Journal of Hospital Medicine®

JUNE 2019 NO. 6 VOL. 14

www.journalofhospitalmedicine.com

@JHospMedicine

An Official Publication of the Society of Hospital Medicine

shm® Society of Hospital Medicine

Accelerate your career in academic medicine.

LEVEL 1
SEPTEMBER 9-12, 2019

LEVEL 2 NEW!
SEPTEMBER 10-12, 2019

Register Today
academichospitalist.org

shm Society of Hospital Medicine | ACLGIM Association of Chiefs & Leaders of General Internal Medicine | SGIM Society of General Internal Medicine

Journal of Hospital Medicine®

Journal of Hospital Medicine®

Publisher: The *Journal of Hospital Medicine*® (Print ISSN 1553-5592; E-ISSN 1553-5606) is published monthly for the Society of Hospital Medicine by Frontline Medical Communications, with business offices at 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609, telephone 973-206-3434, fax 973-206-9378. Periodicals postage paid at Parsippany, NJ and at additional mailing offices.

Postmaster: Send address changes to Journal of Hospital Medicine, Subscription Services, P.O. Box 3000, Denville, NJ 07834-3000.

Reprints: For article reprint requests in the United States and Canada, please contact Wright's Media, toll free: (877) 652-5295; frontline@wrightsmedia.com. For those outside the US/Canada, contact Ray Thibodeau, Content Ed Net, at (267) 895-1758; ray.thibodeau@contentednet.com.

Subscriptions: Individual, USA: $426.00 p.a.; institution, USA: $887.00 p.a.; student, resident, intern, USA: $124.00; $35.00 per copy, USA. Individual, Canada/Mexico: $460.00 p.a.; institution, Canada/Mexico: $971.00 p.a.; $47.00 per copy, Canada/Mexico. Individual, all other nations: $776.00 (surface mail), $998.00 (air mail); institution, all other nations: $971.00; $59.00 per copy, all other nations. For back issues, call (833) 836-2705 to charge to your credit card. Written requests will be accepted and must be accompanied by check or money order. Send payment and request to Journal of Hospital Medicine, Subscription Services, P.O. Box 3000, Denville, NJ 07834-3000.

For subscriptions, please call (833) 836-2705, Journal of Hospital Medicine, Subscription Services, P.O. Box 3000, Denville, NJ 07834-3000 or e-mail custsvc.jhm@fulcoinc.com.

All claims for replacement of missing copies of Journal of Hospital Medicine, without charge, must be made within 3 months of date of missing issue requested. Otherwise, cost of replacement is $47.00 USA, $59.00 Canada/Mexico, $71.00 Other per copy. Produced in the USA.

WEBSITE
www.journalofhospitalmedicine.com

EDITORIAL STAFF

Managing Editor
Susan D. Hite
susanhite@mdedge.com

ART

Creative Director
Mary Ellen Niatas

Art Director
John J. DeNapoli

PRODUCTION AND MANUFACTURING

Production Manager
Mike Wendt
(973) 206-8010
mwendt@mdedge.com

CIRCULATION

Subscription Service:
(833) 836-2705
custsvc.jhm@fulcoinc.com

PUBLISHING STAFF

Publisher
Mark Branca
(973) 290-8246
mbranca@mdedge.com

Advertising Sales
Artie Krivopal
(973) 290-8218
Cell (973) 202-5402
akrivopal@mdedge.com

Valerie Bednarz
(973) 206-8954
Cell (973) 907-0230
vbednarz@mdedge.com

Classified Sales
Linda Wilson
(973) 290-8243
lwilson@mdedge.com
Heather Gonroski
(973) 290-8259
hgentile@mdedge.com

Accounts Receivable
Joan Friedman
(973) 290-8211
jfriedman@mdedge.com

Journal of Hospital Medicine®

shm Society of Hospital Medicine
Empowering hospitalists. Transforming patient care.

TABLE OF CONTENTS

Volume 14 | Number 6 | June 2019

ORIGINAL RESEARCH

BRIEF REPORTS

LEADERSHIP & PROFESSIONAL DEVELOPMENT

REVIEW

CHOOSING WISELY®: THINGS WE DO FOR NO REASON

Continued >

CLINICAL CARE CONUNDRUM

PERSPECTIVES IN HOSPITAL MEDICINE

EDITORIAL

LETTERS TO THE EDITOR

Care Transitions Program for High-Risk Frail Older Adults is Most Beneficial for Patients with Cognitive Impairment

Bjorg Thorsteinsdottir, MD[1,2,3,4]*; Stephanie M Peterson[5]; James M Naessens, ScD[6]; Rozalina G McCoy, MD[1,2]; Gregory J Hanson, MD[1]; LaTonya J Hickson, MD[2,7]; Christina YY Chen, MD[1]; Parvez A Rahman[2]; Nilay D Shah, PhD[3]; Lynn Borkenhagen, PhD, CNP[1]; Anupam Chandra, MD[1]; Rachel Havyer, MD[1,2]; Aaron Leppin, MD[3]; Paul Y Takahashi, MD[1]

[1]Division of Primary Care Internal Medicine, Mayo Clinic, Rochester, Minnesota; [2]Center for the Science of Health Care Delivery, Mayo Clinic, Rochester, Minnesota; [3]Knowledge and Evaluation Research Unit, Mayo Clinic, Rochester, Minnesota; [4]Biomedical Ethics Research Program, Mayo Clinic, Rochester, Minnesota; [5]Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota; [6]Division of Health Care Policy and Research, Mayo Clinic, Rochester, Minnesota; [7]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota.

BACKGROUND: Although posthospitalization care transitions programs (CTP) are highly diverse, their overall program thoroughness is most predictive of their success.

OBJECTIVE: To identify components of a successful homebased CTP and patient characteristics that are most predictive of reduced 30-day readmissions.

DESIGN: Retrospective cohort.

PATIENTS: A total of 315 community-dwelling, hospitalized, older adults (≥60 years) at high risk for readmission (Elder Risk Assessment score ≥16), discharged home over the period of January 1, 2011 to June 30, 2013.

SETTING: Midwest primary care practice in an integrated health system.

INTERVENTION: Enrollment in a CTP during acute hospitalization.

MEASUREMENTS: The primary outcome was all-cause readmission within 30 days of the first CTP evaluation. Logistic regression was used to examine independent variables, including patient demographics, comorbidities, number of medications, completion, and timing of program fidelity measures, and prior utilization of healthcare.

RESULTS: The overall 30-day readmission rate was 17.1%. The intensity of follow-up varied among patients, with 17.1% and 50.8% of the patients requiring one and ≥3 home visits, respectively, within 30 days. More than half (54.6%) required visits beyond 30 days. Compared with patients who were not readmitted, readmitted patients were less likely to exhibit cognitive impairment (29.6% vs 46.0%; $P = .03$) and were more likely to have high medication use (59.3% vs 44.4%; $P = .047$), more emergency department (ED; 0.8 vs 0.4; $P = .03$) and primary care visits (4.0 vs 3.0; $P = .018$), and longer cumulative time in the hospital (4.6 vs 2.5 days; $P = .03$) within 180 days of the index hospitalization. Multivariable analysis indicated that only cognitive impairment and previous ED visits were important predictors of readmission.

CONCLUSIONS: No single CTP component reliably predicted reduced readmission risk. Patients with cognitive impairment and polypharmacy derived the most benefit from the program. *Journal of Hospital Medicine* 2019;14:329-335. Published online first February 20, 2019. © 2019 Society of Hospital Medicine

Unplanned hospital admissions and readmissions have become a major focus of efforts to improve the value of healthcare given that these potentially preventable events exert substantial burden on patients, caregivers, health systems, and the economy.[1] The percentage of patients who are rehospitalized within 30 days have decreased from 20%-21% at the start of the Accountable Care Act and readmission penalties to approximately 18%.[2-5] Rehospitalization rates are 33% at 90 days and approach 40% at six months.[6,7] Readmissions cost Medicare more than $26 billion annually,[4] with one in five Medicare beneficiaries readmitted within 30 days of hospital discharge.[8] Centers for Medicare and Medicaid Services and other payers use condition-specific and all-cause 30-day unplanned readmission rates and potentially preventable admissions among patients with complex or multiple comorbidities for public reporting, value-based purchasing, and performance-based reimbursement.[9,10] Consequently, medical groups and hospitals have begun to place an increasing emphasis on improving the transitions of care following hospitalization with the goal of reducing unplanned readmissions.[11] Care transitions programs have been shown to decrease readmission rates, mortality, and emergency department (ED) visits.[12]

Care transitions programs vary greatly in their scope of intervention and target groups, as well as in their efficacy in reducing readmissions.[13,14] The Mayo Clinic Care Transition Program, hereafter referred to as CTP, was launched in 2011. This program was modeled after other successful programs and in-

***Corresponding Author**: Bjorg Thorsteinsdottir, MD: E-mail: thorsteinsdottir.bjorg@mayo.edu; Telephone: 507-774-5944.

Received: July 19, 2018; **Revised**: October 18, 2018; **Accepted**: October 21, 2018

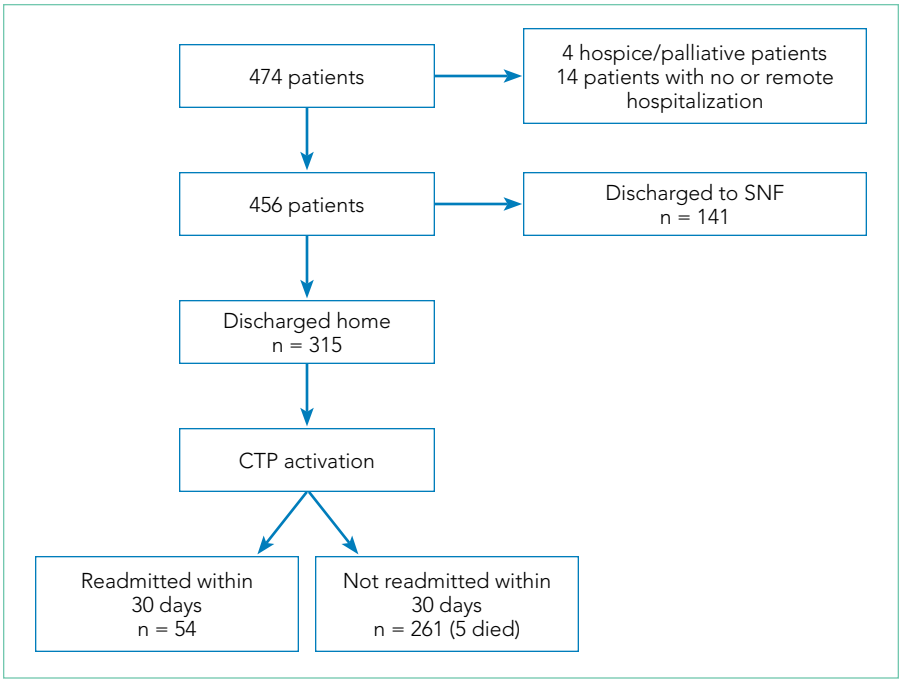


FIG 1. Derivation of the Cohort. Patients who were discharged to a SNF before CTP initiation were excluded.

Abbreviations: CTP care transitions program; SNF skilled nursing facility

volves home visits by a nurse practitioner (NP) and telephonic support and triage provided by a registered nurse (RN). It is offered to high-risk community-dwelling patients during their hospitalization and begins within a week of hospital discharge.

Although the CTP reduces 30-day readmissions from 20% to 17%,[7] it is a highly resource-intensive, multimodal, multidisciplinary program. Moreover, whether some components of the CTP are more critical than others remains unknown. Prior studies that examined the individual components of successful CTPs have suggested that a multipronged approach that includes close patient and caregiver support is most predictive of program efficacy.[13] Long-term program sustainability would benefit from optimization of the most critical components of the program while reducing or eliminating resource-intensive factors that have negligible effects on program success. We therefore examined our CTP to identify whether and which program components are most critical for preventing 30-day readmissions and whether any patient characteristics contribute risk within this complex population.

METHODS

Study Design and Setting

This study is a retrospective cohort study of patients who were enrolled in the care transitions program of Mayo Clinic Rochester during the period January 1, 2010 to June 30, 2013. Patient demographic and clinical data were obtained from electronic health records (EHR), and information regarding CTP processes and interventions was obtained from a prospectively maintained program database. The study complied with the principles of the Declaration of Helsinki and was approved by the Mayo Clinic Institutional Review Board.

Objectives

The study aimed to describe the performance and utilization of a multidisciplinary care transitions program that has been successful in reducing readmissions for high-risk patients. The study also sought to identify patient and/or program factors associated with failure to prevent readmission within 30 days of program enrollment.

Population

Patients who were enrolled in the CTP following hospital discharge and seen for a posthospital in-home visit prior to hospital readmission (for those readmitted) were included. Patients discharged to a skilled nursing facility were excluded. Patients were eligible for CTP enrollment if they were hospitalized for any cause, community dwelling (including assisted living) prior to hospitalization, and ≥60 years old with an Elder Risk Assessment (ERA) score ≥16.[7] The ERA incorporates information regarding previous hospital days, age, and comorbid health burden and has been shown to predict 30-day readmissions, mortality, and critical illness (Figure 1).[15,16]

Intervention

Detailed descriptions of the CTP have been previously published.[7,17] Patients meeting enrollment criteria are enrolled into the CTP by a RN prior to or immediately after hospital discharge. The patient is then seen at home within one to five business days of discharge and again the following week by a NP who performs medication reconciliation; chronic illness management; and acute illness, mobility, safety, and cognition assessments. The NP also provides patient education on self-care and advance care planning. Patient and caregiver support and liaisons with community resources are provided. Home visits by an NP or MD are continued as needed for at least one month. A RN case manager performs weekly phone calls to assess changes in the patient's clinical status and is available for phone triage of acute health issues. An interdisciplinary team composed of MDs, NPs, RNs, and pharmacists review patient management at weekly meetings. Although after-hours or weekend coverage for home visits are unavailable, an on-call primary care physician is available by phone at all times.

Primary Outcome

The primary outcome was all-cause hospital readmission within 30 days of the first CTP home visit, indicating successful program enrollment. Hospitalization was determined on the basis of billing codes from Mayo Clinic hospitals; this approach is 99% reliable in detecting readmissions for this population.[18]

Secondary Outcome Measures

Secondary outcome measures included six-month mortality and hospitalizations, as well as the number of hospital and ICU days and home, ED, primary care, and specialty office visits within 180 days after index hospitalizations as per the EHR. ED visits were counted only when they did not result in a hospital admission.

Independent Variables

Patient characteristics and clinical variables were retrieved from the EHR and included patient age, sex, and marital status. Comorbidities, ERA score,[19] and Charlson comorbidity index (CCI)[20] within two years of program enrollment were determined by using ICD-9 billing codes. The frequencies of primary care and specialty visits within six months of the index hospitalization were also ascertained using the EHR. Mobility limitations and cognitive impairment were categorized as binary variables (yes/no) and were assessed at the first home visit by the NP. The presence of mobility limitations was defined as a Barthel's score of <75[21,22] or Timed up and Go time of >20 seconds.[23] Cognitive impairment was established as Kokmen below the normal cutoff for patient's age group,[24] Mini-Cog ≤2,[25]or AD8 ≥2.[26] If these measures were not specifically documented during the first visit, clinical notes were queried for the description of pertinent cognitive and/or mobility limitations. Dementia diagnosis billing codes (ICD9 Code 290.*) were also included. High medication use was defined as >14 given the reported average medication number ranges from 8-13 in this population.[27]

As previously published, fidelity measures were abstracted from clinical notes by a trained nurse abstractor within 30 days of program enrollment and prior to a readmission.[7] The five program fidelity measures included medication reconciliation, home service evaluation, advanced directives discussion, action plan for acute and chronic disease, safety plan, and discussion of community resources. The presence of advanced care planning was determined on the basis of visit medical notes and/or change of code status within the EHR, the identification or scanning of written advanced directives or "provider order for life-sustaining treatment," and documentation of the discussion of resuscitation status. It was abstracted in duplicate by a nurse abstractor with physician adjudication for disagreement. Moreover, whether the initial visit met the goal of being within five days of discharge was determined by using billing data.

Analysis

The contribution of each independent variable to 30-day readmission was first directly assessed by using a univariate logistic regression model. Five patients died within 30 days without being admitted. These deaths, however, were not censored given that home death (as opposed to hospital death) was considered a positive outcome of the CTP. Multivariable modeling was performed through log rank test with backwards elimination and included all independent variables with $P <$ .05. Variables with P values between .05 and >.1 were tested for interaction with age and sex. Age was categorized as <80 or ≥80 years. The length of hospital stay was categorized as <3 days (not qualifying for a Medicare skilled nursing facility), 3-13 days, or ≥14 days.

This study had 30% power to detect a reduction of 5% in the rates of hospital admissions; 5% is the median absolute risk reduction reported by previous randomized studies on care transitions programs previously reported.[10] All analyses were performed using SAS 6.01 (SAS Inc., Cary, North Carolina).

RESULTS

Study Population

The study cohort included 315 patients who met the inclusion criteria (Fig 1). The demographic and clinical characteristics of the participants were ascertained at the time of CTP enrollment and are shown in Table 1. Patients were, on average, 82.5 (SD, 8.2) years old and had multiple comorbidities with a mean CCI score of 6.2 and ERA score of 18.5. Almost half of the patients (43.2%) exhibited cognitive impairment and more than half (51.7%) had mobility limitations. Among the patients, 42.9% had been hospitalized at least once in the 180 days prior to their CTP-qualifying hospitalization and 14.2% had ≥2 hospitalizations prior to their CTP-qualifying hospitalization. Similarly, 32.4% had at least one emergency department (ED) visit, and 3.5% had ≥3 ED visits. The majority of patients had frequent outpatient visits, with 30.8% having ≥4 office visits in primary care and 32.4% having ≥4 specialty office visits in the preceding six months.

Readmissions, Mortality, ED, and Outpatient Visits

Of the 315 patients, 54 (17.1%) had a readmission within 30 days and seven (2%) had >1 readmission. Among the patients, 126 (40.0%) were readmitted at least once within 180 days with 55 (17.5%) having more than one readmission. A total of 41 patients (13.1%) died during the six-month follow-up period. The need for both office and ED visits was reduced compared to the 180 days prior to admission with the biggest difference in ED visits: 72 (22.9%) of patients needed visits within 180 days of enrollment, as opposed to 102 (32.4%) before enrollment.

Impact of Patient Clinical Variables on Readmission Risk

Readmitted patients were less likely to exhibit cognitive impairment (29.6% vs 46.0%; $P = .03$) and were more likely to have high medication use (59.3% vs 44.4%; $P = .047$) than patients without readmission (Table 1). Readmitted patients had a higher frequency of visits to primary care (4.0 vs 3.0; $P = .02$) in the six months prior to admission and more hospital days in the prior year (4.6 vs 2.5; $P = .04$) than those without readmission.

Multivariable analysis, which included the cognitive status of the patient; the high use of medication; and the number of ED visits, primary care visits, and hospital days in the previous six months, provided a C statistic of 0.665. After backwards elimination, only the cognitive status of the patient and number of ED visits remained predictive of readmission risk.

TABLE 1. **Baseline Demographics, Functional Status, and Comorbidity of Patients Discharged Home**

	Not Readmitted (n = 261)	Readmitted (n = 54)	Total (n = 315)	*P* Value
Age Mean (SD)	82.8 (8.0)	80.8 (8.7)	82.5 (8.2)	.14
Male	132 (50.6%)	31 (57.4%)	163 (51.7%)	.36
Married	139 (53.3%)	33(61.1%)	172 (54.6%)	.29
Clinical Status and Comorbidities				
ERA score Mean (SD)	18.5 (3.1)	18.1 (2.7)	18.5 (3.0)	.22
Charlson score weighted for severity	6.1 (2.9)	6.7 (3.2)	6.2 (3.0)	.12
Congestive heart failure	158 (60.5%)	31 (57.4%)	189 (60.0%)	.67
Chronic pulmonary disease	150 (57.5%)	32 (59.3%)	182 (57.8%)	.81
Diabetes	130 (49.8%)	27 (50%)	157 (49.8%)	.98
Cognitive impairment	120 (46.0%)	16 (29.6%)	136 (43.2%)	.03
Functional impairment	136 (52.1%)	27 (50.0%)	163 (51.7%)	.78
BMI > 30	86 (33.2%)	23 (42.6%)	109(34.8%)	.19
BMI < 18.5	9 (3.5%)	0 (0%)	9 (2.9%)	.17
High medication use	116 (44.4%)	32 (59.3%)	148 (47.0%)	.047
Opioid use	65 (24.9%)	18 (33.3%)	83 (26.3%)	.20
Index Hospitalization				
Length of stay (mean, SD)	4.8(5.5)	5.3 (4.0)	4.9 (5.3)	.11
ICU stay (frequency, percentage)	126 (48.3%)	23 (42.6)	149 (47.3%)	.45
Admission Diagnosis				
Cardiac	68 (26.1%)	13 (24.1%)	81 (25.7%)	.70
Infectious	58 (22.2%)	12 (22.2%)	70 (22.2%)	
Gastrointestinal	21 (8.0%)	6 (11.1%)	27 (8.6%)	
Stroke	19 (7.3%)	2 (3.7%)	21 (6.7%)	
Pulmonary	12 (4.6%)	2 (3.7%)	14 (4.4%)	
Renal	12 (4.6%)	1 (1.9%)	13 (4.1%)	
Fracture/trauma	11 (4.2%)	1 (1.9%)	12 (3.8%)	
Cancer	8 (3.1%)	4 (7.4%)	12 (3.8%)	
Other	52 (19.9%)	13 (24.1%)	65 (20.6%)	
Healthcare Utilization prior 180 Days (6 months)				
Previous care coordination	30 (11.5%)	4 (7.4%)	34 (10.8%)	.38
Primary care visits mean (SD)	3.0 (3.2%)	4.0 (3.3%)	3.1 (3.2)	.02
Specialty visits mean days (SD)	2.7 (3.4)	3.8 (4.5)	2.9 (3.7)	.06
Number of ER visits	0.4 (0.8); 0 (0,1)	0.8 (1.3); 0 (0,1)	0.5 (0.9); 0 (0,1)	.03
Mean number of hospitalizations (SD)	0.6 (1.0)	0.9 (1.2)	0.7 (1.0)	.07
Mean hospital days (SD)	2.5 (5.4)	4.6 (9.0)	2.9 (6.2)	.03

Abbreviations: BMI, body mass index; ERA, elder risk assessment; ICU, intensive care unit; SD, standard deviation.

Impact of Program Interventions on Readmission Risk

The completion of the CTP fidelity measures drastically varied with completion rates between 29.5% (community resource evaluation) and 87.0% (home visit within five days of hospital discharge; Table 2). Only 12.1% of patients received all components of the CTP at the first home visit. Readmission rates among patients who received all program components (13.2%) were lower than those among patients who did not receive all program components. This difference, however, failed to reach statistical significance. No single program component significantly reduced readmission risk. The completion rate of program fidelity measures increased with time (Figure 2). The present findings did not change even after performing sensitivity analysis that excluded the first program year. The overall agreement between chart abstractors on determining whether advance care planning occurred was 69.5% but the Cohens Kappa was only 18.4. This result was largely ascribed to the following: One abstractor counted the presence of a shorthand template used to document the delivery of an advance care planning document as discussion, whereas the other abstractor required further documentation or corroborating evidence (ie, change of code status). The majority of patients required multiple home visits to address ongoing medical needs (mean 2.7; SD = 1.3) over the first 30 days. Among these patients, only 17.1% received one visit, and 54.6% of patients received ≥3

TABLE 2. **Fidelity Measures at First Home Visit and Home Visit within Five Days, Multivariable Analysis**

Fidelity Measures Achieved	Number of Patients with the Measure	Readmission Rate with Measure	Readmission Rate without Measure	Odds Ratio	*P* Value
Home visit within five days	274 (87.0%)	17.2%	17.1%	1.01 (.42,2.41)	.99
Medication reconciliation done	238 (75.6%)	16.4%	19.4%	0.81 (0.42, 1.57)	.53
Safety discussion	160 (50.8%)	15.6%	18.7%	0.81 (.45, 1.45)	.47
Community resource evaluation	93 (29.5%)	15.1%	18.0%	0.81 (.42, 1.57)	.53
Advance directive discussion	176 (55.9%)	14.8%	20.1%	0.69 (.38,1.24)	.21
Action plan completed	223 (70.8%)	19.7%	10.9%	2.02 (.97, 4.20)	.06
All pillars completed	38 (12.1%)	13.2%	17.7%	0.71 (0.26, 1.90)	.49

visits. Eleven (3.5%) patients transitioned to a palliative home-bound program that we began offering toward the end of this study to meet patient needs.[28]

DISCUSSION

The present study met our objective of identifying individual patient factors that are predictive of the success of our CTP. Cognitively impaired patients were less likely to be readmitted than cognitively intact patients. This finding is particularly important because patients with dementia constitute a subgroup that is at an increased risk of readmission after hospitalization[29] and often suffer burdensome transitions at the end of life.[30,31] High medication use and high number of visits to primary care and number of hospital days in the six months leading up to enrollment increase the likelihood of readmission and are plausible measures of disease severity or multi-morbidity that have been identified in previous studies.[32,33] No one program intervention was found to be significantly associated with readmission. This result is consistent with prior works that demonstrated the need for multifaceted and intensive interventions to reduce readmission risk among highly complex and multimorbid patients.[13,14]

Our findings suggest that the provision of an alternative to stressful hospitalization to cognitively impaired patients and their caregivers may be an important benefit of care transitions programs. Having a trusted team to consult in acute situations may have enabled early intervention and crisis avoidance. Avoiding hospitalizations and ED visits may also have been in line with their goals of care.[34,35] Given that program intensity varied on the basis of the discretion of the clinical team, patients with cognitive impairment and their caregivers may also have received more intensive support than cognitively intact patients.

In contrast to recent systematic reviews, our study did not find that advance directive discussion had significant effects on reductions in readmission.[36,37] The lack of discussion surrounding the goals of care for patients with serious illnesses was also listed as one of four factors that are strongly associated with preventability in a national cohort of readmitted general medicine patients.[38] The lack of power and incomplete documentation may have contributed to our null findings. Trust building must also occur before any meaningful discussion of the goals of care could be achieved, and follow-up time may have to be extended. Toward the end of this study, we developed an extension of our program for patients with limited life expectancy and conservative goals of care. In this extension, reductions in hospitalizations were observed among patients who had multiple goals of care discussions.[28]

Previous studies have shown that readmissions reduced with timely follow up among patients with heart failure.[39] Our results showed no difference in readmission rate based on whether or not our patients were visited within five days from discharge, but we may have been underpowered to detect this difference. In addition, we may have missed readmissions that occurred before the enrollment visit.

The elements of the CTP were evidence based. Fidelity to program goals improved over time and reached high levels with program maturity. Only 12% of the patients received all program components at the first home visit. Patients that had all pillars addressed and documented showed a nonsignificant trend toward reduced readmission rates. NPs were given discretion as to how many visits were required to stabilize a patient and achieve program objectives. Heart failure management was driven by protocol with input from cardiology. Medication reconciliation and clinical assessment with action plan were prioritized at the first visit and thus allowed for the completion of other goals at a subsequent visit if time was insufficient. These decisions were deliberated at weekly physician-led multidisciplinary meetings. This variability allowed the team to meet chronic and urgent needs but further confounded the interpretation of our results. One possible way to interpret the lack of significant predictors of success is that through clinical assessment and flexibility, we were able to tailor our program to meet the needs of this complex multi-morbid population.

This study has important limitations. Given that it is a retrospective cohort study, we were unable to include patients who were enrolled but were either readmitted or dropped out before the first program visit. In addition, because of our study's limited sample size and readmission rate, we had limited power to detect other potential predictor variables and test for confounding and interaction. While we included numerous variables in our analyses, we lacked information on mental

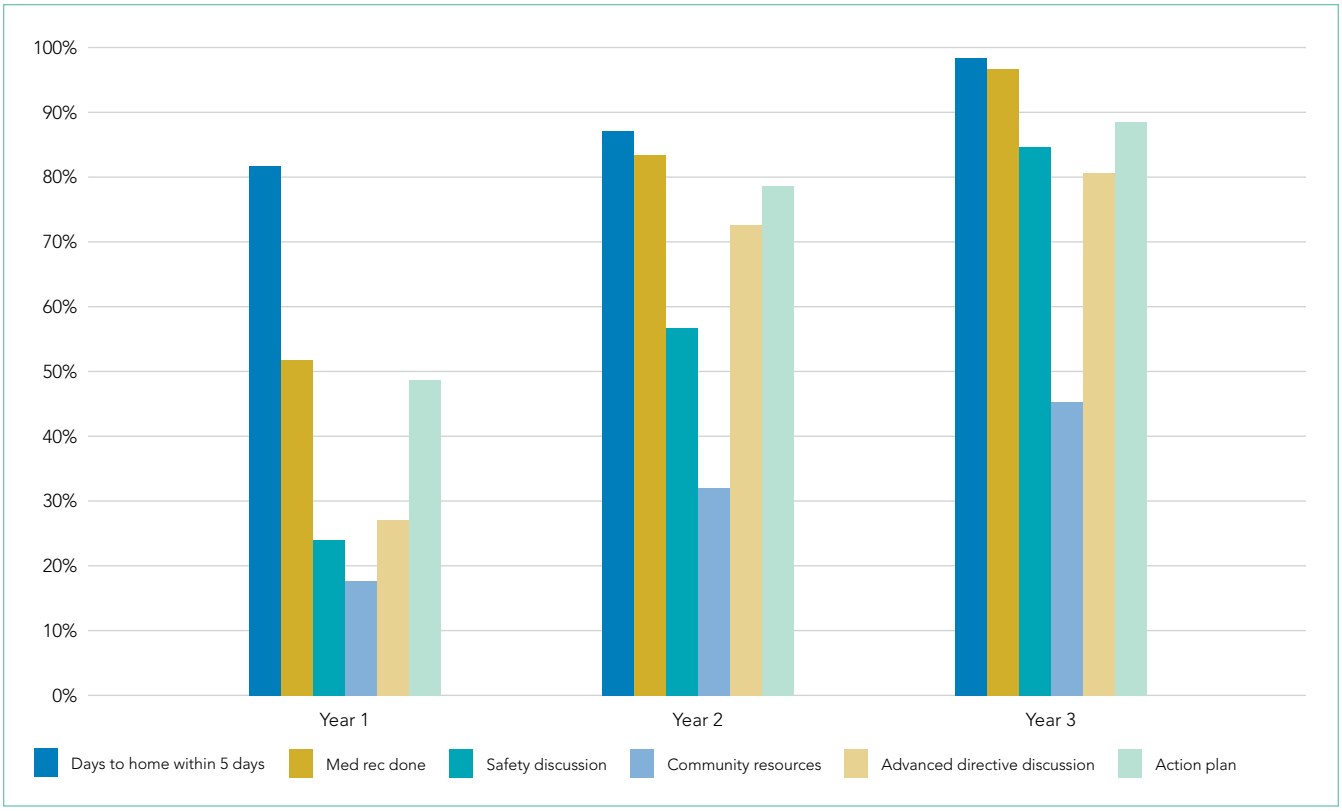


FIG 2. Achievement of Program Fidelity Measures Improved over Time with Increasing Program Maturity.

health and the social determinants of health, which are known to influence readmission risk.[40,41] Similarly, we lacked patient self-reported measures of health and information regarding caregiver support, which are important.[42,43] Several of our predictive measures (cognitive impairment, mobility limitations, and program objective completion) were dependent on supplementing billing codes with heterogeneous data abstracted from usual clinical care as opposed to standardized research protocols. Neither method is completely accurate, nor can the combination of the two be assumed to be without inaccuracies. Failure to adequately document the clinical interventions performed by the clinical team is possibly a major confounder as evidenced by the considerable lack of agreement by our trained abstractors in determining whether advance care planning took place. The generalizability of our results is also a concern because the local population is largely white and highly educated, although our experience tells us that many of our program patients have limited means and thus may more closely resemble the general US population.[44] The strength of our study is that it uses real, practice-based data that can be directly translated to practice.

CONCLUSION

This study focused on a successful high-intensity CTP. Results showed that compared with patients without dementia, patients with dementia were more likely to avoid hospitalizations as a result of enrollment in the investigated CTP. This study, however, failed to identify specific programmatic components critical for the success of the CTP. These findings support the current hypothesis that multidisciplinary, multimodal, and highly intensive interventions are necessary to care for complex and multi-morbid patients. They also suggest that compared with cognitively functional patients, cognitively impaired patients with conservative goals of care may be more likely to avoid burdensome hospitalizations when provided with early intervention in their home.

Acknowledgments

B.T. conceived and designed the study, interpreted the data, drafted and provided final revisions to the manuscript. P.Y.T, N.D.S., and J.M.N obtained funding, contributed to the conception and design of the study, analysis, and interpretation of the data, and provided critical revisions to the manuscript. P.A.R., R.G.M, and G.J.H., contributed to the conception and design of the study, analysis, and interpretation of the data, and provided critical revisions to the manuscript. S.M.P. Assisted with data acquisition and interpretation, performed the data analysis, and drafted parts of the manuscript. C.Y.Y.C, L.J.H., A.L, A.C., L.B., and R.H. helped with methodologic questions and data interpretation, and provided critical revisions to the manuscript.

All authors read and approved the final manuscript and the decision to submit the manuscript for publication.

We thank Donna Lawson, RN for her help with data abstraction and Annika Beck and Anna Jones in Mayo Clinic Biomedical Ethics Research Program for her help in preparing this manuscript for publication.

Disclosures: The authors declare no conflicts of interest.

Funding: This publication was supported by the Mayo Clinic, Robert D and Patricia E. Center for the Science of Health Care Delivery (B.T., R.H., R.G.M, L.J.H), by the Extramural Grant Program by Satellite Healthcare, a not-for-profit renal care

provider (L.J.H., B.T.), and by the National Institute of Health (NIH) National Institute Of Diabetes And Digestive And Kidney Diseases grant K23 DK109134 (L.J.H.) K23DK114497 (RGM) and National Institute on Aging grant K23 AG051679 (B.T.). Additional support was provided by the National Center for Advancing Translational Sciences grant UL1 TR000135. Study contents are the sole responsibility of the authors and do not necessarily represent the official views of NIH.

Funder's Role: The sponsors had no role in the design, execution, or reporting of this study.

Prior Presentations: Part of this data was presented in poster format at the American Geriatrics Society meeting in Washington, DC; 2015.

References

1. Joynt KE, Jha AK. A path forward on Medicare readmissions. *N Engl J Med.* 2013;368(13):1175-1177. doi: 10.1056/NEJMp1300122.
2. Epstein AM, Jha AK, Orav EJ. The relationship between hospital admission rates and rehospitalizations. *N Engl J Med.* 2011;365(24):2287-2295. doi: 10.1056/NEJMsa1101942.
3. Zuckerman RB, Sheingold SH, Orav EJ, Ruhter J, Epstein AM. Readmissions, observation, and the hospital readmissions reduction program. *N Engl J Med.* 2016;374(16):1543-1551. doi: 10.1056/NEJMsa1513024.
4. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med.* 2009;360(14):1418-1428. doi: 10.1056/NEJMsa0803563.
5. Gerhardt G, Yemane A, Hickman P, Oelschlaeger A, Rollins E, Brennan N. Medicare readmission rates showed meaningful decline in 2012. *Medicare Medicaid Res Rev.* 2013;3(2). doi: 10.5600/mmrr.003.02.b01.
6. Naylor MD, Brooten D, Campbell R, et al. Comprehensive discharge planning and home follow-up of hospitalized elders: a randomized clinical trial. *JAMA.* 1999;281(7):613-620.
7. Takahashi PY, Naessens JM, Peterson SM, et al. Short-term and long-term effectiveness of a post-hospital care transitions program in an older, medically complex population. *Healthcare.* 2016;4(1):30-35. doi: 10.1016/j.hjdsi.2015.06.006.
8. Desai NR, Ross JS, Kwon JY, et al. Association between hospital penalty status under the hospital readmission reduction program and readmission rates for target and nontarget conditions. *JAMA.* 2016;316(24):2647-2656. doi: 10.1001/jama.2016.18533.
9. CMS. U.S. Centers for Medicare & Medicaid Services (CMS) measure methodology. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/HospitalQualityInits/Measure-Methodology.html. Accessed December 1, 2017; 2017.
10. National Committee for Quality Assurance. *All-Cause Readmissions: the Number of Acute Inpatient Stays during the Measurement Year That Were Followed by an Acute Readmission for Any Diagnosis within 30 Days and the Predicted Probability of an Acute Readmission, for Patients 18 Years of Age and Older.* Accessed May 18, 2017; 2014.
11. Naylor MD, Hirschman KB, Hanlon AL, et al. Comparison of evidence-based interventions on outcomes of hospitalized, cognitively impaired older adults. *J Comp Eff Res.* 2014;3(3):245-257. doi: 10.2217/cer.14.14.
12. Le Berre M, Maimon G, Sourial N, Guériton M, Vedel I. Impact of transitional care services for chronically ill older patients: A systematic evidence review. *J Am Geriatr Soc.* 2017;65(7):1597-1608. doi: 10.1111/jgs.14828.
13. Leppin AL, Gionfriddo MR, Kessler M, et al. Preventing 30-day hospital readmissions: A systematic review and meta-analysis of randomized trials. *JAMA Intern Med.* 2014;174(7):1095-1107. doi: 10.1001/jamainternmed.2014.1608.
14. Hansen LO, Young RS, Hinami K, Leung A, Williams MV. Interventions to reduce 30-day rehospitalization: a systematic review. *Ann Intern Med.* 2011;155(8):520-528. doi: 10.7326/0003-4819-155-8-201110180-00008.
15. Takahashi PY, Tung EE, Crane SJ, Chaudhry R, Cha S, Hanson GJ. Use of the elderly risk assessment (ERA) index to predict 2-year mortality and nursing home placement among community dwelling older adults. *Arch Gerontol Geriatr.* 2012;54(1):34-38. doi: 10.1016/j.archger.2011.02.012.
16. Biehl M, Takahashi PY, Cha SS, Chaudhry R, Gajic O, Thorsteinsdottir B. Prediction of critical illness in elderly outpatients using elder risk assessment: a population-based study. *Clin Interv Aging.* 2016;11:829-834. doi: 10.2147/CIA.S99419.
17. Takahashi PY, Haas LR, Quigg SM, et al. 30-day hospital readmission of older adults using care transitions after hospitalization: a pilot prospective cohort study. *Clin Interv Aging.* 2013;8:729-736. doi: 10.2147/CIA.S44390.
18. Dunlay SM, Pack QR, Thomas RJ, Killian JM, Roger VL. Participation in cardiac rehabilitation, readmissions, and death after acute myocardial infarction. *Am J Med.* 2014;127(6):538-546. doi: 10.1016/j.amjmed.2014.02.008.
19. Crane SJ, Tung EE, Hanson GJ, Cha S, Chaudhry R, Takahashi PY. Use of an electronic administrative database to identify older community dwelling adults at high-risk for hospitalization or emergency department visits: the elders risk assessment index. *BMC Health Serv Res.* 2010;10:338. doi: 10.1186/1472-6963-10-338.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-383. doi: 10.1016/0021-9681(87)90171-8.
21. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud.* 1988;10(2):61-63. doi: 10.3109/09638288809164103.
22. Sulter G, Steen C, De Keyser J. Use of the Barthel index and modified Rankin scale in acute stroke trials. *Stroke.* 1999;30(8):1538-1541. doi: 10.1161/01.STR.30.8.1538.
23. Bohannon RW. Reference values for the timed up and go test: A descriptive meta-analysis. *J Geriatr Phys Ther.* 2006;29(2):64-68. doi: 10.1519/00139143-200608000-00004.
24. Kokmen E, Naessens JM, Offord KP. A short test of mental status: description and preliminary results. *Mayo Clin Proc.* 1987;62(4):281-288. doi: 10.1016/S0025-6196(12)61905-3.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189-198. doi: 10.1016/0022-3956(75)90026-6.
26. Galvin JE, Roe CM, Powlishta KK, et al. The AD8: A brief informant interview to detect dementia. *Neurology.* 2005;65(4):559-564. doi: 10.1212/01.wnl.0000172958.95282.2a.
27. Farrell B, Szeto W, Shamji S. Drug-related problems in the frail elderly. *Can Fam Phys.* 2011;57(2):168-169.
28. Chen CY, Thorsteinsdottir B, Cha SS, et al. Health care outcomes and advance care planning in older adults who receive home-based palliative care: a pilot cohort study. *J Palliat Med.* 2015;18(1):38-44. doi: 10.1089/jpm.2014.0150.
29. Rao A, Suliman A, Vuik S, Aylin P, Darzi A. Outcomes of dementia: systematic review and meta-analysis of hospital administrative database studies. *Arch Gerontol Geriatr.* 2016;66(Suppl C):198-204. doi: 10.1016/j.archger.2016.06.008.
30. Gozalo P, Teno JM, Mitchell SL, et al. End-of-life transitions among nursing home residents with cognitive issues. *N Engl J Med.* 2011;365(13):1212-1221. doi: 10.1056/NEJMsa1100347.
31. Wang SY, Aldridge MD, Gross CP, Canavan M, Cherlin E, Bradley E. End-of-life care transition patterns of Medicare beneficiaries. *J Am Geriatr Soc.* 2017;65(7):1406-1413. doi: 10.1111/jgs.14891.
32. Pedersen MK, Meyer G, Uhrenfeldt L. Risk factors for acute care hospital readmission in older persons in Western countries: a systematic review. *JBI Database System Rev Implement Rep.* 2017;15(2):454-485. doi: 10.11124/JBISRIR-2016-003267.
33. Edwards ST, Saha S, Prentice JC, Pizer SD. Preventing hospitalization with Veterans Affairs home-based primary care: which individuals benefit most? *J Am Geriatr Soc.* 2017;65(8):1676-1683. doi: 10.1111/jgs.14843.
34. Mitchell SL, Palmer JA, Volandes AE, Hanson LC, Habtemariam D, Shaffer ML. Level of care preferences Among nursing home residents With advanced dementia. *J Pain Symptom Manage.* 2017;54(3):340-345. doi: 10.1016/j.jpainsymman.2017.04.020.
35. D'Avolio DA, Strumpf NE, Feldman J, Mitchell P, Rebholz CM. Barriers to primary care: perceptions of older adults utilizing the ED for nonurgent visits. *Clin Nurs Res.* 2013;22(4):416-431. doi: 10.1177/1054773813485597.
36. Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. *Palliat Med.* 2014;28(8):1000-1025. doi: 10.1177/0269216314526272.
37. Martin RS, Hayes B, Gregorevic K, Lim WK. The effects of advance care planning interventions on nursing home residents: A systematic review. *J Am Med Dir Assoc.* 2016;17(4):284-293. doi: 10.1016/j.jamda.2015.12.017.
38. Auerbach AD, Kripalani S, Vasilevskis EE, et al. Preventability and causes of readmissions in a national cohort of general medicine patients. *JAMA Intern Med.* 2016;176(4):484-493. doi: 10.1001/jamainternmed.2015.7863.
39. Parrinello G, Torres D, Paterna S, et al. Early and personalized ambulatory follow-up to tailor furosemide and fluid intake according to congestion in post-discharge heart failure. *Intern Emerg Med.* 2013;8(3):221-228. doi: 10.1007/s11739-011-0602-y.
40. Barnett ML, Hsu J, McWilliams JM. Patient characteristics and differences in hospital readmission rates. *JAMA Intern Med.* 2015;175(11):1803-1812. doi: 10.1001/jamainternmed.2015.4660.
41. Calvillo–King L, Arnold D, Eubank KJ, et al. Impact of social factors on risk of readmission or mortality in pneumonia and heart failure: systematic review. *J Gen Intern Med.* 2013;28(2):269-282. doi: 10.1007/s11606-012-2235-x.
42. Rönneikkö JK, Mäkelä M, Jämsen ER, et al. Predictors for unplanned hospitalization of New Home care clients. *J Am Geriatr Soc.* 2017;65(2):407-414. doi: 10.1111/jgs.14486.
43. Hasan O, Meltzer DO, Shaykevich SA, et al. Hospital readmission in general medicine patients: a prediction model. *J Gen Intern Med.* 2010;25(3):211-219. doi: 10.1007/s11606-009-1196-1.
44. St Sauver JL, Grossardt BR, Leibson CL, Yawn BP, Melton LJ, 3rd, Rocca WA. Generalizability of epidemiological findings and public health decisions: an illustration from the Rochester Epidemiology Project. *Mayo Clin Proc.* 2012;87(2):151-160. doi: 10.1016/j.mayocp.2011.11.009.

An Advanced Practice Provider Clinical Fellowship as a Pipeline to Staffing a Hospitalist Program

Christina Lackner, PA-C; Shaker Eid, MD, MBA; Tiffani Panek, MA; Flora Kisuule, MD, MPH*

Division of Hospital Medicine, Johns Hopkins Bayview Medical Center, Baltimore, Maryland.

BACKGROUND: Approximately 83% of hospitalist groups around the country utilize advanced practice providers; however, the demand for hospitalists continues to exceed the supply, and this has led to increased utilization of advanced practice providers in hospital medicine. Advanced practice providers receive very limited inpatient training, and there is wide variation in their clinical abilities after graduation.

OBJECTIVE: To determine if an advanced practice provider fellowship is a cost-effective pipeline for filling vacancies within a hospitalist program.

METHODS: In 2014, a one-year advanced practice providers clinical fellowship in hospital medicine was established. Working one-on-one with an experienced hospitalist faculty member, the fellows evaluate and manage patients. The program consists of 80% clinical experience, in the inpatient setting, and 20% didactic instruction. Up to four fellows are accepted each year and are eligible for hire, after training, if there are vacancies.

RESULTS: The duration of onboarding and cost to the division were significantly reduced after implementation of the program (25.4 vs 11.0 weeks, $P = .017$ and $361,714 vs $66,000, $P = .004$).

CONCLUSION: The advanced practice provider fellowship has proven beneficial for the hospitalist division by (1) reducing costs associated with having unfilled vacancies, (2) improving capacity on the hospitalist service, and (3) providing a pipeline for filling nurse practitioners (NP) and physician assistant (PA) vacancies on the hospitalist service. *Journal of Hospital Medicine* 2019;14:336-339. Published online first March 20, 2019. © 2019 Society of Hospital Medicine

There is an increasing utilization of advanced practice providers (APPs) in the delivery of healthcare in the United States.[1,2] As of 2016, there were 157,025 nurse practitioners (NPs) and 102,084 physician assistants (PAs) with a projected growth rate of 6.8% and 4.3%, respectively, which exceeds the physician growth rate of 1.1%.[2] This increased growth rate has been attributed to the expectation that APPs can enhance the quality of physician care, relieve physician shortages, and reduce service costs, as APPs are less expensive to hire than physicians.[3,4] Hospital medicine is the fastest growing medical field in the United States, and approximately 83% of hospitalist groups around the country utilize APPs; however, the demand for hospitalists continues to exceed the supply, and this has led to increased utilization of APPs in hospital medicine.[5-10]

APPs receive very limited inpatient training and there is wide variation in their clinical abilities after graduation.[11] This is an issue that has become exacerbated in recent years by a change in the training process for PAs. Before 2005, PA programs were typically two to three years long and required the same prerequisite courses as medical schools.[11] PA students completed more than 2,000 hours of clinical rotations and then had to pass the Physician Assistant National Certifying Exam before they could practice.[12] Traditionally, PA programs typically attracted students with prior healthcare experience.[11] In 2005, PA programs began transitioning from bachelor's degrees to requiring a master's level degree for completion of the programs. This has shifted the demographics of the students matriculating to younger students with little-to-no prior healthcare experience; moreover, these fresh graduates lack exposure to hospital medicine.[11]

NPs usually gain clinical experience working as registered nurses (RNs) for two or more years prior to entry into the NP program. NP programs for baccalaureate-prepared RNs vary in length from two to three years.[2] There is an acute care focus for NPs in training; however, there is no standardized training or licensure to ensure that hospital medicine competencies are met.[13-15] Some studies have shown that a lack of structured support has been found to affect NP role transition negatively during the first year of practice,[16] and graduating NPs have indicated that they needed more out of their clinical education in terms of content, clinical experience, and competency testing.[17]

Hiring new APP graduates as hospitalists requires a longer and more rigorous onboarding process. On-the-job training in hospital medicine for new APP graduates can take as long as six to 12 months in order for them to acquire the basic skill set necessary to adequately manage hospitalized patients.[15] This extended onboarding is costly because the APPs are receiving a full hospitalist salary, yet they are not functioning at full

***Corresponding author**: Flora Kisuule, MD, MPH; E-mail: fkisuul1@jhmi.edu; Telephone: 410-550-9856

Received: August 4, 2018; **Revised**: January 18, 2019; **Accepted**: January 29, 2019

 DOI 10.12788/jhm.3183

TABLE 1. **Curriculum Highlights**

Time Period	Activities
Day one	Administrative orientation
During the first month	Fellows attend hospital medicine boot camp for five days
First six to eight weeks	Clinical onboarding for the fellow. Paired with a physician. Patient cap slowly raised from baseline of 10 to 13.
40 weeks	• Fellows work alongside a physician caring for patients. The fellows assists with: • being first call on all patients for nurse questions • handing off patients • writing patient notes • discharges • order entries • calling and following up on consults • arranging family meetings • presenting at multi-D rounds • admissions • communicating with primary care doctors • performing medication reconciliation • The physician-fellow dyad sees three more patients
Once a week	The fellow attends weekly didactics
Once a month	The fellow receives training in procedures

capacity. Ideally, there should be an intermediary training step between graduation and employment as hospitalist APPs. Studies have shown that APPs are interested in formal post-graduate hospital medicine training, even if it means having a lower stipend during the first year after graduating from their NP or PA program.[9,15,18]

The growing need for hospitalists, driven by residency work-hour reform, increased age and complexity of patients, and the need to improve the quality of inpatient care while simultaneously reducing waste, has contributed to the increasing utilization of and need for highly qualified APPs in hospital medicine.[11,19,20] We established a fellowship to train APPs. The goal of this study was to determine if an APP fellowship is a cost-effective pipeline for filling vacancies within a hospitalist program.

METHODS

Design and Setting

Johns Hopkins Bayview Medical Center (JHBMC) is a 440 bed hospital in Baltimore Maryland. The hospitalist group was started in 1996 with one physician seeing approximately 500 discharges a year. Over the last 20 years, the group has grown and is now its own division with 57 providers, including 42 physicians, 11 APPs, and four APP fellows. The hospitalist division manages ~7,000 discharges a year, which corresponds to approximately 60% of admissions to general medicine. Hospitalist APPs help staff general medicine by working alongside doctors and admitting patients during the day and night. The APPs also staff the pulmonary step down unit with a pulmonary attending and the chemical dependency unit with an internal medicine addiction specialist.

The growth of the division of hospital medicine at JHBMC is a result of increasing volumes and reduced residency duty hours. The increasing full time equivalents (FTEs) resulted in a need for APPs; however, vacancies went unfilled for an average of 35 weeks due to the time it took to post open positions, interview applicants, and hire applicants through the credentialing process. Further, it took as long as 22 to 34 weeks for a new hire to work independently. The APP vacancies and onboarding resulted in increased costs to the division incurred by physician moonlighting to cover open shifts. The hourly physician moonlighting rate at JHBMC is $150. All costs were calculated on the basis of a 40-hour work week. We performed a pre- and postanalysis of outcomes of interest between January 2009 and June 2018. This study was exempt from institutional review board review.

Intervention

In 2014, a one year APP clinical fellowship in hospital medicine was started. The fellows evaluate and manage patients working one-on-one with an experienced hospitalist faculty member. The program consists of 80% clinical experience in the inpatient setting and 20% didactic instruction (Table 1). Up to four fellows are accepted each year and are eligible for hire after training if vacancies exist. The program is cost neutral and was financed by downsizing, through attrition, two physician FTEs. Four APP fellows' salaries are the equivalent of two entry-level hospitalist physicians' salaries at JHBMC. The annual salary for an APP fellow is $69,000.

Downsizing by two physician FTEs meant that one less doctor was scheduled every day. The patient load previously seen by that one doctor (10 patients) was absorbed by the MD–APP fellow dyads. Paired with a fellow, each physician sees a higher cap of 13 patients, and it takes six weeks for the fellows to ramp-up to this patient load. When the fellow first starts, the team sees 10 patients. Every two weeks, the pair's census increases by one patient

TABLE 2. **Baseline Characteristics and Outcomes of Newly Hired APPs before and after Implementation of the APP Clinical Fellowship Program in 2014**

Variables	Before (2009-2013) Nonfellow Hires n = 7	After (2014-2018) Fellow Hires n = 12	*P* Value
Age, years	27.0 ± 1.8	27.8 ± 7.9	.232
Female	100.0	75.0	.127
Race			—
White	42.8	91.7	
Black	42.8	0.0	
Other	14.4	8.3	
Time from APP school graduation to hire, months	10.5 [4, 20]	3.9 [3.4, 6.4]	.069
Total time with group, months	17.9 ± 10.6	18.3 ± 13.0	.735
Duration of vacancy, weeks (a)	34.9 ± 12.6	0	—
Duration of onboarding, weeks (b)	25.4 ± 11.1	11.0 ± 0.0	.017
*Cost to division, $	361,714 ± 84,122	66,000 ± 0	.004

Data are percentage or mean ± standard deviation or median [IQR]
*($150/hour × 40 hours/week = $6,000) × (a + b)
Abbreviations: APP, Advanced Practice Provider; IQR, interquartile range.

to the cap of 13. Collectively, the four APP fellow–MD dyads make it possible for four physicians to see an additional 12 patients. The two extra patients absorbed by the service per day results in a net increase in capacity of up to 730 patient encounters a year.

Outcomes and Analysis

Our main outcomes of interest were duration of onboarding and cost incurred by the division to (1) staff the service during a vacancy and (2) onboard new hires. Secondary outcomes included duration of vacancy and total time spent with the group. We collected basic demographic data on participants, including, age, gender, and race. Demographics and outcomes of interest were compared pre- (2009-2013) and post- (2014-2018) initiation of the APP clinical fellowship using the chi-square test, the *t*-test for normally distributed data, and the Wilcoxon rank-sum for nonnormally distributed data, as appropriate. The normality of the data distribution was tested using the Shapiro-Wilk W test. Two-tailed *P* values less than .05 were considered to be statistically significant. Results were analyzed using Stata/MP version 13.0 (StataCorp Inc, College Station, Texas).

RESULTS

Twelve fellows have been recruited, and of these, 10 have graduated. Two chose to leave the program prior to completion. Of the 10 fellows that have graduated, six have been hired into our group, one was hired within our facility, and three were hired as hospitalists at other institutions. The median time from APP school graduation to hire was also not different between the two groups (10.5 vs 3.9 months, $P = .069$). In addition, the total time that the new APP hires spent with the group was nonstatistically significantly different between the two periods (17.9 vs 18.3 months, $P = .735$). Both the mean duration of onboarding and the cost to the division were significantly reduced after implementation of the program (25.4 vs 11.0 weeks, $P = .017$ and $361,714 vs $66,000, $P = .004$; Table 2).

The yearly cost of an APP vacancy and onboarding is incurred by doctor moonlighting costs (at the rate of $150 per hour) to cover open shifts. The mean duration of vacancies and onboarding each year was 34.9 and 25.4 weeks, respectively, before the fellowship. The yearly cost of onboarding, after the establishment of the fellowship, is a maximum of $66,000, derived from physician moonlighting to cover the six-week ramp-up at the very beginning of the fellowship and the five weeks of orientation to the pulmonary and chemical dependency units after the fellowship (Table 3).

DISCUSSION

Our APP clinical fellowship in hospital medicine at JHBMC has produced several benefits. First, the fellowship has become a pipeline for filling APP vacancies within our division. We have been able to hire for four consecutive years from the fellowship. Second, the ready availability of high-functioning and efficient APP hospitalists has cut down on the onboarding time for our new APP hires. Many new APP graduates lack confidence in caring for complex hospitalized patients. Following our 12-month clinical fellowship, our matriculated fellows are able to practice at the top of their license immediately and confidently. Third, the reduced vacancy and shortened onboarding periods have reduced costs to the division. Fourth, the fellowship has created additional teaching avenues for the faculty. The medicine units at JHBMC are comprised of hospitalist and internal medicine residency services. The hospitalists spend the majority of their clinical time in direct patient care; however, they rotate on the residency service for two weeks out of the year. The majority of

TABLE 3. **Onboarding Time for Newly Hired Nonfellow and Fellow APPs**

Services for which APPs are trained	Nonfellow APPs Time (weeks)	APP Fellows Time (weeks)
Orientation to CDU	2	1
Orientation to PCU	12	4
Orientation to General Medicine Unit	4	N/A
Gradual increase in patient volume to expected caps	4-12	6
Total training time (weeks)	**22-34**	**11**

Abbreviation: APP, Advanced Practice Provider; CDU, Chemical Dependency Unit; PCU, Progressive Care Unit.

physicians welcome the chance to teach more, and partnering with an APP fellow provides that opportunity.

As we have developed and grown this program, the one great challenge has been what to do with graduating fellows when we cannot hire them. Fortunately, the market for highly qualified, well trained APPs is strong, and every one of the fellows that we could not hire within our group has been able to find a position either within our facility or outside our institution. To facilitate this process, program directors and recruiters are invited to meet with the fellows toward the end of their fellowship to share employment opportunities with them.

Our study has limitations. First, had the $276,000 from the attrition of two physicians been used to hire nonfellow APPs under the old model, then the costs of the two models would have been similar, but this was simply not possible because the positions could not be filled. Second, this is a single-site experience, and our findings may not be generalizable, particularly those pertaining to remuneration. Third, our study was underpowered to detect small but important differences in characteristics of APPs, especially time from graduation to hire, before and after the implementation of our fellowship. Further research comparing various programs both in structure and outcomes—such as fellows' readiness for practice, costs, duration of vacancies, and provider satisfaction—are an important next step.

We have developed a pool of applicants within our division to fill vacancies left by turnover from senior NPs and PAs. This program has reduced costs and improved the joy of practice for both doctors and APPs. As the need for highly qualified NPs and PAs in hospital medicine continues to grow, we may see more APP fellowships in hospital medicine in the United States.

Acknowledgments

The authors thank the advanced practice providers who have helped us grow and refine our fellowship.

Disclosures: The authors have nothing to disclose

References

1. Martsoff G, Nguyen P, Freund D, Poghosyan L. What we know about postgraduate nurse practitioner residency and fellowship programs. *J Nurse Pract.* 2017;13(7):482-487. doi: 10.1016/j.nurpra.2017.05.013.
2. Auerbach D, Staiger D, Buerhaus P. Growing ranks of advanced practice clinicians-implications for the physician workforce. *N Engl J Med.* 2018;378(25):2358-2360. doi: 10.1056/NEJMp1801869.
3. Laurant M, Harmsen M, Wollersheim H, Grol R, Faber M, Sibbald B. The impact of nonphysician clinicians: do they improve the quality and cost-effectiveness of health care services? *Med Care Res Rev.* 2009;66(6 Suppl):36S-89S. doi: 10.1177/1077558709346277.
4. Auerbach DI. Will the NP workforce grow in the future? New forecasts and implications for healthcare delivery. *Med Care.* 2012;50(7):606-610. doi: 10.1097/MLR.0b013e318249d6e7.
5. Kisuule F, Howell E. Hospital medicine beyond the United States. *Int J Gen Med.* 2018;11:65-71. doi: 10.2147/IJGM.S151275.
6. Wachter RM, Goldman L. Zero to 50, 000-The 20th anniversary of the hospitalist. *N Engl J Med.* 2016;375(11):1009-1011. doi: 10.1056/NEJMp1607958.
7. Conrad, K and Valovska T. The current state of hospital medicine: trends in compensation, practice patterns, advanced practice providers, malpractice, and career satisfaction. In: Conrad K, ed. *Clinical Approaches to Hospital Medicine.* Cham, Springer; 2017:259-270.
8. Bryant SE. Filling the gaps: preparing nurse practitioners for hospitalist practice. *J Am Assoc Nurse Pract.* 2018;30(1):4-9. doi: 10.1097/JXX.0000000000000008.
9. Sharma P, Brooks M, Roomiany P, Verma L, Criscione-Schreiber, L. Physician assistant student training for the inpatient setting: a needs assessment. *J Physician Assist Educ.* 2017;28(4):189-195. doi: 10.1097/JPA.0000000000000174.
10. Society of Hospital Medicine. 2016 State of Hospital Medicine Report. Available at: https://www.hospitalmedicine.org/about/press-releases/shm-releases-2016-state-of-hospital-medicine-report/. Accessed July 17, 2018.
11. Will KK, Budavari AI, Wilkens JA, Mishari K, Hartsell ZC. A Hospitalist postgraduate training program for physician assistants. *J Hosp Med.* 2010;5(2):94-8. doi: 10.1002/jhm.619.
12. Naqvi, S. Is it time for Physician Assistant (PA)/Nurse Practitioner (NP) Hospital Medicine Residency Training. Available at: http://medicine2.missouri.e.,-du/jahm/wp-content/uploads/2017/03/Is-it-time-for-PANP-Hospital-Medicine-Residency-Training-Final.pdf. Accessed July 17, 2018.
13. Scheurer D, Cardin T. The Role of NPs and PAs in Hospital Medicine Programs. From July, 2017 *The Hospitalist.* Available at: *https://www.the-hospitalist.org/hospitalist/article/142565/leadership-training/role-nps-and-pas-hospital-medicine-programs.* Accessed July 17, 2018.
14. Furfari K, Rosenthal L, Tad-y D, Wolfe B, Glasheen J. Nurse practitioners as inpatinet providers: a hospital medicine fellowship program. *J Nurse Pract.* 2014;10(6):425-429. doi: 10.1016/j.nurpra.2014.03.022.
15. Taylor D, Broyhill B, Burris A, Wilcox M. A strategic approach for developing an advanced practice workforce: from postgraduate transition-to-practice fellowship programs and beyond. *Nurs Adm Q.* 2017;41(1):11-19. doi: 10.1097/NAQ.0000000000000198.
16. Barnes H. Exploring the factors that influence nurse practitioners role transition. *J Nurse Pract.* 2015;11(2):178-183. doi: 10.1016/j.nurpra.2014.11.004.
17. Hart MA, Macnee LC. How well are nurse practitioners prepared for practice: results of a 2004 questionnaire study. *J Am Acad Nurse Pract.* 2007;19(1):35-42. doi: 10.1111/j.1745-7599.2006.00191.x
18. Torok H, Lackner C, Landis R, Wright S. Learning needs of physician assistants working in hospital medicine. *J Hosp Med.* 2012;7(3):190-194. doi: 10.1002/jhm.1001.
19. Kisuule F, Howell E. Hospitalists and their impact on quality, patient safety, and satisfaction. *Obstet Gynecol Clin N Am.* 2015;42(3):433-446. doi: 10.1016/j.ogc.2015.05.003.
20. Ford, W, Britting L. Nonphysician Providers in the hospitalist model: a prescription for change and a warning about unintended side effects. *J Hosp Med.* 2010;5(2):99-102. doi: 10.1002/jhm.556.

Sepsis Presenting in Hospitals versus Emergency Departments: Demographic, Resuscitation, and Outcome Patterns in a Multicenter Retrospective Cohort

Daniel E Leisman, BS[1,2,3]*; Catalina Angel, MPA[1]; Sandra M Schneider, MD[2,4]; Jason A D'Amore, MD[2]; John K D'Angelo, MD[2]; Martin E Doerfler, MD[5,6]

[1]Icahn School of Medicine at Mount Sinai, New York, New York; [2]Department of Emergency Medicine, Hofstra-Northwell School of Medicine, Hempstead, New York; [3]Global Sepsis Alliance, Jena, Germany; [4]American College of Emergency Physicians, Irving, Texas; [5]Department of Medicine, Hofstra-Northwell School of Medicine, Hempstead, New York; [6]Department of Science Education, Hofstra-Northwell School of Medicine, Hempstead, New York.

BACKGROUND: Differences between hospital-presenting sepsis (HPS) and emergency department-presenting sepsis (EDPS) are not well described.

OBJECTIVES: We aimed to (1) quantify the prevalence of HPS versus EDPS cases and outcomes; (2) compare HPS versus EDPS characteristics at presentation; (3) compare HPS versus EDPS in process and patient outcomes; and (4) estimate risk differences in patient outcomes attributable to initial resuscitation disparities.

DESIGN: Retrospective consecutive-sample cohort.

SETTING: Nine hospitals from October 1, 2014, to March 31, 2016.

PATIENTS: All hospitalized patients with sepsis or septic shock, as defined by simultaneous (1) infection, (2) ≥2 Systemic Inflammatory Response Syndrome (SIRS) criteria, and (3) ≥1 acute organ dysfunction criterion. EDPS met inclusion criteria while physically in the emergency department (ED). HPS met the criteria after leaving the ED.

MEASUREMENTS: We assessed overall HPS versus EDPS contributions to case prevalence and outcomes, and then compared group differences. Process outcomes included 3-hour bundle compliance and discrete bundle elements (eg, time to antibiotics). The primary patient outcome was hospital mortality.

RESULTS: Of 11,182 sepsis hospitalizations, 2,509 (22.4%) were hospital-presenting. HPS contributed 785 (35%) sepsis mortalities. HPS had more frequent heart failure (OR: 1.31, CI: 1.18-1.47), renal failure (OR: 1.62, CI: 1.38-1.91), gastrointestinal source of infection (OR: 1.84, CI: 1.48-2.29), euthermia (OR: 1.45, CI: 1.10-1.92), hypotension (OR: 1.85, CI: 1.65-2.08), or impaired gas exchange (OR: 2.46, CI: 1.43-4.24). HPS were admitted less often from skilled nursing facilities (OR: 0.44, CI: 0.32-0.60), had chronic obstructive pulmonary disease (OR: 0.53, CI: 0.36-0.78), tachypnea (OR: 0.76, CI: 0.58-0.98), or acute kidney injury (OR: 0.82, CI: 0.68-0.97). In a propensity-matched cohort (n = 3,844), HPS patients had less than half the odds of 3-hour bundle compliant care (17.0% vs 30.3%, OR: 0.47, CI: 0.40-0.57) or antibiotics within three hours (66.2% vs 83.8%, OR: 0.38, CI: 0.32-0.44) vs EDPS. HPS was associated with higher mortality (31.2% vs 19.3%, OR: 1.90, CI: 1.64-2.20); 23.3% of this association was attributable to differences in initial resuscitation (resuscitation-adjusted OR: 1.69, CI: 1.43-2.00).

CONCLUSIONS: HPS differed from EDPS by admission source, comorbidities, and clinical presentation. These patients received markedly less timely initial resuscitation; this disparity explained a moderate proportion of mortality differences. *Journal of Hospital Medicine* 2019;14:340-348. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Sepsis is both the most expensive condition treated and the most common cause of death in hospitals in the United States.[1-3] Most sepsis patients (as many as 80% to 90%) meet sepsis criteria on hospital arrival, but mortality and costs are higher when meeting criteria after admission.[3-6] Mechanisms of this increased mortality for these distinct populations are not well explored. Patients who present septic in the emergency department (ED) and patients who present as inpatients likely present very different challenges for recognition, treatment, and monitoring.[7] Yet, how these groups differ by demographic and clinical characteristics, the etiology and severity of infection, and patterns of resuscitation care are not well described. Literature on sepsis epidemiology on hospital wards is particularly limited.[8]

This knowledge gap is important. If hospital-presenting sepsis (HPS) contributes disproportionately to disease burdCHFens, it reflects a high-yield population deserving the focus of quality improvement (QI) initiatives. If specific causes of disparities were identified—eg, poor initial resuscitation— they could be specifically targeted for correction. Given that current treatment guidelines are uniform for the two populations,[9,10] characterizing phenotypic differences could also have implications for both diagnostic and therapeutic recommendations, particularly if the groups display substantially differing clinical

***Corresponding Author:** Daniel E Leisman, BS; E-mail: deleisman@gmail.com; Telephone: 516-941-8468.

Find Additional Supporting Information in the online version of this article.

Received: October 16, 2018; **Revised**: January 17, 2019; **Accepted**: February 2, 2019

presentations. Our prior work has not probed these effects specifically, but suggested ED versus inpatient setting at the time of initial sepsis presentation might be an effect modifier for the association between several elements of fluid resuscitation and patient outcomes.[11,12]

We, therefore, conducted a retrospective analysis to ask four sequential questions: (1) Do patients with HPS, compared with EDPS, contribute adverse outcome out of proportion to case prevalence? (2) At the time of initial presentation, how do HPS patients differ from EDPS patients with respect to demographics, comorbidities, infectious etiologies, clinical presentations, and severity of illness (3) If holding observed baseline factors constant, does the physical location of sepsis presentation inherently increase the risk for treatment delays and mortality? (4) To what extent can differences in the likelihood for timely initial treatment between the ED and inpatient settings explain differences in mortality and patient outcomes?

We hypothesized *a priori* that HPS would reflect chronically sicker patients whom both received less timely resuscitation and who contributed disproportionately frequent bad outcomes. We expected disparities in timely resuscitation care would explain a large proportion of this difference.

METHODS

We performed a retrospective analysis of the Northwell Sepsis Database, a prospectively captured, multisite, real world, consecutive-sample cohort of all "severe sepsis" and septic shock patients treated at nine tertiary and community hospitals in New York from October 1, 2014, to March 31, 2016. We analyzed all patients from a previously published cohort.[11]

Database Design and Structure

The Northwell Sepsis Database has previously been described in detail.[11,13,14] Briefly, all patients met clinical sepsis criteria: (1) infection AND (2) ≥2 (SIRS) criteria AND (3) ≥1 acute organ dysfunction criterion. Organ dysfunction criteria were hypotension, acute kidney injury (AKI), coagulopathy, altered gas exchange, elevated bilirubin (≥2.0 mg/dL), or altered mental status (AMS; clarified in Supplemental Table 1). All organ dysfunction was not otherwise explained by patients' medical histories; eg, patients on warfarin anticoagulation were not documented to have coagulopathy based on international normalized ratio > 1.5. The time of the sepsis episode (and database inclusion) was the time of the first vital sign measurement or laboratory result where a patient simultaneously met all three inclusion criteria: infection, SIRS, and organ dysfunction. The database excludes patients who were <18 years, declined bundle interventions, had advance directives precluding interventions, or were admitted directly to palliative care or hospice. Abstractors assumed comorbidities were absent if not documented within the medical record and that physiologic abnormalities were absent if not measured by the treatment team. There were no missing data for the variables analyzed. We report analysis in adherence with the STROBE statement guidelines for observational research.

Exposure

The primary exposure was whether patients had EDPS versus HPS. We defined EDPS patients as meeting all objective clinical inclusion criteria while physically in the ED. We defined HPS as first meeting sepsis inclusion criteria outside the ED, regardless of the reason for admission, and regardless of whether patients were admitted through the ED or directly to the hospital. All ED patients were admitted to the hospital.

Outcomes

Process outcomes were full 3-hour bundle compliance, time to antibiotic administration, blood cultures before antibiotics, time to fluid initiation, the volume of administered fluid resuscitation, lactate result time, and whether repeat lactate was obtained (Supplemental Table 2). Treatment times were times of administration (rather than order time). The primary patient outcome was hospital mortality. Secondary patient outcomes were mechanical ventilation, ICU admission, ICU days, hospital length of stay (LOS). We discounted HPS patients' LOS to include only days after meeting the inclusion criteria. Patients were excluded from the analysis of the ICU admission outcome if they were already in the ICU prior to meeting sepsis criteria.

Statistical Analysis

We report continuous variables as means (standard deviation) or medians (interquartile range), and categorical variables as frequencies (proportions), as appropriate. Summative statistics with 95% confidence intervals (CI) describe overall group contributions. We used generalized linear models to determine patient factors associated with EDPS versus HPS, entering random effects for individual study sites to control for intercenter variability.

Next, to generate a propensity-matched cohort, we computed propensity scores adjusted from *a priori* selected variables: age, sex, tertiary versus community hospital, congestive heart failure (CHF), renal failure, COPD, diabetes, liver failure, immunocompromise, primary source of infection, nosocomial source, temperature, initial lactate, presenting hypotension, altered gas exchange, AMS, AKI, and coagulopathy. We then matched subjects 1:1 without optimization or replacement, imposing a caliper width of 0.01; ie, we required matched pairs to have a <1.0% difference in propensity scores. The macro used to match subjects is publically available.[15]

We then compared resuscitation and patient outcomes in the matched cohort using generalized linear models, ie, doubly-robust estimation (DRE).[16] When assessing patient outcomes corrected for resuscitation, we used mixed DRE/multivariable regression. We did this for two reasons: first, DRE has the advantage of only requiring only one approach (propensity vs covariate adjustments) to be correctly specified.[16] Second, computing propensity scores adjusted for resuscitation would be inappropriate given that resuscitation occurs after the exposure allocation (HPS vs EDPS). However, these factors could still impact the outcome and in fact, we hypothesized they were potential mediators of the exposure effect. To interrogate this mediating relationship, we recapitulated the DRE model-

TABLE 1. **Selected Patient Characteristics and Outcomes in Unmatched and Matched Cohorts**

	Entire (Unmatched) Cohort			Matched Cohort	
Variable	**All Subjects**	**EDPS**	**(All) HPS**	**EDPS**	**(All) HPS**
N	**11,182**	**8,673 (77.6%)**	**2,509 (22.4%)**	**1,942 (50.0%)**	**1,942 (50.0%)**
Demographics					
Age* - median (IQR)	74 (62, 85)	75 (62, 85)	73 (62, 83)	73 (61-84)	74 (62-84)
Male Sex*	5,740 (51.3%)	4,436 (51.1%)	1,304 (52.0%)	1,025 (52.8%)	1,021 (52.6%)
Admitted from a SNF	2,477 (22.2%)	2,211 (24.5%)	356 (14.2%)	488 (25.1%)	268 (13.8%)
Comorbidities[a]					
Heart Failure	1,647 (14.7%)	1,171 (13.5%)	476 (19.0%)	322 (16.6%)	351 (18.1%)
Renal Failure	1,161 (10.4%)	754 (8.7%)	407 (16.2%)	278 (14.3%)	284 (14.6%)
COPD*	793 (7.1%)	666 (7.7%)	127 (5.1%)	96 (4.9%)	100 (5.1%)
Immune modifying medications	2,346 (21.0%)	1,748 (20.2%)	598 (23.8%)	439 (22.6%)	459 (23.6%)
Presentation and Etiology					
Respiratory Infection Source	4,460 (39.9%)	3,456 (39.8%)	1,004 (40.0%)	728 (37.5%)	787 (40.5%)
Urinary Infection Source	2,802 (25.1%)	2,321 (26.8%)	481 (19.2%)	404 (20.8%)	369 (19.0%)
Skin/Soft Tissue Infection Source	778 (7.0%)	644 (7.4%)	134 (5.3%)	154 (7.9%)	92 (4.7%)
Gastrointestinal Infection Source	1,071 (9.6%)	734 (8.5%)	337 (13.4%)	202 (10.4%)	268 (13.8%)
Other/Unknown Infection Source	2,071 (18.5%)	1,518 (17.5%)	553 (22.0%)	454 (23.4%)	426 (21.9%)
Confirmed Nosocomial Source	1,213 (10.9%)	705 (8.1%)	508 (20.3%)	339 (17.5%)	332 (17.1%)
Fever*	4,040 (36.1%)	3,334 (38.4%)	706 (28.1%)	637 (32.8%)	553 (28.5%)
Leukocytosis	6,596 (59.0%)	5,146 (59.3%)	1,450 (57.8%)	1,123 (57.8%)	1,128 (58.1%)
Severity of Illness					
Initial Lactate (mmol/L)-mean (SD)	3.2 (2.4)	3.3 (2.3)	3.1 (2.7)	3.1 (2.2)	3.1 (2.7)
Hypotension	3,714 (33.2%)	2,551 (29.4%)	1,163 (46.4%)	872 (44.9%)	849 (43.7%)
Altered Gas Exchange[b]	2,412 (21.6%)	1,606 (18.5%)	806 (32.1%)	604 (31.1%)	622 (32.0%)
Altered Mental Status	2,675 (23.9%)	2,060 (23.8%)	615 (24.5%)	461 (23.7%)	469 (24.2%)
Acute Kidney Injury[c]	2,328 (20.8%)	1,847 (21.3%)	481 (19.2%)	380 (19.6%)	372 (19.2%)
Process Outcomes					
Full 3h-bundle compliance (local)	3,056 (27.3%)	2,696 (31.1%)	360 (14.3%)	588 (30.3%)	330 (17.0%)
Full 3h-bundle compliance (SSC)	5,854 (52.4%)	5,127 (59.1%)	727 (29.0%)	1,114 (57.4%)	591 (30.4%)
Antibiotics within 1 h	5,399 (48.3%)	4,317 (49.8%)	1,082 (43.1%)	935 (48.1%)	879 (45.3%)
Antibiotics within 3 h	9,040 (80.8%)	7,437 (85.7%)	1,603 (63.9%)	1,628 (83.8%)	1,285 (66.2%)
Antibiotics within 6 h	9,987 (89.3%)	8,111 (93.5%)	1,876 (74.8%)	1,796 (92.5%)	1,496 (77.0%)
Blood Cultures Before Antibiotics	7,350 (67.3%)	6,170 (71.1%)	1,360 (54.2%)	1,350 (69.5%)	1,036 (53.3%)
Time to Fluid Initiation-mean (SD)	118 (149)	86 (128)	220 (160)	89 (129)	210 (166)
Fluid Volume (mL/kg)-mean (SD)	22.9 (18.7)	25.4 (18.4)	14.1 (16.9)	26.0 (18.8)	15.4 (17.2)
Patient Outcomes					
In-Hospital Mortality	2,241 (20.0%)	1,456 (16.8%)	785 (31.3%)	374 (19.3%)	605 (31.2%)
Mechanical Ventilation	3,265 (29.2%)	2,024 (23.3%)	1,241 (49.5%)	532 (27.4%)	1,000 (51.5%)

All data presented as frequency (percentage) unless otherwise indicated. Full tabulation of patient characteristics and outcomes is available in the online supplement.

*Indicates variable was used in generating propensity score for matching.

[a]Comorbidities reflect status at time zero and would not reflect conditions developing subsequently during hospital stay.

[b]Altered Gas Exchange defined as PaO2 /FiO2 <300 or an increased O2 requirement to maintain SaO2 >90%.

[c]Acute Kidney Injury defined as creatinine >2.0 or 50% increase from a known baseline.

Abbreviations: COPD, chronic obstructive pulmonary disease; EDPS, emergency department-presenting sepsis; HPS, hospital-presenting sepsis, ICU, intensive care unit; IQR, interquartile range; SNF, skilled nursing facility; SD, standard deviation.

ing but added covariates for resuscitation factors. Resuscitation-adjusted models controlled for timeliness of antibiotics, fluids, and lactate results; blood cultures before antibiotics; repeat lactate obtained, and fluid volume in the first six hours.

Since ICU days and LOS are subject to competing risks bias (LOS could be shorter if patients died earlier), we used proportional hazards models where "the event" was defined as a live discharge to censor for mortality and we report output as

TABLE 2. **Adjusted Associations of Patient Characteristics with Hospital vs ED-Presenting Sepsis**

	(All) Hospital-Presenting Sepsis			(Non-ICU) Hospital-Presenting Sepsis		
Variable	**AOR**	**95% CI**	***P***	**AOR**	**95% CI**	***P***
Demographics						
Male Sex	0.98	0.93 to 1.02	.30	1.01	0.84 to 1.20	.96
Age (per 10 years)	1.04	0.86 to 1.27	.67	1.01	0.97 to 1.06	.56
Body Mass Index*	1.01	1.01 to 1.02	<.001	1.01	1.00 to 1.01	.069
Admitted from SNF*	0.44	0.32 to 0.60	<.001	0.49	0.35 to 0.67	<.001
Comorbidities						
Congestive Heart Failure*	1.31	1.18 to 1.47	<.001	1.27	1.12 to 1.44	<.001
Chronic Renal Failure*	1.62	1.38 to 1.91	<.001	1.59	1.29 to 1.95	<.001
COPD*	0.53	0.36 to 0.78	.001	0.52	0.34 to 0.79	.003
Diabetes	0.94	0.86 to 1.03	.20	0.90	0.80 to 1.01	.069
Liver Failure	1.01	0.58 to 1.76	.96	1.10	0.62 to 1.96	.74
Presentation and Etiology						
Infection Source (vs Respiratory):						
Urinary	0.94	0.81 to 1.08	.37	1.03	0.87 to 1.20	.75
Gastrointestinal*	1.84	1.48 to 2.29	<.001	1.96	1.47 to 2.61	<.001
Skin and Soft Tissue*	0.73	0.55 to 0.97	.030	0.97	0.67 to 1.40	.88
Other/Unknown	1.37	0.87 to 2.15	.17	1.39	0.90 to 2.14	.14
Confirmed Nosocomial Etiology*	2.61	1.19 to 5.71	.016	2.98	1.23 to 7.19	.015
Immunocompromized at Presentation	1.05	0.76 to 1.46	.77	1.08	0.83 to 1.41	.58
Tachycardia >90 beats/minute	0.81	0.62 to 1.05	.11	0.88	0.70 to 1.11	.29
Tachypnea >20 breaths/minute*	0.76	0.58 to 0.98	.038	0.69	0.51 to 0.94	.017
Body Temperature (vs Febrile)						
Euthermic (>36.0°C, <38.3°C)*	1.45	1.10 to 1.92	.009	1.35	1.03 to 1.76	.030
Hypothermic (<36.0°C)*	1.56	1.28 to 1.90	<.001	1.40	1.17 to 1.67	<.001
Leukocytosis	0.96	0.81 to 1.13	.62	0.96	0.78 to 1.18	.68
Leukocytopenia	0.95	0.58 to 1.55	.84	0.86	0.52 to 1.40	.54
Severity of Illness						
Initial Lactate (per mmol/L)*	0.95	0.93 to 0.98	.001	0.93	0.89 to 0.97	<.001
Hypotension*	1.85	1.65 to 2.08	<.001	1.57	1.42 to 1.73	<.001
Altered Mental Status	0.93	0.62 to 1.37	.70	0.95	0.66 to 1.37	.80
Altered Gas Exchange*	2.46	1.43 to 4.24	.001	2.35	1.42 to 3.90	.001
Acute Kidney Injury*	0.82	0.68 to 0.97	.022	0.77	0.64 to 0.93	.008
Coagulopathy	0.92	0.53 to 1.57	.75	0.81	0.44 to 1.50	.51
Thrombocytopenia	1.26	0.76 to 2.10	.38	1.28	0.74 to 2.19	.38

Results from two generalized linear models to determine whether sepsis developed after admission or while in the community. Models included the above terms as well as random effects to control for intercenter variability.

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease, SNF, skilled nursing facility.

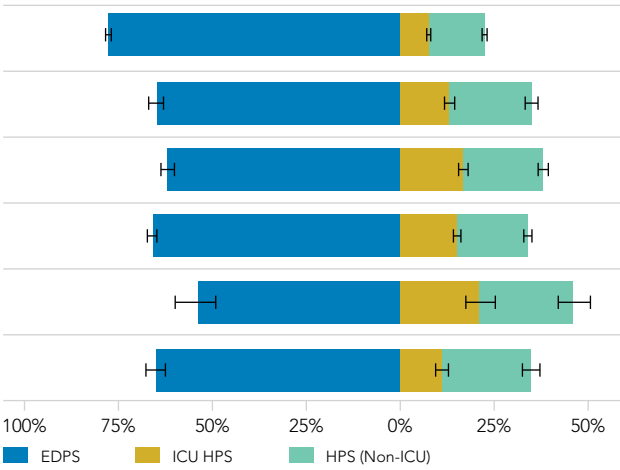
inverse hazard ratios. We also tested interaction coefficients for discrete bundle elements and HPS to determine if specific bundle elements were effect modifiers for the association between the presenting location and mortality risk. Finally, we estimated attributable risk differences by comparing adjusted odds ratios of adverse outcome with and without adjustment for resuscitation variables, as described by Sahai et al.[17]

As sensitivity analyses, we recomputed propensity scores and generated a new matched cohort that excluded HPS patients who met criteria for sepsis while already in the ICU for another reason (ie, excluding ICU-presenting sepsis). We then recapitulated all analyses as above for this cohort. We performed analyses using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Prevalence and Outcome Contributions

Of the 11,182 sepsis patients in the database, we classified 2,509 (22%) as HPS (Figure 1). HPS contributed 785 (35%) of 2,241 sepsis-related mortalities, 1,241 (38%) mechanical ventilations, and 1,762 (34%) ICU admissions. Of 39,263 total ICU days and 127,178 hospital days, HPS contributed 18,104 (46.1%) and 44,412 (34.9%) days, respectively.



Outcome	EDPS	All HPS	Non-ICU	ICU
Prevalance	8,673 (77.8%)	2,509 (22.4%)	1,663 (14.9%)	846 (7.6%)
Hospital Mortalities	1,456 (65.0%)	785 (35.0%)	493 (22.0%)	292 (13.0%)
Mechanical Ventilations	2,024 (62.0%)	1,241 (38.0%)	696 (21.3%)	545 (16.7%)
ICU Admissions	3,423 (66.0%)	1,762 (34.0%)	793 (18.8%)	782 (15.2%)
ICU Days	21,159 (53.9%)	18,104 (46.1%)	9,786 (24.9%)	8,318 (21.2%)
Hospital Days	82,766 (65.1%)	44,412 (34.9%)	30,445 (23.9%)	13.967 (11.0%)

FIG 1. Displays contributions of Hospital vs ED-presenting sepsis to overall case prevalence and patient outcomes. Hospital presentations are also stratified into sepsis presentations that occurred during an ICU admission versus those that occurred outside the ICU on the hospital wards. Brackets indicate 95% CIs.

Abbreviations: EDPS, ED presenting sepsis; HPS, hospital presenting sepsis; ICU, intensive care unit.

Patient Characteristics

Most HPS presented early in the hospital course, with 1,352 (53.9%) cases meeting study criteria within three days of admission. Median time from admission to meeting study criteria for HPS was two days (interquartile range: one to seven days). We report selected baseline patient characteristics in Table 1 and adjusted associations of baseline variables with HPS versus EDPS in Table 2. The full cohort characterization is available in Supplemental Table 3. Notably, HPS patients more often had CHF (aOR [adjusted odds ratio}: 1.31, CI: 1.18-1.47) or renal failure (aOR: 1.62, CI: 1.38-1.91), gastrointestinal source of infection (aOR: 1.84, CI: 1.48-2.29), hypothermia (aOR: 1.56, CI: 1.28-1.90) hypotension (aOR: 1.85, CI: 1.65-2.08), or altered gas exchange (aOR: 2.46, CI: 1.43-4.24). In contrast, HPS patients less frequently were admitted from skilled nursing facilities (aOR: 0.44, CI: 0.32-0.60), or had COPD (aOR: 0.53, CI: 0.36-0.76), fever (aOR: 0.70, CI: 0.52-0.91), tachypnea (aOR: 0.76, CI: 0.58-0.98), or AKI (aOR: 082, CI: 0.68-0.97). Other baseline variables were similar, including respiratory source, tachycardia, white cell abnormalities, AMS, and coagulopathies. These associations were preserved in the sensitivity analysis excluding ICU-presenting sepsis.

Propensity Matching

Propensity score matching yielded 1,942 matched pairs (n = 3,884, 77% of HPS patients, 22% of EDPS patients). Table 1 and Supplemental Table 3 show patient characteristics after propensity matching. Supplemental Table 4 shows the propensity model. The frequency densities are shown for the cohort as a function of propensity score in Supplemental Figure 1. After matching, frequencies between groups differed by <5% for all categorical variables assessed. In the sensitivity analysis, propensity matching (model in Supplemental Table 5) resulted in 1,233 matched pairs (n = 2,466, 49% of HPS patients, 14% of EDPS patients), with group differences comparable to the primary analysis.

Process Outcomes

We present propensity-matched differences in initial resuscitation in Figure 2A for all HPS patients, as well as non-ICU-presenting HPS, versus EDPS. HPS patients were roughly half as likely to receive fully 3-hour bundle compliant care (17.0% vs 30.3%, aOR: 0.47, CI: 0.40-0.57), to have blood cultures drawn within three hours prior to antibiotics (44.9% vs 67.2%, aOR: 0.40, CI: 0.35-0.46), or to receive fluid resuscitation initiated within two hours (11.1% vs 26.1%, aOR: 0.35, CI: 0.29-0.42). Antibiotic receipt within one hour was comparable (45.3% vs 48.1%, aOR: 0.89, CI: 0.79-1.01). However, differences emerged for antibiotics within three hours (66.2% vs 83.8%, aOR: 0.38, CI: 0.32-0.44) and persisted at six hours (77.0% vs 92.5%, aOR: 0.27, CI: 0.22-33). Excluding ICU-presenting sepsis from propensity matching exaggerated disparities in antibiotic receipt at one hour (43.4% vs 49.1%, aOR: 0.80, CI: 0.68-0.93), three hours (64.2% vs 86.1%, aOR: 0.29, CI: 0.24-0.35), and six hours (75.7% vs 93.0%, aOR: 0.23, CI: 0.18-0.30). HPS patients more frequently had repeat lactate obtained within 24 hours (62.4% vs 54.3%, aOR: 1.40, CI: 1.23-1.59).

Patient Outcomes

HPS patients had higher mortality (31.2% vs19.3%), mechanical ventilation (51.5% vs27.4%), and ICU admission (60.6% vs 46.5%) (Table 1 and Supplemental Table 6). Figure 2b shows propensity-matched and covariate-adjusted differences in patient outcomes before and after adjusting for initial resuscitation. aORs corresponded to approximate relative risk differences[18] of 1.38 (CI: 1.28-1.48), 1.68 (CI: 1.57-1.79), and 1.72 (CI: 1.61-1.84) for mortality, mechanical ventilation, and ICU admission, respectively. HPS was associated with 83% longer mortality-censored ICU stays (five vs nine days, HR^{-1}: 1.83, CI: 1.65-2.03), and 108% longer hospital stay (eight vs 17 days, HR^{-1}: 2.08, CI: 1.93-2.24). After adjustment for resuscitation, all effect sizes decreased but persisted. The initial crystalloid

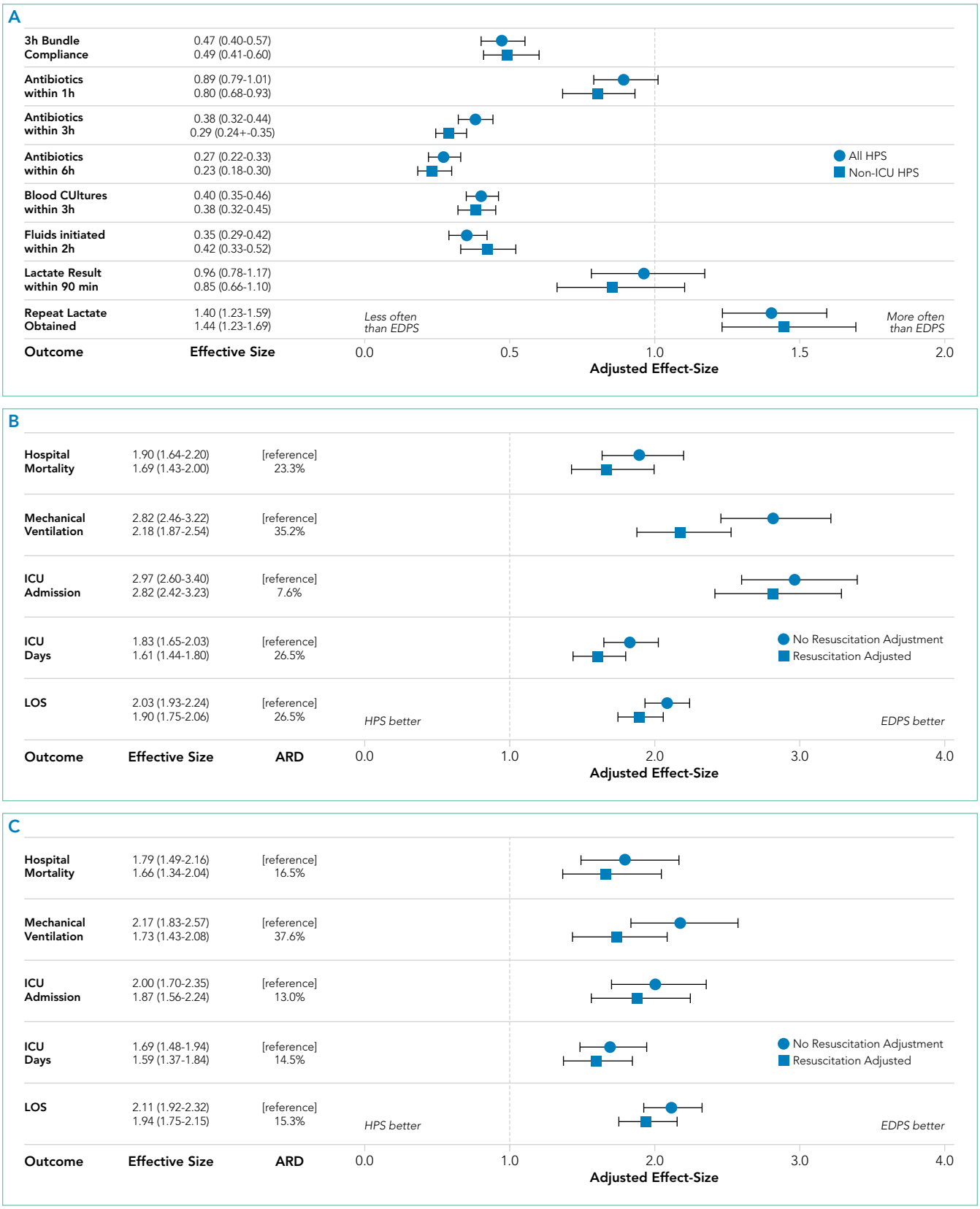


FIG 2. (A) Displays the adjusted likelihood of HPS vs EDPS patients to receive specific initial resuscitation interventions. (B) Displays the adjusted likelihood of all HPS patients to experience the specified outcome, with and without correction for differences in resuscitation delivery. The ARD is the percentage of the outcome difference between HPS and EDPS that was explainable by differences in initial resuscitation delivery. (C) Displays the likelihood of outcome as in (b) but excluding HPS patients whose sepsis presentation occurred in the ICU after admission for another reason. Brackets indicate 95% CIs.

Abbreviations: ARD, adjusted risk-difference; EDPS, ED presenting sepsis; HPS, hospital presenting sepsis; ICU, intensive care unit.

volume was a significant negative effect modifier for mortality (Supplemental Table 7). That is, the magnitude of the association between HPS and greater mortality decreased by a factor of 0.89 per 10 mL/kg given (CI: 0.82-0.97). We did not observe significant interaction from other interventions, or overall bundle compliance, meaning these interventions' association with mortality did not significantly differ between HPS versus EDPS.

The implied attributable risk difference from discrepancies in initial resuscitation was 23.3% for mortality, 35.2% for mechanical ventilation, and 7.6% for ICU admission (Figure 2B). Resuscitation explained 26.5% of longer ICU LOS and 16.7% of longer hospital LOS associated with HPS.

Figure 2C shows sensitivity analysis excluding ICU-presenting sepsis from propensity matching (ie, limiting HPS to hospital ward presentations). Again, HPS was associated with all adverse outcomes, though effect sizes were smaller than in the primary cohort for all outcomes except hospital LOS. In this cohort, resuscitation factors now explained 16.5% of HPS' association with mortality, and 14.5% of the association with longer ICU LOS. However, they explained a greater proportion (13.0%) of ICU admissions. Attributable risk differences were comparable to the primary cohort for mechanical ventilation (37.6%) and hospital LOS (15.3%).

DISCUSSION

In this analysis of 11,182 sepsis and septic shock patients, HPS contributed 22% of prevalence but >35% of total sepsis mortalities, ICU utilization, and hospital days. HPS patients had higher comorbidity burdens and had clinical presentations less obviously attributable to infection with more severe organ dysfunction. EDPS received antibiotics within three hours about 1.62 times more often than do HPS patients. EDPS patients also receive fluids initiated within two hours about 1.82 times more often than HPS patients do. HPS had nearly 1.5-fold greater mortality and LOS, and nearly two-fold greater mechanical ventilation and ICU utilization. Resuscitation disparities could partially explain these associations. These patterns persisted when comparing only wards presenting HPS with EDPS.

Our analysis revealed several notable findings. First, these data confirm that HPS represents a potentially high-impact target population that contributes adverse outcomes disproportionately frequently with respect to case prevalence.

Our findings, unsurprisingly, revealed HPS and EDPS reflect dramatically different patient populations. We found that the two groups significantly differed by the majority of the baseline factors we compared. It may be worth asking if and how these substantial differences in illness etiology, chronic health, and acute physiology impact what we consider an optimal approach to management. Significant interaction effects of fluid volume on the association between HPS and mortality suggest differential treatment effects may exist between patients. Indeed, patients who newly arrive from the community and those who are several days into admission likely have different volume status. However, no interactions were noted with other bundle elements, such as timeliness of antibiotics or timeliness of initial fluids.

Another potentially concerning observation was that HPS patients were admitted much less frequently from skilled nursing facilities, as it could imply that this poorer-fairing population had a comparatively higher baseline functional status. The fact that 25% of EDPS cases were admitted from these facilities also underscores the need to engage skilled nursing facility providers in future sepsis initiatives.

We found marked disparities in resuscitation. Timely delivery of interventions, such as antibiotics and initial fluid resuscitation, occurred less than half as often for HPS, especially on hospital wards. While evidence supporting the efficacy of specific 3-hour bundle elements remains unsettled,[19] a wealth of literature demonstrates a correlation between bundle uptake and decreased sepsis mortality, especially for early antibiotic administration.[13,20-26] Some analysis suggests that differing initial resuscitation practices explain different mortality rates in the early goal-directed therapy trials.[27] The comparatively poor performance for non-ICU HPS indicates further QI efforts are better focused on inpatient wards, rather than on EDs or ICUs where resuscitation is already delivered with substantially greater fidelity.

While resuscitation differences partially explained outcome discrepancies between groups, they did not account for as much variation as expected. Though resuscitation accounted for >35% of attributable mechanical ventilation risk, it explained only 16.5% of mortality differences for non-ICU HPS vs EDPS. We speculate that several factors may contribute.

First, HPS patients are already hospitalized for another acute insult and may be too physiologically brittle to derive equal benefit from initial resuscitation. Some literature suggests protocolized sepsis resuscitation may paradoxically be more effective in milder/earlier disease.[28]

Second, clinical information indicating septic organ dysfunction may become available too late in HPS—a possible data limitation where inpatient providers are counterintuitively more likely to miss early signs of patients' deterioration and a subsequent therapeutic window. Several studies found that fluid resuscitation is associated with improved sepsis outcomes only when it is administered very early.[11,29-31] In inpatient wards, decreased monitoring[32] and human factors (eg, hospital workflow, provider-to-patient ratios, electronic documentation burdens)[33,34] may hinder early diagnosis. In contrast, ED environments are explicitly designed to identify acutely ill patients and deliver intervention rapidly. If HPS patients were sicker when they were identified, this would also explain their more severe organ dysfunctions. Our data seems to support this possibility. HPS patients had tachypnea less frequently but more often had impaired gas exchange. This finding may suggest that early tachypnea was either less often detected or documented, or that it had progressed further by the time of detection.

Third, inpatients with sepsis may more often present with greater diagnostic complexity. We observed that HPS patients were more often euthermic and less often tachypneic. Beyond suggesting a greater diagnostic challenge, this also raises questions as to whether differences reflect patient physiology (response to infection) or iatrogenic factors (eg, prior antipyret-

ics). Higher comorbidity and acute physiological burdens also limit the degree to which new organ dysfunction can be clearly attributed to infection. We note differences in the proportion of patients who received antibiotics increased over time, suggesting that HPS patients who received delayed antibiotics did so much later than their EDPS counterparts. This lag could also arise from diagnostic difficulty.

All three possibilities highlight a potential lead time effect, where the same measured three-hour period on the wards, between meeting sepsis criteria and starting treatment, actually reflects a longer period between (as yet unmeasurable) pathobiologic "time zero" and treatment versus the ED. The time of sepsis detection, as distinct from the time of sepsis onset, therefore proves difficult to evaluate and impossible to account for statistically.

Regardless, our findings suggest additional difficulty in both the recognition and resuscitation of inpatient sepsis. Inpatients, especially with infections, may need closer monitoring. How to cost effectively implement this monitoring is a challenge that deserves attention.

A more rational systems approach to HPS likely combines efforts to improve initial resuscitation with other initiatives aimed at both improving monitoring and preventing infection.

To be clear, we do not imply that timely initial resuscitation does not matter on the wards. Rather, resuscitation-focused QI alone does not appear to be sufficient to overcome differences in outcomes for HPS. The 23.3% attributable mortality risk we observed still implies that resuscitation differences could explain nearly one in four excess HPS mortalities. We previously showed that timely resuscitation is strongly associated with better outcomes.[11,13,30] As discussed above, the unclear degree to which better resuscitation is a marker for more obvious presentations is a persistent limitation of prior investigations and the present study.

Taken together, the ultimate question that this study raises but cannot answer is whether the timely recognition of sepsis, rather than any specific treatment, is what truly improves outcomes.

In addition to those above, this study has several limitations. Our study did not differentiate HPS with respect to patients admitted for noninfectious reasons and who subsequently became septic versus nonseptic patients admitted for an infection who subsequently became septic from that infection. Nor could we discriminate between missed ED diagnoses and true delayed presentations. We note distinguishing these entities clinically can be equally challenging. Additionally, this was a propensity-matched retrospective analysis of an existing sepsis cohort, and the many limitations of both retrospective study and propensity matching apply.[35,36] We note that randomizing patients to develop sepsis in the community versus hospital is not feasible and that two of our aims intended to describe overall patterns rather than causal effects. We could not ascertain robust measures of severity of illness (eg, SOFA) because a real world setting precludes required data points—eg, urine output is unreliably recorded. We also note incomplete overlap between inclusion criteria and either Sepsis-2 or -3 definitions,[1,37] because we designed and populated our database prior to publication of Sepsis-3. Further, we could not account for surgical source control, the appropriateness of antimicrobial therapy, mechanical ventilation before sepsis onset, or most treatments given after initial resuscitation.

In conclusion, hospital-presenting sepsis accounted for adverse patient outcomes disproportionately to prevalence. HPS patients had more complex presentations, received timely antibiotics half as often ED-presenting sepsis, and had nearly twice the mortality odds. Resuscitation disparities explained roughly 25% of this difference.

Disclosures: The authors have no conflicts of interest to disclose.

Funding: This investigation was funded in part by a grant from the Center for Medicare and Medicaid Innovation to the High Value Healthcare Collaborative, of which the study sites' umbrella health system was a part. This grant helped fund the underlying QI program and database in this study.

References

1. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801-810. doi: 10.1001/jama.2016.0287.
2. Torio CMA, Andrews RMA. National inpatient hospital costs: the most expensive conditions by payer, 2011. In. *Statistical Brief No. 160*. Rockville, MD: Agency for Healthcare Research and Quality; 2013.
3. Liu V, Escobar GJ, Greene JD, et al. Hospital deaths in patients with sepsis from 2 independent cohorts. *JAMA*. 2014;312(1):90-92. doi: 10.1001/jama.2014.5804.
4. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):762-774. doi: 10.1001/jama.2016.0288.
5. Jones SL, Ashton CM, Kiehne LB, et al. Outcomes and resource use of sepsis-associated stays by presence on admission, severity, and hospital type. *Med Care*. 2016;54(3):303-310. doi: 10.1097/MLR.0000000000000481.
6. Page DB, Donnelly JP, Wang HE. Community-, healthcare-, and hospital-acquired severe sepsis hospitalizations in the university healthsystem consortium. *Crit Care Med*. 2015;43(9):1945-1951. doi: 10.1097/CCM.0000000000001164.
7. Rothman M, Levy M, Dellinger RP, et al. Sepsis as 2 problems: identifying sepsis at admission and predicting onset in the hospital using an electronic medical record-based acuity score. *J Crit Care*. 2016;38:237-244. doi: 10.1016/j.jcrc.2016.11.037.
8. Chan P, Peake S, Bellomo R, Jones D. Improving the recognition of, and response to in-hospital sepsis. *Curr Infect Dis Rep*. 2016;18(7):20. doi: 10.1007/s11908-016-0528-7.
9. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med*. 2017;45(3):486-552. doi: 10.1097/CCM.0000000000002255.
10. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 Update. *Crit Care Med*. 2018;46(6):997-1000. doi: 10.1097/CCM.0000000000003119.
11. Leisman DE, Goldman C, Doerfler ME, et al. Patterns and outcomes associated with timeliness of initial crystalloid resuscitation in a prospective sepsis and septic shock cohort. *Crit Care Med*. 2017;45(10):1596-1606. doi: 10.1097/CCM.0000000000002574.
12. Leisman DE, Doerfler ME, Schneider SM, Masick KD, D'Amore JA, D'Angelo JK. Predictors, prevalence, and outcomes of early crystalloid responsiveness among initially hypotensive patients with sepsis and septic shock. *Crit Care Med*. 2018;46(2):189-198. doi: 10.1097/CCM.0000000000002834.
13. Leisman DE, Doerfler ME, Ward MF, et al. Survival benefit and cost savings from compliance with a simplified 3-hour sepsis bundle in a series of prospective, multisite, observational cohorts. *Crit Care Med*. 2017;45(3):395-406. doi: 10.1097/CCM.0000000000002184.
14. Doerfler ME, D'Angelo J, Jacobsen D, et al. Methods for reducing sepsis mortality in emergency departments and inpatient units. *Jt Comm J Qual Patient Saf*. 2015;41(5):205-211. doi: 10.1016/S1553-7250(15)41027-X.
15. Murphy B, Fraeman KH. A general SAS® macro to implement optimal N:1

propensity score matching within a maximum radius. In: *Paper 812-2017*. Waltham, MA: Evidera; 2017. https://support.sas.com/resources/papers/proceedings17/0812-2017.pdf. Accessed February 20, 2019.
16. Funk MJ, Westreich D, Wiesen C, Stürmer T, Brookhart MA, Davidian M. Doubly robust estimation of causal effects. *Am J Epidemiol*. 2011;173(7):761-767. doi: 10.1093/aje/kwq439.
17. Sahai HK, Khushid A. *Statistics in Epidemiology: Methods, Techniques, and Applications*. Boca Raton, FL: CRC Press; 1995.
18. VanderWeele TJ. On a square-root transformation of the odds ratio for a common outcome. *Epidemiology*. 2017;28(6):e58-e60. doi: 10.1097/EDE.0000000000000733.
19. Pepper DJ, Natanson C, Eichacker PQ. Evidence underpinning the centers for medicare & medicaid services' severe sepsis and septic shock management bundle (SEP-1). *Ann Intern Med*. 2018;168(8):610-612. doi: 10.7326/L18-0140.
20. Levy MM, Rhodes A, Phillips GS, et al. Surviving sepsis campaign: association between performance metrics and outcomes in a 7.5-year study. *Crit Care Med*. 2015;43(1):3-12. doi: 10.1097/CCM.0000000000000723.
21. Liu VX, Morehouse JW, Marelich GP, et al. Multicenter Implementation of a Treatment Bundle for Patients with Sepsis and Intermediate Lactate Values. *Am J Respir Crit Care Med*. 2016;193(11):1264-1270. doi: 10.1164/rccm.201507-1489OC.
22. Miller RR, Dong L, Nelson NC, et al. Multicenter implementation of a severe sepsis and septic shock treatment bundle. *Am J Respir Crit Care Med*. 2013;188(1):77-82. doi: 10.1164/rccm.201212-2199OC.
23. Seymour CW, Gesten F, Prescott HC, et al. Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med*. 2017;376(23):2235-2244. doi: 10.1056/NEJMoa1703058.
24. Pruinelli L, Westra BL, Yadav P, et al. Delay within the 3-hour surviving sepsis campaign guideline on mortality for patients with severe sepsis and septic shock. *Crit Care Med*. 2018;46(4):500-505. doi: 10.1097/CCM.0000000000002949.
25. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589-1596. doi: 10.1097/01.CCM.0000217961.75225.E9.
26. Liu VX, Fielding-Singh V, Greene JD, et al. The timing of early antibiotics and hospital mortality in sepsis. *Am J Respir Crit Care Med*. 2017;196(7):856-863. doi: 10.1164/rccm.201609-1848OC.
27. Kalil AC, Johnson DW, Lisco SJ, Sun J. Early goal-directed therapy for sepsis: a novel solution for discordant survival outcomes in clinical trials. *Crit Care Med*. 2017;45(4):607-614. doi: 10.1097/CCM.0000000000002235.
28. Kellum JA, Pike F, Yealy DM, et al. relationship between alternative resuscitation strategies, host response and injury biomarkers, and outcome in septic shock: analysis of the protocol-based care for early septic shock study. *Crit Care Med*. 2017;45(3):438-445. doi: 10.1097/CCM.0000000000002206.
29. Seymour CW, Cooke CR, Heckbert SR, et al. Prehospital intravenous access and fluid resuscitation in severe sepsis: an observational cohort study. *Crit Care*. 2014;18(5):533. doi: 10.1186/s13054-014-0533-x.
30. Leisman D, Wie B, Doerfler M, et al. Association of fluid resuscitation initiation within 30 minutes of severe sepsis and septic shock recognition with reduced mortality and length of stay. *Ann Emerg Med*. 2016;68(3):298-311. doi: 10.1016/j.annemergmed.2016.02.044.
31. Lee SJ, Ramar K, Park JG, Gajic O, Li G, Kashyap R. Increased fluid administration in the first three hours of sepsis resuscitation is associated with reduced mortality: a retrospective cohort study. *Chest*. 2014;146(4):908-915. doi: 10.1378/chest.13-2702.
32. Smyth MA, Daniels R, Perkins GD. Identification of sepsis among ward patients. *Am J Respir Crit Care Med*. 2015;192(8):910-911. doi: 10.1164/rccm.201507-1395ED.
33. Wenger N, Méan M, Castioni J, Marques-Vidal P, Waeber G, Garnier A. Allocation of internal medicine resident time in a Swiss hospital: a time and motion study of day and evening shifts. *Ann Intern Med*. 2017;166(8):579-586. doi: 10.7326/M16-2238.
34. Mamykina L, Vawdrey DK, Hripcsak G. How do residents spend their shift time? A time and motion study with a particular focus on the use of computers. *Acad Med*. 2016;91(6):827-832. doi: 10.1097/ACM.0000000000001148.
35. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. *Ann Emerg Med*. 2014;64(3):292-298. doi: 10.1016/j.annemergmed.2014.03.025.
36. Leisman DE. Ten pearls and pitfalls of propensity scores in critical care research: a guide for clinicians and researchers. *Crit Care Med*. 2019;47(2):176-185. doi: 10.1097/CCM.0000000000003567.
37. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Crit Care Med*. 2003;31(4):1250-1256. doi: 10.1097/01.CCM.0000050454.01978.3B.

Follow-Up of Incidental High-Risk Pulmonary Nodules on Computed Tomography Pulmonary Angiography at Care Transitions

Janice L Kwan, MD, MPH[1,2]*; Darya Yermak, MD[2]; Lezlie Markell, MB, BCh BAO[2]; Narinder S Paul, MD[3]; Kaveh G Shojania, MD[2,4]; Peter Cram, MD, MBA[1,2]

[1]Division of General Internal Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada; [2]Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [3]Department of Medical Imaging, Western University, London, Ontario, Canada; [4]Division of General Internal Medicine, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada.

BACKGROUND: Computed tomography pulmonary angiography (CTPA) detects incidental findings that require follow-up. In just over 50% of cases, those incidental findings are pulmonary nodules. Fleischner guidelines recommend that patients with nodules that have a high risk of malignancy should undergo CT follow-up within 3-12 months.

OBJECTIVE: We examined the proportion of patients with pulmonary nodules requiring follow up who received repeat imaging within six weeks of the time frame recommended by the radiologist.

DESIGN: This retrospective cohort study included all patients who underwent CTPA in the emergency department and inpatient settings at three teaching hospitals in Toronto, Canada between September 1, 2014, and August 31, 2015. Natural language processing software was applied to a linked radiology information system to identify all CTPAs that contained pulmonary nodules. Using manual review and prespecified exclusion criteria, we generated a cohort with possible new lung malignancy eligible for follow-up imaging; then we reviewed available health records to determine whether follow-up had occurred.

RESULTS: Of the 1,910 CTPAs performed over the study period, 674 (35.3%) contained pulmonary nodules. Of the 259 patients with new nodules eligible for follow-up imaging, 65 received an explicit suggestion for follow-up by radiology (25.1%). Of these 65 patients, 35 (53.8%) did not receive repeat imaging within the recommended time frame. Explicit mention that follow-up was required in the discharge summary ($P = .03$), attending an outpatient follow-up visit ($P < .001$), and younger age ($P = .03$) were associated with receiving timely follow-up imaging.

CONCLUSIONS: Over 50% of patients with new high-risk pulmonary nodules detected incidentally on CTPA did not receive timely follow-up imaging. Journal of Hospital Medicine 2019; 14 349-352. Published online first February 20, 2019. © 2019 Society of Hospital Medicine

Computed tomography pulmonary angiography (CTPA) is often used in the evaluation of suspected pulmonary embolism (PE). The detection of incidental findings that require follow-up is common; in just over 50% of cases, those incidental findings are pulmonary nodules.[1] Although the majority of these nodules are benign, Fleischner Society guidelines[2] recommend that patients with nodules at high risk for malignancy should undergo follow-up CT imaging within 3-12 months, with patients who smoke and have large nodules requiring closer follow up.

The failure to follow-up on abnormal test results is known to contribute to diagnostic error and can lead to patient harm.[3] We sought to determine the proportion of high-risk pulmonary nodules on CTPA which did not undergo the recommended follow-up imaging.

***Corresponding Author:** Janice L. Kwan; E-mail: janice.kwan@utoronto.ca; Telephone: (416) 586-4800; Twitter: @KwanJanice

Received: July 19, 2018; **Revised**: October 29, 2018; **Accepted**: November 18, 2018

 DOI 10.12788/jhm.3128

METHODS

Study Setting and Design

This retrospective cohort study included all patients who underwent CTPA in the emergency department (ED) and inpatient settings at three academic health centers (Mount Sinai Hospital, Toronto General Hospital, and Toronto Western Hospital) in Toronto, Canada between September 1, 2014, and August 31, 2015.

We examined the proportion of patients with pulmonary nodules requiring follow up who received repeat CT imaging within six weeks of the time frame recommended by the radiologist. Since we were interested in measuring the rate of an important test result that is missed (rather than accuracy of the test itself), we defined "requiring follow up" as the inclusion of explicit recommendations for follow up in the radiology report.

Montage (Philadelphia, Pennsylvania), a natural language processing software, was applied to a linked radiology information system (RIS) to identify all CTPAs that contained pulmonary nodules. We conducted manual chart review to confirm software accuracy. We initially searched the RIS for all CTPAs that were completed within the study period, resulting in the identification of 1932 imaging studies. Following a review of

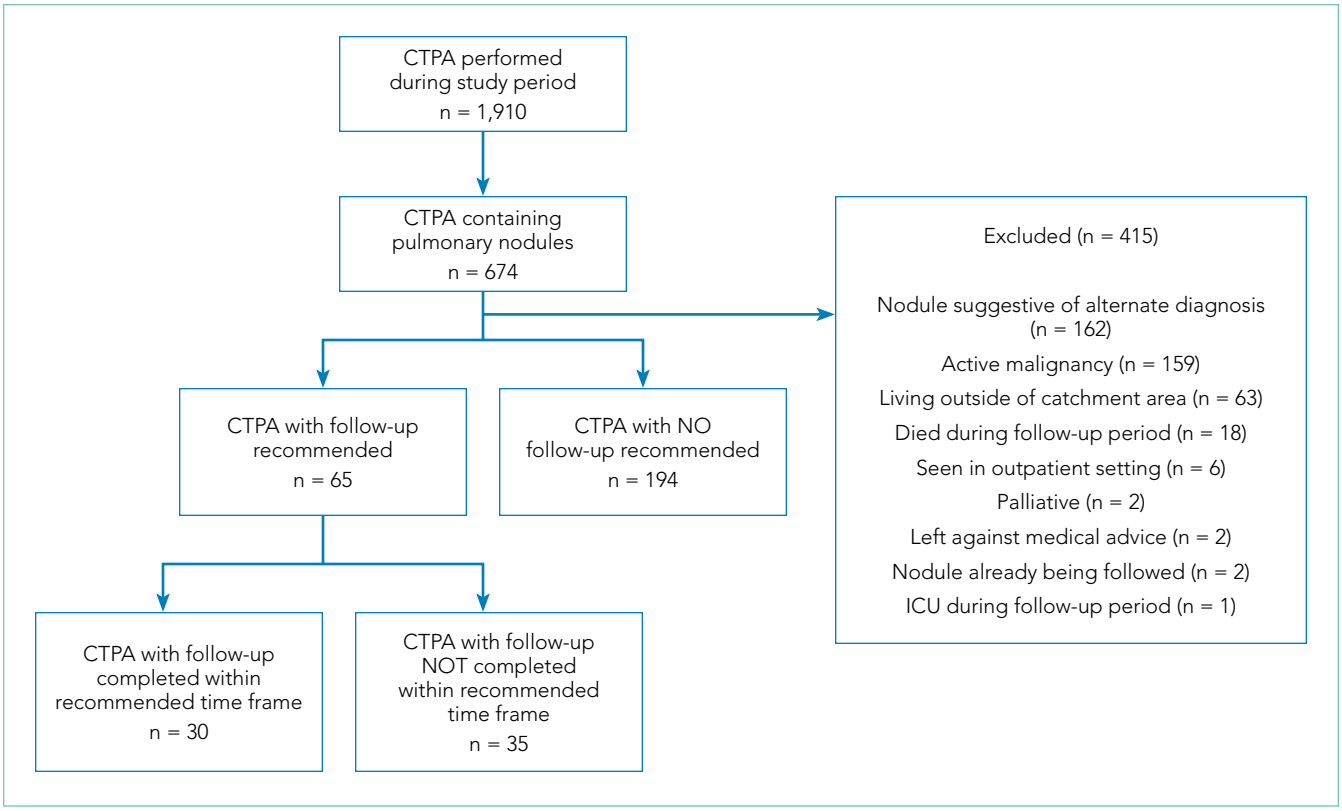


FIG. Flowchart of Computed Tomography Pulmonary Angiography (CTPA) Scans Included in the Study Cohort.

these 1,932 studies, we excluded 22 as they were not CTPAs. We then applied the search term, "nodule-" to 1,910 confirmed CTPAs, resulting in the identification of 836 imaging studies. Following a review of these 836 studies, we excluded 10 as they were duplicate studies. We also excluded 152 studies where the term "nodule" did not identify a pulmonary nodule but instead referred to a radiologist reporting the absence of pulmonary nodules (eg "there were no pulmonary nodules found") or the presence of non-lung nodules (eg thyroid nodules). This resulted in the identification of 674 CTPAs containing pulmonary nodules (Figure 1).

Thereafter, we generated a cohort with possible new lung malignancy eligible for follow-up imaging by reviewing available health records and applying the following prespecified exclusion criteria: (1) patients who died, (2) left against medical advice, (3) were critically ill during the follow-up period, (4) lived outside the hospital catchment area (Greater Toronto Area), (5) were seen in the outpatient setting, (6) identified as palliative, (7) had an active malignancy, (8) had nodules that were already being followed, or (9) had nodules with characteristics suggestive of alternate diagnoses to lung malignancy (such as infection or inflammation) with no follow up recommended as reported by the radiologist. For patients with multiple CTPAs, we included only the first study. For each eligible patient, we determined whether follow-up imaging was completed by manually reviewing the linked RIS. We reviewed available health records to determine whether the pulmonary nodule findings had been discussed with the patient and whether the patient had attended an outpatient follow-up visit. In patients for whom recommended follow-up imaging was not confirmed, we notified the ordering physician by e-mail.

Each radiology department followed the same protocol adherent to the 2005 Fleischner guidelines for identifying nodules requiring follow up.[2] Virtually all CTPAs at the three study institutions are read and reported within 72 hours. The ordering physician is sometimes called at the discretion of the reading radiologist when the findings are judged to be urgent and time-sensitive in nature. For example, the ordering physician may be contacted if a CTPA is positive for segmental PE but is not typically called for incidental pulmonary nodules. It is not common practice for ordering physicians to be notified of incidental findings above and beyond the radiology report. Primary care physicians are not typically copied on radiology reports and usually do not use the same electronic health record.

Statistical Analysis

We calculated simple descriptive statistics for all results. Mean values were compared using two-tailed t-tests, categorical groups using chi-square tests, and median values using Mann-Whitney U tests. We performed all analyses using Microsoft Excel version 16.14.1 (Redmond, Washington).

Ethics Approval

This study was approved by each institution's research ethics board.

TABLE. **Characteristics of Patients with High-Risk Pulmonary Nodules Noted on Computed Tomography Pulmonary Angiography Requiring Follow Up.**

Characteristic	No. (%)			
	All (n = 65)	Follow Up Completed Within the Recommended Time Frame (n = 30)	Follow Up NOT Completed Within the Recommended Time Frame (n = 35)	*P* Value
Sociodemographics				
Mean age (Standard Deviation), y	67.2 (15.2)	62.8 (15.7)	71.0 (14.0)	.03
Women	33 (51)	14 (47)	19 (54)	.29
Lung Cancer Risk Factor				
Never Smoked				
Yes	11 (17)	6 (20)	5 (14)	.42
No	36 (55)	18 (60)	18 (52)	
Unknown	18 (28)	6 (20)	12 (34)	
Chronic Obstructive Pulmonary Disease				
Yes	24 (37)	10 (33)	14 (40)	.58
No	41 (63)	20 (67)	21 (60)	
Imaging				
Lung Nodule				
Single	12 (19)	5 (17)	7 (20)	.73
Multiple	53 (81)	25 (83)	28 (80)	
Median Recommended Follow-Up (Interquartile Range), months	6 (3-12)	6 (3-12)	6 (3-12)	.90
System				
Hospital Department				
Emergency department	27 (42)	14 (47)	13 (37)	.62
Inpatient	38 (58)	16 (53)	22 (63)	
Follow-Up Instructions Included in the Discharge Summary				
Included	36 (55)	21 (70)	15 (43)	.03
Not included	29 (45)	9 (30)	20 (57)	
Attended Outpatient Follow-Up Visit				
Yes	18 (28)	16 (53)	2 (6)	<.001
No	47 (72)	14 (47)	33 (94)	

RESULTS

Follow Up of Incidental High-Risk Pulmonary Nodules

Of the 1910 CTPAs performed over the study period (Figure), 674 (35.3%) contained pulmonary nodules. Of the 259 patients with new pulmonary nodules eligible for follow-up imaging, 194 (74.9%) did not have an explicit suggestion for follow up by the radiologist. Ninety-five percent of radiologists (184 out of 194) provided an explanation for not recommending follow up in the radiology report; the two most common reasons were small nodule size (often described as "tiny") and no interval change compared with the prior imaging study.[2] Of the 65 patients who did receive an explicit suggestion for follow up by radiology, 35 (53.8%) did not receive repeat imaging within the recommended time frame, allowing for a six-week grace period. Of these 35 patients, 10 eventually went on to receive delayed repeat imaging. The median follow-up time for the 30 patients who received timely repeat imaging was four months (IQR 2-6 months); in contrast, the median follow-up time for the 10 patients who received delayed repeat imaging was seven months (IQR 6-8 months), $P = .01$.

Of the 65 patients for whom follow up was recommended, the medical record showed evidence that there was a discussion between the medical team and the patient regarding patient preference for or against follow up in 55.4% (36 out of 65) of the patients. Notably, all 36 patients showed interest in receiving follow up; no patient indicated a preference for no follow up.

Furthermore, of the 65 patients that had follow up recommended, two patients were eventually diagnosed with lung cancer (one via lung biopsy, the other via positron emission

tomography imaging); both patients did not receive timely follow-up imaging. While we did not include nodule size as an exclusion criterion, not one of the 65 patients included in the final cohort had nodules larger than 3 cm.

Physician Notification

In circumstances where we could not confirm that followed up had occurred, we notified the ordering physician by e-mail. Since 10 of the 35 patients who did not receive timely follow-up imaging went on to receive delayed repeat imaging, we notified 25 physicians. Of the 25 physicians that we e-mailed, 24 acknowledged receipt of the information. Of these 24 physicians, 14 reported conducting a detailed review of the chart, from which the following additional information was obtained: one patient expired, and five physicians notified the corresponding primary care physicians (two of whom were unaware of the nodule, and subsequently arranged further follow up with the patient).

Characteristics Associated with Timely Follow Up

Explicit mention that follow up was required in the discharge summary ($P = .03$), attending an outpatient follow-up visit ($P < .001$), and younger age ($P = .03$) were associated with receiving timely follow up; patient sex, smoking history, history of chronic obstructive pulmonary disease, lung nodule count, recommended follow-up time, and hospital department (defined as the discharging service) were not (Table).

DISCUSSION

In this multicenter cohort study, over 50% of patients with new high-risk pulmonary nodules detected incidentally on CTPA did not receive timely follow-up imaging. Including follow-up recommendations in the discharge summary, attending an outpatient follow-up visit, and younger age were associated with timely follow-up imaging.

Few studies have assessed the follow up of incidental nodules identified on CTPA. In a retrospective cohort study of ED patients in the United States, Blagev et al. found that only 29% received timely follow up.[4] Our study contributes to the literature in several ways. First, our study included all hospitalized patients, not only those in the ED. Notably, most of our cohort were inpatients, a group of patients not previously described. Second, we examined factors associated with timely follow up, which may help to inform future quality improvement initiatives and interventions. Third, we included data from three different hospitals, which may improve generalization. Lastly, our study draws on contemporary Canadian data. Most of the studies investigating test result follow up have been conducted in the US[5,6] and Europe,[7] with few empirical studies describing this phenomenon within the Canadian healthcare setting. We believe that our work contributes to the existing evidence that missed test results occur across diverse healthcare systems and have yet to be solved.[5-7]

Our study had limitations. First, we defined follow up as repeat imaging and did not include office visits or biopsy in this definition. Second, we may have missed repeat imaging and outpatient follow-up visits that occurred outside the study hospitals. Although we were able to determine if repeat imaging and outpatient follow-up visits (eg, pulmonology or thoracic surgery clinics) had occurred within the study hospitals, we did not have access to follow-up encounters that occurred outside of the study hospitals (eg primary care clinics). We are unaware of any published regional data on the rate of outpatient follow up at the index facility following discharge. However, we know from provincial data of patients discharged from the ED with a new cardiac diagnosis that just under half are seen by a family physician, cardiologist, or internist within seven days, with just under 80% seen within 30 days.[8] Third, although we attempted to capture patient preference for or against repeat imaging using chart review, the absence of documentation of patient preference did not confirm that a discussion regarding patient preferences had not occurred. Fourth, while we did exclude patients that had an active malignancy, we did not exclude patients who were younger than 35 years or were immunocompromised, which may have led to an overestimation of the percentage of patients who did not receive follow up.

Incidental findings detected on acute diagnostic tests requiring handoffs for chronic follow up are at risk of falling through the cracks. The inclusion of follow-up recommendations in discharge summaries has been shown to increase the likelihood of follow-up completion.[9] Our study provides additional evidence of the urgent need for interventions aimed at closing the loop on test result follow up.[5,6]

Disclosures: None of the authors have any conflicts of interest to disclose in reference to this study.

Funding: JLK is supported by the Mount Sinai Hospital Department of Medicine Research Fund. PC is supported by a K24 award from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (AR062133).

References

1. Hall WB, Truitt SG, Scheunemann LP, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Arch Intern Med* 2009;169(21):1961. doi: 10.1001/archinternmed.2009.360.
2. Macmahon H, Austin JHM, Gamsu G, et al. Guidelines for Management of Small Pulmonary Nodules Detected on CT Scans: A Statement from the Fleischner Society. *Radiology* 2005;237(2):395-400. doi: 10.1148/radiol.2372041887.
3. National Academies of Sciences, Engineering, and Medicine. *Improving diagnosis in health care*. Washington, DC. 2015.
4. Blagev DP, Lloyd JF, Conner K, et al. Follow-up of incidental pulmonary nodules and the radiology report. *J Am Coll Radiol* 2014;11(4):378-383. doi: 10.1016/j.jacr.2013.08.003.
5. Callen J, Georgiou A, Li J, Westbrook JI. The safety implications of missed test results for hospitalized patients: a systematic review. *BMJ Quality Safety* 2011;20(2):194-199. doi: 10.1136/bmjqs.2010.044339.
6. Callen JL, Westbrook JI, Georgiou A, Li J. Failure to follow-up test results for ambulatory patients: a systematic review. *J Gen Intern Med* 2011;27(10):1334-1348. doi: 10.1007/s11606-011-1949-5.
7. Litchfield I, Bentham L, Lilford R, Mcmanus RJ, Hill A, Greenfield S. Test result communication in primary care: a survey of current practice. *BMJ Quality Safety* 2015;24(11):691-699. doi: 10.1136/bmjqs-2014-003712.
8. Atzema CL, Yu B, Ivers NM, et al. Predictors of obtaining follow-up care in the province of Ontario, Canada, following a new diagnosis of atrial fibrillation, heart failure, and hypertension in the emergency department. *Cjem* 2017;20(03):377-391. doi: 10.1017/cem.2017.371.
9. Moore C, McGinn T, Halm E. Tying up loose ends: Discharging patients with unresolved medical issues. *Arch Intern Med* 2007;167(12):1305-1311. doi: 10.1001/archinte.167.12.1305

National Survey of Hospitalists' Experiences with Incidental Pulmonary Nodules

Craig A Umscheid, MD, MS[1,2,3,4]*; Jonathan Wilen, MD[5]; Matthew Garin, MD[1,6]; Jenna D Goldstein, MA[7]; Tessa S Cook, MD, PhD[1]; Yulun Liu, PhD[8]; Yong Chen, PhD[1,4]; Jennifer S Myers, MD[1,3]

[1]University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [2]Center for Evidence-based Practice, University of Pennsylvania Health System, Philadelphia, Pennsylvania; [3]Center for Healthcare Improvement and Patient Safety, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [4]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [5]New York Presbyterian - Columbia University Medical Center, New York, New York; [6]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania; [7]Center for Quality Improvement, Society of Hospital Medicine, Philadelphia, Pennsylvania; [8]Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, Texas.

Incidental pulmonary nodules (IPNs) are common and often require follow-up. The Fleischner Society guidelines were created to support IPN management. We developed a 14-item survey to examine hospitalists' exposure to and management of IPNs. The survey targeted attendees of the 2016 Society of Hospital Medicine (SHM) annual conference. We recruited 174 attendees. In total, 82% were identified as hospitalist physicians and 7% as advanced practice providers; 63% practiced for >5 years and 62% supervised trainees. All reported seeing ≥1 IPN case in the past six months, with 39% seeing three to five cases and 39% seeing six or more cases. Notwithstanding, 42% were unfamiliar with the Fleischner Society guidelines. When determining the IPN follow-up, 83% used radiology report recommendations, 64% consulted national or international guidelines, and 34% contacted radiologists; 34% agreed that determining the follow-up was challenging; only 15% reported availability of automated tracking systems. In conclusion, despite frequent IPN exposure, hospitalists are frequently unaware of the Fleischner Society guidelines and rely on radiologists' recommendations. *Journal of Hospital Medicine* 2019;14:353-356. Published online first February 20, 2019. © 2019 Society of Hospital Medicine

Pulmonary nodules are common, and their identification is increasing as a result of the use of more sensitive chest imaging modalities.[1] Pulmonary nodules are defined on imaging as small (≤30 mm), well-defined lesions, completely surrounded by pulmonary parenchyma.[2] Most of the pulmonary nodules detected incidentally (ie, in asymptomatic patients outside the context of chest CT screening for lung cancer) are benign.[1] Lesions >30 mm are defined as masses and have higher risks of malignancy.[2]

Because the majority of patients will not benefit from the identification of incidental pulmonary nodules (IPNs), improving the benefits and minimizing the harms of IPN follow-up are critical. The Fleischner Society[3] published their first guideline on the management of solid IPNs in 2005,[4] which was supplemented in 2013 with specific guidance for the management of subsolid IPNs.[5] In 2017, both guidelines were combined in a single update.[6] The Fleischner Society recommendations for imaging surveillance and tissue sampling are based on nodule type (solid vs subsolid), number (single vs multiple), size, appearance, and patient risk for malignancy.

For IPNs identified in the hospital, management may be particularly challenging. For one, the provider initially ordering the chest imaging may not be the provider coordinating the patient's discharge, leading to a lack of knowledge that the IPN even exists. The hospitalist to primary care provider (PCP) handoff may also have vulnerabilities, including the lack of inclusion of the IPN follow-up in the discharge summary and the nonreceipt of the discharge summary by the PCP. Moreover, because a patient's acute medical problems often take precedence during a hospitalization, inpatients may not even be made aware of identified IPNs and the need for follow-up. Thus, the absence of standardized approaches to managing IPNs is a threat to patient safety, as well as a legal liability for providers and their institutions.

To better understand the current state of IPN management in our own institution, we examined the management of IPNs identified by chest computed tomographies (CTs) performed for inpatients on our general medicine services over a two-year period.[7] Among the 50 inpatients identified with IPNs requiring follow-up, 78% had no follow-up imaging documented. Moreover, 40% had no mention of the IPN in their hospital summary or discharge instructions.

To inform our approach to addressing this challenge, we sought to examine the practices of hospitalist physicians nationally regarding the management of IPNs, including hospitalists' familiarity with the Fleischner Society guidelines.

METHODS

We developed a 14-item survey to assess hospitalists' exposure to and management of IPNs. The survey targeted attendees of the 2016 Society of Hospital Medicine (SHM) annual conference and was available for completion on a tablet at the conference

***Corresponding Author:** Craig A. Umscheid, MD, MSCE; E-mail: craig.umscheid@gmail.com; Telephone: 215-349-8098.

Additional Supporting Information may be found in the online version of this article.

Received: June 15, 2018; **Revised**: October 2, 2018; **Accepted**: October 18, 2018

TABLE 1. **Demographics of Respondents of a National Survey of Hospitalists' Experience with Incidental Pulmonary Nodules**

Survey Item	Response Choices	n (%)
What is your role in patient care?[a]	Hospitalist Physician	138 (82%)
	Advanced Practitioner (NP, PA)	12 (7%)
	Non-Hospitalist General Internist (I care for inpatients and outpatients)	5 (3%)
	General Internal Medicine Fellow	6 (3%)
How many years have you been in practice?	<5 years	63 (37%)
	5-9 years	36 (21%)
	10-15 years	38 (22%)
	16-20 years	11 (7%)
	>20 years	22 (13%)
What is your current practice setting? (Please specify all that apply)*	University/Teaching hospital	86 (49%)
	Private hospital	21 (12%)
	Veterans Affairs hospital	9 (5%)
	Community hospital	65 (37%)
What is your specialty?[a]	Internal Medicine	147 (87%)
	Family Medicine	19 (11%)
	Pediatrics	0 (0%)
	Obstetrics - Gynecology	0 (0%)
Do you supervise medical students, residents, or fellows in clinical service?	Yes	105 (62%)
	No	65 (38%)
Which one option best describes your current practice location?[a]	Northeast	52 (31%)
	Midwest	34 (20%)
	Southeast	35 (21%)
	Southwest	14 (8%)
	West	19 (11%)
	Pacific Northwest	13 (8%)

[a]This survey item also included "Other, please specify" as a response choice.
Abbreviations; NP, nurse practitioner; PA, physician assistant.

registration desk, the SHM kiosk in the exhibit hall, and at the entrance and exit of the morning plenary sessions. Following the annual conference, the survey was e-mailed to conference attendees, with one follow-up e-mailed to nonresponders.

Analyses were descriptive and included proportions for categorical variables and median and mean values and standard deviations for continuous variables. In addition, we examined the association between survey items and a response of "yes" to the question "Are you familiar with the Fleischner Society guidelines for the management of incidental pulmonary nodules?"

Associations between familiarity with the Fleischner Society guidelines and survey items were examined using Pearson's chi-square test for categorical variables, Fisher's exact test for categorical variables with small sample sizes, the Cochran–Armitage test for trend for ordinal variables, and the t-test for continuous variables. The associations between categorical items were measured by odds ratios with 95% confidence intervals. Statistical tests were two-sided using a $P = .05$ level for statistical significance. All analyses were performed using R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria), with the R packages MASS, stats, and Publish. Institutional review board exemption was granted.

RESULTS

We received 174 responses from a total of 3,954 conference attendees. The majority were identified as hospitalist physicians, and most of them were internists (Table 1). About half practiced at a university or a teaching hospital, and more than half supervised trainees and practiced for more than five years. Respondents were involved in direct patient care (whether a teaching or a nonteaching service) for a median of 28 weeks annually (mean 31.2 weeks, standard deviation 13.5), and practice regions were geographically diverse. All respondents reported seeing at least one IPN case in the past six months, with most seeing three or more cases (Table 2). Despite this exposure, 42% were unfamiliar with the Fleischner Society guidelines. When determining the need for IPN follow-up, most of them utilized radiology report recommendations or consulted national or international guidelines, and a third spoke with radiologists directly. About a third agreed that determining the need for follow-up was challenging, with 39% citing patient factors (eg, lack of insurance, poor access to healthcare), and 30% citing scheduling of follow-up imaging. Few reported the availability of an automated tracking system at their institution, although most of them desired automatic notifications of results requiring follow-up.

TABLE 2. **Results of a National Survey of Hospitalists' Experience with Incidental Pulmonary Nodules**

Survey Item	Response Choices	n (%)
1. How many patients have you encountered with an incidental pulmonary nodule in the last 6 months?	0	0 (0%)
	1-2	39 (22%)
	3-5	67 (39%)
	6-9	43 (25%)
	>9	24 (14%)
2. In addition to your clinical judgment, what additional factor(s) do you use when determining the need for follow-up in your patient(s) with an incidental pulmonary nodule? (Please choose all that apply)[a]	A. Reviewing radiology reports and recommendations	144 (83%)
	B. Speaking to a radiologist directly about a finding for his/her advice	60 (34%)
	C. Speaking to a hospitalist colleague for his/her advice	18 (10%)
	D. Speaking to residents for their advice	4 (2%)
	E. Informally speaking to a pulmonologist for his/her advice	55 (32%)
	F. Getting a formal pulmonary consult for their advice	40 (23%)
	G. Reviewing national/international guidelines for their recommendations	111 (64%)
	H. Reviewing local guidelines for their recommendations	26 (15%)
3. When encountering an incidental pulmonary nodule, I find the process of determining the need for follow-up challenging	A. Strongly Agree	14 (8%)
	B. Agree	45 (26%)
	C. Neither Agree nor Disagree	42 (24%)
	D. Disagree	62 (36%)
	E. Strongly Disagree	10 (6%)
4. If you find follow-up challenging, what specifically made the process of determining the need for follow-up challenging? (Please choose all that apply)[a]	Limited exposure to IPNs	12 (7%)
	No recommendation for FU in radiology report	21 (12%)
	Radiologist recommendations seemed to contradict national guidelines	12 (7%)
	National guideline recommendations did not seem appropriate/applicable for my patient(s)	14 (8%)
	Difficult to schedule FU imaging for patient(s)	52 (30%)
	Patient factors	67 (39%)
5. Does your institution or practice have a system in place to track incidental pulmonary nodules?	A. Yes	26 (15%)
	B. No	94 (55%)
	C. I'm not sure	52 (30%)
6. What features would you find most useful in a system that tracks incidental pulmonary nodules? (Please choose all that apply)[a]	Automatic notification when a nodule is detected	82 (47%)
	Automatic notification when a patient cancels/misses follow-up appointments	80 (46%)
	Automatic notification when a follow-up is completed	53 (30%)
	Automatic notification of concerning results that require further follow-up/action	112 (64%)
	Automatic notifications of all results	20 (11%)
	I'm not sure	17 (10%)

[a]This survey item also included "Other, please specify" as a response choice.

Abbreviations: FU, follow-up; IPN, incidental pulmonary nodule.

Unadjusted analyses revealed that supervision of trainees and seeing more IPN cases significantly increased the odds of a survey respondent being familiar with the Fleischner Society guidelines (OR 1.96, 95% CI 1.04-3.68, *P* =.05, and OR 1.55, 95% CI 1.12-2.18, *P* =.008, respectively; Supplementary Table 1).

DISCUSSION

To our knowledge, the survey reported here is the first to examine hospitalists' knowledge of the Fleischner Society guidelines and their approach to management of IPNs. Although our data suggest that hospitalists are less familiar with the Fleischner Society recommendations than pulmonologists[8] and radiologists,[8-10] the majority of hospitalists in our study rely on radiology report recommendations to inform follow-up. This suggests that embedding the Fleischner Society recommendations into radiology reports is an effective method to promote adherence to these recommendations, which has been demonstrated in previous research.[11-13] Our study also suggests that hospitalists with more IPN exposure and those who supervise trainees are more likely to be aware of the Fleischner Society recommendations, which is similar to findings from studies examining radiologists and pulmonologists.[8-9]

Our findings highlight other opportunities for quality improvement in IPN management. Almost a quarter of hospitalists reported formally consulting pulmonologists for IPN management. Hospitalist groups wishing to improve value could partner with their radiology departments and embed the Fleischner Society recommendations into their imaging reports to potentially reduce unnecessary pulmonary consultations. Among the 59 hospitalists who agreed that IPN management was challenging, a majority

cited the scheduling process (30%) as a barrier. Redesigning the scheduling process for follow-up imaging could be a focus in local efforts to improve IPN management. Strengthening communication between hospitalists and PCPs may provide additional opportunities for improved IPN follow-up, given the centrality of PCPs to ensuring such follow-up. This might include enhancing direct communication between hospitalists and PCPs for high-risk patients, or creating systems to ensure robust indirect communication, such as the implementation of standardized discharge summaries that uniformly include essential follow-up information.

At our institution, given the large volume of high-risk patients and imaging performed, and the available resources, we have established an IPN consult team to improve follow-up for inpatients with IPNs identified by chest CTs on Medicine services. The team includes a nurse practitioner (NP) and a pulmonologist who consult by default, to notify patients of their findings and recommended follow-up, and communicate results to their PCPs. The IPN consult team also sees patients for follow-up in the ambulatory IPN clinic. This initiative has addressed the most frequently cited challenges identified in our nationwide hospitalist survey by taking the communication and follow-up out of the hospitalists' hands. To ensure identification of all IPNs by the NP, our radiology department has created a structured template for radiology attendings to document follow-up for all chest CTs reviewed based on the Fleischner Society guidelines. Compliance with use of the template by radiologists is followed monthly. After a run-in period, almost 100% of chest CT reports use the structured template, consistent with published findings from similar initiatives,[14] and 100% of patients with new IPNs identified on the inpatient Medicine services have had an IPN consult.

The major limitation of our survey study is the response rate. It is difficult to determine in what direction this could bias our results, as those with and without experience in managing IPNs may have been equally likely to complete the survey. Despite the low response rate, our sample targeted the general cohort of conference attendees (rather than specific forums such as audiences interested in quality or imaging), and the descriptive characteristics of our convenience sample align well with the overall conference attendee demographics (eg, conference attendees were 77% hospitalist attendings and 9% advanced practice providers, as compared with 82% and 7% of survey respondents, respectively), suggesting that our respondents were representative of conference attendees as a whole.

Next steps for this work at our institution include developing systems to ensure appropriate follow-up for those with IPNs identified on chest CTs performed for Medicine outpatients. In addition, our institution is collaborating on a national study to compare outcomes resulting from following the traditional Fleischner Society recommendations compared to the new 2017 recommendations, which recommend more lenient follow-up.[15]

Acknowledgments

The authors acknowledge Vivek Ahya, Eduardo Barbosa Jr., Tammy Tursi, and Anil Vachani for their leadership of the local quality improvement initiatives described in our Discussion, namely, the development and implementation of the structured templates for radiology reports and the incidental pulmonary nodule consult team.

Disclosures: Dr. Cook reports relevant financial activity outside the submitted work, including royalties from Osler Institute and grants from ACRIN and Beryl Institute. All other authors report no potential conflicts of interest relevant to this study. There was no financial support for this study.

Previous Presentations: Presented as a poster at the 2017 Society of Hospital Medicine Annual Conference, Las Vegas, NV: Wilen J, Garin M, Umscheid CA, Cook TS, Myers JS. Follow-up of incidental pulmonary nodules: a survey of hospitalists nationwide [abstract]. *Journal of Hospital Medicine*. 2017; 12 (Suppl 2). Available at: https://www.shmabstracts.com/abstract/follow-up-of-incidental-pulmonary-nodules-a-survey-of-hospitalists-nationwide/. Accessed March 18, 2018.

References

1. Ost D, Fein AM, Feinsilver SH. Clinical Practice: the solitary pulmonary nodule. *N Engl J Med*. 2003;348(25):2535-2542. doi: 10.1056/NEJMcp012290
2. Tuddenham WJ. Glossary of terms for thoracic radiology: recommendations of the Nomenclature Committee of the Fleischner Society. *AJR Am J Roentgenol*. 1984;143(3):509-517.
3. Janower ML. A brief history of the Fleischner Society. *J Thorac Imaging*. 2010;25(1):27-28. doi: 10.1097/RTI.0b013e3181cc4cee.
4. Macmahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology*. 2005;237(2):395-400. doi: 10.1148/radiol.2372041887.
5. Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. *Radiology*. 2013;266(1):304-317. doi: 10.1148/radiol.12120628.
6. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology*.2017;284(1):228-243. doi: 10.1148/radiol.2017161659.
7. Garin M, Soran C, Cook T, Ferguson M, Day S, Myers JS. Communication and follow-up of incidental lung nodules found on chest CT in a hospitalized and ambulatory patient population. *J Hosp Med*. 2014:9(2). Available at: https://www.shmabstracts.com/abstract/communication-and-follow-up-of-incidental-lung-nodules-found-on-chest-ct-in-a-hospitalized-and-ambulatory-patient-population/ Accessed June 14, 2018.
8. Mets OM, de Jong PA, Chung K, Lammers JWJ, van Ginneken B, Schaefer-Prokop CM. Fleischner recommendations for the management of subsolid pulmonary nodules: high awareness but limited conformance – a survey study. *Eur Radiol*. 2016;26:3840-3849. doi: 10.1007/s00330-016-4249-y.
9. Eisenberg RL, Bankier AA, Boiselle PM. Compliance with Fleischner Society Guidelines for management of small lung nodules: a survey of 834 radiologists. *Radiology*. 2010;255(1):218-224. doi: 10.1148/radiol.09091556.
10. Eisenberg RL. Ways to improve radiologists' adherence to Fleischner society guidelines for management of pulmonary nodules. *J Am Coll Radiol*. 2013;10(6):439-441. doi: 10.1016/j.jacr.2012.10.001.
11. Blagev DP, Lloyd JF, Conner K, et al. Follow-up of incidental pulmonary nodules and the radiology report. *J Am Coll Radiol*. 2014;11(4):378-383. doi: 10.1016/j.jacr.2013.08.003.
12. Woloshin S, Schwartz LM, Dann E, Black WC. Using radiology reports to encourage evidence-based practice in the evaluation of small, incidentally detected pulmonary nodules: a preliminary study. *Ann Am Thorac Soc*. 2014;11(2):211-214. doi: 10.1513/AnnalsATS.201307-242BC.
13. McDonald JS, Koo CW, White D, Hartman TE, Bender CE, Sykes AMG. Addition of the Fleischner Society Guidelines to chest CT examination interpretive reports improves adherence to recommended follow-up care for incidental pulmonary nodules. *Acad Radiol*. 2017;24(3):337-344. doi: 10.1016/j.acra.2016.08.026.
14. Zygmont ME, Shekhani H, Kerchberger JM, Johnson JO, Hanna TN. Point-of-Care reference materials increase practice compliance with societal guidelines for incidental findings in emergency imaging. *J Am Coll Radiol*. 2016;13(12):1494-1500. doi: 10.1016/j.jacr.2016.07.032.
15. Patient-Centered Outcomes Research Institute Portfolio of Funded Projects. Available at: https://www.pcori.org/research-results/2015/pragmatic-trial-more-versus-less-intensive-strategies-active-surveillance#/. Accessed May 22, 2018.

Managing Eating Disorders on a General Pediatrics Unit: A Centralized Video Monitoring Pilot

Kristin A Shadman, MD[1]*; Ryan J Coller, MD, MPH[1]; Windy Smith, MSN[2]; Michelle M Kelly, MD[1]; Paula Cody, MD[1]; William Taft, MD[1]; Laura Bodine, RD[2]; Daniel J Sklansky, MD[1]

[1]*Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin;* [2]*American Family Children's Hospital, University of Wisconsin Hospital and Clinics, Madison, Wisconsin.*

Adolescents with severe eating disorders require hospitalization for medical stabilization. Supervision best practices for these patients are not established. This study sought to evaluate the cost and feasibility of centralized video monitoring (CVM) supervision on a general pediatric unit of an academic quaternary care center. This was a retrospective cohort study of nursing assistant (NA) versus CVM supervision for girls 12-18 years old admitted for medical stabilization of an eating disorder between September 2013 and March 2017. There were 37 consecutive admissions (NA = 23 and CVM = 14). NA median supervision cost was more expensive than CVM ($4,104/admission vs $1,166/admission, $P <$ .001). Length of stay and days to weight gain were not statistically different. There were no occurances of family refusal of CVM, conversion from CVM to NA, technological failure, or unplanned discontinuation. Video monitoring was feasible and associated with lower supervision costs than one-to-one NA supervision. Larger samples in multiple centers are needed to confirm the safety, acceptability, and efficacy of CVM. *Journal of Hospital Medicine* 2019;14:357-360. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Hospitalizations for nutritional rehabilitation of patients with restrictive eating disorders are increasing.[1] Among primary mental health admissions at free-standing children's hospitals, eating disorders represent 5.5% of hospitalizations and are associated with the longest length of stay (LOS; mean 14.3 days) and costliest care (mean $46,130).[2] Admission is necessary to ensure initial weight restoration and monitoring for symptoms of refeeding syndrome, including electrolyte shifts and vital sign abnormalities.[3-5]

Supervision is generally considered an essential element of caring for hospitalized patients with eating disorders, who may experience difficulty adhering to nutritional treatment, perform excessive movement or exercise, or demonstrate purging or self-harming behaviors. Supervision is presumed to prevent counterproductive behaviors, facilitating weight gain and earlier discharge to psychiatric treatment. Best practices for patient supervision to address these challenges have not been established but often include meal time or continuous one-to-one supervision by nursing assistants (NAs) or other staff.[6,7] While meal supervision has been shown to decrease medical LOS, it is costly, reduces staff availability for the care of other patient care, and can be a barrier to caring for patients with eating disorders in many institutions.[8]

***Corresponding Author:** Kristin A Shadman, MD; E-mail: kshadman@pediatrics.wisc.edu; Telephone: 608-265-8561.

Received: October 20, 2018; **Revised**: January 27, 2019; **Accepted**: January 27, 2019

 DOI 10.12788/jhm.3176

Although not previously used in patients with eating disorders, centralized video monitoring (CVM) may provide an additional mode of supervision. CVM is an emerging technology consisting of real-time video streaming, without video recording, enabling tracking of patient movement, redirection of behaviors, and communication with unit nurses when necessary. CVM has been used in multiple patient safety initiatives to reduce falls, address staffing shortages, reduce costs,[9,10] supervise patients at risk for self-harm or elopement, and prevent controlled medication diversion.[10,11]

We sought to pilot a novel use of CVM to replace our institution's standard practice of continuous one-to-one nursing assistant (NA) supervision of patients admitted for medical stabilization of an eating disorder. Our objective was to evaluate the supervision cost and feasibility of CVM, using LOS and days to weight gain as balancing measures.

METHODS

Setting and Participants

This retrospective cohort study included patients 12-18 years old admitted to the pediatric hospital medicine service on a general unit of an academic quaternary care children's hospital for medical stabilization of an eating disorder between September 2013 and March 2017. Patients were identified using administrative data based on primary or secondary diagnosis of anorexia nervosa, eating disorder not other wise specified, or another specified eating disorder (ICD 9 3071, 20759, or ICD 10 f5000, 5001, f5089, f509).[12,13] This research study was considered exempt by the University of Wisconsin School of Medicine and Public Health's Institutional Review Board.

TABLE 1. **Characteristics of Patients Admitted for Eating Disorder Medical Stabilization**

	Nursing Assistant Supervision (n = 23) %	Central Video Monitoring Supervision (n = 14) %
Gender, female	100	100
Age in years, mean	14.8	15.0
Race, ethnicity		
White, non-Hispanic	92	79
White, Hispanic	4	7
Asian	0	7
Black, non-Hispanic	0	0
Black, Hispanic	0	0
Other/Declined	4	7
Insurance		
Private	80	72
Public	20	28
Suicidality	9	14

Supervision Interventions

A standard medical stabilization protocol was used for patients admitted with an eating disorder throughout the study period (Appendix). All patients received continuous one-to-one NA supervision until they reached the target calorie intake and demonstrated the ability to follow the nutritional meal protocol. Beginning July 2015, patients received continuous CVM supervision unless they expressed suicidal ideation (SI), which triggered one-to-one NA supervision until they no longer endorsed suicidality.

Centralized Video Monitoring Implementation

Institutional CVM technology was AvaSys TeleSitter Solution (AvaSure, Inc). Our institution purchased CVM devices for use in adult settings, and one was assigned for pediatric CVM. Mobile CVM video carts were deployed to patient rooms and generated live video streams, without recorded capture, which were supervised by CVM technicians. These technicians were NAs hired and trained specifically for this role; worked four-, eight-, and 12-hour shifts; and observed up to eight camera feeds on a single monitor in a centralized room. Patients and family members could refuse CVM, which would trigger one-to-one NA supervision. Patients were not observed by CVM while in the restroom; staff were notified by either the patient or technician, and one-to-one supervision was provided. CVM had two-way audio communication, which allowed technicians to redirect patients verbally. Technicians could contact nursing staff directly by phone when additional intervention was needed.

Supervision Costs

NA supervision costs were estimated at $19/hour, based upon institutional human resources average NA salaries at that time. No additional mealtime supervision was included, as in-person supervision was already occurring.

CVM supervision costs were defined as the sum of the device cost plus CVM technician costs and two hours of one-to-one NA mealtime supervision per day. The CVM device cost was estimated at $2.10/hour, assuming a 10-year machine life expectancy (single unit cost $82,893 in 2015, 3,944 hours of use in fiscal year of 2018). CVM technician costs were $19/hour, based upon institutional human resources average CVM technician salaries at that time. Because technicians monitored an average of six patients simultaneously during this study, one-sixth of a CVM technician's salary (ie, $3.17/hour) was used for each hour of CVM monitoring. Patients with mixed (NA and CVM) supervision were analyzed with those having CVM supervision. These patients' costs were the sum of their NA supervision costs plus their CVM supervision costs.

Data Collection

Descriptive variables including age, gender, race/ethnicity, insurance, and LOS were collected from administrative data. The duration and type of supervision for all patients were collected from daily staffing logs. The eating disorder protocol standardized the process of obtaining daily weights (Appendix). Days to weight gain following admission were defined as the total number of days from admission to the first day of weight gain that was followed by another day of weight gain or maintaining the same weight. CVM acceptability and feasibility were assessed by family refusal of CVM, conversion from CVM to NA, technological failure, complaints, and unplanned discontinuation, which were prospectively documented by the unit nurse manager.

Data Analysis

Patient and hospitalization characteristics were summarized. A sample size of at least 14 in each group was estimated as necessary to detect a 50% reduction in supervision cost between the groups using alpha = 0.05, a power of 80%, a mean cost of $4,400 in the NA group, and a standard deviation of $1,600. Wilcoxon rank-sum tests were used to assess differences in median supervision cost between NA and CVM use. Differences in mean LOS and days to weight gain between NA and CVM use were assessed with *t*-tests because these data were normally distributed.

RESULTS

Patient Characteristics and Supervision Costs

The study included 37 consecutive admissions (NA = 23 and CVM = 14) with 35 unique patients. Patients were female, primarily non-Hispanic White, and privately insured (Table 1). Median supervision cost for the NA was statistically significantly more expensive at $4,104/admission versus $1,166/admission for CVM ($P < .001$, Table 2).

Balancing Measures, Acceptability, and Feasibility

Mean LOS was 11.7 days for NA and 9.8 days for CVM ($P = .27$; Table 2). The mean number of days to weight gain was 3.1 and 3.6 days, respectively ($P = .28$). No patients converted from CVM to NA supervision. One patient with SI converted

TABLE 2. **Supervision Costs and Balancing Measures**

	Nursing Assistant Supervision (n = 23)	Centralized Video Monitoring Supervision (n = 14)	*P* Value	Differences (95% CI)
Supervision cost, median, $ (USD)	4,104	1,166	<.001	2,938 (1,998-3,942)
Cost attributed to nursing assistant supervision, (%)	100	39.2	<.001	NA
Monitoring time, median, hours	216	182	.29	34 (–31.9-103)
Length of stay, mean, days	11.7	9.8	0.27	1.9 (–1.5-0.4)
Days to weight gain, mean	3.1	3.6	0.28	–0.5 (–1.4-5.3)

to CVM after SI resolved and two patients required ongoing NA supervision due to continued SI. There were no reported refusals, technology failures, or unplanned discontinuations of CVM. One patient/family reported excessive CVM redirection of behavior.

DISCUSSION

This is the first description of CVM use in adolescent patients or patients with eating disorders. Our results suggest that CVM appears feasible and less costly in this population than one-to-one NA supervision, without statistically significant differences in LOS or time to weight gain. Patients with CVM with any NA supervision (except mealtime alone) were analyzed in the CVM group; therefore, this study may underestimate cost savings from CVM supervision. This innovative use of CVM may represent an opportunity for hospitals to repurpose monitoring technology for more efficient supervision of patients with eating disorders.

This pediatric pilot study adds to the growing body of literature in adult patients suggesting CVM supervision may be a feasible inpatient cost-reduction strategy.[9,10] One single-center study demonstrated that the use of CVM with adult inpatients led to fewer unsafe behaviors, eg, patient removal of intravenous catheters and oxygen therapy. Personnel savings exceeded the original investment cost of the monitor within one fiscal quarter.[9] Results of another study suggest that CVM use with hospitalized adults who required supervision to prevent falls was associated with improved patient and family satisfaction.[14] In the absence of a gold standard for supervision of patients hospitalized with eating disorders, CVM technology is a tool that may balance cost, care quality, and patient experience. Given the upfront investment in CVM units, this technology may be most appropriate for institutions already using CVM for other inpatient indications.

Although our institutional cost of CVM use was similar to that reported by other institutions,[11,15] the single-center design of this pilot study limits the generalizability of our findings. Unadjusted results of this observational study may be confounded by indication bias. As this was a pilot study, it was powered to detect a clinically significant difference in cost between NA and CVM supervision. While statistically significant differences were not seen in LOS or weight gain, this pilot study was not powered to detect potential differences or to adjust for all potential confounders (eg, other mental health conditions or comorbidities, eating disorder type, previous hospitalizations). Future studies should include these considerations in estimating sample sizes. The ability to conduct a robust cost-effectiveness analysis was also limited by cost data availability and reliance on staffing assumptions to calculate supervision costs. However, these findings will be important for valid effect size estimates for future interventional studies that rigorously evaluate CVM effectiveness and safety. Patients and families were not formally surveyed about their experiences with CVM, and the patient and family experience is another important outcome to consider in future studies.

CONCLUSION

The results of this pilot study suggest that supervision costs for patients admitted for medical stabilization of eating disorders were statistically significantly lower with CVM when compared with one-to-one NA supervision, without a change in hospitalization LOS or time to weight gain. These findings are particularly important as hospitals seek opportunities to reduce costs while providing safe and effective care. Future efforts should focus on evaluating clinical outcomes and patient experiences with this technology and strategies to maximize efficiency to offset the initial device cost.

Disclosures: The authors have no financial relationships relevant to this article to disclose. The authors have no conflicts of interest relevant to this article to disclose.

References

1. Zhao Y, Encinosa W. An update on hospitalizations for eating disorders, 1999 to 2009: statistical brief #120. In: Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville, MD: Agency for Healthcare Research and Quality (US); 2006.
2. Bardach NS, Coker TR, Zima BT, et al. Common and costly hospitalizations

for pediatric mental health disorders. *Pediatrics*. 2014;133(4):602-609. doi: 10.1542/peds.2013-3165.
3. Society for Adolescent H, Medicine, Golden NH, et al. Position Paper of the Society for Adolescent Health and Medicine: medical management of restrictive eating disorders in adolescents and young adults. *J Adolesc Health*. 2015;56(1):121-125. doi: 10.1016/j.jadohealth.2014.10.259.
4. Katzman DK. Medical complications in adolescents with anorexia nervosa: a review of the literature. *Int J Eat Disord*. 2005;37(S1):S52-S59; discussion S87-S59. doi: 10.1002/eat.20118.
5. Strandjord SE, Sieke EH, Richmond M, Khadilkar A, Rome ES. Medical stabilization of adolescents with nutritional insufficiency: a clinical care path. *Eat Weight Disord*. 2016;21(3):403-410. doi: 10.1007/s40519-015-0245-5.
6. Kells M, Davidson K, Hitchko L, O'Neil K, Schubert-Bob P, McCabe M. Examining supervised meals in patients with restrictive eating disorders. *Appl Nurs Res*. 2013;26(2):76-79. doi: 10.1016/j.apnr.2012.06.003.
7. Leclerc A, Turrini T, Sherwood K, Katzman DK. Evaluation of a nutrition rehabilitation protocol in hospitalized adolescents with restrictive eating disorders. *J Adolesc Health*. 2013;53(5):585-589. doi: 10.1016/j.jadohealth.2013.06.001.
8. Kells M, Schubert-Bob P, Nagle K, et al. Meal supervision during medical hospitalization for eating disorders. Clin Nurs Res. 2017;26(4):525-537. doi: 10.1177/1054773816637598.
9. Jeffers S, Searcey P, Boyle K, et al. Centralized video monitoring for patient safety: a Denver Health Lean journey. *Nurs Econ*. 2013;31(6):298-306.
10. Sand-Jecklin K, Johnson JR, Tylka S. Protecting patient safety: can video monitoring prevent falls in high-risk patient populations? *J Nurs Care Qual*. 2016;31(2):131-138. doi: 10.1097/NCQ.0000000000000163.
11. Burtson PL, Vento L. Sitter reduction through mobile video monitoring: a nurse-driven sitter protocol and administrative oversight. *J Nurs Adm*. 2015;45(7-8):363-369. doi: 10.1097/NNA.0000000000000216.
12. Prevention CfDCa. ICD-9-CM Guidelines, 9th ed. https://www.cdc.gov/nchs/data/icd/icd9cm_guidelines_2011.pdf. Accessed April 11, 2018.
13. Prevention CfDca. IDC-9-CM Code Conversion Table. https://www.cdc.gov/nchs/data/icd/icd-9-cm_fy14_cnvtbl_final.pdf. Accessed April 11, 2018.
14. Cournan M, Fusco-Gessick B, Wright L. Improving patient safety through video monitoring. *Rehabil Nurs*. 2016. doi: 10.1002/rnj.308.
15. Rochefort CM, Ward L, Ritchie JA, Girard N, Tamblyn RM. Patient and nurse staffing characteristics associated with high sitter use costs. *J Adv Nurs*. 2012;68(8):1758-1767. doi: 10.1111/j.1365-2648.2011.05864.x.

Critical Errors in Inhaler Technique among Children Hospitalized with Asthma

Waheeda Samady, MD, MSCI[1,2]*; Victoria A Rodriguez, MD[1,2]; Ruchi Gupta, MD, MPH[1,2]; Hannah Palac, MS[2]; Marina Karamanis, BS[3]; Valerie G Press, MD, MPH[4]

[1]*Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois;* [2]*Northwestern University Feinberg School of Medicine, Chicago, Illinois;* [3]*Midwestern University, Downers Grove, Illinois;* [4]*University of Chicago, Chicago, Illinois.*

Past studies have not evaluated inhaler use in hospitalized children with asthma. The objectives of this study were to evaluate inhaler technique in hospitalized pediatric patients with asthma and identify risk factors for improper use. We conducted a prospective cross-sectional study in a tertiary children's hospital for children 2-16 years of age admitted for an asthma exacerbation, and inhaler technique demonstrations were analyzed. Of 113 participants enrolled, 55% had uncontrolled asthma, and 42% missed a critical step in inhaler technique. More patients missed a critical step when they used a spacer with mouthpiece instead of a spacer with mask (75% [51%-90%] vs 36% [27%-46%]) and were older (7.8 [6.7-8.9] vs 5.8 [5.1-6.5] years). Patients using the spacer with mouthpiece remained significantly more likely to miss a critical step when adjusting for other clinical covariates (odds ratio 6.95 [1.71-28.23], $P = .007$). Hospital-based education may provide teachable moments to address poor proficiency, especially for older children using a mouthpiece. *Journal of Hospital Medicine* 2018;14:361-365. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Many studies have shown that improved control can be achieved for most children with asthma if inhaled medications are taken correctly and adequately.[1-3] Drug delivery studies have shown that bioavailability of medication with a pressurized metered-dose inhaler (MDI) improves from 34% to 83% with the addition of spacer devices. This difference is largely due to the decrease in oropharyngeal deposition,[1,4,5] and therefore, the use of a spacer with proper technique has been recommended in all pediatric patients.[1,6]

Poor inhaler technique is common among children.[1,7] Previous studies of children with asthma have evaluated inhaler technique, primarily in the outpatient and community settings, and reported variable rates of error (from 45% to >90%).[8,9] No studies have evaluated children hospitalized with asthma. As these children represent a particularly high-risk group for morbidity and mortality,[10,11] the objectives of this study were to assess errors in inhaler technique in hospitalized asthmatic children and identify risk factors for improper use.

METHODS

As part of a larger interventional study, we conducted a prospective cross-sectional study at a tertiary urban children's hospital. We enrolled a convenience sample of children aged 2-16 years admitted to the inpatient ward with an asthma exacerbation Monday-Friday from 8 AM to 6 PM. Participants were required to have a diagnosis of asthma (an established diagnosis by their primary care provider or meets the National Heart, Lung, and Blood Institute [NHLBI] criteria[1]), have a consenting adult available, and speak English. Patients were excluded if they had a codiagnosis of an additional respiratory disease (ie, pneumonia), cardiac disease, or sickle cell anemia. The Institutional Review Board approved this study.

We asked caregivers, or children >10 years old if they independently use their inhaler, to demonstrate their typical home inhaler technique using a spacer with mask (SM), spacer with mouthpiece (SMP), or no spacer (per their usual home practice). Inhaler technique was scored using a previously validated asthma checklist (Table 1).[12] Certain steps in the checklist were identified as critical: (Step 1) removing the cap, (Step 3) attaching to a spacer, (Step 7) taking six breaths (SM), and (Step 9) holding breath for five seconds (SMP). Caregivers only were also asked to complete questionnaires assessing their literacy (Brief Health Literacy Screen [BHLS]), confidence (Parent Asthma Management Self-Efficacy scale [PAMSE]), and any barriers to managing their child's asthma (Barriers to Asthma Care). Demographic and medical history information was extracted from the medical chart.

Inhaler technique was evaluated in two ways by comparing: (1) patients who missed more than one critical step with those who missed zero critical steps and (2) patients with an asthma checklist score <7 versus ≥7. While there is a lot of variability in how inhaler technique has been measured in past studies, these two markers (75% of steps and critical errors) were the most common.[8]

We assessed a number of variables to evaluate their association with improper inhaler technique. For categorical vari-

***Corresponding Author:** Waheeda Samady, MD; E-mail: wsamady@luriechildrens.org; Telephone: 312-227-4000.

Additional Supporting Information may be found in the online version of this article.

Received: November 30, 2018; **Revised**: February 20, 2019; **Accepted**: February 25, 2019

 DOI 10.12788/jhm.3195

TABLE 1. Summary of Asthma Checklist and Missed Asthma Checklist Steps by Method (N = 113)

Step	N Missed	%	95% CI	
			Lower CL (%)	Upper CL (%)
Mask (n = 97)				
Mask 1: Removes cap of inhaler and spacer	10	10.3	4.2	16.5
Mask 2: Shakes inhaler	42	43.3	33.3	53.3
Mask 3: Attaches inhaler to spacer	12	12.4	5.7	19.0
Mask 4: Applies mask over nose and mouth	16	16.5	8.9	24.0
Mask 5: Holds mask firmly to make a seal on face	51	52.6	42.5	62.7
Mask 6: Presses down on canister one time	13	13.4	6.5	20.3
Mask 7: Breathes in an out for six breaths	33	34	24.4	43.6
Mask 8: Removes mask before breathing normally	31	32	22.5	41.4
Mask 9: Breathes normally for 30-60 seconds before repeat	70	72.2	63.1	81.2
Mask 10: Repeats Steps 2-9 for second puff	26	26.8	17.8	35.8
Mouthpiece (n = 16)				
Mouthpiece 1: Removes cap of inhaler and spacer	2	12.5	–5.7	30.7
Mouthpiece 2: Shakes inhaler	7	43.8	16.5	71.1
Mouthpiece 3: Attaches inhaler to spacer	8	50	22.5	77.5
Mouthpiece 4: Breathes out fully	15	93.8	80.4	107.0
Mouthpiece 5: Breathes out away from MDI/spacer	15	93.8	80.4	107.0
Mouthpiece 6: Closes lips around mouthpiece	4	25	1.2	48.8
Mouthpiece 7: Presses down on canister one time	3	18.8	–2.7	40.2
Mouthpiece 8: Breathes in slowly (no whistle)	11	68.8	43.2	94.3
Mouthpiece 9: Holds breath for 5 seconds	7	43.8	16.5	71.0
Mouthpiece 10: Removes spacer from mouth before breathing normally	5	31.3	5.7	56.8
Mouthpiece 11: Breathes normally for 30-60 seconds before repeat	11	68.8	43.2	94.3
Mouthpiece 12: Repeats Steps 2-11 for second puff	6	37.5	10.9	64.1

Items in bold represent critical steps. The darker the shading, the higher the percentage of patients who missed the checklist step.
Abbreviations: CI, confidence interval; CL, confidence limit; MDI, metered-dose inhaler.

ables, the association with each outcome was evaluated using relative risks (RRs). Bivariate *P*-values were calculated using chi-square or Fisher's exact tests, as appropriate. Continuous variables were assessed for associations with each outcome using two-sample *t*-tests. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression analyses. Using a model entry criterion of $P < .10$ on univariate tests, variables were entered into a multivariable logistic regression model for each outcome. Full models with all eligible covariates and reduced models selected via a manual backward selection process were evaluated. Two-sided *P*-values <.05 were considered statistically significant.

RESULTS

Participants

From October 2016 to June 2017, 380 participants were assessed for participation; 215 were excluded for not having a parent available (59%), not speaking English (27%), not having an asthma diagnosis (ie, viral wheezing; 14%), and 52 (14%) declined to participate. Therefore, a total of 113 participants were enrolled, with demonstrations provided by 100 caregivers and 13 children. The mean age of the patients overall was 6.6 ± 3.4 years and over half (55%) of the participants had uncontrolled asthma (NHLBI criteria[1]).

TABLE 2. Demographic and Medical History Characteristics by Missed Critical Step[a]

	SM Missed Critical Step (n = 97)			SMP Missed Critical Step (n = 16)		
	No	Yes	RR (95% CI)	No	Yes	RR (95% CI)
	n = 62	n = 35		n = 4	n = 12	
Patient age, mean ± SD	5.29 ± 2.16	6.31 ± 2.84	N/A	13.50 ± 2.38	12.17 ± 2.51	N/A
Sex						
Female	24 (61.5%)	15 (38.5%)	1.12 (0.65-1.9)	2 (25%)	6 (75%)	1.00 (0.57-1.76)
Male	38 (65.5%)	20 (34.5%)	Ref	2 (25%)	6 (75%)	Ref
Race (N = 112)						
White/Caucasian	9 (52.9%)	8 (47.1%)	Ref	1 (50%)	1 (50%)	Ref
African American	24 (60%)	16 (40%)	1.18 (0.63-2.21)	3 (33.3%)	6 (66.7%)	0.75 (0.17-3.23)
Asian	3 (100%)	0 (0%)	N/A	0 (0%)	0 (0%)	N/A
Mixed	0 (0%)	2 (100%)	0.47 (0.28-0.78)	0 (0%)	1 (100%)	0.50 (0.13-2.00)
Other	24 (77.4%)	7 (22.6%)	2.08 (0.91-4.75)	0 (0%)	4 (100%)	0.50 (0.13-2.00)
Did not report	1 (33.3%)	2 (66.7%)	N/A	0 (0%)	0 (0%)	N/A
Ethnicity						
Hispanic	28 (77.8%)	8 (22.2%)	0.52 (0.26-1.02)	0 (0%)	5 (100%)	1.57 (1.01-2.46)
Non-Hispanic	33 (56.9%)	25 (43.1%)	Ref	4 (36.4%)	7 (63.6%)	Ref
Insurance type	44 (64.7%)	24 (35.3%)	Ref	3 (23.1%)	10 (76.9%)	Ref
Public	1 (100%)	0 (0%)	N/A	0 (0%)	0 (0%)	N/A
Government	16 (59.3%)	11 (40.7%)	0.87 (0.5-1.51)	1 (33.3%)	2 (66.7%)	1.15 (0.49-2.71)
Private						
Asthma control (N = 111)						
Controlled	27 (60%)	18 (40%)	1.33 (0.77-2.32)	2 (40%)	3 (60%)	0.73 (0.34-1.58)
Uncontrolled	35 (70%)	15 (30%)	Ref	2 (18.2%)	9 (81.8%)	Ref
Previous inpatient asthma education (N = 112)						
No	16 (48.5%)	17 (51.5%)	Ref	1 (20%)	4 (80%)	Ref
Yes	46 (71.9%)	18 (28.1%)	0.55 (0.33-0.91)	3 (30%)	7 (70%)	0.88 (0.48-1.59)
Previous asthma PICU admission (N = 107)						
No	44 (59.5%)	30 (40.5%)	Ref	3 (25%)	9 (75%)	Ref
Yes	16 (94.1%)	1 (5.88%)	0.15 (0.02-0.99)	1 (25%)	3 (75%)	1.00 (0.52-1.92)
Controller medication						
No	22 (52.4%)	20 (47.6%)	Ref	3 (42.86%)	4 (57.1%)	Ref
Yes	40 (72.7%)	15 (27.3%)	0.57 (0.34-0.98)	1 (11.11%)	8 (88.9%)	1.56 (0.79-3.08)
Family history of asthma						
No	15 (48.4%)	16 (51.6%)	1.79 (1.08-2.99)	1 (16.67%)	5 (83.3%)	1.19 (0.69-2.04)
Yes in parent/siblings	29 (64.4%)	16 (35.6%)	0.97 (0.57-1.66)	2 (22.22%)	7 (77.8%)	1.09 (0.61-1.95)
Yes in extended family	20 (83.3%)	4 (16.67%)	0.39 (0.15-1.00)	1 (100%)	0 (0%)	N/A
Asthma hospitalizations past 12 months (N = 112)						
0-1	36 (57.1%)	27 (42.9%)	1.77 (0.91-3.44)	2 (18.18%)	9 (81.8%)	1.36 (0.63-2.94)
≥2	25 (75.8%)	8 (24.24%)	Ref	2 (40%)	3 (60%)	Ref

[a]Compared for asthma checklist score <7 versus ≥7, no statistically significant difference was found except the women in the mask group were more likely to have score <7 (46.2% vs 24.1% RR 1.91 [1.08-3.38]).

Abbreviations: CI, confidence interval; SD, standard deviation; PICU, pediatric intensive care unit; RR, relative risk; SM, spacer with mask; SMP, spacer with mouthpiece.

Errors in Inhaler Technique

The mean asthma checklist score was 6.7 (maximum score of 10 for SM and 12 for SMP). A third (35%) scored <7 on the asthma checklist and 42% of participants missed at least one critical step. Overall, children who missed a critical step were significantly older (7.8 [6.7-8.9] vs 5.8 [5.1-6.5] years; *P* = .002). More participants missed a critical step with the SMP than the SM (75% [51%-90%] vs 36% [27%-46%]; *P* = .003), and this was the most prominent factor for missing a critical step in the adjusted regression analysis (OR 6.95 [1.71-28.23], *P* = .007). The most commonly missed steps were breathing normally for 30 seconds for SM, and for SMP, it was breathing out fully and

breathing away from the spacer (Table 1). Twenty participants (18%) did not use a spacer device; these patients were older than those who did use a spacer (mean age 8.5 [6.7-10.4] vs 6.2 [5.6-6.9] years; $P = .005$); however, no other significant differences were identified.

Demographic, Medical History, and Socioeconomic Characteristics

Overall, race, ethnicity, and insurance status did not vary significantly based on asthma checklist score ≥7 or missing a critical step. Patients in the SM group who had received inpatient asthma education during a previous admission, had a history of pediatric intensive care unit (PICU) admission, and had been prescribed a daily controller were less likely to miss a critical step (Table 2). Parental education level varied, with 33% having a high school degree or less, but was not associated with asthma checklist score or missing critical steps. Parental BHLS and parental confidence (PAMSE) were not significantly associated with inhaler proficiency. However, transportation-related barriers were more common in patients with checklist scores <7 and more missed critical steps (OR 1.62 [1.06-2.46]; $P = .02$).

DISCUSSION

Nearly half of the participants in this study missed at least one critical step in inhaler use. In addition, 18% did not use a spacer when demonstrating their inhaler technique. Despite robust studies demonstrating how asthma education can improve both asthma skills and clinical outcomes,[13] our study demonstrates that a large gap remains in proper inhaler technique among asthmatic patients presenting for inpatient care. Specifically, in the mouthpiece group, steps related to breathing technique were the most commonly missed. Our results also show that inhaler technique errors were most prominent in the adolescent population, possibly coinciding with the process of transitioning to a mouthpiece and more independence in medication administration. Adolescents may be a high-impact population on which to focus inpatient asthma education. Additionally, we found that a previous PICU admission and previous inpatient asthma education were associated with missing fewer critical steps in inhaler technique. This finding is consistent with those of another study that evaluated inhaler technique in the emergency department and found that previous hospitalization for asthma was inversely related to improper inhaler use (RR 0.55, 95% CI 0.36-0.84).[14] This supports that when provided, inpatient education can increase inhaler administration skills.

Previous studies conducted in the outpatient setting have demonstrated variable rates of inhaler skill, from 0% to approximately 89% of children performing all steps of inhalation correctly.[8] This wide range may be related to variations in the number and definition of critical steps between the different studies. In our study, we highlighted removing the cap, attaching a spacer, and adequate breathing technique as critical steps, because failure to complete them would significantly reduce lung deposition of medication. While past studies did evaluate both MDIs and discuss the devices, our study is the first to report difference in problems with technique between SM and SMP. As asthma educational interventions are developed and/or implemented, it is important to stress that different steps in inhaler technique are being missed in those using a mask versus mouthpiece.

The limitations of this study include that it was at a single center with a primarily urban and English-speaking population; however, this study population reflects the racial diversity of pediatric asthma patients. Further studies may explore the reproducibility of these findings at multiple centers and with non-English-speaking families. This study included younger patients than in some previous publications investigating asthma; however, all patients met the criteria for asthma diagnosis and this age range is reflective of patients presenting for inpatient asthma care. Furthermore, because of our daytime research hours, 59% of patients were excluded because a primary caregiver was not available. It is possible that these families have decreased access to inpatient asthma educators as well and may be another target group for future studies. Finally, a large proportion of parents had a college education or greater in our sample. However, there was no association within our analysis between parental education level and inhaler proficiency.

The findings from this study indicate that continued efforts are needed to establish that inhaler technique is adequate for all families regardless of their educational status or socioeconomic background, especially for adolescents and in the setting of poor asthma control. Furthermore, our findings support that inhaler technique education may be beneficial in the inpatient setting and that acute care settings can provide a valuable "teachable moment."[14,15]

CONCLUSION

Errors in inhaler technique are prevalent in pediatric inpatients with asthma, primarily those using a mouthpiece device. Educational efforts in both inpatient and outpatient settings have the potential to improve drug delivery and therefore asthma control. Inpatient hospitalization may serve as a platform for further studies to investigate innovative educational interventions.

Acknowledgments

The authors thank Tina Carter for her assistance in the recruitment and data collection and Ashley Hull and Susannah Butters for training the study staff on the use of the asthma checklist.

Disclosures: Dr. Gupta receives research grant support from the National Institutes of Health and the United Healthcare Group. Dr. Gupta serves as a consultant for DBV Technology, Aimmune Therapeutics, Kaleo & BEFORE Brands. Dr. Gupta has received lecture fees/honorariums from the Allergy Asthma Network & the American College of Asthma, Allergy & Immunology. Dr. Press reports research support from the Chicago Center for Diabetes Translation Research Pilot and Feasibility Grant, the Bucksbaum Institute for Clinical Excellence Pilot Grant Program, the Academy of Distinguished Medical Educators, the Develop-

ment of Novel Hospital-initiated Care Bundle in Adults Hospitalized for Acute Asthma: the 41st Multicenter Airway Research Collaboration (MARC-41) Study, UCM's Innovation Grant Program, the University of Chicago-Chapin Hall Join Research Fund, the NIH/NHLBI Loan Repayment Program, 1 K23 HL118151 01, NIH NLBHI R03 (RFA-HL-18-025), the George and Carol Abramson Pilot Awards, the COPD Foundation Green Shoots Grant, the University of Chicago Women's Board Grant, NIH NHLBI UG1 (RFA-HL-17-009), and the CTSA Pilot Award, outside the submitted work. These disclosures have been reported to Dr. Press' institutional IRB board. Additionally, a management plan is on file that details how to address conflicts such as these which are sources of research support but do not directly support the work at hand. The remaining authors have no conflicts of interest relevant to the article to disclose.

Funding: This study was funded by internal grants from Ann and Robert H. Lurie Children's Hospital of Chicago. Dr. Press was funded by a K23HL118151.

References

1. *Expert Panel Report 3: guidelines for the diagnosis and management of asthma: full report*. Washington, DC: US Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute; 2007.
2. Hekking PP, Wener RR, Amelink M, Zwinderman AH, Bouvy ML, Bel EH. The prevalence of severe refractory asthma. *J Allergy Clin Immunol*. 2015;135(4):896-902. doi: 10.1016/j.jaci.2014.08.042.
3. Peters SP, Ferguson G, Deniz Y, Reisner C. Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. *Respir Med*. 2006;100(7):1139-1151. doi: 10.1016/j.rmed.2006.03.031.
4. Dickens GR, Wermeling DP, Matheny CJ, et al. Pharmacokinetics of flunisolide administered via metered dose inhaler with and without a spacer device and following oral administration. *Ann Allergy Asthma Immunol*. 2000;84(5):528-532. doi: 10.1016/S1081-1206(10)62517-3.
5. Nikander K, Nicholls C, Denyer J, Pritchard J. The evolution of spacers and valved holding chambers. *J Aerosol Med Pulm Drug Deliv*. 2014;27(1):S4-S23. doi: 10.1089/jamp.2013.1076.
6. Rubin BK, Fink JB. The delivery of inhaled medication to the young child. *Pediatr Clin North Am*. 2003;50(3):717-731. doi:10.1016/S0031-3955(03)00049-X.
7. Roland NJ, Bhalla RK, Earis J. The local side effects of inhaled corticosteroids: current understanding and review of the literature. *Chest*. 2004;126(1):213-219. doi: 10.1378/chest.126.1.213.
8. Gillette C, Rockich-Winston N, Kuhn JA, Flesher S, Shepherd M. Inhaler technique in children with asthma: a systematic review. *Acad Pediatr*. 2016;16(7):605-615. doi: 10.1016/j.acap.2016.04.006.
9. Pappalardo AA, Karavolos K, Martin MA. What really happens in the home: the medication environment of urban, minority youth. *J Allergy Clin Immunol Pract*. 2017;5(3):764-770. doi: 10.1016/j.jaip.2016.09.046.
10. Crane J, Pearce N, Burgess C, Woodman K, Robson B, Beasley R. Markers of risk of asthma death or readmission in the 12 months following a hospital admission for asthma. *Int J Epidemiol*. 1992;21(4):737-744. doi: 10.1093/ije/21.4.737.
11. Turner MO, Noertjojo K, Vedal S, Bai T, Crump S, Fitzgerald JM. Risk factors for near-fatal asthma. A case-control study in hospitalized patients with asthma. *Am J Respir Crit Care Med*. 1998;157(6 Pt 1):1804-1809. doi: 10.1164/ajrccm.157.6.9708092.
12. Press VG, Arora VM, Shah LM, et al. Misuse of respiratory inhalers in hospitalized patients with asthma or COPD. *J Gen Intern Med*. 2011;26(6):635-642. doi: 10.1007/s11606-010-1624-2.
13. Guevara JP, Wolf FM, Grum CM, Clark NM. Effects of educational interventions for self management of asthma in children and adolescents: systematic review and meta-analysis. *BMJ*. 2003;326(7402):1308-1309. doi: 10.1136/bmj.326.7402.1308.
14. Scarfone RJ, Capraro GA, Zorc JJ, Zhao H. Demonstrated use of metered-dose inhalers and peak flow meters by children and adolescents with acute asthma exacerbations. *Arch Pediatr Adolesc Med*. 2002;156(4):378-383. doi: 10.1001/archpedi.156.4.378.
15. Sockrider MM, Abramson S, Brooks E, et al. Delivering tailored asthma family education in a pediatric emergency department setting: a pilot study. *Pediatrics*. 2006;117(4 Pt 2):S135-144. doi: 10.1542/peds.2005-2000K.

TIME'S UP for Hospital Medicine

Dara Kass, MD[1]*; Rhonda Graves Acholonu, MD[2]

[1]Department of Emergency Medicine, Columbia University Vagelos School of Medicine, New York, New York; [2]Department of Pediatrics, Division of Hospital Medicine, Albert Einstein College of Medicine, Bronx, New York.

"If it is true that the full humanity of women is not our culture, then we can and must make it our culture."

—Chimamanda Ngozi Adichie

A young boy is on the way home from soccer when a driver hits his car head-on. His father dies immediately, but the boy survives. The boy is transported to the hospital and immediately rushed into the OR. The surgeon takes one look at him and says, "I can't operate on this patient. He's my son!" The riddle asks: If the father is dead, who is the surgeon?

Struggling to realize that the surgeon is a mom highlights the depth of gender bias in medicine. Gender bias leads to inequities which are magnified when compounded with differences in race, ethnicity, sexual orientation, gender identity and/or socioeconomic status. The recent National Academies report described the toll of gender inequities, including sexual harassment, and their impact on women in medicine.[1] But like this riddle, the focus was directed towards those at the top of the hierarchy: physicians. It is undeniable that women physicians suffer the effects of inequities, but why exclude other women in healthcare? For example, over 90% of nurses are female, yet male nurses make higher salaries with lower degrees.[2] If we only focus on physicians, we risk ignoring a problem faced by the entirety of our workforce.

Healthcare is a team sport. The practice of hospital medicine is a prime example of how each team member brings critical value. One would never be able to run an effective code without excellent nursing or successfully intubate a patient without a skilled respiratory therapist. Yet, when it comes to conversations about gender bias and sexual harassment, we rarely work together. The work of equity in healthcare must therefore become more like a lattice than a ladder, with many of us advocating for or with one another.

As hospital medicine has grown, hospitalists have become genuine agents of change. Therefore, this change too, must begin with hospitalists. As leaders in healthcare, we must advocate for equity for all, from the lab technician to the CEO. We must engage and respond when direct care workers (often minorities), face gender or racial bias. In short, if we see something, we must say something.

To create a culture of inclusivity and intersectionality in healthcare, we suggest the following:

- **Unite healthcare workers across fields.** View your fellow healthcare worker as a team member, not as a subordinate or ancillary staff. Ask them what their experiences regarding inequity have been. See things from their perspective.
- **Be a champion for those affected by harassment and inequity**. Offer direct support to anyone affected by harassment or inequity. Accompany them to human resources or use your influence to advocate for gender-based salary audits.
- **Raise awareness and knowledge.** Know the resources in your institution and share them with others. Encourage teams to discuss the impact of microaggressions and implicit bias together as opposed to in role-specific groups. Use communication to lend allyship and support. If you see microaggressions based on gender or race, inquire by asking "I'm curious...why would you say that?" or share the impact a statement has on you by noting "The comment doesn't just affect one person, it affects all of us."

People create culture. Meaningful cultural change must be inclusive and intersectional. Historically, movements focused on equity have failed to be inclusive, leading to certain groups feeling marginalized. The time has come to affect change in healthcare across all differences. Whether in the role of physician, nurse, advanced practice provider, or paramedical staff, it's time to stand together and say: "time is up."

Disclosures: Dr Kass and Dr. Acholonu are founding members of TIME'S UP Healthcare

References

1. National Academies of Sciences, Engineering, and Medicine. Sexual harassment of women: climate, culture, and consequences in academic sciences, engineering, and medicine. Washington, DC: National Academies Press, August 2018. (https://www.nap.edu/catalog/24994/sexual-harassment-of-women-climate-culture-and-consequences-in-academic). Accessed March 1, 2019.
2. 2018 Nurse.com. Nursing Salary Research Report. http://mediakit.nurse.com/wp-content/uploads/2018/06/2018-Nurse.com-Salary-Research-Report.pdf. Accessed March 1, 2019..

***Corresponding Author:** Dara Kass, MD; dak2169@cumc.columbia.edu

Received: March 29, 2019; **Accepted**: March 31, 2019

Pharmacologic Management of Malignant Bowel Obstruction: When Surgery Is Not an Option

Kevin Hsu, MD[1]; Eric Prommer, MD, FAAHPM, HMDC[2,3]; Mary C Murphy, MD[2,3], Azadeh Lankarani-Fard, MD[4,5]*

[1]Department of Internal Medicine, Cedars-Sinai Medical Center, Los Angeles, California; [2] Palliative Care Division, VA Greater Los Angeles Healthcare System, Los Angeles, California; [3]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California. [4]Hospitalist Division, VA Greater Los Angeles Healthcare System, Los Angeles, California; [5]Department of Medicine, Hospitalist Division, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California.

Malignant bowel obstruction (MBO) complicates 3%-15% of cancers and often necessitates inpatient admission. Hospitalists are increasingly involved in treating patients with MBO and coordinating their care across multiple subspecialties. Direct resolution of the obstruction via surgical or interventional means is always preferable. When such options are not possible, pharmacological treatments are the mainstay of therapy. Medications such as somatostatin analogs, steroids, H2-blockers, and other modalities can be effective in palliation and possible resolution of obstruction. Awareness of these pharmacologic therapies can aid hospitalists in treating patients who are confronted with this devastating condition. *Journal of Hospital Medicine* 2019;14:367-373. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Malignant bowel obstruction (MBO) is a catastrophic complication of cancer that often requires hospitalization and a multidisciplinary approach in its management. Hospitalists frequently collaborate with such specialties as Hematology/Oncology, Surgery, Palliative Medicine, and Interventional Radiology in arriving at a treatment plan.

Initial management is focused on hydration, bowel rest and decompression via nasogastric (NG) tube. Surgical resection or endoscopic stenting should be considered early.[1] However, patients who present in the terminal stages may be poor candidates for these options due to diminished functional status, multiple areas of obstruction, complicated anatomy limiting intervention, or an associated large volume of ascites.

Presence of inoperable MBO portends a poor prognosis, often measured in weeks.[2] Presentation often occurs in the context of a sentinel hospitalization, signifying a shift in disease course.[3,4] It is essential for hospitalists to be familiar with noninvasive therapies for inoperable MBO given the increasing role of hospitalists in providing inpatient palliative care. Palliative pharmacologic management of MBO can reduce symptom burden during these terminal stages and will be the focus of this paper.

BACKGROUND AND PATHOPHYSIOLOGY

Malignant bowel obstruction occurs in about 3%-15% of patients with cancer.[2] A consensus definition of MBO established the following specific criteria: (1) clinical evidence of bowel obstruction, (2) obstruction distal to the ligament of Treitz, and (3) the presence of primary intra-abdominal cancer with incurable disease or extra-abdominal cancer with peritoneal involvement.[5] The most common malignancies are gastric, colorectal, and ovarian in origin.[1,2] The most common extra-abdominal malignancies associated with MBO are breast, melanoma, and lung. MBO is most frequently diagnosed during the advanced stages of cancer.[2] The obstruction can involve a partial or total blockage of the small or large intestine from either an intrinsic or extrinsic source. Peristalsis may also be impaired via direct tumor infiltration of the intestinal walls or within the enteric nervous system or celiac plexus. Other etiologies of MBO include peritoneal carcinomatosis and radiation-induced fibrosis.[1,6] The obstruction can occur at a single level or involve multiple areas, which usually precludes surgical intervention.[2]

Symptoms of MBO can be insidious in onset and take several weeks to manifest. The most prevalent symptoms are nausea, vomiting, constipation, abdominal pain, and distension.[2,6] The intermittent pattern of symptoms may evolve into continuous episodes with spontaneous remission in between. The etiology of symptoms can be attributed to distension proximal to the site of obstruction with concomitantly increased gastrointestinal and pancreaticobiliary secretions.

The distension creates a "hypertensive state" in the intestinal lumen causing enterochromaffin cells to release serotonin which activates the enteric nervous system and its effectors including substance P, nitric oxide, acetylcholine, somatostatin, and vasoactive intestinal peptide (VIP). These neurotransmitters stimulate the secretomotor actions that cause hypersecretion of mucus from cells of the intestinal crypts. Additional water and sodium secretions accumulate due to the expanded surface area of the bowel.[1,2] Overloaded with luminal contents, the bowel attempts to overcome the obstruction by contracting, which

***Corresponding Author:** Azadeh Lankarani-Fard, MD; E-mail:azadeh.lankarani-fard@va.gov; Telephone: 310-478-3711

Received: August 21, 2019; **Revised**: January 17, 2019; **Accepted**: February 2, 2019

DOI 10.12788/jhm.3187

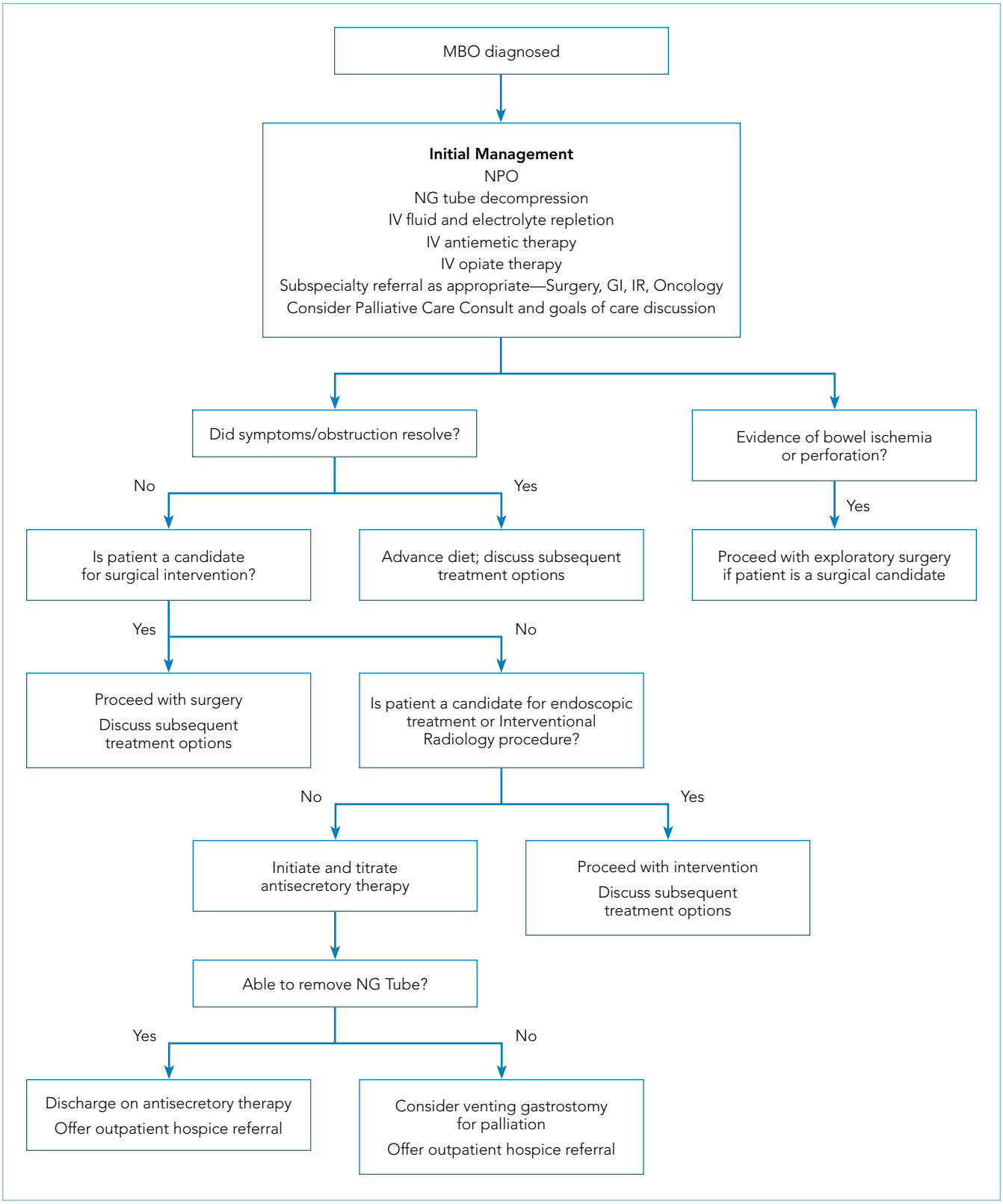


FIG. Management Algorithm for Malignant Bowel Obstruction

Abbreviations: GI, gastroenterology; IR, interventional radiology; IV, intravenous; MBO, malignant bowel obstruction; NG, nasogastric; NPO, *nil per os* (ie, nothing by mouth).

leads to colicky abdominal pain. Tumor burden can also damage the intestinal epithelium and cause continuous pain.

The buildup of secretions can lead to translocation of fluid into the peritoneum ("third spacing"), bowel ischemia, perforation, or sepsis. The combination of poor oral intake, gastrointestinal fluid loss, and sequestration can lead to profound dehydration on presentation.[2,7]

INITIAL MANAGEMENT

Fluid resuscitation, electrolyte repletion, and a trial of NG tube decompression are part of the initial management of MBO (Figure 1). While studies have shown that moderate intravenous hydration can minimize nausea and drowsiness, excessive fluids may worsen bowel edema and exacerbate vomiting.[1,8] NG tube decompression is most effective in patients with proximal obstructions but some studies suggest it can decrease vomiting in patients with colonic obstructions as well.[9] Computed tomography imaging can identify the extent of the tumor, the transition point of the obstruction, and any distant metastases. Surgery, Gastroenterology, and/or Interventional Radiology consultation should be obtained early to evaluate options for direct decompression. Hematology/Oncology and Radiation/Oncology referral may help delineate prognosis and achievable outcomes. Emergent exploratory surgery may be required in cases of bowel perforation or ischemia. Otherwise, a planned surgical resection should be considered in those with an isolated resectable lesion and acceptable perioperative risk. Colorectal or duodenal stents may be an option for those who are not surgical candidates or as a bridge to surgery.

As bowel obstruction is often a late manifestation of advanced malignancy, many patients may not be appropriate candidates for operative/interventional treatment due to malnutrition, comorbid conditions, or anatomic considerations. For these individuals, pharmacologic management is the mainstay of treatment. Additionally, the pharmacologic approaches detailed below may provide benefit as adjunctive therapy for patients undergoing procedural intervention.[7] Consultation for early palliative care can improve symptom control as well as clarify goals of care.

PHARMACOLOGIC MANAGEMENT

Given the pathophysiology of MBO, pharmacologic therapies are focused on controlling nausea and pain while reducing bowel edema and secretions.

Antiemetic Agents

Nausea and vomiting in MBO are due to activation of vagal nerve fibers in the gastric wall and stimulation of the chemoreceptor trigger zone (CTZ).[10] Dopamine antagonists have started to gain favor for MBO compared to more commonly used antiemetics such as the serotonin antagonists. Haloperidol should be considered as a first-line antiemetic in patients with MBO. Its potent D_2-receptor antagonistic properties block receptors in the CTZ. The high affinity of the drug for only the D_2-receptor makes it preferable to alternative agents in the same class such as chlorpromazine. However, haloperidol may cause or worsen QT prolongation and should be avoided in patients with Parkinson's disease. The medication has less sedative and unwanted anticholinergic side effects due to its limited interaction with histaminergic and acetylcholine receptors.[11] Haloperidol has been shown in the past to be efficacious for post-operative nausea but there are few randomized controlled trials in the terminally ill.[12] Nonetheless, recent consensus guidelines from the Multinational Association of Supportive Care recommended haloperidol as the initial treatment of nausea for individuals with MBO based on available systematic reviews.[10]

Other dopamine antagonists remain good options, though they may cause additional side effects due to actions on other receptor types. Metoclopramide, another D_2-receptor antagonist, has been shown to be effective in the treatment of nausea and vomiting due to advanced cancer.[13] However as a prokinetic agent, this medication should be avoided in those with complete MBO and only considered in those with partial MBO.[10,14]

Olanzapine, an atypical antipsychotic, may also have a role in controlling nausea in patients with MBO. It functions as a 5-HT_{2A} and D_2-receptor antagonist, with a slightly greater affinity for the 5-HT_{2A} receptor. Olanzapine thus can target two critical receptors playing a role in nausea and vomiting. A study of patients with incomplete bowel obstruction found the addition of olanzapine significantly decreased nausea and vomiting in patients who were refractory to other treatments including steroids and haloperidol.[15] Olanzapine has the added advantage of single-day dosing as well as an oral disintegrating formulation.[16]

Intravenous and sublingual preparations of 5-HT_3 receptor antagonists such as ondansetron are commonly used in the inpatient setting. These medications are potent antiemetics that exhibit their effects via pathways where serotonin acts as a neurotransmitter.[17] An alternative agent, tropisetron, has shown promise when used alone or in conjunction with metoclopramide but is not currently available in the US.[18] Granisetron is available in a transdermal formulation, which can be very convenient for patients with bowel obstruction. Its mechanism of action differs from ondansetron as it is an allosteric inhibitor rather than a competitive inhibitor.[19] Granisetron needs more specific study with regards to its role in MBO.

Although haloperidol remains the initial choice, combination therapy can help to decrease the risk of extrapyramidal symptoms seen with higher doses of dopaminergic monotherapy.

Analgesics

Pain control is an essential part of the palliative treatment of MBO as bowel distention, secretions, and edema can cause rapid onset of pain. Parenteral step three opioids remain the optimal initial choice since patients are unable to take medications orally and may have compromised absorption. Opioids address both the colicky and continuous aspects of MBO pain.

Short-acting intravenous opioids such as morphine or hydromorphone may be scheduled every four hours with breakthrough dosing every hour in between. Alternatively, analgesics

TABLE 1. **Summary of Preferred Pharmacologic Agents for Malignant Bowel Obstruction**

	Class	Preferred Agents/Dosage	Comments
First-line Antisecretory	Somatostatin analogs	Octreotide initial dose 100 mcg SC tid-qid with titration to effect (max 1 mg/day)[7,12]	1.Expensive 2.Benefit apparent in first 3 days (range 1-5d) 3.Collaboration with palliative medicine recommended with dose titration
	Combination Therapy: Steroids + PPI/ H2-blockers	Steroid: Dexamethasone IV total 8 mg/day in one dose[38] H2-blockers Ranitidine 50 mg IV qid Pantoprazole 40 mg IV qd	1. Combination is noninferior to somatostatin analogues[38] 2. PPI's not as well studied but have significant antisecretory effect[33]
Second-line Antisecretory	Anticholinergic agents	Glycopyrrolate 0.1-0.2 mg IV or SC q6 -8 hours[39] Scopolamine butylbromide 20-120 mg/day IV/IM[1] (not available in US)	1. Scopolamine butylbromide not equivalent to scopolamine hydrobromide (available in US)
Adjunct therapies	Antiemetics	Haloperidol 0.5 mg IV/SC tid-qid, up to 5 mg /24 hours Olanzapine 2.5-7.5 mg po daily (oral disintegrating) [16] Ondansetron 4-8 mg sublingual or IV Metoclopromide 5-10 mg IV/SC qid prn	1. Metoclopramide should be avoided in cases of complete obstruction.
	Analgesics	Dosages will vary across patients. For opioid-naïve patients: Morphine 1 mg IV/SC q4hr PRN Hydromorphone 0.2 mg IV/SC q4hr PRN	1. Consider PCA 2. Collaboration with palliative medicine recommended with dose titration

Abbreviations: IM, intramuscular; IV, intravenous; PCA, patient-controlled analgesia; PPI, proton pump inhibitor; po, *per os* (ie, by mouth); PRN, *pro re nata* (ie, as needed); SC, subcutaneous.

can be administered via a patient-controlled analgesia (PCA) pump.[1] Although doses vary across patients, opioid-naïve patients can be initiated on a low dose therapy such as hydromorphone 0.2 mg IV/SC or morphine 1 mg IV/SC every four hours as needed for pain control.

Ongoing pain management for patients with MBO requires coordination of care. Many patients will elect to receive hospice care following discharge. Direct communication with palliative consultants and hospice providers can help facilitate a smooth transition. In patients for whom bowel obstruction resolves, transition to oral opioids based on morphine equivalent daily dose is indicated with further dose adjustment as patients may have reduced pain at this stage.

Options for patients with unresolved obstruction include transdermal and sublingual preparations as well as outpatient PCA with hospice support. Transdermal fentanyl patch can be useful but onset of peak levels occur within 8-12 hours.[20] The patch is usually exchanged every 72 hours and is most effective when applied to areas containing adipose tissue which may limit its use in cachectic patients. The liquid preparation of methadone can be useful even in patients with unresolved MBO. Its lipophilic properties allow for ease of absorption.[21] A baseline electrocardiogram (EKG) is recommended prior to methadone initiation due to the potential for QT prolongation. Methadone should not be a first-line option for opioid-naïve individuals due to its longer onset of action which limits rapid dose titration. Close collaboration with palliative medicine is highly recommended when using longer acting opioids.

Antisecretory Agents

Antisecretory agents are a mainstay of the pharmacologic management of inoperable MBO. Medications that reduce secretions and bowel edema include: somatostatin analogs, H2-blockers, proton pump inhibitors (PPIs), steroids, and anticholinergic agents. Table 2 summarizes the major studies comparing various antisecretory medications.

Octreotide, a somatostatin analog, has been increasingly used for the palliative treatment of MBO. The mechanism of action involves splanchnic vasoconstriction, reduction of intestinal and pancreatic secretions (via inhibition of VIP), decrease in gastric emptying, and slowing of smooth muscle contractions.[22] Octreotide comes in an immediate-release formulation with an initial subcutaneous dose of 100 µg three or four times per day. Most patients will require 300-800 µg/day, maximum dose being up to 1 mg/day.[22,23] A long-acting formulation, lanreotide, exists but can be difficult to obtain and may not provide the immediate relief needed in an acute care setting.

Initiation of octreotide should be considered in the presence of persistent symptoms. Studies have suggested that the benefit of octreotide is most apparent in the first three days of treatment (range 1-5 days).[6,22,24] The medication should be discontinued if there is no clinical improvement such as reduction of NG tube output. Octreotide has been shown to be more efficacious than anticholinergic agents in reducing secretions as well as frequency of nausea and vomiting.[8,25-28] Octreotide expedites NG tube removal, recovery of bowel function, and improvement in quality of life.[29-32] The medication should also

TABLE 2. **Summary of Major Clinical Trials Comparing the Efficacies of Antisecretory Agents for Malignant Bowel Obstruction**

Study	Patient Population	Intervention	Comparison	Primary Outcome	Summary of Findings
Currow et al. (2015)[38]	87 patients with inoperable MBO on IV dexamethasone (8 mg/24 hours) + ranitidine (200 mg/24 hours) ± IV fluids (10-20 cm3/kg/day)	Octreotide (600 µg/24 hours); n = 45	Placebo; n = 42	Number of days free of vomiting 72 hours after administration	No statistically significant difference in number of days free of vomiting (P = .71).
Peng et al. (2015)[25]	96 patients with inoperable MBO due to ovarian cancer. Concomitant treatment in both groups: NGT, IV fluids	Octreotide (300 µg/24 hours); n = 48	Scopolamine butylbromide (60 mg/24 hours); n = 49	Measured NGT secretions; number of vomiting episodes at each day for 72 hours	Significant reduction in NGT secretions and number of vomiting episodes at each day in the octreotide group (P < .05).
Mariani et al. (2012)[32]	80 patients with inoperable MBO due to peritoneal carcinomatosis with continued symptoms after treatment with steroids and PPI.	Double-blind phase: (10 days): lanreotide (30 mg on day 1); n = 43 Open-label phase: lanreotide (every 10 days until treatment cessation); n = 59	Placebo; n = 37	Proportion of patients with one or fewer vomiting episodes at day 7 or no vomiting recurrence after NGT removal	No statistically significant difference achieving primary outcome in intention to treat analysis (41.9% vs 29.7%; P = .24) Significant decrease in symptoms in per protocol analysis (57% vs.30.4% P < .05) Significant response in investigators assessment: No effect on NG tube removal.
Laval et al. (2012)[31]	64 patients with inoperable MBO due to peritoneal carcinomatosis Concomitant treatment in both groups: methylprednisolone 3-4 mg/kg/day on days 1-6	Octreotide (600 µg/24 hours) on days 1-6 + octreotide LAR (30 mg) on days 1, 29, 57; n = 32	Placebo; n = 32	Proportion of patients with treatment success at day 14, defined as: absence of NGT and vomiting <2 times per day and no use of anticholinergics	Treatment success for octreotide group compared to placebo arm (38% vs.28%)(38%) Treatment success more apparent in those with Karnofsky score >50: (60% vs. 28%) and those without NGT at onset (53%vs 33%).
Mystakidou et al. (2002)[27]	68 with advanced cancer and diagnosed with bowel obstruction Concomitant treatment in both groups: chlorpromazine (15-25 mg/24 hours)	Octreotide (600-800 µg/24 hours); n = 34	Scopolamine butylbromide (60-80 mg/24 hours)); n = 34	Mean percentage change in vomiting episodes; nausea scores at day 0, 3, 6, and 1 day before death	Significant mean percentage reduction in vomiting episodes and nausea scores in the octreotide group between day 0 and 3 (P < .05).
Mercadante et al. (2000)[26]	18 patients with inoperable MBO	Octreotide (300 µg/24 hours); n = 9	Scopolamine butylbromide (60 mg/24 hours); n = 6	Reduction in vomiting episodes at each day for 72 hours	Significant reduction in mean vomiting episodes in the octreotide group mostly noted on day 1 and 2 after administration -2 (P < 0.01; P < .004, respectively).
Ripamonti et al. (2000)[8]	17 patients with inoperable MBO	Octreotide (300 µg/24 hours); n = 9	Scopolamine butylbromide (60 mg/24 hours); n = 8	Daily volume of NGT secretions at each day for 72 hours	Significant reduction in NGT secretions in the octreotide group at days 2-3 (P = .016 and P = .020, respectively).

Abbreviations: IV, intravenous; MBO, malignant bowel obstruction; NGT, nasogastric tube; PPI, proton pump inhibitor.

be considered in cases of recurrent MBO that previously responded to the medication.

Octreotide is considered the first-line agent in the palliative treatment of MBO, however the medication is costly. Recent studies suggest combination therapy with steroids and H2-blockers or PPIs may be an equally effective and less expensive alternative. The primary rationale for the use of steroids in MBO is their ability to decrease peritumoral edema and promote salt and water absorption from the intestine.[1,2] PPIs and H2-blockers decrease distension, pain, and vomiting by reducing the volume of gastric secretions.[33] A recent meta-analysis of phase 3 trials found both PPIs and H2-blockers to be effective in lowering volumes of gastric aspirates with ranitidine being slightly superior.[34]

Initial research into the utility of steroids in MBO garnered mixed results. One study showed marginal benefit for steroid plus octreotide combination therapy compared to octreotide, in a cohort of 27 patients.[35] A subsequent review of practice patterns in the management of terminal MBO in Japan found that patients given steroids in combination with octreotide compared to octreotide alone were more likely to undergo early NG tube removal.[36] A 1999 systematic review of corticosteroid treatment of MBO concluded low morbidity associated with the medications with a trend toward benefit that was not statistically significant.[37] A 2015 study by Currow showed the addition of octreotide in patients already on a regime of dexamethasone and ranitidine did not improve the number of days free from vomiting but did reduce vomiting episodes in those with the most refractory symptoms.[38]

Collectively, the studies suggest that combination therapy

with steroid and PPI or H2 blocker could be a less expensive option in the initial management of MBO. Alternatively, steroids may provide additional relief in patients with continued symptoms on octreotide and H2-blockers. Dexamethasone is preferable given its longer half-life and decreased propensity for sodium retention. Dosing of dexamethasone should be 8 mg IV once a day.[38]

Anticholinergic agents also reduce secretions. However, they are considered second-line therapy given their lower efficacy compared to other treatment options as well as their propensity to worsen cognitive function.[1,2] Anticholinergics may benefit patients with continued symptoms who cannot tolerate the side effects of other treatments. Scopolamine, also known as hyoscine hydrobromide in the US, should be avoided as it crosses the blood-brain barrier. The quaternary formulation, scopolamine butylbromide (hyoscine butylbromide), does not pass this barrier but is currently not available in the US. Glycopyrrolate may be considered as it is also a quaternary ammonium compound that does not cross the blood-brain barrier. Several case reports have described its effectiveness in the resolution of refractory nausea and vomiting in combination with haloperidol and hydromorphone for symptom control.[39] Effective oral care is imperative if anticholinergics are used in order to prevent the unpleasant feeling of dry mouth.

SUBSEQUENT SUPPORTIVE CARE

While initial management of MBO often requires placement of an NG tube, prolonged placement can increase the risk for erosions, aspiration, and sinus infections. Removal of the NG tube is most successful when secretions are minimal, but this may not happen unless the obstruction resolves. Some patients may elect to keep an NG tube if symptoms cannot be otherwise controlled by medications.

A venting gastrostomy tube can be considered as an alternative to prolonged NG tube placement. The tube may help alleviate distressing symptoms and can enhance the quality of life of patients by allowing the sensation of oral intake, though it will not allow for absorption of nutrients.[40] Although a low risk procedure, patients may be too frail to undergo the procedure and may have postprocedure pain and complications. Anatomic abnormalities such as overlying bowel may also prevent the noninvasive percutaneous approach.

In patients with unresolved obstruction, oral intake should be reinitiated with caution with the patient's wishes taken into account at all times. Some patients may prioritize the comfort derived from eating small amounts over any associated risks of increased nausea and vomiting.

Parenteral nutrition should be avoided in those with inoperable MBO in the advanced stages. The risks of infection, refeeding syndrome, and the discomfort of an intravenous line and intermittent testing may outweigh any benefits given the overall prognosis.[41,42]

CONCLUSION

Hospitalists are often involved in the initial care of patients with advanced malignancy who present with MBO. When interventions or surgeries to directly alleviate the obstruction are not possible, pharmacologic options are essential in managing burdensome symptoms and improving quality of life. Early Palliative Care referral can also assist with symptom management, emotional support, clarification of goals of care, and transition to the outpatient setting. While patients with inoperable MBO have a poor prognosis, hospitalists can play a vital role in alleviation of suffering in this devastating complication of advanced cancer.

Disclosures: The authors have nothing to disclose.

References

1. Ripamonti CI, Easson AM, Gerdes H. Management of malignant bowel obstruction. *Eur J Cancer*. 2008;44(8):1105-1115. doi: 10.1016/j.ejca.2008.02.028.
2. Tuca A, Guell E, Martinez-Losada E, Codorniu N. Malignant bowel obstruction in advanced cancer patients: epidemiology, management, and factors influencing spontaneous resolution. *Cancer Manag Res*. 2012;4:159-169. doi: 10.2147/CMAR.S29297.
3. Meier DE. Palliative care in hospitals. *J Hosp Med*. 2006;1(1):21-28. doi: 10.1002/jhm.3.
4. Lin RJ, Adelman RD, Diamond RR, Evans AT. The sentinel hospitalization and the role of palliative care. *J Hosp Med*. 2014;9(5):320-323. doi: 10.1002/jhm.2160.
5. Anthony T, Baron T, Mercadante S, et al. Report of the clinical protocol committee: development of randomized trials for malignant bowel obstruction. *J Pain Symptom Manage*. 2007;34(1 Suppl):S49-S59. doi: 10.1016/j.jpainsymman.2007.04.011.
6. Laval G, Marcelin-Benazech B, Guirimand F, et al. Recommendations for bowel obstruction with peritoneal carcinomatosis. *J Pain Symptom Manage*. 2014;48(1):75-91. doi: 10.1016/j.jpainsymman.2013.08.022.
7. Ferguson HJ, Ferguson CI, Speakman J, Ismail T. Management of intestinal obstruction in advanced malignancy. *Ann Med Surg*. 2015;4(3):264-270. doi: 10.1016/j.amsu.2015.07.018.
8. Ripamonti C, Mercadante S, Groff L, et al. Role of octreotide, scopolamine butylbromide, and hydration in symptom control of patients with inoperable bowel obstruction and nasogastric tubes: A prospective randomized trial. *J Pain Symptom Manage*. 2000;19(1):23-34. doi: 10.1016/S0885-3924(99)00147-5.
9. Rao W, Zhang X, Zhang J, et al. The role of nasogastric tube in decompression after elective colon and rectum surgery: a meta-analysis. *Int J Colorectal Dis*. 2011;26(4):423-429. doi: 10.1007/s00384-010-1093-4.
10. Walsh D, Davis M, Ripamonti C, et al. 2016 updated MASCC/ESMO consensus recommendations: management of nausea and vomiting in advanced cancer. Support Care *Cancer*. 2017;25(1):333-340. doi: 10.1007/s00520-016-3371-3.
11. Murray-Brown F, Dorman S. Haloperidol for the treatment of nausea and vomiting in palliative care patients. *Cochrane Database Syst Rev*. 2015;11(11):CD006271. doi: 10.1002/14651858.CD006271.pub3.
12. Digges M, Hussein A, Wilcock A, et al. Pharmacovigilance in hospice/palliative care: Net effect of haloperidol for nausea or vomiting. *J Palliat Med*. 2018;21(1):37-43. doi: 10.1089/jpm.2017.0159.
13. Bruera E, Belzile M, Neumann C, et al. A double-blind, crossover study of controlled-release metoclopramide and placebo for the chronic nausea and dyspepsia of advanced cancer. *J Pain Symptom Manage*. 2000;19(6):427-435. doi: 10.1016/S0885-3924(00)00138-X.
14. Gupta M, Davis M, LeGrand S, Walsh D, Lagman R. Nausea and vomiting in advanced cancer: the Cleveland clinic protocol. *J Support Oncol*. 2013;11(1):8-13. doi: 10.1016/j.suponc.2012.10.002.
15. Kaneishi K, Kawabata M, Morita T. Olanzapine for the relief of nausea in patients with advanced cancer and incomplete bowel obstruction. *J Pain Symptom Manage*. 2012;44(4):604-607. doi: 10.1016/j.jpainsymman.2011.10.023.
16. Prommer E. Olanzapine: palliative medicine update. *Am J Hosp Palliat Care*. 2013;30(1):75-82. doi: 10.1177/1049909112441241.
17. Currow DC, Coughlan M, Fardell B, Cooney NJ. Use of ondansetron in palliative medicine. *J Pain Symptom Manage*. 1997;13(5):302-307. doi: 10.1016/S0885-3924(97)00079-1.
18. Mystakidou K, Befon S, Trifyllis J, Liossi C, Papadimitriou J. Tropisetron versus metoclopramide in the control of emesis in far-advanced cancer. *Oncologist*. 1997;2(5):319-323. doi: 10.1007/s11136-005-4324-3.

19. Tuca A, Roca R, Sala C, et al. Efficacy of granisetron in the antiemetic control of nonsurgical intestinal obstruction in advanced cancer: A phase II clinical trial. *J Pain Symptom Manage*. 2009;37(2):259-270. doi: 10.1016/j.jpainsymman.2008.01.014.
20. Prommer E. The role of fentanyl in cancer-related pain. *J Palliat Med*. 2009;12(10):947-954. doi: 10.1089/jpm.2009.0051.
21. Shaiova LL, Berger A, Blinderman CD, et al. Consensus guideline on parenteral methadone use in pain and palliative care. *Palliat Support Care*. 2008;6(2):165-176. doi: 10.1017/S1478951508000254.
22. Murphy E, Prommer EE, Mihalyo M, Wilcock A. Octreotide. *J Pain Symptom Manage*. 2010;40(1):142-148. doi: 10.1016/j.jpainsymman.2010.05.002.
23. Prommer EE. Established and potential therapeutic applications of octreotide in palliative care. *Support Care Cancer*. 2008;16(10):1117-1123. doi: 10.1007/s00520-007-0399-4.
24. Mercadante S, Ferrera P, Villari P, Marrazzo A. Aggressive pharmacological treatment for reversing malignant bowel obstruction. *J Pain Symptom Manage*. 2004;28(4):412-416. doi: 10.1016/j.jpainsymman.2004.01.007.
25. Peng X, Wang P, Li S, Zhang G, Hu S. Randomized clinical trial comparing octreotide and scopolamine butylbromide in symptom control of patients with inoperable bowel obstruction due to advanced ovarian cancer. *World J Surg Oncol*. 2015;13:50. doi: 10.1186/s12957-015-0455-3.
26. Mercadante S, Ripamonti C, Casuccio A, Zecca E, Groff L. Comparison of octreotide and hyoscine butylbromide in controlling gastrointestinal symptoms due to malignant inoperable bowel obstruction. *Support Care Cancer*. 2000;8(3):188-191. doi: 10.1007/s005200050283.
27. Mystakidou K, Tsilika E, Kalaidopoulou O, et al. Comparison of octreotide administration vs conservative treatment in the management of inoperable bowel obstruction in patients with far advanced cancer: a randomized, double-blind, controlled clinical trial. *Anticancer Res*. 2002;22(2B):1187-1192.
28. Obita GP, Boland EG, Currow DC, Johnson MJ, Boland JW. Somatostatin analogues compared with placebo and other pharmacologic agents in the management of symptoms of inoperable malignant bowel obstruction: a systematic review. *J Pain Symptom Manage*. 2016;52(6):901-919. doi: 10.1016/j.jpainsymman.2016.05.032.
29. Watari H, Hosaka M, Wakui Y, et al. A prospective study on the efficacy of octreotide in the management of malignant bowel obstruction in gynecologic cancer. *Int J Gynecol Cancer*. 2012;22(4):692-696. doi: 10.1097/IGC.0b013e318244ce93.
30. Hisanaga T, Shinjo T, Morita T, et al. Multicenter prospective study on efficacy and safety of octreotide for inoperable malignant bowel obstruction. *Jpn J Clin Oncol*. 2010;40(8):739-745. doi: 10.1093/jjco/hyq048.
31. Laval G, Rousselot H, Toussaint-Martel S, et al. SALTO: a randomized, multicenter study assessing octreotide LAR in inoperable bowel obstruction. *Bull Cancer*. 2012;99(2):E1-E9. doi: 10.1684/bdc.2011.1535.
32. Mariani PP, Blumberg J, Landau A, et al. Symptomatic treatment with lanreotide microparticles in inoperable bowel obstruction resulting from peritoneal carcinomatosis: a randomized, double-blind, placebo-controlled phase III study. *J Clin Oncol*. 2012;30(35):4337-4343. doi: 10.1200/JCO.2011.40.5712.
33. Clark K, Lam L, Currow D. Reducing gastric secretions--a role for histamine 2 antagonists or proton pump inhibitors in malignant bowel obstruction? *Support Care Cancer*. 2009;17(12):1463-1468. doi: 10.1007/s00520-009-0609-3.
34. Strand DS, Kim D, Peura DA. 25 years of proton pump inhibitors: a comprehensive review. *Gut Liver*. 2017;11(1):27-37. doi: 10.5009/gnl15502.
35. Murakami H, Matsumoto H, Nakamura M, Hirai T, Yamaguchi Y. Octreotide acetate-steroid combination therapy for malignant gastrointestinal obstruction. *Anticancer Res*. 2013;33(12):5557-5560.
36. Minoura T, Takeuchi M, Morita T, Kawakami K. Practice patterns of medications for patients with malignant bowel obstruction using a nationwide claims database and the association between treatment outcomes and concomitant use of H2-blockers/proton pump inhibitors and corticosteroids with octreotide. *J Pain Symptom Manage*. 2018;55(2):413-419. doi: 10.1016/j.jpainsymman.2017.10.019.
37. Feuer DJ, Broadley KE. Systematic review and meta-analysis of corticosteroids for the resolution of malignant bowel obstruction in advanced gynaecological and gastrointestinal cancers. Systematic Review Steering Committee. *Ann Oncol*. 1999;10(9):1035-1041. doi: 10.1023/A:1008361102808.
38. Currow DC, Quinn S, Agar M, et al. Double-blind, placebo-controlled, randomized trial of octreotide in malignant bowel obstruction. *J Pain Symptom Manage*. 2015;49(5):814-821. doi: 10.1016/j.jpainsymman.2014.09.013.
39. Davis MP, Furste A. Glycopyrrolate: a useful drug in the palliation of mechanical bowel obstruction. *J Pain Symptom Manage*. 1999;18(3):153-154.
40. Zucchi E, Fornasarig M, Martella L, et al. Decompressive percutaneous endoscopic gastrostomy in advanced cancer patients with small-bowel obstruction is feasible and effective: a large prospective study. *Support Care Cancer*. 2016;24(7):2877-2882. doi: 10.1007/s00520-016-3102-9.
41. Naghibi M, Smith TR, Elia M. A systematic review with meta-analysis of survival, quality of life and cost-effectiveness of home parenteral nutrition in patients with inoperable malignant bowel obstruction. *Clin Nutr*. 2015;34(5):825-837. doi: 10.1016/j.clnu.2014.09.010.
42. O'Connor B, Creedon B. Pharmacological treatment of bowel obstruction in cancer patients. *Expert Opin Pharmacother*. 2011;12(14):2205-2214. doi: 10.1517/14656566.2011.597382.

Things We Do For No Reason: HIT Testing in Low Probability Patients

Amanda Li, MD[1]; Lisa K Hicks, MD, MSc[2]; Eddy Fan, MD, PhD[3]*

[1]Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [2]Division of Hematology, St. Michael's Hospital, Toronto, Ontario, Canada; [3]Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada.

Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason" series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

A 59-year-old man with cirrhosis secondary to nonalcoholic steatohepatitis was admitted to the intensive care unit (ICU) for management of hepatorenal syndrome and work-up for liver transplantation. On admission, his platelet count was 90 × 109/L (normal 150-400 × 109/L), and he was started on thromboprophylaxis with unfractionated heparin (UFH) 5,000 units subcutaneously twice daily. His platelet count began to fall two days after admission. He did have a history of prior heparin exposure associated with his hemodialysis sessions in the past 30 days. During this period, he also had an episode of fever, and antibiotics were initiated for a presumed line infection. He also required periodic vasopressor support for hypotension. His platelet count reached 14 × 109/L by the end of two weeks. He did not have any symptoms of thrombosis, skin necrosis, or reaction to heparin exposure.

BACKGROUND

Thrombocytopenia is common, especially during critical illness, occurring in up to 50% of patients.[1] In this population, thrombocytopenia is often due to sepsis, hemorrhage, liver dysfunction, and drug reactions.[1,2] Heparin-induced thrombocytopenia (HIT) is an acquired thrombotic drug reaction resulting from platelet activation secondary to antibodies formed against the heparin-modified platelet factor 4 (PF4) complexes.[3] This leads to platelet aggregation and dysregulation of the coagulation cascade, which can result in arterial or venous thromboembolic events in up to 50% of patients.[3] Mortality associated with HIT can be as high as 30% in this critically ill population.[3] Diagnosis of HIT can be made initially through the enzyme-linked immunosorbent assay (ELISA). Management of HIT involves immediate cessation of heparin and initiation of therapeutic anticoagulation with nonheparin agents in order to prevent or treat the thrombotic events.[4,5]

The true incidence of HIT remains low, occurring in 0.2% to 5% of patients exposed to heparin and less than 1% in the ICU population.[2,3,6,7] However, given the high incidence of thrombocytopenia in the ICU, the diagnosis of HIT is often considered, resulting in over-testing in this population. Studies suggest that more than 200 ELISAs are requested per year at many hospitals.[8,9] This can lead to significant clinical and economic consequences.

WHY YOU MIGHT THINK HIT TESTING WITH ELISA IS HELPFUL

Thrombocytopenia is common in hospitalized patients while heparin is frequently used for thromboprophylaxis or therapeutic anticoagulation. As a result, a diagnosis of HIT is often considered.[1] The high stakes of the inpatient environment, coupled with the increased frequency of thrombocytopenia and heparin exposure, has led to increased use of HIT testing in this population.[10]

The most widely available diagnostic test for HIT is the ELISA which detects anti-PF4-heparin antibodies but also nonpathogenic antibodies.[11] As a result, the ELISA has a sensitivity close to 100%, allowing physicians to rule out HIT if the test is negative, as indicated by an optical density (OD) of less than 0.4.[7] Confirmatory testing with the functional serotonin release assay (SRA) is the reference standard as it confers both a high sensitivity and specificity for HIT.[11] Due to technical aspects, SRA, unlike the ELISA, is not available in every center and is often outsourced to external labs. Turn-around time for external SRA testing can vary from days to weeks versus hours for the ELISA. The cost for SRA is approximately $120 (USD) per test compared to $30 (USD) per ELISA. Therefore, the ELISA is the recommended initial test due to its quick turn-around time and lower costs.[12,13] For these reasons, the SRA test should not be used initially, but rather to confirm the diagnosis of HIT in patients with a positive ELISA.

WHY YOU SHOULD NOT TEST LOW PROBABILITY PATIENTS FOR HIT

The "4T's" scoring system is a clinical scoring system that estimates the pretest probability of HIT using clinical and basic laboratory parameters (Table).[14] The 4T's score provides a pretest probability for HIT using four parameters: platelet count, timing of platelet fall, presence of thrombotic events, and the

***Corresponding Author:** Eddy Fan, MD, PhD; E-mail: eddy.fan@uhn.ca; Telephone: 416-340-5483, Twitter: @efan75

Published online first April 8, 2019.

Received: August 24, 2018; **Revised**: December 27, 2018; **Accepted**: January 7, 2019

TABLE. **4T's Score (Adapted from Cuker et al. Blood 2012;120(20):4160-4167. doi: 10.1182/blood-2012-07-443051.14)**

4Ts	2 Points	1 Point	0 Points
Thrombocytopenia	Platelet fall >50% and platelet nadir ≥20 x 10^9/L	Platelet fall 30%-50% or platelet nadir 10-19 x 10^9/L	Platelet fall <30% or platelet nadir <10 x 10^9/L
Timing of platelet count fall	Onset between 5-10 days or platelet fall ≤1 day (prior heparin exposure within 30 days)	Consistent with days 5-10 fall, but not clear (eg, missing platelet counts) or onset after day 10 or fall ≤1 day (prior heparin exposure 30-100 days ago)	Platelet count fall ≤4 days without recent exposure
Thrombosis or other sequalae	New thrombosis (confirmed); skin necrosis; acute systemic reaction after intravenous unfractionated heparin bolus	Progressive or recurrent thrombosis; non-necrotizing (erythematous) skin lesions; suspected thrombosis (not proven)	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

likelihood of another cause of thrombocytopenia. Based on these parameters, the pretest probability for HIT can be divided into three categories: low (4T's score of ≤3), intermediate (score 4-5), or high (score 6-8).[14-16]

Validation of the 4T's score has shown that a low probability score carries a negative predictive value of 99% in a patient population with varying HIT prevalence rates.[14] Therefore, having a low score is sufficient to rule out HIT without the need for further laboratory testing.[14-16] Although the HIT ELISA confers high sensitivity, due to its detection of nonpathogenic antibodies, its specificity can range from 74% to 84%.[15] Therefore, in the setting of a low 4T's score, HIT testing is not only unnecessary, it can be harmful due to the risk of treating a false positive result. For instance, assuming an average HIT prevalence of 1% and a false positive rate of 16% (specificity 84%), 1/17 (5.6%) patients with a positive ELISA will have HIT if testing is pursued in an indiscriminate manner. The American Society of Hematology *Choosing Wisely®* Campaign has highlighted this concern by advising physicians that they should "not test or treat for suspected HIT in patients with a low pretest probability of HIT."[17]

False positive results on HIT tests are not a trivial concern. The most recognizable adverse event associated with HIT treatment is an elevated risk of bleeding while receiving nonheparin agents. Availability of nonheparin anticoagulants vary by center; however, the most commonly used agents include argatroban, danaparoid, bivalirudin, and off-label fondaparinux.[4] Due to its short half-life and hepatic clearance, argatroban is commonly used for cases of confirmed or suspected HIT. A retrospective study assessing the bleeding risk of critically ill patients on argatroban therapy suggests a major bleeding risk of 10% within two days of argatroban initiation.[18] In addition, factors such as the presence of elevated bilirubin, major surgery, weight >90 kg, and platelet count <70 × 109/L were found to be associated with increased risk for major bleeding.[18] These identified risk factors are very common in the inpatient setting. As a result, monitoring and titration of argatroban can be challenging.

Over-diagnosis and over-treatment can also lead to significant costs to the healthcare system. A retrospective study assessing the use of HIT testing found that out of 218 HIT ELISA's sent over a one-year period at a single institution, 161 (74%) were sent inappropriately (ie, in patients with a low pretest probability), with only one resulting in confirmed HIT by SRA. This incurred an additional cost of $33,000 (USD) for testing alone.[8] A retrospective study of 85 patients assessed the costs of treating patients with a false positive HIT assay. They found that the average duration of treatment with a nonheparin agent was three days and the total cost per patient was $982 (USD).[19] Treatment with a nonheparin agent such as argatroban costs more than $700 (USD) per day while the continuation of unfractionated heparin for prophylaxis costs less than $10 (USD) per day.[20]

Lastly, a diagnosis of HIT can also result in late consequences due to heparin re-exposure. Clinicians may be wary of exposing patients to heparin in situations where heparin may be the most appropriate agent such as cardiovascular surgery, percutaneous interventions, routine thromboprophylaxis, or therapeutic anticoagulation. In these situations when heparin is the agent of choice, determining safety for re-exposure requires further antibody testing which may delay procedures or result in the use of alternative agents with their associated risks and cost implications.[4]

WHEN HIT TESTING WITH ELISA MAY BE HELPFUL

Laboratory testing for HIT is appropriate when the pretest probability for HIT is intermediate or high based on the 4T's score.[14-16] Studies assessing the application of the 4T's score have shown that a moderate or high pretest probability carries a probability of having true HIT in 14% and 64% of the cases respectively.[14] However, due to the subjective nature of the 4T's score components, it is important to recognize that in nonexpert hands, the 4T's scoring system can suffer from a lack of interrater reliability.[16]

As discussed above, a negative ELISA (OD < 0.4) helps to rule out HIT and allow heparin to be safely reintroduced without any further testing. If ELISA is positive (OD ≥ 0.4) confirmation testing with SRA should be performed.[5] However, studies suggest that the magnitude of the OD is associated with increased likelihood for true HIT, with an OD of greater than 2.00 associated with a positive SRA approximately 90% of the time.[21] This suggests that if OD values are strongly positive (≥2.00), SRA can be deferred.[5]

Due to the SRA limited availability, confirmatory testing is not always possible or in some situations, SRA results may be negative despite a positive OD. In both these cases, discussion with the Hematology service is recommended.

WHAT WE SHOULD DO INSTEAD OF SENDING ELISA

When presented with a case of thrombocytopenia, it is important for clinicians to consider a broad approach in their differential diagnosis. Hospitalists should investigate common etiologies, consider the coagulation parameters, liver enzymes, nutritional status, peripheral blood smear, and a detailed history and physical exam to identify other common potential cause such as sepsis.

The 4T's score should be applied in patients who have had recent heparin exposure. A score of ≤3 indicates a low pretest probability; therefore, HIT is unlikely and further testing is not needed. A score of ≥4 indicates an intermediate or high pretest probability and should prompt clinicians to consider further HIT testing with ELISA. In these situations, heparin should be held, and nonheparin agents should be initiated to prevent thromboembolic complications. In their study of ICU patients, Pierce et al. found that 17% of patients did not have a concurrent cessation of heparin and initiation of alternative agents despite a high clinical suspicion for HIT.[1] Lastly, if hospitalists have concerns regarding HIT testing or management, expert consultation with the Hematology service is recommended.

RECOMMENDATIONS

- Consider a broad differential diagnosis when presented with a hospitalized patient with new thrombocytopenia given the low incidence of HIT (<5%).
- Apply the 4T's score in those who have thrombocytopenia and recent heparin exposure. A low scores 4T's score (≤3) predicts a low pretest probability and further testing is not required.
- Patients with moderate or high 4T's score (≥4) should have the ELISA test. During this time, heparin should be discontinued and nonheparin agents initiated while waiting for test results.
- Confirmatory testing with SRA should be performed for all positive ELISAs; however, they can be deferred in patients with strongly positive OD (≥2.00) on ELISA.

CONCLUSION

In the opening clinical scenario, the 4T's score would have been 2 (1 point for the platelet count, 1 point for the platelet count fall after 10 days, 0 points for thrombosis, and 0 points for an alternative cause of thrombocytopenia), indicating a low pretest probability. Further HIT testing should be deferred as the likelihood for HIT is low. In this case, the more likely etiology for his thrombocytopenia would be sepsis. Therefore, heparin can be safely reinitiated once the platelet count recovers. This case helps to illustrate the importance of keeping a broad differential in cases of thrombocytopenia in the hospitalized patient while concurrently applying the 4T's score to determine appropriateness for further HIT testing. Ultimately by choosing wisely, we can help reduce the cost and safety implications of a falsely positive HIT diagnosis.

What do you do?

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason"? Let us know what you do in your practice and propose ideas for other "Things We Do for No Reason" topics. Please join in the conversation online at Twitter (#TWDFNR)/Facebook and don't forget to "Like It" on Facebook or retweet it on Twitter.

Disclosures: The authors report no conflict of interest.

References

1. Pierce W, Mazur J, Greenberg C, Mueller J, Foster J, Lazarchick J. Evaluation of heparin-induced thrombocytopenia (HIT) laboratory testing and the 4Ts scoring system in the intensive care unit. *Ann Clin Lab Sci.* 2013;43(4):429-435.
2. Harada MY, Hoang DM, Zaw AA, et al. Overtreatment of heparin-induced thrombocytopenia in the surgical ICU. *Crit Care Med.* 2017;45(1):28-34. doi:10.1097/ccm.0000000000002002.
3. Warkentin TE, Sheppard JAI, Heels-Ansdell D, et al. Heparin-induced thrombocytopenia in medical-surgical critical illness. *Chest.* 2013;144(3):848-858. doi: 10.1378/chest.13-0057.
4. Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia. *Chest.* 2012;141(2):e495S-e530S. doi: 10.1378/chest.11-2303.
5. Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Adv.* 2018;2(22):3360-3392. doi: 10.1182/bloodadvances.2018024489.
6. Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb Haemost.* 2006;4(4):759-765. doi: 10.1111/j.1538-7836.2006.01787.x
7. Cuker A, Cines DB. How I treat heparin-induced thrombocytopenia. *Blood.* 2012;119(10):2209-2218. doi: 10.1182/blood-2011-11-376293.
8. Elmer P, Passero FC, Xavier M. Retrospective Analysis of Heparin-Induced Thrombocytopenia Management at a Large Tertiary Hospital. *J Hematol.* 2014;3(2):27-33. doi: http://dx.doi.org/10.14740/jh157w.
9. Goldman R, Ustun B, Levine RL. Retrospective cost analysis of testing for HIT antibodies in a community hospital. *Blood.* 2008;112(11):4544.
10. Cuker A. Heparin-induced thrombocytopenia (HIT) in 2011: an epidemic of overdiagnosis. *Thromb Haemost.* 2011;106(6):993-994. doi: 10.1160/TH11-09-0677.
11. Warkentin TE. Heparin-induced thrombocytopenia in critically ill patients. *Semin Thromb Hemost.* 2015;41(5):49-60. doi: 10.1055/s-0034-1398381.
12. Caton S, O'Brien E, Pannelay AJ, Cook RG. Assessing the clinical and cost impact of on-demand immunoassay testing for the diagnosis of heparin-induced thrombocytopenia. *Thromb Res.* 2016;140:155-162. doi: 10.1016/j.thromres.2016.01.025
13. Nanwa N, Mittmann N, Knowles S, et al. The direct medical costs associated with suspected heparin-induced thrombocytopenia. *Pharmacoeconomics.* 2011;29(6):511-520. doi: 10.2165/11584330-000000000-00000.
14. Cuker A, Gimotty PA, Crowther MA, Warkentin TE. Predictive value of the 4Ts scoring system for heparin-induced thrombocytopenia: a systematic review and meta-analysis. *Blood.* 2012;120(20):4160-4167. doi: 10.1182/blood-2012-07-443051.
15. Fiorenza MA, Frazee EN, Personett HA, Dierkhising RA, Schramm GE. Assessment of a modified 4T scoring system for heparin-induced thrombocytopenia in critically ill patients. *J Crit Care.* 2014;29(3):426-431. doi: 10.1016/j.jcrc.2013.12.010.
16. Crowther M, Cook D, Guyatt G, et al. Heparin-induced thrombocytopenia in the critically ill: interpreting the 4Ts test in a randomized trial. *J Crit Care.* 2014;29(3):470.e7-470.e15 doi: 10.1016/j.jcrc.2014.02.004.
17. Hicks LK, Bering H, Carson KR, et al. The ASH Choosing Wisely campaign: five hematologic tests and treatments to question. *Blood.* 2013;122(24):3879-3883. doi: 10.1182/blood-2013-07-518423.
18. Doepker B, Mount KL, Ryder LJ, Gerlach AT, Murphy CV, Philips GS. Bleeding risk factors associated with argatroban therapy in the critically ill. *J Thromb Thrombolysis.* 2012;34(4):491-498. doi: 10.1007/s11239-012-0758-y.
19. Marler J, Unzaga J, Stelts S, Oliphant CS. Consequences of treating false positive heparin-induced thrombocytopenia. *J Thromb Thrombolysis.* 2015;40(4):512-514. doi: 10.1007/s11239-015-1236-0.
20. Fowler RA, Mittmann N, Geerts W, et al. Cost-effectiveness of dalteparin vs unfractionated heparin for the prevention of venous thromboembolism in critically ill patients. *JAMA.* 2014;312(20):2135-2145. doi: 10.1001/jama.2014.15101.
21. Warkentin TE, Sheppard JI, Moore JC, Sigouin CS, Kelton JG. Quantitative interpretation of optical density measurements using PF4-dependent enzyme-immunoassays. *J Thromb Haemost.* 2008;6(8):1304-1312. doi: 10.1111/j.1538-7836.2008.03025.x.

Every Nook and Cranny

Siddharth Jain[1]; James Pile[2]; Nitin Gupta[3]; Nathan Houchens[4,5]; Rama Chaudhry[6]; Neeraj Nischal[1]*

This icon represents the patient's case. Each paragraph that follows represents the discussant's thoughts.

[1]*Department of Medicine, All India Institute of Medical Sciences, New Delhi, India;* [2]*Department of Medicine, MetroHealth Medical Center at Case Western Reserve University, Cleveland, Ohio;* [3]*Departments of Medicine and Microbiology, All India Institute of Medical Sciences, New Delhi, India;* [4]*Medicine Service, Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, Michigan;* [5]*Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan;* [6]*Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India.*

A 46-year-old man presented to the emergency room in the postmonsoon month of September with a seven-day history of high fevers as well as a four-day history of a dry cough, dyspnea, and progressive rash. The patient reported no chest pain, hemoptysis, chest tightness, palpitations, wheezing, orthopnea, paroxysmal nocturnal dyspnea, or leg swelling. He lived and sought healthcare in Delhi, India.

Fever followed by a progressive but as yet uncharacterized rash and pulmonary symptoms in a middle-aged man suggests a host of possibilities. While it is tempting to ascribe his symptoms to an infectious process, especially a "tropical" infection based on his residence in Delhi, the location may simply represent a red herring. Potential infections can be divided into those endemic to the Indian subcontinent, and those encountered more globally. The former include diseases such as measles and dengue, while the latter include entities such as *Mycoplasma* pneumonia, varicella, and acute human immunodeficiency virus (HIV) infection. Noninfectious categories of diseases that should be considered include drug reactions and rheumatologic processes. Several rheumatologic diseases, including granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, and systemic lupus erythematosus (SLE) may present with fever, rash, and pulmonary symptomatology.

A history of the patient's exposures, both environmental and pharmaceutical, should be obtained. More information regarding his immunization history, rash characteristics (distribution and nature of the lesions), and other salient exam findings such as organomegaly and joint abnormalities will be helpful.

Fever reached a maximum of 103° Fahrenheit and was associated with chills but not rigors. There were several fever spikes daily, relieved completely with antipyretics. The patient's dyspnea was predominantly noted on exertion, nonpleuritic, not temporally related to cough, and progressively worsening over three days. The skin lesions were first noticed on his trunk and were described as reddish, flat, and pinpoint size. However, the rash spread to the face and extremities sparing the palms and soles. There was no bleeding, nausea, vomiting, abdominal pain, change in bowel habits, dysuria, headache, photophobia, neck stiffness, or joint pain.

The patient reported no significant past medical history, took no medications, and had no recent travel outside of Delhi, India in the past year. He was married and monogamous. He had no pets nor did he report any contact with animals. He did not use tobacco, alcohol, or illicit substances. He did not remember being bitten by an insect. He worked as a software engineer. There was no history of similar illness in the patient's family or at his workplace. He had no history of recent blood transfusion or immunization (including MMR and Tdap).

Several noninfectious and inflammatory conditions can explain his symptoms. Eosinophilic granulomatosis with polyangiitis is considerably less likely in the absence of asthma, and vasculitic processes, in general, are less likely given the nongravity dependent nature of the rash. SLE and sarcoidosis are possible causes of a systemic inflammatory illness presenting acutely with fever, rash, and pulmonary symptoms.

The patient's expanded history makes several infections less likely. Although much of the presentation is consistent with measles, the initial appearance of the truncal rash is atypical, and there is no mention of coryza or conjunctivitis. Likewise, the description of the exanthem is not suggestive of varicella, and dengue and chikungunya are much less likely in the absence of a headache and arthralgias. Other infections including leptospirosis and scrub typhus are possible, and both might be contracted in greater Delhi. Typhoid is another infectious syndrome endemic to the Indian subcontinent that should be considered. The presence of rash involving the face and extremities would be highly atypical, however; and the presence of dyspnea and the absence of a headache argue against typhoid. Acute HIV infection and *Mycoplasma* pneumonia remain possible diagnoses. Toxic shock syndrome is possible, but a faster and fulminant course would be expected.

On physical examination, the temperature was 103° Fahrenheit, heart rate was 120 beats per minute and

***Corresponding Author:** Neeraj Nischal; E-mail: neerajnischal@gmail.com; Telephone: +919811484060

Published online first March 20, 2019.

Received: September 4, 2018; **Revised**: December 22, 2018; **Accepted**: January 6, 2019

 DOI 10.12788/jhm.3163

regular, respiratory rate was 24 breaths per minute, blood pressure was 100/60 mm Hg, and resting oxygen saturation was 93% while breathing ambient air. He appeared uncomfortable. Jugular venous pulse was elevated at 10 cm H_2O. Mild icterus was present, but there was neither conjunctival congestion nor subconjunctival hemorrhage. S1 and S2 heart sounds were loud, but there were no murmurs. Chest auscultation revealed bilateral basal coarse crackles. The abdominal right upper quadrant was mildly tender to palpation, and the liver edge was palpable 2 cm below the subcostal margin. There was neither splenomegaly nor peripheral lymphadenopathy. Kernig and Brudzinski signs were negative, and there were no focal neurological deficits. A generalized, nonpalpable, maculopapular and petechial rash was present on the face, extremities, and trunk.

The patient's presentation must now incorporate the additional findings of bibasilar chest crackles, maculopapular/petechial rash, icterus, modest hypoxia, and hepatomegaly. Some of the noninfectious entities already mentioned (SLE and sarcoidosis) remain possible explanations. Hemophagocytic lymphohistiocytosis (HLH) may also explain most of the patient's presenting signs and symptoms, and several other infectious diseases account for his presentation. Scrub typhus (or a more uncommon rickettsia disease, Indian tick typhus), leptospirosis, and perhaps infective endocarditis seem most likely to provide a unifying diagnosis for the symptoms mentioned above. Leptospirosis presents in a minority of instances as a severe illness known as Weil disease, characterized by several of this patient's findings including icterus, kidney injury, and pulmonary symptoms. However, the rash is relatively uncommon in leptospirosis and when present, is usually more localized. The patient's rash as described is not typically expected in infective endocarditis, although high-grade *Staphylococcus aureus* bacteremia will occasionally present with a diffuse rash that may be confused with that of meningococcemia. The etiology of the patient's elevated jugular venous pressure is not readily apparent, with the cardiac examination making acute valvular insufficiency much less likely. Myocarditis, however, is possible in the setting of several of the diseases listed above, including leptospirosis, scrub typhus, SLE, and dengue.

In addition to basic laboratory studies and a chest radiograph, multiple sets of blood cultures should be obtained, along with a transthoracic echocardiogram and a ferritin level. The evidence to support leptospirosis and scrub typhus is strong enough to justify empiric use of doxycycline once the blood cultures are obtained, especially given the difficulty in definitively diagnosing these diseases in a timely fashion.

Laboratory analysis revealed a total leukocyte count of 13,600/uL (85% neutrophils), hemoglobin 10 g/dL, and platelet count 35,000/uL. Absolute eosinophil count was 136/uL. Serum chemistry showed sodium of 145 meq/L, potassium 4.1 meq/L, blood urea nitrogen 80 mg/dL, creatinine 1.6 mg/dL, aspartate transaminase (AST) 44 U/L (normal, 0-40), alanine transaminase (ALT) 81 U/L (normal, 0-40), direct bilirubin 3 mg/dL, and indirect bilirubin 3 mg/dL. Lactate dehydrogenase, alkaline phosphatase, albumin, and coagulation studies were normal. Erythrocyte sedimentation rate (ESR) was 42 mm (normal, 0-25) and highly sensitive C-reactive protein was 42 mg/L (normal, 0-10). Arterial blood gas on ambient air revealed a pH of 7.52, $PaCO_2$ 24 mm Hg, PaO_2 55 mm Hg, and bicarbonate 20 meq/L. Urinalysis was normal. Blood cultures were obtained. Electrocardiogram (ECG) showed regular narrow complex tachycardia with incomplete left bundle branch block. Old ECGs were not available for comparison. Chest radiograph showed bilateral air space opacities with evidence of vein cephalization. Abdominal and pelvis ultrasonography showed pericholecystic fluid and mild hepatomegaly, but no free fluid, pleural effusion, or evidence of cholecystitis. Point of care immunochromatographic rapid malarial antigen detection test (detects *Plasmodium falciparum*, *Plasmodium vivax, Plasmodium malaria,* and *Plasmodium ovale)* was negative.

Most of the findings described are commonly observed in both scrub typhus and leptospirosis, including cytopenias, parenchymal infiltrates, hepatomegaly, elevated transaminases and bilirubin, cardiac involvement, fever, and rash. The rash described is more consistent with scrub typhus than with leptospirosis. The absence of a headache and joint findings argue modestly against these diagnoses. Likewise, HLH provides an adequate explanation for most of the patient's symptoms, signs, and test results. These include fever, lung involvement, rash, hepatomegaly, elevated bilirubin, and cytopenias; however, leukocytosis and cardiac involvement are less characteristic. SLE also provides a satisfactory explanation for much of the symptoms, although the rash characteristics, normal urinalysis, and leukocytosis make this diagnosis less likely.

Additional testing that should be performed includes serum antinuclear antibody (ANA) and ferritin, since the latter may be markedly elevated in the setting of HLH. Bone marrow aspirate and biopsy should be performed looking specifically for evidence of hemophagocytosis. Finally, a transthoracic echocardiogram (TTE) should be performed to assess evidence of myocardial dysfunction as it may alter the therapeutic approach, although the results will be unlikely to differentiate between the preceding considerations.

Troponin I was negative, but N-terminal probrain natriuretic peptide was elevated at 20,000 pg/mL (normal, 0-900). D-dimer was negative. TTE showed left ventricular ejection fraction (LVEF) of 35% with global left ventricular hypokinesis. On three separate examinations, the peripheral blood smear did not show malarial parasites, atypical lymphocytes, or schistocytes. Three sets of blood cultures, testing for bacteria and fungi, were sterile. A throat culture was sterile. Widal test, as well as *Leptospira* and *Mycoplasma* serologies, were negative. Serology for *Legionella pneumophila* was positive, but the urinary antigen testing was negative. Antibodies to HIV 1 and 2 and anti-hepatitis C virus (HCV) antibody were negative. Dengue IgM ELISA (qualitative) returned positive.

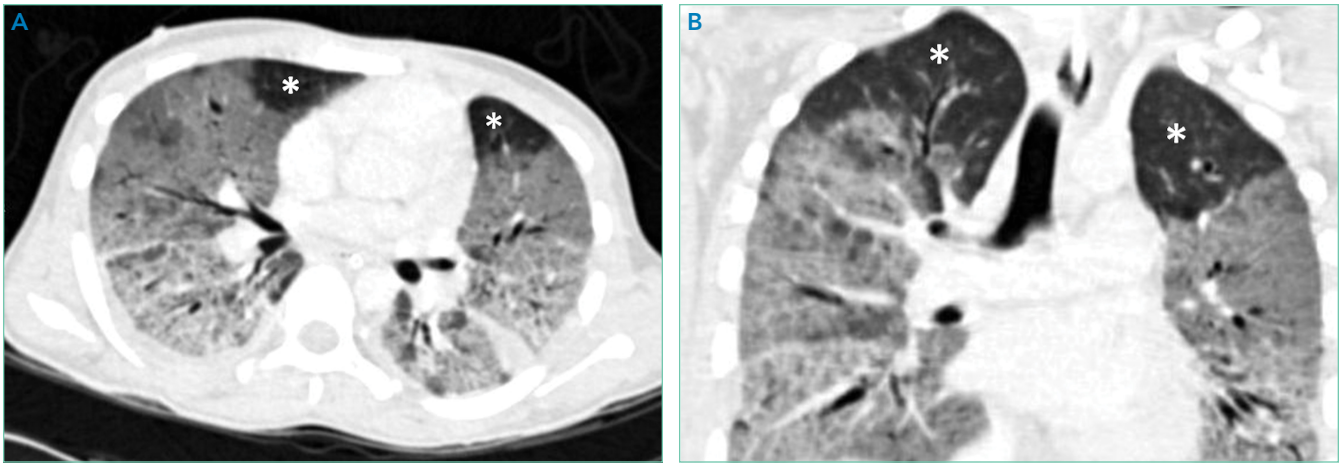


FIG 1. Axial (A) and coronal (B) computed tomography of the thorax showing extensive ground-glass opacities and consolidation sparing the nondependent portions of the lungs (apices and anterior segments, asterisks).

Despite the absence of arthralgias, myalgias, headache, and retro-orbital pain, a positive dengue IgM ELISA supports acute dengue infection, provided the patient did not experience an unexplained febrile illness in the previous months. Most of his presentation may be explained by dengue, including fever, rash, liver abnormalities, myocardial dysfunction, and thrombocytopenia. The bilateral airspace opacities seen on chest radiograph also fit reasonably provided these actually reflect pulmonary edema. Leukocytosis (as opposed to leukopenia) is highly unexpected in dengue, but its presence could be an outlier.

If dengue does indeed explain the entire presentation, defervescence should have occurred by the time the blood cultures and serologic studies returned. Also, by that time, the patient would be expected to demonstrate evidence of improvement, barring the appearance of the serious complications of dengue hemorrhagic fever/dengue shock syndrome. Should fever persist and signs of recovery fail to materialize, the possibility of a superimposed process will need to be considered. Of note, the sensitivity of *Leptospira* serology early in the course of illness is low, and leptospirosis is thus not yet excluded.

A presumptive diagnosis of severe dengue fever was made, based on evidence of pulmonary edema and sepsis. The patient was managed conservatively with oral fluid restriction, low dose of diuretics, and supplemental oxygenation. The patient was also given levofloxacin for possible legionellosis. Despite these therapies, the patient had no improvement in 24 hours. His tachypnea increased, and his measured PaO_2 to FIO_2 (P:F) ratio decreased to 230 from 285 on admission. This prompted the initiation of BiPAP at 10 cm H_2O inspiration PAP and 5 cm H_2O expiration PAP. However, he did not tolerate BiPAP, and his P:F ratio decreased to below 200.

The patient was transferred to the intensive care unit and underwent elective intubation with mechanical ventilation. Axial and coronal computed tomography of the thorax (Figure 1A and 1B, respectively) showed extensive ground-glass opacities and consolidation sparing the nondependent portions of the lungs. On physical inspection, a round, well-defined, painless black lesion surrounded by erythema was noticed in the right axilla (Figure 2). The rest of the examination findings were unchanged.

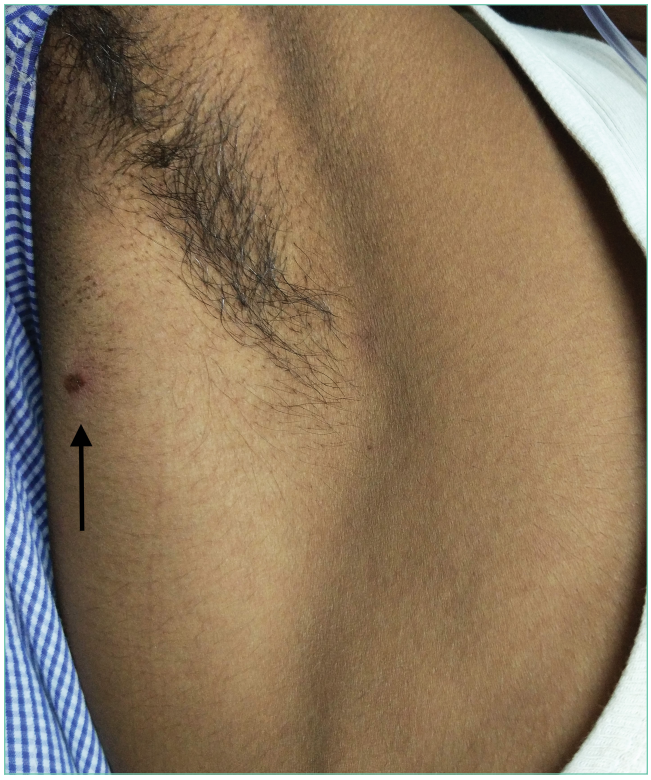


FIG 2. Eschar (arrow) in the right axillary region.

The discovery of eschar in the axilla provides a "pivot point" in determining the cause of the patient's illness. This finding appears to point, with high specificity, toward rickettsia as the explanation of the patient's disease, and this is most likely to be scrub typhus. The report of a positive dengue IgM may repre-

sent concurrent infection or may simply reflect a recent infection in an area that is highly endemic for dengue. Although most of the patient's clinical presentation could be attributed to dengue, multiple features including the leukocytosis, myocarditis, and elevated bilirubin are more likely to be seen in scrub typhus. In any event, dengue cannot satisfactorily explain the eschar.

No mention has been made to the initiation of doxycycline thus far; this agent needs to be started promptly. Polymerase chain reaction (PCR) testing for scrub typhus should be ordered if available; if not, acute and convalescent serology may be obtained.

Given the finding of axillary eschar, the patient was diagnosed with scrub typhus. Doxycycline 100 mg by nasogastric tube twice a day was initiated. The patient began to show marked symptomatic improvement. His P:F ratio improved, and he was successfully weaned off and extubated after 24 hours. Postextubation, he was kept on BiPAP for 12 hours. He was transferred out of the ICU and monitored for 72 hours. With therapy, his cytopenias, liver and renal function, and ECG normalized. Indirect immunofluorescence assay for scrub typhus returned positive at a dilution of > 1:512. PCR assay targeting the 56 kDa region of *Orientia tsutsugamushi* was also positive. Repeated TTE showed an LVEF of 65%. He was subsequently discharged with oral doxycycline and a plan to complete a course of 14 days on an outpatient basis. The final diagnosis was scrub typhus with myocarditis leading to acutely decompensated heart failure with reduced ejection fraction.

DISCUSSION

Scrub typhus is a mite-borne tropical infection caused by the gram-negative intracellular parasite *Orientia tsutsugamushi* from the Rickettsiaceae family that is known to occur in certain parts of Asia and Australia. Although this entity is well known in the Sub Himalayan belt and southern part of India, very few cases have been described in Delhi, the capital state in North India. Scrub typhus, like most other tropical infections, is found most often during the postmonsoon season.[1,2]

Patients with scrub typhus present with fever in addition to a variety of nonspecific symptoms and findings. These often manifest within 10 days of being bitten by a mite. Malaise, headache, myalgias, lymphadenopathy, and maculopapular or petechial rash are common. If present, the rash manifests on the 3rd to 5th day of fever.[3] Disseminated vasculitis due to scrub typhus can frequently result in multiorgan system involvement. Pulmonary involvement often leads to acute respiratory distress syndrome (ARDS) with an incidence of 8%-10%.[1,4] Acute kidney injury, mostly mild and nonoliguric, has been reported in up to 2/3 cases.[4-6] The cardiac myocyte is a known target cell affected by scrub typhus, and therefore patients commonly present with myocarditis.[7] Liver involvement in scrub typhus is evident through elevated liver enzymes and can occur without other clinical evidence of the illness.[4,6,8,9] As in dengue, patients often develop thrombocytopenia, but normal hemoglobin in scrub typhus differentiates it from dengue.[6,8]

Given the nonspecific presentation, it can be challenging to diagnose and treat scrub typhus. The gold standard for diagnosis is the detection of IgM antibodies to *Orientia tsutsugamushi* using an indirect immunofluorescence assay (IFA). For patients from endemic regions, it may be necessary to show a four-fold increase in titers two weeks apart to distinguish from background immunity. Presence of the characteristic eschar, as discussed below, is highly suggestive of scrub typhus. The treatment of choice is doxycycline or azithromycin for seven days.[10,11] Early initiation of doxycycline when considering either scrub typhus or leptospirosis is appropriate and may be life-saving.

Medical decision making is fraught with uncertainty, and physicians must use their experience, evidence base, and cognitive heuristics wisely to care for patients effectively. For this patient, the region of Delhi experiences massive outbreaks of dengue every year during the time the patient presented to the hospital, whereas rickettsia infections are relatively uncommon. The clinical presentation was conceivably consistent with either dengue or scrub typhus, though somewhat more suggestive of the latter. Once the serological diagnosis of recent or concomitant dengue was obtained, however, scrub typhus was considered even less. The team called upon Occam's razor or the heuristic that the simplest and most unifying explanation for any given problem is the one most likely to be correct and that other, less satisfactory explanations (in this case, scrub typhus) are "shaven off." The patient was managed conservatively for dengue. Only when his condition worsened did the team recognize this conflicting information without dismissing it, consider alternative possibilities, and reexamined the patient.

An eschar can be an important clue in the diagnosis of scrub typhus, though it is not often obvious. The presence of this necrotic skin lesion with black crust is highly suggestive of scrub typhus, and in the right clinical context, it is virtually diagnostic. However, it is uncommon (9.5%-45%) in most of the studies from the Indian subcontinent (ie, high specificity but low sensitivity).[1,12] An eschar is often found in obscure locations such as the axillae or groin, areas that may easily be missed or overlooked. Eschars may be seen in a variety of other infectious diseases, including rickettsia pox, Rocky Mountain spotted fever, other members of the spotted fever group, tularemia, and cutaneous anthrax. Given this patient's lack of improvement, repeated examination revealed an eschar in the right axilla, a finding that was either missed or still evolving at the time of presentation.

This case illustrates the challenges in interpreting the significance of multiple positive serological tests in the context of an undifferentiated clinical syndrome. Possible reasons for a positive dengue serology could have been persistent antibodies from a previous infection, recent asymptomatic infection, concurrent infection, or cross-reactivity with flaviviruses such as West Nile Virus or Japanese Encephalitis.[13] The patient also had positive IgM antibodies against *Legionella pneumophila*, but the urinary antigen was negative. In view of a negative antigen test, low specificity of the serologic test,

low incidence of legionellosis in the Indian subcontinent, and absence of therapeutic response to a trial of fluoroquinolones, the diagnosis of legionellosis was considered unlikely in this patient.

With rapid advancements in technology, the importance of history taking and physical examination is at risk of being overshadowed. Approximately 80% of correct diagnoses in medicine can arrive through history and physical examination alone.[14,15] In this case, Occam's razor combined with multiple serological tests was relied on to create the likely list of diagnoses. However, recognition of the limitations of these heuristics and tests proved critical. The life-saving diagnosis was only made when the clinicians returned to basics, looked in every nook and cranny, and found the eschar on physical examination.

KEY TEACHING POINTS

- In patients living in endemic areas who present with an acute febrile illness, the differential diagnosis should include "tropical" infections such as dengue, chikungunya, enteric fever, leptospirosis, malaria, and scrub typhus.
- Serology is commonly employed for diagnosis of tropical infections, which may be misleading. These tests can be falsely positive from past asymptomatic infection or cross reactivity between antibodies, or falsely negative, as in the first few days of infection.
- Presence of eschar is a very useful clue in the diagnosis of scrub typhus, but this finding can be missed since it is often found in obscure locations. A thorough clinical history and physical examination are paramount.

Disclosures: The authors do not report any conflict of interest.

References

1. Gupta N, Chaudhry R, Kabra SK, et al. In search of scrub typhus: a prospective analysis of clinical and epidemiological profile of patients from a tertiary care hospital in New Delhi. *Adv Infect Dis.* 2015;5(4):140. doi: 10.4236/aid.2015.54017.
2. Kamarasu K, Malathi M, Rajagopal V, Subramani K, Jagadeeshramasamy D, Mathai E. Serological evidence for the wide distribution of spotted fevers & typhus fever in Tamil Nadu. *Indian J Med Res.* 2007;126(2):128-130.
3. Mahajan SK. Scrub typhus. *J Assoc Physicians India.* 2005;53:954-958.
4. Mahajan SK, Rolain JM, Kashyap R, et al. Scrub typhus in the Himalayas. *Emerg Infect Dis.* 2006;12(10):1590-1592. doi: 10.3201/eid1210.051697.
5. Attur RP, Kuppasamy S, Bairy M, et al. Acute kidney injury in scrub typhus. *Clin Exp Nephrol.* 2013;17(5):725-729. doi: 10.1007/s10157-012-0753-9.
6. Varghese GM, Trowbridge P, Janardhanan J, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis.* 2014;23:39-43. doi: 10.1016/j.ijid.2014.02.009.
7. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (Orientia tsutsugamushi). *PLoS Negl Trop Dis.* 2015;9(8):e0003971. doi.org/10.1371/journal.pntd.0003971
8. Chrispal A, Boorugu H, Gopinath KG, et al. Scrub typhus: an unrecognized threat in South India-clinical profile and predictors of mortality. *Trop Doct.* 2010;40(3):129-133. doi: 10.1258/td.2010.090452. 9. Mathai E, Rolain JM, Verghese GM, et al. Outbreak of scrub typhus in southern India during the cooler months. *Ann N Y Acad Sci.* 2003;990:359-364. doi: 10.1111/j.1749-6632.2003.tb07391.x
10. Gupta N, Chaudhry R, Kabra SK, et al. Comparative evaluation of serological and molecular methods for the diagnosis of scrub typhus in Indian settings. *Jpn J Infect Dis.* 2017;70(2):221-222. doi: 10.7883/yoken.JJID.2016.139.
11. Rahi M, Gupte MD, Bhargava A, Varghese GM, Arora R. DHR-ICMR Guidelines for diagnosis & management of Rickettsial diseases in India. *Indian J Med Res.* 2015;141(4):417-422. doi: 10.4103/0971-5916.159279.
12. Sharma A, Mahajan S, Gupta ML, Kanga A, Sharma V. Investigation of an outbreak of scrub typhus in the Himalayan region of India. *Jpn J Infect Dis.* 2005;58(4):208-210.
13. Gupta N, Chaudhry R, Mirdha B, et al. Scrub typhus and leptospirosis: the fallacy of diagnosing with IgM enzyme-linked immunosorbent assay. *J Microb Biochem Technol.* 2016;8:71-75. doi: 10.4172/1948-5948.1000265.
14. Peterson MC, Holbrook JH, Von Hales D, Smith NL, Staker LV. Contributions of the history, physical examination, and laboratory investigation in making medical diagnoses. *West J Med.* 1992;156(2):163-165. doi: 10.1097/00006254-199210000-00013
15. Roshan M, Rao AP. A study on relative contributions of the history, physical examination and investigations in making a medical diagnosis. *J Assoc Physicians India.* 2000;48(8):771-775.

Hospital at Home and Emergence of the Home Hospitalist

Per Danielsson, MD[1]*; Bruce Leff, MD[2]

[1]Hospital Medicine Program, Swedish Health Services, Seattle, Washington; [2]Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Ms. P., an 86-year-old woman with a history of hypertension, hyperlipidemia, coronary artery disease, and transient ischemic attack, presents to the emergency department with a three-day history of cough, fever, purulent sputum, fatigue, and dyspnea on exertion. Her vital signs are notable for a fever of 39.0°C, blood pressure 136/92, pulse 102, respiratory rate 30, and room air oxygen saturation of 91%. She looks ill. She has a white blood cell count of 16,000, lactate 1.9, and a right lower lobe infiltrate on imaging. The emergency department attending physician presents the case to you for admission, and you accept the patient into your inpatient hospitalist service.

Now, let's imagine a different future in which you are the attending hospitalist on your institution's Hospital at Home (HaH) service, where you will provide hospital-level care to Ms. P. in the comfort of her own home. Hospitalists should prepare for this paradigm shift.

WHAT IS HOSPITAL AT HOME?

HaH provides hospital-level care in a patient's home, for those with qualifying acute illnesses and appropriate degrees of acuity, as a substitute for traditional inpatient care.[1] This is achieved by bringing the critical elements of hospital care to the home—physician and nursing care, intravenous medications and fluids, oxygen and respiratory therapies, basic radiography and ultrasound, durable medical equipment, skilled therapies, and more.[2]

All hospitalists have cared for patients like Ms. P., and she and many patients like her will have a straightforward hospital trajectory: initial evaluation in the emergency department, inpatient care provided by a hospitalist inpatient service, a few days of intravenous antibiotics and other hospital services, and finally, discharge to home.

A SHARED RATIONALE FOR HOSPITAL MEDICINE AND HOSPITAL AT HOME

However, not all patients will experience a smooth, or safe, hospital course. Studies that launched the hospital safety movement also provide the rationale for HaH, namely, that hospitals are often dangerous environments for patients.[3]

***Corresponding Author:** Per Danielsson, MD; E-mail: per.danielsson@swedish.org; Telephone: 206-215-2370.

Published online first March 20, 2019.

Received: November 12, 2018; **Revised**: December 28, 2018; **Accepted**: January 6, 2019.

A complementary approach to improving outcomes for patients at high risk of iatrogenic illness such as functional decline, falls, delirium, adverse drug events, and hospital-associated disability syndrome,[4-6] is to care for patients outside the traditional inpatient hospital environment. Over the past 20 years, many studies—including dozens of randomized controlled trials and several meta-analyses—have shown better outcomes for patients cared for in HaH: decreased length of stay, decreased incidence of adverse events (including substantially lower six-month mortality), better patient and caregiver care experiences, lower caregiver stress, and lower costs.[7-9]A recent Center for Medicare and Medicaid Innovation (CMMI) Demonstration conducted at the Mount Sinai Health System found similar results.[10]

GROWING INTEREST IN HOSPITAL AT HOME AND CHALLENGES TO DISSEMINATION

Interest in HaH has increased markedly over the past few years with increased penetration of Medicare and Medicaid managed care, the development and spread of accountable care organizations (ACOs), and a shift in focus among some health systems towards value-based care, population health, and community-based care. Recently, commercial entities have entered the HaH space and have raised substantial capital to fund development. Despite this growing interest in HaH and substantial evidence of its effectiveness, HaH has not been widely implemented or scaled in the United States.

Widespread dissemination and implementation of HaH has been hampered by several barriers. First, despite growing interest in HaH, the culture of healthcare and health system leadership, for the most part, remains focused on facility-based care.[11]

Second, while HaH makes financial sense in the managed care arena, given the strong evidence for high-quality, lower-cost care, there is currently no standard payment mechanism for HaH in fee-for-service Medicare or in the commercial insurance space. However, there are indications that this may soon change. In the fall of 2017, a proposal for a bundled payment mechanism for acute HaH care plus 30 days of postacute care was unanimously approved by an Advisory Committee to the Secretary of the Department of Health and Human Services (HHS).[12,13] The HHS Secretary recently noted that "the Department of Health and Human Services is keenly interested in ideas for home-based, hospital-level care, and agrees … that this proposal holds promise for testing."[14]

Third is the need to create the logistics and supply chain to support HaH. There currently exists a well-established supply

chain for providing hospital care. A hospitalist orders a dose of intravenous antibiotic or oxygen, and it is supplied in a timely manner. Similarly, the postacute sector of healthcare has a robust supply chain, though it operates on a somewhat different clock from the acute care setting. However, there is currently no easily replicable supply chain to meet the needs of providing acute care in the home. Each HaH has had to create its own system of logistics with the existing healthcare assets in its local environment. Developing this capacity at scale will require significant capital investment.

There are examples where HaH has scaled. Beginning in 1994, in the state of Victoria, Australia (population 6.3 million), the health authority reimbursed HaH care at the same rates as traditional hospital care. At last report, HaH provided approximately 5% of all hospital bed days of care in Victoria. Providing HaH on this scale helped avoid the need to build a new 500-bed hospital to care for those patients.[15] The avoided costs of building new hospital beds (and the ongoing need to fill those beds) represents significant societal return on investment attributable to HaH.

EMERGENCE OF THE HOME HOSPITALIST?

A key element in implementing a HaH program is its physician staff in terms of the types of doctors who provide HaH care, how they are organized, and how they interact with patients. To date, HaH physicians have been predominantly geriatricians, but internists and family medicine physicians, employed as full-time members of a dedicated HaH team, also provide care by physically visiting patients in their homes. The reason for significant involvement of geriatricians in HaH may relate to the fact that geriatric fellowship training includes training in home-based medical care, whereas this is less common in family medicine and internal medicine residency training programs.

In order to provide HaH on a nationwide scale, there will be a need for a larger workforce. There is an opportunity here to leverage existing hospital physician staff, such as hospitalists. In addition, while there is significant value in physicians seeing patients in their homes, more scalable versions of HaH are being developed and implemented that leverage biometrically enhanced telemedicine approaches for a dedicated physician component of care, with in-person visits provided by other members of an interdisciplinary team.

We believe that hospitalists can play a key role as HaH physicians as the HaH model continues to evolve and expand. Hospitalists bring valuable expertise relevant to HaH care delivery, including extensive experience with the triage of acutely ill patients, an understanding of the natural course of acute illness and team-based care, and for some, experience with telemedicine care.

While a hospitalist providing HaH care would leverage many of the competencies of the traditional hospitalist, we suggest that such a provider should receive additional training and clinical experience in home-based medical care to help them better understand the unique aspects of providing care in patients' homes.[16] Such training could include experience in making house calls, which can be a transformational experience in helping physicians improve their skills in dealing with social determinants of health, diagnosing and managing geriatric syndromes, and mobilizing community resources in the care of their patients, as well as managing care transitions. Hospitalists delivering care in HaH may also need to upgrade specific clinical skills commonly addressed by home-based medical care providers: wound care, caregiver-related issues, social and ethical issues specific to home-based care, problems with functional status, psychiatric and cognitive issues, management of gastrostomy tubes and bladder catheters, dermatologic problems, as well as palliative care and end-of-life symptom management. These skills are slightly different from the usual realm of the typical hospitalists' wheelhouse. However, it is all learnable.[17] Similarly, geriatricians can learn from hospitalists as the HaH model evolves; there are HaH programs in existence today that take care of a sicker tranche of patients than earlier versions of HaH, with continuous telemonitoring of patients and the ability to rapidly deploy providers, labs, imaging, and medications. Going forward, as healthcare organizations begin to develop HaH programs staffed by hospitalists, it is probably wise for hospitalists and geriatricians to collaborate on the optimal physician models for HaH.

There may emerge a new specialty. Ticona and Schulman described a "home intensivist" with competencies including informatics of remote monitoring technology, leadership of multidisciplinary care teams, and the interpersonal skills required for compassionate end-of-life care.[18] We prefer the term Home Hospitalist. Home Hospitalists would develop an enhanced understanding of the transitions of care and social determinants of health, and they would gain valuable knowledge about the social and environmental challenges many patients face after discharge from the hospital.

When this vision is realized, there will be enormous benefits to both HaH and Hospital Medicine. HaH could tap into a large and competent workforce to enhance its implementation and dissemination. Hospital Medicine would gain a new pathway for its providers and could develop new collaborative efforts with geriatric, internal, and family medicine.

Disclosures: Dr. Danielsson has nothing to disclose. Dr. Leff reports personal fees from Medically Home, other from Dispatch Health, other from Landmark Health, personal fees from Medibank, personal fees from Apple, personal fees from Health Affairs, other from Honor, personal fees from Institute for Healthcare Improvement, outside the submitted work; and American Academy of Home Care Medicine - member board of directors, voluntary.

Funding: Dr. Leff was supported in this work by a grant from The John A. Hartford Foundation.

References

1. Leff B, Montalto M. Home hospital-toward a tighter definition. *J Am Geriatr Soc.* 2004;52(12):2141. doi: 10.1111/j.1532-5415.2004.52579_1.x.
2. Leff B, Burton L, Mader SL, et al. Hospital at home: feasibility and outcomes of a program to provide hospital-level care at home for acutely ill older patients. *Ann Intern Med.* 2005;143(11):798-808. doi: 10.7326/0003-4819-143-11-200512060-00008.
3. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negli-

gence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med.* 1991;324(6):370-376. doi: 10.1056/NEJM199102073240604.
4. Creditor MC. Hazards of hospitalization of the elderly. *Ann Intern Med.* 1993;118(3):219-223. doi: 10.7326/0003-4819-118-3-199302010-00011.
5. Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure". *JAMA.* 2011;306(16):1782-1793. doi: 10.1001/jama.2011.1556.
6. Wald HL. The Geometry of Patient Safety: Horizontal and Vertical Approaches to the Hazards of Hospitalization. *J Am Geriatr Soc.* 2017;65(12):2559-2561. doi: 10.1111/jgs.15049.
7. Shepperd S, Doll H, Angus RM, et al. Avoiding hospital admission through provision of hospital care at home: a systematic review and meta-analysis of individual patient data. *CMAJ.* 2009;180(2):175-182. doi: 10.1503/cmaj.081491.
8. Caplan GA, Sulaiman NS, Mangin N, et al. A meta-analysis of "Hospital in the Home". *Med J Aust.* 2012;197:512-519. doi: 10.5694/mja12.10480.
9. Shepperd S, Iliffe S, Doll HA, et al. Admission avoidance hospital at home. *Cochrane Database Syst Rev.* 2016;9:CD007491. doi: 10.1002/14651858.CD007491.pub2.
10. Federman AD, Soones T, DeCherrie LV, Leff B, Siu AL. Association of a bundled hospital-at-home and 30-day postacute transitional care program with clinical outcomes and patient experiences. *JAMA Intern Med.* 2018;178(8):1033-1040. doi: 10.1001/jamainternmed.2018.2562.
11. Stein PD, Hull RD, Matta F, Willyerd GL. Modest response in translation to home management of deep venous thrombosis. *Am J Med.* 2010;123(12):1107-1113. doi: 10.1016/j.amjmed.2010.07.016.
12. Icahn School of Medicine at Mount Sinai. "HaH-Plus" (Hospital at Home Plus) Provider Focused Payment Model. https://aspe.hhs.gov/system/files/pdf/255906/HaHPlusProviderFocusedPaymentModel.pdf. Accessed November 11, 2018.
13. Physician-Focused Payment Model Technical Advisory Committee. Report to the Secretary of Health and Human Services. Comments and Recommendation on "HaH-Plus (Hospital at Home Plus) Provider-Focused Payment Model. https://aspe.hhs.gov/system/files/pdf/255906/MtSinaiHAHReport-Secretary.pdf. Accessed November 11, 2018.
14. The Secretary of Health and Human Services. Response to the Report to the Secretary of Health and Human Services. Comments and Recommendation on "HaH-Plus (Hospital at Home Plus) Provider-Focused Payment Model. https://downloads.cms.gov/files/cmmi/ptac-hhssecresponse-oct17-may18.pdf. Accessed November 11, 2018.
15. Montalto M. The 500-bed hospital that isn't there: the Victorian Department of Health review of the Hospital in the Home program. *Med J Aust.* 2010;193(10);598-601.
16. Hayashi J, Leff B. *Geriatric Home-Based Medical Care.* New York, NY: Springer Publishers; 2015.
17. Reckrey JM, Ornstein KA, Wajnberg A, Kopke MV, DeCherrie LV. Teaching home-based primary care. *Home Healthc Now.* 2017;35(10):561-565. doi: 10.1097/NHH.0000000000000621.
18. Ticona L, Schulman KA. Extreme home makeover - the role of intensive home health care. *N Engl J Med.* 2016;375(18):1707-1709. doi: 10.1056/NEJMp1608301.

Transitions of Care with Incidental Pulmonary Nodules

Raudel Rodriguez, MD[1]*; Luci K. Leykum, MD, MBA, MSc[1,2]

[1]*University of Texas Health Science Center at San Antonio, San Antonio, Texas;* [2]*South Texas Veterans Health Care System, San Antonio, Texas.*

With advancement in imaging techniques, incidental pulmonary nodules (IPNs) are routinely found on imaging studies. Depending on the size, an IPN has diagnostic uncertainty. Is it a benign finding? Will it progress to cancer? These questions have the potential to create anxiety for our patients. Between 2012 and 2014, 19,739 patients were discharged from hospitals in the United States with a diagnosis of a solitary pulmonary nodule.[1] Roughly 7,500 were discharged after an inpatient stay; the remainder from the emergency room. Aggregate costs for these visits totaled $49 million. The exact number of nodules receiving follow-up is unknown.

The Fleischner guidelines, updated in 2017, outline management for IPNs.[2] Depending on nodule size and patient risk factors, repeat imaging is either not indicated or one to two follow-up scans could be recommended. In this issue of the *Journal of Hospital Medicine*®, two reports assess provider awareness of the Fleischner guidelines and examine the proportion of patients receiving follow-up.

Umscheid et al. surveyed hospitalists to understand their approach IPN management. Of 174 respondents, 42% were unfamiliar with the Fleischner guidelines.[3] The authors proposed methods for improving provider awareness, including better communication between hospitalists and primary care providers, better documentation, and in the case of their institution, the development of an IPN consult team. The IPN consult team is composed of a nurse practitioner and pulmonologist. They inform primary care providers of patient findings and need for follow-up. If no follow-up is made, the team will see the patients in an IPN ambulatory clinic to ensure follow-up imaging is obtained.

Kwan et al. found that fewer than 50% of patients with high-risk new pulmonary nodules received follow-up.[4] Although a single-site study, the study is consistent with prior work on tests pending at discharge, which essentially show that there are poor follow-up rates.[5,6] Follow-up was more likely when the IPN was mentioned in the discharge summary. This conclusion builds on previous work showing that IPNs are more likely to be included in a discharge summary if the nodule is noted in the report heading, the radiologist recommends further imaging, and the patient is discharged from a medicine service as opposed to a surgical service.[7] IPN follow-up is less likely if results are mentioned in the findings section alone.[5]

IPN follow-up is a piece of a larger issue of how best to ensure appropriate follow-up of any tests pending after discharge. A systematic review of discharge interventions found improvement in follow-up when discharge summaries are combined with e-mail alerts.[6] A study of the effects of integrated electronic health records (EHR) web modules with discharge specific instructions showed an increase in follow-up from 18% to 27%.[8] Studies also consider provider-to-patient communication. One intervention uses the patient portal to remind patients to pick up their medications,[9] finding a decrease in nonadherence from 65.5% to 22.2%. Engaging patients by way of patient portals and reminders are an effective way to hold both the physician and the patient accountable for follow-up. Mobile technologies studied in the emergency department show patient preferences toward texting to receive medication and appointment reminders.[10] Given wide-spread adoption of mobile technologies,[11] notification systems could leverage applications or texting modalities to keep patients informed of discharge appointments and follow-up imaging studies. Similar interventions could be designed for IPNs using the Fleischner guidelines, generating alerts when patients have not received follow-up imaging.

The number of IPNs identified in the hospital will likely remain in the tens of thousands. From the hospitalist perspective, the findings presented in this month's *Journal of Hospital Medicine* suggest that patients be educated about their findings and recommended follow-up, that follow-up be arranged before discharge, and that findings are clearly documented for patients and primary care providers to review. More study into how to implement these enhancements is needed to guide how we focus educational, systems, and technological interventions. Further study is also needed to help understand the complexities of communication channels between hospitalists and primary care physicians. As hospitalist workflow is more integrated with the EHR and mobile technology, future interventions can facilitate follow-up, keeping all providers and, most importantly, the patient aware of the next steps in care.

Acknowledgments:

Author support is provided by the South Texas Veterans Health Care System. The views expressed are those of the authors and do not reflect the position or policy of the Department of Veterans Affairs.

Disclosures: The authors report no financial conflicts of interest.

References

1. HCUPNet: A tool for identifying, tracking and analyzing national hospital sta-

***Corresponding Author:** Raudel Rodriguez, MD; E-mail: RodriguezRS@uthscsa.edu; Telephone: 210-567-0777.

Received: January 19, 2019; **Revised**: March 5, 2019; **Accepted**: March 6, 2019

 DOI 10.12788/jhm.3199

tistics (2018). Retrieved from https://hcupnet.ahrq.gov/#setup on 10/25/2019
2. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT Images: from the Fleischner Society 2017. *Radiology*. 2017;284(1):228-243. doi: 10.1148/radiol.2017161659.
3. Umscheid CA, Wilen J, Garin M, et al. National Survey of Hospitalists' experiences with incidental pulmonary nodules. *J Hosp Med*. 2019;14(6):353-356. doi: 10.12788/jhm.3115.
4. Kwan JL, Yermak D, Markell L, Paul NS, Shojania KG, Cram P. Follow-up of incidental high-risk pulmonary nodules on computed tomography pulmonary angiography at care transitions. *J Hosp Med*. 2019;14(6):349-352. doi: 10.12788/jhm.3128.
5. Blagev DP, Lloyd JF, Conner K, et al. Follow-up of incidental pulmonary nodules and the radiology report. *J Am Coll Radiol*. 2014;11(4):378-383. doi: 10.1016/j.jacr.2013.08.003.
7. Darragh PJ, Bodley T, Orchanian-cheff A, Shojania KG, Kwan JL, Cram P. A systematic review of interventions to follow-up test results pending at discharge. *J Gen Intern Med*. 2018;33(5):750-758. doi: 10.1007/s11606-017-4290-9.
8. Bates R, Plooster C, Croghan I, Schroeder D, Mccoy C. Incidental pulmonary nodules reported on CT abdominal imaging: frequency and factors affecting inclusion in the hospital discharge summary. *J Hosp Med*. 2017;12(6):454-457. doi: 10.12788/jhm.2757.
9. Lacson R, Desai S, Landman A, Proctor R, Sumption S, Khorasani R. Impact of a health information technology intervention on the follow-up management of pulmonary nodules. *J Digit Imaging*. 2018;31(1):19-25. doi: 10.1007/s10278-017-9989-y.
10. Kerner DE, Knezevich EL. Use of communication tool within electronic medical record to improve primary nonadherence. *J Am Pharm Assoc* (2003). 2017;57(3S):S270-S273.e2. doi: 10.1016/j.japh.2017.03.009.
11. Ray M, Dayan PS, Pahalyants V, Chernick LS. Mobile health technology to communicate discharge and follow-up information to adolescents from the emergency department. *Pediatr Emerg Care*. 2016;32(12):900-905. doi: 10.1097/PEC.0000000000000970.
12. Gallagher R, Roach K, Sadler L, et al. Mobile technology use across age groups in patients eligible for cardiac rehabilitation: survey study. *JMIR mHealth uhealth*. 2017;5(10):e161. doi: 10.2196/mhealth.8352.

In Reference to: "Preventing Hypoglycemia Following Treatment of Hyperkalemia in Hospitalized Patients"

Ahmed Al-Sharefi, MB, ChB, MRCP(UK)[1]; Richard Quinton, MB, BChir, MD, FRCP(E)[2,3]; Graham Roberts, MB, BS, PhD, FRCPI[4,5,6]*

[1]Diabetes, Endocrinology and Metabolic Unit, Sunderland Royal Hospital, City Hospitals Sunderland NHS Foundation Trust, Sunderland, United Kingdom; [2]Endocrine Unit, The Royal Victoria Infirmary, Newcastle-upon-Tyne Hospitals NHS Foundation Trust, United Kingdom; [3]Institute of Genetic Medicine, University of Newcastle upon-Tyne, United Kingdom; [4]HRB-Clinical Research Facility, University College Cork, Cork, Ireland; [5]Diabetes Research Group, Swansea University, Swansea, United Kingdom; [6]Diabetes Translational Research Group, Diabetes Centre, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom.

Boughton et al.[1] reported a high incidence of hypoglycemia resulting from glucose-with-insulin (GwI) infusion used to treat acute hyperkalemia. This has been reported by other investigators—particularly in subjects without preexisting diabetes[2] and resonates with the experiences of clinicians practicing in Internal Medicine or Diabetes.

The authors suggested that patients at risk of hypoglycemia be identified and offered a regimen containing less insulin. However, for subjects without preexisting diagnosis and not at high risk of diabetes, we question the physiological logic and the safety basis for administering insulin.

Infusion of glucose only (GO) to subjects with intact pancreatic function and insulin sensitivity stimulates endogenous insulin secretion in a dose-dependent manner, resulting in a reduction in extracellular fluid potassium with no risk of hypoglycemia.[3,4]

It is unclear why GwI historically entered mainstream practice rather than GO, but the rationale may have been based on the potential risks of paradoxical hyperglycemia-mediated hyperkalemia (HMK) being induced by GO. In practice, HMK was only observed in subjects with diabetes.[5]

As there is an ongoing need to reduce the impact of iatrogenic hypoglycemia, revisiting of the prematurely abandoned GO regimen in hyperkalemia management is warranted. Such approach may offer a safe and physiological alternative to GwI in nondiabetic patients with hyperkalemia.

We advocate that GO be prospectively evaluated against GwI for the treatment of hyperkalemia in subjects without diabetes, against the endpoints being noninferiority in respect of efficacy and maintenance of euglycemia in respect of safety.

***Corresponding Author:** Graham Roberts, MB, BS, PhD, FRCPI; E-mail: Graham.roberts@hse.ie

Received: March 13, 2019;
Accepted: March 20, 2019

Disclosures: Nothing to declare

References

1. Boughton CK, Dixon D, Goble E, et al. Preventing hypoglycemia following treatment of hyperkalemia in hospitalized patients. *J Hosp Med.* 2019;14(5):284-287. doi: 10.12788/jhm.3145.
2. Apel J, Reutrakul S, Baldwin D. Hypoglycemia in the treatment of hyperkalemia with insulin in patients with end-stage renal disease. *Clin Kidney J.* 2014;7(3):248-250. doi: 10.1093/ckj/sfu026.
3. Chothia MY, Halperin ML, Rensburg MA, Hassan MS, Davids MR. Bolus administration of intravenous glucose in the treatment of hyperkalemia: a randomized controlled trial. *Nephron Physiol.* 2014;126(1):1-8. doi: 10.1159/000358836.
4. Groen J, Willebrands AF, Kamminga CE, Van Schothorst HK, Godfried EG. Effects of glucose administration on the potassium and inorganic phosphate content of the blood serum and the electrocardiogram in normal individuals and in non-diabetic patients. *Acta Med Scand.* 1952;141(5):352-366. doi: 10.1111/j.0954-6820.1952.tb14227.x.
5. Nicolis GL, Kahn T, Sanchez A, Gabrilove JL. Glucose-induced hyperkalemia in diabetic subjects. *Arch Intern Med.* 1981;141(1):49-53. doi:10.1001/archinte.1981.00340010045012.

In Response to "In Reference to: 'Preventing Hypoglycemia Following Treatment of Hyperkalemia in Hospitalized Patients'"

Charlotte K Boughton, MBBS, PhD[1,2]; Danielle Dixon, MBBS[1,2]; Emma Goble, MRPharmS[1,3]; Alice Burridge, PhD[1,3]; Alison Cox, RN[1,2]; Georgia Noble-Bell, RN, MSc[1,2]; Charlotte Bell, MRPharmS[1,3]; Ben Fidler[1,4]; James Chudley[1,4]; Caroline Anderson, MRPharmS, FFCI[1,3]; Gillian Cavell, MRPharmS, MSc[1,3]; Omar G Mustafa, MBChB, FRCP[1,2]*

[1]King's Insulin Safety Group, King's College Hospital NHS Foundation Trust, London, United Kingdom; [2]Department of Diabetes, King's College Hospital NHS Foundation Trust, London, United Kingdom; [3]Department of Pharmacy and Medications Safety, King's College Hospital NHS Foundation Trust, London, United Kingdom; [4]Clinical Systems, King's College Hospital NHS Foundation Trust, London, United Kingdom.

We appreciate the comments and interest of Al-Sharefi and colleagues who highlight the use of glucose-only infusion in the management of hyperkalemia.[1] The incidence of hypoglycemia following hyperkalemia treatment with insulin/dextrose is high and measures to reduce this should be pursued.[2] However, evidence of the efficacy of glucose-only infusions on lowering potassium in heterogeneous inpatient populations is lacking. The small study by Chothia et al demonstrated potassium lowering efficacy in ten clinically stable patients without diabetes receiving chronic hemodialysis.[3] In contrast, multiple observational studies consistently show a clinically significant effect of insulin/dextrose on potassium lowering across different populations.[4]

Importantly, inpatient hyperglycemia is associated with increased morbidity and mortality and occurs in those with preexisting diabetes and also those without, due to stress hyperglycemia from acute illness, medication or nutrition support.[5] Determining intact insulin sensitivity during acute illness is not straightforward and deciding on the appropriateness of glucose-only hyperkalemia treatment compared with insulin/dextrose would be challenging. With the rising prevalence of diabetes in the inpatient setting (>30% in our study), the number of eligible individuals for glucose-only treatment would be small and does not justify the use of two separate hyperkalemia treatment protocols.

Given the potential life-threatening consequences of hyperkalemia, rapid potassium lowering is a priority. For glucose-only infusions to be applied, there needs to be more convincing evidence across more representative inpatient populations to ensure efficacy.

***Corresponding Author:** Omar G Mustafa MBChB, FRCP;
E-mail: omarmustafa@nhs.net; Telephone: (020) 3299-1588; Twitter: @OGMustafa

Received: April 2, 2019; **Accepted**: April 2, 2019

DOI 10.12788/jhm.3218

Disclosures: The authors have nothing to disclose.

References

1. Al Sharefi A, Quinton R, Roberts G. In Reference to: "Preventing Hypoglycemia Following Treatment of Hyperkalemia in Hospitalized Patients ". *J Hosp Med*. 2019;14(6):387. doi: 10.12788/jhm.3209.
2. Boughton CK, Dixon D, Goble E, Burridge A, Cox A, Noble-Bell G, et al. Preventing hypoglycemia following treatment of hyperkalemia in hospitalized patients. *J Hosp Med*. 2019;14(5):284-287. doi: 10.12788/jhm.3145.
3. Chothia MY, Halperin ML, Rensburg MA, Hassan MS, Davids MR. Bolus administration of intravenous glucose in the treatment of hyperkalemia: a randomized controlled trial. Nephron Physiol. 2014;126(1):1-8. doi: 10.1159/000358836.
4. Harel Z, Kamel KS. Optimal dose and method of administration of intravenous insulin in the management of emergency hyperkalemia: a systematic review. *PLoS One*. 2016;11(5):e0154963. doi: 10.1371/journal.pone.0154963. e
5. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab*. 2002;87(3):978-982. doi: 10.1210/jcem.87.3.8341.