BRIEF REPORTS

Clinical Presentation and Outcome of Perioperative Myocardial Infarction in the Very Elderly Following Hip Fracture Surgery

Bhanu P. Gupta, MD¹*, Jeanne M. Huddleston, MD^{1,5}, Lisa L. Kirkland, MD¹, Paul M. Huddleston, MD³, Dirk R. Larson, MSc⁴, Rachel E. Gullerud⁴, M. Caroline Burton, MD¹, Charanjit S. Rihal, MD², R. Scott Wright, MD²

¹Division of Hospital Internal Medicine, Department of Medicine, Mayo Clinic, Rochester, Minnesota; ²Division of Cardiology, Department of Medicine, Mayo Clinic, Rochester, Minnesota; ³Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota; ⁴Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁵Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁵Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁶Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁶Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁶Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁶Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; ⁶Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota.

BACKGROUND: Patterns of clinical symptoms and outcomes of perioperative myocardial infarction (PMI) in elderly patients after hip fracture repair surgery are not well defined.

METHODS: A retrospective 1:2 case-control study in a cohort of 1212 elderly patients undergoing hip fracture surgery from 1988 to 2002 in Olmsted County, Minnesota.

RESULTS: The mean age was 85.3 ± 7.4 years; 76% female. PMI occurred in 167 (13.8%) patients within 7 days, of which 153 (92%) occurred in first 48 hours; 75% of patients were asymptomatic. Among patients with PMI, inhospital mortality was 14.4%, 30-day mortality was 29 (17.4%), and 1-year mortality was 66 (39.5%). PMI was associated with a higher inpatient mortality rate (odds ratio

Perioperative myocardial infarction (PMI) often remains unrecognized with higher mortality in the aged.^{1–3} Perioperative ischemic symptoms are often masked by analgesia, sedation, and transient and subtle electrocardiographic (ECG) changes. Postoperative troponin measurement is not routinely done for PMI diagnosis. Hip fracture surgery is the most common non-cardiac surgical procedure in the elderly, with limited data on clinical presentation of PMI.^{4–6} Moreover, the elderly are significantly underrepresented in clinical studies.⁷ We therefore examined the clinical presentation of PMI and its outcomes among elderly patients admitted for hip fracture repair.

METHODS

Study Population

A population-based, retrospective, case-control study was conducted of all residents in Olmsted County, Minnesota undergoing surgery for hip fracture repair from January 1, 1988 through December 31, 2002.

2012 Society of Hospital Medicine DOI 10.1002/jhm.1967 Published online in Wiley Online Library (Wileyonlinelibrary.com). [OR], 15.1; confidence interval [CI], 4.6–48.8), 30-day mortality (hazard ratio [HR], 4.3; CI, 2.1–8.9), and 1-year mortality (HR, 1.9; CI, 1.4–2.7).

CONCLUSION: Elderly patients, after hip fracture surgery, have a higher incidence of PMI and mortality than what guidelines indicate. The majority of elderly patients with PMI did not experience ischemic symptoms and required cardiac biomarkers for diagnosis. The results of our study support the measurement of troponin in postoperative elderly patients for the diagnosis of PMI, in order to implement in-hospital preventive strategies to reduce PMI-associated mortality. *Journal of Hospital Medicine* 2012;7:713–716. © 2012 Society of Hospital Medicine

Primary indication for the surgery was proximal femur (femoral neck or subtrochanteric) fracture. Patients who were <65 years old, had a pathological hip fracture, multiple injuries or fractures, surgery >72 hours after injury (due to higher mortality with delayed surgery),⁸ nonsurgical management of hip fracture repair, or incomplete data were excluded. All patients provided prior authorization to use their medical records for research, per institutional protocols.⁹

Criteria for Perioperative Myocardial Infarction and Death

We utilized the universal definition of acute myocardial infarction¹⁰ to define PMI within the first 7 days following hip fracture surgery. We included creatine kinase-MB fraction (CK-MB) as the biomarker for 1988–July 2000, and troponin as the biomarker for August 2000–2002. Mortality was defined as death from any cause within the first year following hip fracture repair. Deaths were identified through the National Death Index.

Statistical Analysis

For each case of PMI, we identified 2 control patients who were selected at random from the non-PMI patient population. These controls were matched to cases based on age at the time of surgery (± 5 years) and gender in 1:2 ratios. Baseline characteristics across PMI and non-PMI groups were compared using the Kruskal-Wallis test (for continuous data) and the chi-square or Fisher's exact tests (for categorical

^{*}Address for correspondence and reprint requests: Bhanu P. Gupta, MD, Division of Hospital Internal Medicine, Department of Medicine, Mayo Clinic, 200 First St, Rochester, MN 55905; Telephone: 507-255-8715; Fax: 507-284-0164; E-mail: gupta.bhanu@mayo.edu

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

Received: December 2, 2011; Revised: July 4, 2012; Accepted: July 5, 2012

TABLE 1.	Characteristics	and Outcomes	of Patients
----------	-----------------	--------------	-------------

	Patients	Patients	
Characteristics, n (%)	(N = 167)	(N = 334)	P Value*
Age mean \pm SD	85.3 ± 7.4	85.2 ± 7.1	0.5
Weight (kg) mean \pm SD	59.98 ± 16.7	59.80 ± 13.9	0.5
Women	127 (76.4)	254 (76)	0.5
Any symptom of ischemia, n (%)			
Chest/arm pain	11 (7)	4 (1)	0.002
Dyspnea	20 (12)	14 (4)	0.001
Nausea/vomiting	8 (5)	6 (2)	0.08
Diaphoresis	1 (1)	1 (0.3)	1.0
PND	3 (2)	1 (0.3)	0.3
ECG changes, n (%)			
ST-segment elevation MI	12 (7.2)	0	0.01
New ECG changes consistent with ischemia	38 (22.8)	1(0.3)	0.01
Biochemical evidence of ischemia, n (%)			
CK-MB†	147 (88)	20 (6)	±0.01
Troponin±	52 (33)	9 (3)	±0.001
Laboratory markers	. ,		
Hemoglobin gm/dL mean (SD)	8.9 ± 1.0	9.4 ± 1.2	±0.001
Postoperative anemia	22 (13.2)	37 (11.1)	0.5
(<8.0 gm/dL), n (%)			
Length of stay (days), mean \pm SD	11.6 ± 7.7	7.4 ± 6.4	±0.001
In-hospital outcome			< 0.001
Dead	24 (14.4)	4 (1.2)	
Alive	143 (85.6)	330 (98.8)	
30-Day outcome			< 0.001
Dead	29 (17.4)	14 (4.2)	
Alive	138 (82.6)	320 (95.8)	
1-Year outcome			< 0.001
Dead	66 (39.5)	77 (23)	
Alive	101 (60.4)	257 (77)	

Abbreviations: CK-MB, creatine kinase-MB fraction; ECG, electrocardiogram; MI, myocardial infarction; PMI, perioperative myocardial infarction; PND, paroxysmal nocturnal dyspnea; SD, standard deviation. *Univariate analysis, P values for those with PMI vs without PMI. †MI reference value >5.0 ng/ml. ‡MI reference value >0.01 ng/ml.

data). Mean values were utilized in place of the missing values for the following variables: preoperative troponin (missing values 88 [17.5%]), CK-MB (8 [1.6%]), troponin (21 [5.4%]), and postoperative hemoglobin (17 [3.4%]). Univariate predictors of PMI with $P \leq 0.2$ baseline characteristics were entered into a multivariate, conditional, logistic regression analysis. Rates of outcomes were calculated using the Kaplan-Meier method, and by a landmark survival curve for those with and without PMI. Cox proportional hazards analysis was utilized for survival analysis at 30 days and 1 year. All statistical tests were 2-sided, and P values <0.05 were considered significant. All analyses were performed using SAS for UNIX (version 9.1.3; SAS Institute, Inc, Cary, NC).

RESULTS

In the cohort of 1212 with hip fracture surgeries, 167 (13.8%) cases of PMI occurred in the first 7 days, of which 153 (92%) occurred within the first 48 hours. A total of 334 controls were matched with 167 cases of PMI. Table 1 summarizes the demographic characteristics of the study participants. Of the patients with PMI, 25.2% experienced symptoms of ischemia; 7%

TABLE 2. Multivariate and Survival Analysis of Risk Factors for Perioperative Myocardial Infarction, In-Hospital, 30-Day, and 1-Year Mortality

in hoopital, oo bay, and i hoar mortality						
	Unadjusted OR (95% Cl)	Adjusted OR (95% CI)	P Value			
Perioperative myocardial infarction						
Coronary artery disease	3.0 (2.1-4.5)	3.5 (2.2-5.6)	< 0.001			
Serum creatinine >2.0 mg/dL	2.7 (1.6-4.8)	2.4 (1.3-4.4)	0.003			
In-hospital mortality						
Age 85–89	1.7 (0.8-3.7)	5.3 (1.6-17.7)	0.01			
Age \geq 90	2.2 (1.0-4.8)	8.9 (2.6-30.8)	< 0.001			
Male gender	3.0 (1.4-6.4)	5.8 (2.2-15.2)	< 0.001			
Postoperative anemia (<8.0 gm/dL)	4.2 (1.7-10.0)	3.5 (1.2-9.9)	0.02			
Perioperative myocardial infarction	14.0 (5.2-48.0)	15.1 (4.6-49.0)	< 0.001			
30-Day mortality						
Perioperative myocardial infarction	4.1 (2.2-7.8)	4.3 (2.1-8.9)	< 0.001			
1-Year mortality						
Age 85–89	1.3 (0.8-1.9)	1.6 (1.0-2.4)	< 0.03			
Age \geq 90	1.9 (1.3-2.9)	2.0 (1.4-3.1)	0.001			
Male gender	1.9 (1.3-2.6)	2.1 (1.5-3.0)	< 0.001			
Dementia	2.5 (1.8-3.6)	2.7 (1.9-3.8)	< 0.001			
Perioperative myocardial infarction	2.0 (1.5-2.8)	1.9 (1.4-2.7)	0.001			

NOTE: Risk factors adjusted for both logistic regression analysis and Cox proportional hazard ratio: Age >70 years in 5-year increments, male gender, hypertension, coronary artery disease, congestive heart failure, diabetes mellitus, cerebrovascular disease, chronic obstructive pulmonary disease, dementia, preoperative and postoperative aspirin, beta-blocker, angiotensin receptor blockers. Abbreviations: CI, confidence interval; OR, odds ratio.

reported chest pain, and 12% reported dyspnea. Only 22.8% of patients with PMI had ECG changes consistent with ischemia. ST elevation MI was present in 7.2% patients. PMI patients had a lower mean hemoglobin compared to the patients without PMI (8.9 mg/ dL vs 9.4 mg/dL, P < 0.001). Median length of stay (LOS) in the hospital was higher among patients who experienced PMI (11.6 vs 7.4 days, P < 0.001). Overall in-hospital mortality was 5.6%. There were 24 deaths (14.4%) in the PMI group compared to 4 (1.2%) in-hospital deaths in patients without PMI (P < 0.001). A total of 473 (94%) patients survived to discharge. At 30-day follow-up, there were 29 (17.4%) deaths in the PMI group and 14 (4.2%)deaths in non-PMI group. During the follow-up for 1 year, there were 143 (29%) deaths: PMI 66 (39.5%) and 77 (23%) non-PMI group (P < 0.01).

Table 2 describes the risk factors associated with PMI in-hospital, 30-day, and 1-year mortality. Risk factors for PMI were coronary artery disease (CAD) (odds ratio [OR], 3.5; confidence interval [CI], 2.2–5.6), and serum creatinine >2 mg/dL (OR, 2.4; CI, 1.3–4.4). Risk factors for in-hospital mortality were age 85–89 (OR, 5.3; CI, 1.6–17.7), age \geq 90 (OR, 8.9; CI, 2.6–30.8), PMI (OR 15.1; CI, 4.6–48.8), male gender (OR 5.8; CI, 2.2–15.2), dyspnea (OR 5.4; CI, 1.8–16.9), and hemoglobin <8.0 gm/dL (OR, 3.5; CI, 1.2–9.9). PMI was a strong predictor for 30-day mortality (hazard ratio [HR], 4.3; CI, 2.1–8.9). Risk factors for 1-year mortality were: age \geq 90 (HR, 2.0; CI, 1.4–3.1), male gender (HR, 2.1; CI, 1.5–3.0), and PMI (HR, 1.9; CI, 1.4–2.7).



FIG. 1. Kaplan-Meier postoperative survival cure curve for 30-day survival for patients with and without perioperative myocardial infarction (PMI).

Figures 1 and 2 describe the Kaplan-Meier survival curves for patients with and without PMI.

DISCUSSION

We report the high incidence of PMI (13.8%) in the cohort of 1212 elderly patients (mean age 85 years) undergoing hip fracture surgery. Most PMI events (92%) occurred within the first 48 hours of surgery. Most of the events (75%) were asymptomatic. Elderly patients with PMI had an increased hospital LOS by 4.2 days, with high in-hospital mortality (13.8%), 30-day mortality (17.4%), and 1-year mortality (39.5%).

Most of the PMI patients were identified with cardiac biomarkers on the basis of universal definition of MI within the first 48 hours. Although universal definition of MI does not define PMI as a separate type, PMI shares common pathophysiological pathways of Type 1 MI (primary coronary event) and Type 2 MI (myocardial oxygen supply-demand imbalance). Postoperative tachycardia, hemodynamic instability, anemia, and hypoxemia may initiate pathways causing more Type 2 MI. Our study highlights the continued need for active surveillance of clinical symptoms, postoperative ECG monitoring for ST–T changes, and utilizing cardiac troponin in older postoperative patients to improve diagnostic accuracy of PMI.

The current study has higher asymptomatic PMI events when compared to a study of Devereaux et al.¹¹ The current study had an older population undergoing urgent hip fracture surgery, with a higher burden of CAD (60%) and renal failure (20%) with serum creatinine >2 gm/dL (see Supporting Information, Appendix 1, in the online version of this article). Older age and a higher burden of these risk factors may explain the higher incidence of PMI in the current study. Perioperative liberal use of analgesics in hip fracture surgery may explain more asymptomatic patients.

In light of the recently published FOCUS¹² trial, an important finding from our study is that postoperative anemia among elderly (<8.0 gm/dL) is associated with a 3.5-fold increased in-hospital mortality. It is critical to maintain perioperative hemoglobin above 8.0 gm/dL



FIG. 2. Kaplan-Meier postoperative 1-year survival curves for patients with and without perioperative myocardial infarction (PMI).

in very elderly patients, due to asymptomatic presentation of PMI.

In the current study, PMI is associated with a 15fold increased risk of in-hospital death and a 4.3-fold increased risk of 30-day mortality in the elderly. Advanced age (\geq 85 years) is a well known strong predictor of initial hospital admission and death in elderly patients after outpatient surgery.¹³ Furthermore, the odds for an in-hospital death increase by 70% for each 10-year increase in age.¹⁴ Therefore, early detection of silent PMI among at-risk elderly patients by cardiac biomarkers may help in optimization of cardiac pharmacotherapy known to decrease short- and long-term mortality.

There are limitations inherent to the retrospective design and methodology. Data collection was done through the year 2002. CK was used for the period that spans from 1988 to mid-2000. Troponin was used from 2000 to 2002. Statin use was not analyzed for lack of significant data. Limited use of beta-blockers (15%) and angiotensin-converting-enzyme (ACE) inhibitors (25%) may also contribute to higher events (see Supporting Information, Appendix 1, in the online version of this article).

CONCLUSIONS

Elderly patients have a higher incidence of PMI and mortality after hip fracture surgery than what guidelines indicate. The majority of the elderly patients with PMI did not experience ischemic symptoms and required cardiac biomarkers for diagnosis. The results of our study support the measurement of troponin in postoperative elderly patients for the diagnosis of PMI to implement in-hospital preventive strategies to reduce PMI-associated mortality.

Acknowledgements

The authors gratefully acknowledge the assistance of Ms Dawn Bergen in drafting and editing the manuscript.

Disclosures: This research was supported by funding from AHA grant 03-30103N-04, Rochester Epidemiology Project (grant RO1-AR30582 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases). The project was also supported by the National Center for

Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through grant UL1 RR024150. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

- Polanczyk CA, Marcantonio E, Goldman L, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med.* 2001;134(8):637–643.
- Haentjens P, Magaziner J, Colón-Emeric CS, et al. Meta-analysis: 2. excess mortality after hip fracture among older women and men. Ann Intern Med. 2010;152(6):380-390.
- 3. Batsis JA, Huddleston JM, Melton LJ, et al. Body mass index (BMI) and risk of noncardiac postoperative medical complications in elderly hip fracture patients: a population-based study. J Hosp Med. 2009;4(8):E1–E9. Melton LJIII. History of the Rochester Epidemiology Project. Mayo
- 4. Clin Proc. 1996;71(3):266-274.
- Brauer CA, Coca-Perraillon M, Cutler DM, Rosen AB. Incidence and 5. mortality of hip fractures in the United States. JAMA. 2009;302(14): 1573-1579.
- 6. Batsis JA, Huddleston JM, Melton ILJ, et al. Body mass index and risk of adverse cardiac events in elderly patients with hip fracture: a population-based study. J Am Geriatr Soc. 2009;57(3):419-426.
- Alexander KP, Newby LK, Cannon CP, et al. Acute coronary care in 7. the elderly, part I. Non-ST-segment-elevation acute coronary syn-

dromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation*. 2007;115(19):2549–2569.

- Mullen JO, Mullen NL. Hip fracture mortality. A prospective, multi-8. factorial study to predict and minimize death risk. Clin Orthop Relat Res. 1992;280:214-222.
- 9. Gibbons RJ, Chatterjee K, Daley J, et al. ACC/AHA/ACP-ASIM *J Am Coll Cardiol.* 1999;33(7):2092–2190. Thygesen K, Alpert JS, White HD; for the Joint ESC/ACCF/AHA/ WHF Task Force for the Redefinition of Myocardial Infarction. Uni-
- 10. versal definition of myocardial infarction. J Am Coll Cardiol. 2007; 50(22):2173-2195.
- 11. Devereaux PJ, Xavier D, Pogue J, et al. Characteristics and shortterm prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery. Ann Intern Med. 2011;154(8): 523-528.
- 12. Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med. 2011; 365(26):2453-2462.
- 13. Fleisher LA, Pasternak LR, Herbert R, Anderson GF. Inpatient hospital admission and death after outpatient surgery in elderly patients: importance of patient and system characteristics and location of care. *Arch Surg.* 2004;139(1):67–72.
- 14. Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern* Med. 2003;163(19):2345-2353.