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BRIEF REPORT

Refractory Primary Medication Nonadherence: Prevalence and Predictors After Pharmacist Counseling at Hospital Discharge

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Successful secondary prevention of cardiovascular disease relies on medication therapy; thus, minimizing nonadherence is a focus for improving patient outcomes. Receipt of discharge medication counseling has been associated with improved drug knowledge and adherence. We evaluated the prevalence and predictors of postdischarge primary nonadherence (not filling new prescriptions) in patients who received discharge medication counseling by a pharmacist (ie, refractory to intervention) as part of a randomized controlled trial. Of 341 patients, 9.4% of patients did not fill all prescriptions after discharge. Patients who were living alone were more likely to not fill their medications compared to those who were married or cohabitating (odds ratio [OR]: 2.2, 95% confidence interval [CI]: 1.01–4.8, $P = 0.047$). Patients who were discharged with greater than 10 medications were also more likely to demonstrate primary nonadherence (OR: 2.3, 95% CI: 1.05–4.98, $P = 0.036$). Patients with lower income were less likely to fill prescriptions in univariate analysis ($P = 0.04$) but not multivariable analysis. Our study demonstrates that among patients hospitalized for acute cardiovascular events, primary medication nonadherence persisted despite discharge medication counseling. Targeted or multimodal approaches that address patient-specific barriers, such as cost, social isolation, and polypharmacy, in addition to discharge counseling, may further facilitate adherence. *Journal of Hospital Medicine* 2016;11:48–51. © 2015 Society of Hospital Medicine

Medication nonadherence after hospital discharge impacts morbidity and mortality in patients with cardiovascular disease.[1] Primary nonadherence, part of the spectrum of medication underuse, occurs when a patient receives a prescription but does not fill it.[1] Prior studies utilizing retrospective administrative data have found a prevalence of postdischarge primary nonadherence between 24% and 28%,[1,2] similar to findings in a variety of outpatient populations.[3,4]

One strategy for reduction in nonadherence is discharge medication counseling, which has been associated with improved postdischarge outcomes.[1] We evaluated the prevalence and predictors of refractory primary nonadherence in a cohort of patients hospitalized for acute cardiovascular conditions who received pharmacist counseling prior to discharge to guide future adherence interventions.

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METHODS

Setting and Participants

The present study represents a secondary analysis of data from the Pharmacist Intervention for Low Literacy in Cardiovascular Disease (PILL-CVD) study. PILL-CVD was a randomized controlled trial that evaluated the effect of a tailored intervention consisting of pharmacist-assisted medication reconciliation, discharge counseling, low-literacy adherence aids, and follow-up phone calls in adults hospitalized for acute coronary syndromes or acute decompensated heart failure. Patients likely to be discharged home taking primary responsibility for their medication management were eligible. Full study methods and results, including inclusion and exclusion criteria, can be found elsewhere.[5] The institutional review boards of each site approved the study.

For the present analysis, patients were included if they had any new discharge prescriptions to fill and received the study intervention, including a postdischarge follow-up phone call with questions about filling discharge prescriptions.

Baseline Measures

Baseline data were obtained from medical records and patient interviews, including demographic information as well as survey data for cognitive impairment

(Mini-Cog) and health literacy (Short Test of Functional Health Literacy in Adults).[6,7]

Data were also collected related to medication use, including the number of scheduled and as-needed medications listed at discharge, self-reported preadmission adherence, medication understanding, and medication management practices (eg, use of a pillbox, refill reminders). Self-reported medication adherence was measured with the 4-item Morisky scale.[8] Medication understanding was assessed with a tool previously developed by Marvanova et al.[9]

Outcome Measures

The primary outcome was the percentage of patients who reported not filling at least 1 discharge prescription on a telephone call that was conducted 1 to 4 days postdischarge. Patients were asked a dichotomous question about whether or not they filled all of their discharge prescriptions. Further characterization of the class or number of medications not filled was not performed. Patients were asked to provide a reason for not filling the prescriptions.

Analysis

We evaluated the prevalence and possible predictors of primary nonadherence including age, gender, race, marital status, education and income levels, insurance type, health literacy, cognition, presence of a primary care physician, number of listed discharge medications, prehospital medication adherence, medication understanding, and medication management practices using Pearson χ^2, Fisher exact, or Wilcoxon rank sum tests as appropriate. Multiple logistic regression with backward elimination was performed to identify independent predictors, selected with P values < 0.1. We also evaluated reasons that patients cited for not filling prescriptions. Two-sided P values < 0.05 were considered statistically significant. All analyses were conducted using Stata version 13.1 (StataCorp LP, College Station, TX).

RESULTS

Of 851 patients in the PILL-CVD study, the present sample includes 341 patients who received the intervention, completed the postdischarge follow-up call, and had new discharge prescriptions to be filled. This represents 85% of patients who received the intervention.

The mean age of participants was 61.3 years, and 59.5% were male (Table 1). The majority were white (75.1%), and 88% had at least a high school education. Married or cohabitating patients represented 54.3% of the group. Just over half of the patients (54%) had an income of $35K or greater. The primary source of insurance for 82.5% of patients was either Medicare or private insurance, and 7.4% of patients were self-pay. Most patients (80%) had adequate health literacy. The median Mini-Cog score was 4 out of 5 (interquartile range [IQR] = 3–5), and 11% of patients had scores indicating cognitive impairment. Just less than one-fourth of the patients (24.1%) had a Morisky score of 8, indicating high self-reported adherence, and the median score of patients' understanding of medications (range of 0–3) was 2.5 (IQR = 2.2–2.8), reflecting relatively high understanding. The median number of prescriptions on patients' discharge medications lists was 10 (IQR = 8–13).

The prevalence of refractory primary nonadherence was 9.4%. In univariate analysis, single marital status, lower income, and having more than 10 total discharge medications were significantly associated with not filling medications ($P = 0.018$, 0.04, 0.016, respectively; Table 1). In multivariable analysis, single

TABLE 1. Patient Characteristics

Variable	Overall 341 (100.0%)	Filled Prescription309 (90.6%)	Did Not Fill 32 (9.4%)	*P* Value
Age, y, N (%)				0.745*
18–49	69	63 (91.3)	6 (8.7)	
50–64	128	114 (89.1)	14 (10.9)	
65+	144	132 (91.7)	12 (8.3)	
Gender, N (%)				0.056*
Male	203	189 (93.1)	14 (6.9)	
Female	138	120 (87.0)	18 (13.0)	
Race, N (%)				0.712*
White	256	234 (91.4)	22 (8.6)	
African American	60	54 (90.0)	6 (10.0)	
Other	22	19 (86.4)	3 (13.6)	
Education, N (%)				0.054*
Less than high school	40	32 (80.0)	8 (20.0)	
High school	99	91 (91.9)	8 (8.1)	
13–15 years	93	83 (89.2)	10 (10.8)	
≥16 years	109	103 (94.5)	6 (5.5)	
Marital status, N (%)				
Separated/divorced/ widowed/never married	156	135 (86.5)	21 (13.5)	0.018*,†
Married/cohabitating	185	174 (94.1)	11 (5.9)	
Income, N (%)				0.040*,†
<10K–<20K	58	48 (82.8)	10 (17.2)	
20K–35K	86	76 (88.4)	10 (11.6)	
35K–<50K	40	36 (90.0)	4 (10.0)	
50K–<75K	46	43 (93.5)	3 (6.5)	
75K+	83	81 (97.6)	2 (2.4)	
Primary source of payment, N (%)				0.272*
Medicaid	34	28 (82.4)	6 (17.6)	
Medicare	145	131 (90.3)	14 (9.7)	
Private	132	123 (93.2)	9 (6.8)	
Self-pay	25	22 (88.0)	3 (12.0)	
Primary care physician, N (%)				1.000‡
None/do not know	28	26 (92.9)	2 (7.1)	
Yes	313	283 (90.4)	30 (9.6)	
Site, N (%)				0.071*
Nashville, TN	172	151 (87.8)	21 (12.2)	
Boston, MA	169	158 (93.5)	11 (6.5)	

NOTE: Missing values are present in the following categories: race (n = 3), income (n = 28), insurance (n = 5).

*Pearson χ^2 test.

†$P < 0.05$.

‡Fisher exact test (2-sided).

TABLE 2. Patient Medication-Related Characteristics

Variable	Overall 341 (100.0%)	Filled Prescription 309 (90.6%)	Did Not Fill 32 (9.4%)	*P* Value
s-TOFHLA score, range 0–36, N (%)				0.443*
Inadequate, 0–16	40	34 (85.0)	6 (15.0)	
Marginal, 17–22	27	25 (92.6)	2 (7.4)	
Adequate, 23–36	268	244 (91.0)	24 (9.0)	
MiniCog score, range 0–5, N (%)				0.764†
Not impaired, 3–5	304	276 (90.8)	28 (9.2)	
Impaired, 0–2	37	33 (89.2)	4 (10.8)	
Morisky score, range 4–8, N (%)				0.517*
Low/moderate self-reported adherence, 4–7	249	224 (90.0)	25 (10.0)	
High self-reported adherence, 8	79	73 (92.4)	6 (7.6)	
No. of discharge medications, range 1–26, N (%)‡				0.016*
0–10 medications	186	175 (94.1)	11 (5.9)	
11 + medications	155	134 (86.5)	21 (13.5)	
Patient responses to medication behavior questions				
Patient associates medication taking time with daily events	253	229 (90.5)	24 (9.5)	0.913*
Patient uses a pillbox to organize medicine	180	162 (90.0)	18 (10.0)	0.680*
Friends of family help remind patient when it is time to take medicine	89	79 (88.8)	10 (11.2)	0.486*
Patient writes down instructions for when to take medicine	60	55 (91.7)	5 (8.3)	0.758*
Patient uses an alarm or a reminder that beeps when it is time to take medicine	8	6 (75.0)	2 (25.0)	0.167*
Patient marks refill date on calendar	38	35 (92.1)	3 (7.9)	1.000†
Pharmacy gives or sends patient a reminder when it is time to refill medicine	94	84 (89.4)	10 (10.6)	0.624*
Friends or family help patient to refill medicine	60	53 (88.3)	7 (11.7)	0.504*

NOTE: Missing values are present in the following categories: s-TOFHLA (n = 6), Morisky (n = 13). **Abbreviations:** s-TOFHLA, Short Test of Functional Health Literacy in Adults.

*Pearson χ^2 test.

†Fisher exact test (2-sided).

‡Number on discharge medication list.

marital status and having more than 10 total discharge medications maintained significance when controlling for other patient characteristics. Patients who were single had higher odds of failing to fill discharge prescriptions compared to married or cohabitating individuals (odds ratio [OR]: 2.2, 95% confidence interval [CI]: 1.01–4.8, $P = 0.047$). Patients with more than 10 discharge medications also had higher odds of failing to fill compared with patients who had fewer total medications (OR: 2.3, 95% CI: 1.05–4.98, $P = 0.036$).

Filling discharge prescriptions was not associated with health literacy, cognition, prehospital adherence, patients' medication understanding, or any of the surveyed medication management practices (Table 2). Patients' reasons for not filling included lack of time to go to the pharmacy, medications not being delivered or dispensed, or inability to afford prescriptions. Prescription cost was cited by 23.5% of patients who did not fill their prescriptions and provided a reason.

DISCUSSION

Almost 1 in 10 patients hospitalized with cardiovascular disease demonstrated primary nonadherence refractory to an intervention including pharmacist discharge medication counseling. Being unmarried and having greater than 10 medications at discharge were significantly associated with higher primary nonadherence when controlling for other patient factors.

Patients with a cohabitant partner were significantly less likely to exhibit primary nonadherence, which may reflect higher levels of social support, including encouragement for disease self-management and/or support with tasks such as picking up medications from the pharmacy. Previous research has demonstrated that social support mediates outpatient medication adherence for heart failure patients.[10]

Similar to Jackevicius et al., we found that patients with more medications at discharge were less likely to fill their prescriptions.[1] These findings may reflect the challenges that patients face in adhering to complex treatment plans, which are associated with increased coordination and cost. Conversely, some prior studies have found that patients with fewer prescriptions were less likely to fill.[11,12] These patients were often younger, thus potentially less conditioned to fill prescriptions, and unlike our cohort, these populations had consistent prescription coverage. Interventions for polypharmacy, which have been shown to improve outcomes and decrease costs, especially in the geriatric population, may be of benefit for primary nonadherence as well.[13]

Additionally, patients with lower household incomes had higher rates of primary nonadherence, at least in univariate analysis. Medication cost and transportation limitations, which are more pronounced in lower-income patients, likely play influential roles in this group. These findings build on prior literature that has found lower prescription cost to be associated with better medication adherence in a variety of settings.[3,4,14]

Because the prevalence of primary nonadherence in this cohort is less than half of historical rates, we suspect

the intervention did reduce unintentional nonadherence. However, regimen cost and complexity, transportation challenges, and ingrained medication beliefs likely remained barriers. It may be that a postdischarge phone call is able address unintended primary nonadherence in many cases. "Meds to beds" programs, where a supply of medications is provided to patients prior to discharge, could assist patients with limited transportation. Prior studies have also found reduced primary nonadherence when e-prescriptions are utilized.[3]

Establishing outpatient follow-up at discharge provides additional opportunities to address unanticipated adherence barriers. Because the efficacy of any adherence intervention depends on individual patient barriers, we recommend combining medication counseling with a targeted approach for patient-specific needs.

We note several limitations to our study. First, because we studied primary nonadherence that persisted despite an intervention, this cohort likely underestimates the prevalence of primary nonadherence and alters the associated patient characteristics found in routine practice (although counseling is becoming more common). Second, patient reporting is subject to biases that underestimate nonadherence, although this approach has been validated previously.[15] Third, our outcome measure was unable to capture the spectrum of non-adherence that could provide a more nuanced look at predictors of postdischarge nonadherence. Fourth, we did not have patient copayment data to better characterize whether out of pocket costs or pharmacologic classes drove nonadherence. Finally, sample size may have limited the detection of other important factors, and the university setting may limit generalizability to cardiovascular patients in other practice environments. Future research should focus on intervention strategies that assess patients' individual adherence barriers for a targeted or multimodal approach to improve adherence.

In conclusion, we found a prevalence of primary nonadherence of almost 1 in 10 patients who received pharmacist counseling. Nonadherence was associated with being single and those discharged with longer medication lists. Our results support existing literature that primary nonadherence is a significant problem in the postdischarge setting and substantiate the need for ongoing efforts to study and implement interventions for adherence after hospital discharge.

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