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Effect of Gender, Caregiver, on Statin Use and on Low-Density Lipoprotein-Cholesterol Control for Secondary Prevention Among Hospitalized Patients with Coronary Heart Disease

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Abstract

Women with coronary heart disease (CHD) are consistently less likely than men with CHD to be at low density lipoprotein cholesterol (LDL-C) goals, and the reasons for the gender gap are not established. We studied 2190 patients with CHD or equivalent (34% women, 42% racial/ethnic minority) who participated in the Family Cardiac Caregiver Investigation To Evaluate Outcomes (FIT-O) Study and had baseline lipid data, to determine whether having a *paid* or *informal* caregiver was independently associated with adherence to LDL-C goals (<100mg/dL, <70mg/dL) and statin use, and to determine if the association varied by gender. Caregiver status was assessed by standardized questionnaire and lipid levels/statin use were obtained from a hospital-based informatics system. The associations between caregiving and LDL-C and statin use were assessed in univariate and multivariable models, and interaction evaluated in gender stratified models. Men with CHD were more likely to be at LDL-C<100mg/dL, LDL-C<70mg/dL, and on statins than women with CHD (79% vs. 69%, $p<.001$; 48% vs. 36%, $p<.001$; and 73% vs. 67%, $p=.004$, respectively). No significant association was observed between LDL-C<100mg/dL and *informal* caregiving or between *paid* caregiving and lipid goals or statin use. Having an *informal* caregiver was associated with having an LDL-C<70mg/dL ($p=0.016$) which remained significant after adjustment in multivariable models (OR=1.25; 95% CI=1.00–1.56). The multivariable association between *informal* caregiving and LDL-C was significant among men (OR=1.37; 95% CI=1.04–1.80), but not women. In conclusion, there was a significant association between *informal* caregiving and LDL-C control that was limited to men with *informal* caregivers.

Keywords

Gender; Cardiovascular disease prevention; Lipoproteins

Introduction

Low density lipoprotein cholesterol (LDL-C) reduction and statin therapy have proven benefits in the secondary prevention of coronary heart disease (CHD) for both men and women.^{1–2} Despite this, data consistently show that women with CHD are significantly less

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likely to reach LDL-C targets or to be on statin therapy compared to their male counterparts.^{3–8} The reasons for the gender gap remain elusive, and an unexplored mechanism may be differential access to type or quality of caregivers. *Informal* caregivers, such as family members or friends, are often involved in tasks such as assistance with medications and other preventive care that might be associated with better CHD risk factor control.^{9–11} Few data have examined whether caregiving is associated with better lipid management, or the gap in evaluating gender disparities. The purpose of this study was to determine whether having a caregiver (*paid* or *informal*) was associated with adherence to National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) and American Heart Association (AHA) secondary prevention guidelines for LDL-C goals (<100mg/dL and <70mg/dL) and statin use among hospitalized patients with CHD, and whether the association varied by patient gender.^{12–13}

Methods

This was a cross sectional analysis of 2190 patients who participated in the National Heart Lung and Blood Institute (NHLBI) sponsored Family Cardiac Caregiver Investigation To Evaluate Outcomes (FIT-O) Study who had prior CHD or equivalent, and had a documented LDL-C within 12 months of hospital admission (N=2190, 34% women, 42% racial/ethnic minority). The design and methods of FIT-O have been previously reported.¹¹ Briefly, FIT-O was a prospective cohort study that evaluated patterns of caregiving and the association with clinical outcomes among patients with CHD consecutively admitted to an academic medical center (93% enrollment rate, N=4,500).^{11,14} Patients who were unable to read or understand English or Spanish, lived in a full-time nursing facility, had a mental status that made them unable to participate, or refused to participate were excluded from the study. Participants with a documented contraindication to statin use were excluded from this analysis. The institutional review board of Columbia University Medical Center (CUMC) approved the study.

Trained bilingual research staff systematically distributed surveys (available in English and Spanish) to participants to determine whether they had a caregiver within the past year or planned to have one following hospital discharge. The definition of caregiving was adapted from the report of the National Alliance of Caregiving and the AARP.¹⁵ A caregiver was defined as a person who assists the patient with medical and/or preventative care and was categorized into two groups: 1) paid professional (e.g. nurse or home aide) or 2) informal/nonpaid (e.g. family member or friend).¹⁵ If a patient had both a *paid* and an *informal* caregiver, she or he was categorized as having a *paid* caregiver (n=80). Patients who reported having a caregiver in the year prior to hospitalization were classified as having a caregiver in this analysis.

Admission diagnosis, baseline characteristics, past medical history, and prescription medications were documented by standardized electronic chart review by trained professional research staff. A secure and comprehensive electronic clinical information system at CUMC/New York Presbyterian Hospital (NYPH) was used to access and review patient medical records. Admission diagnosis was classified using the *International Classification of Disease*, 9th Revision (ICD-9) billing code for admission or primary diagnosis. The definition and classification of CHD equivalent was adapted from the NHLBI ATP III report.¹⁶ Patients were classified as having CHD or equivalent if they had an ICD-9 billing code consistent with any of the following: ischemic heart disease, myocardial infarction, prior coronary artery bypass graft surgery, non cardiac atherosclerotic disease, peripheral artery disease, abdominal aortic aneurysm, or diabetes mellitus. Comorbidities were determined based on electronic chart review and a summary Ghali Comorbidity index was calculated (range=0–11).¹⁷

LDL-C values obtained closest to within 24 hours of admission were defined as admission LDL-C. If an admission LDL-C was not available (n=362), LDL-C values from within 1 year of hospital admission date were used. LDL-C was calculated according to the Friedewald equation: $\text{LDL-C} = \text{Total cholesterol} - \text{high density lipoprotein cholesterol} - (\text{triglycerides}/5)$.¹⁸ Serum total cholesterol, high density lipoprotein cholesterol, and triglycerides (TG) were measured using the Beckman Coulter analyzer in the core laboratory of CUMC/NYPH. The main results were similar when patients with TG $\geq 400\text{mg/dL}$ (n=13) were excluded, so they were retained in the analyses. LDL-C goals and indication for statin use were defined according to ATP III and AHA secondary prevention guidelines and categorized as minimum goal LDL-C $<100\text{mg/dL}$ and optional goal LDL-C $<70\text{mg/dL}$, and statin use unless contraindicated.^{12–13}

Standardized questionnaires regarding caregiver status and activities were processed using intelligent character recognition software ExDataPro32, version 8.0.7 (Creative ICR, Beaverton, Oregon) and Image Formula, version Dr-2,580C (Canon US, New York, New York). The data were double checked for errors and stored in a Microsoft Access database (Microsoft, Redmond, Washington). Chi-square tests were conducted to determine the association between having a caregiver (*paid* or *informal*) and the baseline characteristics of hospitalized patients with CHD, using a Bonferroni correction for multiple comparisons ($p < 0.017$). The independent associations between caregiving and LDL-C goals and statin use were evaluated using logistic regression adjusted for demographics (age, gender, health insurance status, marital status), Ghali comorbidity index, diabetes, current smoking, being on ≥ 9 medications, and statin use. Gender stratified analyses and interaction terms were evaluated to assess for effect modification by gender.

Results

Baseline characteristics of participants stratified by caregiver status are shown in Table 1. The mean age of hospitalized patients with CHD was 67 ± 12 years. Approximately 34% of the participants were women, and 42% were racial/ethnic minorities. The prevalence of attainment of goal LDL-C $<100\text{mg/dL}$ was 76% overall and differed significantly by gender with men being more likely than women to attain goal LDL-C $<100\text{mg/dL}$ ($p < 0.0001$), as shown in Figure 1. Similarly, attainment of the more intensive goal LDL-C $<70\text{mg/dL}$ which was 44% overall, was more prevalent among men than women ($p < 0.0001$). Overall, 72% of patients in this study were on a statin which also varied significantly by gender with more men than women being on a statin ($p = 0.004$).

The overall prevalence of caregiving in this population was 40% (13% *paid*, 27% *informal*), similar to the larger FIT-O cohort.¹¹ Among men, 13% (n=132) had a *paid* caregiver and 32% (n=426) had an *informal* caregiver. Among women, 26% (n=151) had a *paid* caregiver and 29% (n=170) had an *informal* caregiver. As outlined in Table 2, having a *paid* caregiver was not associated with LDL-C goals $<100\text{mg/dL}$ or $<70\text{mg/dL}$, or statin use. In contrast, having an *informal* caregiver was significantly associated with being more likely to be at LDL-C $<70\text{mg/dL}$ than having no caregiver ($p < 0.05$). There was a non-significant trend that participants with an *informal* caregiver were more likely than participants without a caregiver to be at LDL-C $<100\text{mg/dL}$, however there was no relation between *informal* caregiving and statin use.

Significant correlates ($p < 0.05$) of LDL-C $<70\text{mg/dL}$ were having diabetes mellitus, being on ≥ 9 medications, older age (≥ 65 years old), male sex, and being on a statin at admission. Being a racial/ethnic minority, not being married, not having health insurance, and current smoking were significantly associated with being at minimum and intensive LDL-C goals.

After adjustment for demographics, comorbidities, and confounders, having an *informal* caregiver remained significantly associated with being at LDL-C <70mg/dL.

The results of the gender stratified analysis of the association between caregiver status and attainment of LDL-C goals and statin use are presented in Table 3. Among men, having an *informal* caregiver was significantly associated ($p<.05$) with being at LDL-C <70mg/dL and there was a non-significant trend of an association between *informal* caregiving and being at LDL-C <100mg/dL. In contrast, among women there was no association between having an *informal* caregiver and LDL-C <70 mg/dL or LDL-C <100mg/dL. Table 4 presents the results of the multivariable analysis for *informal* caregiving and attainment of LDL-C <70mg/dL overall, and according to gender. The relation between *informal* caregiving and being at intensive goal LDL-C remained significant among men after adjustment.

Discussion

In this contemporary study of patients hospitalized with CHD, we documented that having an *informal* caregiver was independently associated with meeting ATPIII and AHA defined secondary prevention goal LDL-C <70mg/dL among men but not among women. We also showed that women were less likely to be at minimum and intensive LDL-C goals and less likely to be on a statin compared to men. To our knowledge, this is the first study examining the association between caregivers and ATP III and AHA defined LDL-C goals for secondary prevention among CHD patients.

Our data documenting baseline gender differences in LDL-C control and statin use among a diverse population of hospitalized CHD patients are consistent with numerous studies that have shown similar gender disparities in various patient groups and care settings.^{3–9, 19–21} In a prospective study of a community based cohort of CHD patients sampled from 62 different practices, women had higher baseline LDL-C levels, and also had a lower probability of LDL-C goal attainment after initiation of lipid lowering therapy (median follow up 3.6 years).²² Sambamoorthi et al documented similar disparities among 500,000 veterans with cardiovascular disease (CVD), including 10,582 women: 27% of women versus 17% of men were not at LDL-C goals.⁵ Chou et al reported that among patients in private managed care plans, women with CVD were considerably less likely to be at established LDL-C goals than their male counterparts (47% vs. 55%, respectively).²⁰

The overall prevalence of LDL-C <100mg/dL and <70mg/dL (76% and 44%, respectively) among patients with CHD in our study, and the observed disparity by gender are consistent with previously published works.^{8,23} Karalis et al found similar trends in the overall and gender specific prevalence of LDL-C <100mg/dL (79% overall: 83% men vs. 73% women) and LDL-C <70mg/dL (35% overall: 38% men vs. 31% women) among 10,040 patients with established coronary artery disease seen in a large outpatient cardiology practice.²³ Our findings that participants with more CVD risk factors were more likely to be at LDL-C goal and on a statin are consistent with prior studies that show that those who are perceived to be higher risk may be treated more aggressively,²² or may have more advanced CVD which has been associated with having non-pharmaceutically lowered cholesterol levels.²⁴

Lipid control is multi-factorial and dependent upon various patient, provider, and health care system factors which could provide alternative explanations for our results.²⁵ Appropriate screening, prescription of appropriate therapy and titration/escalation of medical therapy when indicated, as well as adequate education on diet and lifestyle are all examples of provider factors that have been shown to vary by patient gender.⁵ Several studies have documented that women with CHD may be inadequately screened and/or sub optimally treated according to established guidelines.^{26,27}

An important limitation of current reports on gender disparities in LDL-C control and statin use, is that many studies have not been designed to examine patient, provider, and health care system factors at the same time. However, in a recent study of 3,500 patients with CVD, Turner et al demonstrated that even when simultaneously controlling for patient, provider, and health care system factors known to be associated with gender disparities in lipid control and statin use, women were still significantly less likely than men to reach LDL-C goals.²¹ These data emphasize the importance of examining previously unexplored factors such as caregiving and their potential role in gender disparities in LDL-C control and statin use.

The finding that having an *informal* caregiver was associated with achieving LDL-C intensive goal among CHD patients may reflect participation of *informal* caregivers in assistance with medication adherence. Previous studies among cardiac patients have shown that having an *informal* caregiver is associated with adherence to medications as well as other important behaviors such as compliance with physician visit follow up and diet.²⁸ Alternatively, the observed association between *informal* caregiving and LDL-C <70 mg/dL goal attainment could reflect advanced illness among patients with caregivers, as low LDL-C may be seen among patients with advanced CVD,^{24,29} and patients with more advanced disease are more likely to have caregivers.⁹

Strengths of this study include the significant representation of women and racial/ethnic minorities and the high participation with consecutive nature of enrollment that contribute to the generalizability of the results. The observational study design limits our ability to determine cause and effect. Caregiver status was based on self report and there may have been misclassification, however systematic assessment methods reduced the likelihood that misclassification would be differential by caregiver status and therefore results would have been biased towards the null. We did not evaluate lifestyle strategies such as diet and exercise for LDL-C control which may have contributed to gender disparities in LDL-C goal attainment, which should be considered in future studies.

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Figure 1.
Percentage of Participants at LDL-C Targets and on Statins by Gender

Table 1

Prevalence of Demographic Factors and Comorbidities Among 2190 Patients with CHD Stratified by Caregiver Status

Variable	Have a Paid Caregiver (n=283) [A]	Have an Informal Caregiver (n=596) [B]	Have No Caregiver (n=1311) [C]
Age 65	220 (78%) ^{B,C}	349 (59%) ^A	691 (53%) ^A
Men	132 (47%) ^{B,C}	426 (71%) ^A	888 (68%) ^A
Minority Race/Ethnicity [§]	130 (51%) ^C	242 (44%)	497 (39%) ^A
Not Married [¶]	135 (58%) ^{B,C}	191 (38%) ^{A,C}	500 (45%) ^{A,B}
No Health Insurance	66 (23%) ^{B,C}	87 (15%) ^A	154 (12%) ^A
Ghali Co-morbidity index 1	188 (66%) ^{B,C}	277 (47%) ^{A,C}	445 (34%) ^{A,B}
Diabetes Mellitus	169 (60%) ^{B,C}	302 (51%) ^{A,C}	549 (42%) ^{A,B}
Chronic Renal Disease	99 (35%) ^{B,C}	127 (21%) ^{A,C}	199 (15%) ^{A,B}
Prior Stroke	50 (18%) ^C	72 (12%) ^C	110 (8%) ^{A,B}
Prior Coronary Artery Disease	109 (39%) ^{B,C}	337 (57%) ^{A,C}	881 (68%) ^{A,B}
Prior Myocardial Infarction	108 (38%)	239 (40%) ^C	444 (34%) ^B
Prior Coronary Artery Bypass Surgery	86 (30%) ^C	155 (26%) ^C	249 (19%) ^{A,B}
Prior Peripheral Vascular Disease	78 (28%) ^{B, C}	104 (17%) ^A	177 (14%) ^A
Prior Heart Failure	106 (37%) ^{B,C}	140 (23%) ^{A,C}	189 (14%) ^{A,B}
Chronic Obstructive Pulmonary Disease	33 (12%) ^{B,C}	40 (7%) ^{A,C}	52 (4%) ^{A, B}
Hypertension (history)	237 (84%)	502 (84%)	1059 (81%)
Dyslipidemia (history)	204 (72%)	423 (71%)	978 (75%)
9 Medications	176 (62%) ^{B,C}	256 (43%) ^{A,C}	446 (34%) ^{A,B}
Current Smoker	12 (4%) ^{B,C}	52 (9%) ^A	154 (12%) ^A
On Statin at Admission	212 (75%)	418 (70%)	931 (71%)

Superscript A,B,C denote statistically significant differences between column percentages, significance set at $p < 0.017$

[§] Missing race/ethnicity information, n = 122

[¶] Missing Marital status information, n = 329

Table 2

Odds of LDL-C Goal Attainment and Statin Use by Caregiver Status, Demographics, and Covariates

Variable	<u>Low-Density Lipoprotein Cholesterol (mg/dL)</u>		On Statin
	<100 OR (95% CI)	<70 OR (95% CI)	OR (95% CI)
Paid vs. No Caregiver	1.08 (0.8–1.46)	0.93 (0.72–1.21)	1.22 (0.91–1.64)
Informal vs. No Caregiver	1.20 (0.95–1.51)	1.27 (1.05–1.54) [‡]	0.96 (0.78–1.19)
Age 65	1.38 (1.13–1.68) [‡]	1.33 (1.12–1.58) [‡]	1.23 (1.02–1.48) [‡]
Men	1.72 (1.41–2.10) [‡]	1.58 (1.32–1.90) [‡]	1.33 (1.10–1.61) [‡]
Minority Race	0.56 (0.46–0.69) [‡]	0.63 (0.53–0.75) [‡]	0.73 (0.60–0.88) [‡]
Not Married	0.56 (0.45–0.69) [‡]	0.68 (0.57–0.82) [‡]	0.55 (0.45–0.68) [‡]
No Health Insurance	0.51 (0.39–0.66) [‡]	0.57 (0.44–0.73) [‡]	0.95 (0.73–1.24)
Ghali Index 1	1.07 (0.88–1.31)	1.04 (0.87–1.23)	1.05 (0.87–1.27)
Diabetes	1.24 (1.01–1.51) [‡]	1.21 (1.02–1.43) [‡]	1.44 (1.19–1.73) [‡]
9 Medications	1.80 (1.45–2.22) [‡]	1.62 (1.36–1.93) [‡]	2.42 (1.97–2.94) [‡]
Current Smoker	0.59 (0.44–0.80) [‡]	0.56 (0.42–0.76) [‡]	0.64 (0.48–0.85) [‡]
On Statin at Admission	3.83 (3.12–4.72) [‡]	3.21 (2.61–3.99) [‡]	--

[‡] p<.0001[‡] p<.05

Table 3
Association Between Caregiver Status and Attainment of LDL-C Goals and Statin Use

Variable	Low-Density Lipoprotein Cholesterol (mg/dL)				On Statin	
	<100		<70			
	Men OR (95% CI)	Women OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)
Paid vs. No Caregiver	1.27(0.79–2.03)	1.16(0.77–1.75)	1.11(0.77–1.60)	0.91(0.61–1.34)	1.19(0.77–1.82)	1.42(0.93–2.14)
Informal vs. No Caregiver	1.26(0.94–1.68)	1.05(0.72–1.55)	1.35(1.07–1.70) [‡]	1.04(0.72–1.51)	0.95(0.73–1.23)	0.94(0.64–1.36)

Data are presented as ORs (95% CIs)

[‡] p < 0.05

Table 4

Multivariable Analysis for Having an Informal Caregiver and LDL-C <70mg/dL Overall and Stratified by Gender

Variable	LDL-C < 70mg/dL			
	Unadjusted Overall OR (95% CI)	Fully Adjusted Overall OR (95% CI)	Fully Adjusted Men OR (95% CI)	Fully Adjusted Women OR (95% CI)
Paid Caregiver vs. No Caregiver	1.11 (0.77–1.60)	0.82 (0.58–1.14)	1.20 (0.76–1.90)	0.48 (0.29–0.81) [‡]
Informal Caregiver vs. No Caregiver	1.27 (1.05–1.54) [‡]	1.26 (1.00–1.59) [‡]	1.35 (1.03–1.78) [‡]	1.07 (0.69–1.66)
Age ≥ 65		1.16 (0.94–1.42)	1.10 (0.86–1.41)	1.35 (0.91–2.01)
Men		1.48 (1.18–1.86) [‡]	--	--
Minority Race		0.73 (0.59–0.90) [‡]	0.69 (0.53–0.90) [‡]	0.85 (0.59–1.22)
Not Married		0.96 (0.78–1.19)	0.99 (0.76–1.28)	0.95 (0.66–1.38)
No Health Insurance		0.61 (0.45–0.83) [‡]	0.53 (0.35–0.79) [‡]	0.77 (0.48–1.23)
Ghali Index ≥ 1		0.91 (0.74–1.13)	0.87 (0.67–1.13)	0.98 (0.68–1.43)
Diabetes		1.03 (0.83–1.27)	1.04 (0.81–1.35)	1.00 (0.69–1.46)
≥ 9 Medications		1.47 (1.18–1.82) [‡]	1.43 (1.10–1.86) [‡]	1.65 (1.12–2.44) [‡]
Current Smoker		0.79 (0.55–1.12)	0.64 (0.42–0.97) [‡]	1.36 (0.72–2.60)
On Statin at Admission		2.66 (2.10–3.38) [‡]	2.37 (1.78–3.16) [‡]	3.40 (2.21–5.22) [‡]

Data are presented as ORs (95% CIs)

[‡] p < 0.05