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Antilipidemic adherence post-coronary artery disease diagnosis among those with and without an *ICD-9* diagnosis of depression

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Abstract

Objectives: An association between depression and coronary artery disease (CAD) is well established. Poor adherence to cardiac treatments may be one way depression could contribute to the increased risk of coronary events among depressed patients. We sought to evaluate whether adherence to antilipid medication, a therapy shown to be beneficial in secondary prevention of coronary events, differs among CAD patients with and without an *ICD-9* depression diagnosis. **Methods:** Patients were included if, at angiography, they were determined to have CAD (stenosis ≥70%), were discharged on an antilipid medication, and re-filled their prescriptions at a participating pharmacy. A patient was determined to have depression (*ICD-9* codes 296.2–296.36, 311) if the diagnosis occurred prior to angiography or within 6 months of the CAD diagnosis. Adherence and long-term outcomes were evaluated at 6 months, 1 year, 18 months and 2 years. **Results:** A total of 585 patients were included, with 73 (12.5%) having a diagnosis of depression prior to or within 6 months of CAD diagnosis. At all time-points, those with depression had a lower mean adherence compared to those without depression. Differences in adherence rates after adjustment were 7% (P=.001), 6% (P=.02), 13% (P<.0001) and 5% (P=.18) at 6 months, 1 year, 18 months, and 2 years, respectively. Though not statistically significant, there were clinically important associations between adherence and depression on the combined outcome of death, myocardial infarction, and revascularization. **Conclusion:** Depression was the strongest predictor of antilipidemic medication adherence after 2 years of follow-up among CAD patients. Such results suggest that poor antilipid adherence may be one mechanism by which depression contributes to CAD events.

Keywords: Adherence; Antidepressant medication; Coronary artery disease; Depression

Introduction

In the year 2020, the top two contributors of worldwide disease burden are projected to be ischemic heart disease and major depression [1]. An association between these two diseases is well established [2–4]. Poor adherence to cardiac treatments may be one way in which depression could contribute to the increased risk of coronary events among depressed patients.

Depression has been reported to be associated with poor adherence across a variety of disease populations [5–8] and treatments [9–11]. It is known that improving adherence at both the physician and patient level for the prescription of guideline-recommended medications for coronary artery disease (CAD) prevention is associated with a reduction in mortality [12–14]. Guidelines specify that CAD patients should be treated with a lipid-lowering agent (statin, niacin, fibrate, ezetimibe), preferably a statin [15]. The benefits of lipid-lowering therapy after CAD diagnosis have been well established in large randomized clinical trials [16–19], with a recommendation that this therapy should continue indefinitely [15].

Treatments among CAD patients that have been evaluated for their association to depression include the regimen of

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cardiovascular drugs both collectively and individually, diet, and exercise [9–11,20]. Though studies have evaluated statin adherence, no study has collectively assessed the association of depression to lipid-lowering medications. Therefore, the primary purpose of this study was to evaluate whether lipid-lowering adherence differs among CAD patients with and without an *ICD-9* diagnosis of depression. Patients with depression were also evaluated to determine whether treatment by antidepressant medication (ADM) affects adherence. The association of adherence was made to the composite outcome of death, myocardial infarction (MI), and revascularization.

Methods

Patient population

Patients from the Intermountain Heart Collaborative Study (IHCS) were studied [21,22]. The IHCS is a cardiac catheterization registry that includes patients undergoing catheterization at an Intermountain Healthcare hospital (LDS Hospital: Salt Lake City, UT, USA; Intermountain Medical Center: Murray, UT, USA; and McKay Dee Hospital: Ogden, UT, USA). Patients were included if, at angiography, (baseline) they were determined to have CAD (stenosis ≥70%), were discharged on a lipid lowering medication, and refilled their prescriptions at an Intermountain Healthcare pharmacy. The institutional review board approved this study.

Adherence

Adherence was calculated using the medication possession ratio (MPR); however, since the MPR was calculated across multiple refills, the continuous measure of adherence (CMA) was utilized [23]. This formula for this calculation is:

$$\text{CMA} = \mathbf{M} / \mathbf{I}$$

where **M** is the number of days that medication is supplied and **I** is the number of days in the refill interval. Only patients with a CMA score for lipid-lowering medications were included.

Within the Intermountain system, a standardized discharge medication protocol was implemented in 1999 for all those diagnosed with CAD [12]. This protocol included a statin prescription, or other antilipid medication if contraindicated, upon hospital discharge. Thus, a protocol for prescribing a lipid-lowering medication is well established and followed prior to 2002 when information on Intermountain Healthcare pharmacy records became available.

Depression

A patient was determined to have a clinical diagnosis of depression (*ICD-9* codes 296.2–296.36 and 311) if the diagnosis occurred prior to angiography or within 6 months of the CAD diagnosis. Anti-depressant medication use was also assessed and included tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, and other antidepressant (amoxapine, trazodone, venlafaxine, maprotiline, mirtazapine, nefazodone, bupropion). Within this study, no patients were defined as on an ADM without an associated depression diagnosis.

Covariables

Patient baseline characteristics collected included age, sex, smoking (self-reported: included active smokers or those with a >10 pack-year history), family history of CAD (patient-reported if a first-order relative had suffered cardiovascular death, MI, or coronary revascularization before age 65 years), prior MI, prior cerebrovascular accident (CVA), and body mass index. Information on patient clinical conditions included diabetes (fasting blood glucose ≥126 mg/dl, clinical diagnosis of diabetes mellitus, or anti-diabetic medication use), hypertension (systolic blood pressure ≥140 mmHg, diastolic ≥90 mmHg, or anti-hypertensive use), renal failure (clinical renal failure or glomular filtration rate <15 ml/min), and hyperlipidemia (total cholesterol ≥200 mg/dl, LDL ≥130 mg/dl, or cholesterol-lowering medication use). Reason for angiography (clinical presentation) were documented and included stable angina (stable exertional symptoms only), unstable angina (progressive symptoms or symptoms at rest), or acute MI (creatine kinase-MB >6 ng/dl and creatine kinase-MB index >3%). The treatment type that the patient received was defined as treatment with medication only, percutaneous coronary intervention, or coronary artery bypass surgery. The type and the total number of discharge medications were also recorded.

Follow-up and event assessment

Patients were assessed for adherence to lipid-lowering medications and follow-up events (death, MI, or revascularization) for 2 years at 6-month intervals. Deaths were determined by telephone survey, hospital records, Utah State Health Department records (death certificates), and were verified through Social Security death records. MI was defined as a hospitalization where a patient had a creatine kinase-MB >6 mg/dl and creatine kinase-MB index >3%. Revascularization was determined by hospital records and included follow-up angiography or coronary artery bypass surgery. Patients not listed as deceased in any registry were considered to be alive (censor date: April 30, 2007).

Statistical analysis

The chi-square test and Student's *t* test were used to examine univariable associations of an *ICD-9* diagnosis of depression to baseline and clinical characteristics. Linear regression was used to assess the association of adherence to depression and other covariables. To determine the