Is Risk Factor Control and Guideline-Based Medical Therapy Optimal in Patients With Nonobstructive Coronary Artery Disease? A Veterans Affairs Study

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Abstract: *Background:* Aggressive risk factor modification using evidence-based secondary prevention strategies is recommended in coronary artery disease (CAD). Utilization of such strategies was compared in patients with nonobstructive CAD (NOCAD) and obstructive CAD (OCAD). *Methods:* Patients undergoing coronary angiography (excluding normal coronary angiograms), between January 2006 and June 2006, at the Veterans Affairs Medical Center were included. Demographic, clinical and treatment data were compared between the groups at baseline and 1 year. *Results:* Of the 354 patients who underwent coronary angiography, 222 (63%) had follow-up data available at 12 ± 2 months. The mean age in the NOCAD (n = 119) and OCAD (n = 103) groups was similar. There was a lower prevalence of hypertension and heart failure ($P < 0.05$) in the NOCAD group. Compared with the OCAD group, aspirin use was similar but statin use was lower in the NOCAD group ($P = 0.008$). At 1 year, statin use ($P = 0001$) and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use ($P = 0.001$) were significantly lower, whereas the use of aspirin was numerically lower ($P = 0.06$) in the NOCAD group. Mean low-density lipoprotein cholesterol levels were at goal (<100 mg/dL) in the NOCAD group at baseline and 1 year, whereas the same slightly worsened in the OCAD group at 1 year. *Conclusions:* The use of evidence-based medical therapy is lower in patients with NOCAD compared with those with OCAD. Improved awareness among health care providers and a unified effort to implement secondary prevention strategies may help correct such deficiencies.

Key Indexing Terms: Risk factors; Medical therapy; Nonobstructive coronary artery disease. **[Am J Med Sci 2013;345(5):339–342.]**

Risk factor modification remains the cornerstone of secondary prevention in coronary artery disease (CAD). Optimal secondary prevention implies adequate treatment of hypertension, diabetes and hypercholesterolemia using standard guideline-based treatments as outlined in the current American College of Cardiology/American Heart Association (ACC/AHA) guidelines for secondary prevention.[1,2] Backed by strong clinical data, the ACC/AHA CAD guidelines give a class IA recommendation for the use of aspirin, beta-blockers and statins in patients with established CAD.[3] Aggressive use of such therapies for risk factor control is warranted even in nonobstructive CAD (NOCAD) to modify the underlying risk factors and possibly slow the progression of atherosclerosis. Secondary prevention strategies do not differ between obstructive CAD (OCAD) and NOCAD, and therefore, the degree of risk factor control should essentially be identical. It is however unknown if the risk factor control is similar between patients with NOCAD and those with OCAD. We hypothesize that risk factor control in patients with NOCAD may be suboptimal when compared with those with OCAD.

PATIENTS AND METHODS

Patients who underwent coronary angiography, between January 2006 and June 2006 at the Veterans Affairs (VA) Medical Center in Oklahoma City, and for whom 1-year follow-up data were available, were included. Demographic, clinical, laboratory and treatment data were compared between NOCAD and OCAD groups at baseline and 1 year. Of the 354 patients who had coronary angiograms during this period, 222 patients with CAD for whom data were available at baseline and 1 year were analyzed in this study. The local institutional review board and the VA Research and Development Committee approved the study. Based on the evidence of binary stenosis by visual estimate, patients were classified as having either NOCAD (<70% stenosis in the major epicardial vessels and <50% left main stenosis) or OCAD (≥70% stenosis in the major epicardial vessels or ≥50% left main stenosis). All patients with a history of coronary artery bypass graft or percutaneous coronary revascularization and those with normal coronary angiograms were excluded. Baseline demographic and clinical characteristics included the following: age; sex; race; weight; body mass index; smoking status; medical comorbidities such as hypertension (history/antihypertensive medications), diabetes, chronic kidney disease, heart failure and dyslipidemia; serum creatinine level; medications at the time of discharge; fasting lipid profile; and hemoglobin A1C (%). Local and remote VA electronic database was used to collect data on variables at the end of 12 ± 2 months. At follow-up, each patient's blood pressure, medications, lipid profile, serum creatinine level and hemoglobin A1C level were once again recorded.

Statistical Analysis

Continuous data were reported as means with 2 standard deviations. Data were assumed to be nonparametric. Wilcoxon rank sum test was used to compare means within groups, Mann-Whitney's U test for independent samples and χ^2 test for proportion comparison, at a significance level of 0.05. SPSS 17.0 (SPSS, Inc, Chicago, IL) was used for data analysis.

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Submitted November 23, 2011; accepted in revised form April 4, 2012.

The authors have no financial or other conflicts of interest to disclose.

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RESULTS

Patient Characteristics

Of the 222 patients, 119 had NOCAD and 103 had OCAD. Baseline demographic and clinical characteristics are described in Table 1. Prevalence of hypertension (81% versus 91%, $P = 0.02$) and heart failure (17% versus 28%, $P = 0.04$), current smoking status (24% versus 28%, $P = 0.04$), serum triglyceride level (173 versus 206 mg/dL, $P = 0.009$) and use of statins (68% versus 82%, $P = 0.02$) were significantly lower in patients with NOCAD compared with those with OCAD.

TABLE 1. Baseline characteristics of the study population

Baseline characteristics	NOCAD (n = 119)	OCAD (n = 103)	P
Demographics			
Age, yr (mean ± SD)	63 ± 8	62 ± 7	NS
BMI (mean ± SD)	32 ± 8	31 ± 7	NS
Sex (%)			
Male	96	99	NS
Female	4	1	NS
Race (%)			
Caucasian	82	95	0.02
African American	15	3	0.018
Hispanic	1	1	
Other	2	1	
Current smokers (%)	24	28	0.04
Medical comorbidities (%)			
Hypertension	81	91	0.02
Diabetes	44	48	NS
CKD	18	14	NS
Heart failure	17	28	0.04
Dyslipidemia	76	85	NS
Medications (%)			
Aspirin	69	69	NS
Clopidogrel	33	43	NS
Beta-blockers	69	75	NS
Statins	68	82	0.02
Calcium channel blockers	45	39	NS
Long-acting nitrates	31	27	NS
ACEi/ARBs	64	66	NS
Laboratory tests (mg/dL ± SD)			
Total cholesterol	157 ± 46	163 ± 40	NS
Triglycerides	173 ± 147	206 ± 29	0.009
LDL	97 ± 37	97 ± 29	NS
HDL	36 ± 12	36 ± 12	NS
Serum creatinine	1.2 ± 0.9	1.3 ± 1.6	NS
Hemoglobin A1C (%)	7.7 ± 1.7	7.3 ± 1.9	NS
Systolic blood pressure (mm Hg)	132 ± 17	131 ± 24	NS
Diastolic blood pressure (mm Hg)	78 ± 11	75 ± 14	NS

ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BMI, body mass index; CKD, chronic kidney disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NOCAD, nonobstructive coronary artery disease; NS, nonsignificant; OCAD, obstructive coronary artery disease; SD, standard deviation.

One-Year Follow-up Data

In the NOCAD group, there was no statistically significant improvement in the use of aspirin, statins, beta-blockers or ACEi/ARBs when compared with baseline (Table 2). In comparison, in the OCAD group, a greater proportion of patients were on statins and ACEi/ARBs at the end of the follow-up period of 1 year (Table 3). There were greater reductions in the systolic blood pressure and serum triglyceride levels at 1 year in the OCAD group (Table 3).

At 12 months, the NOCAD group continued to show a statistically significantly lower use of statins (74% versus 91%, $P = 0.001$), beta-blockers (70% versus 84%, $P = 0.02$) and ACEi/ARBs (61% versus 82%, $P = 0.001$) and a trend toward lower use of aspirin (68% versus 79%, $P = 0.06$) as compared with the OCAD group (Figure 1; Tables 2 and 3).

The mean low-density lipoprotein (LDL) level in the NOCAD group was <100 mg/dL at both baseline and 1-year follow-up (Table 2). However, in the OCAD group, the mean LDL level actually increased from baseline to 1 year (Table 3). The proportion of patients with target LDL levels of <100 mg/dL at baseline in the NOCAD and OCAD groups were 57% and 61%, respectively. At 1 year, 57% of the patients with NOCAD had a target LDL of <100 mg/dL versus 71% of those with OCAD ($P < 0.05$). Smoking status at follow-up was very difficult to ascertain owing to an underreporting of these important data at follow-up visits. Mean systolic blood pressure in both OCAD and NOCAD groups was <140/90 mm Hg at baseline and follow-up. However, there was a greater reduction of systolic blood pressure in the OCAD group at 1-year follow-up (Tables 2 and 3). Hemoglobin A1C levels were >7.0% at baseline and follow-up in both NOCAD and OCAD groups (Tables 2 and 3).

DISCUSSION

This VA study found less-than-ideal use of evidence-based medical therapies in patients with CAD, especially so in

TABLE 2. Comparison of medical therapies and risk factors in the nonobstructive coronary artery disease (n = 119) group at baseline and 1 year

	Baseline	1 yr	P
Medications (%)			
Aspirin	69	68	NS
Beta-blockers	69	70	NS
Statins	68	74	NS
Calcium channel blockers	45	45	NS
Long-acting nitrates	31	27	NS
ACEi/ARBs	64	61	NS
Laboratory tests (mg/dL ± SD)			
Total cholesterol	157 ± 46	155 ± 40	NS
Triglycerides	173 ± 147	177 ± 132	NS
LDL	97 ± 37	89 ± 34	NS
HDL	36 ± 12	38 ± 14	NS
Serum creatinine	1.2 ± 0.9	1.24 ± 0.7	NS
Hemoglobin A1C (%)	7.3 ± 1.9	7.2 ± 1.7	NS
Systolic blood pressure (mm Hg)	132 ± 17	130 ± 17	NS
Proportion of patients with LDL <100 mg/dL (%)	57	57	NS

ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, nonsignificant; SD, standard deviation.

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