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Statins for Prevention of Cardiovascular Events in a Low-Risk Population With Low Ankle Brachial Index

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ABSTRACT

BACKGROUND Evidence is lacking about the effectiveness of risk reduction interventions in patients with asymptomatic peripheral arterial disease.

OBJECTIVES This study aimed to assess whether statin therapy was associated with a reduction in major adverse cardiovascular events (MACE) and mortality in this population.

METHODS Data were obtained from 2006 through 2013 from the Catalan primary care system's clinical records database (SIDIAP). Patients age 35 to 85 years with an ankle-brachial index ≤0.95 and without clinically recognized cardiovascular disease (CVD) were included. Participants were categorized as statins nonusers or new-users (first prescription or represcribed after at least 6 months) and matched 1:1 by inclusion date and propensity score for statin treatment. Conditional Cox proportional hazards modeling was used to compare the groups for the incidence of MACE (myocardial infarction, cardiac revascularization, and ischemic stroke) and all-cause mortality.

RESULTS The matched-pair cohort included 5,480 patients (mean age 67 years; 44% women) treated/nontreated with statins. The 10-year coronary heart disease risk was low (median: 6.9%). Median follow-up was 3.6 years. Incidence of MACE was 19.7 and 24.7 events per 1,000 person-years in statin new-users and nonusers, respectively. Total mortality rates also differed: 24.8 versus 30.3 per 1,000 person-years, respectively. Hazards ratios were 0.80 for MACE and 0.81 for overall mortality. The 1-year number needed to treat was 200 for MACE and 239 for all-cause mortality.

CONCLUSIONS Statin therapy was associated with a reduction in MACE and all-cause mortality among participants without clinical CVD but with asymptomatic peripheral arterial disease, regardless of its low CVD risk. The absolute reduction was comparable to that achieved in secondary prevention. (J Am Coll Cardiol 2016;67:630–40) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Prescription of statins to prevent cardiovascular disease (CVD) is mainly a "high-risk" strategy focused on detection and intensive management of risk factors in individuals with a high probability of developing CVD (1). In the lipid management arena, this approach is grounded in the knowledge that the absolute risk reduction achieved with statin therapy improves with increasing CVD risk (2).

Detection of asymptomatic peripheral arterial disease (PAD) using the ankle-brachial index (ABI) in screening procedures is a potentially useful strategy to identify candidates for intensive risk-factor management (3) because low ABI values are associated with an increased risk of CVD and total mortality, independent of the CVD risk calculated by the Framingham function (4). Moreover, ABI measurement is reliable, simple, and inexpensive, and therefore suitable for target-population risk screening (5).

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Unfortunately, the usefulness of this screening remains uncertain (6,7), and available guidelines offer heterogeneous recommendations (8). The American College of Cardiology, American Heart Association, and Inter-Society Consensus for the management of patients with PAD have recommended ABI screening, especially for certain groups of asymptomatic individuals (principally subjects age 50 to 69 years who also have diabetes or smoking history, and all patients age >70 years) (9). In contrast, the U.S. Preventive Services Task Force recommends against routine ABI screening in asymptomatic adults (8). One fundamental reason for this uncertainty is the lack of evidence about the effectiveness of risk reduction interventions when asymptomatic PAD is detected (10).

In this study, we aimed to assess whether statin use was associated with a reduction in incidence of CVD and mortality in individuals with asymptomatic PAD detected by ABI measurement.

METHODS

DATA SOURCE. The Information System for the Development of Research in Primary Care (SIDIAP) was created by the Catalan Institute of Health and the Jordi Gol Primary Care Research Institute. This anonymized database contains standardized, cumulated, clinical information about nearly 5 million patients attended by the 3,414 general practitioners (GPs) in the 274 primary care practices managed by the Catalan Institute of Health, consisting of approximately 80% of the Catalan population or 10% of the Spanish population (11). The records include demographic data; clinical diagnoses coded by International Classification of Diseases, 10th revision; referral and hospital discharge information (International Classification of Diseases-9th revision); laboratory tests; and treatments (drug prescriptions and drugs invoiced at any community pharmacy). All GPs follow the same clinical protocols for data recording, and completeness and continuity are assessed externally. A subset of records from GPs who surpass pre-defined data quality standards (12) constitute The Information System for the Development of Research in Primary Care, Quality (SIDIAP^{Q}), which provides anonymized data on approximately 2 million patients, attended by 1,365 GPs, yielding nearly 14 million person-years of clinical data for 2005 through 2013. The high quality of these data and its representativeness of the population of Catalonia in terms of geographic, age, and sex distributions has been previously documented (12), specifically for CVD and cardiovascular risk factors (13). Ethics approval for observational research using SIDIAP^{Q} data was obtained from a local ethics committee.

PARTICIPANTS AND STUDY DESIGN. A cohort study was designed for matched-pair analysis on the basis of study inclusion date and propensity score (PS) for statin treatment. All patients age 35 to 85 years with an ABI measurement recorded in SIDIAP^{Q} between April 2006 and December 2011 were eligible for inclusion. Follow-up lasted till December 2013, guaranteeing at least 2 years of data for each participant. Although individuals with an ABI between 0.91 and 0.95 can be considered to be at "borderline" cardiovascular risk (14), we used an ABI of ≤0.95 instead of 0.90 to identify individuals with asymptomatic PAD, as in a previous clinical trial with aspirin (15). This choice was made because the 0.95 cut-point covered a wider proportion of the population (16), with notably higher risk than patients with ABI between 1 and

ABBREVIATIONS AND ACRONYMS

ABI = ankle-brachial index
CHD = coronary heart disease
GP = general practitioner
MACE = major adverse cardiovascular event
NNT = number needed to treat
PAD = peripheral arterial disease
PS = propensity score
RCT = randomized clinical trial
SIDIAP^{Q} = The Information System for the Development of Research in Primary Care, Quality

authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Ramos and Garcia contributed equally to this work.

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