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Research Article

Regional and physician specialty–associated variations in the medical management of atherosclerotic renal–artery stenosis

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Abstract

For people enrolled in Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL), we sought to examine whether variation exists in the baseline medical therapy of different geographic regions and if any variations in prescribing patterns were associated with physician specialty. Patients were grouped by location within the United States (US) and outside the US (OUS), which includes Canada, South America, Europe, South Africa, New Zealand, and Australia. When comparing US to OUS, participants in the US took fewer anti–hypertensive medications (1.9 ± 1.5 vs. 2.4 ± 1.4; $P < .001$) and were less likely to be treated with an angiotensin–converting enzyme inhibitor or angiotensin II receptor blocker (46% vs. 62%; $P < .001$), calcium channel antagonist (37% vs. 58%; $P < .001$), and statin (64% vs. 75%; $P < .05$). In CORAL, the identification of variations in baseline medical therapy suggests that substantial opportunities exist to improve the medical management of patients with atherosclerotic renal–artery stenosis. J Am Soc Hypertens 2015;9(6):443–452. © 2015 American Society of Hypertension. All rights reserved.

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Introduction

Atherosclerotic renal–artery stenosis (RAS) is associated with secondary hypertension and cardiac morbidity and mortality worldwide.[1,2] A lack of consensus exists regarding optimal treatment strategies for individuals with atherosclerotic RAS. However, the recently completed Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial found that stent revascularization conferred no further benefit to patient outcome in the setting of comprehensive, multifactorial medical therapy for patients with atherosclerotic RAS and either hypertension or chronic kidney disease.[3] Thus, for the majority of these individuals, medical therapy is the preferred management strategy. While medical therapy remains an important foundation in the treatment of atherosclerotic RAS,[4] the optimal anti–hypertensive regimen for patient management remains inconclusive. Limited work in this area suggests that renin–angiotensin inhibitors and HMG–CoA reductase inhibitors (statins) may be beneficial.[5,6] Angiotensin blockade may reduce mortality in people with RAS,[2,7–9] and observational studies have suggested that statin–treated individuals experience a lower rate of RAS progression[10] and improved prognosis.[11] However, these data are derived mostly from retrospective observations.

Little is known specifically about the community use of anti–hypertensive, anti–platelet, and lipid–lowering medications in individuals with atherosclerotic RAS. In particular, questions remain regarding regional and worldwide trends in medication use and how physician specialty influences the medical management of this population.

Geographic region has been shown to influence clinical practice in the treatment of hypertension, with both inter–continental and intra–continental variations reported.[12–20] Variations in non–clinical factors such as region and physician subspecialty may reflect potential barriers to the uniform adoption of recommended clinical guidelines.[21] How exactly these trends apply to the more specific group of people with atherosclerotic RAS, a population with multiple co–morbidities, complex clinical scenarios, and clear indications to treat with certain medications, is unknown. Baseline demographic and medication data from the CORAL trial, a prospective, international, multi–center randomized clinical trial, was used to address these concerns. The CORAL trial enrolled participants with atherosclerotic RAS at sites throughout the United States, North and South America, Europe, South Africa, New Zealand, and Australia. Among the patients enrolled in the CORAL trial, we sought to determine whether variation exists in the use of medical therapy categories between regions and whether this variation was driven by participant characteristics or prescribing physician subspecialty. Specifically, in the current study, we sought to determine if the type and number of baseline medications varied among (1) different regions from which the clinical centers enrolled patients into the trial and (2) specialties of the physicians responsible for overseeing patient care in the trial.

Methods

The CORAL study was a prospective, international, multi–center, non–blinded, two–arm, randomized trial for which the study design, rationale, and methods have been previously reported.[22] In people with hemodynamically significant atherosclerotic RAS who also received optimal medical therapy, the study assessed the effect of revascularization, accomplished through endovascular stenting, on cardiovascular and renal events (ClinicalTrials.gov identifier NCT00081731). All centers obtained institutional review committee approval and followed institutional guidelines. Participants provided written informed consent to join the study. The CORAL trial was undertaken in accordance with the Declaration of Helsinki.

Medication Information

Baseline medication data analyzed in the current study were obtained from the medication logs of the 931 participants randomized into the CORAL trial. The medications were categorized into 12 drug classes: nine classes of anti–hypertensive agents and three separate, additional drug classes that included anti–platelets, lipid–lowering therapies, and nitrates. The anti–hypertensive category consisted of the following nine medication classes: alpha beta blocker, vasodilator, alpha blocker, diuretic, aldosterone antagonist, beta blocker, angiotensin–converting enzyme inhibitor (ACE–I) or angiotensin II receptor blocker (ARB), calcium channel blocker, and renin inhibitor. The number of patients on the renin inhibitor class was too few for appropriate analysis; its data was therefore excluded from presentation. Patients taking one or more medication(s) within a class were identified and counted as being on that class of medication. Medication use at baseline was recorded and classified (yes, no, or unknown). Unknown was designated if the start and stop dates could not be ascertained.

Kidney Function Measurement

Kidney function was assessed using serum creatinine (mg/dL), creatinine–based estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2) calculated using the modified diet in renal disease standard (MDRD–eGFR), and cystatin–C (mg/L). All measurements were centrally analyzed by the Biochemistry Core Lab at the University of Minnesota.

Blood Pressure Measurement and Goal

Blood pressure was measured at the baseline study visit. Participants were seated for 5 minutes in a quiet room, and

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