Associations Between Renal Duplex Parameters and Adverse Cardiovascular Events in the Elderly: A Prospective Cohort Study

Jeffrey D. Pearce, MD,[1] Timothy E. Craven, MSPH,[2] Matthew S. Edwards, MD, MS,[1] Matthew A. Corriere, MD,[1] Teresa A. Crutchley, MD,[1] Shawn H. Fleming, MD,[1] and Kimberley J. Hansen, MD[1]

Background: Atherosclerotic renovascular disease is associated with an increased risk of cardiovascular disease (CVD) events. This study examines associations between Doppler-derived parameters from the renal artery and renal parenchyma and all-cause mortality and fatal and nonfatal CVD events in a cohort of elderly Americans.

Study Design: Cohort study.

Setting: A subset of participants from the Cardiovascular Health Study (CHS). Through an ancillary study, 870 (70% recruitment) Forsyth County, NC, CHS participants consented to undergo renal duplex sonography to define the prevalence of renovascular disease in the elderly, resulting in 726 (36% men; mean age, 77 years) technically adequate complete studies included in this investigation.

Predictor: Renal duplex sonography–derived Doppler signals from the main renal arteries and renal parenchyma. Spectral analysis from Doppler-shifted frequencies and angle of insonation were used to estimate renal artery peak systolic and end diastolic velocity (both in meters per second). Color Doppler was used to identify the corticomedullary junction. Using a 3-mm Doppler sample, the parenchymal peak systolic and end diastolic frequency shift (both in kilohertz) were obtained. Resistive index was calculated as (1 − [end diastolic frequency shift/peak systolic frequency shift]) using Doppler samples from the hilar arteries of the left or right kidney with the higher main renal artery peak systolic velocity.

Outcomes & Measurements: Proportional hazard regression analysis was used to determine associations between renal duplex sonography–derived Doppler signals and CVD events and all-cause mortality adjusted for accepted cardiovascular risk factors. Index CVD outcomes were defined as coronary events (angina, myocardial infarction, and coronary artery bypass grafting/percutaneous coronary intervention), cerebrovascular events (stroke or transient ischemic attack), and any CVD event (angina, congestive heart failure, myocardial infarction, stroke, transient ischemic attack, and coronary artery bypass grafting [CABG]/percutaneous transluminal coronary intervention [PTCI]).

Results: During follow-up, 221 deaths (31%), 229 CVD events (32%), 122 coronary events (17%), and 92 cerebrovascular events (13%) were observed. Renal duplex sonography–derived Doppler signals from the renal parenchyma were associated independently with all-cause mortality and CVD outcomes. In particular, increased parenchymal end diastolic frequency shift was associated significantly with any CVD event (HR, 0.73; 95% CI, 0.62-0.87; $P < 0.001$). Marginally significant associations were observed between increases in parenchymal end diastolic frequency shift and decreased risk of death (HR, 0.86; 95% CI, 0.73-1.00; $P = 0.06$) and decreased risk of cerebrovascular events (HR, 0.78; 95% CI, 0.61-1.01; $P = 0.06$). Parenchymal end diastolic frequency shift was not significantly predictive of coronary events (HR, 0.84; 95% CI, 0.67-1.06; $P = 0.1$).

Limitations: CHS participants showed a "healthy cohort" effect that may underestimate the rate of CVD events in the general population.

Conclusion: Renal duplex sonographic Doppler signals from the renal parenchyma showed significant associations with subsequent CVD events after controlling for other significant risk factors. In particular, a standard deviation increase in parenchymal end diastolic frequency shift was associated with 27% risk reduction in any CVD event.

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INDEX WORDS: Renovascular disease; resistive index; intrarenal Doppler; renal duplex sonography; prospective; population based; cardiovascular events; Cardiovascular Health Study (CHS).

From the [1]Division of Surgical Sciences, Department of Vascular and Endovascular Surgery, and [2]Department of Biostatistical Sciences, Wake Forest University School of Medicine, Winston-Salem, NC.

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Address correspondence to Kimberley J. Hansen, MD, Professor of Surgery, Chairman, Department of Vascular and Endovascular Surgery, Division of Surgical Sciences, Wake Forest University School of Medicine, Winston-Salem, NC 27157-1095. E-mail: kjhansen@wfubmc.edu

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Atherosclerotic renovascular disease is a recognized cause of secondary hypertension and chronic kidney disease (ie, excretory renal insufficiency or ischemic nephropathy).[1-3] Renal duplex sonography is an accurate noninvasive means to diagnose hemodynamically significant renovascular disease in patients with severe hypertension and/or renal insufficiency.[2,4] The presence of renovascular disease assessed using renal duplex sonography has been associated with increased severity of hypertension and decreased renal function.[5,6] Moreover, it appears that the presence of renovascular disease is associated with increased risk of subsequent cardiovascular disease (CVD) events.[7,8]

In addition to providing information about hemodynamically significant atherosclerotic lesions of the main renal artery, renal duplex sonographic Doppler signals can be obtained from the renal hilum and renal parenchyma. Recent studies involving selected patient populations have shown strong associations between renal duplex sonographic measures of renal artery resistance in the hilum (an alternative measure of disease in the renal parenchyma) and severity of hypertension, progressive renal failure, and mortality.[9,10] In prior analyses of a Cardiovascular Health Study (CHS) cohort that had undergone renal duplex sonography, we showed strong associations between renal duplex sonographic measures from the renal parenchyma and severity of hypertension, as well as kidney disease.[11] In contrast, the present study constitutes the first examination of renal duplex sonographic measures from the renal parenchyma and risk of subsequent CVD events in the Forsyth County, NC, CHS cohort participating in the renal duplex sonography ancillary study.

The aim of this study is to examine relationships between renal duplex sonography–derived Doppler signals from the main renal arteries, hilar renal arteries, and renal parenchyma and follow-up mortality and CVD events to better describe previously established links between atherosclerotic kidney disease and CVD morbidity and mortality.

METHODS

The CHS

The design of the CHS has been described previously.[12] Briefly, it is a longitudinal multicenter observational cohort study of CVD risk factors, morbidity, and mortality in Americans aged ≥65 years. The initial CHS cohort was recruited from a randomly selected sample of Medicare-eligible individuals in 4 US communities (Forsyth County, NC; Sacramento County, CA; Washington County, MD; and Allegheny County, PA). Initial recruitment was performed between April 1989 and May 1990, with a supplemental cohort of African American participants recruited using the same method from June 1992 to June 1993.

All CHS enrollees underwent a baseline examination consisting of a detailed medical history and clinical examination. Annual follow-up examinations were performed to update medical data, assess the occurrence of cardiovascular events, and repeat portions of the clinical examination at previously defined intervals. Clinical examination included physical examination, blood pressure measurement, phlebotomy, electrocardiography, and pulmonary function testing. Serum creatinine was measured in conjunction with renal duplex examination.

Renal Duplex Sonography

The renal duplex sonographic examination was performed as part of an ancillary study to the CHS to define the prevalence of renovascular disease in a community-dwelling elderly cohort.[13] For this ancillary study, which was approved by the Wake Forest University Human Subjects Review Committee (Winston-Salem, NC), 1,245 Forsyth County participants were invited to participate on return for the annual examination between January 1995 and February 1997.

The technique of renal duplex sonography has been described previously.[2,13] Briefly, renal duplex sonography was performed by 2 registered vascular technologists using an Ultramark-9 HDI Ultrasound System (Advanced Technologies Laboratories, Bothell, WA) during the participant's return visit for his or her annual examination. After written informed consent and an overnight fast, sagittal B-mode scan images were obtained of the upper abdominal aorta, celiac axis, and superior mesenteric arteries using a 2.25- or 3.0-MHz ultrasound probe with the participant in the supine position. Identification of these 3 vessels was confirmed by the characteristic fasting waveforms from each vessel. Next, using the left renal vein as a reference, the aortic origins of the main renal arteries were identified. While maintaining an angle of insonation $<60°$, Doppler samples were obtained from each renal artery from aortic origin to renal hilum, for a total of 10 Doppler sample sites per renal artery. Spectral analysis from the Doppler-shifted frequencies and angle of insonation were used to estimate the renal artery peak systolic and end diastolic velocities (both in meters per second). Renal artery peak systolic velocity was confirmed using a flank approach with the participant in the right or left lateral decubitus positions, along with B-mode scan imaging of each kidney to determine the greatest longitudinal kidney length. While in the decubitus position, color Doppler was used to identify the corticomedullary junction. Using a 3-mm Doppler sample, the parenchymal peak systolic and end diastolic frequency shift (both in kilohertz) were obtained. Resistive index was calculated as (1 − [end diastolic frequency shift/peak systolic frequency shift]) using Doppler samples from the hilar arteries of the left or right kidney