Suma Vupputuri, PhD, The Center for Health Research, Kaiser Permanente Georgia, Atlanta, Georgia, USA, described the prevalence, incidence, and progression of nephropathy and identified demographic and clinical characteristics that are associated with progression in a US population-based sample.

A total of 11,562 members of a managed care organization (Kaiser Permanente), aged 18 years and older, with hypertension and type 2 diabetes, a urine-to-albumin creatinine ratio (UACR) measurement during 2001-2003, and at least one follow-up UACR, were independently assessed for different stages of nephropathy. Three baseline stages of nephropathy were defined: normal albumin (<30 µm/mg), microalbuminuria (30-299 µm/mg), and macroalbuminuria (≥300 µm/mg). Records through 2008 were searched for individuals who showed progression from baseline to a higher stage of nephropathy, including ESRD. Progression was defined as the first UACR value that was recorded in a stage that was higher than baseline. Incidence was calculated as the number of new cases over the sum of the person-time of the at-risk population. Independent predictors of time to progression were assessed using Cox regression.

At baseline, 59% of subjects had normal albumin (n=6853), 30% had microalbuminuria (n=3492), and 11% had macroalbuminuria (n=1217). The incidence of nephropathy progression (per 1000 person-years) was 94.6, 44.1, and 6.7 for normal albumin, microalbuminuria, and macroalbuminuria, respectively. Table 1 shows the number of patients who progressed to higher stages of nephropathy.

Table 1. Prevalence of Nephropathy and Progression to Subsequent Stages.

	Prevalent Normal Albumin n=6853	Prevalent Microalbuminuria n=3492	Prevalent Macroalbuminuria n=1217
Regressed to normal albumin, n (%)	–	932 (27%)	–
Regressed to microalbuminuria, n (%)	–	–	393 (32%)
No progression, n (%)	3244 (47%)	1656 (47%)	769 (63%)
Progressed to microalbumimuria, n (%)	3216 (47%)	–	–
Progressed to macroalbuminuria, n (%)	387 (6%)	890 (25%)	–
Progressed to ESRD, n (%)	6 (0.09%)	14 (0.4%)	55 (5%)

ESRD=end-stage renal disease

Predictors of progression of nephropathy included age (per 5 years), race (Caucasian), diabetes duration (per year), systolic and diastolic blood pressure (per 5 mm Hg), HbA1C (per 1%), body mass index (per 5 kg/m^2), estimated glomerular filtration rate (per 10 mL/min/1.73m^2), use of ACE inhibitors/ARBs, CVD, and active heart failure.

Although the ability to extend the results of this study to a broader population may be limited by the study sample (ie, only patients with diabetes and hypertension who had health insurance were included), Dr. Vupputuri concluded that in one of the first studies to examine the progression of nephropathy in a US population-based sample of adults with diabetes and hypertension, the lifetime risk of nephropathy and its progression may be greater than previously reported. Developing strategies to slow and/or prevent the progression of nephropathy may reduce the burden of disease.

The Association Between Arterial Stiffness and LV Diastolic Function in T2DM: 8-Year Follow-Up To the Hoorn Study

Individuals with diabetes are more likely to develop congestive heart failure (HF), particularly left-sided HF, than those without diabetes, but the underlying mechanisms remain controversial [Nichols GA et al. *Diabetes Care* 2004]. Arterial stiffness, which is more common in type 2 diabetes mellitus (T2DM), has been suggested as a potential cause of HF, while left ventricular (LV) mass has been shown to be a predictor [Stehouwer CD et al. *Diabetologia* 2008; de Simone G et al. *Eur Heart J* 2008]. Katja van den Hurk, PhD candidate, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands, presented data that addressed the issue of whether arterial stiffness was prospectively associated with a higher LV mass and worse LV diastolic function (indicated by increasing left atrial volume index [LAVI]) and whether this differed in individuals with or without T2DM.

These results were from an 8-year follow-up to the Hoorn Study, a population-based cohort study of diabetes and diabetes complications that began in 1989 [Henry RM et al. *Diabetes Care* 2004]. Echocardiography and arterial ultrasonography were performed in 2000 and again in 2008. Linear regression analyses were performed to

investigate associations between baseline carotid, brachial, and femoral artery distensibility coefficients (DCs, arterial stiffness) with LV mass index (LVMI, $g/m^{2.7}$) and LAVI (mL/m^2). The results were adjusted for age, gender, and mean arterial pressure (MAP). Individuals with moderate or severe mitral or aortic valve disease, or tachycardia (heart rate >90 beats per minute) were excluded.

Of the 796 individuals for whom baseline echocardiograms were available, 394 were included in the present analysis. Subjects with T2DM (n=128; 32%) were older, had a higher LAVI and blood pressure, and stiffer arteries (lower arterial DCs) at baseline compared with those without T2DM. After adjusting for age and gender, more arterial stiffness at baseline was significantly ($p<0.05$) associated with higher LVMI and LAVI. Additional adjustment for baseline MAP showed that blood pressure only partly explained these associations.

Subjects with T2DM have a significantly ($p<0.05$) higher LVMI and LAVI [van den Hurk et al. *Eur J Heart Fail.* 2010]. However, associations between arterial stiffness and LVMI or LAVI were not different for individuals with or without T2DM (p for interaction >0.10). Adjustments for HbA1C, heart rate, LVMI, systolic blood pressure, or use of antihypertensive medication did not change the results.

Arterial stiffness was prospectively associated with worse LV diastolic function, regardless of T2DM. However, individuals with T2DM commonly have stiffer arteries compared with those without T2DM, suggesting that arterial stiffening might be one of the causes of worse LV diastolic function in T2DM.

BNP is a Predictor of Changes in LV Systolic and Diastolic Function Regardless of Diabetes Status

Individuals with type 2 diabetes mellitus (T2DM) have an increased risk of developing heart failure (HF) and a worse prognosis if they already have HF. B-type natriuretic peptide (BNP) is a marker for HF—patients with nonsystolic HF have significantly ($p<0.001$) lower BNP levels than those with systolic HF [Maisel J et al. *J Am Coll Cardiol* 2003].

BNP levels that are well below current thresholds that are used to diagnose HF (<100 pg/mL) have been associated with increases in left ventricular (LV) mass and deterioration of LV systolic and diastolic function and can predict HF and cardiovascular disease (CVD) mortality [Wang TJ et al. *N Eng J Med* 2004]. BNP's association with LV mass and markers of LV diastolic function appears to be particularly strong in individuals with T2DM [Van den Hurk K et al. *Eur J Heart Fail* 2010].

Marieke H. Kroon, VU Medical Center, Amsterdam, The Netherlands, reviewed data from the Hoorn Study, which prospectively investigated whether BNP levels in a nonheart failure range predict LV mass, or LV systolic and diastolic function in individuals with and without T2DM.

Participants with atrial fibrillation, wall movement abnormalities, and moderate or severe aortic or mitral valve disease were excluded from this study. Plasma BNP (pmol/L) levels were measured, and 2D echocardiograms were performed at baseline (2000-2001). Follow-up was 8 years later. The 2D echocardiograms were used to measure LV mass index (LVMI, g/m^2), ejection fraction (% EF, systolic function), and left atrial volume index (LAVI, mL/m^2, diastolic function). Linear regression analyses, adjusted for gender, age, baseline heart function, use of antihypertensive medication, body mass index (BMI), and heart rate (HR), were performed to investigate the association of BNP with LVMI and of LV systolic with diastolic function. In case of significant effect modification ($p<0.10$), the linear regression coefficients for individuals with and without T2DM were reported separately.

Of the 796 participants who had baseline echocardiograms (baseline age 66 years; 32% with T2DM), 301 were available for the follow-up examination. Blood pressure levels were lower in T2DM patients at baseline. LV systolic function (% EF) and BNP were not significantly associated with either T2DM or non-T2DM patients when adjusted for age, gender, baseline EF, use of antihypertensives, BMI, and HR. However, this association was significant ($p<0.05$) when the total population was considered (Table 1). LV diastolic function (LAVI) and BNP levels were significantly ($p<0.05$) associated with T2DM and non-T2DM patients. LV mass (LVMI) and BNP level were significantly ($p<0.05$) associated in T2DM but not non-T2DM patients. The increase in LVMI was greater among those with higher baseline BNP, and the association was stronger among patients with T2DM. In patients without T2DM, the association was explained by baseline LVMI, BMI, and use of antihypertensives; in the T2DM patients, the association was independent. Regardless of T2DM status, a 10-pmol/L higher baseline BNP was associated with a 2.7% lower EF and a 5.0-mL/m^2 higher LAVI at follow-up.

These results suggest that slightly elevated BNP levels are associated with changes in LV systolic and diastolic