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

function. This association was not dependent on T2DM status. Only in T2DM patients were higher BNP levels associated with increase in LV mass. Thus, the presence or absence of T2DM should be taken into account if BNP levels are used to assess CVD risk.

Table 1. LV Function.

LV Systolic Function Regression coefficients, β (95% CI) per 10-pmol/L increase of baseline BNP for EF			
EF (%)	**Non-T2DM n=143**	**T2DM n=62**	**Total population n=205**
Age & gender	-2.5 (-5.4, 0.6)	-3.4 (-8.2, 1.4)	-2.5 (-4.9, -0.01)*
+ baseline EF	-2.6 (-5.6, 0.4)	-3.0 (-7.5, 1.4)	-2.7 (-5.2, -0.3)*
+ use of antihypertensives, BMI, & HR	-2.6 (-5.8, 0.6)	-4.0 (-8.3, 0.2)	-3.2 (-5.8, -0.7)*
LV Diastolic Function Regression coefficients, β (95% CI) per 10-pmol/L increase of baseline BNP for LAVI			
LAVI (mL/m²)	**Non-T2DM n=165**	**T2DM n=71**	**Total population n=236**
Age & gender	5.3 (2.8, 7.7)*	6.8 (2.5, 11.2)*	5.3 (3.2, 7.4)*
+ baseline EF	4.3 (1.7, 6.9)*	5.6 (1.2,10.1)*	4.2 (2.0, 6.4)*
+ use of antihypertensives, BMI, & HR	4.5 (1.8, 7.1)*	6.1 (1.7, 10.5)*	4.5 (2.4, 6.7)*
LV Mass Regression coefficients, β (95% CI) per 10-pmol/L increase of baseline BNP for LVMI			
LVMI (g/m²)	**Non-T2DM n=151**	**T2DM n=73**	
Age & gender	4.6 (-1.5, 10.0)	31.0 (14.7, 47.3)*	
+ baseline EF	1.0 (-4.9, 6.9)	26.4 (10.3, 42.5)*	
+ use of antihypertensives, BMI, & HR	0.1 (-5.9, 6.2)	30.6 (14.3, 46.8)*	

LV=left ventricular; CI=confidence interval; BNP= B-type natriuretic peptide; EF=ejection fraction; LAVI=left atrial volume index; LVMI-left ventricular mass index; *p <0.05

An Update on the DIGAMI Studies

Acute myocardial infarction (AMI) in patients with diabetes increases the risk of poor outcome. In the Diabetes Mellitus-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study, insulin-glucose infusion, followed by multidose insulin treatment, improved long-term prognosis in diabetic patients with AMI at 1 year [Malmberg K et al. *J Am Coll Cardoiol* 1995].

In DIGAMI 2, patients with type 2 diabetes or blood glucose >11 mmol/L and suspected myocardial infarction (MI) were randomized to one of three treatment strategies: Group 1–acute insulin-glucose infusion followed by insulin-based long-term glucose control (n=474); Group 2–insulin-glucose infusion followed by standard glucose control (n=473); or Group 3–routine metabolic management according to local practice (n=306) [Malmberg K et al. *Eur Heart J* 2005]. Subjects were treated for a mean of 2.1 years and, in an extended part of the trial, followed up for a maximum of 8.3 years (median 4.1). At the end of the study, there were no significant differences in morbidity, expressed as nonfatal reinfarctions and strokes, among the three groups. The data did suggest that glucose level is a strong, independent predictor of long-term mortality in this patient category, indicating that glucose control seems to be an important part of their management.

Results of a later post hoc analysis from DIGAMI 2, assessing the impact of glucose-lowering treatment with insulin, sulfonylureas, or metformin on long-term mortality and morbidity prognosis, showed no significant difference in mortality between the three treatments. The risk of nonfatal MI and stroke increased significantly with insulin, while metformin was protective [Mellbin LG et al. *Eur Heart J* 2008].

Linda Mellbin, MD, Department of Cardiology, Karolinska Institutet, Stockholm, Sweden, discussed recent data from the extended follow-up (maximum 8.3 years; median 4.1 years) for 1145 subjects in the DIGAMI 2 study. Total mortality was 34% (24% cardiovascular [CV]; 9.5% malignancies). Cox regression analysis did not show any difference in total or CV mortality among the treatment groups. The total number of fatal malignancies was 37, with the highest risk in Group 1 (HR vs Group 2, 1.83; 95% CI, 0.90 to 3.71; p=0.10 and Group 3, 3.57; 95% CI, 1.22 to 10.39; p=0.02). Treatment with insulin was associated with a significant increase in the risk of nonfatal MI and stroke (OR, 1.90; 95% CI, 1.38 to 2.60; p<0.0001) but not mortality (OR, 1.30; 95% CI, 0.94 to 1.80; p=0.11), while metformin was associated with a lower mortality (HR, 0.65; 95% CI, 0.47 to 0.90) and a lower risk of death due to malignancies (HR, 0.25; 95% CI, 0.08 to 0.83).

Long-term mortality is high after MI in patients with type 2 diabetes. The drug that is used for glucose control appears to have a prognostic impact. Prof. Mellbin suggested that the beneficial effects of metformin may be due to 5' AMP-activated protein kinase-induced improved endothelial