Cardiovascular Risk Factors and Systolic and Diastolic Cardiac Function: A Tissue Doppler and Speckle Tracking Echocardiographic Study

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Background: The aim of this study was to determine whether blood pressure, body mass index (BMI), serum lipids, glucose, and renal function are associated with left ventricular (LV) and right ventricular function in a low-risk population.

Methods: The associations of common risk factors with cardiac function were assessed, using multiple linear regression, in a random sample of 1,266 individuals free from hypertension, diabetes, and cardiovascular disease. A combination of conventional echocardiographic, speckle-tracking, and tissue Doppler methods was used to assess cardiac function.

Results: Older age and higher BMI, systolic and diastolic blood pressure, and non–high-density lipoprotein (HDL) cholesterol were associated with lower LV function. Thus, LV strain was reduced by approximately 5% per 5 kg/m^2 increase in BMI and by 4% per 10 mm Hg increase in diastolic blood pressure. Corresponding reductions in peak early diastolic mitral annular velocity were 7% for both BMI and diastolic blood pressure. Higher HDL cholesterol was associated with better LV function. In women, smoking was also associated with reduced LV function. LV function was lower also at low levels of diastolic pressure and BMI. Reduced right ventricular function was related to older age, smoking, higher diastolic blood pressure and non-HDL cholesterol, and lower HDL cholesterol.

Conclusions: These findings suggest that conventional risk factors may predict cardiac function many years before clinical disease. The J-shaped associations related to diastolic blood pressure and BMI may suggest that in some individuals, low levels of these factors may indicate underlying but unknown disease. (J Am Soc Echocardiogr 2011;24:322-32.)

Keywords: Blood pressure, Cholesterol, Obesity, Population, Strain

Unfavorable levels of blood pressure, body weight, and serum lipids, as well as smoking, diabetes, and impaired renal function, increase the risk for cardiovascular morbidity and mortality,[1,2] but little is known about their influence on cardiac function in the general population. Previous studies using ejection fraction (EF) to assess cardiac function have shown little effect of age[3] and no clear association with clinical symptoms of heart failure.[4] The restricted appropriateness of EF for quantification of left ventricular (LV) function[5-7] may be explained by increased radial shortening as longitudinal LV systolic function declines.[7,8] However, studies using tissue Doppler and speckle-tracking echocardiography have shown reduced LV function in patients with hypertension, diabetes mellitus, or ischemic heart disease and reduced LV function with increasing age in individuals without known cardiovascular disease.[9-15] Data on the association of cardiac function with risk factors in low-risk population are scarce.[10,11] Also, studies using blood flow Doppler have shown reduced LV diastolic function with increasing age but no age-related effect on systolic function.[15-17]

Longitudinal indices may be the best measures of LV function.[18] We hypothesized that unfavorable levels of blood pressure, body mass index (BMI), serum lipids, glucose, and renal function were associated with reduced cardiac function, on the basis of echocardiographic measurements. We used tissue Doppler and speckle-tracking echocardiography, as well as traditional echocardiographic measures, to study the association of these risk factors with cardiac function in a population sample of 1,266 individuals without known cardiovascular disease, hypertension, or diabetes.

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Abbreviations

BMI = Body mass index

EF = Ejection fraction

eGFR = Estimated glomerular filtration rate

HDL = High-density lipoprotein

LV = Left ventricular

pwTD = Pulsed-wave tissue Doppler

RV = Right ventricular

METHODS

Study Population

The third wave of the Nord-Trøndelag Health Study (HUNT) in Norway was conducted from 2006 to 2008. A total of 93,210 adults aged ≥ 20 years were invited, and 50,839 (54%) participated. Within the third wave of HUNT, the echocardiography study was conducted among participants in predetermined communities.[14,15] To be eligible, subjects had to be free from known cardiovascular disease, diabetes, or hypertension.[19] A total of 1,296 participants who met the inclusion criteria were randomly selected. In 30 participants, we discovered pathology on echocardiography that could influence the deformation analysis, and these 30 participants were therefore excluded.[14] Validation of the inclusion criteria was performed by the physician echocardiographer (H.D.), who also obtained the medical histories of the participants. The echocardiography study was approved by the Regional Committee for Medical Research Ethics and conducted according to the second Declaration of Helsinki. Written informed consent was obtained from all participants.

Anthropometrics and Laboratory Tests

The HUNT included self-administered questionnaires (medical history and smoking habits), clinical measurements (anthropometry and blood pressure), and blood samples, as previously described.[19] Renal function was assessed by the Modification of Diet in Renal Disease equation to calculate the estimated glomerular filtration rate (eGFR),[20] whereby reduced renal function is usually indicated by values <60 mL/min/1.73 m^2.[21] Smoking information was categorized as never, former, occasional, or current smoking, and the latter three categories were grouped into a category of "ever smoking" in the analyses. Blood pressure was measured three times by trained staff members using a Dinamap 845XT (GE Healthcare, Milwaukee, WI). Measurements were made after 2 min of rest with the arm on a table, and the average of the second and third measurements was used in the analyses.[19] Nonfasting blood samples were collected at study attendance, centrifuged, and placed in a refrigerator before transportation to the IEC 17025–accredited laboratory at Levanger Hospital on the same day. Serum analyses were performed on fresh blood samples using an Architect ci8200 (Abbott Laboratories, Abbott Park, IL). All analyses were performed by photometric methods. The coefficients of variation at the laboratory were 1.4% to 1.7% for glucose, 1.1% to 1.3% for cholesterol, 1.0% to 1.7% for high-density lipoprotein (HDL) cholesterol, and 1.9% to 2.4% for creatinine.

Echocardiographic Acquisition, Analysis, and Reproducibility

All examinations were conducted by one experienced physician echocardiographer (H.D.), and participants were examined in the left lateral decubitus position with a Vivid 7 scanner (version BT06; GE Vingmed Ultrasound AS, Horten, Norway) using a phased-array transducer (M3S and M4S).

Blood flow Doppler recordings were done in four-chamber and five-chamber views as described in the recommendations of the American Society of Echocardiography and the European Association of Echocardiography.[22] Mitral flow was measured with sample volume between the mitral leaflets and analyzed for early (E) and late (A) diastolic filling, and the E/A ratio was calculated. LV internal dimensions were analyzed on parasternal M-mode echocardiograms with the ultrasound beam at the tip of the mitral leaflet. Longitudinal end-systolic strain, defined as the percentage shortening of myocardial segments during contraction, was analyzed semiautomatically by a combination of tissue Doppler and speckle tracking[14] using customized software (GcMat; GE Vingmed Ultrasound AS) that runs on a MATLAB platform (The MathWorks, Inc., Natick, MA). Seven search boxes sized 5 × 5 mm defining segment borders were tracked with tissue Doppler along the ultrasound beam and grayscale speckles perpendicular to the ultrasound beam. Segmental strain was calculated from the variation of segment length. Because the 18-segment model gives too much weight to the apex for global strain measurements, global longitudinal end-systolic strain was analyzed as the global average in a 16-segment model of the left ventricle.[23] Strain values from the inferolateral and anterolateral apical segments, and the inferoseptal (septal) and anteroseptal apical segments were averaged to refer to the lateral and septal apical segments, respectively. Mitral and tricuspid annular systolic and early diastolic velocities were assessed by pulsed-wave tissue Doppler (pwTD) using a Vivid 7 scanner (version BT06).[15] Peak systolic (S′) and peak early diastolic (e′) velocities were measured in the base of the lateral, septal, anterior, and inferior LV wall, and the average of the four myocardial walls is presented as a global measure of LV function. Right ventricular (RV) function was assessed by pwTD by measuring S′ and e′ in the base of the RV free wall at the tricuspid annulus. The localizations used for measurement of S′ and e′ are shown in Figure 1. All Doppler and tissue Doppler measurements reflect the average of three consecutive cardiac cycles.

Reproducibility of the echocardiographic analyses has previously been described.[14,15,24] Briefly, the interobserver mean error (the absolute difference between two measurements on separate recordings divided by the mean of the measurements) of the indices of cardiac function was 4% to 8% in the left ventricle and 12% to 14% in the right ventricle. The intraobserver mean error was 2% and 4%, respectively.

Other Measures of LV Systolic Function

Association of cardiac risk factors with peak systolic longitudinal strain rate, peak systolic mitral annular velocities by color tissue Doppler, and EF are shown in the Supplementary Data only. However, except for EF, these data were in line with those presented in the "Results" section.

Statistical Analysis

Because all cardiac function indices were mutually correlated (all Pearson's R values ≥ 0.20, all P values < .001), associations between cardiovascular risk factors and cardiac function were estimated using multivariate linear regression analyses, with the different cardiac function measures as dependent variables. The cardiac function measures were log transformed, and the regression coefficients are presented as the percentage difference in cardiac function per standard deviation higher risk factor level with the corresponding 95% confidence intervals. In the analyses, age was included as a continuous covariate, and in the analyses of lipids and glucose, we also included time since last meal as a covariate, because the blood samples were nonfasting.