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Research paper

Atrial function, atrial volume and cardiovascular clinical outcomes in patients with end-stage renal disease – A study of cardiac computed tomography

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ABSTRACT

Background: Patients with chronic kidney disease (CKD) have an increased risk of cardiovascular events. Previous studies using 2-dimensional echocardiography show that left atrial end-diastolic volume (LAEDV) predicts cardiovascular outcomes and mortality in patients with CKD. However, contrast-enhanced cardiac CT may offers a more precise measure of atrial dimensions and function than 2-dimensional echocardiography and may provide improved predictionof patient outcome.
Aim: The aim of the present study was to examine the association of LAEDV and left atrial ejection fraction (LAEF) assessed by CT with left ventricle end-diastolic volume (LVEDV), left ventricular mass, left ventricular ejection fraction and N-terminal plasma-pro-brain natriuretic peptide (NT-PRO-BNP). Furthermore, we examined LAEDV and LAEF as predictors of major adverse cardiac events (MACE) and mortality.
Methods: Kidney transplant candidates (n = 117) underwent contrast-enhanced CT screening for coronary artery disease as part of the work-up prior to kidney transplantation before being accepted on the transplantation waiting list. Left atrial (LA) and left ventricular (LV) volume and function were determined by cardiac CT. MACE and mortality data were extracted from the Western Denmark Heart Registry, a review of patient records and patient interviews.
Results: Baseline patient characteristics did not differ between LAEDV tertiles. LAEDV was positively associated with measures of LV function – both LVEDV ($\beta = 0.36$, $p < 0.05$) and LV mass ($\beta = 0.30$, $p < 0.05$). LAEF was not associated with measures of LV function. LAEDV was positively and LAEF negatively associated with NT-PRO-BNP (LAEDV: $\beta = 10.28$, $p < 0.05$. LAEF: $\beta = -0.06$, $p < 0.05$).
During a median follow-up of 3.7-years, 19 (16.2%) patients died and 19 (16.2%) patients suffered MACE. MACE and survival analysis showed no relation to LAEDV or LAEF.
Conclusions: Using contrast-enhanced CT, we demonstrated a correlation between atrial and ventricular functional parameters. However, we found no association with either LAEF or LAEDV or MACE and mortality in this cohort of kidney transplant candidates.

1. Introduction

Patients with chronic kidney disease (CKD) have a very high risk of cardiovascular (CV) events.[1] However, traditional clinical screening tools, including general population-based risk prediction models, are limited in their predictive accuracy for CV events in patients with advanced stages of CKD.[2] Left atrial (LA) end-diastolic volume (LAEDV) predicts CV events in the general population and in high-risk patients with, e.g., acute myocardial infarction.[3,4] Specifically, LA volume predicts CV outcome and all-cause mortality in CKD patients.[4] The prognostic value of LA volume is independent of left ventricular (LV) mass and ejection fraction (LVEF)

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Abbreviations

CKD	Chronic kidney disease
LAEDV	left atrial end-diastolic volume
CCTA	cardiac computed tomography angiography
LAEF	left atrial ejection fraction
LVEDV	left ventricle end-diastolic volume
LVESV	left ventricle end-systolic volume
NT-PRO-BNP	N-terminal plasma-pro-brain natriuretic peptide
MACE	major adverse cardiac events
LA	left atrial
LV	left ventricular
CV	cardiovascular
2D-ECHO	two-dimensional echocardiography
MRI	magnetic resonance imaging
ERSD	end-stage renal disease
STEMI	ST-elevation myocardial infarction
Non-STEMI	non-ST-elevation myocardial infarction
BSA	body surface area
eGFR	estimated glomerular filtration rate
BMI	body mass index
PD	peritoneal dialysis
HD	haemodialysis

both in the general population and in CKD patients, and LA volume is related to functional parameters of cardiac function.[5]

Previous studies used two-dimensional echocardiography (2D-echo) to analyze LAEDV in CKD patients.[5–8] Two-dimensional estimation of the three-dimensional LA structure by 2D-echo is challenging and displays high inter- and intraobserver variability.[9] Not unlike the gold standard magnetic resonance imaging (MRI),[10] cardiac computed tomography angiography produces high-resolution three-dimensional images throughout the cardiac cycle. The three-dimensional images enable accurate measurement of LA volumes and LA ejection fraction (LAEF). Determining LA volume by cardiac CT provides more accurate cardiac chamber assessment than 2D-echo.[11–13]

To our knowledge, no previous study has investigated LAEF determined by CT in patients with CKD. We hypothesised that determination of LA function by cardiac CT may offer further prognostic value in addition to LA-volume assessment in a high-risk population with CKD.

Using CT the aim of the present study was to examine LAEDV and LAEF as risk markers of major adverse cardiac events (MACE) and overall mortality in CKD patients. Moreover, we investigated the correlation between LAEDV, LAEF, cardiac functional parameters and N-terminal plasma pro-brain natriuretic peptide (NT-PRO-BNP).

2. Methods

We included 167 adult kidney transplant candidates from 9 hospitals in Northern and Central Denmark from February 2011 to February 2014 in our study. All patients were enrolled in a prospective, observational study investigating the diagnostic accuracy of coronary CT angiography to identify coronary stenoses in comparison to invasive coronary angiography.[14]

Inclusion criteria were end-stage renal disease (ESRD) and the need for cardiac evaluation prior to kidney transplantation. Patients were included if at least 1 of the following characteristics was present: age >40 years, treatment with dialysis for >5 years, diabetes, registered on kidney transplant waiting list >3 years without cardiac screening or symptoms of CV disease. Exclusion criteria were age <18 years, known atrial fibrillation (AF) or unstable angina pectoris.

Written informed consent was obtained from all patients. The study was approved by the Danish Data Protection Agency and the Regional Ethics Committee, and followed the principles of the Declaration of Helsinki. The study was registered at ClinicalTrials.gov (Identifier: NCT01344434).[14]

Serum levels of NT-PRO-BNP were measured using a two-site electrochemiluminescence immunoassay according to clinical guidelines. Cardiac valve disease was visualised using 2D-echo according to clinical guidelines.[15]

2.1. Cardiac computed tomography acquisition and interpretation

The CT protocol has been described previously.[14] In short, cardiac CT was performed on a dual-source scanner (Siemens Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany) using a fixed contrast dose of intra-venous ioversol (90 ml, Optiray® 350 mg/ml, Mallinckrodt Deutschland GmbH, Hennef, Germany). Contrast-enhanced CT data sets were acquired with a spiral acquisition protocol (0%–100% of the heart cycle). Tube voltage was 80–120 kV according to patient weight and tube current was selected according to local standards. Detector configuration was $2 \times 64 \times 0.6$ mm collimation with z-flying focal spot. Gantry rotation time was 280 ms (temporal resolution: 75 ms). Tube current was reduced to 20% in either the systolic or diastolic phase depending on heart rate. Using raw-data iterative reconstruction, cardiac images (512×512 matrix, slice thickness 0.6 mm, reconstruction increment of 0.4 mm) were reconstructed for every 5% of the cardiac cycle.

All patients received glyceryl nitrate (0.8 mg) sublingually before the scan. Intravenous beta blockers were used optionally to obtain a heart rate of <65 beats/min to optimise coronary visualization in the CT data sets.

LA volume was determined with commercially available software (VitreaAdvanced, ViTAL Images, Toshiba Medical Systems Europe, Zoetermeer, The Netherlands). The software automatically traces the LA endocardium in 3D. Correct tracing and appendage and pulmonary vein exclusion were ensured by visual control and, if necessary, optimised by manual adjustment. Using commercially available software (Syngo.via, Siemens Healthcare, Forchheim, Germany), LVEDV, LV mass and LVEF were assessed in a similar manner, manually optimising automatically reconstructed and traced CT images throughout the cardiac cycle. All cardiac chamber measurements were indexed to body surface area. In total, 117 patients underwent LA volume assessment (Fig. 1).

Intraobserver variability was assessed by randomly selecting 10 patients and re-determining LAEDV, LA end-systolic volume (LAESV) and LAEF. The following coefficients of variation were found: LAEDV = 1.19%, LAESV = 2.29%.

2.2. Clinical endpoints

Clinical endpoint data were extracted from patient records, standardised patient interviews and the Western Denmark Heart Registry.[16] Endpoints were determined prior to data analysis and to patient record review. The primary endpoint was defined as MACE

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