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Detection of left atrial thrombus during routine diagnostic work-up prior to pulmonary vein isolation for atrial fibrillation: Role of transesophageal echocardiography and multidetector computed tomography ☆

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ABSTRACT

Background: Transesophageal echocardiography (TEE) and multidetector computed tomography (MDCT) are frequently used imaging modalities prior to pulmonary vein isolation (PVI) in order to exclude left atrial (LA) and left atrial appendage (LAA) thrombus and to visualize the anatomy of LA and pulmonary veins. This study aimed to identify predictors of LA/LAA thrombus and to analyze the diagnostic yield of routine pre-procedural TEE and MDCT.

Methods: 329 patients with drug-refractory atrial fibrillation (AF) (age 62 ± 10 years; 65% males; 247 paroxysmal AF) referred for pulmonary PVI were included. Prior to the procedure, all patients underwent 64-slice MDCT and TEE, which was used as the gold standard. Risk parameters for thrombus formation were determined, including the $CHADS_2$ and CHA_2DS_2-VASc scores.

Results: MDCT identified 10 LA/LAA thrombi (3.0%) (8 false positive, 2 true positive), whereas 7 actual thrombi (2.1%) were detected by TEE (5 false negative by MDCT). Sensitivity and specificity of MDCT was 29% and 98%, respectively, with a negative predictive value of 98% and a positive predictive value of 20%. All patients with thrombus were on effective anticoagulation. In multivariate analysis, diabetes mellitus, $CHADS_2$ score ≥3, and CHA_2DS_2-VASc score ≥4 were significantly associated with LA/LAA thrombus. No thrombus was seen in patients without risk factors.

Conclusions: In patients presenting for PVI, MDCT does not reliably exclude LA/LAA thrombus. Our study revealed a small but significant prevalence of thrombus despite effective anticoagulation. Diabetes mellitus, $CHADS_2$ score ≥3, and CHA_2DS_2-VASc score ≥4 were independent risk predictors of LA/LAA thrombus.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with increased morbidity and mortality as well as decreased quality of life [1,2]. Catheter ablation of AF has evolved over the past decade and is currently recommended for symptomatic patients who are refractory to drug therapy [3]. Imaging of the LA and related intrathoracic structures prior to ablation is important for procedural planning [4,5]. Multidetector computed tomography (MDCT) allows visualization of the entire left atrium (LA), including the left atrial appendage (LAA) and the number and anatomy of the pulmonary veins. In addition, pre-segmented 3D-MDCT data sets might be integrated with advanced electroanatomical mapping systems to assist during the mapping and ablation procedure, and to avoid complications [6].

Thromboembolism, usually originating from the LA and LAA, is a major complication of AF and may result in transitory ischemic attack (TIA) and stroke [1]. The presence of LA/LAA thrombus is a contraindication to catheter ablation of AF since navigation of ablation catheters inside the LA may lead to the dislodgement of in situ thrombi [3]. Accordingly, the 2007 Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society consensus statement recommends pre-procedural transesophageal echocardiography (TEE) in order to screen for the presence of thrombus, especially in patients with persistent AF at the time of ablation [3]. Although TEE is still considered the gold standard to exclude LA/LAA thrombus, recent studies have investigated the usefulness and limitations of MDCT in excluding LA/LAA thrombus

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[7–14]. However, the results are conflicting and diagnostic accuracy has varied widely between studies. It has further been demonstrated that LA/LAA thrombus may form during effective oral anticoagulation with a vitamin K antagonist such as phenprocoumon [15]. However, the prevalence of LA/LAA thrombus also varies between different reports and recommendations regarding TEE screening in patients with paroxysmal AF or low-risk profile are less clear [3,16–18].

The aim of this study was to prospectively analyze the diagnostic yield of routine pre-procedural TEE and cardiac MDCT in patients undergoing pulmonary vein isolation (PVI) and to identify predictors of LA/LAA thrombus formation despite effective anticoagulation.

2. Methods

2.1. Patient population

A single-center study was done in 329 patients with drug-refractory, symptomatic paroxysmal or persistent AF scheduled to undergo PVI between October 2007 and April 2010 at the Heart Center of Georg-August-University Göttingen, Germany. All patients were included in a registry and all clinical, imaging and procedural data were prospectively recorded. Paroxysmal AF was defined as self-terminating episodes of AF lasting less than 7 days. Persistent AF was defined as AF sustained >7 days, and requiring electrical or pharmacological cardioversion [19]. All patients underwent TEE screening and contrast-enhanced MDCT for anatomical evaluation of the LA and pulmonary veins. Written informed consent was obtained from all patients prior to the procedures.

2.2. Anticoagulation

According to the $CHADS_2$ risk score, patients were divided into a low ($CHADS_2$ score = 0), intermediate ($CHADS_2$ score = 1) and a high risk group ($CHADS_2$ score ≥ 2) [20]. Anticoagulation with phenprocoumon was administered to all AF patients with $CHADS_2$ scores of 2 or more (target INR 2.0–3.0) (Fig. 1). Patients with ineffective anticoagulation (INR <2) were not included. The anticoagulation strategy of patients with a $CHADS_2$ score of 1 was left to the discretion of the treating cardiologist. Patients with a $CHADS_2$ score of 0 received aspirin or no antithrombotic therapy. Patients were treated with phenprocoumon for at last 4 weeks prior to the ablation procedure and were instructed to stop phenprocoumon 5 days prior to the procedure. High-risk patients were bridged with weight-adjusted enoxaparin (100 IU/kg twice daily). Following PVI, all patients received phenprocoumon for at least 6 ± 3 months (Fig. 1).

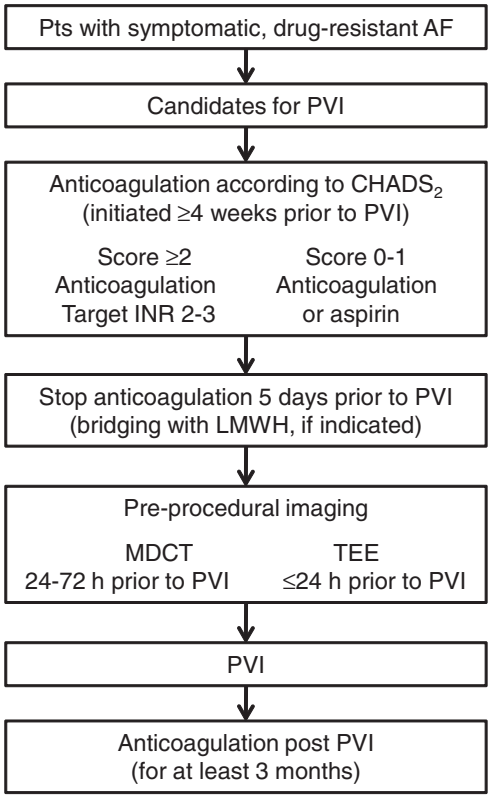

Fig. 1. Flow chart illustrating the evaluation and treatment sequence of the study population. AF — atrial fibrillation; $CHADS_2$ — congestive heart failure, hypertension, age, diabetes, stroke; LMWH — low molecular weight heparin; MDCT — multidetector computed tomography; PVI — pulmonary vein isolation; TEE — transesophageal echocardiogram.

2.3. Clinical risk factors

The $CHADS_2$ score is a useful stroke risk stratification tool [21,22]. The $CHADS_2$ score assigns 1 point for each of the presence of heart failure, hypertension, age ≥75 years, and diabetes mellitus; and 2 points for a history of stroke or TIA. We calculated the $CHADS_2$ score (ranging from 0 to 6) for each of our patients at the time of TEE. The CHA_2DS_2-VASc score was calculated in retrospect and was not used by clinicians during any patient's treatment. The CHA_2DS_2-VASc score extends the classic $CHADS_2$ score and assigns 2 points for a history of stroke or TIA, or age ≥75; and 1 point each is assigned for the presence of heart failure, hypertension, age 65–74, diabetes mellitus, vascular disease (prior myocardial infarction, peripheral artery disease, or complex aortic plaque), and female sex [23,24]. Clinical risk analysis also assessed other risk factors for LA/LAA thrombus formation including LA size, valvular disease, cardiomyopathy, and chronic kidney disease [25,26].

2.4. Echocardiography

Left atrial size and left ventricular (LV) ejection fraction were assessed by transthoracic echocardiography (TTE). The TTE images were obtained from parasternal long- and short-axis views, apical four-chamber, two-chamber, and long-axis views. Chambers were quantified according to methods described by the American Society of Echocardiography [27]. All patients underwent TEE within 24 h prior to the PVI procedure (Fig. 1). TEE was defined as gold standard for thrombus detection. The TEE was performed using a GE Vivid E9 ultrasound system (GE Ultrasound, Horten, Norway) with a 5.0 MHz multiplane probe as previously described [28]. In particular, cine loops of the LAA were acquired during a continuous sweep from 0° to 180°. The presence of LA thrombus was considered if there was an intracavitary echogenic mass that could be distinguished from the surrounding tissue in more than one imaging plane. If serial TEE were necessary in case of thrombus, the findings were compared with the previous study in order to assess thrombus resolution. All TEEs were performed and interpreted by highly experienced cardiologists (M.P., R.W.) (>100 TEEs per year per cardiologist) who were blinded to the results of other examinations and patients' history.

2.5. Multidetector computed tomography

All patients were examined with the same 64-slice MDCT scanner (VCT LightSpeed, GE Healthcare, Milwaukee, WI, USA) within 24 h to 72 h prior to the PVI procedure (Fig. 1) using our local LA protocol. If the heart rate was >70 bpm, beta adrenergic blocking agents were administered before the scan procedure (in 86% of the investigated patients). A spiral scan was performed within a single breath-hold covering a range from the supraaortic region to the heart base and the upper abdomen. Eighty milliliters of intravenous contrast agent (Imeron 400, Bracco Imaging, Konstanz, Germany) was injected in all cases. Imaging parameters included gantry rotation time of 500 ms, detector collimation of 64 × 0.625 mm, and a tube voltage of 120 kV. An ECG gated half scan algorithm was used to reconstruct the data into axial images with a slice thickness of 0.625 mm. Numerous phases within the cardiac cycle were reconstructed and the best phase with least motion artifacts was selected. MDCT images were analyzed off-line by experienced independent readers (at least one radiologist and one cardiologist) on a standard workstation with a dedicated cardiac imaging software package (VolumeShare 2, GE Healthcare, Milwaukee, WI, USA). For each patient, anatomy of the LA and the pulmonary veins was identified. A LA/LAA thrombus was defined as an intracavitary contrast filling defect with attenuation values similar to non-enhanced tissue. Intracavitary thrombi were differentiated from normal pectinate muscles and from filling, motion, and acquisition artifacts. The MDCT readers were forced to make a definitive decision on the presence or absence of LA/LAA thrombus solely based on the MDCT images. On the day of the PVI procedure, 3D-MDCT images of the LA and the pulmonary veins were reconstructed on a separate workstation and integrated with electroanatomical mapping (Carto Merge, Biosense Webster, Diamond Bar, CA, USA).

2.6. Statistical analysis

Continuous data are presented as mean ± SD and categorical data are given as frequencies and percentages. Comparisons were performed with the 2-tailed Student's *t* test for continuous variables or the Chi-square test or Fisher's exact test for categorical variables (depending on field values). A value of $P<0.05$ was considered statistically significant. Multivariate logistic regression analysis was performed to assess those factors that achieved significance in univariate analysis. Ninety-five percent confidence intervals were calculated for sensitivity, specificity, and for negative (NPV) and positive predictive values (PPV). Concordance between