Institutionen för molekylär medicin och kirurgi

Aortic valve calcification
- in vivo and ex vivo evaluation

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Thoraxaulan N2:U1, Karolinska Universitetssjukhuset, Stockholm

Fredagen den 19 september 2014, kl. 09:00

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Stockholm 2014

Abstract

Aortic valve calcification (AVC) or thickening is found in around one fifth of the general population between 65-75 years of age and increasingly thereafter. The process of aortic valve thickening and calcification is not only an aging (wear and tear) process of the valve leaflets. It is now considered to be closely related to atherosclerosis. The presence and the degree of AVC have been shown to have prognostic value in patients with cardiovascular diseases and in the general population. Despite its importance, there is no widely agreed upon scoring system that objectively quantifies AVC.

The aim of this project was to investigate different methods for evaluating AVC, using transthoracic and transoesophageal echocardiography (TTE and TOE), intra-operative assessment of the valve (IOS) and ex vivo evaluation based on computed tomography (CT) of the excised aortic valves and based on valve weight. A 5-grade scoring system was used for the visual assessment of AVC on real-time and still TTE and TOE images of the aortic valve, as well as intra-operatively. Computer-based greyscale measurement (GSM) software was used to obtain a quantitative-ultrasound-based AVC measure, which was compared with the visual AVC score from TTE and TOE, whereas IOS was used as the gold-standard method. We also aimed at identifying the most suitable ex vivo conditions and CT parameters for optimal AVC scanning by CT in a calcium hydroxyapatite (CaHA) phantom study. The TTE and TOE AVC scores and IOS were compared to the weight and the CT CaHA mineral mass (MM) index of the explanted aortic valves. The study cohorts were recruited among patients undergoing aortic valve replacement because of aortic valve disease and/or ascending aorta aneurysm.

In Study I, which included 185 patients, we showed that the visual evaluation of AVC using real-time TTE images yielded better correlations with IOS than did quantitative still frame measures based on GSM (r = 0.83 vs 0.64, respectively). In Study II, AVC scores based on TTE and TOE real-time images from 169 patients showed strong correlations with IOS (r = 0.83 and 0.82, respectively). GSM-based measures correlated less well with IOS, even for TOE (r = 0.52). In Study II, we also showed that TOE was more accurate than TTE in diagnosing the aortic valve phenotype. In the CT-phantom-based, methodological Study III, we identified optimal CT scanning and reconstruction parameters, as well as the most suitable medium (normal saline) for ex vivo tissue CT-based calcium scoring. In Study IV, 155 operatively explanted aortic valves were weighed and scanned ex vivo by CT, and CaHA MM was measured. The CaHA MM exhibited a strong correlation with valve weight (r = 0.91), whereas AVC scores based on TTE, TOE and IOS showed weaker correlations. Conversely, echocardiographic and intra-operative AVC evaluation showed a better correlation with haemodynamic parameters compared with ex vivo CT AVC scoring.

In conclusion, real-time echocardiographic images are crucial for accurate AVC scoring, regardless of whether TTE or TOE is used. Echocardiographic AVC scoring was as accurate as intra-operative assessment, according to valve weight and ex vivo CT. For ex vivo calcium scoring by CT, in addition to scanning and reconstruction parameters, using saline as the surrounding medium seems to be important. TOE is more accurate than TTE in detecting the bicuspid aortic valve.

ISBN 978-91-637-6159-1