Short communication

Clinical validation of an ultrasound quantification score for aortic valve calcifications

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image might add additional information, we also aimed to semi-automatically select calcified valvular regions.

2. Materials and methods

2.1. Experimental protocol

We prospectively enrolled 52 patients above 18 years old, who were scheduled for a cardiac CT for valvular or coronary evaluation, and performed a TTE within three months. Patients with previous valve surgery were excluded. TTE and CT analyses were performed offline by trained specialists in cardiology and radiology respectively, blinded for results of the other imaging technique. The local ethical committee approved the study. All participants gave their informed consent.

2.2. Computed tomography

Multi-slice CT (MSCT) was performed using a 16-detector Philips MX 8000IDT 16 (Philips Medical Systems, Andover, MA, USA). A scan run consisted of 40×3-mm thick contiguous transverse slices, covering ascending aorta to cardiac apex, without contrast nor β-blocker administration. Acquisition time 0.5 s/slice, electrocardiography triggered at 75% of the RR interval. AVC was defined as calcification within aortic leaflets, aortic annulus or aortic wall immediately adjacent to leaflet or annular calcification. Calcification was defined as four adjacent pixels with density > 130 Hounsfield units. The Agatston score was calculated offline (heart beat calcium scoring software; Philips Medical Systems, USA), as previously described [9]. The scores of two MSCT runs, performed with 1 or 2 mm initial interval, were averaged. Radiation exposure was 2 to 3 mSv.

2.3. Transthoracic echocardiography

Two-dimensional (2D) TTE was performed using a Vivid 7 Pro system (GE100 Medical Systems, Milwaukee, WI, USA). The AS severity was evaluated according to the ESC guidelines [15].

For calcium scoring, parasternal long (PLAx) and short axis (PSAx) images were obtained using a 3S probe (GE100 Medical Systems, USA), maintaining settings constant at 1.7 MHz and 60 FPS. The global calcium score (GC score) was calculated offline using imaging software OsiriX 3.6.1 (Pixmeo, Geneva, Switzerland). Multiple regions of interest (ROIs) were placed in end-diastole (Fig. 1A). Three in PLAx view: at anterior annulus, posterior annulus and leaflets. Five in PSAx view: one delineating the annulus, one at each leaflet, and one delineating the cusps free edges. The mean grayscale value of each ROI was averaged over three heart cycles and calibrated by subtracting the mean grayscale value of the left ventricular outflow tract (LVOT) blood pool (BP) or right ventricular (RV) BP in PLAx or PSAx view respectively. Next, all calibrated ROIs were averaged in PLAx view (PLAx score) and PSAx view (PSAx score). Finally, the GC score was calculated as the mean of the PLAx score and PSAx score (Fig. 1B).

Calcifications have higher grayscale values than interventricular septal (IVS) myocardium. Therefore, the mean IVS grayscale value (GS_{ivs}) + 2 standard deviation (SD) was determined as calcium threshold in PLAx view. In PSAx images, where myocardium cannot be used as internal reference, a threshold of $130 + RV\ BPmax$ was applied, based on the grayscale value of calcium [13] with the adjacent blood pool as correction for inter-individual attenuation. Semi-automatic calcium selection and visualization was obtained

1. Introduction

Aortic valve calcification (AVC) is a predictor of morbidity and mortality in calcific aortic valve disease (CAVD) and an important prognostic factor, associated with faster progression of aortic valve stenosis (AS) [1–3]. The AVC amount is an indicator for stenosis severity in low-flow low-gradient (LFLG) AS [4–6] and the localization and extent determines the risk of paravalvular regurgitation after transcatheter aortic valve implantation (TAVI) [7,8]. AVC is usually quantified by computed tomography (CT) Agatston score [9,10], an ionizing technique not suitable for serial follow-up of CAVD progression. Imaging modalities are required to evaluate AVC progression, determining the ideal moment for intervention [1,2] and to evaluate the effect of treatments [11,12]. Ultrasound seems an interesting technique for this purpose [11,12], but in clinical practice AVC assessment with transthoracic echocardiography (TTE) remains subjective and semi-quantitative, and objective calcium quantification is lacking. Preclinical research showed it is possible to objectively quantify calcifications *in vitro* and *in vivo* in rats, using echocardiography [13,14]. Therefore, we aimed to validate TTE as a technique to accurately quantify AVC in patients with CAVD, compared to CT Agatston score. As visualization of calcifications on the ultrasound

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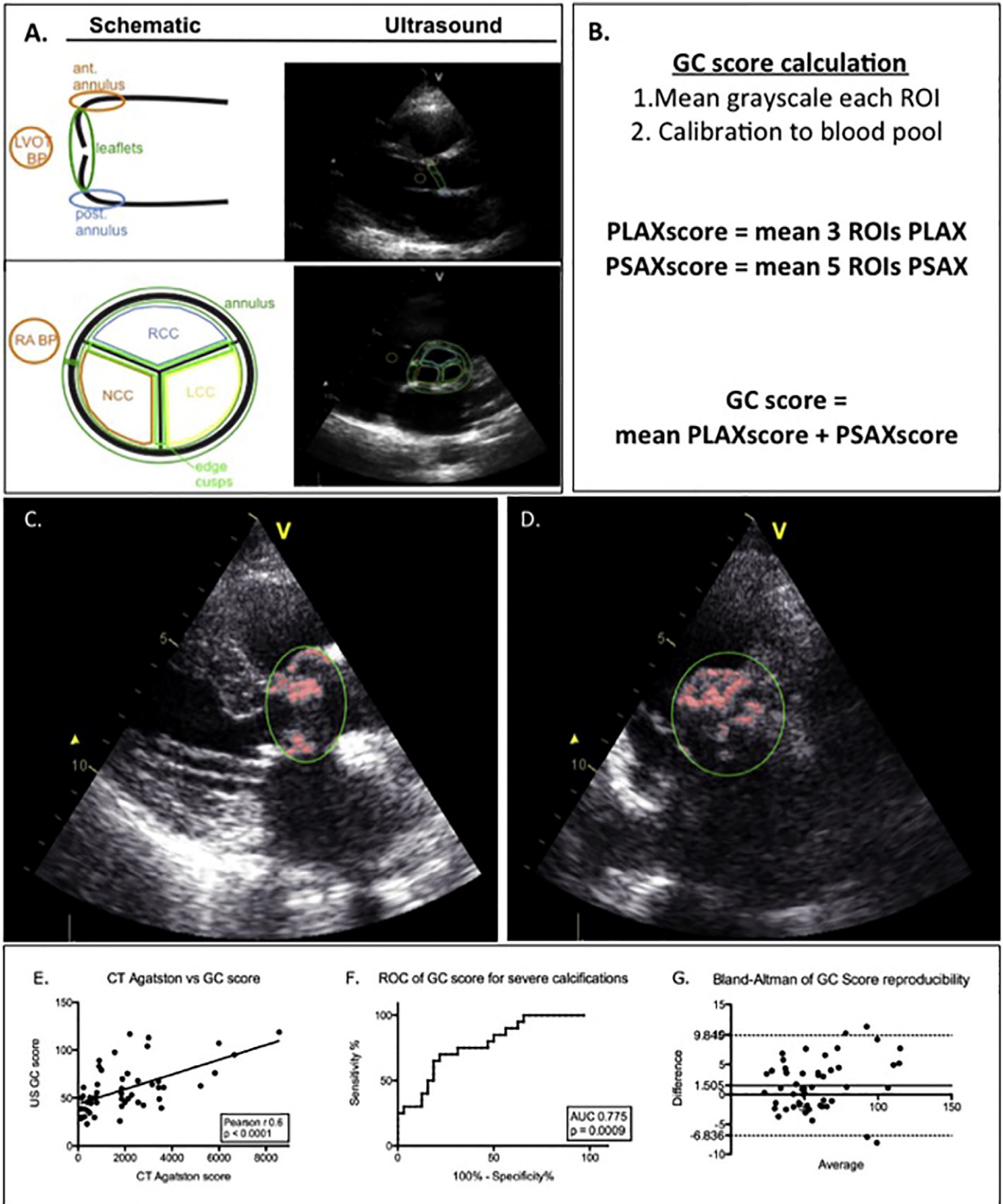 E-mail address: Kris.Gillis@uzbrussel.be (K. Gillis).

Fig. 1. The ultrasound global calcium score and calcium selection method and comparison to computed tomography. A. Schematic representation and ultrasound image of the placement of regions of interest in PLAx (upper panel) and PSAx (lower panel) views. B. Method for GC score calculation. C&D. Semi-automatic calcium selection: a green circle was drawn as ROI around the AV. Application of a calcification threshold of $GS_{ivs} + 2SD$ in PLAx view (C) and $130 + RVBPmax$ in PSAx view (D) allowed calcium selection. Red = calcification within the region of interest. E. Correlation between GC score and Agatston score. F. ROC-curve of the GC score for severe calcifications, determined by a CT Agatston >2000 arbitrary units. G. The Bland-Altman plot for intra-observer variability of the GC score, bias is shown as full line, 95% limits of agreement are shown as dotted lines. Ant annulus, anterior annulus; AUC, area under the curve; AV, aortic valve; BP, blood pool; CT, computed tomography; GC score, global calcium score; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; PLAx, parasternal long axis; post annulus, posterior annulus; PSAx, parasternal short axis; RCC right coronary cusp; ROC, receiver operating curve; ROI, region of interest; US, ultrasound.