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Computed tomography calcium scoring in routine clinical daily practice for assessing

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**Short title:** Computed tomography calcium scoring in routine clinical daily practice

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INTRODUCTION

Aortic valve stenosis (AS) is the most common valvular heart disease requiring intervention,

with its incidence rising due to the aging population [1]. Treatment decisions rely on AS

severity and symptoms, but accurate assessment can be challenging in some patients [2, 3].

Transthoracic echocardiography (TTE) is the standard for evaluating AS, though it has

methodological limitations that can hinder proper qualification for invasive treatment [4].

Contemporary AS assessment also incorporates cardiac biomarkers, computed tomography

(CT), and cardiac magnetic resonance [5, 6]. CT calcium scoring (CTCS) offers valuable

insights into AS severity and is endorsed by the European Society of Cardiology, although its

use is primarily limited to university centers [7, 8].

To the authors' knowledge, there are no reports on the use of CTCS in everyday clinical

practice beyond the topics of low-gradient AS or the validation of cutoff values. Therefore, the

study aimed to identify the main indications for CTCS in assessing AS in an unselected population and to evaluate patients' outcomes.

#### **METHODS**

We retrospectively analyzed data from all consecutive AS patients who underwent CTCS between November 2017 and September 2021 at a single heart valve center. This confirmatory study included patients with suspected low-gradient severe AS and those with potential errors in AV evaluation. The only exclusion criterion was inaccessible TTE recording. The study adhered to the principles of the Declaration of Helsinki and received approval from the local ethics committee. The follow-up was conducted for up to 12 months after the CTCS.

The TTE recordings, stored in DICOM format, were analyzed in accordance with current guidelines, by two independent cardiologists certified by the European Association of Cardiovascular Imaging, who were blinded to the clinical data and CTCS results. The image analysis was facilitated using ComPACS (Medimatic S.R.L., Genova, Italy).

CT scans were conducted using a second-generation dual-source scanner (SOMATOM Drive, Siemens Medical Solutions, Forchheim, Germany), following guidelines. Two independent radiologists evaluated the data on a Syngo.via Multimodality workstation (Siemens-Healthineers, Munich, Germany 2020). AV calcification was categorized according to European Society of Cardiology guidelines [1]. Participants were stratified into two groups: the highly likely group (HLG) with CTCS >3000AU in men and >1600AU in women, and the non-very likely group (NVLG) with CTCS below this threshold.

#### Statistical analysis

Normality was assessed using Shapiro–Wilk test. Descriptive statistics were used, presenting continuous variables with non-normal distribution as median (interquartile range [IQR]), and categorical variables as numbers (percentages). Wilcoxon rank-sum test was used for non-normally distributed variables. Pearson's  $\chi^2$  test and Fisher's exact test were employed for unpaired categorical data. Statistical analyses were conducted using Statistica 13.3 (Tibco Software, Inc., Palo Alto, CA, US), with a two-tailed *P*-value <0.05 considered statistically significant.

#### RESULTS AND DISCUSSION

One hundred patients (median age 78.5 years, [IQR 72.5–83]) were included, with 57 (57%) being female. They were mostly (70, 70%) overweight or obese and predominantly in New

York Heart Association functional class II or III (40 [40%] and 38 [38%], respectively). The median AV area (AVA) was 0.9 cm<sup>2</sup> (IQR 0.8–1), and the median mean gradient (MG) was 31 mm Hg (IQR 25.5–40).

The primary indication for CTCS was the MG-AVA mismatch. Echocardiographic discordance was found in 60 (60%) patients, mainly due to AVA <1 cm<sup>2</sup> and MG <40 mm Hg coexistence in 57 (95%) patients. In this group, severe AS was observed in only 33.3% of patients. This observation is consistent with published data indicating that significant low-gradient AS with preserved ejection fraction occurs in approximately 20%–30% of cases [2].

The second reason for CTCS was the suspicion of AS underestimation. Concordant values of AVA <1 cm<sup>2</sup> and MG >40 mm Hg, and AVA >1 cm<sup>2</sup> and MG <40 mm Hg were observed in 21 (21%) and 19 (19%) patients, respectively. Technical issues, such as the underestimation of Doppler velocities and inaccurate assessment of the left ventricular outflow tract, are the most common causes of AS underestimation [9]. Other factors contributing to echocardiographic ambiguity include impaired filling pressures, atrial fibrillation, ventricular remodeling, and the pressure recovery phenomenon [4].

The median CTCS was 1703.2 AU (IQR 1103.7–2739.5). Thirty-five patients (35%) were assigned to the HLG, while 65 (65%) were in the NVLG. The median CTCS in the HLG was 3432 AU (IQR 2398–5144), while in the NVLG, it was 1310 AU (IQR 881–1707.4); P < 0.001. CTCS values were higher in men compared to women: 2282 AU (IQR 1469–3072) vs. 1473 AU (IQR 1015–2495); P = 0.03. However, we found no significant difference in the incidence of severe stenosis between the sexes (P = 0.09). The median AVA was lower in the HLG:  $0.8 \text{ cm}^2$  (IQR 0.6–0.9) vs.  $0.9 \text{ cm}^2$  (IQR 0.8–1.1); P = 0.001, while the median MG was higher in the HLG: 36 mm Hg (IQR 27–51) vs. 30 mm Hg (IQR 23–36); P = 0.001. More patients in New York Heart Association class III or IV were in the HLG (71.4%) compared to the NVLG (36.4%; P = 0.003). Moreover, patients in the HLG were 5 years older than those in the NVLG (82 years [IQR 74–84]) vs. 77 years [IQR 72–81; P = 0.01]). This aligns with current studies, suggesting that CTCS correlates with age and the frequency of severe AS, reaching 10% in octogenarians [10].

After evaluation, 45 patients (45%) were qualified for the observational group with optimal medical therapy. 55% patients were reviewed by the Heart Team. Of these, 35 (66%) were deemed eligible for transcatheter aortic valve implantation, while 15 (28.3%) were recommended for aortic valve replacement. Only 3 (5.7%) patients were eligible for palliative balloon aortic valvuloplasty. The number of patients qualifying for invasive treatment (55,

55%) exceeded the number with confirmed severe AS (35, 35%), owing to concurrent valvular or coronary artery disease necessitating surgery.

Twelve-month all-cause mortality in the study group was 17%, lower than reported by Clavel et al. [11]. The HLG experienced five deaths (14.3%), while the NVLG had twelve (18.5%; P = 0.6). However, cardiovascular mortality at 12-months was 11%, with 5 deaths in the HLG (14.3%) and 6 in the NVLG (9.2%; P = 0.44). CTCS in non-survivors measured 1719 AU (IQR 1100–2692), compared to 1561 AU (IQR 1150–3072; P = 0.048) in survivors. In the HLG, 2 deaths occurred while awaiting transcatheter aortic valve implantation or aortic valve replacement. However, it's important to note that the study took place during the SARS-CoV-2 pandemic.

CT has greatly enhanced our understanding of heart diseases. While not yet widely adopted, CTCS offers promising advantages in AS evaluation, often surpassing echocardiography in accuracy [12]. We are the first to describe the use of CTCS in everyday clinical practice for indications beyond low-gradient AS. Given the critical role of accurate AS assessment in treatment decisions, broader utilization of CTCS could provide valuable diagnostic insights.

Our study's limitations include a small sample size and a retrospective analysis from a single-center registry. Additionally, TTEs were conducted by various echocardiographers, which reflects real-life practice.

In conclusion, the primary reason for assessing AS severity with CTCS was the discordance between AVA (<1 cm²) and MG (<40 mm Hg), where CTCS often indicated non-severe AS. In older symptomatic patients with inconclusive echocardiographic results, CTCS generally confirmed significant AS. Higher valve calcification was linked to poorer twelvementh outcomes.

#### **Article information**

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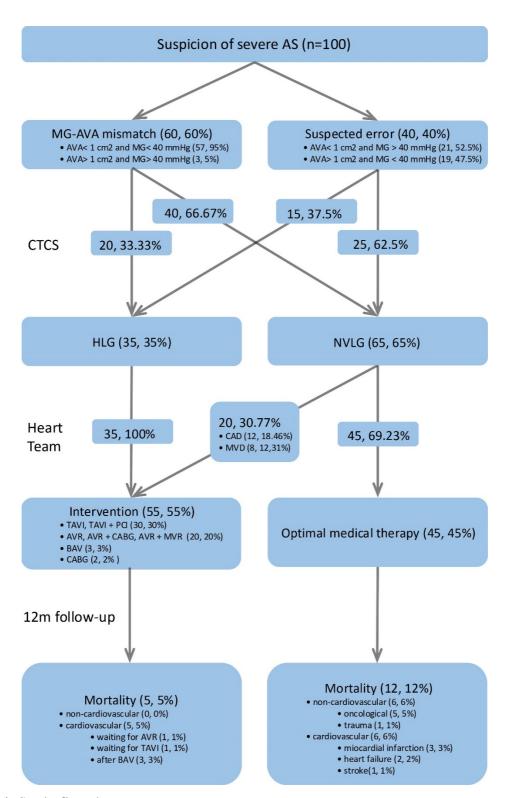


Figure 1. Study flowchart

Abbreviations: AVA, atrioventricular area; AVR, aortic valve replacement; BAV, balloon aortic valvuloplasty; CABG, coronary artery bypass graft; CAD, coronary artery disease; CTCS, computed tomography calcium scoring; HLG, highly likely group; MG, mean gradient; MVD, mitral valve disease; MVR, mitral valve replacement; NVLG, non-very likely group; PCI, percutaneous coronary intervention; TAVI, transcatheter pulmonary valve implantation