



Reproducibility of aortic valve calcification scoring with computed tomography – An interplatform analysis



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ABSTRACT

Background: To investigate whether aortic valve calcification (AVC) scoring performed with different workstation platforms generates comparable and thus software-independent results.

Methods: In this IRB-approved retrospective study, we included 100 consecutive patients with symptomatic aortic stenosis undergoing CT prior to transcatheter aortic valve implantation. Two independent observers performed AVC scoring on non-enhanced images with commercially available software platforms of four vendors (GE, Philips, Siemens, 3mensio). Gender-specific Agatston score cut-off values were applied according to current recommendations to assign patients to different likelihood categories of aortic stenosis (unlikely to very likely). Comparative analysis of Agatston scores between the four platforms were performed by using Kruskal-Wallis analysis, Spearman rank correlation, linear regression analysis, and Bland-Altman analysis. Differences in category assignment were compared using Fisher's exact test and Cohen's kappa.

Results: For both observers, each workstation platform produced slightly different numeric AVC Agatston scores, however, without statistical significance ($p = 0.96$ and $p = 0.98$). Excellent correlation was found between platforms, with $r = 0.991$ – 0.996 (Spearman) and $r^2 = 0.981$ – 0.992 (regression analysis) for both observers. Bland-Altman analyses revealed small mean differences with narrow limits of agreement between platforms (mean differences: 6 ± 128 to 100 ± 179), for inter-observer (mean differences: 1 ± 43 to 12 ± 70), and intra-observer variability (mean differences: 9 ± 42 to 20 ± 96). Observer 1 assigned 11 (kappa: 0.85–0.97) and observer 2 assigned 10 patients (kappa: 0.88–0.95) to different likelihood groups of severe aortic stenosis with at least one platform. Overall, there was no significant difference of likelihood assignment between platforms ($p = 0.98$ and $p = 1.0$, respectively).

Conclusion: While absolute values differ slightly, common commercially available software platforms produce comparable results for AVC scoring, which indicates software-independence of the method.

1. Introduction

The prevalence of severe aortic stenosis in the elderly (> 75 years of age) is 3.4% and constitutes a significant health problem.^{1,2} Most often the pathogenesis is degenerative.¹ Aortic valve calcification (AVC) induces aortic valve stenosis and correlates with severity of the stenosis.^{3–6} Moderate or severe AVC is a strong and independent risk factor for adverse clinical outcome in patients with asymptomatic aortic stenosis and delayed surgery.^{7,8}

Echocardiography is the key diagnostic tool to confirm the presence of aortic stenosis and to quantify its severity.⁹ However, the diagnosis of low-flow, low-gradient aortic stenosis with preserved ejection fraction

(aortic valve area $< 1 \text{ cm}^2$, mean gradient $< 40 \text{ mmHg}$, ejection fraction $\geq 50\%$, indexed stroke volume $\leq 35 \text{ ml/m}^2$) remains challenging and requires careful exclusion of measurement errors and other reasons for such echocardiographic findings.^{9,10} In this setting, quantification of AVC by computed tomography (CT) has gained in importance as the AVC Agatston Score is related to aortic stenosis severity and outcome.^{6,8,11} Previously, the European Society of Cardiology recommended cut-off values for the AVC Agatston Score to assess the likelihood of severe aortic stenosis according to AVC load (Table 1).^{9,12} In patients with paradoxical low-flow, low-gradient aortic stenosis, AVC load could be an important adjunct to hemodynamic assessment.¹²

On dedicated workstation platforms, AVC scoring is performed on

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Abbreviations

AVC	aortic valve calcification
CT	computed tomography
ROI	region of interest
WS	workstation

non-enhanced CT using the method proposed by Agatston, initially designed for quantification of coronary calcifications.^{9,13–15} While the reproducibility of coronary calcium quantification by multidetector CT has been tested for various workstation platforms before,^{16,17} the same has not been performed so far for AVC quantification. A certain variation in AVC scoring across workstation platforms in patients with paradoxical low-flow, low-gradient aortic stenosis, however, would have implications for patient treatment.^{9,12}

Hence, the purpose of our study was to investigate whether AVC scoring performed with different common workstation platforms generates comparable and thus vendor-independent results.

2. Methods

2.1. Patient population

Between September 2016 and April 2017, we screened 104 consecutive patients with symptomatic aortic stenosis planned to undergo transcatheter aortic valve replacement and who underwent CT as part of the pre-procedural protocol.^{18,19} Patients with previous aortic valve replacement (n = 4) were excluded, resulting in the inclusion of 100 patients (median age 81 years, inter-quartile range: 77–85 years; 56 females) into this study. Further baseline clinical characteristics are provided in Table 2.

Baseline data collection was performed in the context of a nationwide prospective registry (SWISS TAVI registry). This study had institutional and local ethics committee approval. All patients provided written informed consent.

2.2. CT data acquisition and image reconstruction

All patients underwent CT on a 192-slice dual-source CT scanner (Somatom Force; Siemens Healthineers, Forchheim, Germany). Non-enhanced CT was performed with prospective electrocardiography-gating in the step-and-shoot mode, acquiring data at 70% of the RR-interval using the following scan parameters: quality reference tube current-time product, 50mAs/rotation using automated attenuation-based tube current modulation (CAREDose); tube voltage, 120 kVp; gantry rotation time, 0.25s. Reconstructed slice thickness was 3 mm with an increment of 1.5 mm using a soft tissue convolution kernel using filtered back projection (Qr36). The scan was performed in a craniocaudal direction, ranging from the level of the tracheal bifurcation to the diaphragm. Subsequent contrast-enhanced, electrocardiography-gated CT angiography of the thoracoabdominal aorta was not part of this study and thus is not detailed further.

Table 1
Grading of aortic stenosis likelihood according to AVC score by CT (modified from¹²).

Likelihood of severe aortic stenosis	Agatston Score	
	Men	Women
Very likely	≥ 3000	≥ 1600
Likely	2000–2999	1200–1599
Intermediate	1600–1999	800–1199
Unlikely	< 1600	< 800

2.3. AVC scoring

Two independent observers (R.H. and M.P., with 3 and 5 years of experience in cardiovascular radiology and experience in TAVI planning CT) performed quantification of AVC with four common, commercially available software platforms: workstation platform 1, Syngo.via Calcium Scoring (Siemens Healthineers, Erlangen, Germany); workstation platform 2, Heartbeat-CS, Intellispace 8.0 (Philips Healthcare, Eindhoven, The Netherlands); workstation platform 3, SmartScore 4.0, Advantage Workstation platform Volume Share 7 (GE Healthcare, Waukesha, Wisconsin, USA), and workstation platform 4, Calcium Scoring, 3mensio Structural Heart 7.3 (Pie Medical Imaging, Maastricht, The Netherlands) (Fig. 1). M.P. performed analysis of 25 randomly selected cases twice to determine the intra-observer agreement.

AVC scoring was performed in each data set by using the default settings of the respective calcium scoring software platform. Platform 1, 3, and 4 define calcium plaques as 2 adjacent pixels with an attenuation ≥ 130 HU at 120 kVp. Platform 2 defines calcium plaques as an area of ≥ 0.5 mm² with an attenuation ≥ 130 HU at 120 kVp. The observers marked each calcified aortic valve lesion by carefully placing regions-of-interest (ROI) and excluding calcification of the left ventricular outflow tract, the aortic wall, the coronary arteries and/or the mitral annulus and valve. The Agatston scores for individual calcifications of the aortic valve were added to derive the total AVC score.

2.4. Statistical analysis

Non-parametric, continuous variables are presented as median values with interquartile ranges. The total range of Agatston scores, median scores, and inter-quartile ranges were calculated for all workstation platforms. As previously shown,¹⁶ comparative analysis of Agatston scores between the four workstation platforms were performed by using Kruskal-Wallis analysis, Spearman rank correlation, linear regression analysis, and Bland-Altman analysis.

Spearman rank correlation as a nonparametric measure was chosen to assess the strength of the statistical dependence, and regression analysis was used to assess the relationship between workstation platforms.¹⁶ Furthermore, Bland-Altman analysis was applied to assess differences between software platforms and observers, and for intra-observer variability.

For likelihood stratification, patients were categorized into likelihood categories of severe aortic stenosis according to gender by using AVC Agatston scores, as previously described (Table 1).^{9,12} Fisher's exact test was applied to assess inconsistencies between these likelihood categories. The agreement of likelihood categories between software

Table 2
Baseline patient characteristics.

	Overall cohort (n = 100)
Age (years)	81, 77-85
BMI (kg/m ²)	26.8, 23.4–29.1
Weight (kg)	76, 64-86
Height (cm)	167, 162-172
Females	56
Diabetes	24
Dyslipidemia	32
Hypertension	83
Coronary artery disease	51
Cerebrovascular disease	26
PAD	21
COPD	10
Previous coronary bypass graft	57

Data is expressed as median (interquartile-range) or count. Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease.

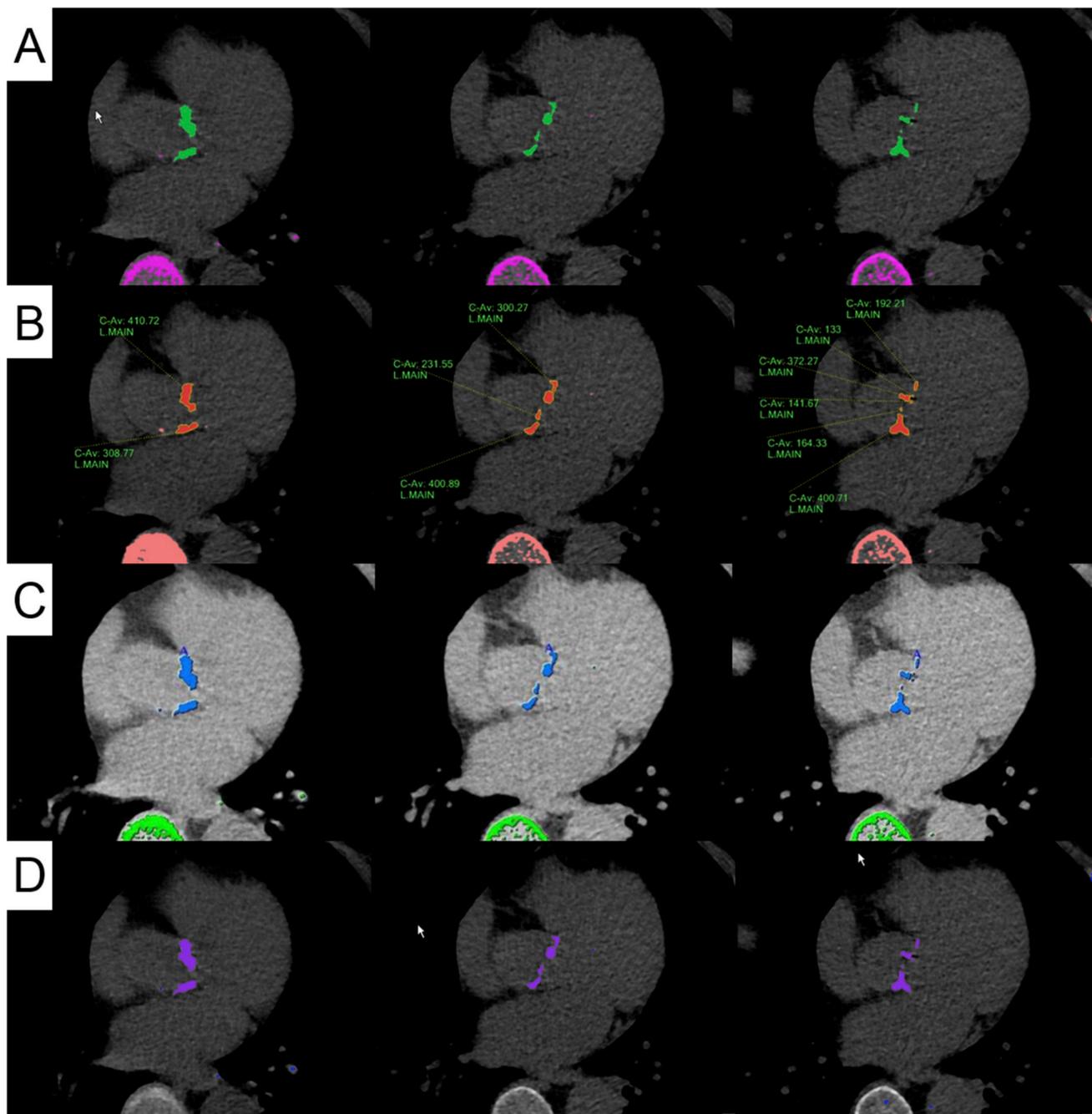


Fig. 1. Representative images of a 90-year-old male patient with severe aortic stenosis planned to undergo transcatheter aortic valve implantation. A–D, Transverse CT sections (same slice positions) evaluated with all workstation platforms (A, workstation 1, Siemens; B, workstation 2, Philips; C, workstation 3, GE; D, workstation 4, Pie Medical).

Table 3
Comparison of Agatston scores of the aortic valve for each observer with four different workstation platform (WS) platforms.

	Parameters	WS1	WS2	WS3	WS4	p-value ^a
Observer 1	Median (IQR)	1908 (1160–3021)	1876 (1144–2822)	1785 (1148–2862)	1826 (1141–2807)	0.96
	Range	282–6037	304–5863	277–6264	280–5684	
Observer 2	Median (IQR)	1886 (1185–2948)	1834 (1147–2826)	1839 (1188–2911)	1818 (1141–2807)	0.98
	Range	287–6005	309–5727	313–6264	281–5644	
	p-value ^b	0.93	0.98	0.89	0.98	

Data were compared using Kruskal-Wallis-Test^a and Mann-Whitney-U-Test^b.

Abbreviations: IQR, inter-quartile range; WS, workstation platform.

Workstation platform 1, Siemens; Workstation platform 2, Philips; Workstation platform 3, GE; Workstation platform 4, Pie Medical.

platforms and observers, and for intra-observer variability was assessed using Cohen's kappa coefficient.

All analyses were performed using commercially available software (SPSS 25, IBM Corporation, Armonk, NY, USA). A two-tailed $P < 0.05$ was considered statistically significant.

3. Results

3.1. Aortic valve calcification scoring

Each of the four workstation platforms generated numerically different results for the Agatston scores (Table 3). For both observers, WS 1 produced the highest overall absolute values with a median score of 1908 (interquartile-range: 1160–3021) for observer 1 and a median score of 1886 (interquartile-range: 1185–2948) for observer 2. However, there were no significant differences between Agatston scores quantified with the different workstation platforms for both observers ($p = 0.96$ and $p = 0.98$).

Comparing Agatston score results of all four workstation platforms, we found an excellent correlation between platforms with $r = 0.991$ – 0.996 for observer 1 and 2 (Table 4). Regression analysis revealed a strong relationship between measurements of all platforms

with $r^2 = 0.981$ – 0.992 for observer 1 and $r^2 = 0.981$ – 0.989 for observer 2 (see Table 4).

Results of Bland-Altman analysis detailing the level of agreement between workstation platforms are shown in Table 4. All Bland-Altman plots showed small mean differences between workstation platforms (6 ± 128 – 100 ± 179). Largest differences of Agatston scores between platforms were found for WS1 in comparison to WS 2 (91 ± 186 for observer 1 and 87 ± 175 for observer 2) and WS1 in comparison to WS4 (100 ± 179 for observer 1 and 81 ± 180 for observer 2). Bland-Altman-Plots for comparing platforms indicated a proportional bias with higher differences at higher Agatston scores (see Fig. 2).

Bland-Altman analysis showed minimal mean differences with narrow limits of agreement (1 ± 43 to 12 ± 70) between observers using the same workstation platform (Fig. 3). Furthermore, Bland-Altman analysis showed minor mean differences with narrow limits of agreement for intra-observer variability using the same workstation platform (9 ± 122 for WS1, 9 ± 42 for WS2, 20 ± 96 for WS3, and 14 ± 77 for WS4). Bland-Altman plots for both inter-observer and intra-observer variability showed no bias.

Table 4

Spearman's rank correlation (A), regression analysis (B) and Bland-Altman analysis of Agatston scores assessed by two observers with four workstation platforms. Cohen's kappa (D) of likelihood categories of severe aortic stenosis according to gender by using AVC Agatston scores, as previously described.^{9,12}

A		Spearman rank correlation (r)			
Observer 1		WS1	WS2	WS3	WS4
	WS1	–	0.991	0.995	0.992
	WS2	0.991	–	0.993	0.996
	WS3	0.995	0.993	–	0.995
	WS4	0.992	0.996	0.995	–
Observer 2		WS1	WS2	WS3	WS4
	WS1	–	0.991	0.994	0.994
	WS2	0.991	–	0.992	0.996
	WS3	0.994	0.992	–	0.994
	WS4	0.994	0.996	0.994	–
B		Linear regression analysis (r^2)			
Observer 1		WS1	WS2	WS3	WS4
	WS1	–	0.981	0.987	0.984
	WS2	0.981	–	0.986	0.992
	WS3	0.987	0.986	–	0.985
	WS4	0.984	0.992	0.985	–
Observer 2		WS1	WS2	WS3	WS4
	WS1	–	0.982	0.985	0.986
	WS2	0.982	–	0.984	0.989
	WS3	0.985	0.984	–	0.981
	WS4	0.986	0.989	0.981	–
C		Bland-Altman analysis			
Observer 1		WS1	WS2	WS3	WS4
	WS1	–	91 ± 186	64 ± 149	100 ± 179
	WS2	91 ± 186	–	-36 ± 160	-8 ± 110
	WS3	64 ± 149	-36 ± 160	–	27 ± 150
	WS4	100 ± 179	-8 ± 110	27 ± 150	–
Observer 2		WS1	WS2	WS3	WS4
	WS1	–	87 ± 175	42 ± 157	81 ± 180
	WS2	87 ± 175	–	-44 ± 175	-6 ± 128
	WS3	42 ± 157	-44 ± 175	–	39 ± 154
	WS4	81 ± 180	-6 ± 128	39 ± 154	–
D		Cohen's Kappa			
Observer 1		WS1	WS2	WS3	WS4
	WS1	–	0.85	0.91	0.88
	WS2	0.85	–	0.89	0.97
	WS3	0.91	0.89	–	0.89
	WS4	0.88	0.97	0.89	–
Observer 2		WS1	WS2	WS3	WS4
	WS1	–	0.90	0.89	0.90
	WS2	0.90	–	0.88	0.95
	WS3	0.89	0.88	–	0.91
	WS4	0.90	0.95	0.91	–

Abbreviations: WS, workstation platform.

Workstation platform 1, Siemens; Workstation platform 2, Philips; Workstation platform 3, GE; Workstation platform 4, Pie Medical.

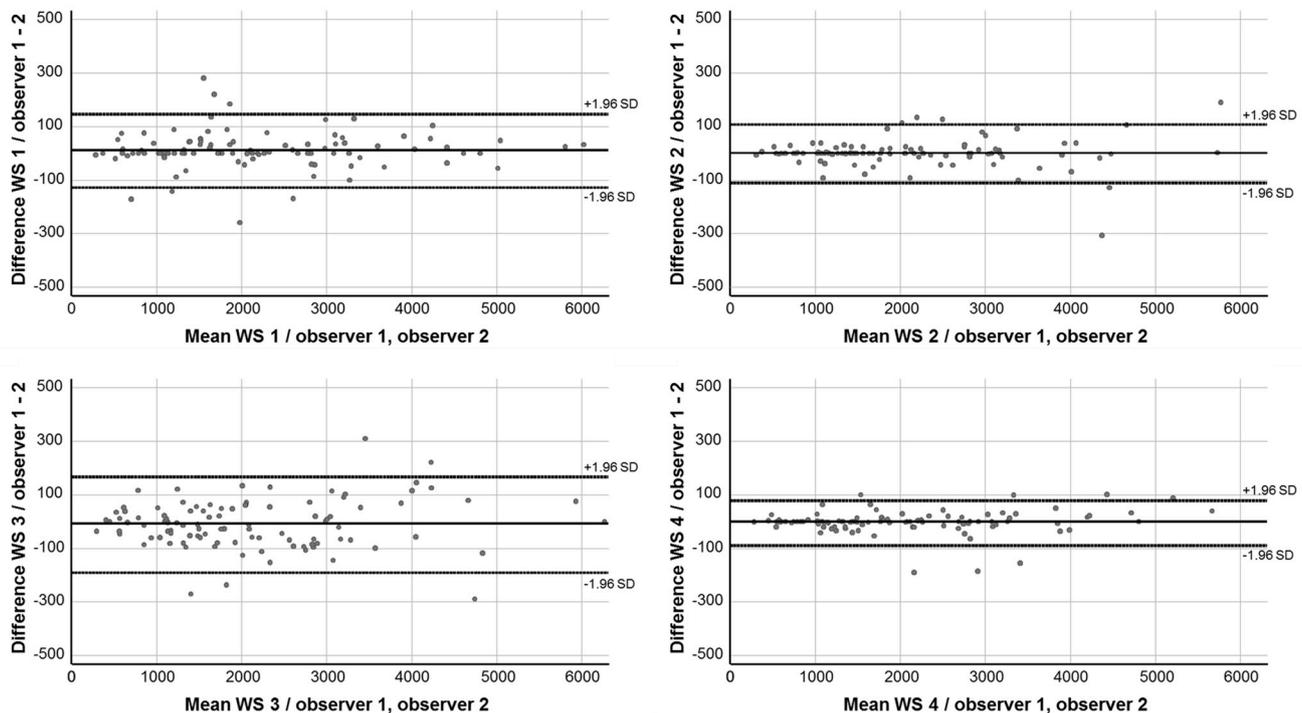


Fig. 2. Bland-Altman-Plots illustrate the mean error and limits of agreement between both observers for Agatston scores of the aortic valve (Workstation platform 1, Siemens; Workstation platform 2, Philips; Workstation platform 3, GE; Workstation platform 4, Pie Medical). SD, standard deviation; WS, workstation platform.

3.2. Likelihood stratification

Most patients (33–36%) had a very high likelihood of severe aortic stenosis according to the Agatston Score. We found minor inconsistencies in gender-specific likelihood classifications depending on the workstation platform and observer (Fig. 4). Further evaluation of aortic stenosis likelihood grading revealed that 11 of 100 patients (11%) and 10 of 100 patients (10%) were assigned to different likelihood groups by at least two of the four workstation platforms by observer 1 and observer 2. For both observers, these classification discrepancies were not statistically significant ($p = 0.98$ and $p = 1.0$).

Cohen's kappa showed a strong to almost perfect agreement between workstations for likelihood classification of severe aortic stenosis for observer 1 (kappa: 0.85–0.97) and observer 2 (kappa: 0.88–0.95), see Table 4. Furthermore, Cohen's kappa showed a strong to almost perfect agreement between observers using the same workstation (WS1: kappa = 0.92; WS2: kappa = 0.97; WS3: kappa = 0.93; WS4: kappa = 1.0) and for intra-observer agreement using the same workstation (WS1: kappa = 0.95; WS2: kappa = 1.0; WS3: kappa = 1.0; WS4: kappa = 1.0).

4. Discussion

The aim of the present study was to investigate whether AVC scoring performed with different workstation platforms generates similar and thus vendor-independent results. On the basis of the CT data of 100 patients we could show that - while mere numeric AVC Agatston scores between software-platforms might differ slightly - the AVC Agatston scores were closely correlated and different workstation platforms produced similar results also for likelihood classification of aortic stenosis according to the AVC load. Furthermore, we found low inter-observer and intra-observer variability for AVC Agatston scores using the same software-platform with substantial agreement regarding likelihood classification.

Current recommendations to assess the likelihood of severe aortic

stenosis according to AVC load are based on the Agatston score from non-enhanced CT.^{9,12} It is known that the coronary Agatston score and the AVC Agatston score are influenced by several factors including the time point of CT data acquisition throughout the cardiac cycle, tube potential and tube current, slice thickness, reconstruction kernel and beam hardening artifacts.^{5,20–22} Furthermore, motion artifacts leading to cusp motion may influence AVC Agatston scores, similar to the effect reported for the coronary arteries.²³

There are various workstation platforms dedicated to calcium scoring. Each calcium scoring software has individual calculation algorithms and innate ROI placement options (volume-based versus slice-based). It was previously shown that results from coronary calcium quantification might differ depending on the software platforms used, but results were overall comparable with minor inconsistencies in risk group assignments.^{16,17} In patients with a small coronary calcium load, however, Weininger et al.¹⁶ reported higher inconsistencies between platforms.

To the best of our knowledge, our study is the first to describe the interplatform reproducibility of AVC Agatston scores on the basis of identical CT data sets. Precise, reproducible and vendor-independent assessment of AVC scores represents a prerequisite for the clinical application of the technique, having an impact on patient management and treatment. In contrast to coronary calcifications, AVC consists of larger plaques. In our study largest AVC scores amounted to 6'264, and the literature reports values of above 10'000.²⁴ In contrast to Weininger et al.,¹⁶ we found - at an overall higher median Agatston score level - higher inconsistencies of scoring results between workstation platforms at higher AVC scores. While we found that some patients were assigned to different likelihood categories, we did not find significant differences regarding assignment to these categories for aortic stenosis.

Each workstation platform uses different algorithms and labeling methods for the demarcation of calcifications. Workstation platform 4 (Pie Medical) enables a volumetric selection of the entire calcification with the possibility of subsequent manual adjustments. Workstation platforms 2 (Philips) and 3 (GE) allow plaque tracing on each CT slice

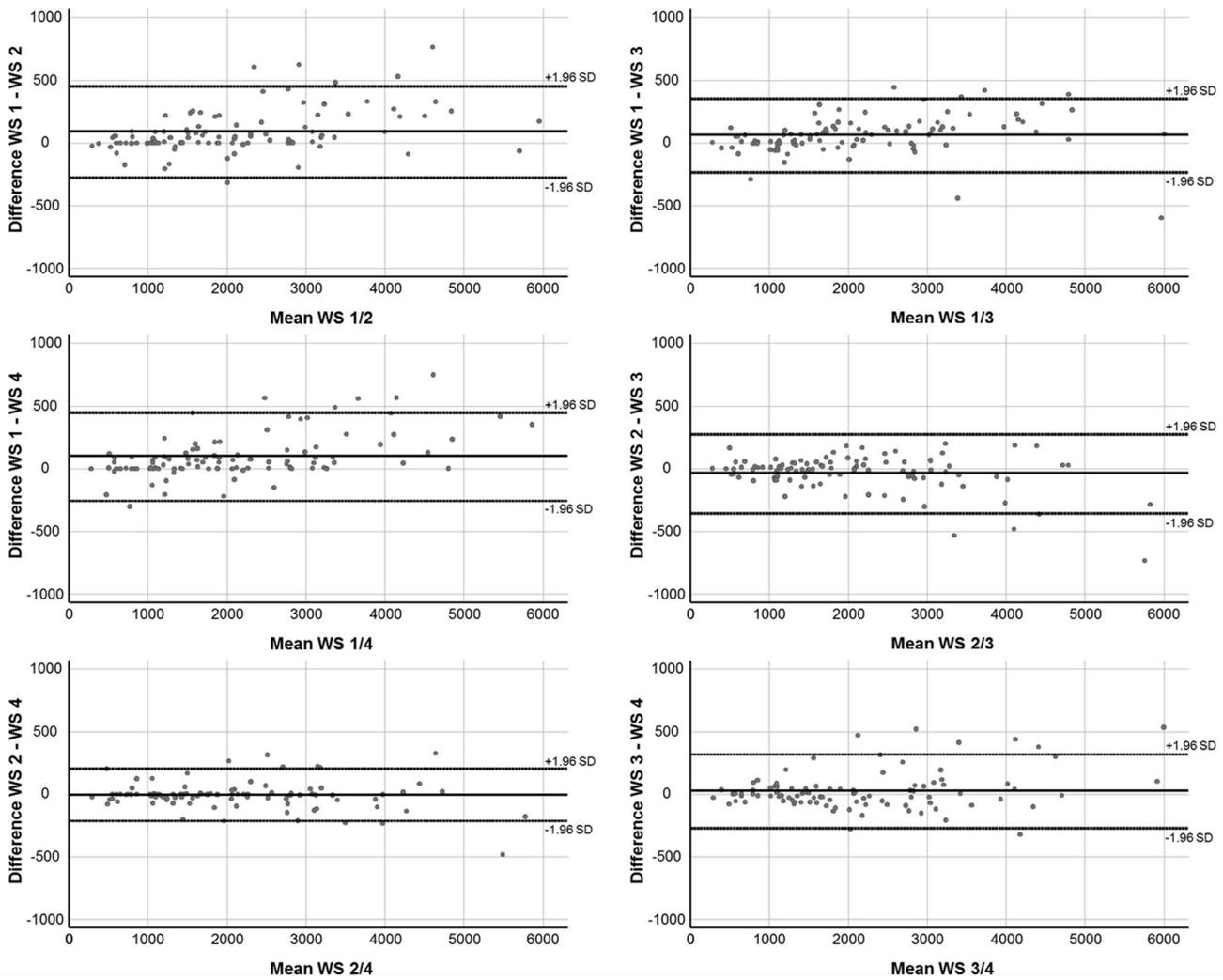


Fig. 3. Bland-Altman-Plots illustrate the mean error and limits of agreement between workstation platforms (Workstation platform 1, Siemens; Workstation platform 2, Philips; Workstation platform 3, GE; Workstation platform 4, Pie Medical) for Agatston scores of the aortic valve assessed by observer 1. SD, standard deviation; WS, workstation platform.

and calcification area restriction by using freehand ROIs. On Workstation platform 1 (Siemens), AVC scoring can be performed with a mixture of both methods. These differences in calcium segmentation

might explain some of the inter-platform variation found.

Another effect of the calcium segmentation issue may also result in observers' differences of AVC segmentation in patients having a

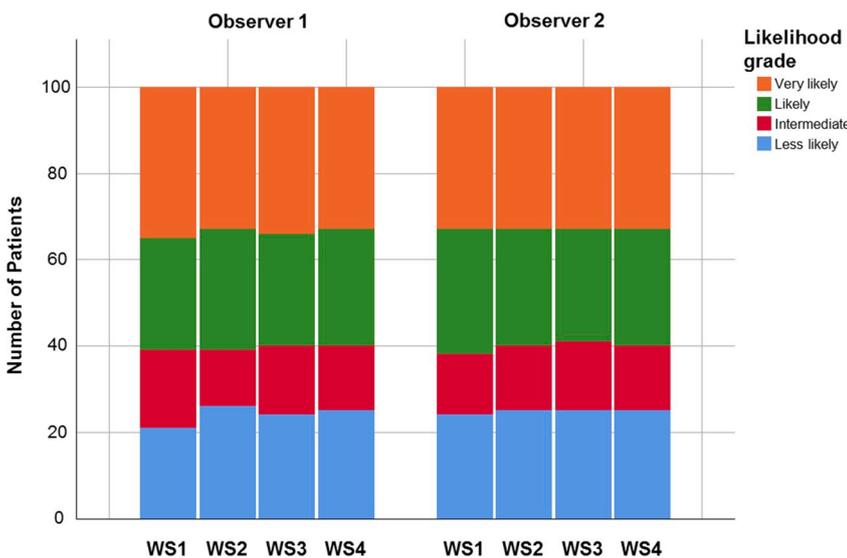


Fig. 4. Differences of the gender-specific likelihood assessment of severe aortic stenosis according to the Agatston Score assessed with different workstation platforms (Workstation platform 1, Siemens; Workstation platform 2, Philips; Workstation platform 3, GE; Workstation platform 4, Pie Medical) by two observers. Bars are colored according to likelihood of severe aortic stenosis using the Agatston score as previously described.⁹ WS, workstation platform.

continuity of aortic calcifications into the left ventricular outflow tract, aortic wall, coronary arteries and/or the mitral valve apparatus. Disagreement in exclusion of such calcifications may lead to differences in AVC scores. This effect may be relevant in borderline AVC scores near the cut-off values for different likelihood categories. Thus, patients with calcifications adjacent to the aortic valve are more likely to be put into different likelihood categories by different observers and different platforms than those having calcifications limited to the aortic valve. Still, Bland-Altman analyses showed that inter-observer and intra-observer variations of AVC scoring were small for all software solutions, being in line with previous studies.^{4,25} Furthermore, Cohen's kappa statistics showed that agreement of likelihood categorization according to AVC scores between workstations and between observers is substantial.

Our study has some limitations which should be addressed in future research. First, we did not assess interplatform variability of volume score and mass score as current recommendations on CT assessment of aortic stenosis are based on the Agatston Score.^{9,12} Second, we performed measurements on CT data sets of 100 consecutive patients acquired on one CT scanner with an identical CT acquisition protocol. Thus, it remains to be elucidated whether our results are generalizable to other CT scanners as well. Third, our study is based on a limited number of patients with symptomatic aortic stenosis. Future studies should address whether our results can be generalized to patient cohorts having valve calcifications also at the lower range. Finally, we included four commonly used software platforms for calcium quantification, however, there exist further products from other vendors on the market.

5. Conclusion

Our study shows high correlation and concordance of CT-derived AVC Agatston scores calculated with four common, commercially available software platforms and analyzed by two independent observers. This finding indicates a software- and observer-independence of AVC scoring regarding the CT assessment of patients with severe aortic stenosis, which is a prerequisite for a wide application of the technique in clinical routine.

Conflicts of interest

Francesco Maisano is consultant for Abbott Vascular, St Jude Medical, Medtronic, ValtechCardio and receives royalties from Edwards Lifesciences. Fabian Nietlispach is consultant for Edwards Lifesciences, Medtronic, St Jude Medical. All other authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcct.2019.01.016>.

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