Aortic valve calcification is associated with increased incidence of cognitive decline

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Abstract

Background: To our knowledge, there has only been only one prior study examining the relationship between aortic valve calcification (AVC) and dementia, which was found to be statistically insignificant. We aimed to examine this relationship in US Veterans receiving clinically indicated lung cancer screening CT (LCSCTs), and determine if quantification of AVC has predictive value in determining early signs of cognitive decline.

Methods: We identified 1654 US Veterans who received LCSCTs under USPSTF guideline recommendations between October 1, 2013 and July 30, 2014. Primary outcome was a diagnosis of dementia, as defined by a MOCA score less than 26, MMSE score of less than 24, or ICD diagnosis. AVC was calculated using the Agatston method and cardiac risk factor adjustments were made using regression modeling. Similar to prior investigations, AVC underwent logistic transformation with log2(AVC+1) to achieve normal distribution.

Results: The patient population was predominantly Caucasian males (95% and 96% respectively) and the median age of our population was 65 (IQI: 61, 68). 124 patients were identified with new diagnosis of dementia after LCSCT. Dementia and logAVC demonstrated a strong correlation in both the univariate and multivariate Cox regression analysis, ([95% CI] 1.13 [1.09, 1.17]; p<0.001) and ([95% CI] 1.08 [1.04, 1.13]; p<0.001) respectively.

Conclusion: AVC retained statistical significance with dementia both in the univariate and multivariate regression analysis. The difference in significance between coronary artery calcification (CAC) and AVC may highlight a separate subclinical vascular process whose mechanism may require further investigation.

Cohort Flow Diagram

1654 Providence VA Medical Center patients receiving LCSCT between Oct 2013-July 2014

- **Prior aortic valve replacements (N=18)**
- **Prior percutaneous coronary interventions (N=154)**
- **Clinical indications of cognitive decline prior to LCSCT (N=94)**

1388 final patients for analysis

Baseline Demographics and Clinical Characteristics

Characteristic	Overall (N=1388)
CACS, median (IQI)	455.0 (93.1, 1317.4)
AVCS, median (IQI)	56.3 (0, 313)
Age, years, median (IQI)	65 (61, 68)
BMI, median (IQI)	28.6 (25.3, 32.4)
Male, n (%)	1331 (96.0)
Caucasian, n (%)	1305 (94.0)
Diabetes, n (%)	364 (26.2)
Hypertension, n (%)	827 (59.6)
Hyperlipidemia, n (%)	1010 (72.8)
Total cholesterol, median (IQI)	178 (154, 205)
HDL Cholesterol, median (IQI)	43 (37, 52.5)
Statin Use, n (%)	781 (56.3)
Current Smoker, n (%)	767 (55.3)
Family History of Early CAD, n (%)	163 (11.7)
Prior CAD, n (%)	218 (15.7)
Prior MI, n (%)	69 (5.0)
Prior CABG, n (%)	23 (1.7)
ASCVD Risk Score, median (IQI)	18.3 (12.3, 27.5)

Table 1. Baseline demographics and clinical characteristics for overall population. Abbreviations: IQI=Interquartile range, CACS=coronary artery calcium score, AVCS=aortic valve calcium score, BMI=body mass index, CAD=coronary artery disease, MI=myocardial infarction, CABG=coronary artery bypass graft, ASCVD=atherosclerotic cardiovascular disease

Aortic Valve Calcium Scoring

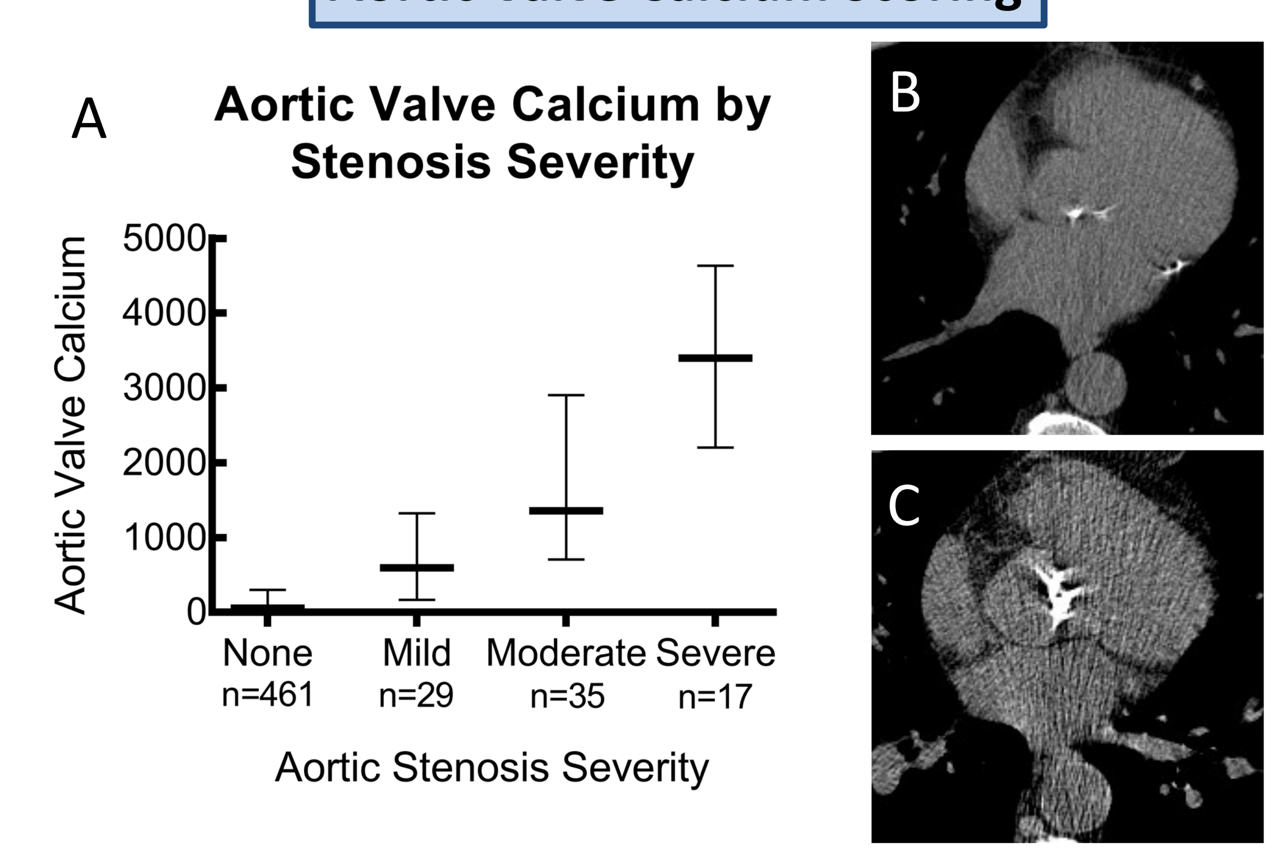

Figure 1. Aortic valve calcification by aortic stenosis. Left: graph of AVC by level of aortic valve stenosis demonstrating the median and interquartile range of each (A). Right: examples of AVC detected on LCSCT in a single-slice plane at the level of the aortic valve. Images from a patient with total AVCS of less than 100 (B) and from a patient with total AVCS of more than 3000 (C).

Normalization of AVCS distribution

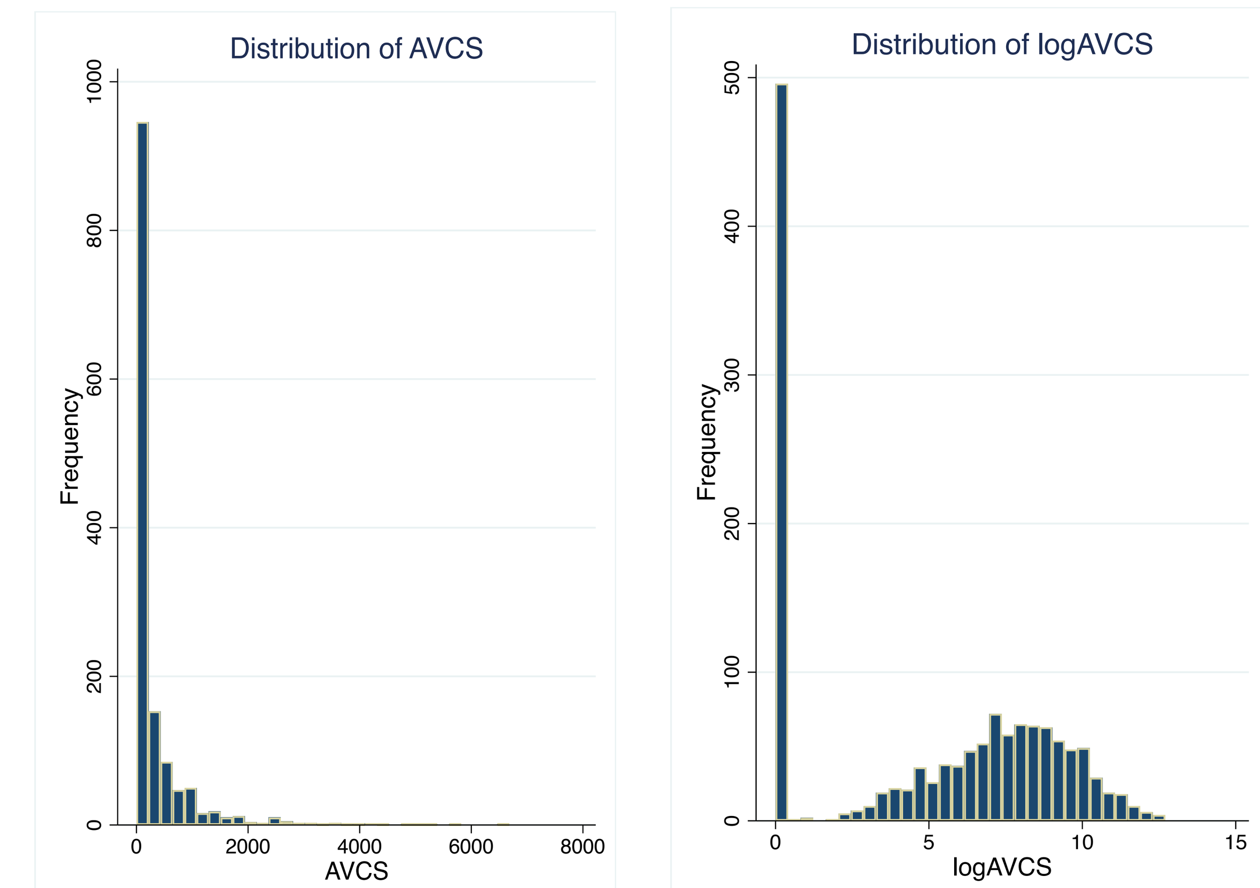

Figure 2. Normalization of AVC scores using log transformation. We treated AVC score as continuous using base-2 logarithm of AVCS+1 (log2 [CAC+1]) in accordance with previous studies to achieve normal distribution.

Increasing AVC predicts increased cognitive decline

Univariate model	Hazard Ratio	95% Confidence Interval	Standard Error	z	P Value
logAVC	1.13	1.09, 1.17	0.02	6.21	<0.001
Age	1.06	1.04, 1.08	0.01	6.55	<0.001
Male	0.99	0.52, 1.87	0.32	-0.04	0.968
BMI	1.00	0.98, 1.02	0.01	0.00	0.999
Hypertension	1.47	1.10, 1.97	0.22	2.58	0.010
Hyperlipidemia	1.02	0.75, 1.38	0.16	0.13	0.898
DM	1.33	0.99, 1.78	0.20	1.88	0.060
Prior CAD	1.79	1.30, 2.48	0.30	3.52	<0.001
Current statin use	1.32	1.00, 1.75	0.19	1.97	0.049
CVA event	1.58	0.90, 2.80	0.46	1.59	0.113

Table 2. Univariate cox regression model. Dementia and logAVC demonstrated a strong correlation in the univariate analysis. Hazard ratio 1.13 (CI: 1.09, 1.17; p<0.001).

Multivariate model	Hazard Ratio	95% Confidence Interval	Standard Error	z	P Value
logAVC	1.08	1.04, 1.13	0.02	3.87	<0.001
Age	1.04	1.02, 1.06	0.01	4.15	<0.001
Hypertension	1.20	0.88, 1.65	0.19	1.17	0.244
DM	1.04	0.76, 1.42	0.17	0.24	0.809
Prior CAD	1.51	1.07, 2.12	0.26	2.35	0.019
Current statin use	0.92	0.68, 1.25	0.14	-0.55	0.584
CVA event	1.17	0.66, 2.08	0.34	0.52	0.601

Table 3. Multivariate cox regression model. Dementia and logAVC also demonstrated a strong correlation in the multivariate analysis. Hazard ratio 1.08 (CI: 1.04, 1.13; p<0.001).

Conclusions

- **AVC as a continuous variable is associated with increased rates of mild cognitive decline as defined by ICD codes, MMSE <24, and MOCA <26**
- This association remained significant when controlling for time to diagnosis in months

Future Studies

- Compare relationship between CAC and AVC with diagnosis of mild cognitive decline, to characterize how different vascular beds are affected.
- Preliminary data suggests that CAC is not significant when compared to AVC. This may represent differing inflammatory vascular processes between CAC and AVC, which warrants further investigation.

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