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RECEIVED 10 February 2023

ACCEPTED 04 April 2023

PUBLISHED 28 April 2023

## CITATION

Walker J, Christianson A, Athar M, Waqar F and Gerson M (2023) Prediction of angiographic coronary disease and mortality with a cadmium-zinc-telluride camera: a comparison of upright and supine ejection fractions and left ventricular volumes.  
Front. Nucl. Med. 3:1162784.  
doi: 10.3389/fnume.2023.1162784

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# Prediction of angiographic coronary disease and mortality with a cadmium-zinc-telluride camera: a comparison of upright and supine ejection fractions and left ventricular volumes

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**Introduction:** Perfusion imaging strongly predicts coronary artery disease (CAD), whereas cardiac volumes and left ventricular ejection fraction (LVEF) strongly predict mortality. Compared to conventional Anger single-photon emission computed tomography (SPECT) cameras, cadmium-zinc-telluride (CZT) cameras provide higher resolution, resulting in different left ventricular volumes. The cadmium-zinc-telluride D-SPECT camera is commonly used to image in the upright position, which introduces changes in left ventricular loading conditions and potentially alters left ventricular volumes. However, little or no data exist on the predictive value of left ventricular volumes and ejection fraction when acquired in the upright position. We investigated models for the prediction of CAD and mortality, comparing upright and supine imaging.

**Methods:** A retrospective study of patients with upright/supine stress and rest imaging and coronary angiography within 3 months was performed. Univariate and multivariable analyses were performed to predict abnormal angiograms and all-cause mortality.

**Results:** Of the 392 patients, 210 (53.6%) had significant angiographic CAD; 78 (19.9%) patients died over 75 months. The best multivariable model for CAD included the supine summed stress score and supine stress LVEF, with an area under the receiver operating characteristic of 0.862, a sensitivity of 76.7%, and a specificity of 82.4%, but this model was not statistically superior to the best upright model. The best multivariable models for mortality included age, diabetes, history of cardiovascular disease, and end-systolic volume, with the upright and supine models being equivalent.

## Abbreviations

CZT, cadmium-zinc-telluride; SPECT, single-photon emission computed tomography; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; SSS, summed stress score; AUROC, area under the receiver operating characteristic; AIC, Akaike information criterion.

**Discussion:** Angiographic CAD was best predicted by the supine summed stress score and LVEF but was not statistically superior to the next-best upright model. Mortality was best predicted by end-systolic volume in combination with age, diabetes status, and cardiovascular disease status, with equivalent results from the upright and supine images.

#### KEYWORDS

CZT SPECT, D-SPECT, upright SPECT, supine SPECT, LVEF, ESV

## 1. Introduction

The advent of digital cadmium-zinc-telluride (CZT) single-photon emission computed tomography (SPECT) imaging ushered in an era of faster, more patient-friendly perfusion stress testing (1, 2). With these new devices came the need to validate and reconcile the effects of increased spatial resolution on attenuation artifacts and volumetric measurements (3–5). With respect to clinical outcomes, the resulting CZT SPECT literature has focused primarily on myocardial perfusion findings for the prediction of coronary artery disease (CAD), cardiac events, and mortality (6–14). Although left ventricular ejection fraction (LVEF) and volumes are known to be strong predictors of mortality, the prognostic value of CZT SPECT volumetric measurements has been less explored (15–22). In a multicenter comparative study of the Anger camera and CZT camera measurements of LVEF, the mean LVEF was found to be significantly higher with the CZT camera (23). The prognostic implications of this difference in LVEF are unknown.

An important factor affecting CZT SPECT volumetric measurements is patient positioning. Unlike other imaging modalities obtained in a single supine position, CZT SPECT studies are commonly performed in two positions to reduce the risk of incorrectly interpreting attenuation artifacts as perfusion abnormalities (24–28). This potentially provides the imager with both upright and supine LVEF and volume data. No study, however, has directly compared the relative prognostic power of LVEF vs. left ventricular volumes on a CZT camera, and no study has addressed whether the prognostic implications are different in the upright vs. supine position.

There is limited previous research on the accuracy of LVEF and volume measurements obtained in the upright position (24, 29–31). Previous data in healthy participants (30, 32) and patients referred for evaluation of angina pectoris (24) have shown that resting end-diastolic volumes (EDV) and end-systolic volumes (ESV) are generally smaller in the upright position compared to the supine position, whereas LVEF is more variable. It is unclear whether these differences may affect the prognostic value of upright volumetric measurements on a CZT SPECT camera.

The aim of this study was to compare the prognostic value of upright vs. supine volumetric imaging for the prediction of CAD and mortality by creating multivariable prediction models. Because left ventricular volumes and ejection fractions differ due to differences in ventricular loading, we hypothesized that there may be a difference in the prediction of mortality between the upright and supine images acquired with a CZT camera.

## 2. Materials and methods

### 2.1. Study population and clinical data collection

All methods for this retrospective cohort study were reviewed and approved by the Institutional Review Board of the University of Cincinnati, with an exception for informed consent. The study population underwent upright and supine SPECT myocardial perfusion imaging with a Spectrum Dynamics D-SPECT camera (Spectrum Dynamics Inc., Palo Alto, CA, United States) between 20 June 2014 and 4 February 2016. All patients who underwent selective coronary angiography within 3 months of perfusion imaging were included in the present study, regardless of other medical histories.

Clinical data were obtained from the electronic medical record (Epic Systems, Verona, WI, USA). All-cause mortality data were acquired from the local medical record and from communicating institutions utilizing the same electronic medical record. Follow-up was terminated at death or last contact with the electronic medical record.

### 2.2. SPECT protocol

Our SPECT protocol was conducted as follows. Patients were counseled to avoid caffeinated beverages 24 h before testing and to avoid beta-blockers or calcium channel antagonists 24–48 h before testing, unless otherwise requested by the referring physician. Exercise testing was performed on a treadmill using the Bruce protocol. Pharmacologic stress was performed with regadenoson 0.4 mg intravenously when exercise testing was not possible.

Upright and supine stress and rest images were acquired with a D-SPECT CZT dedicated cardiac camera. Upright imaging was performed with the imaging chair at an angle of 65°–70°. Rest images were acquired for 3–11 min at 60 min following a weight-based injection of 9.4–14 mCi (mean 0.11 mCi/kg) of technetium-99 m tetrofosmin. Stress images were acquired for at least 3 min at 30–45 min following a weight-based injection of 27.7–42 mCi (mean 0.33 mCi/kg) of technetium-99 m tetrofosmin.

### 2.3. Image processing

Images were processed using iterative reconstruction (ordered subset expectation maximization) on a Spectrum Dynamics

Cedars View processing station (Spectrum Dynamics Inc., Palo Alto, CA, United States). Processed images were reviewed by a physician reader and inaccurate computer identification of endocardial borders, the left ventricular long axis, and apical or basal planes was corrected at the time of image interpretation. The interpretation was performed by two experienced nuclear cardiologists using Corridor4DM SPECT software (INVIA Medical Imaging Solutions, Ann Arbor, MI, United States). Differences in interpretation were resolved by consensus agreement. The studies were read independently, without knowledge of the test indication or clinical data other than gender, height, and weight. Summed stress score (SSS), summed rest score, and summed difference score were recorded from the upright and supine positions. Upright and supine rest and post-stress LVEF, ESV, and EDV were calculated from the gated images by the 4DM SPECT software.

## 2.4. Method for CAD assessment

Coronary angiographic images were blinded for the patient's age, gender, past medical history, presenting symptoms, and SPECT results. Angiographic CAD was defined as a stenosis of  $\geq 50\%$  in the left main coronary artery and/or  $\geq 70\%$  in the left anterior descending, left circumflex, right coronary artery, or main branch. Angiographic CAD was assessed by an independent, blinded interventional cardiologist. This assessment was compared to the documented reading in the patient's

medical chart, and any differences were resolved by a second blinded interventional cardiologist.

## 2.5. Statistical methods

Categorical variables were summarized using frequencies and percentages, with chi-squared tests used for comparisons. Continuous variables were summarized using means and standard deviations, and *t*-tests were used for comparisons. Logistic regression models were used to predict angiographic CAD, and Cox regression models were used to predict mortality. For each outcome, demographic and clinical variables were evaluated in univariate models. Multivariable models were then constructed using forward stepwise selection, using demographic variables only, demographic variables plus upright stress results, demographic variables plus upright rest results, demographic variables plus supine stress results, and demographic variables plus supine rest results. The best logistic and Cox models were chosen using the C-statistic and Akaike information criterion (AIC), respectively; models were compared using Vuong's closeness test and partial likelihood ratio test, respectively. All statistical analyses were performed with SAS version 9.4. Figures were generated using SAS 9.4 software.

## 3. Results

### 3.1. Demographic results

Between 20 June 2014 and 4 February 2016, 2,779 patients underwent SPECT testing in the Nuclear Cardiology Laboratory. Of these patients, 395 underwent both upright and supine rest and stress imaging and subsequently underwent selective coronary angiography within 3 months and were included in the

TABLE 1 Study population demographics and outcome frequencies.

	Total ( <i>n</i> = 392)	Survivors ( <i>n</i> = 314, 80.1%)	Non-survivors ( <i>n</i> = 78, 19.9%)	<i>p</i> -value
Age (mean, SD)	58.9 (10.4)	62.9 (9.5)	57.9 (10.4)	0.0001*
Gender ( <i>n</i> , %)				0.0139*
Men	223 (56.9)	169 (53.8)	54 (69.2)	
Women	169 (43.1)	145 (46.2)	24 (30.8)	
BMI (mean, SD)	32.6 (8.1)	30.6 (6.7)	33.1 (8.4)	0.0044*
BSA (mean, SD)	2.1 (0.3)	2.1 (0.3)	2.1 (0.3)	0.4082
Pharm/exercise test ( <i>n</i> , %)				0.3065
Pharm	294 (75.0)	232 (73.9)	62 (79.5)	
Exercise	98 (25.0)	82 (26.1)	16 (20.5)	
Diabetes ( <i>n</i> , %)	156 (39.8)	119 (37.9)	37 (47.4)	0.1235
Hypertension ( <i>n</i> , %)	314 (80.1)	247 (78.7)	67 (85.9)	0.1520
HLD ( <i>n</i> , %)	188 (48.0)	143 (45.5)	45 (57.7)	0.0545
CAD ( <i>n</i> , %)	98 (25.0)	65 (20.7)	33 (42.3)	<0.0001*
CVD ( <i>n</i> , %)	148 (37.8)	103 (32.8)	45 (57.7)	<0.0001*
CMP ( <i>n</i> , %)	77 (19.6)	50 (15.9)	27 (34.6)	0.0002*
Angiographic CAD ( <i>n</i> , %)	210 (53.6)	154 (49.0)	56 (71.8)	0.0003*

SD, standard deviation, BMI, body mass index; BSA, body surface area; HLD, hyperlipidemia; CAD, history of coronary artery disease; CVD, cardiovascular disease, defined as previously; CAD, cerebrovascular disease and/or peripheral arterial disease; CMP, cardiomyopathy, defined as a history of reduced ejection fraction and/or heart failure.

\*Significant *p*-values < 0.05.

TABLE 2 Upright vs. supine perfusion and volumetric variables.

	Upright (mean, SD)	Supine (mean, SD)	<i>p</i> -value, upright vs. supine
SSS	4.4 (5.7)	4.6 (5.6)	0.1971
SRS	2.7 (4.0)	2.9 (4.4)	0.2096
SDS	2.3 (2.9)	2.3 (2.8)	0.9691
Stress LVEF	51.9 (13.9)	52.9 (13.6)	0.0006*
Rest LVEF	52.2 (14.1)	53.3 (13.7)	0.0015*
Difference stress vs. rest LVEF	0.0 (0.1)	0.0 (0.1)	0.968
Stress ESV	68.8 (50.2)	68.5 (48.4)	0.5074
Rest ESV	65.5 (46.8)	65.2 (44.6)	0.5653
Difference stress vs. rest ESV	3.3 (10.9)	3.3 (12.1)	0.9869
Stress EDV	130.4 (57.3)	133.5 (55.9)	<0.0001*
Rest EDV	125.4 (53.9)	128.6 (51.5)	<0.0001*
Difference stress vs. rest EDV	5.0 (13.5)	4.9 (15.1)	0.9261

SRS, summed rest score; SDS, summed difference score; SSS, summed stress score; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume.

\*Significant *p*-values < 0.05.

present study. Three patients were excluded from the final analysis due to missing perfusion data. Of the 392 patients, 169 (43.1%) were women; 98 (25.0%) patients underwent exercise stress, and the remaining patients underwent pharmacological stress. Of the 392 patients, 210 (53.6%) had significant angiographic CAD, and 78 (19.9%) died during a median follow-up of 75 months. See **Table 1** for complete patient demographic data.

### 3.2. Perfusion scores and left ventricular volumes

Perfusion scores and volumetric data are presented in **Table 2**. The mean differences in perfusion scores between the upright and supine positions were not statistically significant. Stress and rest LVEF and stress and rest EDV were all lower in the upright position than in the supine position, but the absolute differences were small. The differences between upright and supine ESV at rest (0.3 ml) and stress (0.3 ml) were minimal and not statistically different.

### 3.3. Univariate analysis for CAD prediction

**Table 3** shows the univariate analysis for CAD. The strongest upright predictors for CAD were SSS [area under the receiver operating characteristic (AUROC) 0.823], summed difference score (AUROC 0.778), summed rest score (AUROC 0.709), and stress LVEF (AUROC 0.706). The strongest supine predictors were SSS (AUROC 0.848), summed difference score (AUROC 0.781), summed rest score (AUROC 0.738), and stress LVEF (AUROC 0.682). Supine SSS was not independently statistically superior to upright SSS for the prediction of CAD. The presence of hyperlipidemia (AUROC 0.568,  $p = 0.0073$ ), known

cardiovascular disease (AUROC 0.570,  $p = 0.0044$ ), cardiomyopathy (AUROC 0.581,  $p < 0.0001$ ), and a pharmacological stress type (AUROC 0.544,  $p = 0.0477$ ) were all significantly but weakly predictive of CAD.

### 3.4. Multivariable analysis for CAD prediction

Multivariable modeling for CAD prediction demonstrated that the supine SSS and supine stress LVEF model was the best predictor of CAD with an AUROC of 0.862, a sensitivity of 76.7%, and a specificity of 82.4%. The best upright model consisted of upright SSS, supine LVEF, and a history of hyperlipidemia with an AUROC of 0.839, a sensitivity of 70.5%, and a specificity of 81.9% (**Figure 1**). Vuong’s closeness test was performed between these upright and supine models and showed no statistical difference.

### 3.5. Univariate analysis for mortality prediction

The univariate analysis for all-cause mortality is presented in **Table 4**. The strongest upright predictor of mortality was stress EDV, followed by stress ESV, rest ESV, and rest EDV in ascending order of AIC. The lower the AIC value, the better the

TABLE 3 Individual SPECT variables AUROC for prediction of CAD.

	Upright		Supine	
	AUROC	p-value	AUROC	p-value
SSS	0.823	<0.0001*	0.848	<0.0001*
SRS	0.709	<0.0001*	0.738	<0.0001*
SDS	0.778	<0.0001*	0.781	<0.0001*
Stress LVEF	0.706	<0.0001*	0.682	<0.0001*
Rest LVEF	0.643	<0.0001*	0.662	<0.0001*
Stress EDV	0.646	<0.0001*	0.65	<0.0001*
Rest EDV	0.645	<0.0001*	0.633	<0.0001*
Stress ESV	0.679	<0.0001*	0.671	<0.0001*
Rest ESV	0.648	<0.0001*	0.654	<0.0001*
Difference stress LVEF – rest LVEF <sup>a</sup>	0.585	0.0017*	0.537	0.2946
Difference stress EDV – rest EDV <sup>a</sup>	0.569	0.0083*	0.611	0.0004*
Difference stress ESV – rest ESV <sup>a</sup>	0.634	<0.0001*	0.622	0.0003*

SPECT, single-photon emission computed tomography; AUROC, area under the receiver operating characteristic; CAD, coronary artery disease; SRS, summed rest score; SDS, summed difference score; SSS, summed stress score; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume. \*Significant p-values < 0.05. <sup>a</sup>Difference values refer to the absolute difference between stress and rest measurements.

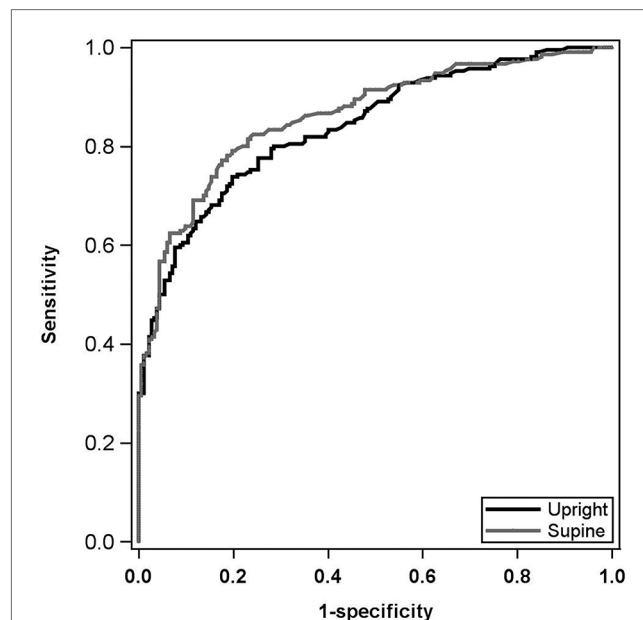


FIGURE 1 Multivariable CAD AUROC curves. Black curve: best upright CAD prediction model. Includes upright SSS, upright stress LVEF, and HLD status. AUROC: 0.839; sensitivity: 70.5%; specificity: 81.9%. Gray curve: best supine CAD prediction model. Includes supine SSS and supine stress LVEF. AUROC: 0.862; sensitivity: 76.7%; specificity: 82.4%. Models were not statistically different by Vuong’s closeness test. CAD, coronary artery disease; AUROC, area under the receiver operating characteristic; SSS, summed stress score; LVEF, left ventricular ejection fraction; HLD, hyperlipidemia.

TABLE 4 Individual SPECT variables and AIC for prediction of all-cause mortality.

	Upright		AIC	Supine		AIC
	HR	p-value		HR	p-value	
SSS	1.08 (1.05–1.11)	<0.0001*	871.5	1.07 (1.04–1.10)	<0.0001*	877.3
SRS	1.09 (1.05–1.13)	<0.0001*	877.1	1.08 (1.04–1.12)	0.0002*	879.5
SDS	1.11 (1.05–1.18)	0.0003*	880.1	1.09 (1.02–1.16)	0.0129*	885.9
Stress LVEF	0.97 (0.95–0.98)	<0.0001*	873.6	0.97 (0.95–0.98)	<0.0001*	871.0
Rest LVEF	0.97 (0.95–0.98)	<0.0001*	872.4	0.96 (0.95–0.98)	<0.0001*	867.0
Stress EDV	1.01 (1.01–1.01)	<0.0001*	862.9	1.01 (1.01–1.01)	<0.0001*	865.0
Rest EDV	1.01 (1.01–1.01)	<0.0001*	869.1	1.01 (1.01–1.01)	<0.0001*	870.8
Stress ESV	1.01 (1.01–1.01)	<0.0001*	863.3	1.01 (1.01–1.01)	<0.0001*	863.2
Rest ESV	1.01 (1.01–1.01)	<0.0001*	865.7	1.01 (1.01–1.01)	<0.0001*	866.3
Difference stress LVEF – rest LVEF <sup>a</sup>	1.72 (0.07–43.08)	0.7427	890.9	5.71 (0.19–167.74)	0.3125*	890.0
Difference stress EDV – rest EDV <sup>a</sup>	1.03 (1.01–1.04)	0.0003*	878.7	1.03 (1.01–1.04)	0.0001*	878.4
Difference stress ESV – rest ESV <sup>a</sup>	1.03 (1.01–1.05)	0.0093*	884.5	1.02 (1.01–1.04)	0.005*	884.0

SPECT, single-photon emission computed tomography; AIC, Akaike information criterion; SRS, summed rest score; SDS, summed difference score; SSS, summed stress score; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume.

\*Significant p-values < 0.05.

<sup>a</sup>Difference values refer to the absolute difference between stress and rest measurements.

predictive ability of the variable. The strongest supine predictor was stress ESV, followed by stress EDV, rest ESV, and rest LVEF in ascending order of AIC. The demographic variables that predicted mortality were increasing age, male gender, increasing body mass index (BMI), cardiovascular disease, and cardiomyopathy. The change in the left ventricular end-diastolic volume between the upright (mean 129.3 ml) and supine (mean 132.8 ml) positions in patients with a body mass index <35 kg/m<sup>2</sup> was 3.5 ml. For a body mass index ≥35 kg/m<sup>2</sup>, the mean change in the left ventricular end-diastolic volume between the upright (mean 132.5 ml) and supine (mean 135.0 ml) positions was 2.5 ml (p = NS).

### 3.6. Mortality prediction by LVEF subgroup

Although ESV outperformed LVEF in predicting all-cause mortality, LVEF is a practical and widely used prognostic indicator. Table 5 shows the hazard ratios for mortality for stress and rest LVEF divided into three groups: LVEF >50% (reference group); LVEF 35%–50%; and LVEF <35%. For example, the

hazard ratio for upright stress LVEF <35% compared to LVEF >50% was 3.00 (95% CI: 1.68–5.34), and for LVEF 35%–50% it was 1.95 (95% CI: 1.18–3.25). Hazard ratios showed similar trends for upright rest, supine stress, and supine rest LVEF.

### 3.7. Multivariable analysis for mortality prediction

Multivariable modeling for all-cause mortality demonstrated that upright stress ESV, combined with age, diabetes, and cardiovascular disease status, was the best predictor of all-cause mortality with the lowest AIC. The best model for the supine

TABLE 5 Mortality hazard ratios by LVEF >50%, 35–50%, and <35%.

	vs. >50%	Upright		Supine	
		HR	p-value	HR	p-value
Stress LVEF			0.0005*		0.0002*
	<35%	3.00 (1.68–5.34)		3.24 (1.81–5.79)	
	35–50%	1.95 (1.18–3.25)		1.85 (1.12–3.08)	
Rest LVEF			<0.0001*		<0.0001*
	<35%	3.70 (2.16–6.34)		3.67 (2.05–6.58)	
	35–50%	1.42 (0.83–2.44)		2.32 (1.40–3.85)	

HR, hazard ratio; LVEF, left ventricular ejection fraction.

\*Significant p-values < 0.05.

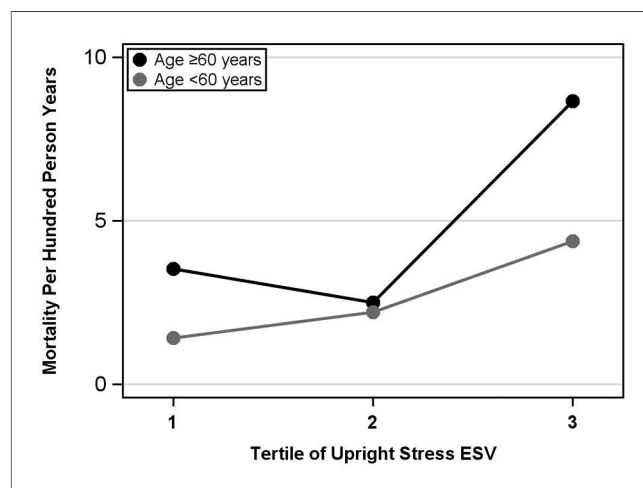


FIGURE 2

Upright stress ESV tertiles vs. mortality, ages <60 years and ages ≥60 years. Upright stress ESV is divided into tertiles, ordered from lowest to highest ESV, vs. mortality events per hundred person-years. The gray curve represents patients aged <60 and the black curve represents ages ≥60. The overall mortality rate was significantly higher in the third tertile compared with the second, but not significantly different between the first and second tertiles. ESV, end-systolic volume.

position included the same demographic variables in addition to supine resting ESV. The partial likelihood ratio test showed the equivalent predictive ability of these two best models. See [Figure 2](#) for a graphical representation of the mortality rate per 100 person-years by upright stress ESV tertile.

### 3.8. Indexed volumes sensitivity analysis

A sensitivity analysis was performed using volumetric indices corrected for body surface area for the ESV and EDV areas. The indices were included in the multivariable prediction models but did not provide additional predictive ability and were therefore removed from the final analyses.

## 4. Discussion

This study demonstrates that upright and supine D-SPECT data provide the equivalent predictive ability for identifying angiographic CAD and risk for all-cause mortality. In multivariable models that include commonly available demographic variables, the addition of left ventricular volume measurements provides a similar prediction of all-cause mortality, whether acquired in the supine or upright position.

This study helps address the question of the optimal imaging position for volumetric measurements on the D-SPECT camera. It has previously been suggested that volumetric measurements are best obtained in the supine position for adequate comparison with other cardiac imaging modalities (33). Nevertheless, a validation study comparing upright CZT volumes on the D-SPECT camera with cardiac magnetic resonance volumes showed a good correlation for LVEF, although upright CZT images underestimated supine ESV and EDV (31). This underestimation probably reflects reduced left ventricular filling in the upright position. The present study does not compare the accuracy of upright vs. supine measurements of LVEF with a reference standard such as cardiac magnetic resonance. It does suggest, however, that the prognostic values of upright and supine volumes are similar. It also shows that, while LVEF and EDV are statistically smaller in the upright position, the absolute differences are likely clinically insignificant (a 1% difference in LVEF).

Obese patients in the present study had a higher mortality rate than non-obese patients. It has been previously observed that obese patients have higher end-diastolic volumes than non-obese patients (34). In the present study, we also noted that end-diastolic volumes were statistically higher in the supine position compared to the upright position, but the change in end-diastolic volumes by imaging position was minimal. The observed differences in upright vs. supine end-diastolic volumes may be more closely related to left ventricular loading conditions than to body weight.

An important additional implication from this study is that ESV is a stronger predictor of all-cause mortality than LVEF, regardless of whether it is measured in the supine or upright position. A possible physiological explanation is that ESV is a proxy for systolic dysfunction and remodeling. Numerous previous studies have supported the strength of ESV as a predictor of events (17, 19,

35–39), although not all studies have demonstrated the strength of ESV over LVEF for prediction (40).

The final major finding of this study was that SSS is the strongest predictor of angiographic CAD, whether performed in the upright or supine position. This finding is in contrast to a previous, smaller sample that showed improved prediction in the supine position (6). This, however, does not detract from the value of imaging in multiple projections to avoid confounding attenuation artifacts with true perfusion defects.

There are some potential limitations to the present study. This was a retrospective review of patients at a single urban academic medical center. Our patients had a high mortality rate of nearly 20% over a median follow-up of 75 months. We suspect that this is due to the complex multimorbidity of our patient population and thus may not be easily generalizable. We measured all-cause mortality rather than cardiovascular death, which may capture unrelated mortality events. We did not correlate upright and supine volumetric measurements with another imaging modality, such as cardiac magnetic resonance, but other generally applied imaging modalities are not available for upright imaging. Finally, the administered radioactivity at the time of the present study was higher than the substantially lower doses used with the CZT camera in our current practice, but this is not expected to alter the present findings.

In conclusion, in the present study, angiographic CAD was best predicted by the combination of supine SSS and LVEF, although this supine model was not statistically superior to the next-best upright model. The study demonstrates that all-cause mortality was best predicted by ESV, in combination with age, DM status, and cardiovascular disease (CVD) status, with equivalent predictive ability in both the upright and supine positions. Finally, it shows that LVEF and EDV measurements are statistically different in the upright compared to the supine position, but their absolute differences are clinically insignificant.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

This study involving human participants was reviewed and approved by the University of Cincinnati Institutional Review Board. Written informed consent for participation was not required for this study in accordance with national legislation and institutional requirements.

## Author contributions

JW performed the study design, clinical data collection, and manuscript writing. AC performed the statistical analyses, prepared the tables, and designed the figures. MA and FW performed the SPECT variable data collection and organization.

MA and FW contributed equally to this manuscript. MG served as the principal investigator and performed the study design and manuscript writing. All authors contributed to the article and approved the submitted version.

## Funding

The study was supported in part by the John R. Strauss Fund for Research and Education in Cardiac Imaging.

## Acknowledgments

The authors would like to acknowledge that the opportunity for this research was made possible by the University of Cincinnati Medical Center Cardiac Stress Laboratory.

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