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ORIGINAL ARTICLE

A systemic congestive index (systemic pulse pressure to central venous pressure ratio) predicts adverse outcomes in patients undergoing valvular heart surgery

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Abstract

Background and Aims: Invasive hemodynamics may provide a more nuanced assessment of cardiac function and risk phenotyping in patients undergoing cardiac surgery. The systemic pulse pressure (SPP) to central venous pressure (CVP) ratio represents an integrated index of right and left ventricular function and thus may demonstrate an association with valvular heart surgery outcomes. This study hypothesized that a low SPP/CVP ratio would be associated with mortality in valvular surgery patients.

Methods: This retrospective cohort study examined adult valvular surgery patients with preoperative right heart catheterization from 2007 through 2016 at a single tertiary medical center (n = 215). Associations between the SPP/CVP ratio and mortality were investigated with univariate and multivariate analyses.

Results: Among 215 patients (age 69.7 ± 12.4 years; 55.8% male), 61 died (28.4%) over a median follow-up of 5.9 years. A SPP/CVP ratio <7.6 was associated with increased mortality (relative risk 1.70, 95% confidence interval [CI] 1.08–2.67, p = .019) and increased length of stay (11.56 ± 13.73 days vs. 7.93 ± 4.92 days, p = .016). It remained an independent predictor of mortality (adjusted odds ratio 3.99, 95% CI 1.47–11.45, p = .008) after adjusting for CVP, mean pulmonary artery pressure, aortic stenosis, tricuspid regurgitation, smoking status, diabetes mellitus, dialysis, and cross-clamp time.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; ROC, receiver operating characteristic; SPP, systemic pulse pressure; STS, Society of Thoracic Surgeons.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2022 The Authors. *Journal of Cardiac Surgery* published by Wiley Periodicals LLC. **Conclusions:** A low SPP/CVP ratio was associated with worse outcomes in patients undergoing valvular heart surgery. This metric has potential utility in preoperative risk stratification to guide patient selection, prognosis, and surgical outcomes.

KEYWORDS

heart failure, hemodynamic monitoring, perioperative mortality, pulmonary hypertension, valvular surgery, ventricular dysfunction

1 | INTRODUCTION

Proper risk stratification of patients undergoing valvular heart surgery is crucial in improving surgical outcomes. A robust risk score may adequately inform patient selection, guide patient-clinician shared decision making, and in specific instances enhance presurgical optimization to facilitate improved operative outcomes.¹ Many of the risk scores used in cardiac surgery have multivariable inputs heavily weighted on patient-specific factors such as the presence or absence of comorbid conditions, as well as procedural factors such as case urgency.² More recently there has been a growing recognition of the importance of physiological markers integrating the overall performance of left and right circulatory systems.²⁻⁴ However, there is a paucity of risk modeling frameworks integrating global cardiac functional assessment in risk status.

Cardiac valvular lesions often have pathophysiological consequences beyond the proximal location that may have deterministic import on postoperative outcomes. For example, severe mitral valve stenosis is associated with pulmonary hypertension that may negatively impact the right ventricle and incrementally increase the risks of surgical intervention.⁵ Systemic pulse pressure (SPP), calculated as systemic systolic pressure minus diastolic pressure, is a hemodynamic variable that reflects the contractile efficiency of the left ventricle. A low pulse pressure may be a proxy for low cardiac output or ventricular-arterial uncoupling.⁶ Similarly, central venous pressure (CVP) is a hemodynamic variable that reflects right ventricular preload.⁷ Accordingly, SPP indexed to CVP may represent an integrated index of the left and right ventricles. Leveraging this rationale of using an original index that considers the physiological integrity of right and left ventricular function, we hypothesized that a low SPP/CVP ratio would be associated with increased mortality among patients undergoing valvular heart surgery.

2 | MATERIALS AND METHODS

2.1 | Study design and population

This retrospective cohort study investigated adult valvular surgery patients at a single academic medical center from May 2007 to October 2016. All patients were prospectively enrolled in the Society of Thoracic Surgeons (STS) National Database, with queried variables collected as part of routine care. Aortic valve replacement, mitral valve replacement, and mitral valve repair surgeries were included. Concurrent coronary artery bypass grafting was not an exclusion criterion, however, the frequency of this concurrent procedure is reported within the study results. In accordance with the study objectives, patients were excluded if they did not undergo preoperative right heart catheterization with simultaneous systemic blood pressure measurement. Patients were also excluded if their preoperative echocardiographic parameters were unavailable. While the patient selection was limited to May 2007–October 2016, mortality was followed through May 2020, the time at which statistical analysis began.

The study protocol was approved by the Institutional Review Board with a waiver of written consent.

2.2 | Measurements and data handling

The primary endpoint was mortality. To reduce length-time bias, patients were followed for 10 years or until May 2020, whichever came first. For nondeceased patients, survival in May 2020 was assumed after verifying >95% adherence to at least one documented postoperative medical encounter. Postoperative length of stay was investigated as a secondary endpoint.

The independent variable of interest was the SPP/CVP ratio. CVP was obtained from invasive pressure transduction during right heart catheterization, and SPP was obtained simultaneously after validation by procedural staff. Cardiac preoperative right heart catheterization was performed as clinically indicated in this retrospective observational study. At the authors' institution, an estimated 11.6% of all valvular surgery patients undergo preoperative right heart catheterization.⁸

2.3 | Baseline characteristics

Independent variables also included age, sex, current smoker, hypertension diagnosis, diabetes diagnosis, preoperative end-stage renal disease on dialysis, preoperative atrial fibrillation, heart failure preoperative clinical diagnosis, preoperative ejection fraction (%), mean pulmonary artery pressure (mPAP), aortic stenosis, aortic insufficiency, tricuspid regurgitation, STS predicted risk of operative mortality, urgent/emergent case status, valve procedure, concurrent coronary artery bypass, and aortic cross-clamp time. Urgent and emergent cases were grouped together due to the low frequency (n = 3) of emergent cases. Aortic stenosis was categorized as present or absent per the STS registry. Aortic insufficiency and tricuspid regurgitation were initially graded as trivial/trace, mild, moderate, or severe. Given the low frequency of severe aortic insufficiency (n = 10) and severe tricuspid regurgitation (n = 2), the reported rates of aortic insufficiency and tricuspid regurgitation represent moderate to severe grading of valvular pathology. Otherwise, no modifications were made to the raw data in the registry.

2.4 | Sample size calculation

An a priori power analysis was conducted. To detect an absolute mortality difference of 10% among two SPP/CVP cohorts (mortality risks 25% and 15% respectively, effect size $\omega = 0.25$) with 80% power, a sample size of n > 124 was needed.⁹ The mortality risk estimates of 15%–25% for a presumed 5–10 year study duration were based on preliminary exploratory analyses by other investigators at the authors' institution. The final sample size obtained by applying the above inclusion and exclusion criteria to this observational study of consecutive cases acceptably exceeded this minimum value.

2.5 | Statistical analyses

Statistical analysis was performed with R version 4.1.2 (R Core Team).¹⁰ Continuous variables were summarized by mean ± standard deviation, while categorical variables were summarized by frequency (%). All hypothesis tests were two-sided, with significance defined by α = .05.

The SPP/CVP ratio was discretized according to a receiver operating characteristic (ROC) analysis applied to patient mortality.¹¹ Youden's index identified an optimal SPP/CVP ratio to use for discretization. The sensitivity and specificity of this SPP/CVP ratio were calculated.

Kaplan–Meier survival curves were generated for the SPP/CVP strata. Survival differences were assessed with the log-rank p value for the test statistic.^{12,13}

Baseline differences between SPP/CVP strata were investigated with univariate analyses. The Student's *t* test was applied to continuous variables while Pearson's chi-square test without continuity correction was applied to categorical variables. Associations between SPP/CVP ratio and the primary and secondary endpoints were also investigated with the above univariate tests.

A multivariate analysis was then conducted, modeling mortality against SPP/CVP and/or other relevant predictors. Preoperative and operative characteristics demonstrating marginal association (p < .10) with mortality on univariate analysis were considered potential predictors in the multiple logistic regression model. Variable selection was accomplished by backward stepwise model adjustment by Akaike information criterion. Adjusted odds ratios (AOR) and accompanying confidence intervals (CI) are reported for the CARDIAC SURGERY -WILEY-

TABLE 1 Demographic data

Characteristic	Mean ± SD or Frequency (%)	n
Preoperative		
Age (years)	69.73 ± 12.42	215
Sex (male)	120/215 (55.8%)	215
Current smoker	35/215 (16.3%)	215
Hypertension	168/215 (78.1%)	215
Diabetes	76/215 (35.3%)	215
Dialysis	14/215 (6.5%)	215
Atrial fibrillation	30/215 (14.0%)	215
Heart failure	173/215 (80.5%)	215
Ejection fraction (%)	54.72 ± 14.06	198
SPP	65.01 ± 24.08	207
CVP	8.18 ± 4.77	210
SPP/CVP ratio	13.07 ± 14.78	202
mPAP	31.25 ± 11.88	215
Aortic stenosis	145/215 (67.4%)	215
Aortic insufficiency	29/215 (13.5%)	215
Tricuspid regurgitation	27/215 (12.6%)	215
STS predicted mortality	0.07 ± 0.07	215
Operative		
Urgent/emergent	85/215 (39.5%)	215
AV replacement	153/215 (71.2%)	215
MV repair	27/215 (12.6%)	215
MV replacement	35/215 (16.3%)	215
Coronary artery bypass	58/215 (27.0%)	215
Cross-clamp time (mins)	77.92 ± 25.62	207
Outcomes		
Deceased	61/215 (28.4%)	215
Postoperative length of stay (days)	9.68 ± 10.05	215

Abbreviations: AV, aortic valve; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; MV, mitral valve; SD, standard deviation; SPP, systemic pulse pressure; STS, Society of Thoracic Surgeons.

independent predictor(s) of mortality. Model discrimination was assessed with the c-statistic. $^{\rm 14}$

3 | RESULTS

3.1 | Demographics

Among 215 patients (age 69.7 ± 12.4 years; 55.8% male), 61 died (28.4%) over a median follow-up of 5.9 years (Table 1). Only nine

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FIGURE 1 Receiver operating characteristic analysis, mortality versus SPP/CVP ratio. AUC, area under the curve

patients (4.2%) were missing a documented postoperative encounter. All nine of these patients were living at hospital discharge and were ultimately classified as survivors in May 2020 after cross-validating with the institutional Decedent Affairs department and the state and neighboring states' Departments of Health. Thus none of the 215 patients were excluded from the analysis. Preoperative right heart catheterization and echocardiography preceded surgery by median of 6 days and 14 days, respectively.

3.2 | Receiver operating characteristic and survival analyses

ROC analysis demonstrated that a SPP/CVP ratio < 7.6 predicted mortality with 59.6% sensitivity and 58.6% specificity (Figure 1). The SPP/CVP ratio < 7.6 did not achieve statistical significance on survival analysis over the study period (p = .064) (Figure 2).

3.3 Univariate analyses comparing SPP/CVP strata

Compared to those with SPP/CVP ratio ≥ 7.6, an SPP/CVP ratio < 7.6 was associated with younger age, male sex, decreased incidence of hypertension, lower ejection fraction, greater mPAP, decreased incidence of aortic stenosis, decreased incidence of aortic insufficiency, and decreased incidence of aortic valve correction. Of note, SPP/CVP cohorts did not differ in their incidence of tricuspid regurgitation or STS predicted risk of operative mortality.



FIGURE 2 Survival analysis by SPP/CVP ratio. CVP, central venous pressure; SPP, systemic pulse pressure

A SPP/CVP ratio < 7.6 was associated with increased mortality (34/94 vs. 23/108, p = .019), and increased length of stay (11.56 ± 13.73 days vs. 7.93 ± 4.92 days, p = .016) (Table 2).

3.4 | Multivariate analysis modeling mortality against predictors

Mortality was associated with SPP/CVP ratio < 7.6 (unadjusted relative risk = 1.70, 95% CI [1.08–2.67]) along with smoking status, diabetes mellitus, dialysis, urgent/emergent case status, coronary artery bypass grafting, and cross-clamp time. SPP demonstrated no association (63.69 ± 22.76 vs. 65.53 ± 24.64 , p = .609), CVP demonstrated marginal association (9.24 ± 4.96 vs. 7.76 ± 4.64 , p = .051), and mPAP demonstrated a significant association with mortality (34.85 ± 12.64 vs. 29.82 ± 11.28 , p = .008). Aortic insufficiency demonstrated no association (unadjusted relative risk = 0.83, 95% CI [0.42–1.65]), aortic stenosis demonstrated marginal association (unadjusted relative risk = 1.62, 95% CI [0.96–2.74]), and tricuspid regurgitation demonstrated a significant association with mortality (unadjusted relative risk = 1.89, 95% CI [1.19–2.99]). Mortality was associated with an increased STS predicted risk of operative mortality (0.10 ± 0.09 vs. 0.05 ± 0.06, p < .001) (Table 3).

The above characteristics demonstrating at least a marginal (p < .10) association with mortality were considered predictors in a multiple logistic regression model with subsequent variable selection accomplished by backwards stepwise model adjustment by Akaike information criterion. The SPP/CVP ratio < 7.6 was independently predictive of mortality (AOR = 3.99, 95% CI [1.47–11.45], p = .008) after adjusting for CVP (AOR = 0.87, 95% CI [0.76–0.99], p = .043), mPAP (AOR = 1.04, 95% CI [1.00–1.09], p = .071), aortic stenosis (AOR = 6.83, 95% CI [2.56–20.86], p < .001), and tricuspid regurgitation (AOR = 5.43, 95% CI [1.88–16.32],

TABLE 2 Univariate analyses comparing SPP/CVP strata

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Characteristic	SPP/CVP ≥ 7.6 n = 108	SPP/CVP < 7.6 n = 94	n	p value
Preoperative				
Age (years)	73.70 ± 9.86	66.62 ± 12.86	202	<.001
Sex (male)	52/108 (48.1%)	61/94 (64.9%)	202	.017
Current smoker	14/108 (13.0%)	18/94 (19.1%)	202	.230
Hypertension	93/108 (86.1%)	68/94 (72.3%)	202	.015
Diabetes	34/108 (31.5%)	37/94 (39.4%)	202	.242
Dialysis	5/108 (4.6%)	7/94 (7.4%)	202	.398
Atrial fibrillation	14/108 (13.0%)	15/94 (16.0%)	202	.545
Heart failure	83/108 (76.9%)	80/94 (85.1%)	202	.138
Ejection fraction (%)	57.62 ± 12.03	52.62 ± 14.96	185	.014
mPAP	26.00 ± 10.45	36.89 ± 10.81	202	<.001
Aortic stenosis	87/108 (80.6%)	52/94 (55.3%)	202	<.001
Aortic insufficiency	20/108 (18.5%)	8/94 (8.5%)	202	.040
Tricuspid regurgitation	10/108 (9.3%)	17/94 (18.1%)	202	.066
STS predicted mortality	0.06 ± 0.05	0.07 ± 0.08	202	.066
Operative				
Urgent/emergent	39/108 (36.1%)	40/94 (42.6%)	202	.349
AV replacement	90/108 (83.3%)	56/94 (59.6%)	202	<.001
MV repair	8/108 (7.4%)	19/94 (20.2%)	202	<.001
MV replacement	10/108 (9.3%)	19/94 (20.2%)	202	<.001
Coronary artery bypass	34/108 (31.5%)	22/94 (23.4%)	202	.201
Cross-clamp time (mins)	77.04 ± 23.17	79.49 ± 29.63	195	.528
Outcomes				
Deceased	23/108 (21.3%)	34/94 (36.2%)	202	.019
Postoperative length of stay (days)	7.93 ± 4.92	11.56 ± 13.73	202	.016

Abbreviations: AV, aortic valve; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; MV, mitral valve; SPP, systemic pulse pressure; STS, Society of Thoracic Surgeons.

p = .002), along with smoking status, diabetes mellitus, dialysis, and aortic cross-clamp time in hours (Table 4). Adjustments for SPP and aortic insufficiency were not made due to the insignificant associations demonstrated by the preceding univariate analyses. The model demonstrated good discrimination (c-statistic = 0.803).

4 | DISCUSSION

The present study demonstrated that a low SPP/CVP ratio is independently predictive of mortality after adjusting for covariates. However, the SPP/CVP ratio alone showed only a marginal association with mortality on ROC and survival analysis. In conjunction, these findings suggest that the SPP/CVP index is unlikely to serve as a standalone early marker of mortality, but rather aid in risk stratification when considered alongside other established risk factors. It is worth noting that the STS predicted risk of operative mortality demonstrated a strong univariate association with mortality over the entire study period. Despite this, the multivariate model containing just SPP/CVP ratio and eight additional routine predictors performed outstandingly well (c-statistic = 0.803).

The significance of aortic stenosis, tricuspid regurgitation, and preoperative end-stage renal disease cannot be understated. The adjusted odds with which these characteristics predicted mortality exceeded that of the SPP/CVP ratio and of the other model predictors. Additionally, each of these comorbidities has an associated hemodynamic profile which will be discussed in more details. Regardless, an SPP/CVP ratio < 7.6 remained independently predictive of mortality even after adjusting for valve lesions and renal dysfunction.

The cardiovascular system is intrinsically pulsatile in nature and is characterized by both ventricular-arterial and ventricular-ventricular

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Characteristic	Alive <i>n</i> = 154	Deceased n = 61	n	p value
Preoperative				
Age (years)	69.10 ± 12.45	71.31 ± 12.30	215	.238
Sex (male)	84/154 (54.5%)	36/61 (59.0%)	215	.552
Current smoker	31/154 (20.1%)	4/61 (6.6%)	215	.015
Hypertension	117/154 (76.0%)	51/61 (83.6%)	215	.222
Diabetes	44/154 (28.6%)	32/61 (52.5%)	215	<.001
Dialysis	6/154 (3.9%)	8/61 (13.1%)	215	.014
Atrial fibrillation	22/154 (14.3%)	8/61 (13.1%)	215	.823
Heart failure	123/154 (79.9%)	50/61 (82.0%)	215	.727
Ejection fraction (%)	55.21 ± 13.73	53.43 ± 14.98	198	.448
SPP	65.53 ± 24.64	63.69 ± 22.76	207	.609
CVP	7.76 ± 4.64	9.24 ± 4.96	210	.051
SPP/CVP ratio < 7.6	60/145 (41.4%)	34/57 (59.6%)	202	.019
mPAP	29.82 ± 11.28	34.85 ± 12.64	215	.008
Aortic stenosis	98/154 (63.6%)	47/61 (77.0%)	215	.058
Aortic insufficiency	22/154 (14.3%)	7/61 (11.5%)	215	.587
Tricuspid regurgitation	14/154 (9.1%)	13/61 (21.3%)	215	.015
STS predicted mortality	0.05 ± 0.06	0.10 ± 0.09	215	<.001
Operative				
Urgent/emergent	53/154 (34.4%)	32/61 (52.5%)	215	.015
AV replacement	106/154 (68.8%)	47/61 (77.0%)	215	.104
MV repair	24/154 (15.6%)	3/61 (4.9%)	215	.104
MV replacement	24/154 (15.6%)	11/61 (18.0%)	215	.104
Coronary artery bypass	35/154 (22.7%)	23/61 (37.7%)	215	.026
Cross-clamp time (mins)	75.39 ± 25.17	84.75 ± 25.78	207	.022

TABLE 3 Univariate analysis identifying potential predictors (*p* < .10) for model selection

Abbreviations: AV, aortic valve; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; MV, mitral valve; SPP, systemic pulse pressure; STS, Society of Thoracic Surgeons.

interactions.¹⁵⁻¹⁷ As shown in previous studies, ventricular-arterial interactions have been associated with adverse outcomes in patients undergoing cardiac surgery.¹⁸ SPP is influenced by ventricular-arterial interactions and encompasses the combined effects of left ventricular contractile properties and arterial characteristics such as input impedance.^{19,20} Thus, the SPP serves as a proxy for ventriculararterial interactions and can be utilized as a prognostic tool for patients undergoing valvular heart surgery.²¹ Unfavorable ventricular-ventricular interactions as reflected by a high mean arterial pressure to mPAP ratio have also been associated with increased morbidity and mortality among patients undergoing valvular heart surgery.⁸ Specifically, right ventricular function has been shown to be an important prognostic indicator for patients with various cardiac conditions including those undergoing surgery.^{22,23} CVP, a proxy for right ventricular function, reflects the right ventricular preload and by extension marks the right ventricular

contractile response to afterload imposed on it. Thus a rising CVP signals a compensatory adaptation to right ventricular workload.

These physiologic principles are of the utmost importance in valvular surgery patients, as patients with severe left-sided valvular cardiac lesions not only have impaired left ventricular mechanical efficiency as a consequence of these pathologies, but often develop right ventricular dysfunction via mechanisms related to increased passive filling pressures causing pulmonary vascular remodeling. It is estimated that up to 100% of patients with severe mitral valve disease and 65% of patients with severe aortic valve disease have elevated pulmonary artery pressure.^{24–26} In line with this pathophysiologic rationale, patients with a low SPP/CVP ratio had lower left ventricular ejection fraction, elevated mPAP, and increased CVP profiles reflecting putative left and right heart interactions and pulmonary hypertension as a potential modulator. Patients with a low SPP/CVP ratio had echocardiographic profiles that were only partially

TABLE 4Multivariate analysismodeling mortality against predictors

Characteristic	β	Standard error	Adjusted odds ratio [95% CI]	p value
Preoperative				
Current smoker	-0.91	0.64	0.40 [0.10-1.27]	.152
Diabetes	1.04	0.41	2.83 [1.28-6.36]	.010
Dialysis	1.86	0.77	6.41 [1.47-31.59]	.016
CVP	-0.14	0.07	0.87 [0.76-0.99]	.043
SPP/CVP ratio < 7.6	1.38	0.52	3.99 [1.47-11.45]	.008
mPAP	0.04	0.02	1.04 [1.00-1.09]	.071
Aortic stenosis	1.92	0.53	6.83 [2.56-20.86]	<.001
Tricuspid regurgitation	1.69	0.55	5.43 [1.88-16.32]	.002
Operative				
Cross-clamp time (h)	1.14	0.42	3.12 [1.36-7.26]	.007

Abbreviations: CI, confidence interval; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; SPP, systemic pulse pressure.

concordant with what was expected. Those with a low SPP/CVP ratio did have a significantly lower incidence of aortic insufficiency (8.5% vs. 18.5%, p = .040) and a nonsignificant trend towards greater incidence of tricuspid regurgitation (18.1% vs. 9.3%, p = .066). In the case of aortic stenosis, the predominant profile was that of a lower SPP/CVP ratio.

This study is limited both by its novelty and its design. Given that the SPP/CVP ratio has not been studied previously, it was discretized following ROC analysis. This methodology was thought to yield a more objective and replicable SPP/CVP ratio than discretization by quartile or percentile as was done in a preliminary investigation. However, the authors recognize that different study samples may identify different SPP/CVP thresholds for predicting mortality and/or other adverse events.²⁷ The accuracy of this threshold alone was fair, at best. Estimating early mortality (within 30 days or 1 year) will require investigation of a multicenter cohort, given the favorable early survival rates demonstrated by this analysis. It is possible that the effect demonstrated by the SPP/CVP ratio may be attributable to patient cardiopulmonary disease burden, rather than represent a unique modifiable risk factor. However, elective surgical patients (60.5% in the present sample) can presumably undergo medical optimization, which may improve their hemodynamic indices and surgical risk profiles. Only patients with complete hemodynamics from preoperative right heart catheterization were included in this study. Thus, there exists a potential for selection bias given that the right heart catheterization may have been obtained in patients who were relatively sicker requiring invasive hemodynamics. Finally, the present results are contingent on the validity of the study sample's hemodynamic measurements. Reliability could have been improved with dynamic invasive arterial pressure transduction, however, this was not clinically indicated during routine diagnostic testing.^{28,29} It is the authors' hope that future prospective studies can test the replicability of these results. Investigating a

multi-center cohort will also allow for adequately powered investigation of more homogenous subgroups, either by specific procedure (aortic valve replacement vs. mitral valve repair/ replacement, with or without coronary artery bypass), or by valvular pathology.

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CONCLUSION In summary, the SPP/CVP ratio is a readily calculable hemodynamic index that reflects both ventricular-arterial and ventricular-ventricular coupling mechanisms. Mortality was predicted by an SPP/CVP ratio less than 7.6 with higher odds than those of the SPP or CVP in isolation, as well as that of mPAP. Valvular pathology remained an important independent predictor of mortality. Further, an SPP/CVP was also associated with increased length of stay which might have a direct bearing on increased utilization of health care resources. Assessment of this hemodynamic index may help inform the patient selection and preoperative optimization in the valvular surgery population. Future studies are needed to validate the prognostic utility of the SPP/CVP ratio in cardiac surgical patients and investigate whether optimization of the index before surgery would be associated with favorable outcomes.

AUTHOR CONTRIBUTIONS

Ziyad O. Knio: Methodology, software, validation, formal analysis, writing-original draft. Frances L. Morales: Investigation, writingreview & editing, visualization. Kajal P. Shah: Data curation, visualization. Olivia K. Ondigi: Data curation, investigation. Christian E. Selinski: Data curation, investigation. Cherisse M. Baldeo: Conceptualization, investigation. David X. Zhuo: Conceptualization, data curation. Kenneth C. Bilchick: Methodology, software, formal analysis. Nishaki K. Mehta: Conceptualization, investigation. Younghoon Kwon: Conceptualization, investigation. Khadijah Breathett: Conceptualization, investigation. Robert H. Thiele: Resources, supervision. Matthew C. Hulse: Resources, supervision. Sula Mazimba: Writing-review & editing, supervision, project administration.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

- Wessler BS, Lundquist CM, Koethe B, et al. Clinical prediction models for valvular heart disease. J Am Heart Assoc. 2019;8(20): e011972. doi:10.1161/JAHA.119.011972
- Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. *Circulation*. 2005;112(2):224-231. doi:10.1161/CIRCULATIONAHA. 104.515049
- Goepfert MS, Richter HP, Zu Eulenburg C, et al. Individually optimized hemodynamic therapy reduces complications and length of stay in the intensive care unit: a prospective, randomized controlled trial. *Anesthesiology*. 2013;119(4):824-836. doi:10.1097/ ALN.0b013e31829bd770
- Lopes MR, Oliveira MA, Pereira VOS, Lemos IPB, Auler JOC, Michard F. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care*. 2007;11(5):R100. doi:10.1186/cc6117
- Hugenholtz PG, Ryan TJ, Stein SW, Abelmann WH. The spectrum of pure mitral stenosis. hemodynamic studies in relation to clinical disability. *Am J Cardiol*. 1962;10:773-784. doi:10.1016/0002-9149(62)90171-6
- Petrie CJ, Damman K, Jhund PS, Hillege HL, Van Veldhuisen DJ, Voors AA. Low pulse pressure as a poor-man's indicator of a low cardiac index in patients with severe cardiac dysfunction. *J Cardiovasc Med (Hagerstown)*. 2014;15(4):315-321. doi:10.2459/ JCM.0b013e328365b51e
- Mercat A, Diehl JL, Meyer G, Teboul JL, Sors H. Hemodynamic effects of fluid loading in acute massive pulmonary embolism. *Crit Care Med.* 1999;27(3):540-544. doi:10.1097/00003246-199903000-00032
- Schubert SA, Mehaffey JH, Booth A, et al. Pulmonary-Systemic pressure ratio correlates with morbidity in cardiac valve surgery. *J Cardiothorac Vasc Anesth*. 2019;33(3):677-682. doi:10.1053/j.jvca. 2018.08.190
- Chameply S. pwr: Basic Functions for Power Analysis. R package version 1.3-0.2020. https://CRAN.R-project.org/package=pwr
- R Core Team. R: A Language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2021;89:419-427. https://www.R-project.org/
- Robin X, Turck N, Hainard A, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics. 2011;12:77. doi:10.1186/1471-2105-12-77
- 12. Therneau TM, Grambsch PM. Modeling survival data: extending the cox model. Springer; 2000.
- Therneau T. A package for survival analysis in R. R package version 3.2-7. 2020. https://CRAN.R-project.org/package=survival
- 14. Harrell FE Jr. rms: Regression modeling strategies. R package version 6.0-0. 2020. https://CRAN.R-project.org/package=rms
- Ky B, French B, May Khan A, et al. Ventricular-arterial coupling, remodeling, and prognosis in chronic heart failure. J Am Coll Cardiol. 2013;62(13):1165-1172. doi:10.1016/j.jacc.2013.03.085

- Li JKJ, Atlas G. Left Ventricle-Arterial system interaction in heart failure. *Clin Med Insights Cardiol.* 2015;9(suppl 1):93-99. doi:10. 4137/CMC.S18742
- Weber KT, Janicki JS, Shroff S, Fishman AP. Contractile mechanics and interaction of the right and left ventricles. *Am J Cardiol.* 1981;47(3):686-695. doi:10.1016/0002-9149(81)90556-7
- Wang X, Long Y, He H, et al. Left ventricular-arterial coupling is associated with prolonged mechanical ventilation in severe post-cardiac surgery patients: an observational study. BMC Anesthesiol. 2018;18(1):184. doi:10.1186/s12871-018-0649-7
- Laskey WK, Wu J, Schulte PJ, et al. Association of arterial pulse pressure with Long-Term clinical outcomes in patients with heart failure. JACC Heart Fail. 2016;4(1):42-49. doi:10.1016/j.jchf.2015. 09.012
- Stergiopulos N, Westerhof N. Determinants of pulse pressure. Hypertension. 1998;32(3):556-559. doi:10.1161/01.hyp.32.3.556
- Monge García MI, Jian Z, Hatib F, Settels JJ, Cecconi M, Pinsky MR. Dynamic arterial elastance as a ventriculo-arterial coupling index: an experimental animal study. *Front Physiol.* 2020;11:284. doi:10.3389/ fphys.2020.00284
- 22. Towheed A, Sabbagh E, Gupta R, et al. Right ventricular dysfunction and short-term outcomes following left-sided valvular surgery: an echocardiographic study. J Am Heart Assoc. 2021;10(4):e016283. doi:10.1161/JAHA.120.016283
- Haddad F, Denault AY, Couture P, et al. Right ventricular myocardial performance index predicts perioperative mortality or circulatory failure in high-risk valvular surgery. J Am Soc Echocardiogr. 2007;20(9):1065-1072. doi:10.1016/j.echo.2007.02.017
- Badesch DB, Champion HC, Gomez Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. J Am Coll Cardiol. 2009;54(suppl 1):S55-S66. doi:10.1016/j.jacc.2009.04.011
- Oudiz RJ. Pulmonary hypertension associated with left-sided heart disease. Clin Chest Med. 2007;28(1):233-241. x doi:10.1016/j.ccm. 2006.12.001
- Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2012;33(19): 2451-2496. doi:10.1093/eurheartj/ehs109
- Maslove DM, Podchiyska T, Lowe HJ. Discretization of continuous features in clinical datasets. J Am Med Inform Assoc. 2013;20(3): 544-553. doi:10.1136/amiajnl-2012-000929
- Schroeder B, Mark J, Barbeito A. Chapter 36: cardiovascular monitoring. *Miller's Anesthesia*. 9th ed. Elsevier; 2020:1145-1193.
- Mark JB. Atlas of Cardiovascular Monitoring. Churchill Livingstone; 1998.

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