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Preexisting right ventricular systolic dysfunction in high-risk patients undergoing non-emergent open abdominal surgery: A retrospective cohort study

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ABSTRACT

Background: The prognostic value of right ventricular systolic dysfunction in high-risk patients undergoing non-emergent open abdominal surgery is unknown. Here, we aim to evaluate whether presence of preexisting right ventricular systolic dysfunction in this surgical cohort is independently associated with higher incidence of postoperative major adverse cardiac events and all-cause in-hospital mortality.

Methods: This is a single-centered retrospective study. Patients identified as American Society Anesthesiology Classification III and IV who had a preoperative echocardiogram within 1 year of undergoing non-emergent open abdominal surgery between January 2010 and May 2017 were included in the study. Incidence of postoperative major cardiac adverse events and all-cause in-hospital mortality were collected. Multivariable logistic regression was performed in a step-wise manner to identify independent association between preexisting right ventricular systolic dysfunction with outcomes of interest.

Results: Preexisting right ventricular systolic dysfunction was not associated with postoperative major adverse cardiac events ($P = 0.26$). However, there was a strong association between preexisting right ventricular systolic dysfunction and all-cause in-hospital mortality ($P = 0.00094$). After multivariate analysis, preexisting right ventricular systolic dysfunction continued to be an independent risk factor for all-cause in-hospital mortality with an odds ratio of 18.9 (95% CI: 1.8-201.7; $P = 0.015$).

Conclusion: In this retrospective study of high-risk patients undergoing non-emergent open abdominal surgery, preexisting right ventricular systolic dysfunction was found to have a strong association with all-cause in-hospital mortality.

Keywords: Major adverse cardiac events, mortality, open abdominal surgery, preexisting right ventricular systolic dysfunction

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INTRODUCTION

Major adverse cardiac events (MACE) following non-cardiac surgery have significant implications for morbidity and mortality.^[1-3] Although various definitions exist for MACE, it often includes non-fatal cardiac arrest, myocardial

infarction, development of congestive heart failure, cerebrovascular event such as stroke, and cardiovascular mortality.^[4-6] The revised cardiac risk index (RCRI) is a commonly used tool to predict perioperative cardiac

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events in patients undergoing non-cardiac surgery.^[7] In addition, the RCRI has also been shown to have prognostic value for morbidity and mortality in various non-cardiac surgery.^[8] While ischemic heart disease and congestive heart failure are two cardiovascular diseases included in RCRI as clinical risk factors, the associated left or right ventricular dysfunction is not part of the risk indices.^[9]

Currently, it is still controversial whether left ventricular (LV) dysfunction, systolic or diastolic, poses as an independent risk factor for perioperative morbidity and mortality in patients undergoing non-cardiac surgery.^[10-14] Moreover, knowledge about the predictive value of right ventricular (RV) dysfunction in non-cardiac surgical cohort is largely unknown. Recently, we published the finding that among high-risk patients undergoing major vascular surgery, preexisting RV systolic dysfunction was more predictive of postoperative MACE than LV systolic dysfunction. Indeed, our group found that while reduced left ventricular ejection fraction (LVEF) was not an independent risk factor for MACE, presence of preexisting RV systolic dysfunction by itself was associated with a six-fold increase in incidence of post-operative MACE.^[15]

Building on other authors' previous findings in which the RCRI score was shown to have predictive value for morbidity and mortality in patients undergoing major abdominal procedures,^[16] and in which LVEF did not have independent association with overall outcomes,^[17] we aimed to determine whether the effect of preexisting RV systolic dysfunction on postoperative cardiac morbidity and overall mortality would be similar in an open abdominal surgery cohort to what we observed in our previous study in vascular patients. Our hypothesis was that preexisting RV systolic dysfunction would be more prognostic than LV systolic dysfunction for postoperative major adverse cardiac events. As a secondary outcome, we also hypothesized that preexisting RV systolic dysfunction would be associated with higher all-cause in-hospital mortality in major abdominal surgery.

METHODS

This study was approved by the Institutional Review Board at the University of California Irvine Medical Center (UCI IRB HS# 2017-4099).

Data collection

We performed a retrospective single-centered chart review of all patients undergoing open abdominal surgery between 2010 and 2017 [Figure 1]. Inclusion criteria for the search were any non-emergent open abdominal procedures

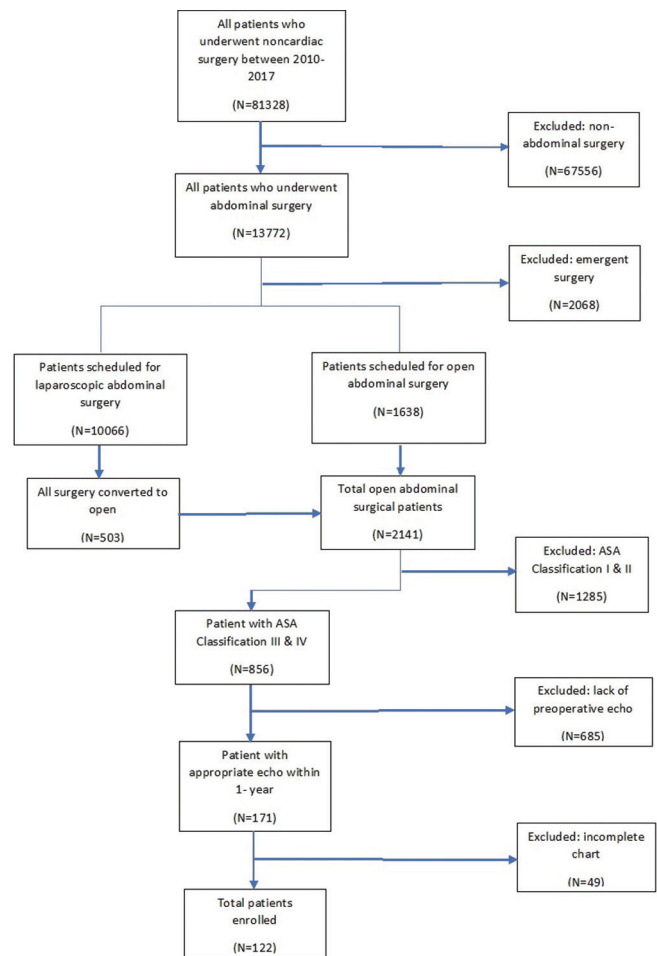


Figure 1: Inclusion and Exclusion Diagram

including gastrointestinal procedure (colorectal, gastric, small bowel, hepatic, and pancreatic involvement), urological procedure including nephrectomy or cystectomy, renal transplant, general exploratory laparotomy with or without lysis of adhesion, open removal of retroperitoneal mass, gynecological procedures involving open hysterectomy with or without oophorectomy, open gynecologic-oncological tumor debulking, and all other open abdominal surgeries that involved a combination of the procedures mentioned above. Procedures that involved major vascular surgery such as involvement of the abdominal aorta or inferior vena cava were not included in this cohort. The study only included adult patients between the age of 18 and 89. We defined high-risk patients as those who were identified as American Society of Anesthesiologist (ASA) Physical Status Classification of III or IV. Finally, we included only patients with a preoperative echocardiogram performed within one-year of the indexed surgery, and for which the study report included evaluation and determination of the RV function. In patients who had multiple echo studies within a year of the indexed surgery, we selected the study that was closest to the indexed surgery for final review.

To collect patients' demographic and perioperative data, we performed manual chart review using the hospital's electronic record. While intraoperative variables were collected from Surgical Information Systems (Surgical Information Systems Corp, Alpharetta GA), demographic and postoperative variables were obtained from Quest (Allscripts Corporation, Alpharetta GA). For those who met the inclusion criteria, the following pre-operative variables were collected: age, gender, body mass index (BMI), preoperative hemoglobin and creatinine level, presence or absence of history of congestive heart failure (CHF), coronary artery disease (CAD), hypertension (HTN), cerebrovascular accident (CVA), diabetes (DM), chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), and pulmonary hypertension. Since abdominal procedures can often be performed as part of a cancer treatment plan, presence of active cancer requiring the indexed abdominal surgery was also collected. Finally, an RCRI score was calculated and collected based on presence of its six clinical predictors.^[18]

For intraoperative variables, length of surgery, need for intraoperative transfusion of allogeneic blood products, intraoperative total fluid balance, intraoperative hypotension, and intraoperative infusion of inotropic or vasopressor agents were collected. Furthermore, post-operative variables including post-operative development of respiratory complications and acute kidney injury, as well as, post-operative infections and need for subsequent surgeries during the same admission were also collected so they could be evaluated as confounding factors. Finally, diagnosis of sepsis made anytime during the entire hospital admission was also collected and evaluated as a confounder, as presence of sepsis continues to be an important risk factor for morbidity and mortality in surgical patients.^[19]

For assessment of intraoperative hypotension, both non-invasive and invasive blood pressure measurements were extracted from the Surgical Information System (SIS). Data points without both a systolic and diastolic value were excluded. In addition, any systolic values outside of 20-300 mmHg and diastolic values outside of 5-200 mmHg were excluded as they were considered to be non-physiological.^[20] Blood pressure data from the noninvasive and invasive monitor were then combined in the following manner: if a systolic or diastolic value had another observation of the same type (systolic or diastolic) regardless of the source (noninvasive or invasive) and was within one minute of each other, the two values would be replaced with the average of the two. Mean arterial pressure (MAP) was calculated for each systolic/diastolic pair according to the following

equation: $1/3 \times \text{systolic blood pressure} + 2/3 \times \text{diastolic blood pressure}$. Intraoperative hypotension was defined using MAP <60 mmHg as the threshold. This threshold was chosen because previous studies have been able to show an increased risk for myocardial injury and mortality when MAP is less than an absolute threshold of 60 for various duration during general surgery.^[20] An episode of intraoperative hypotension was derived by calculating area under the threshold (AUT). AUT was calculated in the same manner as previously described by Vernooij *et al.*^[21] Finally, total AUT was obtained by adding all AUTs for each surgical encounter. All blood pressure data processing described was performed via Python version 2.7 using SciPy and NumPy library of packages (Python Software Foundation, Wilmington, DE).

Post-operative MACE was defined broadly as composite events including non-fatal cardiac arrest, myocardial infarction, development of congestive heart failure, cerebrovascular accident (Stroke), and cardiovascular mortality defined as death attributable to any or a combination of the adverse cardiovascular events just described.^[4-6] Post-operative respiratory complication was defined as prolonged intubation for more than 24 hours or need for re-intubation or tracheostomy. Post-operative acute kidney injury was defined as patients with a post-operative rise of creatinine greater than 60% from the baseline.^[22] Post-operative need for subsequent surgeries included all procedures that required anesthesia care. Post-operative infection was defined as a composite event including wound or surgical site infection, urinary tract infection, pulmonary infection, and systemic infection. Finally, diagnosis of sepsis was made according to guidelines set by the International Sepsis Definitions Conference.^[23]

The pre-operative echocardiogram obtained within one year of the index surgery was used to identify patients with RV systolic dysfunction. All of the echo studies were originally performed by the cardiology service at the study institution. The majority of the echo studies were performed via transthoracic echocardiogram (96%). All of the echo images were interpreted by the cardiologist from the study institution with the final results reported and stored in the institution's cardiovascular imaging database (Syngo Dynamics – Siemens Healthcare, Tarrytown, NY). All study reports were reviewed and the following collected: LVEF, right ventricular systolic pressure (RVSP), any valvular pathology categorized as severe, presence of LV diastolic dysfunction, and RV function. RV function was reported as a binary variable (normal versus abnormal). RV function collected from the official report was

determined based on visual estimation by the cardiologists. Visual estimation of the RV function was determined based on multiple acoustic windows including apical 4-chamber (lateral wall of the RV and RV apex), parasternal short-axis (anterior, lateral, and inferior wall of the RV), parasternal RV inflow (anterior and inferior wall of the RV), and subcostal 4-chamber (inferior wall of the RV). For descriptive purpose, an independent cardiologist was asked to grade RV systolic dysfunction as mild, moderate, or severe.

Statistical analysis

All statistical analysis was performed using SPSS for windows version 24 (SPSS Inc, Chicago, IL). The cohort was divided into 2 groups: those with and without RV systolic dysfunction. For comparative analysis, Fisher's exact test was used for dichotomous variables while Student *t*-test or Mann-Whitney U test were used for continuous variables with normal and non-normal distribution respectively. For test of normality, Shapiro-Wilk test was employed. Dichotomous variables are reported as counts and percentages while continuous variables are described as either mean and standard deviation for normal distribution or median with interquartile range for non-normal distribution. Of note, a subgroup analysis of patients with different degree of RV systolic dysfunction was not performed due to its small sample size.

Logistic regression analysis was performed to estimate odds ratio (OR) and 95% confidence interval (CI) for effect of RV systolic dysfunction on binary outcomes. The selection of variables to include in the univariable logistic model was based on both group differences and *a priori* predictors. Variables that were individually associated with outcome of interest with *P* value <0.1 in univariable analysis were further included into multivariable analysis in a step-wise manner. Since RV systolic dysfunction, CHF, and RCRI are highly correlated with each other and are expected to exhibit multicollinearity, they were not included in the same regression models during the step-wise multivariable analysis. For goodness-of-fit of the regression model, Hosmer and Lemeshow test was employed. For all tests, a *P* value <0.05 was considered statistically significant.

RESULTS

A total of 122 patients met final inclusion criteria and were included for data analysis [Figure 1]. 5.7% (N = 7) of the patients in this cohort had preexisting RV systolic dysfunction evident on pre-operative echocardiogram at the time of surgery. A comparison of demographic data using either Fisher's exact test or Mann-Whitney U

test in patients with and without RV systolic dysfunction showed that there was no difference in gender, age, and BMI between the groups [Table 1]. For other pre-operative covariates, a higher percentage of patients with RV systolic dysfunction had a history of CAD and CHF (*P* = 0.0098 and *P* = 0.00052 respectively). In addition, a higher percentage of patients with RV systolic dysfunction had an RCRI score >3 (*P* = 0.00072).

For the remaining pre-operative covariates such as history of COPD, OSA, hypertension, pulmonary hypertension, and preoperative hemoglobin level, no differences were found between the groups [Table 1]. Similarly, there were no statistical differences between the groups when evaluating other echo parameters such as diastolic dysfunction, LVEF, and right ventricular systolic pressure (RVSP). In regards to valvular pathology, only two patients had severe valvular pathology (mitral regurgitation and aortic stenosis). Both patients had normal RV function.

For intraoperative covariates, all patients underwent general anesthesia with or without epidural catheter. A higher proportion of patients with RV systolic dysfunction received inotropic or vasopressor infusion during surgery compare to those without RV systolic dysfunction (*P* = 0.014). There was no difference in area under the threshold (AUT) for MAP <60 mmHg in the analysis of intraoperative

Table 1: Baseline demographic and comorbidity data between groups

	Normal Right ventricular function (n=115)	Right Systolic ventricular dysfunction (n=7)	<i>P</i>
Male	44 (51)	56 (4)	0.70
Age	65 [55, 74]	56 [45, 68]	0.13
BMI	25.4 [22.7, 30.4]	22.2 [20.4, 30.3]	0.23
CAD	22 (25)	71 (5)	0.0098
CHF	10 (12)	71 (5)	0.00052
COPD	13 (15)	29 (2)	0.25
OSA	4 (4)	14 (1)	0.26
Pulmonary HTN	15 (17)	17 (1)	1.00
HTN	71 (81)	43 (3)	0.20
Diastolic dysfunction	69 (59)	43 (3)	1.00
EF	63 [57, 67]	62 [45, 71]	0.66
EF <30%	2 (2)	14 (1)	0.16
RVSP	32.7 [27.2, 44.3]	31.3 [23.4, 64.2]	0.84
Preop Hgb	10.8 [9.6, 12.2]	11.2 [8.0, 11.9]	0.70
Cancer	50 (58)	43 (3)	1.00
RCRI >3	6 (7)	57 (4)	0.00072
Smoking	47 (43)	14 (1)	0.42

BMI: Body mass index, CAD: Coronary artery disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, OSA: Obstructive sleep apnea, Pulmonary HTN: Pulmonary hypertension, HTN: Hypertension, EF: Ejection fraction, RVSP: Right ventricular systolic pressure, Preop Hgb: Preoperative hemoglobin, RCRI: Revised cardiac risk index. All categorical variables are reported as % (n). All continuous variables exhibit non-normal distribution; as such, they are reported as median [25th, 75th]. All statistical tests were performed using Fisher's exact test for categorical variables and Mann-Whitney U test for non-normal distributed variables

hypotension ($P = 0.41$). Moreover, no differences were found between the groups for both intraoperative fluid balance, need for transfusion of blood products, and total surgical time [Table 2]. A total of 7 (5.7%) patients developed postoperative acute kidney injury. Of note, all 7 patients belonged to the normal RV group ($P = 1.00$). A total of 31 (25%) patients had postoperative respiratory complications. Of those patients with normal RV function, 23.5% developed postoperative respiratory complications. Among patients with preexisting RV systolic dysfunction, 57.1% had postoperative respiratory complications. Using Fisher's exact test, this trend for higher incidence of postoperative respiratory complications in patients with preexisting RV systolic dysfunction was not statistically significant ($P = 0.070$).

Complications

A total of 5 (4.1%) patients developed postoperative MACE: 3.5% ($N = 3$) among patients with normal RV function and 14.3% ($N = 1$) among patients with abnormal RV function. Using Fisher's exact test, this difference in incidence of MACE did not reach a statistical significance ($P = 0.20$). Of note, the patient with preexisting RV systolic dysfunction who had developed postoperative MACE had an isolated preexisting RV systolic dysfunction that was graded as severe (Patient #113, Table 3). Of the patients who had developed postoperative MACE, 2 patients had postoperative myocardial infarction with elevated troponin while 3 patients had postoperative development of heart failure. Neither RV systolic dysfunction nor LVEF were found to be associated with development of postoperative

MACE in univariable analysis. In addition, there was no association between low EF (EF <30%) and outcome MACE ($P = 0.881$). An RCRI score >3 on the other hand was found to be associated with higher incidence of MACE ($P = 0.0030$). In addition, CHF and CAD were also found to be associated with higher incidence of MACE ($P = 0.012$ and $P = 0.021$, respectively). Multivariable analysis was not carried out due to expected multicollinearity among MACE, CHF, and CAD [Table 4].

A total of 7 (5.7%) patients had expired during the hospital stay: 3.5% ($N = 4$) among patients with normal RV function and 42.9% ($N = 3$) among patients with abnormal RV function ($P = 0.0037$). 1 patient died from sepsis resulting from ischemic bowel, 2 patients died from multi-organ failure relating to sepsis, 1 patient died from protracted course relating to organ rejection after renal transplant, 1 patient died from protracted hospital course relating to severe gastrointestinal bleed, 1 patient died from decompensated heart failure, and 1 patient died from multi-organ failure relating to metastatic cancer. There were no intraoperative deaths; all deaths occurred postoperatively during hospital admission. Among the total 7 patients who had expired during the hospitalization, 3 had preexisting RV systolic dysfunction. Among these 3 patients, one had severe RV systolic dysfunction with an LVEF 31% (patient #6), one had mild RV systolic dysfunction with a normal LVEF and had developed postoperative sepsis (patient #48), and one had severe RV systolic dysfunction with a normal LVEF who had developed postoperative MACE (patient #113) [Table 3].

Table 2: Intraoperative and post-operative variables

	Normal right ventricular function	Right ventricular systolic dysfunction	<i>P</i> *
Inotrope	16 (13.9)	4 (57.1)	0.014
Intraoperative blood transfusion	52 (45.2)	3 (42.8)	1.00
AUT	27.1 [0, 82.6]	61.4 [2.6, 81.1]	0.41
Intraoperative fluid balance (mL)	1700 [898, 2955]	825 [170, 2000]	0.33
Surgical Time (min) (median, 25%, 75%)	309 [194, 450]	332 [268, 690]	0.35
Death	4 (3.5)	3 (42.9)	0.0037
MACE	4 (3.5)	1 (14.3)	0.26
AKI	7 (7.7)	0 (0)	1.00
Postoperative Respiratory Complication	27 (23.5)	4 (57.1)	0.07

AUT: Area under threshold; MACE: Major adverse cardiac event; AKI: Acute Kidney Injury. **P* calculated by Chi-square for counts and by Mann-Whitney U for scalar data

Table 3: Description of grading of RV systolic dysfunction in relation to LVEF and outcomes

Patient Number	Preexisting RVD	Degree of RVD	EF (%)	Postoperative MACE	Postoperative Sepsis	All Cause In-Hospital Mortality
6	Yes	Severe	31	No	No	Yes
28	Yes	Mild	52	No	No	No
34	Yes	Mild	68	No	No	No
48	Yes	Mild	73	No	Yes	Yes
108	Yes	Severe	45	No	No	No
113	Yes	Severe	71	Yes	No	Yes
122	Yes	Moderate	67	No	No	No

RVD: Right ventricular dysfunction; LVEF: Left ventricular ejection fraction; EF: Ejection fraction; MACE: Major adverse cardiac events

Table 4: Results of logistic regression models for MACE and all-cause in-hospital mortality

Model (MACE)	OR	P	95% CI	OR	P	95% CI
Univariate Regression			Multivariate Regression			
RVD	4.63	0.20	(0.45, 48.02)	* Not performed		
Sepsis	3.41	0.30	(0.34, 34.18)			
CHF	11.04	0.012	(1.69, 71.91)			
CAD	14.00	0.021	(1.50, 130.75)			
EF	0.97	0.52	(0.91, 1.03)			
LVEF<50%	2.68	0.40	(0.27, 26.29)			
RCRI>3	18.56	0.0030	(2.70, 127.73)			
Model (Mortality)	OR	P	95% CI	OR	P	95% CI
Univariate Regression			**Multivariate Regression			
RVD	20.81	0.00094	(3.44, 125.76)	18.86	0.015	(1.76, 201.67)
Sepsis	13.623	0.0027	(2.47, 75.16)	9.12	0.054	(0.96, 86.21)
MACE	14.93	0.0081	(2.02, 110.45)	5.46	0.21	(0.39, 77.11)
Multiple Surgery	3.00	0.169	(0.63, 14.35)			
CHF***	5.41	0.038	(1.10, 26.74)			
EF	1.00	0.881	(0.93, 1.07)			
CAD	4.56	0.056	(0.96, 21.71)			
Post-infection	2.30	0.293	(0.49, 10.92)			
Inotrope	4.32	0.070	(0.89, 21.05)			
Dialysis	1.62	0.673	(0.17, 15.15)			
Age	0.99	0.833	(0.94, 1.05)			
RCRI >3	9.09	0.0092	(1.73, 47.90)	6.99	0.07	(0.89, 55.08)
Respiratory Complication	21.36	0.0055	(2.46, 185.77)	8.09	0.09	(0.72, 90.47)
AKI	2.767	0.386	(0.277, 27.633)			
Cancer	0.380	0.259	(0.071, 2.037)			

RVD: Right ventricular (systolic) dysfunction, CHF: Congestive heart failure, CAD: Coronary artery disease, EF: Ejection fraction, RCRI: Revised cardiac risk index, MACE: Major adverse cardiac events, AKI: Acute kidney injury, OR: Odds ratio, CI: Confidence interval. *Multivariate logistic regression model was not performed for MACE due to non-significant finding for RVD and multicollinearity among RCRI, CAD, & CHF, **Only results from the final models are shown for the multivariate logistic regression analysis for all-cause in-hospital mortality. RVD and RCRI>3 were analyzed in separate models due to multicollinearity. ***CHF was not included in the multivariate logistic regression due to expected multicollinearity with RVD and RCRI

In univariate logistic regression, the odds ratio (OR) for all-cause in-hospital mortality in presence of preexisting RV systolic dysfunction was 20.8 (95% CI, 3.4-125.8; $P = 0.00094$). Other covariates found to have significant association with all-cause in-hospital mortality included sepsis, MACE, CHF, RCRI >3, and postoperative development of respiratory complications [Table 4]. Accounting for all other covariates, RV systolic dysfunction remained independently associated with higher incidence of all-cause in-hospital mortality with an OR = 18.9 (95% CI, 1.8-201.7; $P = 0.015$). This is demonstrated in Figure 2, in which preexisting RV systolic dysfunction is the only predictor with a confidence interval that excluded the null value. RCRI >3 was not included in the same regression model as RV systolic dysfunction because of expected multicollinearity. Evaluating RCRI >3 in a separate multivariable regression model, unlike RV dysfunction, it was not an independent risk factor for all-cause in-hospital mortality [Table 4].

DISCUSSION

In this retrospective single-centered study, we evaluated the association of preexisting RV systolic dysfunction with postoperative major adverse cardiac event (MACE)

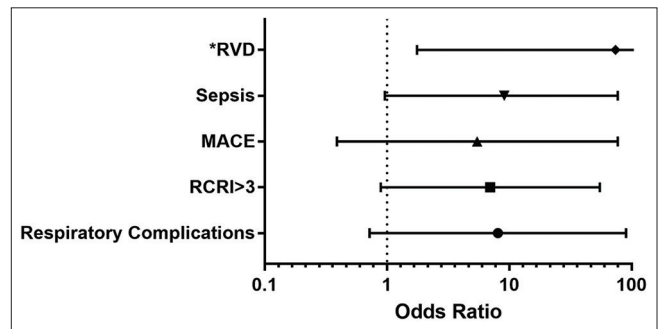


Figure 2: Multivariate Logistic Regression on all-cause in-hospital mortality. RVD = Right ventricular (systolic) dysfunction, MACE = Major adverse cardiac events, RCRI = Revised cardiac risk index. * $P < 0.05$

and all-cause in-hospital mortality in high-risk patients undergoing open abdominal surgery.

We found that, unlike our previous study in vascular surgery patients, preexisting RV systolic dysfunction in this cohort was not shown to be associated with postoperative MACE but was associated with higher all-cause in-hospital mortality with a nearly 20-fold increase in the odds ratio for risk, even when controlling for other high-risk factors such as sepsis. In regards to postoperative MACE and the lack of confirmation of our previous results, the low incidence rate (4.1%)

together with the study's small sample size likely result in the study being underpowered to detect the true effect of preexisting RV systolic dysfunction on postoperative MACE. By contrast, despite the low sample size in the RV dysfunction group, the finding of a strong association between preexisting RV systolic dysfunction and mortality in this current surgical cohort reinforces the possibility that RV dysfunction may have clinical significance. Of note, while we did not find a significant difference in incidence of all-cause in-hospital mortality in our previous vascular cohort, there was a trend for higher mortality in the group with preexisting RV systolic dysfunction compare to those with normal RV function (20% versus 6%). This previously observed trend may further lend support to our current finding.

In our evaluation of the impact of LV systolic dysfunction on outcomes, we shared similar findings with those of others. Indeed, in the investigation conducted by Gundes *et al.*^[17] on patients with malignancies of the gastrointestinal system undergoing major abdominal surgery, LV systolic dysfunction was not associated with higher incidence of postoperative MACE or mortality. Similar to our subgroup analysis, their findings were consistent across all categories of LV systolic dysfunction includes those with worse LVEF defined as an EF <30%. In the study conducted by Vest *et al.* in which the significance of LV systolic dysfunction on postoperative outcomes was evaluated in obese patients undergoing bariatric surgery,^[24] it was also observed that LV systolic dysfunction did not predict higher incidence of post-operative mortality. Unlike our observation and those made by Gundes *et al.*, their study did find that patients with LV systolic dysfunction defined as those with an EF <50% had significant higher incidence of postoperative MACE compare to those with normal LV function. However, it is important to note that Vest *et al.* did not account for potential confounding factors in their study. Indeed, it was noted in their study that patients with LV systolic dysfunction was significantly older than those with normal LV function. Therefore, it is possible age may have been a confounding factor.

It has been shown that among patients in the intensive care unit with diagnosis of sepsis, 47% have isolated RV dysfunction and 53% have combined biventricular dysfunction evident on echocardiogram.^[25] In our surgical cohort, 3 of the 7 patients ultimately died from sepsis. While 2 of the 3 patients had normal biventricular function preoperatively, one had mild preexisting RV dysfunction with normal LV function (patient #48, Table 3). In this patient with preexisting RV dysfunction, it is possible that

development of sepsis in this patient exacerbated the ventricular function in an already compromised RV. Since the RV plays a critical role in delivering deoxygenated blood to the lungs, maintaining forward flow from venous return thereby preventing organ congestion, as well as global systemic circulatory hemostasis,^[26] it is reasonable to assume that a preexisting RV dysfunction in a septic patient may contribute to increased mortality. For the remaining 6 patients in the cohort who had preexisting RV systolic dysfunction, 2 additional patients expired during their hospital stay. While both had severe preexisting RV dysfunction, one had an EF of 31% while the other had an EF of 71%. Interestingly, it was the patient with the normal LVEF who had developed post-operative MACE (patient #113, Table 3).

For the 4 patients with preexisting RV systolic dysfunction who had survived their hospital stay, 2 of the patients had mild RV systolic dysfunction with normal LVEF (EF >50%), 1 had severe RV systolic dysfunction with an EF of 45%, and 1 had moderate RV systolic dysfunction with a normal LVEF [Table 3]. In this small cohort study, we were unable to perform additional subgroup analysis to further describe the impact of severe versus mild or moderate RV systolic dysfunction on outcomes of interest. However, we suspect that an RV systolic dysfunction of worse severity would have higher predictive value for postoperative mortality. Furthermore, we suspect that sepsis has a significant negative impact on RV function such that worse mortality may be predicted even in patients with just mildly compromised RV function pre-operatively. Of note, the simultaneous effect of LV systolic dysfunction in presence of preexisting RV dysfunction cannot be evaluated in this study due to the study's small sample size. Future studies with larger sample size of patients with preexisting RV systolic dysfunction will be needed in order to provide more insights.

From clinical experience, management of critically-ill patients with concomitant RV systolic dysfunction can be quite difficult. Aside from addressing the underlying problems or causes of RV dysfunction such as infarction of the right coronary artery or acute pulmonary hypertension (i.e., pulmonary embolism or acute pulmonary edema of any etiology), optimization of RV function in a patient with preexisting RV dysfunction is challenging. Part of this challenge results from the fact that an already compromised RV, unlike that of a healthy RV, is not only sensitive to pressure overload, but also exquisitely sensitive to volume loading. In other words, while preload may be important for optimal RV

function, the safety margin in which the rate of fluid replacement and total volume given without further exacerbating ventricular dysfunction can be quite narrow in a dysfunctional RV. Combining this challenge with the frequent hemodynamic derangement of hypotension resulting from postsurgical bleed, fluid shift, or in setting of sepsis, the clinical problem and management often becomes much more complex.^[27] Currently, there is a lack of guideline in how fluids should be administered and what kind of parameters can be used for optimal fluid management in a patient with RV dysfunction. Based on the author's own experience in managing patients with RV dysfunction undergoing open heart surgery, titrating a combination of vasopressor with careful fluid administration (if patient is deemed hypovolemic) under transesophageal echo guidance in which the shape of the interventricular septum and the excursion of the lateral RV free wall are used as a way to gauge the effectiveness of the therapy have been helpful. However, official recommendation cannot be given at this point due to paucity of scientific studies in this area.

In addition to the challenge of when and how to optimally replace fluid in a patient with RV systolic dysfunction, avoiding factors that can worsen pulmonary vascular resistance may be just as difficult in a critically-ill patient. This is because a postsurgical and critically-ill patient is often faced with multitude of clinical problems that have negative effect on pulmonary vascular resistance and therefore RV function. These problems may include physiological changes relating to surgically induced stress,^[28] pulmonary complication resulting in hypoxemia or hypercarbia, mechanical ventilatory setting that increases intrathoracic pressure, or systemic hypotension that requires use of vasoconstrictor agents.^[29] In a critically-ill patient with preexisting RV systolic dysfunction, any one or a combination of the above processes would undoubtedly add complexity to the clinical care of the patient. In summary, sepsis may play a role in worsening RV or biventricular function; in a critically-ill patient with preexisting RV systolic dysfunction, development of sepsis may therefore further exacerbate ventricular function and contribute to mortality. Moreover, preexisting RV systolic dysfunction in a post-surgical and critically-ill patient can be particularly challenging and may also contribute to overall in-hospital mortality.

Different from the study performed by Jakobson *et al.*,^[16] in which RCRI >3 was evaluated for in-hospital mortality, as well as both short- and long-term mortality, our group only investigated the association between RCRI >3 and all-cause in-hospital mortality.

In agreement with this prior study,^[16] our multivariable analysis did not find RCRI >3 to have independent association with all-cause in-hospital mortality. This finding is consistent with the understanding that while RCRI predicts perioperative cardiac events well, it does not reliably predict death in non-cardiac surgical cohorts.^[30]

Limitations

While the findings in this study may have clinical implications and, despite the small sample size, were strongly statistically significant, the statistical power was limited. Finding agreement with these results in a larger surgical cohort will be needed. In addition to this, the impact of severity of RV systolic dysfunction cannot be addressed in the current study due to the small number of patients with preexisting RV systolic dysfunction. This will be an important area to address using a larger cohort in the future. The retrospective nature of the study means that the quality of the study findings is dependent on accuracy of medical charting. Since our finding of a mortality rate of 5.7% is comparable with prior studies, this suggests that quality of the study was not likely compromised,^[31-33] but this cannot be ruled out. In addition, the retrospective nature of the study allowed evaluation of well-documented covariates only. As such, there are important *a priori* variables relevant to this surgical cohort that the study could not account for.^[34,35] Including pre-operative echocardiogram as far as 1 year prior to the indexed surgery may not accurately capture changes in ventricular function which may have occurred closer to the surgical date. However, the majority of the patients (89%) had preoperative echocardiogram (echo) performed within 6 months of the surgery. Moreover, it is the practice of the institution in which repeat echo is obtained during pre-operative evaluation for non-emergent surgery when patient either demonstrate or endorse clinical changes that may have cardiac relevance.

Lastly, unlike our previous finding in the vascular cohort in which patients with RV systolic dysfunction had lower LVEF and higher RVSP,^[15] we did not find a significant difference in LVEF and RVSP between patients with and without RV systolic dysfunction in the current surgical cohort [Table 1]. While this may be a reflection of an inherent difference between the vascular versus the abdominal surgical cohort, it may represent a skewed sampling of the population resulting from the study's small sample size. If the latter is true, the study would have additional limitation in that it does not reflect the true epidemiology of patients with

RV systolic dysfunction undergoing open abdominal surgery.

CONCLUSION

The present study demonstrated that 5.7% of the patients classified as ASA III and above undergoing non-emergent open abdominal surgery had preexisting RV systolic dysfunction. The presence of RV systolic dysfunction was independently associated with all-cause in-hospital mortality with an almost 20-fold increase in odds. LV systolic dysfunction such as EF <30% on the other hand, was not associated with overall in-hospital mortality. Further studies with larger sample size that includes additional relevant covariates are required to validate current findings.

List of abbreviations

MACE: Major adverse cardiac events

RCRI: Revised cardiac risk index

LV: Left ventricle

RV: Right ventricle

LVEF: Left ventricular ejection fraction

ASA: American Society of Anesthesiology

BMI: Body mass index

CHF: Congestive heart failure

CAD: Coronary artery disease

HTN: Hypertension

CVA: Cerebral vascular accident

DM: Diabetes

COPD: Chronic obstructive pulmonary disease

OSA: Obstructive sleep apnea

SIS: Surgical information system

MAP: Mean arterial pressure

AUT: Area under the threshold

RVSP: Right ventricular systolic pressure

OR: Odds ratio

CI: Confidence interval.

DECLARATIONS

Ethics approval and consent to participate

This study was approved by the Institutional Review Board at the University of California Irvine Medical Center (UCI IRB HS# 2017-4099). Approved initially in 2016, and revision made and approved in 2017.

Consent for publication

Not applicable.

Availability of data and material

All datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

J. Rinehart is a consultant for Edwards Lifesciences and has ownership interest in Sironis Inc. All other authors do not have any competing interest.

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Conflicts of interest

There are no conflicts of interest.

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