

Right ventricular assessment can improve prognostic value of Euroscore II

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Abstract

Background: The aim of this multicenter prospective study was to evaluate the prognostic weight of preoperative right ventricular assessment on early mortality in cardiac surgery.

Methods: This is a multicenter prospective observational study performed by the Italian Group of Research for Outcome in Cardiac Surgery (GIROC) including 11 centers. From October 2017 to March 2019, out of 923 patients undergoing cardiac surgery, 28 patients with some missing data were excluded and 895 patients were

enrolled in the study right ventricular dilatation was defined as a basal end-diastolic diameter >42 mm. The right ventricle (RV) function was assessed using the combination of three parameters: fractional area changing (FAC), tricuspid annular plane systolic excursion (TAPSE), and S'-wave using tissue Doppler imaging (TDI-S'); RV dysfunction was defined as the presence of at least two of the following cutoffs: FAC <35%, TAPSE <17 mm, and TDI S' <9.5 mm

Results: Among the entire cohort, 624 (70%) showed normal RV, 92 (10%) isolated RV dilatation, 154 (17%) isolated RV dysfunction, and 25 (3%) both RV dilatation and dysfunction. Non-surviving patients showed a significantly higher rate of RV alteration at multivariable analysis, RV status was found to be an independent predictor for higher in-hospital mortality beside Euroscore II.

Conclusions: This prospective multicenter observation study shows the importance to assess RV preoperatively and to include both RV function and dimension in a risk score model such as Euroscore II to implement its predictivity, since PH cannot always mirror the status of the right ventricle.

KEYWORDS

Euroscore II, right ventricle, right ventricular dilatation, right ventricular dysfunction

1 | INTRODUCTION

The prognostic role of right ventricle has been clearly demonstrated in patients with myocardial infarction (MI),^{1,2} heart failure (HF), either ischemic or not,^{3,4} receiving cardiac resynchronization therapy,⁵ and in small cohorts of patients undergoing cardiac surgery.⁶⁻¹⁰ In last decades several risk score models were introduced to estimate perioperative risk in cardiac surgery, mainly Euroscore I and Euroscore II^{11,12} and STS score.^{13,14} However, while left ventricular function has been considered as risk factor in all of them, the right ventricle function and size have not been included.

Ghio et al¹⁵ demonstrated in a heart failure model that certain patients have normal pulmonary pressure and low right ventricular ejection fraction (RVEF); they reported as this subset accounted for roughly 6% if patients with HF and their prognosis was similar to those patients with high pulmonary pressure but normal RVEF. In a cohort of patients undergoing mitral and tricuspid surgery, Di Mauro et al,¹⁶ reported a subset of patients with normal systolic pulmonary artery pressure (sPAP) and abnormal right ventricle (RV) accounting for roughly 3%. Similarly in this study, the prognostic impact of RV on in-hospital mortality was independent from pulmonary hypertension (PH), and the presence of both PH and RV alteration showed the worst outcome.

So, although many surgeons and cardiologists consider systolic pulmonary pressure as mirror of right ventricular condition, there are some evidence that this is not particularly true.^{15,16}

Hence, the aim of this multicenter study was to evaluate the weight of preoperative right ventricular assessment as add-on to implement Euroscore II.

2 | MATERIALS AND METHODS

2.1 | Study population

This is a multicenter prospective observational study performed by the Italian Group of Research for Outcome in Cardiac Surgery (GIROC), endorsed by The Italian Society for Cardiac Surgery (SICCH), including 11 centers. Inclusion criteria were: (a) patients undergoing cardiac surgery; (b) elective or urgent surgery; (c) complete preoperative echocardiogram with data regarding RV. Patients undergoing surgery on emergency or patients with technical difficulty to assess the right ventricle with 2D-TT echocardiogram were excluded. All the data were prospectively collected using SICCH database. The study was approved by IRB and ethical committee of all participating centers (Prot. 0086656|07/11/2017 Principal Ethical Committee). From October 2017 to March 2019, out of 923 patients undergoing cardiac surgery, 28 patients with some missing data were excluded and 895 patients were enrolled in the study

2.2 | Definition of terms, end-points, and echocardiography

All the variables collected in the dataset were defined according to Euroscore II.¹³ The primary end-points were in-hospital mortality.

The right ventricle was assessed from a right ventricle-focused apical four-chamber view¹⁷: RV basal dimension is best estimated at end-diastole; right ventricular dilatation was defined as a basal end-diastolic diameter >42 mm. The RV function was assessed using the

combination of three parameters: fractional area changing (FAC), tricuspid annular plane systolic excursion (TAPSE) and S'-wave using tissue Doppler imaging (TDI-S'); RV dysfunction was defined as the presence of at least two of the following cutoffs: FAC <35%, TAPSE <17 mm, and TDI S' <9.5 mm.¹⁷

Thus, RV status was classified as: 0 no dilatation and dysfunction; 1 isolated dilatation; 2 isolated dysfunction; 3 dilatation and dysfunction; RV alteration was defined as RV status from 1 to 3

Systolic pulmonary artery pressure was estimated using tricuspid regurgitation (TR) velocity using the simplified Bernoulli equation and combining this value with an estimate of the right atrium (RA) pressure. PH was defined as the presence of sPAP equal or higher than 31 mm Hg.¹²

2.3 | Statistics

The normal distribution of continuous variables was assessed by Kolmogorov-Smirnov test. Normally distributed variables are reported as mean and standard deviation; conversely non-normally distributed variables are reported as median and quartiles. Pairwise comparison was performed with *t*-test or the Mann-Whitney *U*-test in case of continuous variables and χ^2 with Fisher exact test in case of categorical variables. To verify the impact of RV-status beside Euroscore II, these two variables were tested using a parsimonious logistic regression model was built to identify the best predictors for early outcome. Results are reported as odds ratio (OR), 95% confidence limits (95CLs) and *P*-value. The final model was internally validated using bootstrapping. Receiver operating characteristic (ROC) curve was used to estimate the discrimination power of Euroscore II and Euroscore II plus RV dysfunction and/or dilatation (Euroscore + RV). The ROC curves were compared by DeLong test. Calibration of both risk model was assessed with Brier score. The effect on risk classification of adding anemia to the reference model was evaluated with the use of net reclassification improvement (category-free NRI)¹⁸

All the analyses were performed with SPSS (IBM Corp. IBM SPSS Version 24.0. Armonk, NY), Med-Calc (MedCalc Software bv, Ostend, Belgium) and R-project (Core Team 2013. R Foundation for Statistical Computing, Vienna, Austria); *P* < .05 was considered as the threshold for statistical significance.

3 | RESULTS

The mean age was 67 ± 12 (19-89 years) and 35% were females. Isolated coronary artery bypass grafting (CABG) was performed in 234 (31%), isolated non-CABG procedure in 313 (35%), two procedures in 234 (26%), and three procedures in 70 (8%) cases. All pre-operative data are summarized in the Table 1.

Among the entire cohort, 624 (70%) showed normal RV, 92 (10%) isolated RV dilatation, 154 (17%) isolated RV dysfunction, and 25 (3%) both RV dilatation and dysfunction. Non-surviving patients

TABLE 1 Preoperative data

Age, y	67 ± 12
Female gender	311 (35%)
Smoker	291 (33%)
Hypertension	555 (62%)
Dyslipidemia	376 (42%)
NIDDM	141 (16%)
IDDM	70 (8%)
ECV	156 (17%)
Previous stroke	33 (4%)
CRF	
Moderate	127 (14%)
Severe	23 (3%)
Dialysis	7 (1%)
COPD	
Mild	25 (3%)
Moderate	39 (4%)
Severe	4 (0.5%)
Previous cardiac surgery	49 (6%)
NYHA class	
I	320 (36%)
II	286 (32%)
III	273 (31%)
IV	16 (2%)
CCS class	
1	54 (6%)
2	95 (11%)
3	104 (12%)
4	70 (8%)
EF (%)	56 ± 10
Moderate impairment	148 (17%)
Severe impairment	30 (3%)
PH	
Moderate	202 (23%)
Severe	43 (5%)
Elective surgery	668 (75%)
Urgent surgery	227 (25%)
Euroscore II	1.7 (1.0-3.1)

Abbreviations: CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; ECV, extracardiac vasculopathy; EF, ejection fraction; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; NYHA, New York Heart Association; PH, pulmonary hypertension.

showed a significantly higher rate of RV alteration as shown in the Figure 1.

Stratifying the entire cohort according to the presence of PH and RV status, 422 (47%) patients showed neither PH nor RV alteration, 202 (23%) showed PH but not RV alteration, 145 (16%) showed RV alteration but not PH, and 126 (14%) showed both conditions.

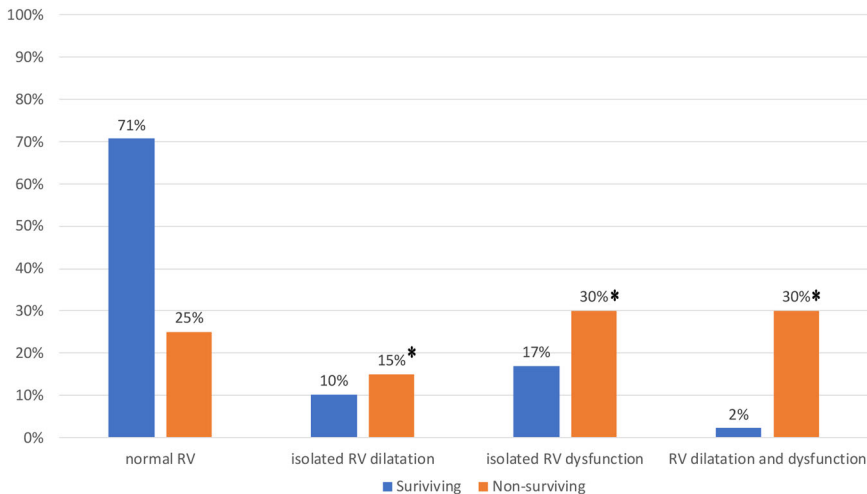


FIGURE 1 The rate of right ventricular (RV) dilatation and/or dysfunction between surviving (blue columns) and non-surviving (orange columns) patients

In-hospital mortality was 2.2% (20 cases). Surviving patients showed significantly higher TAPSE [22 mm (19-24) vs 19 mm (15-21); $P = .001$], TDI S' [14 cm/s (13-16) vs 11 cm/s (9-14), $P < .001$] and FAC [44% (39-49) vs 34% (32-39); $P < .001$] along with significantly less dilated RV [36 mm (33-40) vs 40 mm (35-43); $P = .025$] (Figures 2-3).

At multivariable analysis, RV status was found to be an independent predictor for higher in-hospital mortality (Table 2), beside Euroscore II. The Euroscore II showed an area under the curve (AUC) significantly lower than Euroscore II + RV (0.86, 0.84-0.88 vs 0.96, 0.94-0.97, difference 0.095, $P = .045$) (Figure 4). The net reclassification index was 0.5126 (0.0706-0.9545); P -value, .023. Calibration was similar: Brier score was 0.0197 for Euroscore II and 0.0196 Euroscore II + RV

The predicted mortality by Euroscore II + RV is closer to observed mortality than Euroscore II (Figure 5). This finding was confirmed also in subgroups: isolated CABG, isolated non-CABG, two or more procedures (Figure 6).

4 | DISCUSSION

The estimation of RV dimensions and function can be well achieved with cardiac magnetic resonance (CMR),¹⁷ but preoperative evaluation cannot include routine CMR due to its cost, availability, and technical issues (PMK/ICD, claustrophobia, etc). In most of centers, even 3D echocardiography cannot be considered as a routine preoperative exam, since it is performed in

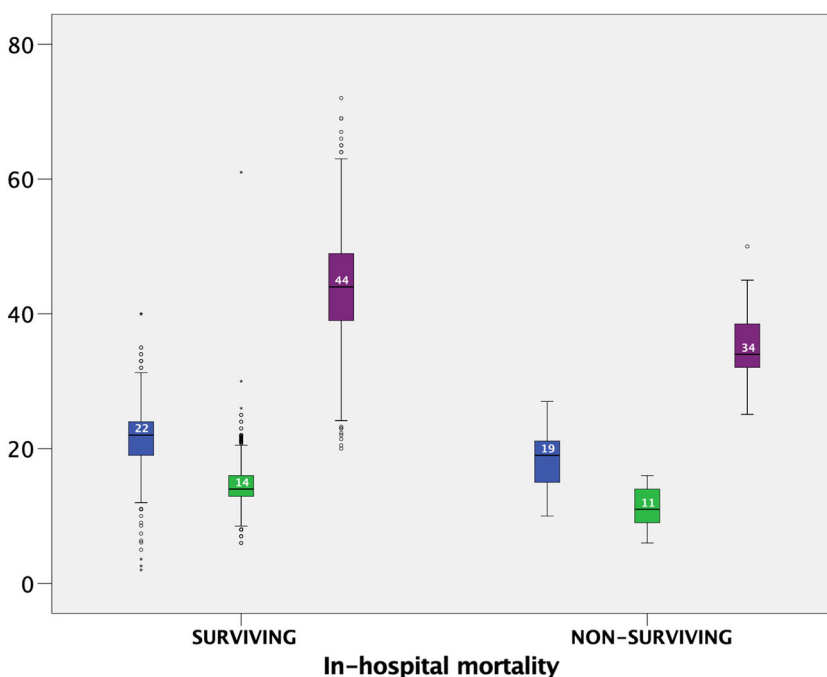


FIGURE 2 Preoperative right ventricular function comparing surviving and non-surviving patients; tricuspid annular plane systolic excursion (TAPSE, red box); tricuspid annular plane velocity by tissue Doppler pulse wave (TDI S', green box); fractional area change (FAC%, purple box)

FIGURE 3 Preoperative right ventricular diameter comparing surviving and non-surviving patients; basal right ventricular diameter (red box)

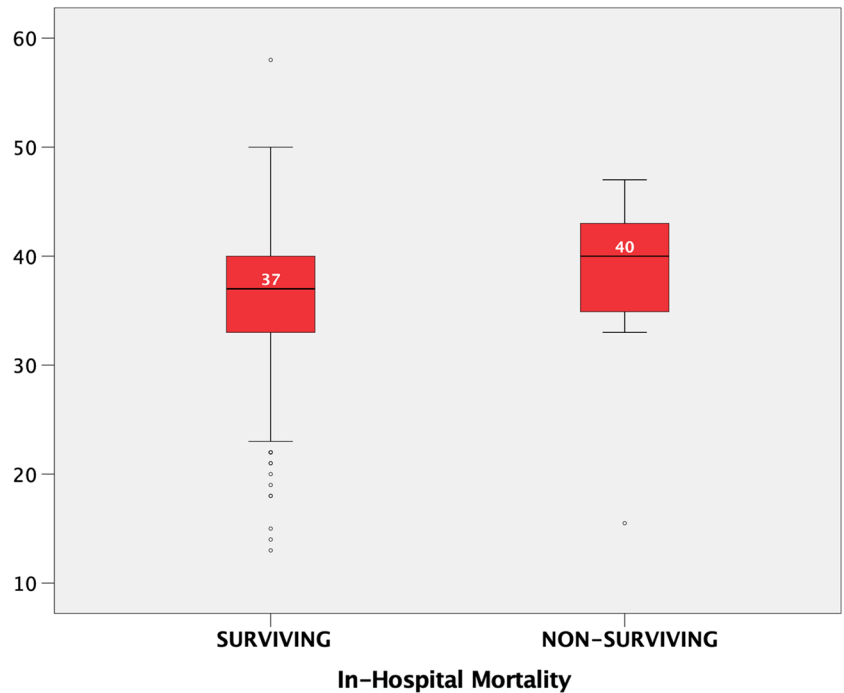


TABLE 2 Multivariable analysis

	Beta-coefficient	OR	Lower 95%CL	Upper 95%CL	P-value
Euroscore II	0.053	1.054	1.024	1.085	<.001
Normal RV (ref.)					
Isolated RV dilatation	1.678	5.355	1.174	24.417	.030
Isolated RV dysfunction	1.790	5.991	1.679	21.383	.006
RV dilatation and dysfunction	3.813	45.298	11.840	173.311	<.001
Constant	-5.211				

Abbreviations: CL, confidence limits; OR, odds ratio; RV, right ventricle.

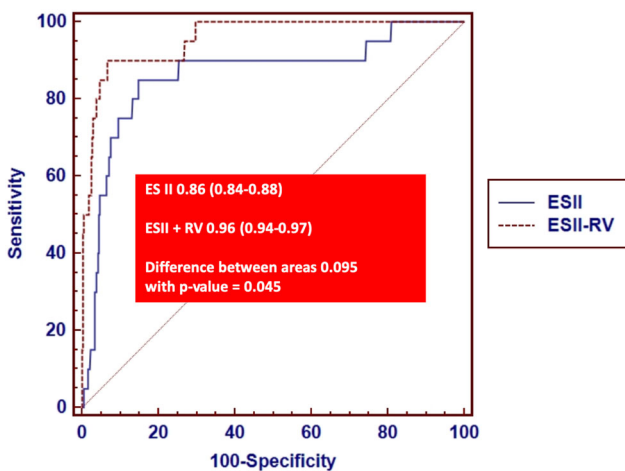


FIGURE 4 The Euroscore II showed an AUC significantly lower than Euroscore II + RV. AUC, area under the curve; RV, right ventricle

the operating room where hemodynamic conditions is somehow altered by the anesthesia. So, actually, 2D-echocardiography remains the easiest tool to assess RV function and size, playing a paramount role using surrogate index as TAPSE, FAC, or TDI S',¹⁹ even with the limitation of a poor sonographic windows in some cases.

The importance of the right ventricle in cardiac surgery has been demonstrated in a variety of clinical settings such as CABG or valvular heart disease, congenital heart disease, heart transplantation, in patients requiring ventricular assist devices.⁶⁻¹⁰ However, almost all the studies focusing on prognostic role of RV are retrospective with a small sample size, so the independent prognostic role of RV has not been well evidenced.

The present multicenter study account for roughly 900 cases, exploring the usefulness to add RV function and size to Euroscore II to avoid underestimation of the risk.

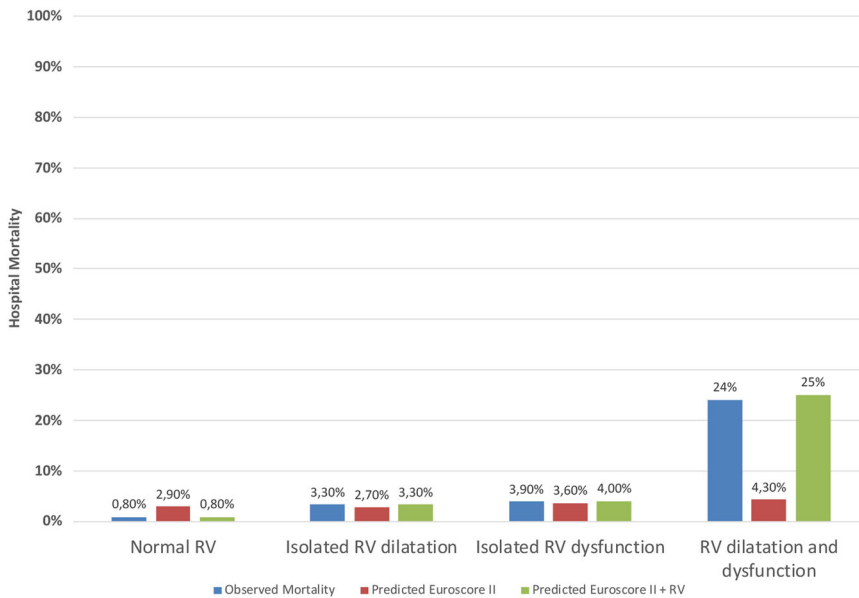


FIGURE 5 Observed (blue columns) versus predicted mortality by either Euroscore II (red columns) and Euroscore II + RV (green columns), stratified by right ventricular status. RV, right ventricle

In fact, in presence of a reduction of RV function or of low forward RV stroke volume, as in case of tricuspid regurgitation, pulmonary pressure can be normal or low, even in presence of high pulmonary resistances²⁰ Moreover, in case of RV volume overload and dilatation, the primary involvement of RV by myocardial disease or overtreatment with diuretic can reduce pulmonary pressure, but not necessarily influence the right ventricle prognostic role. In this condition, the actual predictive models underestimate the perioperative risk. Conversely, some patients show good RV function despite high pulmonary pressure; in fact, despite similar RV afterload not all the patients develop maladaptive RV hypertrophy, characterized by dilatation, ischemia, fibrosis, and then RV failure.²¹

So, considering pulmonary hypertension strictly linked to right ventricular dysfunction and dilatation and vice versa is not always true, and this is particularly important in the case of prognosis assessment, even in cardiac surgery.¹⁶

In our series, PH and RV dilatation and/or dysfunction were present only in 14% of cases, while in 23% of cases patients had PH without any alteration of RV as well as in 16% of cases RV alteration was not associated with PH.

Longitudinal RV excursion is the major contributor to RV ejection, accounting for 80% of RV stroke volume.²² Some reports demonstrated as patients undergoing cardiac surgery show a reduction of longitudinal RV contraction up to 40% that can persist even for

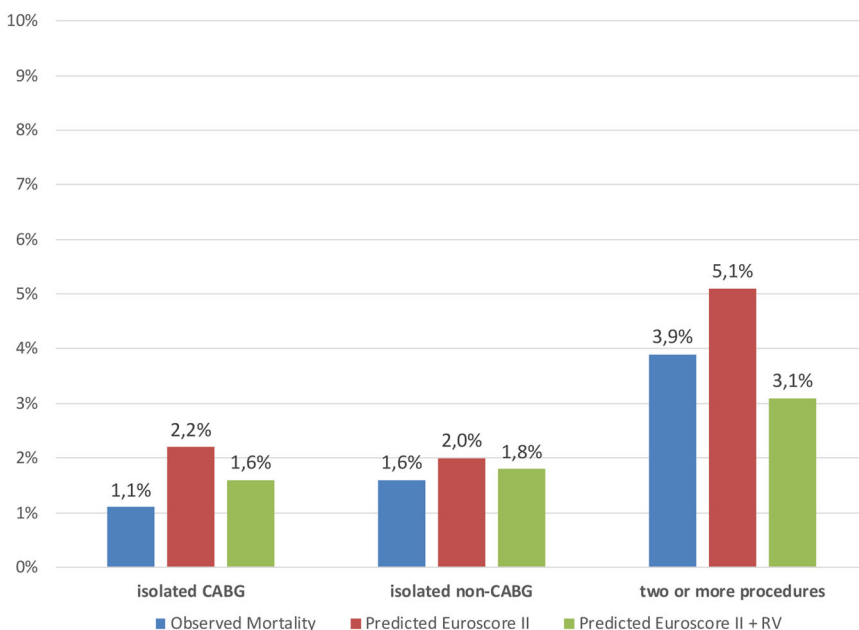


FIGURE 6 Observed (blue columns) vs predicted mortality by either Euroscore II (red columns) and Euroscore II + RV (green columns), stratified by weight of procedure: isolated CABG, isolated non-CABG, two or more procedures. CABG, coronary artery bypass grafting; RV, right ventricle

months after surgery.²³⁻²⁵ Singh et al²⁶ have recently demonstrated in a cohort of 109 patients as the RV function reduction starts soon after CPB discontinuation, with the greatest change after chest closure, regardless of the procedure and the chest access; TAPSE decreased from 2.2 to 1.4 and FAC from 46% to 38%. This reduction seems to be CPB-correlated or due to cardioplegic arrest.²⁵⁻²⁷ However, the real correspondence between surrogate echocardiographic indexes and RVEF in postoperative period remains still largely controversial. Some studies^{24,28} reported preserved RVEF despite reduced echocardiographic TAPSE and TDI S', but, conversely, others defined TAPSE as a robust measure well correlating with RVEF²⁹

Nevertheless, the reduction of RV function is well-tolerated in almost the patients with preoperative normal RV size and function, and normal RV afterload. Though, in presence of pre-existing RV alteration, surgery can be so deleterious to compromise the outcome. Therefore, the present study support the necessity to add RV assessment to actual risk models such as Euroscore II, showing a significant improvement of both calibration and discrimination power of the model.

The strength of the present study was to identify RV dilatation as well as RV dysfunction as risk factors independently from other pathological conditions already included into Euroscore II such as PH or COPD. This new stratification tool could be helpful to identify those patients with normal pulmonary pressure but RV dilatation and dysfunction, not only to merely establish the perioperative risk, but also to adopt all that strategies to prevent a further impairment of the right ventricle (off-pump surgery, lung protection, pulmonary vasodilatation, volume management) to be willing to treat postoperative RV failure (pulmonary vasodilatation, ventilatory management, ECLS).

4.1 | Practical implication

Using beta-coefficient and constant reported in the Table 2, Euroscore II + RV score model should become according to the following formula: $\exp[-5.211 + (\text{EuroSCORE II} \times 0.53) + 1.678]$ (in case of isolated RV dilatation) or $+1.790$ (in case of isolated RV dysfunction) or $+3.813$ in case of contemporary RV dilatation and dysfunction).

4.2 | Study limitations

The right ventricular dysfunction was assessed by TAPSE, FAC, and TDI S' that, although are well correlated with RVEF,³⁰ ignores the outlet portion and the septal contribution to RV ejection, which may become important to maintain overall RV function. Moreover, neither 3D echocardiographic RV assessment nor novel echocardiographic indexes as speckle tracking was used. Another limitation is the small number of events (only 20) is a limitation for the multi-variable analysis according to the role of thumb 1:10. Finally, the most important limitation of the study is the use of the internal

rather than an external validation, as consequent we have such an extremely high discrimination value (0.96) for the new ES II + RV model. So, this model deserves to be validated in a larger and different cohort of patients undergoing cardiac surgery.

5 | CONCLUSIONS

Although the above-mentioned limitations, this prospective multicenter observational study confirms the importance to assess RV preoperatively and to include both RV function and dimension in a risk score model such as Euroscore II to implement its predictivity, since PH cannot always mirror the status of the right ventricle.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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