Prognostic role of different findings at echocardiography in acute pulmonary embolism: a critical review and meta-analysis

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Shareable abstract (@ERSpublications)
Echocardiography is a useful tool for risk stratification in all-comers with acute PE but standardisation is required https://bit.ly/3HR8rdw

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Abstract

Background Right ventricle dysfunction (RVD) at echocardiography predicts mortality in patients with acute pulmonary embolism (PE), but heterogeneous definitions of RVD have been used. We performed a meta-analysis to assess the role of different definitions of RVD and of individual parameters of RVD as predictors of death.

Methods A systematic search for studies including patients with confirmed PE reporting on right ventricle (RV) assessment at echocardiography and death in the acute phase was performed. The primary study outcome was death in-hospital or at 30 days.

Results RVD at echocardiography, regardless of its definition, was associated with increased risk of death (risk ratio 1.49, 95% CI 1.24–1.79, I^2=64%) and PE-related death (risk ratio 3.77, 95% CI 1.61–8.80, I^2=0%) in all-comers with PE, and with death in haemodynamically stable patients (risk ratio 1.52, 95% CI 1.15–2.00, I^2=73%). The association with death was confirmed for RVD defined as the presence of at least one criterion or at least two criteria for RV overload. In all-comers with PE, increased RV/left ventricle (LV) ratio (risk ratio 1.61, 95% CI 1.90–2.39) and abnormal tricuspid annular plane systolic excursion (TAPSE) (risk ratio 2.29 CI 1.45–3.59) but not increased RV diameter were associated with death; in haemodynamically stable patients, neither RV/LV ratio (risk ratio 1.11, 95% CI 0.91–1.35) nor TAPSE (risk ratio 2.29, 95% CI 0.97–5.44) were significantly associated with death.

Conclusion Echocardiography showing RVD is a useful tool for risk stratification in all-comers with acute PE and in haemodynamically stable patients. The prognostic value of individual parameters of RVD in haemodynamically stable patients remains controversial.

Introduction

Pulmonary embolism (PE) is a life-threatening disease [1]. Death is related to prevalent comorbidities in a variable proportion of patients; however, in the acute phase, PE itself accounts for the majority of deaths [2]. Right ventricle (RV) failure plays a major role in mortality due to PE, and its assessment could be used to identify patients at increased risk for death [3, 4, 5]. Current international guidelines recognise an essential role of RV dysfunction (RVD) at echocardiography in the risk stratification process of patients with acute PE [6, 7]. Risk stratification is crucial for decision making in patients with acute PE concerning disposition, treatment and early discharge [8].

However, the definition of RVD at echocardiography differed across studies in patients with acute PE, and this may have influenced study results. Several qualitative and quantitative findings of RVD at echocardiography have been reported in clinical studies and are used in daily clinical practice to diagnose RVD [9]. The most commonly reported parameters are RV hypokinesis, McConnell's sign, RV

end-diastolic diameter, pulmonary artery pressure (PAP), tricuspid annular plane systolic excursion (TAPSE) and right ventricle/left ventricle (RV/LV) diameter ratio. Previous studies comparing different measures of RVD suggested that all of these were associated with an increased risk of death, but with different accuracy of the individual findings [10, 11].

This critical review and meta-analysis aimed at assessing the accuracy of different parameters of RVD at echocardiography for the prediction of short-term all-cause mortality, PE-related death and adverse outcome.

Methods

The study protocol for the meta-analysis was registered in PROSPERO (Prospero ID: CRD42021266948) and the findings were reported according to the PRISMA guidelines. Firstly, a critical review was conducted to assess the available evidence on RVD as combination of findings as well as on individual parameters of RV overload at echocardiography and short-term death. Quantitative meta-analyses were subsequently performed on the association between individual echocardiographic parameters and short-term death, whenever data were available.

MEDLINE and EMBASE databases were searched from inception to October 2021 (Supplementary Appendix 1).

Studies meeting the following criteria were eligible for inclusion in the critical review: 1) inclusion of patients with acute PE; 2) echocardiography performed in the early phase of PE; 3) availability of data on all-cause in-hospital death or death at 30 days; and 4) availability of data on in-hospital adverse outcome or at 30 days.

The following parameters at echocardiography were considered: RV diameter, RV/LV, RV hypokinesis, PAP, TAPSE and RVD as a comprehensive definition based on the presence of pre-specified numbers of criteria at echocardiography.

Studies were excluded in case of: 1) case reports; 2) case series <50 patients; 3) thrombus in transit studies; and 4) language other than English.

To be included in the meta-analysis, studies had to report on the number of patients dying/surviving among those with a specific finding at echocardiography. Study authors were contacted whenever data for meta-analysis could not be extrapolated from the text; as an alternative, study data available in previous meta-analyses were reported. In case provision of unpublished data was not possible, risk measurements (odds ratios (ORs), hazard ratios (HRs)) with 95% confidence interval (CI) were used for the meta-analyses, if available.

Study selection and data extraction

Three investigators (L.A. Cimini, M. Candeloro and M. Phywaczewska) independently reviewed the search list by title and abstract and determined study eligibility. Candidate records were then reviewed and selected for data retrieval. Two authors (L.A. Cimini and G. Maraziti) independently reviewed each study for inclusion in the critical review and in the meta-analysis and performed quality assessment and data extraction using standardised extraction forms. Disagreements were resolved through revision by an additional reviewer (M. Candeloro) and by discussion. Extracted data included information on study design (retrospective, prospective, date of publication), patient features (mean age, sex, severity of PE, *etc.*), definitions of RVD, prevalence of RVD, all-cause mortality, PE-related mortality and adverse outcome.

The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) risk of bias tool was used to assess the quality of included studies [12]. QUADAS-2 is the currently recommended tool to evaluate the risk of bias and applicability of primary diagnostic accuracy studies. QUADAS-2 consists of four key domains: patient selection, index test, reference standard, and flow and timing. Each is assessed in terms of risk of bias and the first three in terms of concerns regarding applicability.

Study outcome and measurements

The primary outcome of the meta-analysis was short-term death, defined as death occurring in-hospital or within 30 days since PE diagnosis. Secondary outcomes were: 1) short-term PE-related death; and 2) short-term adverse outcome, according to the definition used in the individual studies.

For each RV parameter at echocardiography, the following measurements were collected: number of patients with/without study outcome event based on presence/absence of the parameter; risk measurements (OR, HR) with 95% CI.

Statistical analysis

For each echocardiographic parameter, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, negative likelihood ratio, prediction intervals and 95% CI were calculated [13, 14]. For the meta-analysis, different statistics were used based on the type of available data (see supplementary material) [15, 16, 17]. We planned separate analyses for: 1) all-cause short-term death; 2) PE-related death; and 3) short-term adverse outcome.

The appropriateness of pooling data across studies was assessed using the Cochran's Chi-squared test and the I^2 test for heterogeneity [18]. I^2 statistic over 50% identified significant heterogeneity. We examined potential sources of heterogeneity by conducting sensitivity analyses in the following categories: 1) studies including only patients with echocardiography available; 2) studies including >100 patients; 3) studies published after 2010; 4) number of criteria at echocardiography used to define RVD (*e.g.*, at least one, at least two, *etc.*); 5) different echocardiographic cut-offs; 6) haemodynamically stable patients; and 7) prospective studies. The exclusion of outlier studies from the analysis was also used to address significant heterogeneity.

We also performed specific analyses for each echocardiographic parameter, whenever possible.

The statistical analyses, forest plots and publication bias analyses were performed using R version 4.0.5.

The study was performed without any external support. The authors had full access to and take full responsibility for the integrity of all the data. All authors have read and agreed to the manuscript as it is written.

Results

Critical review

Our search identified 26 052 records. After removal of 21 675 papers that did not fulfil the inclusion criteria, 265 records were retrieved for full-text examination (figure 1). 63 studies were finally retained for the systematic review.

We identified seven parameters at echocardiography for which data on mortality were reported in at least three studies: 1) RVD as a variable combination of parameters of RV overload; 2) RV/LV ratio; 3) TAPSE; 4) RV hypokinesis; 5) RV diameter; 6) PAP and 7) McConnell's sign (table 1).

Overall, 41 studies, all observational, reported on RVD at echocardiography and mortality (supplementary table S1) [19–59].

16 different definitions of RVD were used across these studies, and in particular the presence of a single criterion of RV overload was used in 16 studies, the presence of at least two criteria in eight studies and the presence of at least three parameters of RV overload were required in one study only. The most commonly used criteria of RV overload used for definition of RVD were: 1) RV dilatation; 2) RV/LV ratio; 3) paradox septal systolic motion; 4) pulmonary hypertension; 5) hypokinesis of the RV free wall; 6) tricuspid regurgitation systolic velocity over 2.6 $m \cdot s^{-1}$ from the apical or subcostal four-chamber view; 7) absence of the inspiratory collapse of the inferior vena cava; 8) McConnell's sign; and 9) TAPSE. The majority of the studies (58% of examined studies) described an association between RVD and short-term death. A meta-analysis on the association between RVD at echocardiography and clinical outcome is reported below.

The role of RV/LV ratio as predictor of clinical course in patients with acute PE was reported in 16 studies [10, 11, 23, 24, 28, 45, 60–69] (supplementary table S2).

Three different cut-off values were used across the individual studies: 0.6, 0.9 and 1.0. Controversial results were reported across studies on the association between increased RV/LV ratio and the risk of death. Published and unpublished data were pooled in a meta-analysis to assess the role of RV/LV ratio as predictor of death, and the results are reported below.

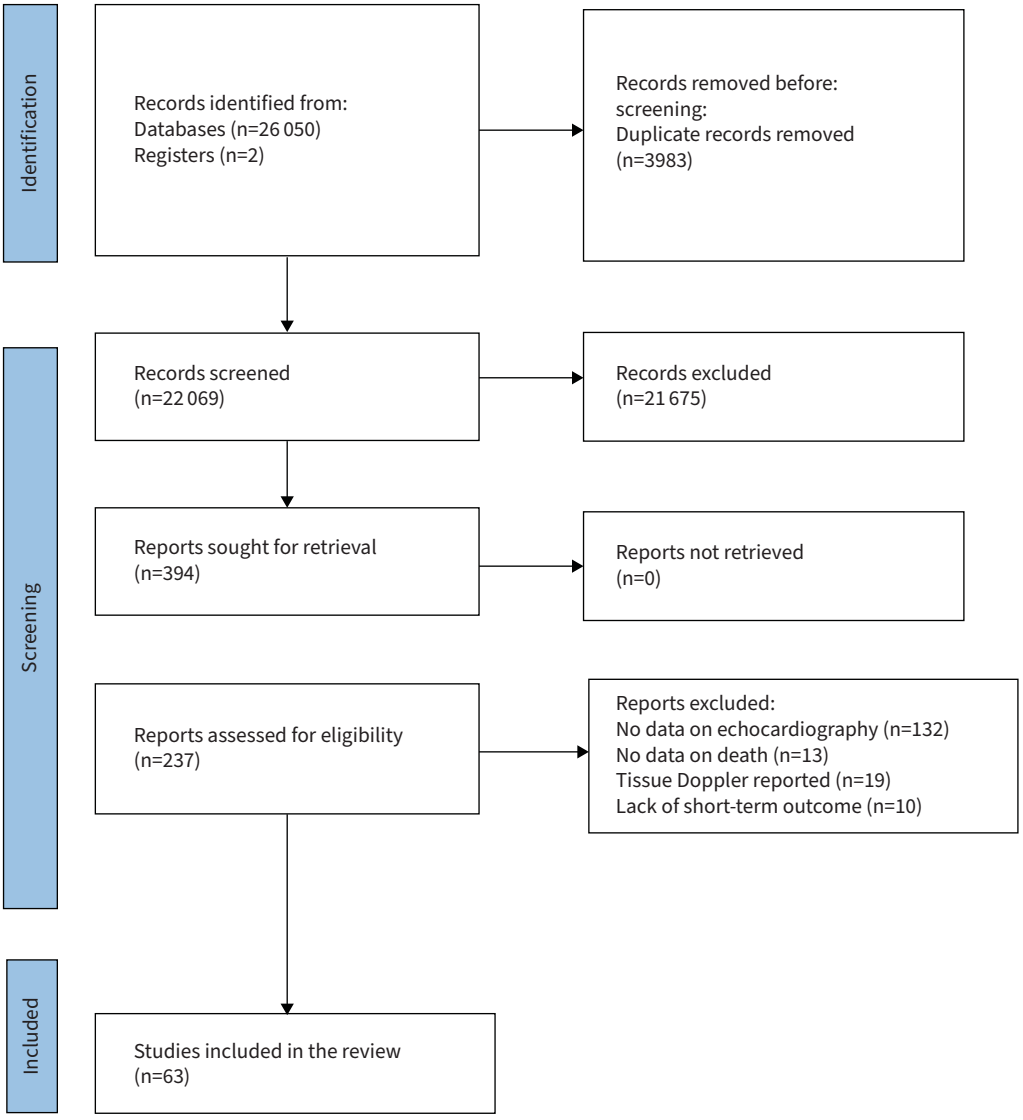

FIGURE 1 Prisma diagram of the study.

TABLE 1 Characteristics of studies according to different echocardiographic parameters

Parameter at echocardiography	Studies	Overall patients	Retrospective	Single-centre	Found an association with mortality	Found an association with adverse outcome
RVD	41	12 209	10	17	NA	NA
Hypokinesis	6	17 510	3	3	3	3
McConnell's sign	4	1078	2	4	3	NA
PAP	6	1104	3	6	6	NA
RV diameter	10	2091	4	5	7	NA
RV/LV ratio	16	6391	8	6	6	5
TAPSE	14	5697	7	8	9	1

NA: not applicable; RVD: right ventricular dysfunction as comprehensive definition; PAP: pulmonary artery pressure; RV/LV ratio: right ventricle/left ventricle diameter ratio; TAPSE: tricuspid annular plane systolic excursion.

14 observational studies assessed the role of TAPSE in the prediction of short-term death [10, 11, 45, 60, 62–65, 70–75] (supplementary table S3). A formal meta-analysis on the association between TAPSE and clinical outcome is reported below.

Among the studies reporting on TAPSE, two also described the role of TRPG/TAPSE (tricuspid regurgitation peak gradient/TAPSE) (890 patients, one retrospective, one prospective) in predicting all-cause short-term death. In both the studies, TRPG/TAPSE was associated with increased risk of all-cause short-term death. A meta-analysis was not possible for this parameter.

Six studies (17 510 patients), all observational, reported on the association between RV hypokinesis and clinical outcome [39, 60, 70, 76–78] (supplementary table S4). In all these studies, RV hypokinesis was associated with increased risk of death or adverse outcome. A meta-analysis of available data is reported below.

Four studies reported on the association between McConnell's sign and clinical outcome [10, 61, 62, 70] (supplementary table S5). All these studies, except for one, found a significant association between McConnell's sign and death.

Six observational studies (1104 patients; three prospective, three retrospectives) reported on the association between PAP and clinical outcome [48, 61, 63, 71, 79, 80] (supplementary table S6) and found an increased risk of short-term death in patients with increased PAPs; however, a meta-analysis on this parameter was not possible.

10 studies (2091 patients) assessed the association between RV diameter and clinical course in patients with acute PE [10, 11, 20, 26, 45, 48, 61, 62, 79, 80] (supplementary table S7). A meta-analysis on the prognostic role of RV diameter is reported below.

Of all included studies, four reported long-term outcomes (605 patients): two studies assessed the association between RV/LV and long-term course of PE patients, two RVD as a combination of findings and long-term course [41, 41, 61, 63]. RV/LV >1 was associated with an increased risk of long-term death (two studies, 331 patients) [61, 62]. In one study, RVD was not associated with an increased risk of long-term death [40]. However, the heterogeneity on data reporting did not allow a formal meta-analysis on the long-term value of RVD.

Quality assessment and risk of bias

Results of QUADAS-2 assessments are reported in supplementary tables S8 and S9. Several studies were judged to be at low or uncertain risk of bias. The main reasons were un-blinding of echocardiography with respect to clinical status and other risk stratification strategies, and extrapolation of PE patients with echocardiography performed from PE populations for whom echocardiography was not mandatory; the latter could have led to selection bias. Furthermore, the timing of echocardiography was not uniformly defined.

Meta-analysis: RVD and short-term death, PE-related death or adverse outcome

Out of 41 studies reporting on RVD and clinical outcome, one was excluded from the meta-analysis for lack of data [57]. Of the remaining studies, 24 (8121 patients) had data available on short-term death (in four studies after direct contact with the author) and were included in a meta-analysis [19–30, 44, 46–56, 59]. RVD was associated with increased risk of short-term death in all-comers with PE, with the presence of significant heterogeneity (risk ratio 1.49, 95% CI 1.24–1.79, I^2=64%) (figure 2, table 2). Heterogeneity decreased after excluding studies with <100 patients or studies published beyond 2010 (table 3); heterogeneity also decreased after excluding the study by Palmieri *et al.* (23 studies, 8032 patients, risk ratio 1.56, 95% CI 1.38–1.77, I^2=14%) [49]. In this single-centre study, rates of death and of haemodynamic deterioration were particularly high (13.3 and 37%, respectively) and RVD was not associated with short-term death. Among the 24 studies, RVD was associated with short-term death in studies defining RVD as the presence of at least one criterion of RV overload and in studies requiring at least two criteria but not in the single study requiring at least three criteria (one study, 89 patients, risk ratio 0.44, 95% CI 0.30–0.65) (table 3, supplementary figure S1A). When the analysis focused on studies only including haemodynamically stable patients, RVD was associated with short-term death (15 studies, 5453 patients, risk ratio 1.52, 95% CI 1.15–2.00, I^2=73%) (table 4, supplementary figure S1B).

Pooled sensitivity, specificity, PPV and NPV of RVD for short-term death are reported in table 4.

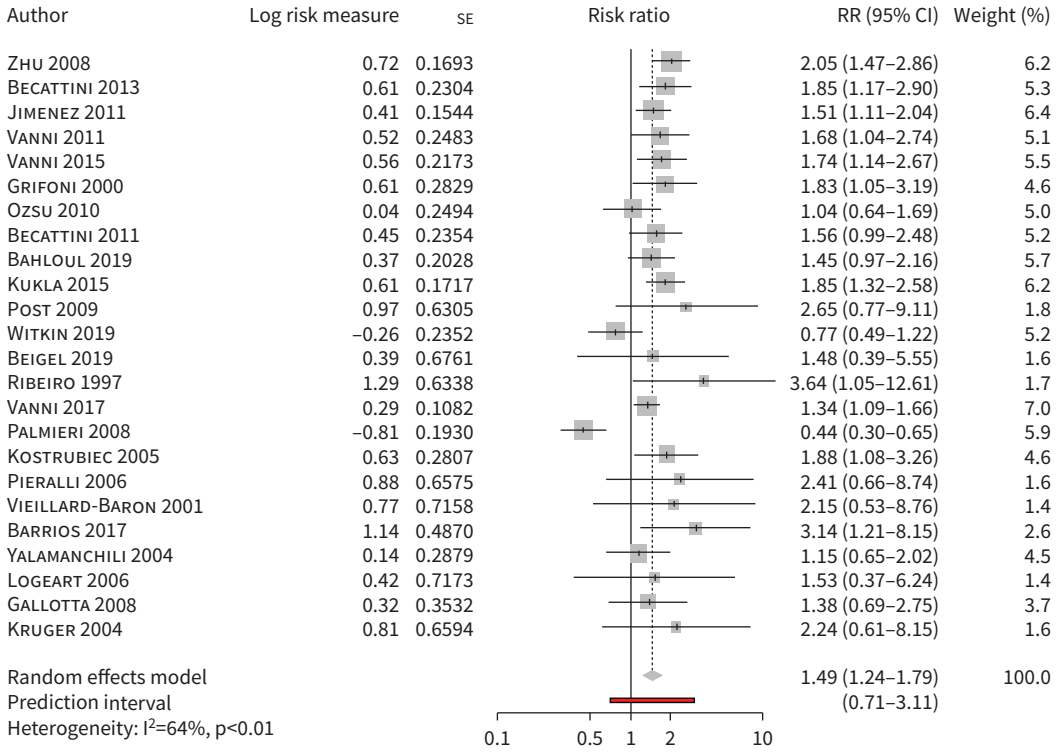

FIGURE 2 Short-term all-cause mortality in pulmonary embolism patients with *versus* without right ventricle dysfunction defined as a combination of findings at echocardiography. RR: risk ratio.

26 studies reported on the association between RVD and secondary outcomes and allowed specific meta-analyses (supplementary table S1) [19, 21, 25–28, 30–44, 49, 55, 56, 58]. Different definitions of adverse outcome were used across the included studies (supplementary table S7). RVD at echocardiography was associated with increased risk of PE-related death both in all-comers (11 studies, 3909 patients; 5.3% *versus* 2.1%, risk ratio 3.31, 95% CI 1.84–5.97, $I^2 = 0\%$) and in haemodynamically stable patients (eight studies, 2656 patients; 4.1% *versus* 2.2%, risk ratio 3.16, 95% CI 1.51–6.60) (supplementary figure S2A and SB), and of adverse outcome (20 studies, 5264 patients; risk ratio 1.68, 95% CI 1.40–2.02, I^2=55%) (supplementary figure S3).

Meta-analyses on individual parameters of RV overload and clinical outcome

Among 16 studies reporting on RV/LV diameter ratio, four were excluded from the meta-analysis due to lack of data that was not resolved after contact with the authors; finally, 12 studies were included in the meta-analysis (supplementary table S2). Increased RV/LV diameter ratio was associated with increased risk

TABLE 2 Meta-analyses on the role of RVD or individual findings at echocardiography in predicting all-cause death in all-comers with acute pulmonary embolism

Parameter at echocardiography	Studies/patients n	Risk ratio (95% CI)
RVD	24/8121	1.49 (1.24–1.79)
RV diameter	5/944	0.58[#] (0.05–1.21)
RV/LV	12/4019	1.61 (1.09–2.39)
TAPSE	11/4095	2.29 (1.45–3.59)
Hypokinesis[¶]	6/17 510	1.60 (1.14–2.25)

RVD: right ventricular dysfunction as comprehensive definition; CI: confidence interval; RV/LV ratio: right ventricle/left ventricle diameter ratio; TAPSE: tricuspid annular plane systolic excursion. [#]: standardised mean difference. [¶]: the outcome of this analysis is short-term adverse outcome.

TABLE 3 Sensitivity analyses

	Studies/patients n	Risk ratio (95% CI), I^2 (%)	Haemodynamically stable patients only risk ratio (95% CI), I^2 (%)
RVD			
Number of criteria for RVD definition:			
⩾1 echo criterion	16/5488	1.50 (1.28–1.87), 24	
⩾2 echo criteria	7/2633	1.76 (1.46–2.12), 0	1.52 (1.15–2.00), 73
⩾3 echo criteria	1/89	0.44 (0.30–0.65)[#]	
Studies including >100 patients	16/7502	1.59 (1.36–1.87), 36	-
Studies published beyond 2010	12/6318	1.47 (1.24–1.74), 33	-
RV/LV			
Different cut-offs:			
⩾1	9/2079	1.57 (0.93–2.65), 35	1.11 (0.91–1.35), 0
>1	2/990	1.09 (0.91–1.35), 0	
>0.6	1/950	3.47 (1.72–6.98)[#]	
TAPSE			
Different cut-offs:			
⩾15 mm	3/828	3.23 (1.45–7.18), 0	2.29 (0.97–5.44), 71
>16 mm	6/1159	2.19 (0.80–6.03), 66	
>20 mm	1/2108	1.68 (0.78–3.64), 0	

CI: confidence interval; RVD: right ventricular dysfunction as comprehensive definition; RV/LV ratio: right ventricle/left ventricle diameter ratio; TAPSE: tricuspid annular plane systolic excursion. [#]: the result is obtained for one study only, thus I^2 is not calculated.

of short-term death in all-comers (4019 patients; 8.3% *versus* 5.7%, risk ratio 1.61, 95% CI 1.09–2.39, I^2=46%) (supplementary figure S4, supplementary table S2). Sensitivity analyses were performed in studies including haemodynamically stable patients (table 3, supplementary figure S5A) and by grouping for different cut-offs (table 3, supplementary figure S5B). Pooled sensitivity, specificity, PPV and NPV of RV/LV diameter ratio for short-term death are reported in table 4.

Overall, 14 studies reported on the prognostic role of TAPSE. After exclusion of four studies due to lack of data, 11 were included in the meta-analysis (supplementary table S3). The risk of short-term death was higher in all-comers with reduced *versus* normal TAPSE (11 studies, 4095 patients; 9.7% *versus* 5.2%, risk ratio 2.29, 95% CI 1.45–3.59, I^2=49%) (table 2, supplementary figure S6). This result was consistent for different TAPSE cut-offs (>15 mm and ⩽15 mm) (table 3, supplementary figure 7A). When the analysis was restricted to six studies including haemodynamically stable patients only, a marginally significant association between TAPSE and short-term death was observed, with significant heterogeneity (3240 patients; risk ratio 2.29, 95% CI 0.97–5.44, I^2=71%) (table 3, supplementary figure S7B). In haemodynamically stable patients, TAPSE was not associated with PE-related death (OR 1.55, 95% CI 0.82–2.59, I^2=90%) (supplementary figure S7C). Pooled sensitivity, specificity, PPV and NPV are reported in table 4.

Six studies reported on the association between RV hypokinesis at echocardiography and short-term outcomes and were included in the meta-analysis [39, 60, 70, 76–78]. A meta-analysis on death was not possible. Hypokinesis was associated with an increased risk of short-term adverse outcome with significant heterogeneity (17 510 patients, risk ratio 1.60, 95% CI 1.14–2.25, I^2=79%) (table 2, supplementary figure S8).

TABLE 4 Accuracy of different echocardiographic parameters in predicting prognosis

Echocardiographic parameter	Sensitivity	Specificity	PPV	NPV	Positive likelihood ratio	Negative likelihood ratio
RVD	0.74 (0.6–0.9)	0.51 (0.4–0.6)	0.09 (0.06–0.12)	0.97 (0.94–0.98)	1.51	0.51
RV/LV	0.44 (0.3–0.5)	0.64 (0.6–0.7)	0.08 (0.05–0.12)	0.64 (0.57–0.71)	1.22	0.88
TAPSE	0.57 (0.5–0.6)	0.65 (0.5–0.8)	0.06 (0.04–0.1)	0.65 (0.51–0.76)	1.63	0.66

Data calculated from studies reporting number of patients with/without study outcome event based on presence/absence of the parameter. PPV: positive predictive value; NPV: negative predictive value; RVD: right ventricular dysfunction as comprehensive definition; RV/LV ratio: right ventricle/left ventricle diameter ratio; TAPSE: tricuspid annular plane systolic excursion.

The study by Bikdeli *et al.* [76] excluded from the analysis over 50% of patients who did not undergo echocardiography. After exclusion of this study from the current analysis, heterogeneity was significantly reduced and the association was confirmed (risk ratio 1.42, 95% CI 1.0–2.02, I^2=53%).

Overall, five studies reported on the association between mean RV diameter and clinical outcome and were included in the meta-analysis [10, 11, 48, 61, 62]. One study had adverse outcome and one had PE-related death as primary outcome [10, 11]. An increased RV diameter was not associated with increased risk of death or adverse outcome (five studies, 944 patients; standardised mean difference 0.58, 95% CI 0.05–1.21, I^2=63%) (table 2, supplementary figure S9).

Discussion

Our study shows that RVD, defined as a combination of findings of RV overload at echocardiography, is a predictor of short-term death in all-comers with acute PE and in haemodynamically stable patients. Among individual parameters of RVD, increased RV/LV ratio and abnormal TAPSE but not RV diameter were associated with increased risk of short-term death in all-comers with PE. In haemodynamically stable patients, neither TAPSE nor increased RV/LV ratio showed a significant association with death. RV hypokinesis was associated with the risk for short-term adverse events in all-comers. In addition, the study shows relevant heterogeneity in the definition of RVD at echocardiography in studies in patients with acute PE. This leads to a high degree of heterogeneity in almost all the estimates on the prognostic value of RVD and claims for a standardisation in the definition of RVD in patients with acute PE.

PE is a life-threatening disease, with death mainly related to acute RV failure [33], and, consequently, the identification of RV overload is considered an essential step of risk stratification for early death [3]. Echocardiography has been consistently reported as a tool for identification of RV overload and risk stratification for short-term death. However, echocardiography is an operator-dependent technique and lacks standardisation for the definition of acute RVD. The guidelines of the European Society of Cardiology report that, due to the peculiar RV geometry, no individual echocardiographic parameter can provide fast and reliable information on RV size or function [6]. Our critical review shows that 16 different definitions of RVD were used across 41 studies that reported on the prognostic role of RVD in patients with acute PE. These definitions differed for the number and type of signs of RV overload that were required for the diagnosis of RVD. Indeed, nine parameters of RV overload were described at echocardiography. In this meta-analysis we found that RVD, defined as the presence of at least one sign of RV overload or as two or more signs, is associated with ∼50% increase in the risk of short-term death in patients with acute PE. This wide range of definitions of RVD could have caused the significant heterogeneity observed in the meta-analysis of RVD in all-comers and in haemodynamically stable patients with acute PE and the wide prediction interval for this parameter. Our findings call for a standardisation in the definition of RVD at echocardiography in patients with acute PE in order to use RVD efficiently for decision making concerning patient management. Whether standardisation should refer to the role of specific signs of RV overload or to implementation of technical accuracy (*e.g.*, echocardiography with ECG trace) or to the skills of the operator (*e.g.*, differential diagnosis between chronic and acute RV overload, accuracy of measurements) remains to be defined.

Our critical review shows a correlation with death for several individual findings of RV overload at echocardiography. We were able to run formal meta-analyses for four of these findings. An association with short-term death was confirmed in all-comers with acute PE for increased RV/LV ratio, abnormal TAPSE and RV hypokinesis but not RV diameter. The lack of association between RV diameter and death is not surprising as a combined assessment of the right and left ventricle is necessary to make a final judgement. Moreover, we did not observe a significant association with death when the single parameters were evaluated in haemodynamically stable patients. The absence of significant association could be due to underpower for TAPSE, while it seems questionable for RV/LV ratio. In a recent meta-analysis, increasing RV/LV was a predictor of all-cause short-term death in haemodynamically stable patients (three studies, meta-analysis of continuous values) [81]. In our study, RV/LV was not a predictor of death in haemodynamically stable patients (six studies, meta-analysis of proportions). It is conceivable that different study methodologies led to different results; this difference again reinforces the concept of the need for standardisation of echocardiographic assessment in patients with acute PE.

Taken together our results seem to support the statement of the European Society of Cardiology (ESC) guidelines on the need for more than one abnormality at echocardiography to predict prognosis accurately. Good-quality studies suggested that a clearly increased RV/LV (RV/LV >1) combined with TAPSE <16 mm could be used to identify a group of normotensive patients with acute PE at increased risk for death [45].

PPVs and NPVs were suboptimal for the use of echocardiography as a stand-alone test for decision making. Recently, a systematic review and meta-analysis showed that RVD can be detected by computed tomography (CT) imaging; the diagnostic accuracy of CT compared with echocardiography varies depending on specific findings [82]. The assessment of multiple CT findings of RVD seems to have improved diagnostic accuracy compared to stand-alone findings. This finding is in keeping with the results of our meta-analysis, showing that the assessment of combined parameters at echocardiography has improved prognostic value in comparison to stand-alone findings.

This information is crucial for clinicians dealing with patients with acute PE as these patients may have a wide range of causes of death, and not all of them are related to RV overload. In fact, echocardiography can detect acute RVD in ∼25% of all PE patients. In haemodynamically unstable patients, bedside echocardiography is the first imaging method for the initial assessment and to guide further management including life-saving therapies [6]. In haemodynamically stable patients with suspected PE, echocardiography provides important information regarding prognosis and differential diagnosis. However, clinical assessment and laboratory markers should be integrated with echocardiographic findings for risk stratification.

Our study has some limitations. First, pooling the results from different studies resulted in significant heterogeneity that was assessed through several methods and sensitivity analyses. Only few studies reported data on more than one finding of RV overload. As a consequence, results on different findings were often obtained from different combinations of studies. Overall, 35.8% of the studies included in our meta-analyses had an uncertain risk of bias, which was due to the lack of information on several domains. We excluded all studies dealing with Doppler tissue imaging in patients with acute PE. This technique is promising, but not commonly available in the urgent setting.

Our study also has some strengths. By including over 40 studies, this is one of the most comprehensive meta-analyses on the prognostic role of RVD at echocardiography in patients with acute PE. By providing several sensitivities analyses we were able to describe the specific prognostic value of different findings and of different cut-offs.

In conclusion, echocardiography is a useful tool for risk stratification in all-comers and in haemodynamically stable patients with acute PE, but standardisation is required. The prognostic value of individual parameters of RVD in haemodynamically stable patients remains controversial indicating comprehensive assessment of RV function These results can inform future studies, guidelines and clinicians dealing with management of patients with acute PE.

Provenance: Submitted article, peer reviewed.

This study is registered at https://www.crd.york.ac.uk/prospero/ with identifier number CRD42021266948.

Conflict of interest: None declared.

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