Supplementary data

Search strategy

1. exp heart ventricle function/
2. ventricular dilation.mp. or exp ventricular dilatation/
3. pulmonary hypertension or exp pulmonary hypertension/
4. exp tricuspid annular plane systolic excursion/
5. septal motion.mp.
6. paradoxal septal motion.mp.
7. paradoxical septal motion.mp.
8. echocardiography.mp. or exp.echocardiography/
9. Exp heart right ventricular failure/
10. 2 or 3 or 4 or 5 or 7 or 8 or 9
11. Pulmonary embolism.mp. or exp lung embolism/
12. 10 and 11

Statistical analysis

We determined Risk Ratio (RR), 95% CI for all-cause short-term death in patients with RVD as assessed at echocardiography. Prediction intervals have been also calculated [14]. Data from individual studies were pooled using the Mantel-Haenszel method; we reported results according to a fixed-effects model in the absence of significant heterogeneity and to a random-effects model in the presence of significant heterogeneity [14,15]. In case data for a meta-analysis of proportions were not available, a meta-analysis of effect size was performed. We calculated the summary ORs with 95% CI from ORs or HRs extracted from the study or calculated as crude ORs from rates. Unadjusted ORs and HRs were considered for the meta-analysis and analyzed together, due to the short-term follow-up (in-hospital or ≤30 days) [16].

Funnel plots were used to assess for publication bias.

Supplementary Table 1. Characteristics of studies reporting on RVD and included in the critical review. *= mean and standard deviation or median and range. D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients; RVD: right ventricular dysfunction as comprehensive definition. sPAP: systolic pulmonary artery pressure; RV/LV ratio: right ventricle/left ventricle diameter ratio; TAPSE: Tricuspid Annular Plane Systolic Excursion; PE: pulmonary embolism; ICU: intensive care unit; CCUS: complete compression ultrasonography; cTnI: cardiac troponin I; TTE: transthoracic echocardiography; MDCT: multi-detector CT; MPA: main pulmonary artery; RVPO: right ventricular pressure overload; ESC: European Society of Cardiology; BNP: brain peptide natriuretic peptide; RHT: right heart thrombus; AF: atrial fibrillation; HsTnt: high-sensitive troponin T.

Study	Design	Follow up	Pts. (N)	Age*	Male %	Un-stable	RVD %	Objective	RVD definition
Ozsu 2010	OBP	30d	108	70 (21-90)	44	no	40	I) to define low risk patients in an outpatient setting. II) to define high risk patients	end-diastolic RV/LV, end-diastolic RV diameter or sPAP (calculated by using the maximal velocity of tricuspid regurgitation)
Bahloul 2019	OBP	In-hospital	75	53 (18)	83	y	45	to evaluate the rate and the outcome of PE in the ICU	RV dilatation or hypokinesia or abnormal movement of the interventricular septum with or without tricuspid regurgitation
Jimenez 2011	OBP	30d	591	74 (65-82)	43	no	20	to assess if a combined strategy with lower CCUS, cTnI, and TTE might offer an advantage in risk stratification	RV dilatation, hypokinesis of the RV free wall, or tricuspid systolic velocity greater than 2.6 m/s from the apical or subcostal four-chamber view
Becattini 2011	OBP	In-hospital	460	67 (16)	46	y	50	To identify a criterion for RV dysfunction at MDCT and to evaluate its prognostic value	at least two among: RV/LV >0.9 in the apical four-chamber view, or RV/LV >0.7 in the parasternal long-axis or subcostal four-chamber views, or paradoxical interventricular septal motion, or sPAP over 30 mmHg
Vanni 2011	OBR	In-hospital	160	70 (15)	42	Y	56	To assess the association between plasma lactate concentration and in-hospital mortality in patients with acute PE.	One of the following: 1) RV dilatation; 2) paradoxical septal systolic motion, or 3) pulmonary hypertension (Doppler pulmonary acceleration time < 90 msec or presence of a right ventricle ⁄ atrial gradient > 30 mm Hg).

Vanni 2015	OBP	30d	496	69 (16)	49	no	40	To determine the role of plasma lactate levels in risk assessment of normotensive patients with acute PE	At least one of the following: 1) RV dilatation (end-diastolic diameter >30 mm or RV/ LV end-diastolic diameter ratio ≥1 in apical four-chamber view); (2) pulmonary hypertension (estimated RV–right atrial trans-tricuspidal gradient over 30 mm Hg); (3) hypokinesis of the RV free wall (any view).
Vanni 2009	OBP	In-hospital	386	67 (16)	40	no	52	To investigate the prognostic value of electrocardiography alone or in combination with echocardiography in normotensive PE patients	At least one of the following: RV dilatation (end-diastolic diameter >30 mm or RV/LV >1 in apical 4-chamber view); paradoxical septal systolic motion; and/or pulmonary hypertension (Doppler pulmonary acceleration time <90 ms or presence of a right ventricular/atrial gradient >30 mm Hg)
Grifoni 2000	OBP	In-hospital	209	65 (15)	60	y	53	To evaluate the prevalence and short-term prognosis of patients with PE	One of the following: RV dilatation, systolic flattening of the interventricular septum, and Doppler evidence of pulmonary hypertension.
Becattini 2013	OBP	In-hospital	1106	68 (15)	45	y	68	To validate a model for risk stratification	Two of the following: (1) RV/LV > 1 in apical four-chamber view, (2) RV/LV 0.6 in parasternal long-axis or subcostal four-chamber view, and (3) right ventricular-to-right atrial pressure gradient> 30 mm Hg.
Zhu 2008	OBP	14d	520	57 (14)	62	no	48	To assess RVD for prognosis in PE patients identifying optimal echocardiographic indexes	at least two of the following. (1) RV dilatation: RV/LV the parasternal long-axis view >0.6 or RV/LV>1.0; (2) RV hypokinesis; (3) loss of inspiratory collapse of IVC; (4) tricuspid regurgitant jet velocity >2.8 m/s.
Krüger 2004	OBP	In-hospital	50	62(16)	72	y	62	To determine how BNP levels are affected by PE with and without RVD	Presence of any: 1) dilation of the RV (diastolic diameter >30 mm) or a RV/LV >1 in the 4-chamber view; 2) hypokinesis of the RV; 3) abnormal motion of the interventricular septum; or 4) tricuspid valve regurgitation (jet velocity >2.5 m/s).
Post 2009	OBP	14d	192	57 (17)	47	y	74	To evaluate the local therapy regimen	RV dilatation, RV hypokinesis in the apical or subcostal view and/or the presence of paradoxical

									septal wall motion or a newly developed tricuspid regurgitation
George 2014	OBR	30d	785	58.4 (17)	62	NR	44	To compare the prognostic significance of CT-derived RV/LV and TTE detection of RV strain in patients with PE	Any of following: 1) reduced RV systolic function assessed qualitatively on the basis of the RV free wall motion or presence of RV hypokinesia/ dyskinesia/ akinesia; (2) sPAP >36mm Hg; (3) moderate or severe dilatation of the RV determined qualitatively; and (4) abnormal interventricular septal movement
Kumamaru 2016	OBR	14d	236	54.8 (17)	38	Y	22	To develop a clinical prediction rule to identify the subpopulation for which CT-derived data can be used to predict normal RV function	Any of the following: (1) reduced RV systolic function assessed qualitatively based on the RV wall motion; (2) RV hypokinesia/dyskinesia/akinesia; (3) sPAP>36 mmHg; (4) moderate or severe dilatation of RV; and (5) abnormal interventricular septal movement.
Lankeit 2010	OBP	30d	156	67 (53–75)	45	no	45	To assess the role of cardiac cTnT levels using hsTnT in risk assessment	dilatation of the RV in the absence of left ventricular or mitral valve disease
Weekes 2017	OBP	30d	116	59 (26)	59	no	22	To assess early use of POC RVD testing to accurately identify RVD in PE patients	Blunt RV apex; basal RV diameter > 3.8 cm; RV > LV; Minimal to absent movement of RV free wall annulus (tricuspid annular plane systolic excursion < 1.0 cm) and diminished inward movement of RV free wall (fractional change < 18%); Flattened or bowed toward LV.
Binder 2005	OBP	In-hospital	124	60 (18)	40	y	27	To investigate whether the combination of NT-proBNP with imaging increase the prognostic value of either method alone	RV dilatation (end-diastolic diameter >30 mm from the parasternal view or the RV appearing larger than the LV from the subcostal or apical view) combined with right atrial hypertension, ie, absence of inspiratory collapse of the inferior vena cava.
Taylor 2013	OBR	In-hospital	161	60 (18)	46	y	24	To assess the prognostic value of POC for PE patients in hospital adverse events	RV/LV of ≥1 by qualitative estimate, RV hypokinesis, or a McConnell's sign. RVS was determined by the initial consciousness, lethargy, or delirium.

Dudzinski 2016	OBP	5d	104	58 (17)	52	y	40	To test the hypothesis that CT provides information on RV analogous to TTE	presence of either RV hypokinesis, RV dilatation, or interventricular septal bowing in concordance with American Society of Echocardiography guidelines
Ohigashi 2010	OBR	In-hospital	50	66 (54-78)	58	y	64	To evaluate the usefulness of biomarkers for the diagnosis of RVD	RV dilatation >30 or RV/LV>1 or RV hypokinesis or paradoxyc septal motion or sPAP>30 mmHg
Zhu 2007	OBP	14d	90	56.8 (14)	57	y	56	to assess 14-day adverse events in combined RVD at TTE and cTnI	At least 2 of the following: RV dilatation (without hypertrophy), loss of inspiratory collapse of inferior vena cava (IVC), RV hypokinesis, tricuspid regurgitant jet velocity > 2.8 m/s
Dellas 2010	OBP	30d	126	67 (51-74)	NR	no	39	To determine H-FABP, alone or in combination with clinical or echocardiographic findings, might reliably predict poor prognosis	RV dilation (end-diastolic diameter >30 mm from the parasternal view or a RV/LV diameter ratio >1.0 from the subcostal or apical views), combined with right atrial hypertension (absence of the inspiratory collapse of the inferior vena cava) in the absence of LV or mitral valve disease
Kaeberich 2015	OBP	30d	588	NR	NR	no	37	Optimised cut-off values for hsTnT and adjustment for age might provide superior prognostic value	RV dilatation combined with right atrial hypertension (absence of the inspiratory collapse of the inferior vena cava)
Lankeit 2008	OBP	30d	112	68 (55-76)	42	y	42	GDF-15 levels on admission to identify serious complications during the acute or long-term phase of PE	RV dilatation (end-diastolic diameter > 30 mm from the parasternal view, or a RV/LV > 1.0 from the subcostal or apical views), combined with right atrial hypertension (absence of the inspiratory collapse of the inferior vena cava)
Keller 2019	OBP	30d	511	69 (54-77)	44	y	51	To investigate the impact of symptoms and initial presentation on treatment and outcome	RV dilatation (RV/LV) or end-diastolic RV diameter>30mm combined with absence of the inspiratory collapse of the inferior vena cava on TTE
Beigel 2019	OBR	In-hospital	179	66 (16)	47	no	66	To evaluate a cohort of intermediate-risk PE patients with evidence of RV involvement, to	One of the following: a) an increased RV/LV ratio; b) an enlarged RV diameter of>35mm at the mid-ventricular level or>41mm at the base of the RV; or c) RV contractile dysfunction

								identify poor outcomes	
Pruszczyk 2020	OBP	30d	490	64 (18)	53	no	12	to compare echocardiographic parameters for the prediction of adverse 30-day outcome	TAPSE<16 mm and RV/LV <1
Vanni 2017	OBR	30d	994	74 (64-81)	50	no	29	to compare the efficiency of the 2014 ESC model, Bova and TELOS scores	At least one of the following: (1) RV dilatation (end-diastolic diameter); (2) sPAP >30 mmHg); and (3) hypokinesis of the RV-free wall (any view).
Witkin 2019	OBR	7d	326	NR	NR	NR	45	To assess mortality and need for intensive therapies in patients with PE who had TTE evidence of chronic RVPO than patients without chronic RVPO	RV dilatation, hypokinesis or septal bowing or flattening without fulfilling the criteria for chronic RVPO
Ribeiro 1997	OBP	In-hospital	126	NR	56	y	55	To evaluate if the degree of systolic RVD is a predictor of mortality during hospitalization	RV systolic dysfunction was assessed by qualitative evaluation of the RV wall motion; tricuspid regurgitation was assessed qualitatively; A normal PASP was defined as <30 mmHg
Palmieri 2008	NR	In-hospital	89	NR	NR	no	NR	increased cTnI and RVD had prognostic relevance in addition to a novel clinically based prognostic risk score	RV dilatation associated with paradoxical interventricular septal motion, and with depressed RV systolic function either global (tricuspid anulus peak systolic excursion \15 mm) or segmental (basal segments)
Kostrubiec 2010	OBP	30d	212	64 ± 18	38	y	58	renal dysfunction as independent marker of early mortality in PE, and in addition to troponin-based risk stratification.	RV free wall hypokinesis and RV/LV > 0.9 in a four-chamber view, and/or (ii) an elevated tricuspid valve pressure gradient exceeding 30 mmHg with a shortened acceleration time of pulmonary ejection below 80 ms
Pieralli 2006	OBP	In-hospital	61	75 ± 14	26	no	57	to investigate the value of BNP for the identification of RV	(1) RV dilation (end-diastolic diameter 30 mm or RV/LV in 4-chamber view), (2) RV free wall hypokinesia, (3) paradoxic septal systolic motion,

								dysfunction and its prognostic value	and (4) pulmonary hypertension (Doppler pulmonary acceleration time 90 ms or the presence of a RV or right atrial gradient 30 mm Hg)
Vieillard-Baron 1001	OBR	In-hospital	98	NR	NR	y	NR	To examine the prevalence of acute cor pulmonale in PE, diagnosed on the basis of TTE criteria	Combining RV enlargement, as indicated with RV/LV end diastolic area with septal dyskinesia
Barrios 2017	OBP	30d	848	67.4 ± 16.7	49	no	23	to evaluate the optimal approach to assess RV function in normotensive PE patients	Dilatation of the RV (end-diastolic diameter > 30 mm from the parasternal view or the RV larger than LV from the subcostal or apical view), hypokinesis of the RV free wall (any view), and estimated systolic pulmonary artery pressure over 30 mm Hg
Yalamanchili 2004	OBR	In-hospital	81	NR	NR	y	27	To report in-hospital mortality in patients with PE with and without increased cardiac troponin I	RV dilation (RV end-diastolic diameter 30 mm), hypokinesia, and paradoxic RV septal systolic motion
Logeart 2007	OBP	In-hospital	67	69 ± 15	56	no	54	to compare the value of BNP and troponin as well as clinical and electrocardiographic characteristics for diagnosing RVD	RV/LV diameter ratio > 0.7, hypokinesis of the RV free wall, inferior cava vena diameter > 10 mm during inspiration, interventricular septum bulging in the LV, and tricuspid regurgitant jet velocity > 2.7 m/s.
Gallotta 2008	OBP	In-hospital	90	67 ± 18	26	no	59	To assess adverse outcomes in association with increased troponin I at admission independently of clinical, electrocardiographic, echocardiographic and laboratory information	any of the following findings: 1) paradoxical interventricular septal motion; 2) RV dilation (diastolic diameter >15 mm/m2); 3) low RV systolic function (systolic excursion of the tricuspid anulus <15 mm)

Samaranayake 2015	NR	30d	61	63.1 (27–97)	47	no	86	to determine the rates and factors associated with the development of persistent RVD and/or PHT and all-cause mortality	main pulmonary artery (MPA) diameter >33 mm or MPA to aorta diameter ratio >1.1 and/or (ii) signs of RV dilatation or straightened or leftward bowed interventricular septum
Jimenez 2014	OBP	30d	848	72 (59–80)	49	no	23	to derive a multimarker model for estimating risk in normotensive patients with PE.	dilatation of the RV, hypokinesis of the RV free wall, and estimated systolic pulmonary artery pressure greater than 30 mm Hg
Kukla 2015	OBR	In-hospital	975	65.8 (14)	41	y	76	to determine the prevalence of RHT and AF and to assess their impact on outcomes in PE patients	RV diameter >30 mm in the parasternal view or RV/LV ratio >1, acceleration time of RV ejection <90 ms or tricuspid insufficiency peak gradient >30 mm Hg without RV hypertrophy, paradoxical systolic movement of the septum, presence of hypokinesia or akinesia of the RV free wall, or presence of RHT

Supplementary Table 2. Characteristics of studies reporting on RV/LV and included in the critical review. *= mean and standard deviation or median and range. D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients; RVD: right ventricular dysfunction; RV/LV ratio: right ventricle/left ventricle diameter ratio; PE: pulmonary embolism; cTnI: cardiac troponin I; TTE: transthoracic echocardiography; MDCT: multi-detector CT; TAPSE: Tricuspid Annular Plane Systolic Excursion.

Study	Design	Follow up	Pts. (N)	Age*	Male %	Unstable	Altered RV/LV %	RV/LV cut off	Objective
Khemasuwan 2015	OBR	In-hospital	211	61 (15)	49	y	52	≥1	To identify the most important echocardiographic parameters that predict adverse clinical outcomes in patients with acute PE.
Zanobetti 2013	NR	30d	120	73 (14)	43	y	50	≥1	identify 1 or more ECG indices of RV anatomy and function predictors of short-term RV dysfunction in patients with PE
Pruszczyk 2014	OBP	In-hospital	411	64 (18)	43	no	29	≥1	evaluate the prognostic value of echocardiographic indices of RVD for prediction of adverse clinical outcomes in initially normotensive patients with acute pulmonary embolism
Ciurzyński 2018	OBR	30d	400	66 (20-101)	48	no	36	≥1	to analyses the prognostic value of a new echocardiographic parameter, TRPG/ TAPSE, for prediction of adverse clinical outcomes in initially normotensive APE patients
Paczyńska 2015	OBP	30d	76	68 (19-94)	46	no	39	≥1	to compare right ventricular RV/LV measured by echocardiography and MDCT with TAPSE as a prognostic factor of APE-related 30-day mortality
Dahhdan 2016	OBR	30d	65	55 (43-72)	48	y	14	≥1	the addition of quantitative echocardiographic markers of RV function would add to clinical parameters to predict outcomes in patients with acute PE
Stein 2010	OBR	In-hospital	900	65 (17)	64	no	26	>1	to further assess in-hospital mortality of stable patients with PE who have RV enlargement and/or an increase of cTnI
Frémont 2008	OBR	In-hospital	950	69 (14)	40	y	28	≥0.6	to determine whether that criterion had independent prognostic value and, if so, to determine the critical cutoff of the ratio with respect to predicting hospital mortality
Kanar 2019	OBR	In-hospital	142	56.9 (13)	58	y	13	>1	was to evaluate RV mechanical functions and dyssynchrony and to consider their relationship with early hospital mortality in patients with APE
Zhu 2008	OBP	14d	520	57 (14.4)	62	y	NR	0.6	To assess RVD for prognosis in PE patients identifying optimal echocardiographic indexes
Sanchez 2010	OBP	30d	570	68 (52–	47	y	NR	NR	to assess the additional prognostic value of echocardiography and biomarkers for stratifying patients with PE in different risk categories

				77)					
Sanchez 2013	OBP	30d	592	67 (52–77)	47	no	NR	>0.9	to determine whether the combination of echocardiography and biomarkers with the PESI improves the risk stratification of patients with PE compared with the PESI alone
Pruszczyk 2003	OBR	In-hospital	64	61 (17)	53	no	NR	NR	We checked whether the detection of ongoing RV myocardial injury by the monitoring of cardiac troponin T (cTnT) levels might help in the risk stratification of patients with PE
Pruszczyk 2020	OBP	30d	490	64 (18)	53	no	36	>1	to compare echocardiographic parameters for the prediction of adverse 30-day outcome in normotensive patients with acute pulmonary embolism, and to develop an optimal definition of RVD
Vanni 2011	OBR	In-hospital	384	70 (15)	42	y	43	≥1	To assess the association between plasma lactate concentration and in-hospital mortality in patients with PE
Vanni 2015	OBP	30d	496	69 (16)	49	no	41	≥1	To determine the role of plasma lactate levels in the risk assessment of normotensive patients with acute PE

Supplementary Table 3. Characteristic of studies reporting on TAPSE and included in the critical review

*= mean and standard deviation or median and range. D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients; RVD: right ventricular dysfunction; RV/LV ratio: right ventricle/left ventricle diameter ratio; PE: pulmonary embolism; MDCT: multi-detector CT; TAPSE: Tricuspid Annular Plane Systolic Excursion; LVOT VTI: left ventricular outflow tract velocity time; BUN: blood urea nitrogen.

Study	Design	Follow up	P (N)	Age*	Male (%)	Unstable	Altered TAPSE (%)	TAPSE cut off (mm)	Objective
Lobo 2014	OBP	30d	782	73(59-80)	49	no	45	>20	To establish the relationship between TAPSE and clinical outcomes in normotensive patients with acute symptomatic PE.
Lobo 2014	OBR	30d	1326	72 (58-80)	48	no	46	>20	To establish the relationship between TAPSE and clinical outcomes in normotensive patients with acute symptomatic PE.
Khemasuwan 2015	OBR	In-hospital	211	61 (15)	49	y	31	≥16	To identify the most important echocardiographic parameters that predict adverse outcome in patients with acute PE.
Zanobetti 2013	NR	30d	120	73 (14)	43	y	47	≥16	To identify 1 or more ECG indices of RV anatomy and function predictors of short-term RV dysfunction in patients with PE
Pruszczyk 2014	OBP	In-hospital	411	64 (18)	43	no	9	≥16	To evaluate the prognostic value of echocardiographic indices of right ventricular dysfunction (RVD) for adverse outcomes in initially normotensive patients with acute pulmonary embolism
Yuriditsky 2019	OBR	In-hospital	188	57 (17)	49	y	20	≥16	To determine the association between LVOT VTI and in-hospital mortality or adverse outcomes
Ciurzyński 2018	OBR	30d	400	66 (20-101)	48	no	12	≥15	To analyses the prognostic value of a new echocardiographic parameter, TRPG/ TAPSE, for prediction of adverse outcomes in initially normotensive APE patients
Paczyńska 2015	OBP	30d	76	68 (19-94)	46	no	17.1	≥15	To compare RV/LV measured by echocardiography and multidetector computed tomography (MDCT) with TAPSE as a prognostic factor of APE-related 30-day mortality
Dahhdan 2016	OBR	30d	65	55 (43-72)	48	y	20	≥16	The addition of quantitative echocardiographic markers of RV function would add to clinical parameters to predict outcomes in patients with acute PE
Tatlisu 2017	OBR	In-hospital	252	64 (15)	47	y	37.6	≤15	To investigate the association of BUN levels with in-hospital and long-term adverse clinical outcomes in APE patients treated with the tissue plasminogen activator
Carroll 2018	OBR	In-hospital	455	63 (16)	47	y	27	<16	to determine the potential additive value of multiple parameters of RV strain and to evaluate the association of each individual parameter with adverse events in acute PE
Lee 2019	OBP	In-hospital	144	56 (17)	50	no	NR	NR	We aimed to evaluate the prognostic value of echocardiographic measurements of RV systolic function for clinical outcomes in patients with acute non-massive PE.

Kanar 2019	OBP	In-hospital	142	57 (13)	58	y	NR	NR	To evaluate RV mechanical functions and dyssynchrony and to consider their relationship with early hospital mortality in patients with APE
Pruszczyk 2020	OBP	30d	490	64 (18)	53	no	18	<16	to compare echocardiographic parameters for the prediction of adverse 30-day outcome in normotensive patients with acute pulmonary embolism, and to develop an optimal definition of RVD
Osken 2021	OBR	In-hospital	635	62 (16.3)	46	NR	31	<16	we aimed to compare the ECG and echocardiographic parameters between older and younger patients and to evaluate the predictors of in-hospital mortality among APE patients.

Supplementary Table 4. Characteristics of studies reporting on hypokinesis and included in the critical review

*= mean and standard deviation or median and range. D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients; RVD: right ventricular dysfunction; RV/LV ratio: right ventricle/left ventricle diameter ratio; PE: pulmonary embolism; MDCT: multi-detector CT; TTE: transthoracic echocardiography.

Study	Design	Follow up	Pts (N)	Age*	Male (%)	Unstable	Hypokinesis (%)	Objective
Zhu 2008	OBP	14d	520	57 (14.4)	62.1	no	78	RVD for prognosis in APE patients identifying optimal echocardiographic indexes
Bikdeli 2018	OBP	30d	15375	65.9 (17.2)	46	y	23	to report the real-world use and predictors of early TTE (within the first 72 hours from diagnosis) in patients with PE, and to explore the association between some of the main TTE findings and 30-day PE-related mortality in unadjusted and adjusted analyses
Kucher 2005	OBP	30d	1035	67 (21-91)	44.1	No	42	we investigated whether echocardiographic RV hypokinesis helps predict early death in the large group of patients enrolled in the International Cooperative Pulmonary Embolism Registry (ICOPER) who presented with a preserved systemic arterial pressure
Dahhan 2016	OBR	30d	69	55 (43-72)	52	y	45	the addition of quantitative echocardiographic markers of RV function would add to clinical parameters to predict outcomes in patients with acute PE
Park 2012	OBR	30d	56	63.5 (52–71)	50	y	36	we aimed to test the hypothesis that chest CT is a valuable rapid method of identifying RV dysfunction and predicting poor clinical outcomes, by comparing the two imaging methods in the same patients
Carroll 2018	OBR	In-hospital	455	63 (16.2)	47	y	62	to determine the potential additive value of multiple parameters of RV strain and to evaluate the association of each individual parameter with adverse events in acute PE

Supplementary Table 5. Characteristics of studies reporting on McConnell's sign and included in the critical review

*= mean and standard deviation or median and range. RV: right ventricular dysfunction; D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients

Study	Design	Follow up	Pts (N)	Age*	Male (%)	Unstable	McConnell's sign (%)	Objective
Pruszczyk 2014	OBP	In-hospital	411	64 (18)	43	no	18	evaluate the prognostic value of echocardiographic indices of RVD prediction of pulmonary embolism–related 30-day mortality or need for rescue thrombolysis in initially normotensive patien with acute pulmonary embolism
Carroll 2018	OBR	In-hospital	455	63 (16.2)	47	y	14	to determine the potential additive value of multiple parameters of RV strain and to evaluate the association of each individual parameter with adverse events in acute PE
Khemasuwan 2015	OBR	In-hospital	211	61 (15)	49	y	14	To identify the most important echocardiographic parameters that predict medical ICU, hospital, an long-term mortality in patients with acute PE.
Zanobetti 2013	NR	30d	120	73 (14)	43	y	39	identify 1 or more ECG indices of RV anatomy and function predictors of short-term RV dysfunction in patients with PE

Supplementary Table 6. Characteristics of studies reporting on sPAP and included in the critical review

*= mean and standard deviation or median and range. RV: right ventricular dysfunction; D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients**;** sPAP: systolic pulmonary artery pressure

Study	Design	Follow up	Pts (N)	Age*	Male %	Unstable	Increased PAPs %	PAPs cut off (mmHg)	Objective
Ribeiro 1997	OBP	In-hospital	126	NR	56	y	76	≤30	The degree of RV systolic dysfunction, as assessed by ED at the time of diagnosis of PE, is a predictor of mortality rate during hospitalization and within 1 year.
Sukhija 2005	OBR	In-hospital	190	58 (15)	45	y	34	50	The association of in-hospital mortality with different echocardiographic signs of RV dysfunction
Tatlisu 2016	OBR	In-hospital	252	64(15)	47	y	NR	NR	To investigate the association of BUN levels with in-hospital and long-term adverse clinical outcomes in APE patients treated with the tissue plasminogen activator
Meneveau 2003	OBP	In-hospital	183	66 (14)	44	y	74	>30	To evaluate the in-hospital course and long-term evolution of patients with massive PE submitted to thrombolytic therapy, and to determine the independent predictors of short and long-term prognosis in these patients
Khemasuwan 2015	OBR	In-hospital	211	61 (15)	49	y	NR	NR	To identify the most important echocardiographic parameters that predict medical ICU, hospital, and long-term mortality in patients with acute PE.
Kanar 2019	OBP	In-hospital	142	56.9 (13)	58	y	NR	NR	To evaluate RV mechanical functions and dyssynchrony and to consider their relationship with early hospital mortality in patients with APE

Supplementary Table 7. Characteristics of studies reporting on RV diameter and included in the critical review

*= mean and standard deviation or median and range. RV: right ventricle dysfunction; D: days; OBP: observational prospective; OBR: retrospective; NR: not reported; y: yes; Unstable: hemodynamic instability; Pts: patients**;** TAPSE: Tricuspid Annular Plane Systolic Excursion; ED: echocardiography Doppler; ICU: intensive care unit.

Study	Design	Follow up	P (N)	Age*	Male %	Unstable	Altered RV diameter %	RV diameter cut off (mm)	Objective
Pruszczyk 2014	OBP	In-hospital	411	64 (18)	43	no	NR	NR	To evaluate the prognostic value of echocardiographic indices of RVD for prediction of pulmonary embolism–related 30-day mortality or need for rescue thrombolysis in initially normotensive patients with acute pulmonary embolism
Sukhija 2005	OBR	In-hospital	190	58 (15)	45	y	34	≥4.5	The association of in-hospital mortality with different echocardiographic signs of RV dysfunction
Paczyńska 2015	OBP	30d	76	68 (19-94)	46	no	NR	NR	To compare RV/LV ratio measured by echocardiography and multidetector computed tomography (MDCT) with TAPSE as a prognostic factor of APE-related 30-day mortality
Meneveau 2003	OBP	In-hospital	183	66 (14)	44	y	83	NR	To evaluate the in-hospital course and long-term evolution of patients with massive PE submitted to thrombolytic therapy, and to determine the independent predictors of short and long-term prognosis in these patients
Khemasuwan 2015	OBR	In-hospital	211	61 (15)	49	y	NR	NR	To identify the most important echocardiographic parameters that predict medical ICU, hospital, and long-term mortality in patients with acute PE
Zanobetti 2013	NR	30d	120	73 (14)	43	y	NR	NR	To identify 1 or more ECG indices of RV anatomy and function predictors of short-term RV dysfunction in patients with PE
Ribeiro 1997	OBP	In-hospital	126	NR	56	Y	NR	NR	the degree of RV systolic dysfunction, as assessed by ED at the time of diagnosis of PE, is a predictor of mortality rate during hospitalization and within 1 year.
Bahloul 2019	OBP	In-hospita	75	53 (18)	83	y	NR	NR	to evaluate the rate and the outcome of PE in the ICU

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Grifoni 2000	OBP	In-hospital	209	65 (15)	60	y	42.5	>30	To evaluate the prevalence and short-term prognosis of patients with objectively confirmed PE, normal blood pressure, and echocardiographic RV dysfunction
Pruszczyk 2020	OBP	30d	490	64 (18)	53	no	NR	NR	to compare echocardiographic parameters for the prediction of adverse 30-day outcome in normotensive patients with acute pulmonary embolism, and to develop an optimal definition of RVD

Supplementary Table 7. Adverse outcome definition across different studies included in the meta-analysis of RVD

Study	Adverse outcome definition
Lankeit 2008	need for catecholamine administration (except for dopamine at a rate of 5 mg/kg/min or less) to maintain adequate tissue perfusion and prevent or treat cardiogenic shock, endotracheal intubation, or cardiopulmonary resuscitation
Becattini 2013	clinical worsening from a stable to an unstable hemodynamic condition that required at least one of the following: (1) IV catecholamine infusion to maintain adequate tissue perfusion and prevent or treat cardiogenic shock, (2) endotracheal intubation, or (3) CPR.
Binder 2005	Not reported
Kaeberich 2015	adverse 30-day outcome defined as pulmonary embolism-related death, need for mechanical ventilation, cardiopulmonary resuscitation, or catecholamine administration (except for dopamine at an infusion rate of ⩽5 μg per kg of body weight per minute)
Vanni 2009	composite of death for any cause and clinical deterioration (defined as progression to shock, mechanical ventilation, or cardiopulmonary resuscitation, or the need for infusion of a catecholamine, except for dopamine infused at a rate ≤5 μg /kg/min)
Dellas 2010	1) need for catecholamine administration (except for dopamine at a rate of ≤5 μg/kg/min) to maintain adequate tissue perfusion and prevent or treat cardiogenic shock; 2) endotracheal intubation; or 3) cardiopulmonary resuscitation
Keller 2019	adverse outcome (primary study outcome) was defined as PE-related death, need for mechanical ventilation, cardiopulmonary resuscitation or administration of catecholamines (except for dopamine at an infusion rate of ≤5 μg/kg body weight/min)
Lankeit 2010	(i)need for catecholamine administration (except for dopamine at a rate of ≤5 mg/kg/min) to maintain adequate tissue perfusion and prevent or treat cardiogenic shock; (ii) endotracheal intubation; and (iii) cardiopulmonary resuscitation.
Weekes 2017	Signs of clinical deterioration after admission, including escalating ventilatory support, systolic blood pressure at or below 90 mm Hg, new dysrhythmia, the need for systemic or catheter-based thrombolysis, or advanced PE therapy such as embolectomy or extracorporeal membrane oxygenation
Beigel 2019	any one of the following: 1. A drop in systolic blood pressure to<90 mmHg for at least 15 min, or a drop of blood pressure of>30 mmHg from baseline, accompanied by signs of end-organ hypoperfusion; 2. The need for vasopressor support to maintain adequate organ perfusion or blood pressure of>90 mmHg; 3.The need for cardiopulmonary resuscitation; 4. The need for mechanical ventilation; 5. The need for reperfusion (either by thrombolysis or surgical embolectomy) and 6. Mortality during hospitalization
Taylor 2013	shock (systolic blood pressure persistently <100 mm Hg refractory to volume loading and requiring vasopressors), respiratory failure requiring intubation, death, and recurrent venous thromboembolism (according to Kline et al.). Additionally, clinical deterioration as evidenced by transition to higher level of care (floor to stepdown, or stepdown to intensive care unit), and major bleeding during hospital admission were included as adverse outcomes.
Pruszczyk 2020	at least one of the following: PE-related death, rescue thrombolysis, or hemodynamic collapse (which was defined as cardiopulmonary resuscitation; or systolic blood pressure <90 mm Hg for at least 15 minutes with signs of end-organ hypoperfusion; or a need for intravenous catecholamine administration
Zhu 2007	defined as death or at least one of the following: need for vasoactive agents, endotracheal intubation, cardiopulmonary resuscitation
Jimenez 2014	death from any cause, hemodynamic collapse, or adjudicated recurrent PE
Gallotta 2008	development of hemodynamic instability, defined as systolic blood pressure b90 mm Hg or a blood pressure drop ≥40 mm Hg for N15 min with signs of organ hypoperfusion not due to hypovolemia or sepsis; death due to shock or arrhythmias
Post 2009	Not reported

Grifoni 2000	Not reported
Logeart 2006	In-hospital death or circulatory failure
Dudinski 2016	a composite of severe clinical deterioration occurring within 5 days of PE diagnosis, defined as: need for cardiopulmonary resuscitation or advanced cardiac life support, respiratory support with positive pressure ventilation or intubation and mechanical ventilation, hemodynamic support with inotropes and/or vasopressors, unstable dysrhythmia including ventricular tachycardia or ventricular fibrillation, or need for systemic or catheter-directed thrombolysis or surgical thromboembolectomy
Ohigashi 2010	a composite of severe clinical deterioration occurring within 5 days of PE diagnosis, defined as: need for cardiopulmonary resuscitation or advanced cardiac life support, respiratory support with positive pressure ventilation or intubation and mechanical ventilation, hemodynamic support with inotropes and/or vasopressors, unstable dysrhythmia including ventricular tachycardia or ventricular fibrillation, or need for systemic or catheter-directed thrombolysis or surgical thromboembolectomy

Table 8 Risk of bias of RVD studies based on QUADAS2

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Grifoni 2000	☺	☺	☺	☺	☺	☺	☺
Ribeiro 1997	☹	☹	☺	☺	☺	☺	☺
Post 2009	☺	☺	☺	?	☺	☺	☺
Becattini 2013	☺	?	?	?	☺	?	?
Kruger 2004	☹	☺	☺	☺	☺	☺	☺
Jiménez 2011	☹	☺	☺	☺	☹	☺	☺
George 2014	☹	☹	☺	?	☹	☺	☺
Zhu 2008	?	☹	☹	☺	☺	☺	☺
Dellas 2010	☹	☺	?	?	☺	?	?
Kaeberich 2015	☹	?	?	?	☺	☹	☹
Becattini 2011	☹	☹	☺	☺	☺	☺	☺
Vanni 2011	☹	☹	☹	☺	☺	☺	☺
Vanni 2015	☺	☹	☹	☺	☺	☺	☺
Vanni 2009	☹	?	?	?	☹	?	?
Bahloul 2019	☹	☹	☹	?	?	☹	☹
Ozsu 2010	☺	☺	☺	?	☺	☺	☺
Keller 2019	☺	☹	☹	☹	☺	?	?
Beigel 2019	☺	☹	☹	☺	☺	☹	?
Kumamaru 2016	☹	☹	☺	☹	☹	☹	☺
Taylor 2013	☹	☺	☺	☹	☹	☺	☺
Dudzinski 2016	?	☺	☺	☺	?	☺	☺
Lankeit 2010	☹	?	?	☺	☺	☺	☺
Weekes 2017	☺	☺	☺	☺	☺	☺	☺
Lankeit 2008	☺	☺	?	☺	☺	☺	☺
Ohigashi 2010	☹	☺	☺	☺	☹	☺	☺
Zhu 2007	☹	?	?	?	☹	?	?
Binder 2005	☹	☺	☺	☺	☹	☺	☺
Kukla 2015	☺	?	?	?	☺	?	?
Witkin 2019	☺	?	?	☺	☺	?	☺
Vanni 2017	☺	☺	?	☺	☺	☺	☺
Palmieri 2008	☺	?	☹	☺	☺	?	☺
Kostrubiec 2005	☺	☹	☹	☺	☺	☺	☺
Pieralli 2006	☹	☺	☺	?	☹	☺	☺
Vieillard-Baron 2001	☹	?	?	☺	☹	?	☺
Barrios 2016	?	?	?	☺	?	?	?
Yalamanchili 2004	☹	☹	☹	?	☹	☹	☹
Logeart 2006	☺	☺	☺	☺	☺	☺	☺
Gallotta 2008	☺	?	☹	?	☺	?	☺

Pruszczyk 2020	☺	☹	☹	☺	☺	☹	?
Jimenez 2014	☺	?	?	☺	☺	?	?

Table 9 Risk of bias of individual parameters of RV overload based on QUADAS2

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Lobo 2014	☺	☺	☺	☺	☺	☺	☺
Dahhan 2016	?	☹	☹	☺	☹	☺	☺
Ciurzyński2018	☺	☹	☺	☺	☺	☹	☺
Paczyńska 2015	☹	?	?	☺	☹	☺	☺
Frémont 2008	☺	?	?	☹	☹	☹	?
Khemasuwan 2015	☺	☺	☺	☺	☺	☺	☺
Pruszczyk 2014	☺	?	?	☺	☺	☺	☺
Stein 2010	?	☹	?	?	☺	☹	☹
Yuriditsky 2019	☺	☺	?	☺	☺	☺	?
Zanobetti 2013	?	☺	☺	?	☺	☺	☺
Tatlisu 2017	?	☹	☹	☹	?	☹	☹
Kanar 2019	☺	☺	☺	☺	☺	☺	☺
Kucher 2005	☺	☹	☹	?	☺	☹	☹
Carroll 2018	☹	?	?	☺	☹	?	?
Bikdeli 2018	☹	?	?	?	☹	?	?
Park 2012	☹	?	?	?	☹	?	?

Figure 1A. Meta-analysis on the association between RVD and death by number of criteria used for the definition of RVD

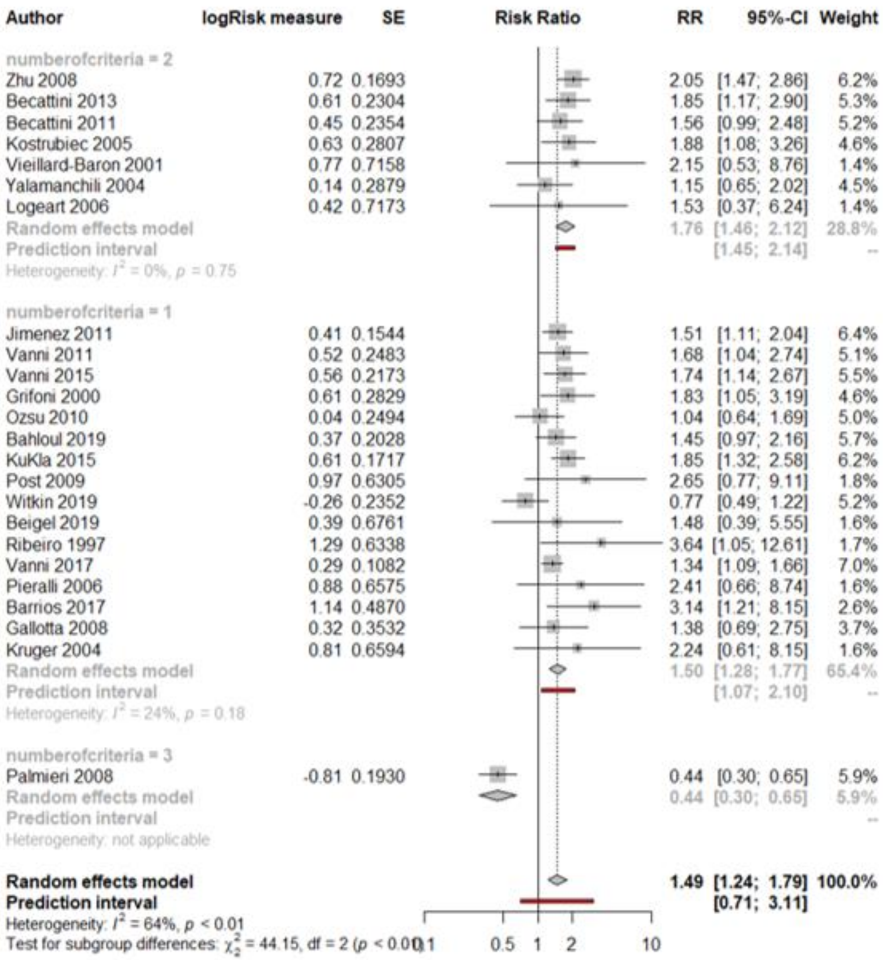

Figure 1B. Sensitivity analysis for RVD studies for hemodynamic stable patients

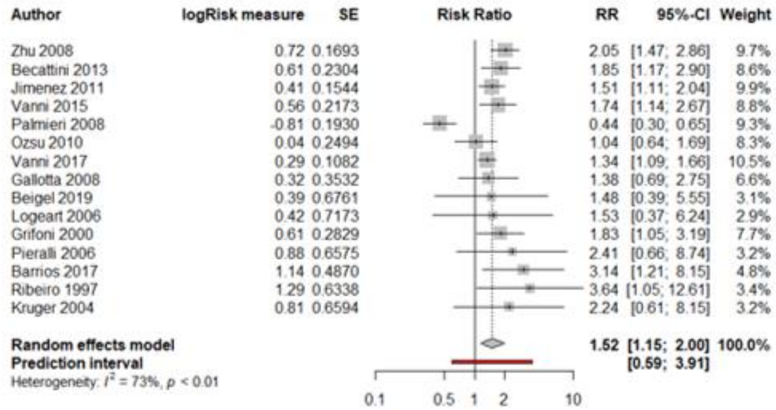

Figure 2A. Meta-analysis on the association between RVD and PE-related death

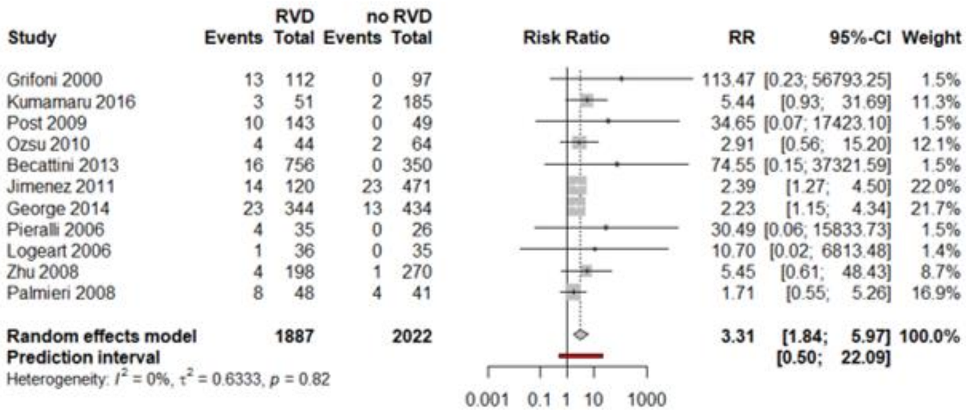

Figure 2B Meta-analysis on the association between RVD and PE-related death in hemodynamically stable patients.

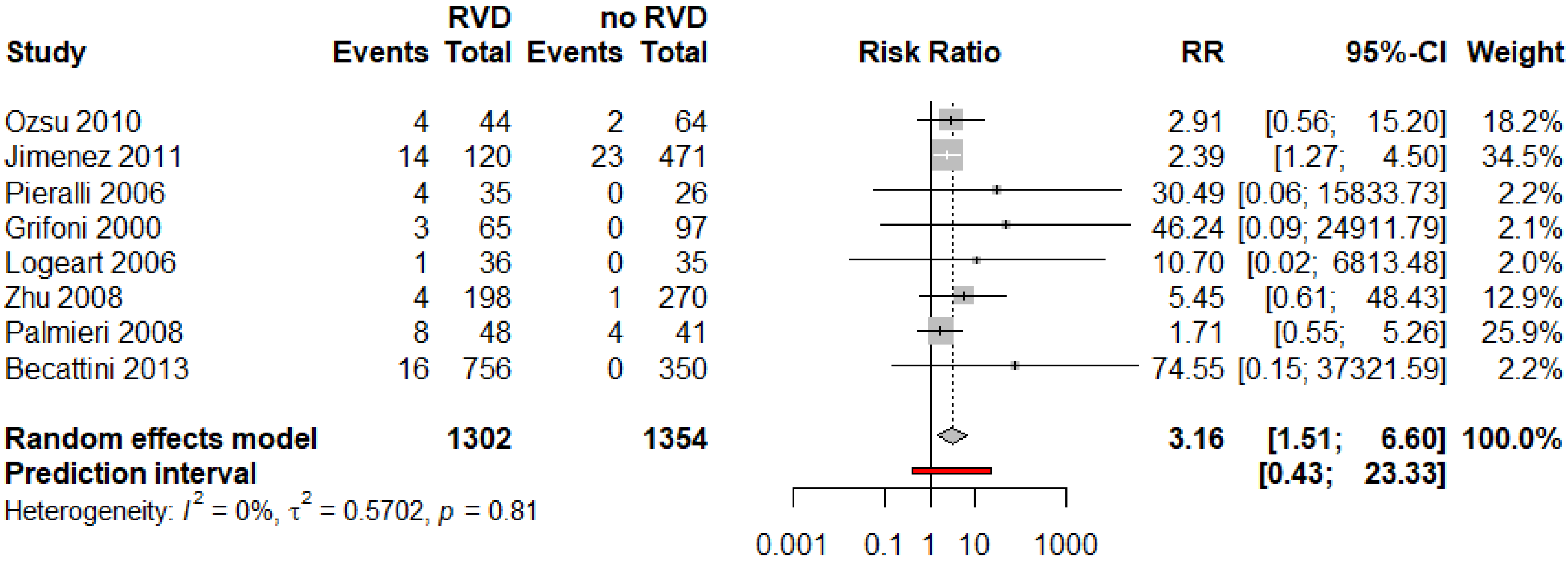

Figure 3 Meta-analysis on the association between RVD and adverse outcome.

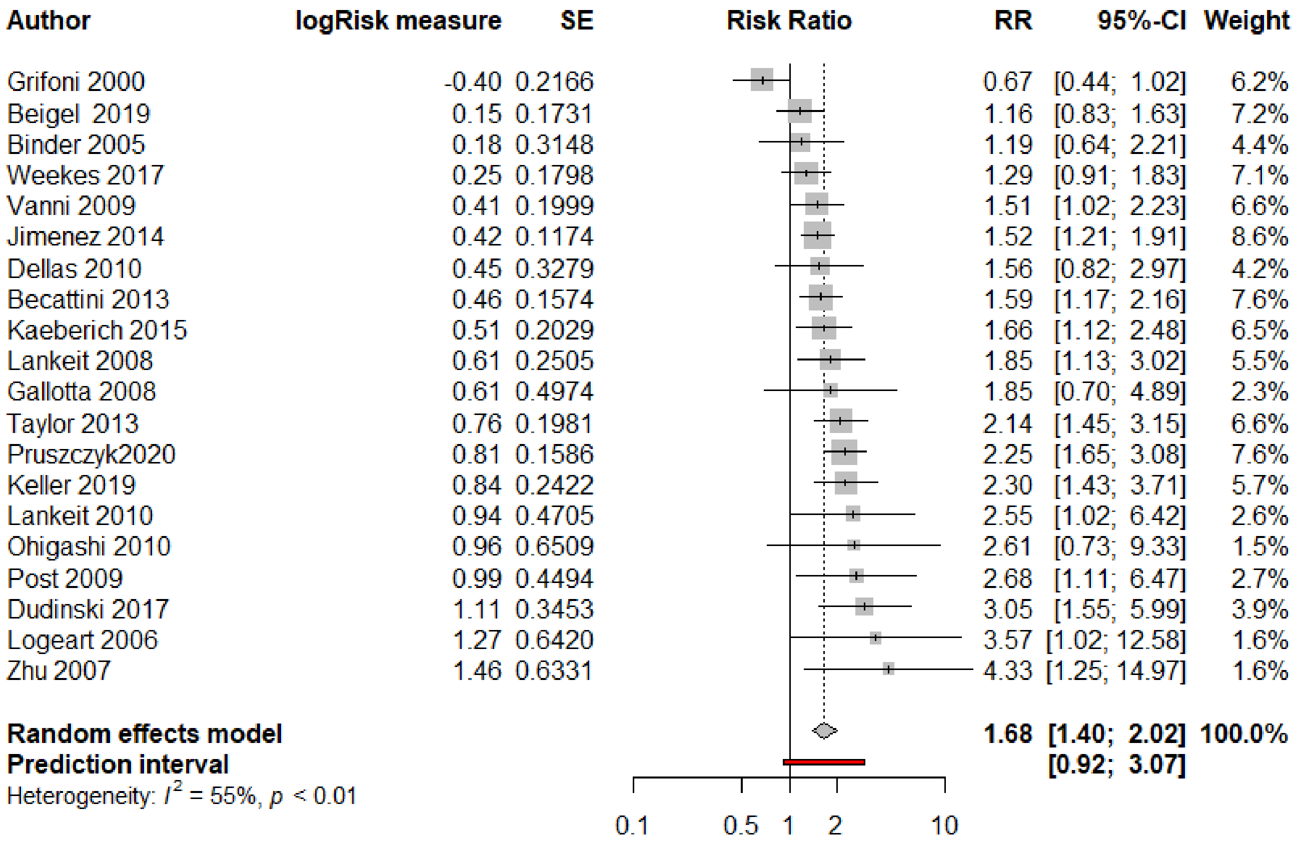

Figure 4. Meta-analysis on the association between RV/LV and death

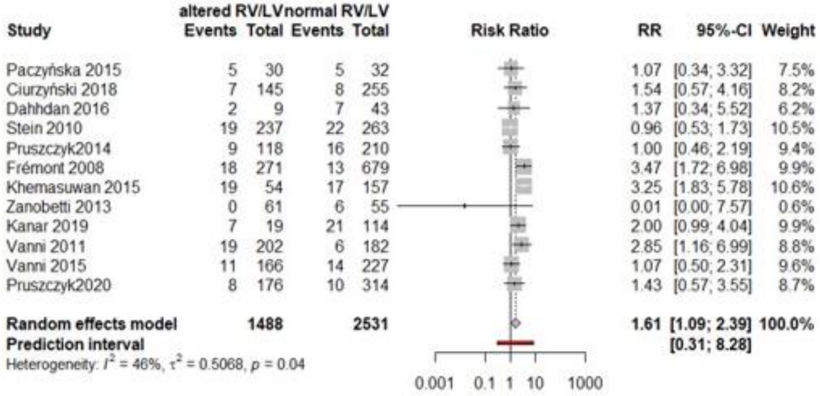

Figure 5A. Sensitivity analyses on the association between RV/LV ratio and death in studies that excluded hemodynamically unstable patients.

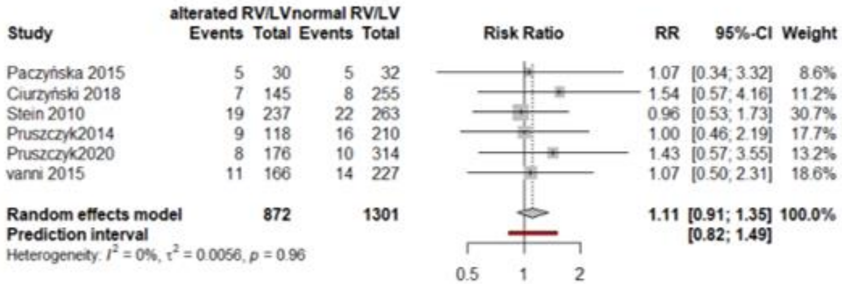

Figure 5B. Sensitivity analysis on the association between RV/LV ratio and death according to different cut-offs.

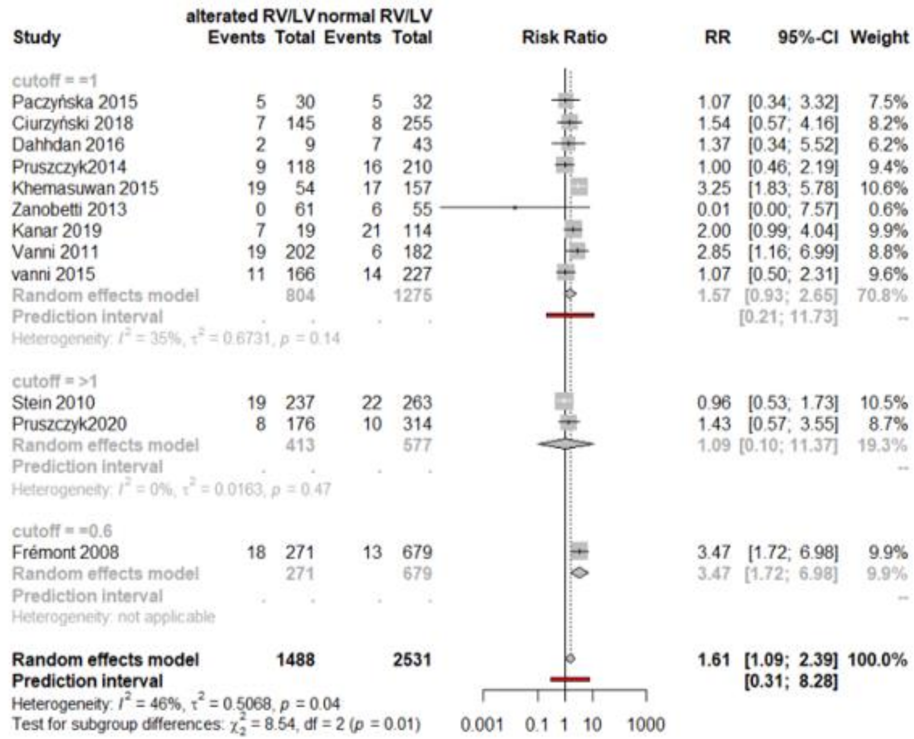

Figure 6 Meta-analysis on the association between TAPSE and death. For one study, the derivation and validation cohorts were analyzed separately [66].

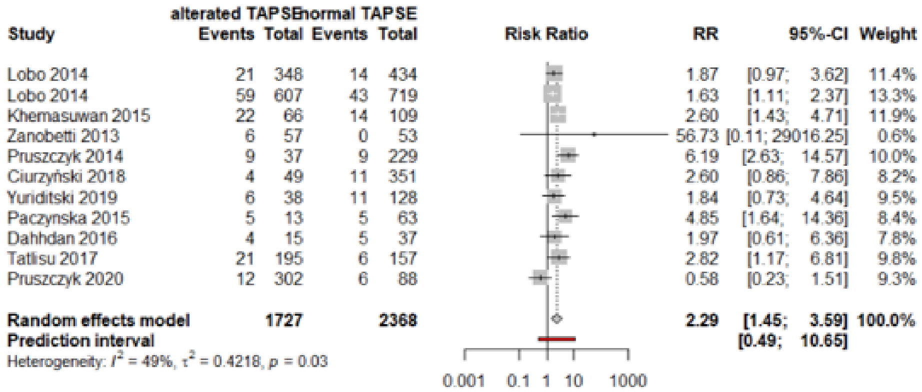

Figure 7B. Sensitivity analysis on the association between TAPSE and death in studies only including hemodynamically stable patients.

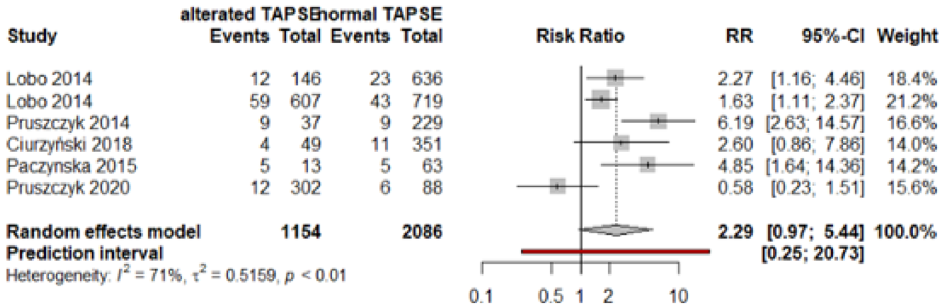

Figure 7A. Sensitivity analysis on the association between TAPSE and death according to different cut-offs.

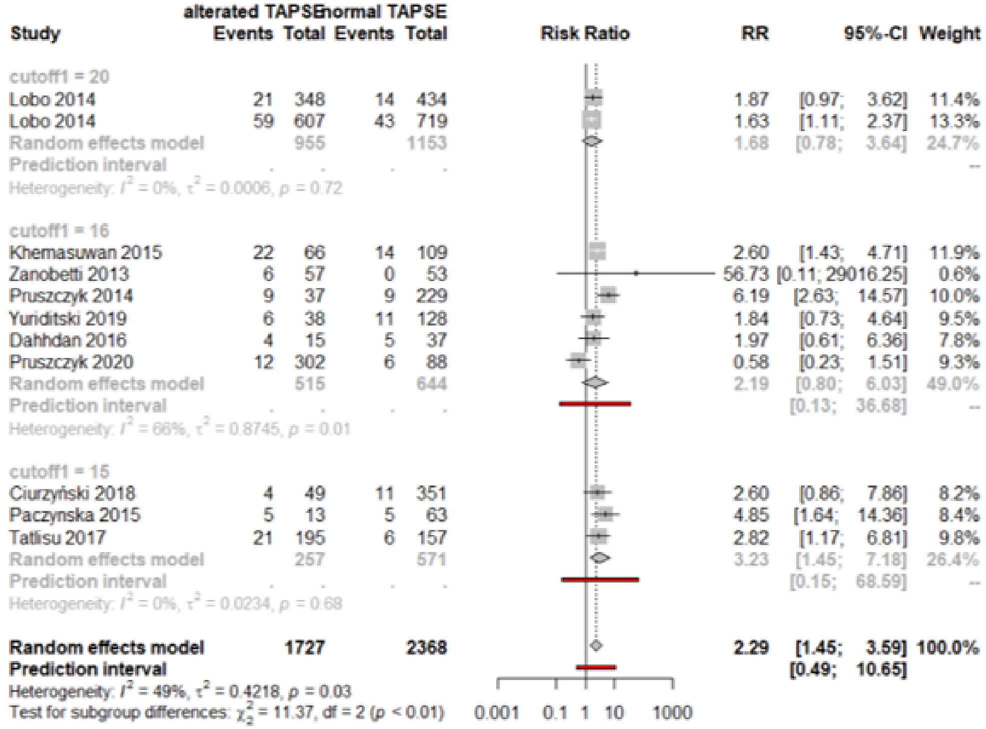

Figure 7C. Sensitivity analysis on the association between TAPSE and PE-related death in hemodynamically stable patients

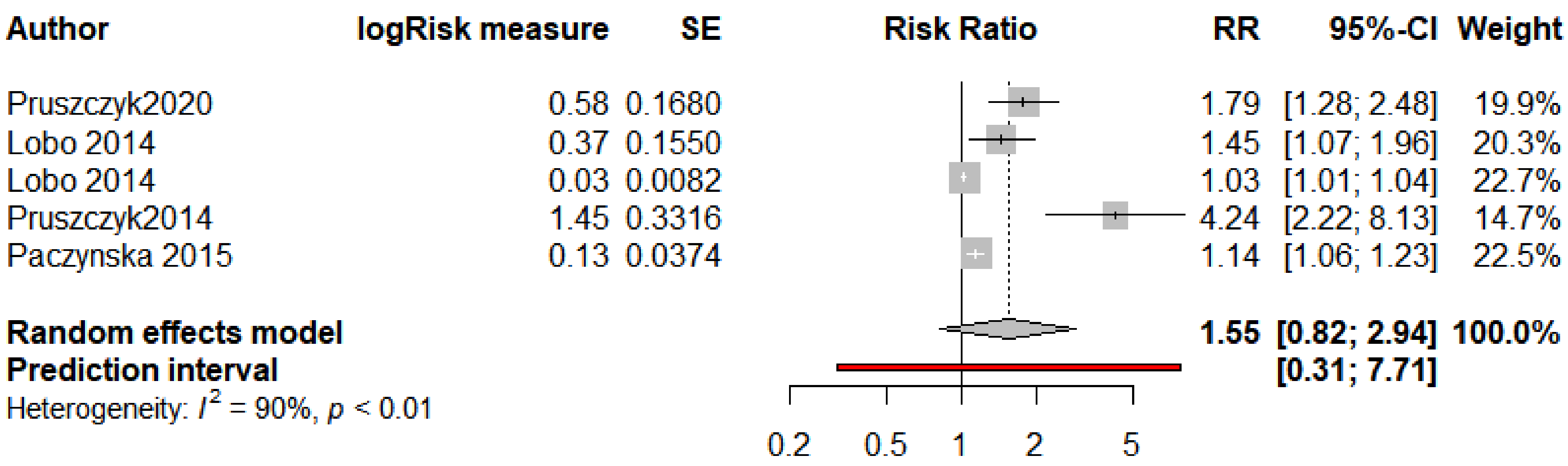

Figure 8. Meta-analysis on the association between hypokinesis and adverse outcome in the short-term

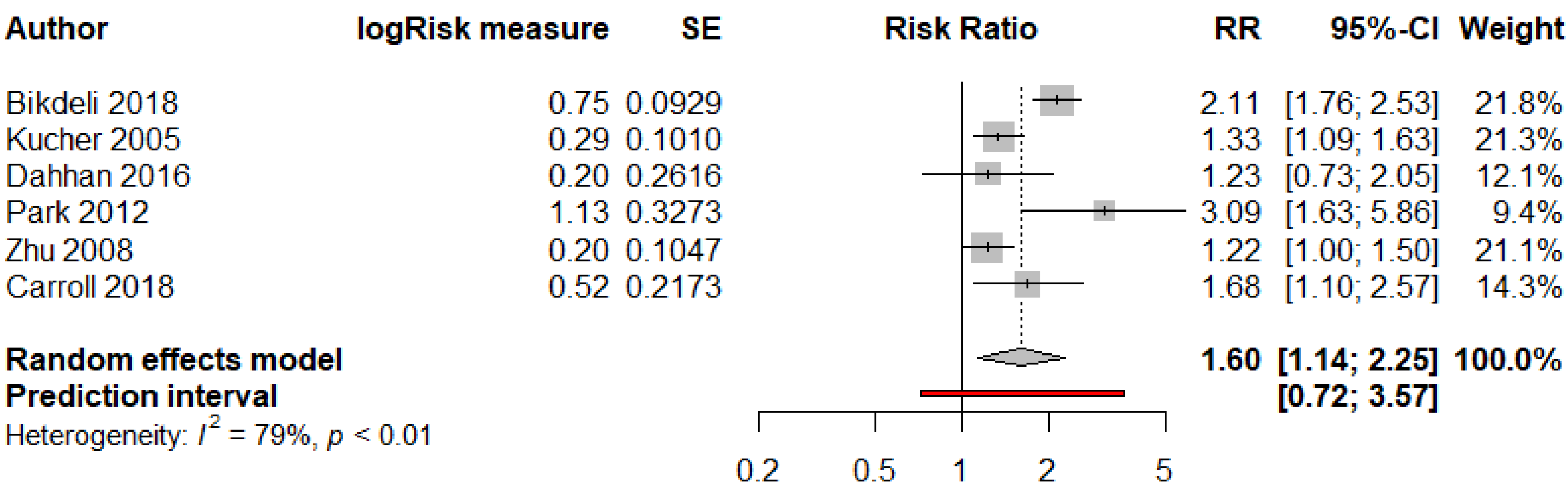

Figure 9. Meta-analysis on the Mean difference of RV diameter in survivors and non survivors

Study	Experimental Total	Experimental Mean	Experimental SD	Control Total	Control Mean	Control SD	SMD	95%-CI	Weight
Paczyńska 2015	8	41.60	8.9000	68	37.50	7.0000	0.56	[-0.17; 1.30]	16.4%
Khemasuwan 2015	82	40.00	9.0000	82	37.00	9.0000	0.33	[0.02; 0.64]	27.2%
Zanobetti 2013	6	29.00	7.0000	115	27.00	6.0000	0.33	[-0.49; 1.15]	14.7%
Ribeiro 1997	10	40.00	4.0000	116	31.00	6.0000	1.52	[0.85; 2.20]	17.8%
Pruszczyk 2014	21	39.00	10.0000	390	36.00	9.5000	0.31	[-0.13; 0.75]	23.8%
Random effects model	**127**			**771**			**0.58**	**[-0.05; 1.20]**	**100.0%**

Heterogeneity: $I^2 = 63\%$, $\tau^2 = 0.1529$, $p = 0.03$