

Supplementary Table 1S: Comparison between included and excluded patients due to missing echocardiographic data

Variable	Study population	Excluded patients	P value
	N = 517	N = 89	
Age, years	52 ± 15	55 ± 17	0.132
Female (%)	316 (64.8)	70 (78.7)	0.010
WHO FC III-IV (%)	339 (66.1)	64 (71.9)	0.281
Monotherapy, %	160 (32.4)	29 (33.3)	0.862
Combination therapy, %	215 (43.5)	32 (36.8)	0.241

List of abbreviations: WHO FC, World Health Organization functional class

Supplementary Table 2S: Adjusted HRs for all-cause mortality per 1 increase in echocardiographic risk category

Adjusted for	HR per 1 echocardiographic risk category increase (95% CI)	P value
1) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF	1.96 (1.55-2.46)	<0.001
2) Age, gender, incident/prevalent, year of publication, WHO FC, heart rate, LVEF	1.86 (1.46-2.37)	<0.001
3) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF, PAH etiology	2.11 (1.65-2.71)	<0.001
4) Age, gender, incident/prevalent, year of publication, 6MWD, LVEF	2.38 (1.45-3.91)	0.001
5) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF, AcT	1.96 (1.50-2.55)	<0.001
6) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF, RVEDA	2.01 (1.31-3.08)	0.001
7) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF, RA area	1.92 (1.32-2.80)	0.001
8) Age, gender, incident/prevalent, year of publication, WHO FC, LVEF, PASP	1.94 (1.49-2.53)	<0.001

These analyses were conducted based on data availability, multivariable Cox regression model 1 included 444 patients, model 2 405 patients, model 3 367 patients, model 4 135 patients, model 5 385 patients, model 6 194 patients, model 7 277 patients, and model 8 352 patients.

List of abbreviations: AcT, acceleration time; HR, hazard ratio; LVEF, left ventricular ejection fraction; PAH, pulmonary arterial hypertension; RA, right atrial; RV EDA, right ventricular end diastolic area; 6MWD, 6-minute walking distance; WHO FC, World Health Organization functional class

Supplementary Table 3S. Univariable and multivariable Cox regression analysis with a multivariable Cox

regression model including: age, gender, incident prevalent, WHO FC, RA area, and LVEF

	Univariate Analysis HR (95% CI)	P value	Multivariate Analysis HR (95% CI)	P value
Age	1.02 (1.01-1.03)	<0.001	1.03 (1.02-1.05)	<0.001
Female sex	0.71 (0.53-0.94)	0.017	0.87 (0.57-1.33)	0.521
Heart rate	1.02 (1.01-1.03)	0.002		
PVOD*	5.00 (2.50-10.00)	<0.001		
Scleroderma PAH*	1.50 (0.90-2.50)	0.121		
Connective tissue disease PAH*	2.80 (1.49-5.26)	0.001		
Incident PAH [§]	1.67 (1.16-2.41)	0.006	1.83 (0.78-4.33)	0.165
Combination therapy [°]	1.16 (0.88-1.54)	0.293		
Study published in 2016-18 ^Δ	0.55 (0.36-0.83)	0.005	0.26 (0.03-2.01)	0.196
Data from retrospective study [£]	0.90 (0.66-1.21)	0.484		
WHO FC III-IV	2.96 (2.02-4.34)	<0.001	2.30 (1.36-2.89)	0.002
6MWD, per 10 m increase	0.96 (0.94-0.98)	<0.001		
Center location in USA	0.83 (0.60-1.18)	0.301		
TAPSE [#]	0.92 (0.89-0.94)	<0.001		
TAPSE ≤17 mm	2.37 (1.78-3.14)	<0.001		
RVEDD	1.01 (1.00-1.02)	0.076		
RVEDA	1.05 (1.02-1.07)	<0.001		
FAC	0.97 (0.95-0.99)	0.008		
AcT	0.98 (0.97-0.99)	<0.001		
PASP	1.01 (1.00-1.01)	0.006		
RA area	1.04 (1.02-1.06)	<0.001	1.04 (1.02-1.06)	<0.001
Pericardial effusion	1.33 (0.69-2.59)	0.396		
Dilated IVC	1.95 (1.46-2.64)	<0.001		
TR moderate to severe	2.00 (1.43-2.79)	<0.001		
LVEDV	0.99 (0.97-0.99)	0.005		
LVEF	0.98 (0.97-0.99)	0.002	1.01 (0.99-1.02)	0.509
Intermediate- [†] vs low-risk [‡]	2.15 (1.38-3.37)	0.001		
High- [¥] vs low-risk [‡]	4.54 (2.88-7.15)	<0.001		

* versus idiopathic PAH

§ versus prevalent PAH

° versus monotherapy or no specific therapy

Δ versus 2006-2011

£ versus prospective study

as a continuous variable

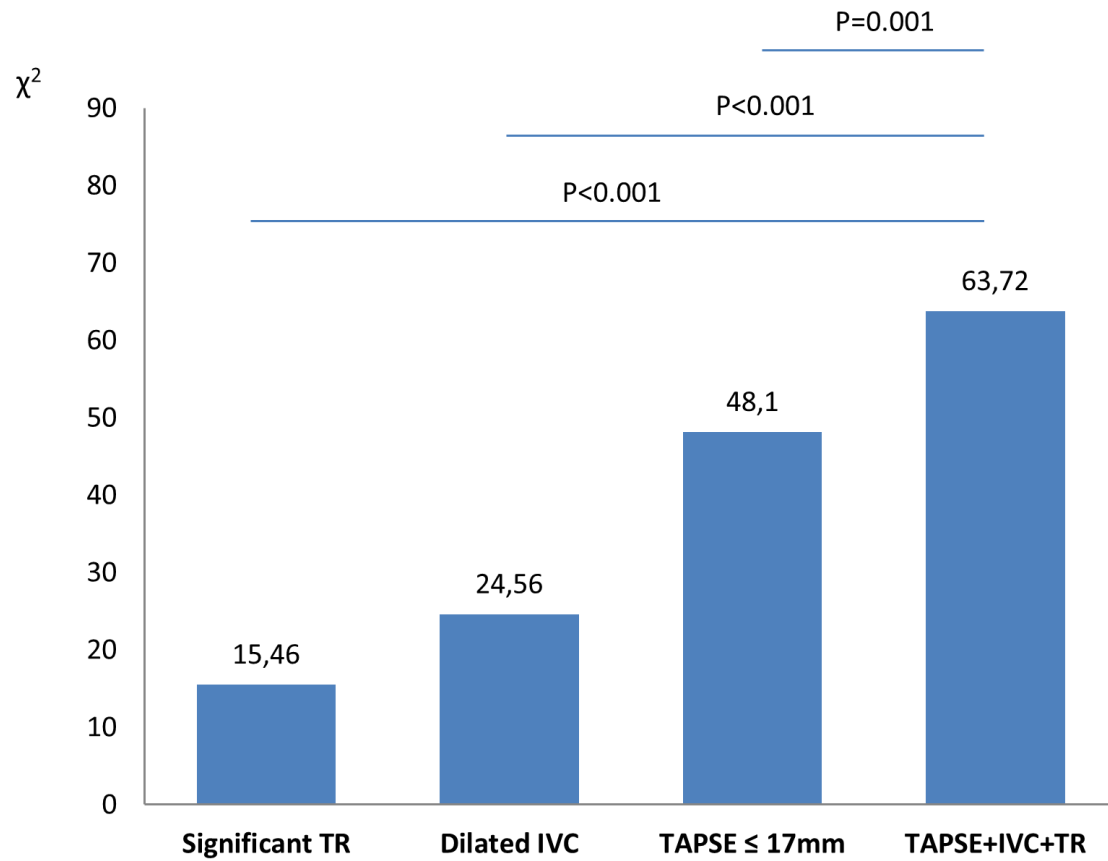
† Group 2 and 3

‡ Group 1

¥ Group 4

List of abbreviations: HR, hazard ratio; CI, confidence interval; PAH, pulmonary arterial hypertension; WHO FC, world health organization functional class; 6MWD, six-minute walking distance; TAPSE, tricuspid annular plane systolic excursion; RVEDD, right ventricular end diastolic diameter; RVEDA, right ventricular end diastolic area; FAC, fractional area change; AcT, acceleration time; PASP, pulmonary arterial systolic pressure; RA, right atrial; IVC, inferior vena cava; TR, tricuspid regurgitation; LVEDV, left ventricular end diastolic volume; LV EF, left ventricular ejection fraction.

Supplementary Figure 1S: Association between individual and combined echocardiographic parameters with all-cause mortality.

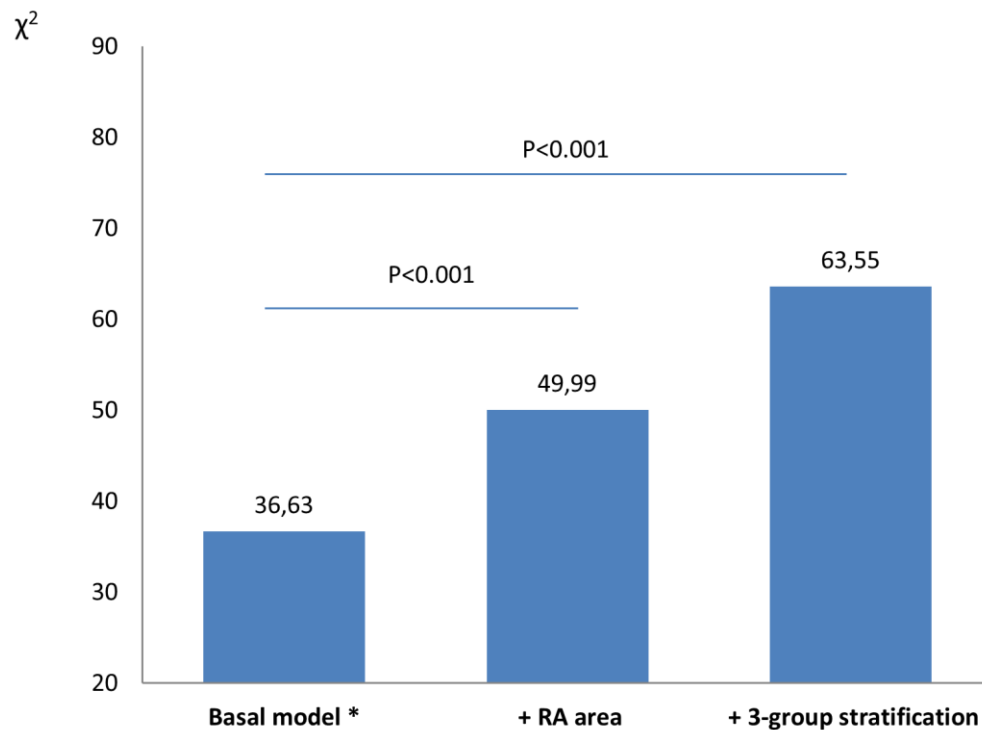


The model χ^2 values are presented for a series of Cox regression analysis model: the combination of significant TR, dilated IVC and decreased TAPSE is associated with a significant increase in χ^2 value compared with the use of these parameters individually.

This analysis was conducted on patients that had all the parameters included in the Cox regression models available (440).

IVC = inferior vena cava; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation

Supplementary Figure 2S. Incremental prognostic value of the proposed stratification model compared with RA area



*The basal model includes age, gender, WHO class III-IV, year of study publication, incident/prevalent, and LVEF. This analysis was conducted based on data availability and included 277 patients.

The model χ^2 values are presented for a series of Cox regression analysis model: the proposed risk stratification into 3 groups based on TAPSE, IVC dilation and TR severity when added to the basal model is associated with a higher increase in the χ^2 value compared with the addition of RA area.

The first blue bar from the left shows the χ^2 of the basal model; the second one the χ^2 value of the basal model + RA area and the third the χ^2 value of the basal model + our 3-groups risk stratification.

IVC = inferior vena cava; RA = right atrial; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation