Predictors of cardiovascular outcomes after surgery in severe tricuspid regurgitation: clinical, imaging and hemodynamic prospective study

SUPPLEMENTARY DATA

CMR PROTOCOL

All CMR studies were performed with a 1.5 T clinical scanner (Sonata or Avanto scanner Siemens, Erlangen, Germany) using a phased-array cardiac receiver coil. Electrocardiogram-gated breath-hold short-axis cine views were performed to quantify volumes and ejection fraction (SSFP sequences; slice thickness: 6 mm; space between slices 67%; matrix: 256x256: field of view: 300-370mm; temporal resolution < 50ms). Additional 2-chamber, 3-chamber and 4-chamber views were also obtained. LGE images were acquired at identical slice positions to the cine images after the administration of 0.2 mmol/kg of body weight Gadolinium-DTPA (Gd-DTPA) (Berlex, Montville, NJ, USA).

A segmented inversion-recovery (seg-IR) gradient-echo sequence was acquired starting at 10-15 min after contrast administration (Matrix 256 x 197, voxel size 2.0 x 1.6 x 6 mm, TE 4.91 ms, TR 700 ms, flip angle 30º; and the bandwidth 140 z/pixel) for late gadolinium enhancement (LGE) quantification.

Image analysis

Left ventricular (LV) and right ventricular (RV) end-diastolic volumes (EDV), end-systolic volumes (ESV), ejection fraction (EF) and LV mass were performed by manually tracing the epicardial and endocardial borders as previously described. Volume indices were calculated by dividing the EDV or ESV by body surface area.

Quantification of the infarcted/fibrotic myocardium was assessed by delineating the regions of LGE with ≥ 5 standard deviations (± SD) over remote signal intensity on each of the contrast enhanced CMR tomograms and summed, as previously described.

Right atrial (RA) diameters were measured from the RA posterior wall to the tricuspid annular plane (AP diameter) and from the septum to the lateral wall (LM diameter) in the four-chamber orientation. Right atrial area in the four-chamber orientation was planimetered by tracing the endocardial border at maximal atrial diastole with exclusion of the confluence of the vena cava and the RA appendage. RA volume was measured by manually drawing the endocardial borders using the stack of short axis cine images as previously described.

Tissue tracking CMR

All strain parameters were quantified offline by an experienced observer blinded to patient data. These analyses were carried out retrospectively using currently available certified software (CMR42, Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada). Data were expressed on a per-patient basis. The global peak longitudinal strain (LS), circumferential strain (CS), and radial strain (RS) were calculated as the mean of the respective peak values in the 16 segments.

Statistical analysis

The linearity assumption for the Cox models for the prediction of the composite endpoint and for the prediction of cardiovascular mortality, was graphically represented by Martingale residuals against values of iRVEDV (figure 1A of the supplementary data and figure 2A of the supplementary data). Based on this analysis, it is possible to conclude from the Martingale residuals distribution that there is only a small deviation from linearity at higher levels of the variable iRVEDV. As the representation does not improve with the log iRVEDV (figure 1B of the supplementary data and figure 2B of the supplementary data) the original values of iRVEDV were used in the final model.

Table 1 of the supplementary data

Baseline characteristics of the entire study group and patients with or without cardiovascular mortality

	All patients (n = 43)	**Cardiovascular mortality (n = 7)**	**Patients alive (n = 36)**	***P***
	n (%)	**n (%)**	**n (%)**	
Demographics				
Age (year)	66.9 ± 9.6	72 ± 5.1	65.9 ± 9.9	.152
Female	67%	4 (57%)	25 (69%)	.565
Weight (Kg)	70.6 ± 10.7	66.1 ± 12.1	71.5 ± 10.4	.181
Height (cm)	161.3 ± 9.2	159.6 ± 8.1	161.6 ± 9.5	.540
BMI	27.3 ± 4.7	26 ± 4.4	27.5 ± 4.7	.396
Medical history				
Hypertension	23 (54%)	5 (71%)	18 (50%)	.300
Dyslipidemia	16 (37%)	3 (43%)	13 (36%)	.638
Diabetes	7 (16%)	3 (43%)	4 (11%)	.071
CAD	4 (9%)	0 (0%)	4 (11%)	
Atrial fibrillation	37 (86%)	6 (86%)	31 (86%)	.904
Previous cardiac surgery	19 (44%)	3 (43%)	16 (44%)	.805
Asthma/COPD	5 (12%)	0 (0%)	5 (14%)	
NYHA Classification				.749
I	1 (2.4%)	0 (0%)	1 (2.9%)	
II	13 (31.0%)	2 (28.6%)	11 (31.4%)	
III	27 (64.3%)	5 (71.4%)	22 (62.9%)	
IV	1 (2.4%)	0 (0%)	1 (2.9%)	
EuroSCORE II	4.8 ± 3.5	6.06 ± 3.61	4.55 ± 3.48	.351
Aortic cross-clamping duration (minute)	90.6 ± 30.6	102.8 ± 38.6	88.6 ± 29.4	.259
Isolated tricuspid surgery	12 (27.9%)	3 (43%)	9 (25%)	.442
Tricuspid annuloplasty	43 (100%)			
Blood test				
Hemoglobin (g/dL)	12.6 ± 1.7	12.1 ± 1.2	12.8 ± 1.8	.369
Hematocrit (%)	39.0 ± 5.1	37.4 ± 3.6	39.3 ± 5.3	.429
Urea (mg/dL)	59.9 ± 46.2	56 ± 30.0	60.6 ± 49.1	.783
Creatinine (mg/dL)	1.0 ± 0.6	1.0 ± 0.2	1.0 ± 0.6	.963
eGFR (ml/min/1.73m²)	73.6 ± 26.2	64.6 ± 9.4	75.3 ± 28.1	.343
AST (UI/L)	31.2 ± 15.3	30.4 ± 23.8	31.3 ± 13.5	.847
ALT (UI/L)	24.3 ± 14.1	22.9 ± 26.6	24.6 ± 10.6	.643
ALP (UI/L)	111.1 ± 41.7	160.8 ± 47.8	98.6 ± 30.4	.014
GGT (UI/L)	145.6 ± 159.5	275.5 ± 318.2	113.1 ± 79.6	.157
Bilirubin (mg/dL)	1.1 ± 0.5	1.1 ± 0.4	1.1 ± 0.5	.767
Protein (g/dL)	7.3 ± 0.7	7.3 ± 0.8	7.3 ± 0.6	.933
Albumin (g/dL)	3.9 ± 0.4	3.6 ± 0.2	4.0 ± 0.4	.031
Renin (ng/mL/h)	8.5 ± 10.9	17.6	7.4 ± 11.1	.416
Aldosterone (ng/dL)	24.5 ± 17.2	50.2	22.0 ± 15.8	NP

BNP (pg/mL)	321.1 ± 250.3)	216.7 ± 22.7)	347.3 ± 276.7	.537
Right catheterization				
sPAP (mmHg)	41.5 ± 14.8	46 ± 29.0	40.7 ± 11.4	.403
mPAP (mmHg)	28.0 ± 8.6	29.8 ± 15.6	27.6 ± 7.2	.537
dPAP (mmHg)	19.4 ± 6.3	19.3 ± 10.1	19.5 ± 5.7	.904
iPVR (dyn*m²/cm^5)	371.3 ± 172.3	352.8 ± 169.5	375.0 ± 178.5	.760
RA pressure (mmHg)	14 ± 6.67	18.33 ± 7.09	13.4 ± 6.6	.305
Echocardiography				
LVEF (%)	57.2 ± 7.3	59.6 ± 9.6	56.8 ± 6.8	.341
TAPSE (mm)	17 ± 3.7	17.7 ± 3.3	16.9 ± 3.8	.498
S' Tricuspid annulus (cm/s)	9.3 ± 2.5	10.7 ± 4.3	9.0 ± 1.8	.053
sPAP (mmHg)	53.5 ± 12.1	61.2 ± 8.8	52.2 ± 12.2	.132
Right atrium area (cm²)	35.7 ± 9.6	37 ± 14.1	35.5 ± 9.3	.969
Tricuspid annulus diameter (mm)	42.8 ± 7.5	43.6 ± 6.3	42.6 ± 7.8	.767
Inferior cava vein diameter (mm)	23.2 ± 5.3	26 ± 2.6	22.7 ± 5.5	.181
Massive tricuspid regurgitation	37 (86%)	6 (86%)	31 (86%)	.993
Magnetic resonance				
iRVEDV (mL)	102.3 ± 36.2	126.9 ± 28.0	97.5 ± 36.0	.069
iRVESV (mL)	50.7 ± 18.8	62.7 ± 12.7	48.4 ± 19.0	.087
RVEF (%)	49.3 ± 8.2	49.6 ± 5.9	49.2 ± 8.6	.926
iLVEDV (mL)	79.1 ± 28.6	85.3 ± 39.1	77.8 ± 26.4	.522
iLVESV (mL)	38.4 ± 20.6	44.3 ± 32.3	37.2 ± 17.6	.388
LVEF (%)	57.2 ± 7.3	51.4 ± 10.5	53.2 ± 8.3	.614
Right atrium area (cm²)	35.7 ± 9.6	35.4 ± 9.5	36 ± 10.6	.866
Tricuspid annulus diameter (mm)	43.6 ± 7.3	41 ± 5.7	44.1 ± 7.5	.289
Longitudinal strain (%)	-17.2 ± 6.1	-20.6 ± 4.8	-16.5 ± 6.2	.178
Circumferential strain (%)	-14.9 ± 3.6	-16.0 ± 2.5	-14.7 ± 3.7	.488
Radial strain (%)	24.7 ± 7.5	26.6 ± 5.6	24.4 ± 7.9	.564
Right atrium volume (mL)	215.9 ± 112.8	207.7 ± 131.1	217.0 ± 113.5	.805
Right atrium diameter AP (mm)	87.6 ± 87.9	73.1 ± 13.2	90.4 ± 95.8	.743
Right atrium diameter LM (mm)	59.7 ± 14.7	63 ± 13.0	59 ± 15.1	.595
Treatment at discharge				
Betablocker	9 (23.7%)	0 (0%)	9 (25.7%)	1
ACEi/ARB	19 (50%)	1 (33.3%)	18 (51.4%)	.578
MRA	16 (42.1%)	3 (100%)	13 (37.1%)	1
Furosemide	35 (92.1%)	3 (100%)	32 (91.4%)	.597
Furosemide dosage	65.1 ± 44.3	133.3 ± 100.7	58.8 ± 31.7	.04

Values are mean ± standard deviation or n (%).

BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; eGFR, glomerular filtration rate; AST, aspartate aminotransferase ; ALT, alanine aminotransferase; ALP,

alkaline phosphatase; GGT, gamma-glutamyltransferase; BNP, brain natriuretic peptide; sPAP, systolic pulmonary artery pressure; mPAP, mean pulmonary artery pressure; dPAP, diastolic pulmonary artery pressure; iPVR, indexed pulmonary vascular resistance; LVEF, left ventricular ejection fraction; iRVEDV, indexed right ventricular end-diastolic volume; iRVESV, indexed right ventricular end-systolic volume; RVEF, right ventricular ejection fraction; iLVEDV, indexed left ventricular end-diastolic volume; iLVESV, indexed left ventricular end-systolic volume; AP, anteroposterior; LM, lateral-medial.

Table 2 of the supplementary data

Baseline characteristics of the entire study group and patients with or without recurrence of significant tricuspid regurgitation

	All patients (n = 40)	**Significant tricuspid regurgitation (n = 13)**	**No significant tricuspid regurgitation (n = 27)**	***P***
	n (%)	**n (%)**	**n (%)**	
Demographics				
Age (year)	66.8 ± 9.8	69.8 ± 1.9	65.3 ± 2.1	.174
Female	27 (67.5)	9 (69.2)	18 (66.7)	1
Weight (Kg)	70.8 ± 11.0	71.5 ± 9.7	70.4 ± 11.8	.781
Height (cm)	161.5 ± 9.4	160.9 ± 2.8	161.7 ± 9.3	.801
BMI	27.3 ± 4.8	27.7 ± 3.5	27.1 ± 5.3	.728
Medical history				
Hypertension	21 (52.5)	9 (69.2)	12 (44.4)	.186
Dyslipidemia	14 (35.0)	7 (53.9)	7 (25.9)	.155
Diabetes	6 (15.0)	4 (30.8)	2 (7.4)	.075
CAD	4 (10.0)	2 (15.4)	2 (7.4)	.584
Atrial fibrillation	35 (87.5)	12 (92.3)	23 (85.2)	1.000
Previous cardiac surgery	18 (45.0)	5 (38.5)	13 (48.2)	.737
Asthma/COPD	5 (12.5)	2 (15.4)	3 (11.1)	1.000
NYHA Classification				.770
I	1 (2.6%)	0 (0%)	1 (3.9%)	
II	12 (30.8%)	3 (23.1%)	9 (34.6%)	
III	10 (64.1%)	10 (76.9%)	15 (57.7%)	
IV	1 (2.6%)	0 (0%)	1 (3.9%)	
Euroscore II	5.0 ± 3.6	5.6 ± 3.9	4.6 ± 3.5	.435
Aortic cross-clamping duration (minute)	90.6 ± 31.1	80.9 ± 40.6	94.1 ± 27.0	.281
Isolated tricuspid surgery	11 (27.5)	6 (46.2)	5 (18.5)	.067
Tricuspid annuloplasty	43 (100%)			
Blood test				
Hemoglobin (g/dL)	12.6 ± 1.7	12.2 ± 1.3	12.8 ± 1.9	.322
Hematocrit (%)	38.9 ± 5.2	38.2 ± 4.0	39.29 ± 5.7	.526
Urea (mg/dL)	61.6 ± 47.4	75.1 ± 62.7	55.1 ± 37.8	.216
Creatinine (mg/dL)	1.0 ± 0.6	1.1 ± 0.9	1.0 ± 0.4	.416
eGFR (mL/min/1.73m²)	73.2 ± 26.9	67.4 ± 22.7	76.0 ± 28.6	.349
AST (UI/L)	31.4 ± 15.7	27.9 ± 18.1	33.1 ± 14.5	.328
ALT (UI/L)	24.2 ± 14.0	22.2 ± 19.4	25.2 ± 10.5	.547
ALP (UI/L)	107 ± 38.6	111.1 ± 50.6	104.6 ± 32.0	.732
GGT (UI/L)	150.1 ± 162.5	205.3 ± 243.3	117.9 ± 88.6	.270

Bilirubin (mg/dL)	1.1 ± 0.5	1.0 ± 0.3	1.1 ± 0.6	.604
Protein (g/dL)	7.3 ± 0.7	7.1 ± 0.6	7.3 ± 0.7	.399
Albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.5	3.9 ± 0.4	.877
Renin (ng/mL/h)	8.5 ± 10.9	16.6 ± 12.4	2 ± 1.9	.033
Aldosterone (ng/dL)	24.5 ± 17.2	27.9 ± 19.8	21.8 ± 16.1	.589
BNP (pg/mL)	331.0 ± 263.5	336.5 ± 331.0	324.1 ± 197.1	.949
Right catheterization				
sPAP (mmHg)	43 ± 14.3	45.6 ± 18.2	41 ± 10.8	.457
mPAP (mmHg)	29.0 ± 8.1	29.9 ± 9.1	28.4 ± 7.5	.665
dPAP (mmHg)	20.4 ± 5.8	19.8 ± 5.9	20.8 ± 5.8	.698
iPVR (dyn*m²/cm^5)	396.8 ± 163.0	412.7 ± 169.6	387.3 ± 167.5	.774
RA pressure (mmHg)	14.19 ± 1.48	16.89 ± 5.33	12.17 ± 7.26	.117
Echocardiography				
LVEF (%)	56.7 ± 7.1	56.9 ± 5.7	56.5 ± 7.8	.869
TAPSE (mm)	16.9 ± 3.6	17.1 ± 3.3	16.7 ± 3.9	.789
S' Tricuspid annulus (cm/s)	8.9 ± 1.9	8.9 ± 1.7	8.9 ± 2.0	.966
sPAP (mmHg)	53.3 ± 12.4	56.5 ± 17.3	52.2 ± 10.6	.406
Right atrium area (cm²)	35.5 ± 9.8	33.4 ± 9.9	36.6 ± 9.9	.455
Tricuspid annulus diameter (mm)	42.7 ± 7.5	42.6 ± 5.4	42.7 ± 8.6	.972
Inferior cava vein diameter (mm)	22.9 ± 5.4	22.8 ± 5.3	23 ± 5.5	.902
Massive tricuspid regurgitation	34 (85.0)	12 (92.3)	22 (81.5)	.762
Magnetic resonance				
iRVEDV (mL)	101.4 ± 36.0	119.5 ± 38.0	92.6 ± 32.2	.025
iRVESV (mL)	50.4 ± 18.9	53.8 ± 16.6	48.8 ± 20.1	.446
RVEF (%)	49.1 ± 8.5	54 ± 6.0	46.7 ± 8.6	.009
iLVEDV (mL)	81.4 ± 28.3	77.3 ± 21.9	83.4 ± 31.1	.543
iLVESV (mL)	39.8 ± 20.6	35.3 ± 14.5	42 ± 23.0	.365
LVEF (%)	52.4 ± 8.7	54 ± 10.6	51.7 ± 7.8	.455
Right atrium area (cm²)	35.9 ± 10.4	34.2 ± 8.4	36.7 ± 11.3	.486
Tricuspid annulus diameter (mm)	43.8 ± 7.4	42.3 ± 5.6	44.4 ± 8.2	.401
Longitudinal strain (%)	-16.7 ± 6.1	-20.4 ± 3.3	-14.0 ± 6.3	.002
Circumferential strain (%)	-14.7 ± 3.7	-17.0 ± 2.3	-13.6 ± 3.7	.009
Radial strain (%)	24.3 ± 7.6	28.5 ± 5.2	22.3 ± 7.9	.025
Right atrium volume (mL)	217.4 ± 114.9	183.3 ± 79.0	244.1 ± 133.4	.194
Right atrium diameter AP (mm)	88.4 ± 91.1	73 ± 9.4	95.7 ± 110.6	.467
Right atrium diameter LM (mm)	60.4 ± 13.3	58.5 ± 15.5	61.3 ± 12.3	.529
Treatment at discharge				

Betablocker	9 (23.7%)	4 (33.3%)	5 (19.2%)	.423
ACEi/ARB	19 (50%)	7 (58.3%)	12 (46.2%)	.485
MRA	16 (42.1%)	7 (58.3%)	9 (34.6%)	.169
Furosemide	35 (92.1%)	12 (100%)	23 (88.5%)	.220
Furosemide dosage	65.1 ± 44.3	65 ± 58.5	65.2 ± 36.3	.231

BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; eGFR, glomerular filtration rate; AST, aspartate aminotransferase ; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyltransferase; BNP, brain natriuretic peptide; sPAP, systolic pulmonary artery pressure; mPAP, mean pulmonary artery pressure; dPAP, diastolic pulmonary artery pressure; iPVR, indexed pulmonary vascular resistance; LVEF, left ventricular ejection fraction; iRVEDV, indexed right ventricular end-diastolic volume; iRVESV, indexed right ventricular end-systolic volume; RVEF, right ventricular ejection fraction; iLVEDV, indexed left ventricular end-diastolic volume; iLVESV, indexed left ventricular end-systolic volume; AP, anteroposterior; LM, lateral-medial.

Values are mean ± standard deviation or n (%).

Figure 1 of the supplementary data

Martingale residuals distribution for primary end-point

Fig 1A

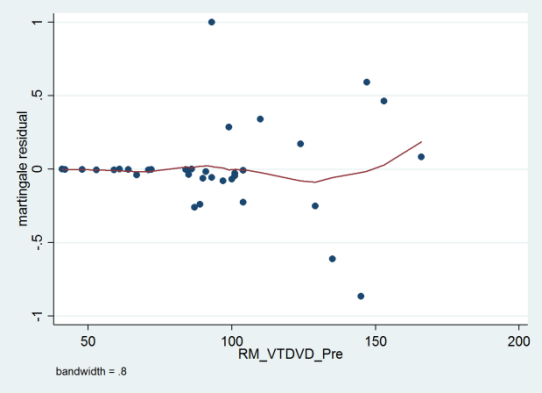

Fig 1B

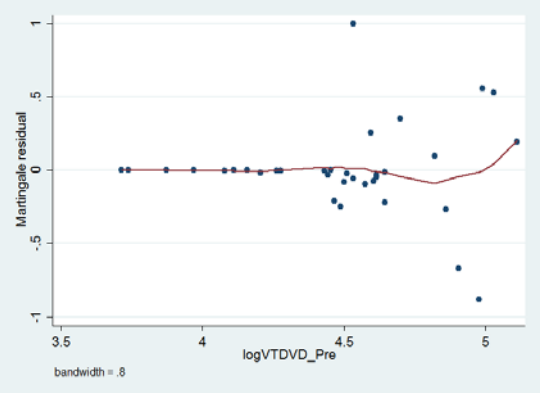

Figure 2 of the supplementary data

Martingale residuals distribution for cardiovascular mortality

Fig 2A

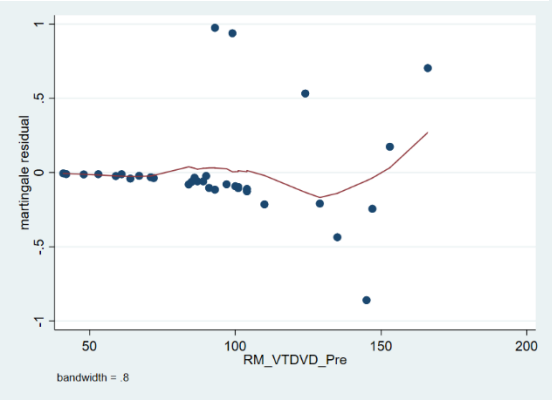

Fig 2B