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Pre-procedural CT angiography inferior vena cava measurements: a predictor of mortality in patients undergoing transcatheter aortic valve implantation

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Abstract

Objectives To assess the value of pre-procedural computed tomography angiography (CTA) measurements of the suprahepatic inferior vena cava (IVC) to detect elevated central venous pressure (CVP) assessed by right heart catheterisation (RHC), and to predict post-procedural 1-year mortality in a cohort of patients undergoing transcatheter aortic valve implantation (TAVI).

Methods We retrospectively evaluated 408 consecutive patients undergoing CTA before TAVI between January 2011 and December 2014. Two hundred and five patients were included in the RHC cohort, who underwent RHC and CTA within ≤1 day prior to TAVI. Two hundred and three patients not fulfilling this requirement were included in the validation cohort. Measurements of the IVC were performed between diaphragm and right atrium on axial slices. Receiver operating characteristic (ROC) analyses, Kaplan-Meier analyses and Cox regression analyses were performed.

Results In the RHC cohort, ROC curve analyses for IVC area measurements indicated an AUC of 0.77 ($p < 0.001$) to detect CVP ≥10mmHg and an area under the ROC curve (AUC) of 0.72 ($p < 0.001$) to predict 1-year mortality. An IVC area cut-off of ≥665 mm^2 predicted 1-year mortality with a specificity of 84% and a sensitivity of 63%. Kaplan-Meier analysis showed that patients with an IVC area ≥665 mm^2 had a significantly higher post-procedural 1-year mortality (38% versus 7%, log-rank $p < 0.001$) with a hazard ratio of 5.5 (95% CI, 2.2-13.6; $p < 0.001$). Applying this cut-off value to the validation cohort confirmed a significantly higher 1-year mortality after TAVI (34% versus 11%; log-rank $p = 0.004$) for patients with an IVC area ≥665 mm^2.

Conclusions Pre-procedural enlargement of the suprahepatic IVC is a predictor of post-procedural 1-year mortality in patients evaluated for TAVI.

Key Points

- *IVC measurements are moderate predictors of an elevated CVP in TAVI patients.*
- *Pre-procedural IVC enlargement is a predictor of 1-year mortality after TAVI.*
- *IVC enlargement is associated with right heart dysfunction in TAVI patients.*

Keywords Aortic valve stenosis · Central venous pressure · Computed tomography angiography · Vena cava; inferior · Transcatheter aortic valve replacement

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Abbreviations

BSA	Body surface area
CVP	Central venous pressure
IVC	Inferior vena cava
PCWP	Pulmonary capillary wedge pressure
RHC	Right heart catheterisation
TAVI	Transcatheter aortic valve implantation

Introduction

Transcatheter aortic valve implantation (TAVI) has emerged as the treatment of choice for symptomatic severe aortic stenosis in patients with high surgical risk [1–4]. Electrocardiogram-gated computed tomography angiography (CTA) plays an integral part in pre-procedural planning of TAVI [5–8]. CTA provides critical information on the eligibility for peripheral vascular access, aortic root assessment and aortic annulus sizing [5–7].

Recently, right heart dysfunction has gained increasing attention in patients with left heart disease and was shown to adversely affect survival in these patients [9–13]. Aortic stenosis, right ventricular dysfunction and pulmonary hypertension were shown to have impact on a patient's survival even after cardiac surgery or TAVI [11, 14, 15]. Current guidelines suggest measurements of the inferior vena cava (IVC) as part of the echocardiographic assessment of the right heart [16, 17]. There are many publications regarding non-invasive assessment of central venous pressure (CVP) using ultrasound [18–20]. To our best knowledge, the correlation of CT measurements of the suprahepatic IVC and CVP has not yet been described.

The primary objective of our study was to correlate CTA measurements of the suprahepatic IVC with CVP assessed by right heart catheterisation (RHC) in a cohort of patients undergoing TAVI. The second objective of our study was to assess the prognostic value of pre-procedural IVC measurements on post-procedural mortality after TAVI.

Materials and methods

Patient selection

We retrospectively screened data of all patients undergoing TAVI at the University Hospital Zurich between January 2011 and December 2014 (n = 468). We only included patients undergoing CT dedicated for TAVI planning at our hospital (n = 408). Three hundred and twenty-seven patients (80%) underwent pre-procedural RHC as part of the clinical routine. Subsequently, patients were subdivided into two groups. Patients undergoing RHC and CTA within 1 day prior to TAVI were included in the RHC cohort (n = 205), to assess correlation of IVC measurements with CVP and 1-year mortality. Patients not fulfilling these requirements (n = 203) were included in the validation cohort to assess whether cut-off values obtained in the RHC cohort are also applicable in the validation cohort (Fig. 1).

Data collection was performed in the context of a nationwide prospective registry (SWISS TAVI registry). This study had institutional and local ethics committee approval. Written informed consent was obtained from each patient.

Data collection and definitions

Patient demographics [age, gender, weight, height, body mass index (BMI), body surface area (BSA), Logistic EuroSCORE II, STS risk score], cardiac risk factors (diabetes mellitus, hyperlipidaemia, hypertension) and past medical history (coronary artery disease, cerebrovascular disease, previous kidney transplantation, peripheral vascular disease, chronic obstructive pulmonary disease, previous coronary artery bypass graft) were recorded preoperatively. Clinical follow-up data were obtained after 30 days, at 12 months, and yearly thereafter at our institution or by a local cardiologist. Median observation period was 371 days with a range of 0-1,721 days.

RHC was performed for haemodynamic evaluation before TAVI. Elevated CVP was defined as ≥10 mmHg. Pulmonary hypertension was defined as mean pulmonary artery pressure ≥25 mmHg. Pre-procedural transthoracic echocardiography was acquired with commercially available transducers and analysed by certified staff members.

CT protocol

CTA was performed on a second-generation, dual source, 128-slice CT (Somatom Definition Flash; Siemens Healthineers, Erlangen, Germany) for evaluation of peripheral vascular access, assessment of the aortic root and aortic annulus sizing before TAVI. The prospective electrocardiogram-gated CT scan ranged from the apex of the lungs to the pubic symphysis and started automatically to reach the 60% RR-interval at the level of the sinotubular junction. The CT scan was performed during a single mid-inspiratory breath-hold with the following scan parameters: tube voltage, 100kVp; tube current, automated attenuation-based tube current modulation was used with a reference tube current-time product of 320 mAs/rotation; pitch, 3.2; gantry rotation time, 0.25 s; collimation, 128 × 0.6 mm. Images were reconstructed with a slice thickness of 2.0 mm, an increment of 1.5 mm and a soft tissue convolution kernel (B30f). First, 45 mL Iopromide (Ultravist 370; Bayer Vital, Leverkusen, Germany) at a flow rate of 5 mL/s was intravenously injected, directly followed by 35 mL of a second bolus of Iopromide and with a 60-mL bolus of saline chaser, both at the flow rate of 2.5 mL/s. Bolus tracking was performed in the ascending aorta with a signal attenuation threshold of 100 Hounsfield units at a tube voltage of 120 kV.

IVC measurements on CTA

We performed IVC measurements at the suprahepatic segment between the diaphragm and the right atrium (Fig. 2a, b). Measurements of short diameter, long diameter, and area were performed on standard axial plane (Fig. 2c, d). Additionally, in the RHC cohort we performed measurements of the suprahepatic IVC segment on multiplanar reformatted

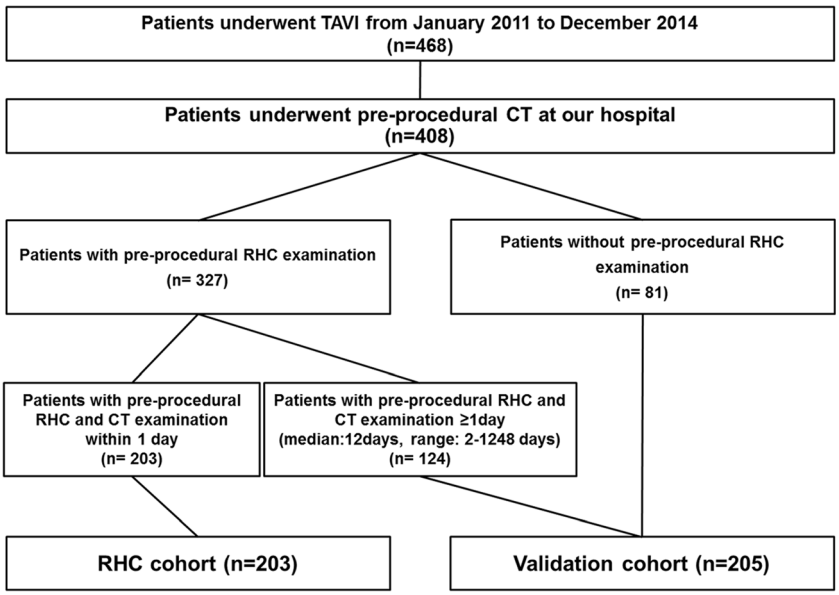

Fig. 1 Flowchart shows details of the selection process for our RHC and validation cohort. Patients who underwent RHC and CT within ≤1 day prior to TAVI were put in the RHC cohort. All other patients were put in the validation cohort. *CT* computed tomography, *RHC* right heart catheterisation, *TAVI* transcatheter aortic valve implantation

(MPR) images perpendicular to the IVC axis to assess differences between axial and MPR measurements.

Measurements were performed on a dedicated workstation (Impax, V. 6.6.1; Agfa-Gevaert, Mortsel, Belgium) without knowledge of RHC or clinical data. A radiologist with 5-years' experience in thoracic radiology performed measurements of all patients. To assess interobserver variability, a radiologist with 4-years' experience in thoracic radiology repeated these measurements in 75 patients of the RHC cohort.

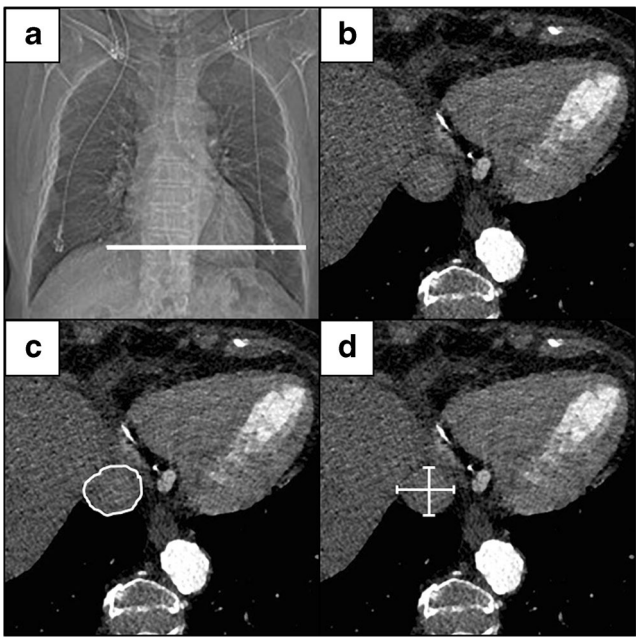

Fig. 2 The suprahepatic IVC segment was evaluated just superior to the hepatic veins, below the junction with the right atrium (**a**) on axial CT slices (**b**). Area measurements (**c**) as well as measurements of short and long diameter (**d**) were performed

Statistical analysis

Non-normally distributed continuous data are shown as median and interquartile range (IQR) and categorical data are shown as counts with percentages. Continuous variables with a non-parametric distribution were compared using Mann-Whitney *U* test. Categorical variables were compared using the chi-squared or Fisher's exact test wherever appropriate. In the RHC cohort, we assessed correlation of IVC measurements and CVP using Pearson's correlation coefficient. The performance of IVC measurements to detect CVP ≥10 mmHg and 1-year mortality was assessed using the area under the curve (AUC) of the receiver operating characteristics (ROC). The AUC derived from the ROC curve is expressed with 95% confidence interval (95% CI). An axial area cut-off of 665 mm^2 showed the highest diagnostic accuracy to predict 1-year mortality and was chosen for further survival analysis. Inter-reader reproducibility of IVC measurements was assessed using the intra-class correlation coefficient (ICC) expressed with 95% CI and by calculating the mean percentage error (absolute difference divided by the mean of two observers). Kaplan-Meier analysis of survival was applied to assess cumulative 1-year mortality. Log-rank test was used to declare significance. Univariate Cox regression analysis was performed to estimate risk-adjusted hazard ratio (HR) for 1-year mortality. In the RHC cohort, univariate Cox regression analysis was performed for baseline characteristics shown in Table 1, IVC area ≥665 mm^2, elevated CVP and pulmonary hypertension. Variables with $p < 0.10$ were then subjected to multivariate Cox regression analysis to control for potential confounders as previously described [21]. The final multivariate Cox regression model included IVC area ≥665 mm^2, categorised STS risk score (category 1, <5; category 2, 5-10; category 3, >10), coronary artery disease, peripheral vascular

Table 1 Baseline characteristics with demographics, cardiac risk factors, comorbidities and echocardiographic data overall, and compared between the RHC and validation cohorts

	Overall (n = 405)	RHC cohort (n = 204)	Validation cohort (n = 201)	p value
Age [years]	83; 79-87	83; 80-88	82; 78-86	0.013*
Sex, female [n, (%)]	203 (50)	106 (52)	96 (48)	0.427
Body mass index [kg/m^2]	26.0; 23.0-30.4	25.3; 22.9-29.2	26.9; 23.8-30.9	0.020*
Body surface area [m^2]	1.8; 1.7-2.0	1.8; 1.7-2.0	1.8; 1.7-2.0	0.056
Weight [kg]	72; 64-81	70; 62-80	73; 66-84	0.014*
Height [cm]	165; 158-172	165; 158-172	165; 168-173	0.617
Logistic EuroSCORE II	4.2; 2.5-7.1	4.1; 2.3-6.4	5.3; 3.6-7.6	0.187
STS risk score	5.0; 3.5-7.5	4.5; 3.3-6.9	5.3; 3.6-8.1	0.03*
Cardiac risk factors				
Diabetes mellitus [n, (%)]	99 (25)	44 (22)	55 (28)	0.203
Hyperlipidaemia [n, (%)]	158 (39)	71 (35)	87 (44)	0.083
Hypertension [n, (%)]	313 (78)	149 (73)	164 (82)	0.033*
Medical history				
Coronary artery disease [n, (%)]	226 (56)	107 (53)	119 (60)	0.162
Cerebrovascular disease [n, (%)]	47 (12)	26 (13)	21 (11)	0.536
Previous kidney transplantation [n, (%)]	14 (4)	7 (3)	7 (4)	1.0
Peripheral vascular disease [n, (%)]	87 (22)	27 (13)	60 (30)	<0.001*
Chronic obstructive pulmonary disease [n, (%)]	69 (17)	32 (16)	37 (19)	0.509
Previous coronary artery bypass graft [n, (%)]	62 (18)	30 (20)	32 (16)	0.399
NYHA-Classification III or IV [n, %]	73 (19)	23 (12)	50 (26)	<0.001*
Echocardiography				
Ejection fraction [%]	57; 45-63	58; 46-63	55; 45-63	0.248
Mean trans-aortic pressure gradient [%]	41; 29-53	41; 30-54	40; 26-53	0.275
Indexed aortic valve area [cm^2/m^2]	0.4; 0.3-0.5	0.4; 0.3-0.5	0.4; 0.3-0.5	0.663

*$p < 0.05$

Data are expressed as median and inter-quartile range or count and percentage

Aortic valve area is indexed to body surface area

CVP central venous pressure, *NYHA* New York Heart Association, *RHC* right heart catheterisation

disease, chronic obstructive pulmonary disease, and pulmonary hypertension. HR is stated with 95% CI.

A p value of less than 0.05 was considered statistically significant. Statistical analyses were retrospective and conducted using IBM SPSS, version 25.

Results

In three patients (0.7%; one patient of the RHC cohort, two patients of the validation cohort) we could not measure the suprahepatic IVC as it was not possible to sufficiently discriminate between IVC, the right atrium and the liver. These patients were excluded for further analysis reducing the patient numbers to 204 patients in the RHC cohort and 201 patients in the validation cohort.

Patient baseline characteristics

Overall baseline characteristics and comparison of baseline characteristics between the RHC and validation cohort are shown in Table 1. Patients in the validation cohort were significantly older (p = 0.013), had a significantly higher weight (p = 0.014), a higher BMI (0.020) and a higher STS risk score (0.031). More patients in the validation cohort had NYHA stage 3 or 4 ($p < 0.001$), arterial hypertension (0.033) and peripheral vascular disease (<0.001) compared to the RHC cohort.

Correlation of IVC measurements and central venous pressure in the RHC cohort

Median CVP in the RHC cohort was 7 mmHg (IQR, 5-9 mmHg). Forty-six patients (23%) of the RHC cohort were diagnosed with elevated CVP at pre-procedural RHC.

Table 2 shows correlation of suprahepatic IVC measurements with CVP. The strongest correlation with CVP was

Table 2 Multiplanar measurements and indexing axial measurements of the suprahepatic inferior vena cava (IVC) in the RHC cohort did not improve performance to predict elevated central venous pressure (CVP ≥10 mmHg) and 1-year all-cause mortality, compared to IVC measurements on standard axial CT slices

RHC cohort (n = 204)	ROC curve to detect CVP ≥10 mmHg		Pearson correlation IVC measurements - CVP		ROC curve to predict 1-year all-cause mortality	
	AUC	p value	r value	p value	AUC	p value
Non-indexed measurements						
Axial measurements						
Area [mm^2]	0.77 (95% CI, 0.70-0.84)	<0.001*	0.44	<0.001*	0.72 (95% CI, 0.60-0.85)	<0.001*
Short diameter [mm]	0.77 (95% CI, 0.69-0.84)	<0.001*	0.45	<0.001*	0.63 (95% CI, 0.50-0.77)	0.034*
Long diameter [mm]	0.67 (95% CI, 0.58-0.76)	<0.001*	0.28	<0.001*	0.66 (95% CI, 0.53-0.79)	0.010*
Multiplanar measurements						
Area [mm^2]	0.76 (95% CI, 0.68-0.84)	<0.001*	0.39	<0.001*	0.68 (95% CI, 0.55-0.80)	0.005*
Short diameter [mm]	0.71 (95% CI, 0.64-0.79)	<0.001*	0.36	<0.001*	0.63 (95% CI, 0.51-0.74)	0.047*
Long diameter [mm]	0.70 (95% CI, 0.61-0.79)	<0.001*	0.28	<0.001*	0.63 (95% CI 0.49-0.77)	0.035*
Indexed measurements						
Axial measurements						
Area [mm^2]	0.69 (95% CI, 0.61-0.78)	<0.001*	0.19	0.005*	0.62 (95% CI, 0.50-0.73)	0.065
Short diameter [mm]	0.63 (95% CI, 0.53-0.72)	0.010*	0.06	0.36	0.52 (95% CI, 0.40-0.65)	0.74
Long diameter [mm]	0.55 (95% CI, 0.46-0.65)	0.27	0.09	0.21	0.54 (95% CI, 0.43-0.65)	0.54

Furthermore, the correlation between IVC measurements and CVP was not strengthened using multiplanar or indexed measurements

*$p < 0.05$

Axial measurements were performed on standard axial CT slices

Multiplanar measurements were performed on double-oblique reformatted images perpendicular to the direction of the IVC

Indexed measurements are indexed to body surface area

Area under the curve (AUC) is displayed with 95% confidence interval (95% CI)

AUC area under the curve, *CVP* central venous pressure, *IVC* inferior vena cava, *ROC* receiver operating characteristics

found for axial short diameter (r = 0.45, $p < 0.001$) and axial area measurements (r = 0.44; $p < 0.001$). IVC measurements indexed to BSA and MPR IVC measurements did not improve correlations with CVP, compared to non-indexed axial measurements.

Performance of IVC CT measurements to detect elevated CVP and mortality in the RHC cohort

Table 2 shows the AUC (derived from ROC analysis) to detect elevated CVP for all IVC CT measurements. Axial IVC area measurements (AUC, 0.77; 95% CI, 0.70-0.84; $p < 0.001$; Fig. 3), axial IVC short diameter (AUC, 0.77; $p < 0.001$) and MPR IVC area measurements (AUC, 0.76; $p < 0.001$) showed the largest AUC to detect CVP ≥10 mmHg. IVC measurements indexed to BSA and MPR IVC measurements did not improve performance to detect elevated CVP, compared to non-indexed axial measurements.

To predict 1-year mortality, ROC analysis for axial IVC area measurements showed an AUC of 0.72 (95% CI, 0.60-0.85; p = 0.001; Fig. 4). Indexing axial IVC area measurements or MPR measurements did not improve performance to predict 1-year mortality (shown in Table 2). A cut-off of 665 mm^2 for axial IVC area measurements showed the highest diagnostic accuracy with a specificity of 84% and a sensitivity of 63% to predict 1-year mortality and was chosen for further survival analysis.

Reproducibility of axial IVC measurements

IVC axial area measurements showed an ICC of 0.998 (95% CI, 0.997-0.999; $p < 0.001$) and an absolute percentage error of 0.05 ± 1.92% between observers. ICC for long- and short-diameter IVC measurements were 0.983 (95% CI, 0.973-0.989; $p < 0.001$) and 0.966 (95% CI, 0.947-0.979; $p < 0.001$), respectively. Absolute percentage errors for long- and short-diameter IVC measurements were 0.16 ± 2.88% and 0.16 ± 4.70%, respectively.

Correlation of IVC axial area measurements with baseline characteristics in the RHC cohort

Further analyses were only performed with axial area measurements, as ROC analysis showed the highest AUC to predict 1-year mortality for axial area measurements.

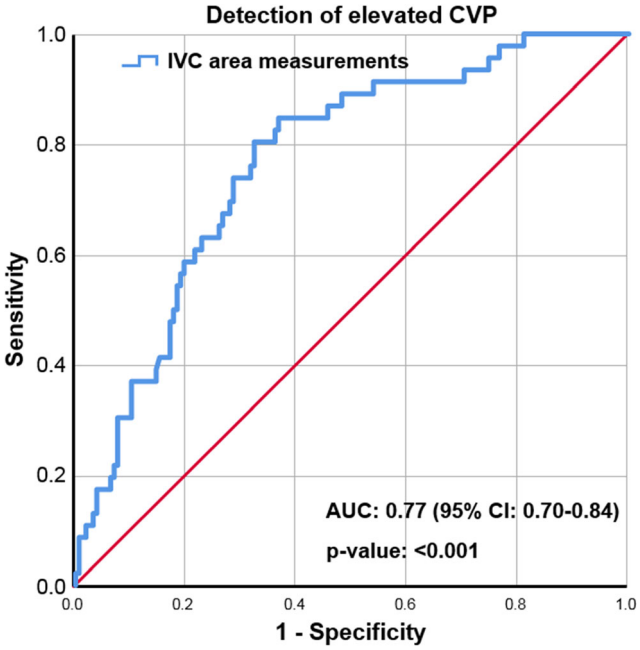

Fig. 3 The ROC curve indicates moderate strength of suprahepatic IVC area measurements to detect elevated central venous pressure in the RHC cohort (AUC, 0.77; 95% CI,0.70-0.84; $p < 0.001$; *blue line*). The true-positive rate (sensitivity) is plotted in function of the false-positive rate (100-specificity). The *red line* represents the diagonal reference line. *AUC* area under the curve, *CI* confidence interval, *IVC* inferior vena cava

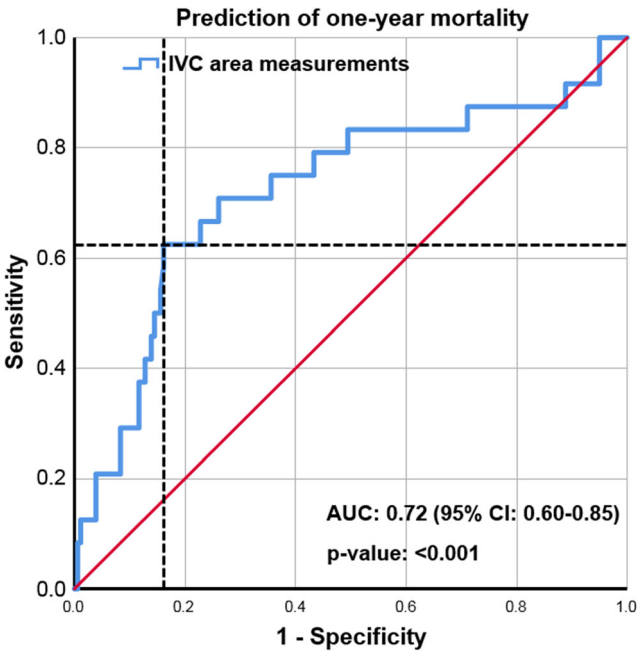

Fig. 4 The ROC curve indicates moderate strength of suprahepatic IVC area measurements to predict 1-year mortality in the RHC cohort (AUC, 0.72; 95% CI, 0.60-0.85; $p < 0.001$; *blue line*). The true positive rate (sensitivity) is plotted in function of the false-positive rate (100-specificity). The *red line* represents the diagonal reference line. A cut-off of 665 mm^2 (marked with *dotted lines*) showed a specificity of 84% and a sensitivity of 63% to predict 1-year mortality. *AUC* area under the curve, *CI* confidence interval, *IVC* inferior vena cava

There were significant but weak correlations of axial IVC area measurements with weight ($r = 0.24$; $p < 0.001$), height ($r = 0.28$; $p < 0.001$) and BSA ($r = 0.28$; $p < 0.001$), but not with BMI ($p = 0.157$). There was no significant correlation of IVC area measurements with age ($p = 0.616$).

Patients with an axial IVC area ≥665 mm^2 showed a higher median NT-pro-BNP-level ($p = 0.011$) at baseline. Furthermore, patients with an IVC area ≥665 mm^2 had higher end-diastolic ventricular pressures ($p = 0.001$), end-systolic right ventricular pressures ($p = 0.031$), higher systolic ($p = 0.002$), mean ($p = 0.003$) and diastolic ($p = 0.004$) pulmonary artery pressures, and higher pulmonary capillary wedge pressures (PCWP; $p = 0.001$) assessed by RHC. Additionally, patients with an IVC area ≥665 mm^2 had a larger right atrium in end-systole (long axis, $p < 0.001$; short axis, $p < 0.001$) and a larger right ventricle in end-diastole ($p = 0.008$), assessed by echocardiography (Table 3).

Correlation of IVC axial area measurements with echocardiography in the validation cohort

In the validation cohort, patients with an IVC area ≥665 mm^2 had a larger right atrium in end-systole (long axis, $p < 0.001$; short axis, $p = 0.001$) and a larger right ventricle in end-diastole ($p = 0.038$), assessed by echocardiography (Table 4).

Analysis of survival

Median time to death or follow-up was 371 days (interquartile range, 87-637 days). In the RHC cohort, Kaplan-Meier analysis of survival showed that patients with an axial IVC area ≥665 mm^2 at pre-procedural CTA had a significantly higher 1-year mortality after TAVI, compared to patients with an axial IVC area <665 mm^2 (38% versus 7%; log-rank p value <0.001; Fig. 5) and a HR of 6.9 (95% CI, 3.0-15.8; $p < 0.001$) in univariate Cox regression analysis. In multivariate Cox regression analysis IVC area ≥665 mm^2 showed a HR of 5.5 (95% CI, 2.2-13.6; $p < 0.001$).

In the validation cohort, patients with an axial IVC area ≥665 mm^2 also showed a significantly higher 1-year mortality after TAVI (34% versus 11%; log-rank p value = 0.004).

Discussion

This study suggests that pre-procedural CTA measurements of the suprahepatic IVC have moderate diagnostic strength to non-invasively detect CVP in a cohort of patients undergoing TAVI. Suprahepatic IVC enlargement, defined as an axial area ≥665 mm^2, is associated with more pronounced right heart dysfunction and is a predictor of post-procedural 1-year mortality after TAVI.

Table 3 Right heart catheterisation and echocardiographic parameters in patients of the RHC cohort with an axial suprahepatic inferior vena cava area ≥665 mm^2 and <665 mm^2, assessed in electrocardiogram-gated CT angiography

Axial IVC area (*RHC cohort*)		<665 mm^2 (*n* = 160)	≥665 mm^2 (*n* = 44)	*p* value
Right heart catheterisation				
CVP [mmHg]		6 (4-8)	9 (7-11)	<0.001*
Patients with elevated CVP [*n*, (%)]		27 (17)	19 (43)	<0.001*
End-diastolic right ventricular pressure [mmHg]		8 (5-11)	10 (8-12)	0.001*
End-systolic right ventricular pressure [mmHg]		45 (37-56)	54 (44-62)	0.031*
Diastolic pulmonary artery pressure [mmHg]		17 (13-21)	20 (17-23)	0.004*
Mean pulmonary artery pressure [mmHg]		27 (21-35)	32 (27-39)	0.003*
Systolic pulmonary artery pressure [mmHg]		43 (34-55)	53 (42-61)	0.002*
Patients with pulmonary hypertension [*n*, (%)]		99 (62)	40 (91)	<0.001*
Pulmonary capillary wedge pressure [mmHg]		17 (13-21)	20 (18-25)	0.001*
Echocardiography				
Ejection fraction [%]		59 (50-65)	55 (40-60)	0.026*
Mean trans-aortic pressure gradient [%]		43 (31-55)	36 (30-48)	0.084
Indexed aortic valve area [cm^2/m^2]		0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.52
End-systolic right atrium long axis [cm]		5.0 (4.6-5.5)	5.7 (5.1-6.3)	<0.001*
End-systolic right atrium short axis [cm]		3.8 (3.3-4.2)	4.6 (4.2-5.0)	<0.001*
End-diastolic right ventricle short axis [cm]		3.0 (2.6-3.5)	3.3 (3.1-3.8)	0.008*
Moderate or severe tricuspid regurgitation	no	113 (93)	33 (85)	0.100
	yes	8 (7)	6 (15)	

Data are expressed as median and inter-quartile range or count and percentage

CVP central venous pressure, *CT* computed tomography, *IVC* inferior vena cava, *RHC* right heart catheterisation

Right ventricular size and function can be adversely affected by pulmonary hypertension, including secondary pulmonary hypertension caused by left heart disease such as myocardial infarction and aortic stenosis [11, 22, 23]. Right ventricular dysfunction is a powerful predictor of mortality in patients with chronic left heart failure [11–13]. Furthermore, pulmonary hypertension is a strong predictor of mortality after TAVI, even though aortic valve replacement has shown to improve right ventricular filling pressures and pulmonary artery pressure immediately after treatment [15, 21, 24, 25]. Elevated CVP independently predicts mortality in patients with pulmonary hypertension [26]. Current guidelines recommend echocardiographic assessment of the IVC to estimate CVP as part of the evaluation of right ventricular dysfunction [16, 17]. Recently, Testa et al [11] have shown that severe right ventricular dysfunction limits expected benefit of TAVI, as patients with severe right ventricular dysfunction showed a significantly higher 1-year mortality, compared to patients with normal right ventricular function and patients with mild to moderate right ventricular dysfunction. In

Table 4 Echocardiographic parameters in patients of the validation cohort with an axial suprahepatic inferior vena cava area ≥665 mm^2 and <665 mm^2, assessed on electrocardiogram-gated CT angiography

Axial IVC area (*validation cohort*)		<665 mm^2 (*n* = 145)	≥665 mm^2 (*n* = 56)	*p* value
Echocardiography				
Ejection fraction [%]		56 (45-64)	55 (42-60)	0.246
Mean trans-aortic pressure gradient [%]		40 (29-53)	42 (26-54)	0.969
Indexed aortic valve area [cm^2/m^2]		0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.288
End-systolic right atrium long axis [cm]		4.9 (4.3-5.3)	5.9 (5.3-6.5)	<0.001*
End-systolic right atrium short axis [cm]		3.8 (3.4-4.1)	4.2 (3.8-4.7)	0.001*
End-diastolic right ventricle short axis [cm]		3.1 (2.9-3.4)	3.5 (3.0-3.7)	0.038*
Moderate or severe tricuspid regurgitation	no	105 (86)	42 (82)	0.495
	yes	17 (14)	9 (18)	

*$p < 0.05$

Data are expressed as median and inter-quartile range or count and percentage

CT computed tomography, *IVC* inferior vena cava

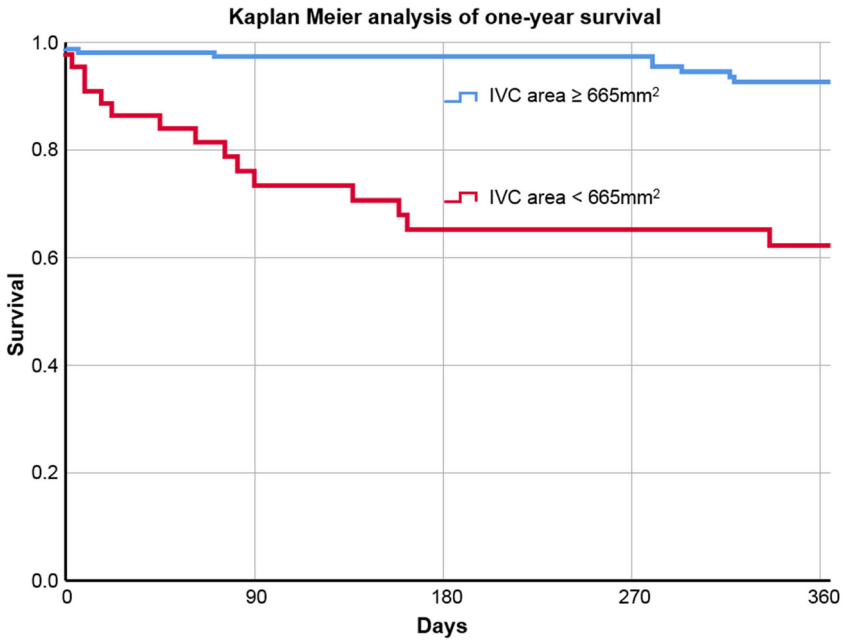

Fig. 5 In the RHC cohort, Kaplan-Meier analysis of survival shows significantly increased 1-year mortality in patients with an axial suprahepatic IVC area ≥665 mm^2 (*blue curve*) at pre-procedural CT (log-rank $p < 0.001$), compared to patients with an IVC area <665 mm^2 (*red curve*). *IVC* inferior vena cava, *RHC* right heart catheterisation

contrast, Koifman et al [27] did not find a significant difference in 1-year mortality between patients with severe aortic stenosis and right ventricular dysfunction and patients with normal right ventricular function, but in contrast to Testa et al [11] they did not subclassify right ventricular dysfunction according to severity. In our study, patients with suprahepatic IVC enlargement on CTA, showed a significantly higher CVP, higher right ventricular pressures, pulmonary artery pressures and PCWP, assessed by RHC, Furthermore, these patients showed larger right heart dimensions assessed by echocardiography. Therefore, our results indicate that suprahepatic IVC enlargement, assessed on pre-procedural CTA, may represent more severe right heart dysfunction in TAVI patients. As CTA is routinely performed prior to TAVI, IVC enlargement may be used as an additional, easily accessible parameter to predict post-procedural outcome without the need for additional radiation. Supporting our data, Franzone et al [28] recently showed that CVP, estimated with ultrasound, is significantly higher in patients dying within 2 years after TAVI, compared to patients with 2-year survival after TAVI but they did not compare actual echocardiographic IVC measurements.

IVC dilation is a recognised marker of haemodynamic congestion [19]. In the literature we did not find a study evaluating CT measurements of the hepatic or suprahepatic IVC segment to predict CVP. Size and shape of the IVC varies with changes in CVP and intravascular volume [18, 19]. Additionally, several factors influence measurements of the IVC, such as negative intrathoracic pressure secondary to inspiration and image assessment during systole, which both lead to a decrease in IVC size [18, 29]. Ultrasound is a fast and easy to use screening tool allowing for real-time imaging of the IVC during the respiratory cycle and estimation of CVP without ionising radiation [16,, 18]. In our study, CTA was performed as a high-pitch scan in mid-inspiration to assess aortic annulus size in diastole, allowing for standardised evaluation of the IVC. Nonetheless, differences in inspiration depth and changes in cardiac rhythm may affect CTA measurements of the IVC. Furthermore, due to our CT protocol, we could only assess the IVC area at one time point of the cardiac cycle but could not assess IVC area changes during the cardiac cycle. Further studies may be warranted to assess if changes during the cardiac cycle may provide incremental value to detect elevated CVP or to predict mortality after TAVI. Our results show only moderate correlation of IVC area measurements with CVP, comparable to the results of Seo et al [20] assessing correlation of 3D echocardiographic area measurements and CVP. In contrast to their results, CT short-diameter measurements of the IVC did not notably increase the correlation with CVP in our study [20]. Interestingly, indexing measurements did also not strengthen correlation between IVC measurements and CVP, a finding which was also previously reported [20]. Our measurements of the suprahepatic IVC may not be comparable to echocardiographic measurements, as guidelines suggest the assessment of the hepatic segment of the IVC just inferior to the hepatic veins [16, 17]. But in CTA dedicated for TAVI evaluation, the hepatic segment of the IVC is usually not evaluable. In contrast to echocardiography, CT measurements of the IVC probably have the advantage to have a higher reproducibility as these measurements are not influenced by transducer angles and are less operator-dependent, compared to ultrasound measurements of the IVC. Indeed, we could show that IVC CT measurements are highly reproducible. A recent review of the existing literature about diagnostic accuracy and clinical

utility of ultrasound measurements of the IVC, as a method to assess CVP, indicated that most studies showed moderate strength correlation between IVC measurements and CVP despite heterogeneous measurement techniques, as correlation ranged from weak and not significant to very strong correlations and results were also influenced by patient cohorts [19]. In this review, AUC to detect elevated CVP for different ultrasound measurement techniques ranged between 0.66 and 0.93, which would locate the performance of CT measurements in our cohort in the middle of that spectrum [19].

This study has some limitations. First, this study has the inherent bias of a retrospective, single-centre design. Further studies are required to prove whether our results are transferable to other CT scanners, CT protocols and patient cohorts. Second, CTA and RHC were not performed simultaneously, which may facilitate significant changes in cardiac haemodynamics. To restrict this limitation, we decided to only include patients with RHC and CTA within 1 day into our RHC cohort. Third, we did not assess whether TAVI had an impact on haemodynamic profiles and whether these changes had an impact on post-procedural mortality. Fourth, in establishing a cut-off to predict 1-year mortality in the RHC cohort, we introduced a selection bias. Therefore, we chose to validate this cut-off in our validation cohort. Fifth, we could not compare our CT measurements to echocardiographic IVC measurements, or echocardiographic functional assessment of the right heart, such as tricuspid annular plane systolic excursion (TAPSE) or estimated systolic pulmonary artery pressure (PASP) as in our cohort echocardiographic IVC measurements and functional right heart assessment were not regularly performed before TAVI.

Conclusions

Our study shows that suprahepatic IVC area measurements on CTA are moderate predictors of an elevated CVP in patients undergoing TAVI. Furthermore, pre-procedural enlargement of the suprahepatic IVC, defined as an area ≥665 mm^2 on axial CT slices, is an independent predictor of 1-year all-cause mortality and may add prognostic value to CT evaluation of TAVI candidates.

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Compliance with ethical standards

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Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported in:

1. Eberhard M, Mastalerz M, Frauenfelder T et al (2017) Quantification of aortic valve calcification on contrast-enhanced CT of patients prior to transcatheter aortic valve implantation. EuroIntervention 13:921-927
2. Eberhard M, Mastalerz M, Pavicevic J et al (2017) Value of CT signs and measurements as a predictor of pulmonary hypertension and mortality in symptomatic severe aortic valve stenosis. Int J Cardiovasc Imaging 33:1637-1651
3. Possner M, Vontobel J, Nguyen-Kim TD et al (2016) Prognostic value of aortic regurgitation after AVI in patients with chronic kidney disease. Int J Cardiol 221:180-187
4. Stahli BE, Abouelnour A, Nguyen TD et al (2014) Impact of three-dimensional imaging and pressure recovery on echocardiographic evaluation of severe aortic stenosis: a pilot study. Echocardiography 31:1006-1016

While the previous studies assessed quantification of aortic valve calcification, prognostic value of aortic regurgitation after TAVI, impact of three-dimensional imaging and pressure recovery on echocardiographic evaluation of severe aortic stenosis and value of previously reported CT signs and measurements as a predictor of pulmonary hypertension and mortality in severe aortic stenosis, this work focused on whether IVC measurements are correlated with central venous pressure and the predictive value of IVC measurements on one-year mortality after TAVI. Thus, this work is substantially different from the previous reports. Additionally, in contrast to the aforementioned studies the present study is the only one including all patients undergoing TAVI between 01/2011 and 12/2014 at our institution.

Methodology

- retrospective
- diagnostic or prognostic study
- performed at one institution

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