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Early safety outcome following transcatheter aortic valve implantation: is the amount of contrast media used a matter of concern?

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Summary

QUESTIONS UNDER STUDY: The study objective was to evaluate the impact of the amount of contrast medium used for transcatheter aortic valve implantation (TAVI) on short-term outcome. Patients undergoing TAVI are exposed to repeat contrast medium application both for preprocedural screening and during the TAVI procedure itself. Whether the amount of contrast media is associated with worse outcome is unclear.

METHODS: A total of 257 patients were included (median age 82.7 years) and divided into two groups with preserved and reduced kidney function (glomerular filtration rate <60 ml/min/1.73 m^2), respectively. Total volume of contrast media administered during and within 5 days prior to TAVI was analysed. A combined early safety endpoint at 30 days was evaluated.

RESULTS: The early safety endpoint was reached by 31 patients and acute kidney injury occurred in 22 patients. The median total volume of contrast media administered was 144 ml (interquartile range 81–225 ml). The amount of contrast did not independently predict the early safety endpoint in the overall population (odds ratio [OR] 0.93, 95% confidence interval [CI] 0.56 to 1.53, p = 0.774) and in subgroups with preserved and reduced kidney function. Change in creatinine was an independent strong predictor of the early safety endpoint in the overall population (OR 18.13, 95% CI 4.70 to 69.99, p <0.001), as well as in subgroups with preserved and reduced kidney function. The amount of contrast did not predict a change in creatinine within 72 hours following TAVI (r = 0.02, 95% CI –0.02 to 0.07, p = 0.368).

CONCLUSION: Decreased kidney function after TAVI influences outcome. When rather small amounts of contrast media are used for screening and the TAVI procedure itself, the amount of contrast media seems not to be an independent predictor of outcome, further suggesting that decreased kidney function after TAVI is multifactorial.

Key words: *TAVI; contrast media; short-term outcome; early safety outcome*

Introduction

Transcatheter aortic valve implantation (TAVI) has become an accepted percutaneous procedure for the treatment of advanced aortic valve disease [1]. Patients undergoing TAVI are usually older and suffer from a number of comorbidities. The mean age range of patients undergoing TAVI in high-volume registries has been reported to be between 81 and 84 years old, and the prevalence of comorbidities such as chronic obstructive pulmonary disease (COPD), coronary and peripheral artery disease, as well as chronic kidney disease (CKD), arterial hypertension and diabetes is high [2–6]. CKD is one of the most frequently encountered comorbidities, with a prevalence ranging from 20% to 60% in large studies [7–9]. In most centres, preprocedural screening includes – besides echocardiography – investigations necessitating application of contrast media (coronary angiography, aortic root angiography, peripheral angiography, computed tomography). This is followed by repeat contrast media application during the TAVI procedure itself. Repeat contrast media applications potentially expose this vulnerable population to an increased risk of acute kidney injury (AKI). AKI following TAVI is associated with significant morbidity and in-hospital mortality [10] and concomitant CKD increases the incidence of kidney disorders after TAVI up to 30% [11].

The volume of contrast media is considered a major risk factor associated with AKI in patients undergoing percu-

taneous coronary intervention (PCI) [12]. Usually systemic and kidney perfusion change only marginally after PCI, but haemodynamics are dramatically changed immediately after TAVI, thereby *per se* improving kidney perfusion. However, data concerning the effect of contrast media on kidney function following TAVI are conflicting [13–16]. While Madershahian et al. reported a possible association between the extensive use of contrast media during TAVI and the incidence of contrast-induced nephropathy and mortality in patients with impaired kidney function [13], a large multicentre Italian study could not confirm this [14]. The fact that many patients receive additional contrast media shortly prior to TAVI during computed tomography and/or angiography has been neglected in previous studies and not been taken into account in the evaluation of AKI and short-term outcome.

Thus, the aim of the present study was to evaluate the impact on short-term outcome of the total amount of contrast media administered shortly prior to and during the TAVI procedure, as well as the association between contrast media and kidney function deterioration following TAVI.

Methods

Patient population, screening process and TAVI procedure

Between April 2012 and June 2014, 257 consecutive patients undergoing TAVI for severe native aortic valve stenosis at the University Heart Centre Zurich were prospectively included in a nationwide registry (Swiss TAVI registry). Eligibility for TAVI was based on the consensus of the heart team. Baseline characteristics, procedural and follow-up data from each patient were entered in the registry. Each patient signed an informed consent for data collection and analysis. The registry was approved by the local ethics committee.

Each patient underwent transthoracic echocardiography prior to TAVI. Transoesophageal echocardiography has not been performed routinely. Multi-detector computed tomography (CT) to accurately assess the aortic valvular complex for exact prosthesis sizing and to assess vascular access site was performed in most patients prior to TAVI. A bolus of 80–130 ml iodinated contrast media (Iomeprol, Bracco, Italy) was injected via an antecubital vein. Before intervention, left or both left and right heart catheterisation to evaluate coronary and aortic anatomy as well as haemodynamic status was performed in most patients. The time interval between preprocedural CT, angiography and TAVI was variable, depending on the urgency of valve replacement. Iopromide (Bayer HealthCare Pharmaceuticals, Germany) was used as contrast medium for both coronary angiography and the TAVI procedure.

The default access for TAVI was transfemoral, as was local anaesthesia. Transaxillary, transapical, or direct aortic access was used as alternative access route in cases where peripheral arterial disease was limiting. Valve implantation was performed under rapid pacing (for balloon-expandable valves) or fast pacing (for self-expanding valves).

Standard blood samples for haematology and serum chemistry were taken 1 day prior to TAVI and daily thereafter up to 72 hours after the procedure. Further blood samples were drawn, depending on the treating physician's decision. To prevent contrast-induced AKI, nonuniform protocols, depending on the treating physician's preference, were applied in patients with pre-existing impaired kidney function. Usually, patients received periprocedural hydration with intravenous normal saline (100 ml/h) starting at least 12 hours prior to and ending 24 hours after TAVI. Intravenous n-acetylcysteine was additionally administered at a dose of 1 200 mg 12 hours before and after TAVI. In patients with diabetes, metformin was stopped 1 day prior to the intervention and reinstituted after the procedure, depending on kidney function. Contrast-sparing approaches to minimise the risk of contrast-induced nephropathy are routine measures and were chosen in all patients with CKD, if possible [17].

Follow-up

Clinical follow-up was performed at 30 days and 12 months, and yearly thereafter either at our institution or by a local cardiologist. Telephone interviews were used to complete follow-up. In the case of events, medical records were reviewed and all events were independently adjudicated by a clinical event committee. All events were defined according to the Valve Academic Research Consortium (VARC)-2 consensus document criteria [18].

Transthoracic echocardiography was performed before intervention, before hospital discharge, at 30 days and 12 months, and yearly thereafter.

Kidney function and contrast media

Baseline kidney function in the form of glomerular filtration rate (GFR) was determined in each patient based on the last preprocedural serum creatinine value and the Modification of Diet in Renal Disease (MDRD) equation [19]. Patients with preserved kidney function at baseline (GFR ≥60 ml/min/1.73 m^2) were compared with patients with reduced kidney function (GFR <60 ml/min/1.73 m^2). Patients on chronic haemodialysis before intervention were excluded from the analysis (n = 6, 2.3%).

To evaluate the impact of contrast media, all iodinated contrast media administered during and within 5 days prior to TAVI (CT, angiography, PCI) were included in the analysis.

Endpoints

The primary endpoint was the VARC-2 early safety endpoint [18], comprising all-cause mortality, all stroke, life-threatening bleeding, AKI stage 2 or 3, coronary artery obstruction requiring intervention, major vascular complication and valve-related dysfunction requiring repeat procedure (balloon aortic valvuloplasty, surgical aortic valve replacement, TAVI) up to 30 days.

AKI was defined as a reduction in kidney function within 48 hours following TAVI according to the VARC-2 criteria [18]: increase in serum creatinine to ≥150% or an increase of ≥26.4 mmol/l (stage 1); increase in serum creatinine to 200–299% (stage 2); increase in serum creatinine to ≥300% or an increase in serum creatinine of ≥354 mmol/l with an acute increase of at least 44 mmol/l or the new installation of dialysis after TAVI (stage 3).

Statistical analysis

Continuous variables were expressed as median ± interquartile range (IQR) or mean ± standard deviation, depending on variable distribution, and categorical variables as numbers and percentages. Comparisons between groups of patients with preserved and reduced kidney function and between groups split according to the occurrence of the early safety endpoint were performed with Mann-Whitney U test, t test or χ^2 test, as appropriate. Firstly, the impact of the total amount of contrast media on the early safety endpoint was analysed with a multivariate logistic regression analysis with adjustment for the total contrast media volume administered during and within 5 days prior to TAVI and the Society of Thoracic Surgeons (STS) score [20]. Secondly, the impact of the change of creatinine within 72 hours following TAVI on the early safety endpoint was analysed with a multivariate logistic regression analysis, adjusted for the change of creatinine within 72 hours after TAVI and the STS score. Finally, the association between the total amount of contrast media and the change of creatinine was studied. A multivariate linear regression model was performed with adjustment for the total amount of contrast media administered during and within 5 days prior to TAVI and the STS score to evaluate their impact on the change of creatinine within 72 hours following TAVI. Change in creatinine was defined as any change in creatinine within 72 hours following TAVI, thus including increased, decreased or unchanged creatinine. As STS score includes comorbidities such as hypertension, diabetes, prior coronary or peripheral artery disease, prior stroke and lung disease, this integrated score has been included into the multivariate model instead of each single risk factor. The amount of contrast was log transformed to correct for non-normal distribution. Subgroup analyses have been performed for groups of patients with preserved and reduced kidney function. Results of logistic regression analysis are reported as odds ratio (OR) and 95% confidence interval (CI). Correlation is reported as correlation coefficient r and 95% CI. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using a commercially available software package (STATA 12.1, StataCorp. 4905 Lakeway Drive, College Station, Texas 77845 USA and SPSS Statistics, Version 22, IBM, Chicago, IL, USA).

Results

A total of 257 patients were included in the study. Baseline characteristics are described in tables 1a and 1b. Almost half of the patients had preserved kidney function (GFR ≥60 ml/min/1.73 m^2) at baseline (122 patients [47.5%]), whereas reduced kidney function (GFR <60 ml/min/1.73 m^2) was present in 135 patients (52.5%). Overall, CT and cardiac catheterisation were performed in 218 (84.8%) and 237 (92.2%) patients, respectively, prior to TAVI. However, in only 91 (35.4%) and 57 (22.2%) patients, respectively, CT and cardiac catheterisation were performed within the critical 5-day period prior to TAVI. Four patients additionally underwent PCI within 5 days prior to TAVI. The following devices were used for implantation: CoreValve (Medtronic Inc., Minneapolis, MN, USA, 108 patients, 42%), Edwards Sapien (Edwards Life science, Irvine, CA, USA, 141 patients, 54.9%), Symetis Acurate (Symetis ACURATE TA, Symetis Inc., Ecublens, VD, Switzerland, three patients, 1.2%), St. Jude Medical Portico (St. Jude Medical, St. Paul, MN, USA, three patients, 1.2%), Direct Flow Medical (Direct Flow Medical Inc., Santa Rosa, CA, USA, two patients, 0.8%).

The median amount of contrast used was 80 ml (IQR 40–130 ml) for CT and 84 ml (IQR 60–104 ml) for angiography. Overall, the median amount of contrast media administered during TAVI was 99 ml (IQR 65–147 ml). Median contrast volume during TAVI in patients with preserved versus reduced kidney function was 100 ml (IQR 70–157 ml) versus 88 ml (IQR 60–130 ml, p = 0.035). Overall, the median total amount of contrast media used in each patient within the 5-day period was 144 ml (IQR 81–225 ml), with 150 ml (IQR 88–251 ml) in the preserved kidney function group versus 135 ml (IQR 77–207 ml) in the reduced kidney function group (p = 0.120).

Early safety endpoint

The early safety endpoint occurred in 31 patients (12.1%; 19 patients [15.6%] in the group with preserved kidney function, and 12 [8.9%] in the group with reduced kidney function, p = 0.298). An overview on the events is presented in table 2.

The amount of contrast administered was not an independent predictor of the early safety endpoint (table 3), both in the overall population (OR 0.93, 95% CI 0.56 to 1.53, p = 0.774) and in subgroups with preserved (OR 1.73, 95% CI 0.66 to 4.53, p = 0.266) and reduced kidney function (OR 0.75, 95% CI 0.42 to 1.35, p = 0.340), without evidence for effect modification (p for interaction = 0.19).

On the other hand, the change in creatinine from baseline up to 72 hours following TAVI was an independent and strong predictor of the early safety endpoint (OR 18.13, 95% CI 4.70 to 69.99, p <0.001; table 4). In subgroup analyses, this creatinine change remained independently associated with the early safety endpoint in groups with preserved (OR 17.48, 95% CI 2.86 to 106.92, p = 0.002) and reduced kidney function (OR 25.75, 95% CI 2.86 to 231.92, p = 0.004), without evidence for effect modification (p for interaction = 0.46).

Association between amount of contrast media administered and change in kidney function

AKI occurred in 9 patients (7.4%) with preserved kidney function at baseline and in 13 patients (9.6%) with reduced kidney function (p = 0.519). A small, but statistically nonsignificant difference was found in the amount of contrast media administered to patients who experienced AKI (159 ml, IQR 80–216 ml) compared with patients without AKI (142 ml, IQR 83–226 ml, p = 0.798).

Median amount of contrast administered in patients with postimplant decline in kidney function was higher (154 ml, IQR 97–236 ml) than in patients with improved kidney function (139 ml, IQR 77–207 ml). However, the difference was not statistically significant (p = 0.213). No association between the amount of contrast media administered

during and within 5 days prior to TAVI and a change of creatinine within 72 hours following TAVI was found (r = 0.02, 95%CI –0.02 to 0.07, p = 0.368; table 5, fig. 1). Furthermore, no such association was found in either subgroup (subgroup with preserved kidney function [r = 0.06, 95% CI –0.01 to 0.13, p = 0.112] and reduced kidney function [r = –0.01, 95% CI –0.07 to 0.05, p = 0.698]). Again, there was no evidence for effect modification (p for interaction = 0.14).

Bleeding complications

Bleeding complications occurred significantly more often in patients with reduced kidney function (19 patients [14.1%]) compared with patients with preserved kidney function (5 patients [4.1%], p = 0.009). No significant difference was found for life-threatening bleeding (p = 0.390), whereas nonlife-threatening bleeding occurred significantly more frequently in patients with reduced kidney function (p = 0.006).

Discussion

This was a retrospective cohort study analysing the impact of contrast media used for screening and the TAVI procedure itself on short-term outcome. No association between the amount of contrast media and the short-term outcome 30 days after TAVI was found, in subgroups with preserved and reduced kidney function. Surprisingly, the amount of contrast media was not associated with a change in creatinine shortly after TAVI. However, change in creatinine was associated with worse short-term outcome.

While operator experience [21], patient selection and advances in technology [22] lead to a decrease in the incidence of early safety events following TAVI, occurrence of

Table 1a: Patient characteristics according to the early safety endpoint.

	Overall population (n = 257)	No event* (n = 226)	Event* (n = 31)	p-value
Age (years), median (IQR)	82.7 (78.4–87.3)	82.6 (78.4–87.1)	84.9 (77.8–88.0)	0.55
Males, n (%)	127 (49.4)	110 (48.7)	17 (54.8)	0.52
Body mass index (kg/m^2), median (IQR)	25.9 (23.4–29.1)	25.85 (23.4–29.1)	26.1 (24.1, 29.8)	0.62
Diabetes, n (%)	63 (24.5)	54 (23.9)	9 (29.0)	0.53
Hypertension, n (%)	191 (74.3)	170 (75.2)	21 (67.7)	0.37
Dyslipidaemia, n (%)	79 (30.7)	68 (30.1)	11 (35.5)	0.54
COPD, n (%)	47 (18.3)	43 (19.0)	4 (12.9)	0.41
Prior CVI, n (%)	30 (11.7)	26 (11.5)	4 (12.9)	0.82
Prior PCI, n (%)	56 (21.8)	50 (22.1)	6 (19.4)	0.73
Prior MI, n (%)	28 (10.9)	26 (11.5)	2 (6.5)	0.40
Known CAD, n (%)	124 (48.2)	110 (48.7)	14 (45.2)	0.71
Known PAD, n (%)	37 (14.4)	29 (12.8)	8 (25.8)	0.05
Prior cardiovascular surgery, n (%)	34 (13.2)	31 (13.7)	3 (9.7)	0.53
Kidney function				
GFR >90 ml/min/1.73 m^2, n (%)	26 (10.1)	23 (10.2)	3 (9.7)	0.82
GFR 60–89 ml/min/1.73 m^2, n (%)	96 (37.4)	87 (38.5)	9 (29.0)	
GFR 45–59 ml/min/1.73 m^2, n (%)	70 (27.2)	62 (27.4)	8 (25.8)	
GFR 30–44 ml/min/1.73 m^2, n (%)	37 (14.4)	31 (13.7)	6 (19.4)	
GFR 15–29 ml/min/1.73 m^2, n (%)	22 (8.6)	18 (8.0)	4 (12.9)	
GFR <15 ml/min/1.73 m^2, n (%)	6 (2.3)	5 (2.2)	1 (3.2)	
Dialysis, n (%)	6 (2.3)	5 (2.2)	1 (3.2)	0.73
Creatinine at baseline (µmol/l), median (IQR)	97 (81–126)	97 (81–123)	111 (84–137)	0.26
GFR at baseline (ml/min/1.73 m^2), mean ± SD	59.8 ± 24.1	60.2 ± 23.8	56.6 ± 25.9	0.43
STS score, median (IQR)	4.62 (3.1–7.67)	4.59 (2.9–7.0)	5.89 (3.2–9.34)	0.08
Aortic valve area at baseline (cm^2), median (IQR)	0.70 (0.60–0.90)	0.70 (0.60–0.90)	0.70 (0.60–0.90)	0.98
Mean gradient at baseline (mm Hg), mean ± SD	43 ± 16	43 ± 16	44 ± 16	0.68
LVEF at baseline (%), median (IQR)	58.5 (47–65)	59 (47–65)	56 (45–65)	0.78
Contrast volume				
Contrast for CT (ml), median (range)	80 (40–130)	80 (40–130)	80 (60–80)	0.16
Contrast for angiography (ml), median (IQR)	98 (75–144)	101 (75–145)	90 (60–130)	0.21
Contrast for TAVI (ml), median (IQR)	99 (65–145)	95 (65–145)	104 (60–160)	0.67
Total contrast during and within 5 days prior to TAVI (ml), median (IQR)	144 (81–225)	139.5 (84–220)	159 (60–270)	0.77
Devices				
Medtronic CoreValve, n (%)	108 (42.0)	93 (41.2)	15 (48.4)	0.63
Edwards Sapien, n (%)	141 (54.9)	126 (55.8)	15 (48.4)	
Symetis Acurate, n (%)	3 (1.2)	2 (0.9)	1 (3.2)	
SJM Portico, n (%)	3 (1.2)	3 (1.3)	0 (0.0)	
Direct Flow Medical, n (%)	2 (0.8)	2 (0.9)	0 (0.0)	

* Early safety endpoint at 30 days

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CT = computed tomography; CVI = cerebrovascular insult; GFR = glomerular filtration rate; IQR = interquartile range; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; SD = standard deviation; STS = Society of Thoracic Surgeons; TAVI = transcatheter aortic valve implantation.

AKI is still a relevant problem. In our study the incidence of AKI was 9%. This is in line with other studies, where the incidence of AKI was reported to be between 8–28% and was associated with a higher 30-day mortality [11, 15, 23–29]. Therefore, any measures to reduce AKI incidence are important.

Table 1b: Patient characteristics according to kidney function at baseline.

	GFR <60 ml/min/1.73 m^2 (n = 135)	GFR ≥60 ml/min/1.73 m^2 (n = 122)	p-value
Age (years), median (IQR)	82.4 (79.4–88.4)	82.0 (76.8–85.3)	0.01
Males, n (%)	54 (40.0)	73 (59.8)	<0.01
Body mass index (kg/m^2), median (IQR)	26.5 (23.9–29.8)	25.7 (23.4–28.1)	0.47
Diabetes, n (%)	41 (30.4)	22 (18)	0.02
Hypertension, n (%)	105 (77.8)	86 (70.5)	0.18
Dyslipidaemia, n (%)	43 (31.9)	36 (29.5)	0.68
COPD, n (%)	23 (17.0)	24 (19.7)	0.59
Prior CVI, n (%)	12 (8.9)	18 (14.8)	0.14
Prior PCI, n (%)	34 (25.2)	22 (18.0)	0.17
Prior MI, n (%)	17 (12.6)	11 (9.0)	0.36
Known CAD, n (%)	71 (52.6)	53 (43.4)	0.14
Known PAD, n (%)	26 (19.3)	11 (9.0)	0.02
Prior cardiovascular surgery, n (%)	22 (16.3)	12 (9.8)	0.13
Absolute change in creatinine (µmol/l), median (IQR)*	–4.5 (–18 to 11.8)	–3.0 (–9.5 to 4.0)	0.24
Absolute change in GFR (ml/min/1.73 m^2), median (IQR)*	+1.7 (–4.0 to 9.3)	+3.7 (–4.7 to 12.3)	0.43
GFR at baseline (ml/min/1.73 m^2), median (IQR)	44.9 (32.0–52.3)	75.0 (67.7–87.4)	<0.01
STS score, median (IQR)	6.50 (4.20–10.70)	3.6 (2.5–5.0)	<0.01
Aortic valve area at baseline (cm^2), median (IQR)	0.70 (0.60–0.90)	0.72 (0.60–0.90)	0.26
Mean gradient at baseline (mm Hg), mean ± SD	43 ± 16	43 ± 16	0.97
LVEF at baseline (%), median (IQR)	57 (45–65)	59 (50–65)	0.49
Contrast volume			
Contrast for CT (ml), median (range)	80 (80–130)	80 (40–130)	0.02
Contrast for angiography (ml), median (IQR)	95 (70–138)	103 (75–154)	0.24
Contrast for TAVI (ml), median (IQR)	88 (60–130)	100 (70–157)	0.04
Total contrast during and within 5 days prior to TAVI (ml), median (IQR)	135.0 (77–207)	150 (88–251)	0.10
Devices			
Medtronic CoreValve, n (%)	62 (45.9)	46 (73.7)	0.35
Edwards Sapien, n (%)	69 (51.1)	72 (59.0)	
Symetis Acurate, n (%)	2 (1.5)	1 (0.8)	
SJM Portico, n (%)	2 (1.5)	1 (0.8)	
Direct Flow Medical, n (%)	0 (0.0)	2 (1.6)	

* Minus means a decrease in creatinine or GFR, plus means an increase in creatinine or GFR
CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CT = computed tomography; CVI = cerebrovascular insult; GFR = glomerular filtration rate; IQR = interquartile range; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PAD = peripheral artery disease; PCI; percutaneous coronary intervention; SD = standard deviation; STS = Society of Thoracic Surgeons; TAVI = transcatheter aortic valve implantation.

Table 2: Events at 30 days.

Event	All n = 257	GFR ≥60 ml/min/1.73 m^2 n = 122	GFR <60 ml/min/1.73 m^2 n = 135	p-value
Early safety endpoint	31 (12.1)	19 (15.6)	12 (8.9)	0.30
All-cause mortality	9 (3.5)	3 (2.5)	6 (4.4)	0.39
Cardiovascular mortality	8 (3.1)	3 (2.5)	5 (3.7)	0.57
Noncardiovascular mortality	1 (0.4)	0	1 (0.7)	0.34
Myocardial infarction	0	0	0	
Stroke/TIA	8 (3.1)	4 (3.3)	4 (3.0)	0.88
Bleeding	24 (9.3)	5 (4.1)	19 (14.1)	0.01
Life-threatening	9 (3.5)	3 (2.5)	6 (4.4)	0.39
Nonlife-threatening	15 (5.8)	2 (1.6)	13 (9.6)	0.01
Acute kidney injury	22 (8.6)	9 (7.4)	13 (9.6)	0.52
Stage 1	18 (7.0)	9 (7.4)	9 (6.7)	0.82
Stage 2 or 3	4 (1.6)	0	4 (3.0)	0.06
Conduction disturbances and arrhythmias	34 (13.2)	17 (13.9)	17 (12.6)	0.75
Valve-related dysfunction requiring repeat procedure	2 (0.8)	1 (0.8)	1 (0.7)	0.94

Values are expressed as n (%)
GFR = glomerular filtration rate; TIA = transient ischaemic attack.

Interestingly, the amount of contrast administered in our study was relatively low and was not an independent predictor of the early safety endpoint (median 99 ml, IQR 65–147 ml). Our findings are in line with the findings of Bagur et al., where a similarly low amount of contrast was used (mean 97 ± 57 ml) [25]. This indicates that AKI in TAVI patients is most likely multifactorial. Several different reasons for a decline of kidney function following TAVI have been reported [25], for example, major bleeding requiring red blood cell transfusion has been shown to increase the risk of AKI following TAVI [11, 25]. In the present study, 14% of all patients received red blood cell transfusion. Thus, efforts to reduce bleeding complications are important to improve the outcome following TAVI – this is particularly true for patients in atrial fibrillation who are at high-risk for major bleeding complications [30]. Left atrial appendage occlusion may offer an attractive treatment option in these patients [31].

Secondly, short periods of severe hypotension during TAVI have been suggested to be risk factors for AKI, although Bagur et al. did not find an association between the number of rapid pacing runs and the occurrence of AKI [25].

Thirdly, most patients with severe aortic stenosis undergoing TAVI suffer from diffuse atherosclerosis and manipulation with catheters in the aorta and on the aortic valve may expose patients to the risk of arteriosclerotic microembolism with temporary deterioration of kidney function.

In clinical practice we try to save contrast in every patient, but particularly in patients with decreased renal function. We recently showed that TAVI with minimal amounts of contrast can be safely performed [17]. Therefore, the findings of the present study came as some surprise. Although the amount of contrast for TAVI can be reduced to as little as 8 ml [17], the total amount of contrast used in this study was rather low (144 ml, including screening CT and screening angiograms performed within 5 days prior to the procedure). Furthermore, only a few patients in our cohort had severely decreased kidney function (GFR <30 ml/min/1.73 m^2), precluding a separate subgroup analysis for these patients.

The fact that the amount of contrast media was not associated with a change in creatinine within 72 hours following TAVI was surprising, as contrast media are well-known risk factors of renal impairment. Contrast-induced nephropathy affects predominantly patients with chronic kidney disease [32]. The prevalence of moderate to severe kidney failure was rather low in the present study, which might in part explain our findings. Contrast-sparing approaches and periinterventional hydration therapy were used and may further have influenced our results. Furthermore, treatment of the severe aortic stenosis itself leads to an increased cardiac output and reduced venous congestion, thereby improving renal perfusion and thus glomerular filtration rate immediately after the intervention [33].

Other factors are also associated with worsening kidney function, such as the use of nonfemoral approaches (8.9%

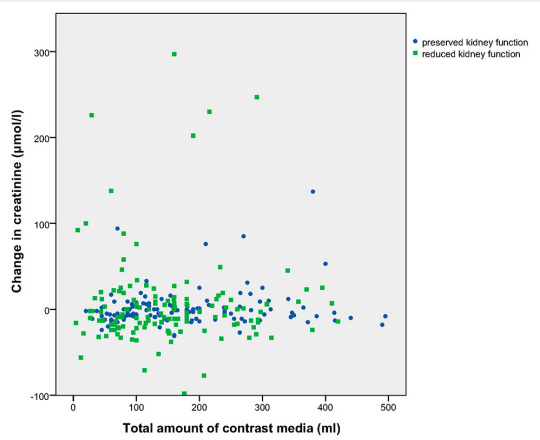

Figure 1

Association between the total amount of contrast media (in ml) administered during and within 5 days prior to TAVI and absolute changes in creatinine (in µmol/l) within 72 hours following TAVI in each patient according to preinterventional kidney function (preserved kidney function: GFR ≥60 ml/min/1.73 m^2 versus reduced kidney function: GFR <60 ml/min/1.73 m^2).

Table 3: Impact of contrast media as a predictor of events (n for events = 31) at multivariable regression.

	All patients		GFR ≥60 ml/min/1.73 m^2		GFR <60 ml/min/1.73 m^2	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Log total contrast media	0.93	0.56 to 1.53	1.73	0.66 to 4.53	0.75	0.42 to 1.35
STS score	1.03	0.98 to 1.09	0.98	0.85 to 1.14	1.03	0.97 to 1.10

CI = confidence interval; GFR = glomerular filtration rate; OR = odds ratio; STS = Society of Thoracic Surgeons

Table 4: Impact of change of creatinine as a predictor of events (n for events = 31) at multivariable regression.

	All patients		GFR ≥60 ml/min/1.73 m^2		GFR <60 ml/min/1.73 m^2	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Change of creatinine within 72 hours	18.13	4.70 to 69.99	17.48	2.86 to 106.92	25.75	2.86 to 231.92
STS score	1.04	0.99 to 1.10	0.98	0.85 to 1.15	1.05	0.99 to 1.12

CI = confidence interval; GFR = glomerular filtration rate; OR = odds ratio; STS = Society of Thoracic Surgeons

Table 5: Impact of contrast media as a predictor of change of creatinine within 72 hours after transcatheter aortic valve implantation.

	All patients		GFR ≥60 ml/min/1.73 m^2		GFR <60 ml/min/1.73 m^2	
	r	**95% CI**	**r**	**95% CI**	**r**	**95% CI**
Log total contrast media	0.02	–0.02 to 0.07	0.06	–0.01 to 0.13	–0.01	–0.07 to 0.05
STS score	0.00	–0.01 to 0.00	0.00	–0.01 to 0.01	0.00	–0.01 to 0.00

CI = confidence interval; GFR = glomerular filtration rate; STS: Society of Thoracic Surgeons

in our study population) [34], the occurrence of major vascular complications (2.3% in our study population) [35] or moderate and severe postimplant aortic regurgitation (2.3% in our population) [36]. Whether the amount of contrast applied during TAVI procedures differently influences outcome in patients with or without one of the above mentioned risk factors needs to be evaluated in further studies.

In the present study, patients with reduced kidney function experienced significantly more bleeding complications compared with patients with preserved kidney function, which is in line with previous data [37]. This finding should especially be taken into account in patients with atrial fibrillation, as with simultaneous left atrial appendage occlusion anticoagulation can be stopped and thus bleeding complications can further be reduced. However, simultaneous left atrial appendage occlusion requires additional contrast media application, thus further underlining the efforts to reduce the amount of contrast media in this population.

Taken together, despite our findings, we still consider efforts to reduce the amount of contrast before or during the procedure beneficial, particularly in patients with reduced kidney function. Areas to reduce the amount of contrast in such patients are the screening CT, which can either be omitted [17], replaced by (3D-)echocardiography [38], or reduced to a minimal-contrast selective CT of the peripheral vessels [39]. A screening coronary angiogram can be omitted, as can a peripheral angiogram [17]. If it is felt that a screening angiogram and a CT need to be performed, the procedures should be staged in order to allow the kidneys to recover and to minimise the temporal contrast exposure. An important phase in which to reduce the amount of contrast is intraprocedurally, with techniques previously described.

If measures to minimise the risk of AKI are taken, we should still opt for an as safe procedure as possible, including selective administration of contrast media where needed. Therefore, the findings presented here should encourage us to use contrast media, but to use them wisely and selectively, always keeping in mind that an optimal TAVI result should be the primary goal of each procedure.

Limitations

This study has several limitations. The association between the amount of contrast media and changes in creatinine has been evaluated only within 72 hours following TAVI. Thus, we cannot exclude the possibility that longer follow-up of kidney function may be necessary to find an association between the amount of contrast media and a change in creatinine.

The time interval between preprocedural evaluations with contrast media administration (CT, angiography) and the TAVI procedure was variable. This might have introduced a bias in the analysis of the impact of the amount of contrast media on the kidney function, as it could be expected that patients with known CKD might have had a longer time interval between procedures to reduce the risk of AKI. Consequently, the cumulative dose of contrast media was lower in patients with CKD in the present study. Furthermore, patients with CKD were routinely treated with hydration and n-acetylcysteine to reduce further the potential risk of AKI.

The smaller amount of contrast media administered in the group of patients with reduced kidney function compared with the group with preserved kidney function might have introduced a bias in the results of the multivariate analysis. However, as our data reflect daily clinical routine, these results might be of more practical importance. Prospective studies with administration of the same amount of contrast in patients with preserved and reduced kidney function seem not to be feasible because of ethical concerns.

Finally, the sample size of 257 patients might have influenced the results of the present study. Considering the number of TAVI procedures performed per year, the sample size of our study represents the experience of a high-volume centre in a time-period with increasing acceptance of TAVI as an alternative to open aortic valve surgery in selected patients. Multicentre studies to increase the sample size are needed to assess further the impact of contrast media on short-term outcome, and in particular to evaluate the high-risk patient group with moderately to severely reduced kidney function.

Conclusion

AKI following TAVI has a major impact on outcome. The occurrence of AKI is most likely multifactorial. Contrast-sparing approaches are probably beneficial particularly in patients with severely decreased kidney function, but if rather small amounts of contrast media are used for screening and the TAVI procedure itself, the amount of contrast seems not to be an independent predictor of outcome in an overall TAVI-cohort.

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Figures (large format)

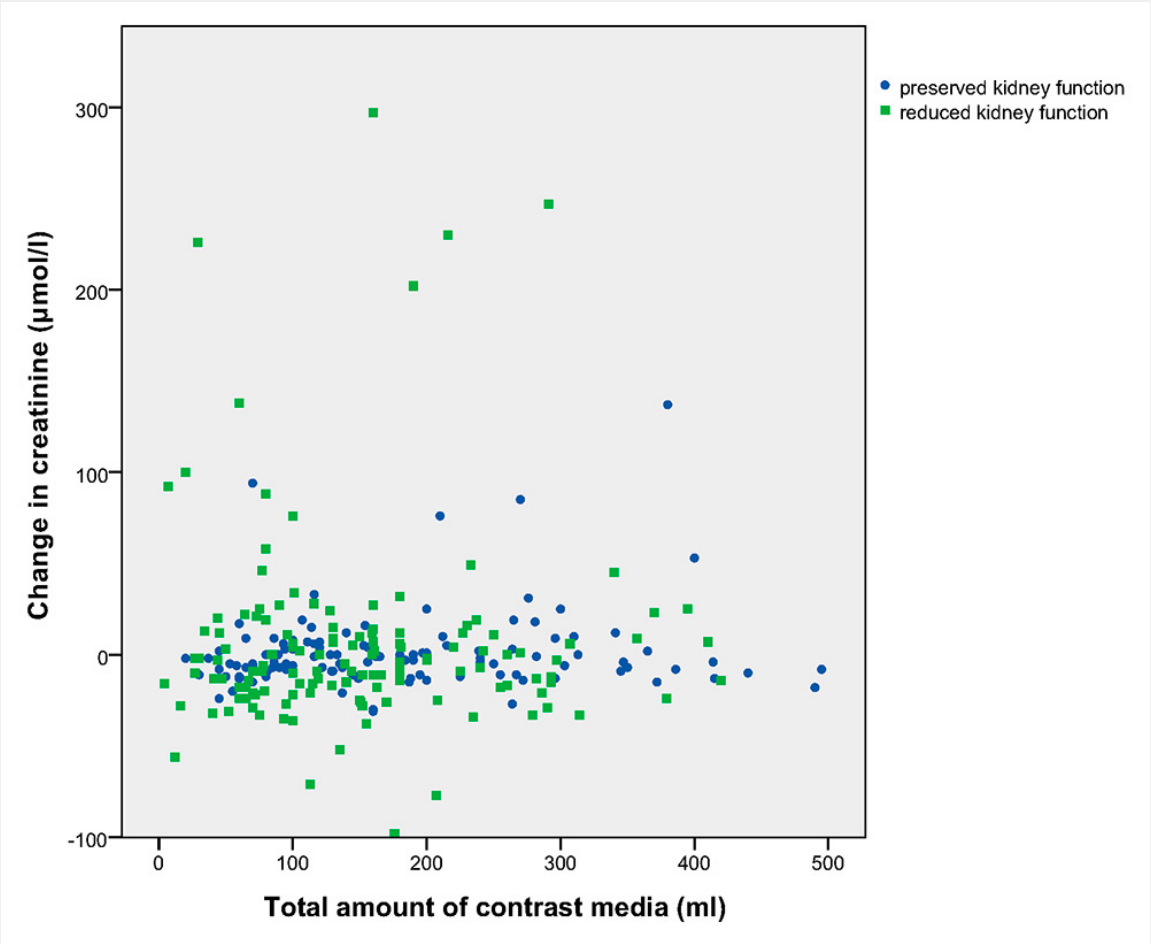

Figure 1

Association between the total amount of contrast media (in ml) administered during and within 5 days prior to TAVI and absolute changes in creatinine (in µmol/l) within 72 hours following TAVI in each patient according to preinterventional kidney function (preserved kidney function: GFR ≥60 ml/min/1.73 m^2 versus reduced kidney function: GFR <60 ml/min/1.73 m^2).