

Does Preoperative Computed Tomography Angiography Lead to an Increased Incidence of Postoperative Acute Kidney Injury Following Transcatheter Aortic Valve Implantation in Patients with Impaired Renal Function?

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Abstract

Aim: Although the superiority of information derived from computed tomography angiography (CTA) compared to transesophageal echocardiography (TOE) for aortic annulus sizing has been proved, the CTA is considered critically due to the contrast media (CM) application, especially in patients with compromised renal function. We aimed to evaluate the impact of CTA on the incidence of postoperative acute kidney injury (AKI) following transapical transcatheter aortic valve implantation (TA-TAVI).

Methods: Two hundred and thirteen high-risk patients with severe aortic stenosis who underwent TA-TAVI in our institution between 01/2011 and 08/2016, were analyzed. In conformity with our policy switch in 01/2014 from TOE to CTA for annulus sizing, the cohort was divided in two groups, (TOE-group/CTA-group) and retrospectively analyzed. The occurrence of a post-procedural AKI was defined according to the VARC-2 criteria.

Results: The preoperative risk evaluation was similar in both groups (EuroSCORE II: $8.2 \pm 6.5\%$ in CTA vs. $7.8 \pm 6.2\%$ in TOE). Overall AKI occurred in 75 patients (35.2%), with no group difference (33% in CTA vs. 37.4% in TOE; $p=0,567$). Preoperative chronic kidney disease (CKD) was seen in 97 patients (45.5%). Here AKI occurrence was 32.4% in CTA vs. 39.3% in TOE; $p=0,888$. A post-procedural renal replacement therapy (RRT) was needed in 26 patients (12.2%); the need was less in case of patients with CTA (6.6% in CTA vs. 17.8% in TOE; $p=0,01$). Patients with pre-existing CKD needed RRT postoperatively in 15.6% in CTA, vs. 25.4% in TOE ($p<0,001$).

Conclusion: The preoperative CTA is a safe investigation method prior to TA-TAVI and is not associated with an increased incidence of AKI, even in patients with CKD.

Keywords: computed tomography angiography, contrast media, TA-TAVI, postoperative acute kidney injury.

1. INTRODUCTION

A key factor for the success of transcatheter aortic valve implantation (TAVI) techniques is the accurate anatomical measurements of the aorta. Dimensions such as the aortic annulus diameter, perimeter, orifice area, and the distance to the coronary orifices or detailed analysis of calcification patterns have a major relevance not only to achieve good operative results, but also to avoid catastrophic, life-threatening complications during TAVI

procedures. The superiority of the computed tomography angiography (CTA) compared to transesophageal echocardiography (TOE) in terms of annulus sizing and post-procedural complications is well documented [1, 2]. At this point, due to the advantages of CTA compared to TOE [3], CTA has become the standard method of evaluation in pre-TAVI procedures [4, 5].

On the other hand, CTA represents a source for kidney injury, due to need for contrast media

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(CM) application. The TAVI population typically includes elderly patients with significant pre-existing renal dysfunction. The acute kidney injury (AKI) represents a severe complication following TAVI, which is known to increase the post-procedural morbidity and mortality [6–9]. We aimed to assess whether the preoperative CTA examination leads to an increased incidence of postoperative AKI after transapical (TA)-TAVI.

2. METHODS

Patients with aortic valve stenosis, deemed high-risk candidates for surgical aortic valve replacement were considered for TA-TAVI, according to our standardized interdisciplinary heart-team protocol. We retrospectively analyzed patients who underwent TA-TAVI in our institution between 01/2011 and 08/2016. Initially, in our TA-TAVI era, we preoperatively employed TOE (Philips CX50, Revision 3.1.1, Philips Ultrasound; Andover, MA, USA) for annulus sizing. Since 01/2014, in conformity to our policy switch, almost all TA-TAVI candidates preoperatively underwent CTA for annulus sizing. We performed CTA using a mono-source CT machine (Somatom Definition Edge, Simens, Germany; 128 detector rows, rapid ECG gated, spiral acquisition, covering the heart and the thoracic aorta) 24h before TA-TAVI, with intravenous application of 60 ml CM (370 mg iodine/ml; Solustrast 370; Bracco Imaging, Milan, Italy). A CM volume bolus was injected at the rate of 4 ml/s followed by a crystalloid solution of 40 ml. The imaging parameters for the reference tube current and voltage were set to 160–190mAs and 120 kVp, respectively. The image acquisition was performed in cranio-caudal scan direction. The applied CM volume was the same in all patients (60 ml). All patients gave written informed consent before the CTA examination. We did not use a standardized hydration regime. All patients intraoperatively underwent intra-arterial CM exposure (370 mg iodine/ml; Solustrast 370; Bracco Imaging, Milan, Italy) during

fluoroscopy performance. For the patient group with CTA, there was a second CM exposure within 24 h. This patient cohort intraoperatively received for fluoroscopy on average 69 ± 20 ml of CM in contrast to the TOE which received 77 ± 27 ml of CM for fluoroscopy [Fig.5]. We performed a CTA examination by all patients, independently of chronic kidney disease (CKD) co morbidity. We defined CKD here as Stage 3 or 4 according to renal dysfunction, injury to the kidney, failure or loss of kidney function, and end-stage kidney disease (RIFLE) classification. So we were able to divide the cohort into two groups: 107 (50. 2%) patients who received TOE and 106 (49. 8%) who received CTA preoperatively. After the exclusion of patients with chronic dialysis, 213 patients were included in this study. The postoperative AKI was defined according to Valve Academic Research Consortium Consensus Document (VARC-2) criteria. Ethics Committee approval has been obtained (Reg. Nr.18-6339).

3. STATISTICAL ANALYSIS

For continuous variables, data are reported as mean with standard deviation. The categorical variables are reported as frequency (percentage). Data comparison was done using the χ^2 test, the Fisher's exact test, Kruskal-Wallis test and the Mann-Whitney test as appropriate. All statistical tests were 2-sided, and p values of 0.05 or less were considered statistically significant. The statistical analyses were conducted using SPSS 23.0.0.2 software (IBM, Chicago, IL, USA).

4. RESULTS

A total of 229 patients (84 ± 7 years, 53.5% male, EuroSCORE II $8 \pm 6\%$) who underwent TA-TAVI in our institution were analyzed. After excluding patients with chronic dialysis, 213 patients were included in this study. Preoperatively, for annulus sizing, 107 patients underwent TOE (50.2%) and 106 CTA (49.8%). Preoperative variables of the entire cohort and of the two subgroups, CTA and TOE, are shown in Table1.

Table1: Baseline clinical characteristics (* left ventricular ejection fraction)

Table 1	All N=213; n= (%)	TOE N=107;n= (%)	CTA N=106;n= (%)	p Value
Age	84 ± 7	86 ± 6	82 ± 6	$p < 0,0001$
Male sex	114 (53,5)	58 (54,2)	56 (52,3)	$p = 0,677$
EuroScore II	$8 \pm 6,32$	$7,81 \pm 6,22$	$8,23 \pm 6,47$	$p = 0,703$
Arterial Hypertension	189 (88,7)	99 (92,5)	90 (84,9)	$p = 0,117$
Diabetes mellitus	73 (34,2)	37 (34,5)	36 (33,9)	$p = 1$

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LVEF*	49 ± 11	47 ± 10	51 ± 11	<i>p</i> = 0,001
Peripheral artery disease	68 (31,9)	32 (29,9)	36 (33,9)	<i>p</i> = 0,236
Chronic kidney failure	97 (45,5)	59 (55,1)	38 (35,8)	<i>p</i> = 0,007
Preoperative creatinine (mg/dL)	1,3 ± 0,6	1,4 ± 0,7	1,2 ± 0,5	<i>p</i> < 0,0001
Atrial fibrillation	82 (38,5)	52 (48,5)	30 (28,3)	<i>p</i> = 0,002
Previous cardiac operation	37 (17,4)	13 (12,1)	24 (22,6)	<i>p</i> = 0,03

Overall, postoperative AKI, after TA-TAVI in 213 patients occurred in 75 patients (35.2%). A postoperative AKI in the CTA cohort occurred in 33% of patients (n= 35) and 37.4% in the TOE cohort (n=40), [33% CTA vs. 37.4% TOE; *p* = 0.567] [Fig.1]. Preoperatively, 97 patients (45.5%) of the entire cohort were

burdened with CKD. We documented a postoperative AKI in 32.4% of the cases in this population in the CTA group. We found almost the same postoperative AKI rate (39.3%) occurring in the TOE group, [32.4% CTA with CKD vs. 39.3% TOE with CKD; *p* = 0.888] [Fig.2]

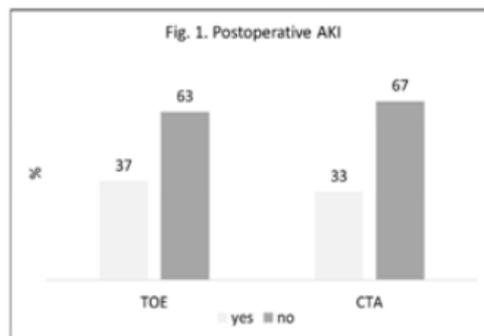


Fig1: Comparison of the postoperative acute kidney injury (AKI) occurrence among patients who received CTA and TOE preoperatively for annulus sizing.

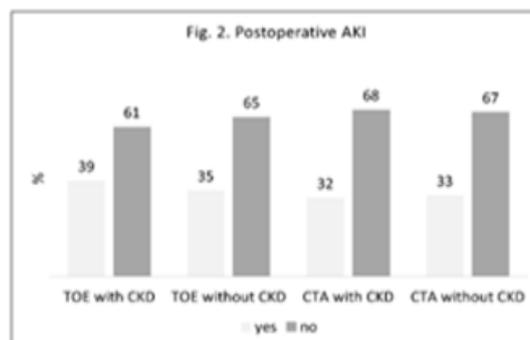


Fig2: Comparison of the postoperative acute kidney injury (AKI) occurrence among CTA and TOE groups of patients with chronic kidney disease (CKD).

From a total of 213 patients, postoperative renal replacement therapy (RRT) was necessary in 26 patients (12.2%). In the CTA group, we registered RRT in 6.6% of the cases, in the TOE group in 17.8% of the cases, [6.6% CTA vs.

17.8% TOE; *p* = 0.01]. We also documented a significantly more RRT in the TOE group compared to the CTA group, in the patients with CKD, [15.6% CTA with CKD vs. 25.4% TOE with CKD; *p* < 0.001] [Fig.3].

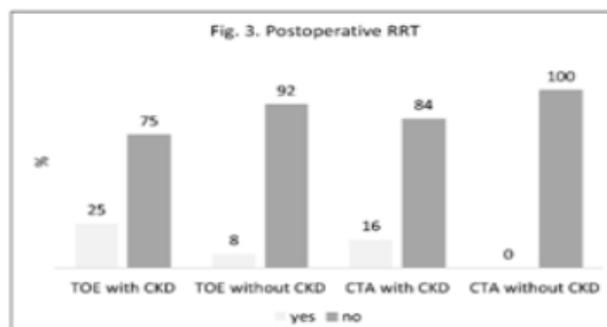


Fig3: Comparison of patients who needed renal replacement therapy (RRT) postoperatively in CTA and TOE groups with and without chronic kidney disease (CKD).

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The intraoperative CM application during fluoroscopy was 73 ± 24 ml in the entire cohort and 69 ± 20 ml / 77 ± 27 ml in the CTA / TOE group respectively ($p = 0.015$). The perioperative total CM volume applied was significantly higher in the CTA group (CTA + fluoroscopy) compared to the TOE group

(fluoroscopy), [129 ± 20 ml CTA vs. 77 ± 27 ml TOE; $p < 0.001$] [Fig.4]. The 30-day- all-cause-mortality of the entire cohort was 10.1%. Owing to postoperative AKI-related complications 3 patients died from the TOE group but none from the CTA group. Further perioperative characteristics are shown in Table 2, 3.

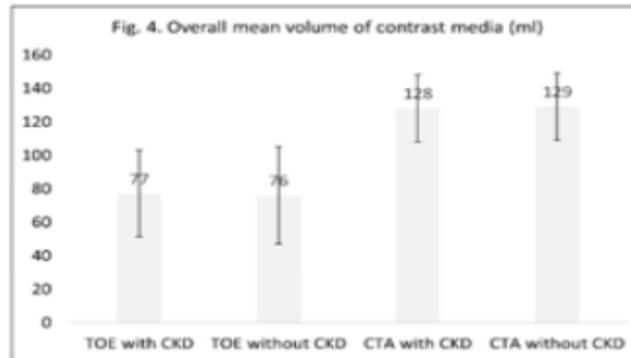


Fig4: Perioperative applied total volume contrast media in both CTA and TOE groups.

Table2: Procedural and postprocedural characteristics (* cardio-pulmonary bypass)

Table 2	All N=213;n= (%)	TOE N=107;n= (%)	CTA N=106;n= (%)	p Value
TOE-derived annulus diameter (mm)	/	$23 \pm 2,1$	/	/
CTA-derived annulus diameter (mm)	/	/	$24,2 \pm 2,5$	/
Prosthesis diameter (mm)	$25,5 \pm 2,1$	$25,57 \pm 2,1$	$25,45 \pm 2,1$	$p = 1$
Contrast medium application (mL)	103 ± 41	77 ± 27	129 ± 20	$p < 0,001$
Mean procedural time (h/min)	$01:47 \pm 00:44$	$01:53 \pm 00:55$	$01:40 \pm 00:24$	$p = 0,354$
Conversion to CPB*	9 (4,2)	7 (6,5)	2 (1,9)	$p = 0,178$
Bleeding (mL)	465 ± 305	502 ± 338	420 ± 256	$p = 0,08$
AKI-related-30-day-mortality	3 (1,4)	3 (2,8)	0 (0)	$p = 0,260$

Table3: AKI-related post-procedural characteristics (* acute kidney injury; ** renal replacement therapy (continuous veno-venous hemodialysis))

Table 3	All N=213;n= (%)	TOE N=107;n= (%)	CTA N=106;n= (%)	p Value
Postprocedural AKI*	75 (35,2)	40 (37,4)	35 (33,0)	$p = 0,567$
AKI Stage 1	48 (64)	27 (67,5)	21 (60)	$p = 0,507$
AKI Stage 2	20 (26,7)	11 (27,5)	9 (25,7)	$p = 0,863$
AKI Stage 3	7 (9,3)	2 (5)	5 (14,3)	$p = 0,186$
RRT (CVVHD)**	26 (12,2)	19 (17,8)	7 (6,6)	$p = 0,01$
Creatinine max. (mg/dL)	$1,8 \pm 0,9$	$1,9 \pm 0,9$	$1,6 \pm 0,9$	$p = 0,001$

5. DISCUSSION

The occurrence of AKI after TAVI procedures is one of most frequent complication with an incidence of 11–40%. The AKI occurs as an independent predictor of mortality, increasing the risk more than four-fold in the TAVI population [6–9]. Moreover, kidney function impairment is very common issue in high risk elderly TAVI candidates and the fact that the CM exhibits nephrotoxic features in this population is beyond doubt [10, 11, and 17].

However, there is a lack of evidence about the clinical relevance of CM-induced AKI (such as

the influence on postoperative RRT), particularly in patients with CKD undergoing TAVI. Furthermore, the favorable timing of a dual CM exposition (CTA and intra-operative fluoroscopy) in high-risk elderly patients with compromised renal function is not clear. In this study, we aimed to find out if our CTA protocols with an intra-venous application of CM, 24 h prior to TA-TAVI, led to postoperative AKI and what the clinical impact was on elderly patients with CKD co morbidity undergoing TA-TAVI. Although, significantly more CM volume was applied peri-operatively in the CTA group compared to the TOE group,

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we found that peri-operative additional intravenous application of 60 ml Solustrast 370 for CTA examination did not lead to an increased postoperative AKI incidence in TA-TAVI patients. In this study, we specially focussed on the patient group with prior CKD. Surprisingly, we did not observed any association between the CTA group with CKD and increased postoperative AKI occurrence. In fact, we saw here a lower AKI incidence compared to the TOE-group with CKD.

The data on the risk of AKI requiring RRT after TA-TAVI in patients who received CM are limited. We were able to show that even in patients with CKD in our cohort, who received CTA with CM, required significantly lesser use of postoperative RRT compared to the TOE-group with CKD. Nobody from the CTA-group died postoperatively due to AKI-related complications. These facts could be explainable by the baseline and perioperative characteristics of the cohorts. The TOE cohort includes older patients, higher preoperative serum creatinine level, longer operation time and more patients with congestive heart failure. Moreover, the postoperative bleeding volume was higher in the TOE group. All these features have been identified in other studies [6–9] as independent predictors of AKI after TAVI procedures. However, the CTA did not influence the TA-TAVI procedure in terms of the use of various prosthesis sizes. We measured at average bigger annulus via CTA but saw similar implanted prosthesis size in both groups.

Furthermore, the incidence of AKI after intra-arterial administration of CM is up to three-times higher than after intra-venous administration of CM [6, 20, and 21]. This might be another explanation to why postoperative AKI and its clinical complications occurred more frequently in the TOE group. We administrated on average 8 ml more intra-arterial CM for fluoroscopy in the TOE group, which was statistically significant [Fig.5]. Recent studies [12, 13] have shown, that not only high CM volumes but also a repetitive administration of CM within a short period of time (<24 h) correlate with increased risk of contrast-induced nephropathy.

We performed CTA examination on all patients 24 h before the TAVI procedure, independently of CKD co morbidity. Our strategy for TAVI immediately after CTA examination, with repetitive CM application within 24 h, have been shown to be safe in terms of postoperative AKI, and cost-effective and useful in emergency TAVI cases. CTA-TAVI protocols described in the literature [5, 14–16] usually use large CM volumes up to 120 ml, to ensure the optimal exposure of the aorta and peripheral arteries. Accordingly, the next goal is the development of protocols with very low CM volumes to avoid contrast-induced AKI. The first steps in this field have been taken. The feasibility of 55 ml or even 20 ml CM volume CTA for TAVI has been tested [18, 19]. For such protocols, we have limited data in terms of postoperative CM-induced AKI.

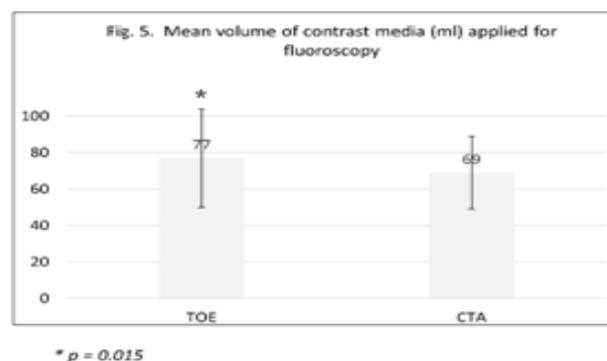


Fig5: Intraoperatively applied intra-arterial volume contrast media for fluoroscopy in both CTA and TOE groups.

6. CONCLUSION

We found that a CTA with 60 ml CM application was a safe method prior to TA-TAVI, and did not trigger the post-procedural AKI occurrence. A consecutive and immediate (within 24 h) intra-arterial application of CM

does not influence the occurrence of the postoperative AKI, even in patients with CKD. The application of CM volumes up to 73 ml during fluoroscopy is a safe course. Intra-arterial administration of CM in elderly patients who undergo TA-TAVI seems to be relevant in CM-

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induced nephropathy, so that a reducing volume of CM application during fluoroscopy should be considered.

7. LIMITATIONS

This is an observational retrospective study and the evidence value provided in our study is inferior compared to randomized trials. This science has the usual flaws inherent in retrospective observational studies. The biggest flaw is that the addition of CTA with CM is not the only change in the practice between the groups. The procedure time of the groups has been changed. As this compares a service at one time point with another, there could be changes in the experience of the surgeons that might have influenced the results. Other professionals such as anaesthetists involved will also have gained more experience and could, therefore, have refined their skills at recognizing and treating renal issues around the time of TAVI. Another limitation is that the group studied is selected. This is only for CTA performed solely for patients assessed for TA-TAVI, which is a less common procedure than transfemoral TAVI, to which the results cannot necessarily be extrapolated.

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