Continued Versus Interrupted Oral Anticoagulation During Transfemoral Transcatheter Aortic Valve Implantation and Impact of Postoperative Anticoagulant Management on Outcome in Patients With Atrial Fibrillation

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The role of continued versus interrupted oral anticoagulation (OAC) in patients with atrial fibrillation (AF) who underwent transfemoral transcatheter aortic valve implantation (TF-TAVI) for severe aortic stenosis is uncertain. The aim of this retrospective investigation was to evaluate the impact (1) of continued versus interrupted OAC on early safety and (2) of postoperative anticoagulant management on the 1-year mortality in patients with AF who underwent TF-TAVI. Consecutive patients with AF and on OAC at admission (n = 598) were stratified according to interrupted (iVKA) versus continued vitamin K antagonist (cVKA) versus continued direct oral anticoagulants (DOAC) at the time of TF-TAVI. Valve Academic Research Consortium-2 early safety was the primary outcome measure. Patients with iVKA (n = 299), cVKA (n = 117), and DOAC (n = 182) had comparable baseline characteristics including age (p = 0.25), gender (p = 0.33), and STS-Score (p = 0.072). The proportion of patients having a CHA_2DS_2-VASc-Score ≥3 (p = 0.791) and HAS-BLED-Score ≥3 (p = 0.185) was not different between groups. The rate of early safety events (with lower values indicating superior safety) was lowest in DOAC (13.2%) and not increased in cVKA (19.7%) compared to iVKA (23.1%) (p = 0.029). Valve Academic Research Consortium-2 defined stroke (p = 0.527) and bleeding (p = 0.097) did not differ between groups. Renal failure occurred more often in iVKA compared to cVKA and DOAC (p = 0.02). All-cause 1-year mortality was 20.1% in iVKA, 13.7% in cVKA, and 8.8% in DOAC (p = 0.015). Multivariate analysis revealed DOAC to be associated with reduced all-cause 1-year mortality (HR 0.56 (95%-CI 0.32 to 0.99), p = 0.047) whereas cVKA was comparable to iVKA (HR 0.75 (95%-CI 0.43 to 1.31), p = 0.307). In conclusion, cVKA did not increase the rate for the composite end point of early safety at 30 days in this cohort of patients. Treatment with a DOAC was associated with a significantly reduced rate of early safety end points at 30 days and lower 1-year mortality. **(Am J Cardiol 2019;123:1134−1141)**

Aortic stenosis (AS) is associated with a higher burden of atrial fibrillation (AF) due to pressure overload of the left heart chambers.[1] The prevalence of pre-existing AF in patients who underwent surgical aortic valve replacement is reported to be 8% to 13%[2−4] whereas new-onset AF occurs in up to 40% leading to increased risk of cardiac and cerebrovascular events and mortality.[4] Transcatheter aortic valve implantation (TAVI) has become a valid treatment option in high-[5] and intermediate-risk patients[6] with severe AS. Since TAVI has been performed predominantly in older patients, rates of pre-existing AF have been reported to be 16% to 59%.[4,7−10] Oral anticoagulation (OAC), either using vitamin K antagonists (VKA) or direct oral anticoagulants (DOAC), reduces the rate of stroke and systemic embolism in patients with AF[11] with a better safety profile and improved survival of patients treated with a DOAC.[12−15] In patients who underwent catheter ablation for AF, continued compared to interrupted OAC is associated with reduced bleeding and comparable or even reduced thromboembolic complications.[16,17] Uninterrupted Dabigatran seems to yield even a greater benefit compared to uninterrupted VKA by showing fewer bleeding complications.[18] The aim of this retrospective analysis was to evaluate the impact (1) of continued versus interrupted OAC on early safety and (2) of postoperative anticoagulant management on the 1-year

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mortality in patients with atrial fibrillation who underwent transfemoral TAVI (TF-TAVI).

Methods

From 01/2011 to 03/2016, 598 patients with pre-existing AF and a prescribed OAC at baseline received TF-TAVI for severe aortic stenosis or bioprosthetic valve failure in aortic position. Patients were analyzed according to the anticoagulation status during TAVI procedure: interrupted VKA (iVKA), continued VKA (cVKA) and continued DOAC (DOAC). In January 2013, we decided to systematically perform TAVI under continued VKA, prior to this date (2011/2012) it was generally recommended to stop VKA and bridging with heparin was initiated. The below mentioned regime in DOAC was not changed since the first patient on DOAC was treated in our center (March 2012). The decision to continue or interrupt OAC was also dependent on other clinical characteristics and concomitant therapeutic procedures carrying a high bleeding risk, e.g. pleurocentesis.

Baseline characteristics, procedural data and outcome data were prospectively collected. Follow-up was performed after 30 days and 12 months. Presence of lung disease was defined according to the EuroScore definition.[19] Immunosuppressant medication, diabetes mellitus, coronary heart disease, and peripheral artery disease were defined according to the Society of Thoracic Surgeons-Predicted Risk of Mortality score.[20] Society of Thoracic Surgeons-Predicted Risk of Mortality was determined and CHA_2DS_2-VASc-Score and HAS-BLED-Score were calculated as recommended in current guidelines.[21] The registry was approved by the Ethics Committee of the University of Leipzig (registration number: 167-10-12072010) and all patients gave written informed consent.

Patients with iVKA had interrupted administration of VKA and were bridged with low molecular heparin (LMH) or unfractionated heparin according to their comorbidities, in particular in severe kidney disease as soon as an INR drop below 2.0 was observed. LMH was not administered at the day of intervention and intravenous heparin was stopped at least 4 hours before intervention and restarted 24 hours after a successful intervention. VKA was reinitiated 24 to 48 hours after successful TAVI. Patients with cVKA remained on VKA therapy during the whole periprocedural phase with a goal directed INR between 2.0 and 3.0. Patients receiving DOACs remained on their direct oral anticoagulant during the whole periprocedural phase except the day of intervention with the last dose of DOAC administered the day before and restarted in the morning of the next day after successful TAVI. During the TAVI procedure, intravenous heparin was administered to reach an activated clotting time around 300 seconds in all groups. All patients received clopidogrel for 6 months after TAVI in addition to their anticoagulation strategy with VKA (recommended INR 2.0 to 2.5) or DOACs administered in their approved reduced dose for stroke prevention.

The primary outcome measure was early safety at 30 days, which is a composite of all-cause mortality, all stroke, life-threatening bleeding, acute kidney injury stage 2 and 3, coronary obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure. The 30-day and 1-year all-cause mortality was assessed. The latest vital status was known in 100%. However, at 30 days, vital status was censored in 33 patients (5.5%) ranging from day 6 to day 29. The mean survival time for 30-day mortality was 29.4 days (95%-CI 29.1 to 29.7). At 1 year, vital status was censored in 171 patients (28.6%) ranging from day 6 to day 364. The mean survival time for 1-year mortality was 323 days (95%-CI 315 to 331). All single Valve Academic Research Consortium-2 (VARC-2) defined outcome measure up to 30 days were evaluated.[22] Causes of death were categorized into cardiovascular and noncardiovascular causes, according to VARC-2. Cause of death was verified by two investigators (NM, FW) reviewing medical records and death certificates to receive consensus. According to VARC-2, patients with unknown cause of death were categorized as cardiovascular mortality.

The statistical analysis was performed using SPSS Statistics version 22.0 (IBM Corporation, Armonk). Categorical variables are expressed as numbers and percentage and were compared with the use of the chi-squared test. Continuous variables are expressed as the median with corresponding 25th and 75th percentile and were compared using the Kruskal−Wallis-Test due to non-normal distribution assessed by the Shapiro−Wilk-Test. The 30-day and 1-year mortality were analyzed according to the method of Kaplan−Meier and group comparisons were made applying the log-rank test. Since there were two hypotheses, p values for the primary outcome measure early safety at 30 days and 1-year mortality were corrected using the Bonferroni method. A p value <0.05 was considered significant. All other p values should be interpreted as exploratory. Factors associated with the occurrence of the primary outcome measure, overall stroke, and bleeding were evaluated using a binary logistic regression analysis. Factors showing a p value ≤ 0.1 in univariate analysis were included in the multivariate model and status of anticoagulation was forced into the model if it failed to reach a p value ≤ 0.1 in univariate analysis. Independent predictors of 1-year all-cause mortality were determined with a Cox proportional hazard regression model. Clinically relevant baseline variables with a p value ≤ 0.1 in univariate analysis were included in the model. Oral anticoagulation was tested both as a dichotomous variable (continued vs interrupted OAC) and as a trichotomous variable with iVKA as reference (iVKA vs cVKA vs DOAC).

Results

Out of 598 patients, 299 patients (50.0 %) were classified as iVKA, 117 patients (19.6 %) as cVKA and 182 patients (30.4 %) as DOAC. The later one consisted of 111 patients receiving rivaroxaban, 41 patients receiving apixaban, 29 patients receiving dabigatran and 1 patient receiving edoxaban. Baseline characteristics are shown in Table 1 and were balanced between the groups except for a higher rate of previous myocardial infarction and diabetes mellitus in iVKA. Comparing the frequencies of patients with CHA_2DS_2-Vasc ≥ 3 and HAS-BLED Score ≥ 3 groups, no significant difference was detectable. Indication, type of

Table 1
Baseline characteristics and procedural data.

Variable	iVKA (n = 299)	cVKA (n = 117)	DOAC (n = 182)	p value
Age (years)	80 (76; 83)	80 (77; 83)	80 (77; 84)	0.250
Males	127/299 (42.5%)	46/117 (47.9%)	89/182 (48.9%)	0.330
Body mass index (kg/m^2)	27.9 (25.0; 32.0)	27.8 (24.2; 31.2)	27.7 (24.5; 31.6)	0.693
STS-score (%)	6.9 (4.2; 10.8)	6.7 (4.4; 10.8)	5.9 (3.6; 9.5)	0.072
CHA_2DS_2-Vasc score	6 (5; 6)	5 (5; 6)	5 (5; 6)	0.008
CHA_2DS_2-Vasc score ≥3	298/299 (99.7%)	116/117 (99.1%)	180/181 (99.4%)	0.791
HAS-BLED score	3 (3; 4)	3 (3; 4)	3 (3; 4)	0.006
HAS-BLED score ≥3	242/299 (80.9%)	100/117 (85.5%)	139/181 (76.8%)	0.177
New York Heart Association Class III/IV	238/293 (81.2%)	86/110 (78.2%)	130/180 (72.2%)	0.072
Coronary artery disease	131/299 (43.8%)	55/117 (47.0%)	71/181 (39.2%)	0.387
Previous myocardial infarction	46/299 (15.4%)	15/117 (12.8%)	12/182 (6.6%)	0.016
Previous coronary artery bypass grafting	30/299 (10.0%)	16/117 (13.7%)	14/182 (7.7%)	0.244
Previous percutaneous coronary intervention	53/290 (18.3%)	24/116 /20.7%)	32/182 (17.6%)	0.787
Arterial hypertension	289/299 (96.7%)	116/117 (99.1%)	175/182 (96.2%)	0.299
Diabetes Mellitus	162/299 (54.2%)	49/116 (42.2%)	77/182 (42.3%)	0.015
Previous stroke	39/299 (13.0%)	22/117 (18.8%)	26/182 (14.3%)	0.323
Peripheral artery disease	33/299 (11.0%)	15/117 (12.8%)	26/182 (14.3%)	0.569
Chronic obstructive lung disease	47/299 (15.7%)	21/117 (17.9%)	26/182 (14.3%)	0.697
Chronic kidney disease ≥3b	101/298 (33.9%)	45/116 (38.8%)	50/181 (27.6%)	0.120
Glomerular filtration rate [mL/min/1.73 m^2)	55 (39; 68)	52 (37; 72)	56 (43; 71)	0.255
Immunosuppressive therapy	20/298 (6.7%)	12/117 (10.3%)	11/180 (6.1%)	0.358
LV-ejection fraction (%)	56 (44; 65)	56 (44; 64)	55 (43; 64)	0.767
Aortic valve area (cm^2)	0.7 (0.6; 0.8)	0.7 (0.6; 0.8)	0.7 (0.6; 0.9)	0.711
Mean gradient (mm Hg)	37 (27; 46)	36 (27; 43)	38 (29; 48)	0.368
Mitral regurgitation 2/3	46/270 (17.0%)	16/110 (14.5%)	26/157 (16.6%)	0.836
Indication				
Native valve	289/299 (96.7%)	109/117 (93.2%)	172/182 (94.5%)	0.261
valve-in-valve	10/299 (3.3%)	8/117 (6.8%)	10/182 (5.5%)	
Type of valve				
Self-expandable	212/299 (70.9%)	70/117 (59.8%)	122/182 (67.0%)	0.094
Balloon-expandable	87/299 (29.1%)	47/117 (40.2%)	60/182 (33.0%)	
Procedure time (min)	44 (36; 57)	45 (37; 56)	48 (40; 58)	0.077
Contrast dye (mL)	120 (95; 140)	100 (80; 125)	110 (90; 130)	<0.001
Device success	266/284 (93.7%)	106/113 (93.8%)	174/181 (96.1%)	0.495
Residual mean gradient (mm Hg)	8 (6; 12)	9 (6; 12)	8 (7; 12)	0.090
Aortic valve area (cm^2)	1.8 (1.5; 2.1)	1.9 (1.5; 2.2)	1.8 (1.5; 2.2)	0.747
Residual aortic regurgitation ≥2	7/274 (2.5%)	4/111 (3.6%)	8/168 (4.8%)	0.463

Variables are expressed as numbers and percentages or median (25th to 75th percentile).

valve and procedural success rate did not vary between the groups (Table 1).

The outcomes at 30 days are summarized in Table 2. The primary outcome measure was lowest in DOAC (13.2%) and not increased in cVKA (19.7%) compared to iVKA (23.1%) (p = 0.029). The overall rate of VARC-2 defined stroke was not statistically different between iVKA, cVKA and DOAK. There were also no significant differences in the rate of major and minor stroke and TIA. The incidence of VARC-2 defined bleeding complications did not differ significantly between iVKA, cVKA, and DOAC. No significant differences were detected evaluating the incidence of life-threatening, major and minor bleeding complications. The median number of packed red blood cells and the proportion of patients receiving any red blood cells was higher in iVKA compared to cVKA and DOAC (Table 2). Compared to iVKA, the rate of VARC-2 defined renal failure was significantly lower in cVKA and DOAC. The other overall rates of VARC-2 defined outcomes did not differ between groups. All-cause mortality at 30 days was numerically lower in DOAC without reaching statistical significance (iVKA: 4.3% vs cVKA: 3.4% vs DOAC: 0.5%, p = 0.061 by logrank). Cardiovascular mortality at 30 days was lower in DOAC (iVKA: 4.3% vs cVKA: 2.6% vs DOAC: 0%, p = 0.017 by logrank).

Continued versus interrupted OAC (HR 0.64 (95%-CI 0.42 to 0.97), p = 0.034) and STS-Score (HR 1.08 (95%-CI 1.01 to 1.17), p = 0.035) were associated with the occurrence of the primary outcome measure. This was primarily driven by DOAC (HR 0.58 (95%-CI 0.35 to 0.97), p = 0.039) whereas cVKA was comparable to iVKA (HR 0.80 (95%-CI 0.47 to 1.38), p = 0.428) (Table 3 and *Online-only Table 1 and 2*). Including continued versus interrupted OAC, there were no clinical factors associated with the occurrence of stroke in this cohort of patients (*Online-only Table 3 and 4*). In contrast, bleeding was associated with male gender (HR 0.65 (95%-CI 0.43 to 0.97), p = 0.036), STS-Score (per 1% increase) (HR 1.06 (95%-CI 1.03 to

Table 2
Outcome at 30 days.

Variable	iVKA (n = 299)	cVKA (n = 117)	DOAC (n = 182)	p value
Early safety	69/299 (23.1%)	23/117 (19.7%)	24/182 (13.2%)	**0.029**
All-cause mortality	13/299 (4.3%)	4/117 (3.4%)	1/182 (0.5%)	0.059
Cardiovascular mortality	13/299 (4.3%)	3/117 (2.6%)	0/182 (0%)	0.035
VARC stroke	12/290 (4.1%)	4/115 (3.5%)	4/182 (2.2%)	0.527
Major	11/290 (3.8%)	2/115 (1.7%)	2/182 (1.1%)	0.162
Minor	0/290 (0%)	1/115 (0.9%)	1/182 (0.5%)	0.338
Transient ischemic attack	1/290 (0.3%)	1/115 (0.9%)	1/182 (0.5%)	0.797
VARC bleeding	101/290 (34.8%)	45/116 (38.8%)	50/182 (27.5%)	0.097
Life-threatening	11/290 (3.8%)	5/116 (4.3%)	5/182 (2.7%)	0.747
Major	43/290 (14.8%)	14/116 (12.1%)	20/182 (11.0%)	0.453
Minor	47/290 (16.2%)	26/116 (22.4%)	25/182 (13.7%)	0.140
Red packed blood cells	0 (0; 1)	0 (0; 0)	0 (0; 0)	<0.001
Patients receiving any red packed blood cells	91/263 (34.6%)	22/112 (19.6%)	36/143 (20.1%)	0.001
VARC access site complication	93/290 (32.1%)	47/116 (40.5%)	55/182 (30.2%)	0.661
Major	36/290 (12.4%)	12/116 (10.3%)	18/182 (9.9%)	0.661
Minor	50/290 (17.2%)	32/116 (27.6%)	32/182 (17.6%)	0.045
Closure device failure	7/290 (2.4%)	3/116 (2.6%)	5/182 (2.7%)	0.975
VARC renal failure	46/291 (15.8%)	11/116 (9.5%)	14/182 (7.7%)	0.020
Stage 1	27/291 (9.3%)	6/116 (5.2%)	11/182 (6.0%)	0.247
Stage 2	9/291 (3.1%)	3/116 (2.6%)	2/182 (1.1%)	0.378
Stage 3	10/291 (3.4%)	2/116 (1.7%)	1/182 (0.5%)	0.106
VARC myocardial infarction	2/289 (0.7%)	0/115 (0%)	0/180 (0%)	0.359
New permanent pacemaker/ Implantable cardioverter defibrillator	93/299 (31.1%)	31/116 (26.7%)	55/181 (30.4%)	0.678
Postoperative hospital stay, days	12 (9; 15)	11 (8; 14)	10 (8; 13)	<0.001

Variables are expressed as numbers and percentages or median (25th to 75th percentile). **Bold:** significant at 5% after correction for multiple testing.

1.09), p < 0.001), and LV-EF (per 10% decrease) (HR 1.23 (95%-CI 1.07 to 1.42), p = 0.005) but not continued versus interrupted OAC (HR 1.09 (95-CI 0.74 to 1.60), p = 0.677) (Table 4 and *Online-only Table 5 and 6*).

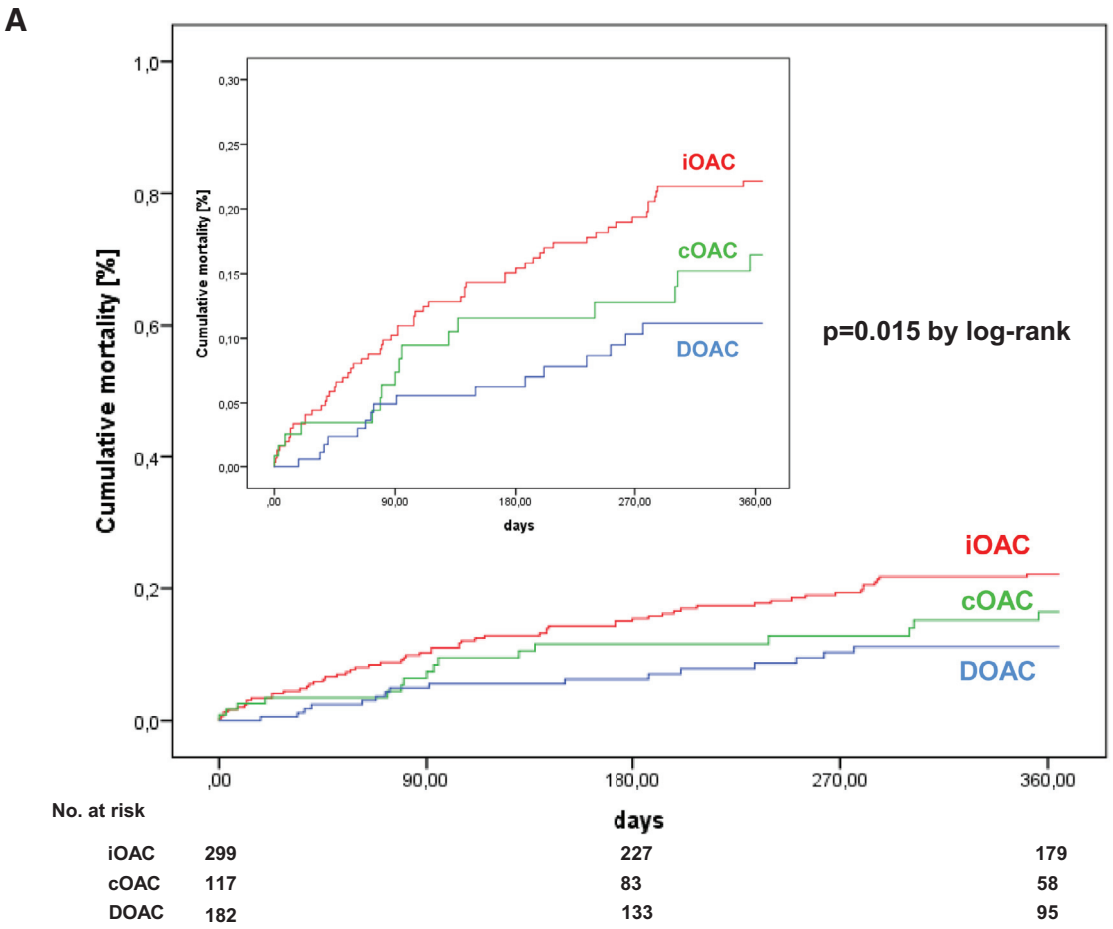
The 1-year-mortality was lowest in DOAC (iVKA: 20.1% vs cVKA: 13.7% vs DOAC: 8.8%, p = 0.015 by logrank and p = 0.003 after Bonferroni correction) (Figure 1). This was mainly driven by a lower cardiovascular mortality in DOAC compared to iVKA and cVKA (Figure 1). Factors associated with 1-year mortality are shown in Table 5 and *Online-only Table 7 and 8*). New York Heart Association class III/IV at baseline (HR 2.23 (95%-CI 1.15 to 4.31), p = 0.017), CAD (HR 1.61 (95%-CI 1.06 to 2.45), p = 0.027) and continued versus interrupted OAC (HR 0.59 (95%-CI 0.38 to 0.91), p = 0.018) were associated with 1-year mortality. The mortality benefit in the dichotomous comparison was mainly driven by DOAC (HR 0.56 (95%-CI 0.32 to 0.99), p = 0.047) whereas cVKA was comparable to iVKA (HR 0.75 (95%-CI 0.43 to 1.31), p = 0.307).

Table 3
Factors associated with 30-day early safety.

Parameter	Oral anticoagulation dichotomous	
	HR (95% CI)	p value
STS-score (per 1% increase)	1.08 (1.01-1.17)	0.035
Oral anticoagulation (continued vs discontinued)	0.64 (0.42-0.97)	0.034
	Oral anticoagulation trichotomous	
Parameter		
STS-score (per 1% increase)	1.04 (1.01-1.07)	0.008
Oral anticoagulation		
Interrupted vitamin K antagonist (reference)	1	
Continued vitamin K antagonist	0.80 (0.47-1.38)	0.428
Direct oral anticoagulant	0.58 (0.35-0.97)	0.039

Table 4
Factors associated with 30-day bleeding.

Parameter	Oral anticoagulation dichotomous	
	HR (95% CI)	p value
Male gender	0.65 (0.43-0.97)	0.036
STS-score (per 1% increase)	1.06 (1.03-1.09)	<0.001
LV-ejection fraction (per 10% decrease)	1.23 (1.07-1.42)	0.005
Oral anticoagulation (continued vs discontinued)	1.09 (0.74-1.60)	0.677
	Oral anticoagulation trichotomous	
Parameter		
STS-score (per 1% increase)	1.16 (1.07-1.24)	<0.001
LV-ejection fraction (per 10% decrease)	1.24 (1.07-1.43)	0.003
Oral anticoagulation		
Interrupted vitamin K antagonist (reference)	1	
Continued vitamin K antagonist	1.38 (0.84-2.26)	0.208
Direct oral anticoagulant	0.79 (0.51-1.22)	0.284



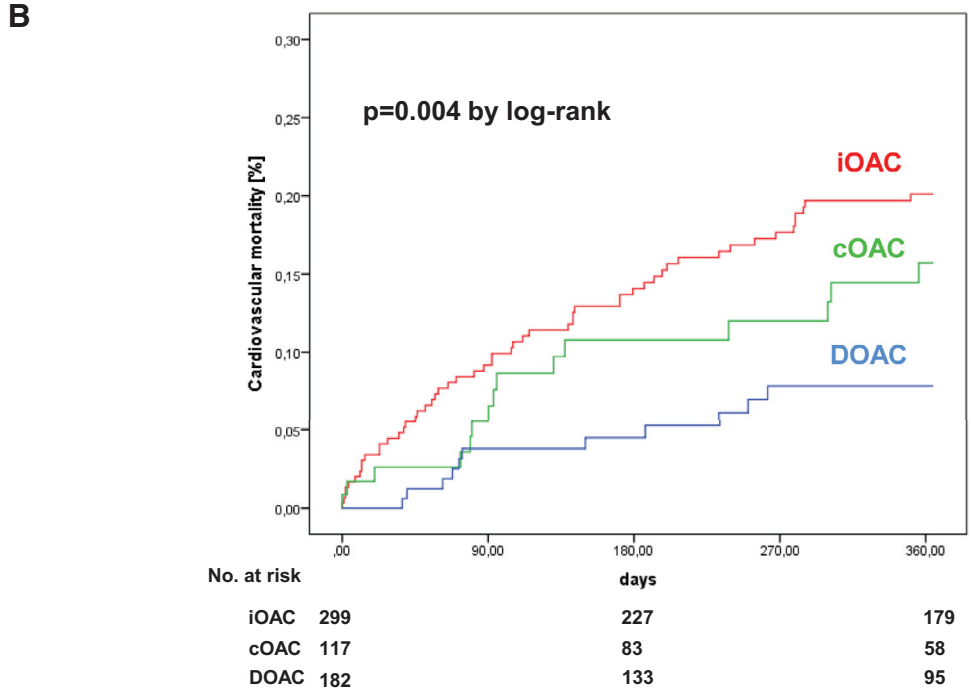


Figure 1. Kaplan–Meier analysis showing all-cause *(A)*, and cardiovascular *(B)* mortality. The inset in (A) shows the same data on an expanded y axis

Table 5
Factors associated with all-cause 1-year mortality.

Parameter	Oral anticoagulation dichotomous	
	HR (95% CI)	p value
New York Heart Association Class III/IV	2.23 (1.15-4.31)	0.017
Coronary artery disease	1.61 (1.06-2.45)	0.027
Oral anticoagulation (continued vs discontinued)	0.59 (0.38-0.91)	0.018
	Oral anticoagulation trichotomous	
Parameter		
New York Heart Association Class III/IV	2.19 (1.13-4.24)	0.020
Coronary artery disease	1.58 (1.04-2.41)	0.033
Oral anticoagulation		
Interrupted vitamin K antagonist (reference)	1	
Continued vitamin K antagonist	0.75 (0.43-1.31)	0.307
Direct oral anticoagulant	0.56 (0.32-0.99)	0.047

Discussion

In this cohort of patients, continued OAC did not increase the risk for the primary outcome measure. Overall rates of stroke and bleeding were not different between continued and interrupted OAC. Treatment with a DOAC was associated with a significantly reduced rate of early safety events and with a reduced 1-year mortality.

Performing invasive procedures in patients on therapeutic OAC is still feared because of the perceived higher risk of bleeding complications. However, several controlled studies proved the opposite in the field of ablation therapy for atrial fibrillation and noncardiac operations. The COMPARE trial randomized patients who underwent ablation procedures into an on-warfarin and off-warfarin arm with the latter one bridged with LMH.[16] The incidence of thromboembolic events within 48 hours was significantly reduced in on-warfarin. In the BRIDGE trial,[17] patients were randomized to bridging or no bridging before different noncardiac operations after stopping OAC. Patients with bridging had higher rates of major and minor bleeding without an impact on thromboembolic complications. The RE-CIRCUIT trial[18] investigated the safety of continued dabigatran versus continued warfarin in patients who underwent ablation of atrial fibrillation. The incidence of major bleeding events during and up to 8 weeks after ablation was lower with dabigatran than with warfarin (1.6% vs 6.9%; $p < 0.001$). Dabigatran was associated with fewer pericardial tamponades and groin hematomas than warfarin. These trials show that it is safe to perform ablation therapy under continued OAC and that forgoing bridging with heparin during noncardiac surgery is associated with a decreased risk of bleeding.

In our study, DOAC showed superior early safety compared to iVKA whereas no safety concerns were noticed in cVKA compared to iVKA indicating that TAVI under continued OAC, either with VKA or DOAC, seems to be safe and effective. Numerically lower rates of life-threatening/major bleedings and stroke were noticed in DOAC despite a high risk for bleeding and stroke. This is in line with randomized clinical trials comparing the use of different DOACs compared to VKA showing lower life-threatening/major bleeding events in patients treated with DOAC for prevention of thromboembolism in AF.[12–15] Rates of renal failure were lower in cOAC and DOAC despite a comparable rate of chronic kidney disease at baseline. Acute kidney injury after TAVI is known to be associated with bleeding events and consecutive need for blood transfusion[23] indicating that the lower number of bleeding events and significantly lower rates of blood transfusion in cOAC and DOAC might have contributed to this finding.

The reduction of 1-year mortality in DOAC is in line with a study evaluating the safety and efficacy of apixaban compared to VKA in patients with AF after TAVI.[24] The rate of the early safety end point at 30 days was also lower with apixaban compared to VKA although therapy was stopped during the procedure. Similar to our study, a lower rate of acute kidney injury stage 2/3 was observed in the apixaban group compared to VKA. Periprocedural stroke, bleeding and acute kidney injuries are important risk factors affecting even 1- and 3-year survival.[7,10] Therefore, the reduction of those events in patients treated with DOAC may have led to the improved outcome at 1 year observed in in our study and the one by Seeger et al. [24] Moreover, treatment with DOAC compared to VKA was also associated with improved survival in clinical trials evaluating the safety and efficacy of different DOACs for prevention of thromboembolism in AF.[12–15] The mortality difference at 1 year in our analysis was mainly driven by cardiovascular mortality mirroring the results of clinical trials with apixaban[14] and edoxaban.[13] Additionally, a recent study documented a lower risk of myocardial infarction in patients with AF treated by DOAC compared to VKA, supporting the hypothesis that prevention of cardiovascular events is the main contributor for the reduction of all-cause mortality.[25]

Yet, there is no evidence from randomized trials for the use of DOACs after TAVI. In surgical mechanical valve implantation, the use of dabigatran was associated with a higher rate of thromboembolic and bleeding complications.[26] For bioprosthetic valves, a retrospective analysis demonstrated the prevention of thromboembolic events, but documented a higher rate of bleeding.[27] Our study and the one by Seeger et al [24] provide signals that DOAC might be a reasonable option in patients after TAVI with AF. The ATLANTIS trial will test the superiority of apixaban versus the recommended standard of care in an all comer population,[28] whereas GALILEO tested the hypothesis that rivaroxaban reduces the risk of thromboembolic complications post-TAVI compared with an antiplatelet therapy-based strategy in subjects without an indication for oral anticoagulation.[29] However, GALILEO was stopped during the follow-up period due to safety concerns in the rivaroxaban group.

Our analysis has limitations. This was a nonrandomized, retrospective analysis in a single center and is, therefore, prone to bias inherent to registries and not necessarily conferrable to other cohorts. DOAC comprised of different active ingredients with a predominance of rivaroxaban. However, clinical trials evaluating the safety and efficacy of DOACs pointed in the same direction with an advantage for DOAC indicating a class rather than a substance effect.

A learning curve and the examined time frame might have had an impact on the outcome measures. To address these limitations we restricted the analysis to the time frame from 2011 to 2016. First, our TAVI program already started in 2006 assuming that the learning curve was completed in 2011 and second, applying this strategy, we also avoided the inclusion of too many first generation devices. We are aware that there was a trend to lower risk patients during the examined time frame and DOAC use increased in the later years. However, risk prediction, in particular using the STS-Score, might be misleading since yearly changes to the STS score algorithm can result in significant reduction in STS scores for patients who underwent TAVI.[30] This is reflected by a comparable age (79, 79, 80, 80, 80, and 80 years, $p = 0.72$) and only a nonsignificant trend regarding mean logEuroScore I (21.5, 19.1; 16.8, 18.8, 17.9, and 19.1%, $p = 0.06$) in the total cohort from 2011 to 2016. Another possible bias is that the decision to continue or interrupt OAC was also dependent on other clinical characteristics and concomitant therapeutic procedures. It is a limitation that we do not have complete data on stroke and bleeding beyond day 30 and, thereby, limiting the statistical power for analyzing predictors of those events, in particular stroke due to a low number of events until day 30.

In conclusion, continued OAC did not increase the rates of early safety events at 30 days in this cohort of patients suffering from atrial fibrillation treated by OAC before TAVI. Overall rates of stroke and bleeding were not different between continued and interrupted OAC. Treatment with a DOAC was associated with a significantly reduced rate of early safety events at 30 days and with a reduced 1-year mortality.

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