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# Incidence, predictors, impact, and treatment of vascular complications after transcatheter aortic valve implantation in a modern prospective cohort under real conditions

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1 **Incidence, predictors, impact, and treatment of vascular complications following**  
2 **transcatheter aortic valve implantation in a modern prospective cohort under real**  
3 **conditions**

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19

20 Short title: Vascular complications after TAVI in the era of low profile devices

1 Article highlights

2 Type of research: Multicenter, prospective, nonrandomized cohort study

3 Key findings: The incidence of vascular complications was high (26.1%) following 479  
4 transcatheter aortic valve implantation (TAVI), but 88.8% were minor and survival was not  
5 affected. Major complications were rare. they were treated with surgery and had a significant  
6 impact on survival at 30 days (69.3%) and 1 year (59.4%) .

7 Take Home Message: Vascular complications after TAVI are frequent and challenging, despite  
8 routine use of low profil devices and sheathless techniques.

9

10 Table of contents Summary

11 In this prospective study the incidence of vascular complications was high (26.1%) following  
12 479 transcatheter aortic valve implantation (TAVI), but 88.8% were minor and survival was not  
13 affected. Major complications were rare. they were treated with surgery and had a significant  
14 impact on survival at 30 days (69.3%) and 1 year (59.4%) .

## 1 **Abstract**

2 **Objective:** Vascular complications (VCs) occurring in TAVI procedures have frequently been  
3 reported in the past. Considering significant technical improvements in delivery systems and  
4 vascular closure devices, the goal of this study was to determine the incidence, impact, and  
5 prognostic factors of VCs in a recent real-world cohort.

6 **Methods and results:** We report a bicentric prospective analysis of 479 consecutive patients  
7 who underwent TAVI between January 2017 and December 2017. Vascular complications were  
8 defined according to criteria set out by the Valve Academic Research Consortium Criteria-2  
9 (VARC-2).

10 The incidence of VCs was 26.1% (n = 125 patients), of which 2.9% were major (n = 14) and  
11 23.2% were minor (n = 111) . Vascular complications were related to the primary puncture point  
12 in 69% of cases, compared to 31%, at the secondary puncture site. Treatments implemented were  
13 medical in 76% of cases and surgical in 24% of cases. The risk factors for VCs were as follows:  
14 iliac morphology score, sheath-to-iliofemoral artery ratio (SIFAR), and moderate-to-severe  
15 iliofemoral calcifications or tortuosity. In the case of major VCs, only SIFAR was a risk factor.  
16 Major VCs significantly increased intra-hospital mortality (30.7% vs. 1.1% for minor VCs and  
17 1.3% for no VCs, log rank  $p < 0.0001$ ) and 1-year mortality (40.6% vs. 5.6% for minor VCs and  
18 5.6% for no VCs, log rank  $p < 0.0001$ ).

19 **Conclusion:** Using strictly VARC-2 endpoint definitions, more than one-quarter of TAVI  
20 procedures were associated with VCs, primarily minor ones. Secondary puncture points were  
21 responsible for one-third of VCs and should, therefore, also be actively monitored. Major VCs  
22 significantly impact short and mid-term survival.

23

## 1 **Keywords**

- 2 • Transcatheter aortic valve implantation
- 3 • Vascular complications
- 4 • Valve Academic Research Consortium-2
- 5 • Sheath-to-iliofemoral artery ratio
- 6 • Iliofemoral calcifications
- 7 • Iliofemoral tortuosity

## 8 **Abbreviations**

- 9 • TAVI: transcatheter aortic valve implantation
- 10 • VARC: valve academic research consortium
- 11 • VCs: vascular complications
- 12 • PVA: primary vascular access
- 13 • SVA: secondary vascular access
- 14 • BMI: body mass index
- 15 • SIFAR: sheath-to-iliofemoral artery ration
- 16 • IMS: iliac morphology score

17

## 18 **Conflict of interest statement/funding statement**

19 No funding has to be declared.

20 Dr Bourguignon reports personal fees from Edwards Lifesciences, outside the submitted work.

21 Other authors have no conflicts of interest to declare

## 1 **Introduction**

2 Transcatheter aortic valve implantation (TAVI) has, in recent years, developed into a standard  
3 treatment for severe aortic valve stenosis among patients at high and intermediate operative risk  
4 (1–4). Although transfemoral access for TAVI is generally the preferred approach in most  
5 experienced treatment centers, vascular complications (VCs) account for significant morbidity  
6 and mortality (5–7). The incidence of VCs varies according to the literature, as studies have  
7 employed different definitions for such events. The valve academic research consortium (VARC)  
8 standardized definitions of VCs following TAVI to allow for better comparison between studies  
9 (8). Research addressing VCs has generally been conducted among older-generation prostheses  
10 and has involved larger delivery systems compared to those currently in use, which may also  
11 have had an impact on VCs rates. Moreover, indications for TAVI have shifted toward patients  
12 who are of lower surgical risk, whereas institutional and operator experience has increased.  
13 These developments may have changed the incidence and outcome of VCs over time.  
14 The objective of this study was to report the incidence, predictors, and impact of VCs during the  
15 TAVI procedure in the era of low profil devices, using a standardized definition of events.

16

## 17 **Methods**

### 18 **Study design**

19 In this study, we enrolled all patients who underwent a TAVI procedure from January 2017 to  
20 December 2017 at the Tours and Rennes University hospitals in France. All procedures and  
21 approaches were reviewed and established to have accurate and exhaustive estimates of VCs  
22 over a period of 1 year.

23 Consent was obtained from each patient using an agreement of the Institutional Ethics

1 Committee , and registered in the France TAVI database. All patients underwent computed  
2 tomography (CT) angiography to evaluate the size of the prosthesis and vascular anatomy. Prior  
3 to TAVI implantation, a multidisciplinary meeting was held to check medical indications  
4 according to international recommendations and select the best access approach (9,10). Baseline  
5 characteristics, risk score, and procedural data were collected from the medical records of each  
6 patient.

7 The two most common implanted prostheses were the balloon-expandable SAPIEN 3 (sizes 23,  
8 26, and 29 mm; Edwards Lifesciences, Irvine, California) and the self-expanding CoreValve  
9 EVOLUT R (sizes 23, 26, 29, 31, and 34 mm; Medtronic, Minneapolis, Minnesota). For  
10 SAPIEN 3 prostheses, the eSheath expandable introducer system (Edwards Commander delivery  
11 catheter; Edwards Lifesciences) was used with a 14-French inside diameter sheath of 23 and 26  
12 mm (equivalent to 5.8 mm at the outer diameter unexpanded) or a 16-French inside diameter for  
13 29 mm prostheses (equivalent to 6.5 mm at the outer diameter unexpanded) (11). In the case of  
14 CoreValve EVOLUT R 23-, 26-, and 29 mm prostheses, the EnVeo delivery system (Medtronic,  
15 Inc ) was used, with a 14-French equivalent InLine sheath, which is equal to 18-French (6 mm)  
16 at the outer diameter.

17 The transfemoral approach was selected as the preferred method in this study. Procedural steps  
18 were previously described (12,13). To take a true percutaneous approach, ProStar XL  
19 Percutaneous Vascular Surgical System (Abbott Vascular, Santa Clara, California) or ProGlide  
20 (Abbott Vascular) preclosing devices were used for the primary puncture site. FemoSealTM  
21 (Terumo Corporation), AngiosealTM (Terumo Corporation), or manual compression was  
22 employed for the secondary puncture site. Primary vascular access (PVA) was defined as access  
23 by which the valve was introduced. Secondary vascular access (SVA) was defined as access by

1 which aortography was performed.

2 Anatomical parameters were measured by an investigator using EndoSize® software, prior to  
3 collection of clinical outcomes. Anatomical parameters were automatically extracted from the  
4 vessel's centerline. Common iliac arteries, external iliac arteries, and common femoral arteries  
5 were treated as three segments. Parameters were as follows: minimal iliofemoral diameter,  
6 iliofemoral calcifications, and iliofemoral tortuosity. An iliac morphology score (IMS) was  
7 calculated for each patient (14). The calcification rate of iliofemoral access was graded from 0–3  
8 (0 = no calcification; 1 = calcification < 25% of the vessel length; 2 = calcification ranging from  
9 25% to 50%; and 3 = calcification > 50% or circumferential calcification) (15). Tortuosity rate  
10 for iliofemoral access was also graded from 0–3 (0 = tortuosity angle <30° at any point of  
11 iliofemoral access; 1 = tortuosity angle ranging from 30° to 60°; 2 = tortuosity angle ranging  
12 from 60° to 90°; 3 = tortuosity angle >90° (13). SIFAR was calculated using the minimum  
13 iliofemoral artery diameter and the maximal delivery sheath diameter (16).

14 Baseline characteristics and procedural and follow-up data were prospectively collected in our  
15 local database. Mortality data were obtained using the Social Security Death Index, thereby  
16 ensuring complete survival follow-up for all patients.

17

## 18 **Study endpoints**

19 The primary endpoint of the study was identified as the occurrence of any vascular complication,  
20 defined according to the Valve Academic Research Consortium Criteria-2 (VARC-2) (8), and  
21 these were divided into major and minor VCs. Minor VCs included all access-related criteria and  
22 those not meeting the criteria for major VCs. Vascular complications were recorded for all types  
23 of vascular access: transfemoral (percutaneous or surgical), transcarotid, subclavian, transapical,



1 and transaortic.

2 Treatment of VCs was registered according to three classes: medical treatment (echo-guided  
3 compression), endovascular treatment (stenting), and surgical treatment (open surgery). Survival  
4 analysis was performed at 30 days and one year.

5 To conduct statistical analysis of baseline characteristics, procedural data, and general outcomes,  
6 we compared patients with both major and minor VCs with patients without VCs. Categorical  
7 data were presented as numbers with percentages and compared using the Pearson chi-squared  
8 test or Fisher's exact test, accordingly. A normal distribution of continuous variables was  
9 verified using the Shapiro–Wilk test, and data were expressed as mean  $\pm$  standard deviation and  
10 compared using either Student's t-test or Mann–Whitney U test. Thirty-day mortality and 1-year  
11 mortality were described using the Kaplan–Meier method and compared using the log-rank test.  
12 A p value  $<0.05$  was considered statistically significant.

13 To determine predictors of VCs, a univariate logistic regression analysis was performed using  
14 the following covariates found in the literature: age, sex, body mass index (BMI), diabetes,  
15 peripheral artery disease, chronic kidney failure, logistic EuroSCORE, anticoagulant use,  
16 femoral secondary puncture site, IMS, SIFAR, iliofemoral moderate-to-severe calcification, and  
17 tortuosity. To determine clinical thresholds for quantitative data, we performed a receiver  
18 operating characteristic curve analysis. Multivariate logistic regression analysis was performed,  
19 including variables with a p value  $< 0.20$  in the univariate analysis. For analysis of SIFAR, IMS  
20 score, calcification, and tortuosity, we excluded patients with non-transfemoral access.

21 Statistical analyses were conducted using SPSS software version 25.0 (IBM Corporation,  
22 Chicago, Illinois), and the survival analysis was conducted using R statistical software (version  
23 3.5.0; R Foundation for Statistical Computing, Vienna, Austria).

1

## 2 **Results**

### 3 **Study population**

4 The total number of patients included was 479. The patient flow chart is presented in Figure 1.

5 Baseline characteristics were divided into three groups (no VCs, minor VCs, and major VCs) and  
6 are described in Table I. Procedural and CT angiography parameters are presented in Table II.

7 The overall incidence of VCs was 26.1% (171 events among 125 patients ). Among them were  
8 14 major VCs (2.9%) and 111 minor VCs (23.2%). The distribution of VCs is described in  
9 Figures 2 and 3. The proportion of VCs related to the second puncture site was 31.8% in the  
10 group with minor VCs and 21.4% in the group with major VCs.

### 11 **Risk factors**

12 Using multinomial logistic regression, predictors for all VCs were as follows: IMS score ( $p =$   
13  $0.003$ ), sheath-to-iliofemoral ratio ( $p = 0.002$ ), moderate-to-severe iliofemoral calcification ( $p =$   
14  $0.002$ ), and moderate-to-severe iliofemoral tortuosity ( $p < 0.001$ ) (Table III ). Importantly,  
15 neither valve type nor vascular closure device were found to significantly influence the risk of  
16 VCs. SIFAR was the only predictor of major VCs ( $p = 0.001$ ) (Table III).

17 The SIFAR cutoff point was 0.91 for all VCs and 0.95 for major VCs (Supplementary Figures 1  
18 and 2). The minimal iliofemoral diameter cutoff point was 6.4 mm for all VCs, excluding major  
19 VCs, for which it was 6.2 mm.

### 20 **Treatments**

21 Surgery (open or endovascular) was performed for 41 patients (8.5%). Emergency treatment of  
22 major VCs performed as open vascular surgery accounted for eight patients (57.1%),  
23 endovascular stenting involved three patients (21.4%), and medical treatment was provided for

1 three patients (21.4%). Minor VCs were primarily treated by prolonged compression (82.9%).  
2 Fourteen patients needed delayed vascular surgery, performed  $8.8 \pm 9.8$  days following the TAVI  
3 procedure and included surgical closure for false aneurysm in six patients (42.8%), surgical  
4 drainage in five patients (35%), amputation in two patients (14%), and axillofemoral bypass in  
5 one patient ( ).

### 6 **In-hospital results**

7 The median total length of hospital stay for all patients was  $6.8 \pm 4.2$  days, of which  $1 \pm 1.8$  days  
8 were spent in the intensive care unit. Patients who developed VCs had a significantly longer total  
9 length of hospitalization ( $7.7 \pm 4.8$  days vs.  $6.5 \pm 3.8$  days,  $p = 0.004$ ) and intensive care unit  
10 length stay ( $1.4 \pm 2.3$  days vs.  $0.9 \pm 1.6$  days,  $p = 0.013$ ). Moreover, VCs were significantly  
11 associated with in-hospital major bleeding ( $p = 0.001$ ), transfusion ( $p < 0.001$ ), stroke (major  
12 stroke,  $p = 0.018$ ; minor stroke,  $p = 0.003$ ), and delayed reintervention ( $p < 0.001$ )  
13 (Supplementary Table I).

### 14 **Survival results**

15 On comparing the three groups (major VCs, minor VCs, and no VCs), it was observed that the  
16 in-hospital mortality rate was 30.7%, 1.1%, and 1.3% (log rank  $p < 0.0001$ ), respectively. At 1  
17 year, mortality rates were 40.6% among patients with major VCs, 5.6% for those with minor  
18 VCs, and 5.6% for those without VCs (log rank  $p < 0.0001$ , Figure 4). In pairwise comparisons,  
19 the mortality rate in patients with major VCs was statistically higher than in those without VCs  
20 ( $p < 0.0001$ ) and with minor VCs ( $p < 0.0001$ ). Major VCs were associated with increased 1-year  
21 mortality in univariate and multivariate analyses (adjusted HR (95%CI) = 18.69 (7.72–61.13),  $p$   
22  $< 0.0001$ ) (see Table IV).

23

## 1 **Discussion**

2 This study found a high incidence of VCs after TAVI (26.1%), however, only 2.9% were major.  
3 The predictive factors of VCs found are : IMS score, SIFAR, moderate/severe iliofemoral  
4 calcification and tortuosity. Major VCs had a significant impact on 30-day (30.7%) and 1-year  
5 (40.6%) mortality rates.

## 6 **Definition and incidence**

7 Assessments of the accurate incidence of VCs from existing trials were limited by the initial lack  
8 of standardized definitions, with reported rates varying widely, from 1.9% to 30.7% (1,5,13).  
9 Using updated VARC-2 criteria, incidences of VCs in the case of older-generation prostheses  
10 were observed as ranging from 7.4% to 21.4% in several registries (5,13). The relationship  
11 between larger sheath diameter and higher vascular access site complications is well established.  
12 In a registry analysis of 26,414 patients comparing outcomes in patients who underwent TAVI  
13 between 2012 and 2013 with those who did so in 2014, incidences of major bleeding, life-  
14 threatening bleeding, and major VCs declined from 5.5% to 4.2%, 6.4% to 4.3%, and 5.6% to  
15 4.2%, respectively (17).  
16 More recently, in a monocentric prospective cohort employing SAPIEN 3 prostheses, Van  
17 Kesteren et al. (6) described incidences of major VCs in 5.8% and minor VCs in 15% of cases.  
18 The incidence of major VCs at a rate of 2.9% (reported in our series) was in line with these  
19 results and confirmed improvements in technology and the benefits of low-profile sheaths. The  
20 higher incidence of minor VCs (23.2%) in our series can potentially be explained by the less  
21 frequent use of vascular ultrasound, which was not systematic in 2017 as a means for guiding  
22 arterial puncture. Subsequently, research reported its beneficial impact on the prevention and  
23 management of VCs (18).

## 1 **Impact on clinical outcomes**

2 Consistent with previous studies (5,6,17), we demonstrated that minor VCs were not associated  
3 with in-hospital and 1-year survival. However, 25.2% of minor VCs were actively managed by  
4 invasive treatment (unplanned endovascular treatment or open surgery). The bulk of minor VCs  
5 were benign and resolved using medical treatment. Our results indicated 1-year mortality rates  
6 for minor (5.6%) and no VCs (5.6%). Proper management of minor VCs by experienced  
7 healthcare teams was not indicated as affecting mid- and long-term survival (5,6).

8 Conversely, major VCs were found to be strongly associated with in-hospital mortality (30.7%)  
9 and 1-year mortality (40.6 %, log rank < 0.0001), compared to minor and no VCs. Our 1-year  
10 mortality rate for major VCs was high (40.6%) but similar to a pooled analysis of PARTNER IA  
11 and IB trials (39.4%) (5,19-21). In keeping with recent literature (6,22-24), we observed that  
12 major VCs led to open surgery in half of presenting cases and were associated with an increase  
13 in the length of the hospital stay, thereby adding to the total cost of the procedure.

14 Concerning the links between VCs and other in-hospital outcomes, we observed an association  
15 between VCs, bleeding (minor and major), and transfusion rates. Among these bleeding events,  
16 69.8% (n = 44) were linked to the primary puncture site, 25.4% (n = 16) were linked to the  
17 secondary puncture site, and other localizations were retroperitoneal (n = 2) and intrapericardial  
18 (n = 1). According to the literature, VCs and bleeding events are linked, because they arise as a  
19 result of the same cause (puncture sites).

20 Global stroke rate was 2.3% within our cohort, similar to other studies reporting a 30-day risk of  
21 stroke ranging from 2%–5% (25,26). We also found an association between VCs and strokes,  
22 particularly in the case of major VCs. Five patients who presented major VCs had experienced a  
23 stroke, likely due to hemodynamic variation related to conversion to general anesthesia,

1 bleeding and/or arterial manipulation with the aim of treating VCs. This finding highlights taking  
2 care of hemodynamic conditions and optimizing cerebral protection in the case of VCs.

### 3 **Risk factors**

4 Several clinical predictors of VCs are reported in the literature: female sex, renal insufficiency,  
5 diabetes mellitus, moderate-to-severe iliofemoral calcifications, and concomitant peripheral  
6 vascular disease (21). Procedural factors include a sheath size >19Fr (5,25), operator and clinical  
7 center experience (26,27), and SIFAR, which appear to be the major predictors of VCs (6,19).  
8 In our study, we distinguished predictors for all VCs, as well as predictors for major VCs. We  
9 identified four factors of all VCs in the multivariate analysis: IMS score, SIFAR, moderate-to-  
10 severe iliofemoral calcification, and moderate-to-severe iliofemoral tortuosity. Concerning IMS  
11 score, Blakeslee–Carter et al. reported that an  $IMS \geq 5$  had the best discriminatory power for  
12 predicting VCs (sensitivity: 54%, specificity: 90%) (12). However, our results were less  
13 convincing (AUROC: 0.58, 95% CI: 0.40–0.76 vs. AUROC: 0.82, 95% CI: 0.65–0.98).  
14 Concerning major VCs, SIFAR was the only predictor of complications in our series. Receiver  
15 operating characteristic curves described an area under the curve of 0.62, in line with outcomes  
16 reported by Van Kesteren et al. (6). Indeed, the expandability and flexibility of new introducers  
17 make the use of this ratio less relevant than  
18 older-generation introducers. Moreover, measurements of the outer diameter of expandable  
19 introducer sheaths can vary during the procedure (9). We chose the outer diameter for the  
20 calculation of SIFAR, prior to the introduction of the introducer, which represented the most  
21 constant measure.

22 Complete percutaneous transfemoral access is the reference access route for the TAVI  
23 procedure. We reported 13% of alternative access in our study with an incidence of 1.5% major

1 VCs and 12.7% minor VCs. Vascular complications were significantly less frequent in  
2 alternative access cases, compared to percutaneous transfemoral access (14.3% vs. 27.9%,  $p$   
3 =0.034). In our series, very few patients underwent a transfemoral TAVI using a surgical  
4 cutdown. We were, therefore, unable to confirm the data of Hernandez–Enriquez et al., who  
5 reported a 30-day vascular complication rate of 18% in the puncture group vs. 6.9% in the  
6 surgical cutdown group (28).

7 Regarding the impact of introducer systems on VCs, similar to others (29,30), we could not find  
8 any difference between different types of implanted valves. Moreover, comparison of closure  
9 device systems indicated no difference in VCs concerning the primary access site or the  
10 secondary access site, which is supported by conflicting results in the literature (31,32).

### 11 **Prevention**

12 As VCs are a major determinant of outcome following the TAVI procedure, prevention of these  
13 issues is paramount. A CT angiogram of the vascular anatomy plays a major role in procedural  
14 planning. Attention should be given to precise access techniques, including the secondary  
15 puncture point, to avoid any possible vessel injury. The use of echo-guided puncture techniques  
16 can improve the first-pass success rate and reduce the number of attempts needed (33). This  
17 technique should, therefore, be recommended in clinical settings. Additionally, we believe that  
18 active collaboration with cardiovascular surgeons may be necessary in this regard.

19 Other access-site considerations and strategies have been described. In case of unfavorable  
20 anatomy, surgical conduits techniques can be performed through the axillary artery or the  
21 retroperitoneal iliac artery (34). Too, the « paving and cracking » technique using covered stents  
22 improves iliac access by dilation and relining of calcified and/or tortuous arteries (34-35).

### 23 **Limitations**

1 Our study includes several limitations. First, the research was bicentric and included all TAVIs  
2 regardless of vascular access, which increased cohort heterogeneity. Second, because the major-  
3 VCs group was small in size, the search for risk factors in this group may have been skewed by  
4 the numerical disproportion between groups.

5 Our study was specifically designed to focus on VCs following TAVI procedures. We employed  
6 strict VARC-2 criteria and exhaustively reported all VCs, regardless of access, delivery system,  
7 and closure device. We, therefore, propose that a comprehensive overview of this life-  
8 threatening complication be conducted in a real-world setting, involving a recent cohort.

9

## 10 **Conclusion**

11 Despite smaller caliber delivery systems and the introduction of new-generation prostheses, VCs  
12 remain a significant issue for TAVI procedures, particularly transfemoral cases. Although most  
13 VCs are minor in nature and not associated with negative outcomes, major VCs are linked with  
14 an increased risk of mortality at 30 days and at one year. More attention should be focused on  
15 establishing adequate pre-operative access imaging, clinical assessment, cardiovascular surgery  
16 team involvement in high risk cases and ultrasound guided arterial puncture, including  
17 approaches to the secondary puncture point.

18

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1 **Figure legends**

2 Figure 1 : Flow chart of the cohort

3 Figure 2 : Distribution of minor VCs according to the arterial puncture point, 157 events are  
4 reported for 111 patients, 46 patients cumulated two minor VCs.

5 Figure 3 : Distribution of major VCs according to the arterial puncture point, 14 events are  
6 reported for 14 patients.

7 Figure 4 : Kaplan-Meier curves of survival probability at 1-year follow-up after TAVI procedure.

8 Numbers at risk are the cumulative incidence at each landmark point. Percentages are the  
9 cumulative incidence of death at 1-year follow-up for each group.

10

11 **Text tables legends**

12

13 Table 1 : Preoperative characteristics aggregate to vascular complications

14 p-values are for comparison in two groups: without VCs and with VCs.

15 STS-PROM = Society of Thoracic Surgery predicted risk of mortality; NYHA = New York

16 Heart Association; MMSE = Mini-Mental State Evaluation

17 <sup>a</sup> Glomerular filtration rate < 60ml/min

18 <sup>b</sup> Including only angioplasty and/or coronary stenting

19

20 Table 2 : Procedural and CT- angiography characteristics aggregate to vascular complications

21 <sup>a</sup> : Cardiogenic shock or acute decompensated heart failure

22 Closure device primary puncture was missing in 14 patients

23 Closure device secondary puncture was missing in 25 patients

1

2 Table 3 : Predictors of all vascular complications in multivariate analysis. Predictors of major  
3 vascular complications in multivariate analysis

4

5 Table 4 : Univariate and multivariate analysis with hazard ratio of survival curves at one year

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## Tables

Table 1

Preoperative characteristics aggregate to vascular complications

Characteristics	Vascular complications			p-value
	No VC n = 354	Minor VC n = 111	Major VC n = 14	
Age (years)	82.6±6.5	83.4±6.0	82.2±5.7	0.283
Women	156 (45.9%)	53 (47.7%)	9 (64,3%)	0.286
Body Mass Index (kg/m <sup>2</sup> )	27±5	26.7±7.1	24±4.6	0.184
<b>Medical history</b>				
Hypertension	295 (84.3%)	86 (77.5%)	13 (92,9%)	0.194
Diabetes all types	98 (27.9%)	28 (25.2%)	3 (21,4%)	0.500
Dyslipidemia	204 (58.1%)	65 (58.6%)	3 (21.4%)	0.471
History of smoke	78 (22.3%)	22 (20%)	2 (14.3%)	0.495
Chronic obstructive pulmonary disease	63 (17.9%)	25 (22.5%)	5 (35.7%)	0.143
Cirrhosis	8 (2,3%)	2 (1.8%)	0	0.649
History of neoplasia	64 (18.2%)	18 (16.2%)	2 (14.3%)	0.574
Chronic renal failure <sup>a</sup>	136 (38.9%)	46 (41.4%)	5 (35.7%)	0.703
Ischemic heart disease	127 (36.3%)	39 (35.1%)	4 (28.6%)	0.706
Coronary bypass	24 (6.9%)	11 (10%)	0	0.461
Valvular heart surgery	15 (4.3%)	8 (7.2%)	0	0.345
Percutaneous aortic valvuloplasty	10 (2.9%)	7 (6.4%)	0	0.153
Percutaneous coronary intervention <sup>b</sup>	82 (23.6%)	31 (28.2%)	3 (21.4%)	0.135
Permanent pacemaker	29 (8.2%)	20 (18%)	0	0.014
Permanent atrial fibrillation	105 (29.8%)	42 (37.8%)	6 (42.9%)	0.078
NYHA class III or IV	173 (49.3%)	57 (51.8%)	9 (64.3%)	0.451
Chronic cardiac angina	46 (13.1%)	20 (18.2%)	2 (14.3%)	0.209
Pulmonary arterial hypertension moderate/severe	149 (46%)	50 (47.2%)	5 (41.7%)	0.908
History of stroke	30 (8.6%)	8 (7.2%)	2 (14.3%)	0.843
Logistic EuroSCORE	15.2±11	16.4±12.1	13.4±9.6	0.457
STS-PROM score	4.6±2.3	4.3±1.9	6.8±3.7	0.654
Peripheral vascular disease	44 (13.3%)	16 (16%)	1 ( 7.7%)	0.149
<b>Echocardiography</b>				
Left ventricular ejection fraction (%)	56.8±0.7	57.8±1.3	52.7±3.8	0.759



<i>Aortic valve area (cm<sup>2</sup>)</i>	0.73±0.01	0.77±0.02	0.64±0.05	0.175
<b><i>Biology at baseline</i></b>				
<i>Hemoglobin level (g/dL)</i>	12.5±0.1	12.6±0.2	12.1±0.6	0.813
<i>Platelets (G/L)</i>	217.7±3.9	203.9±7.2	275±20.6	0.432
<i>Prothrombin time (%)</i>	83±1.2	83.8±2.3	77.3±6	0.967
<i>Creatinine (μmol/L)</i>	107.6±2.7	110.9±5	107.6±2.7	0.191
<b><i>Preoperative treatment</i></b>				
<i>Anticoagulant</i>	104 (29.4%)	41 (37%)	5 (35.7%)	0.124
<i>Antiplatelet monotherapy</i>	138 (39%)	40 (36%)	3 (21.4%)	0.364
<i>Antiplatelet bitherapy</i>	46 (13%)	15 (13.5%)	2 (14.3%)	0.863
<i>Oral direct anticoagulants use (OADs)</i>	47 (13.3%)	15 (13.5%)	1(7.2%)	0.892

p-values are for comparison in two groups: without VCs and with VCs.

STS-PROM = Society of Thoracic Surgery predicted risk of mortality; NYHA = New York Heart Association; MMSE = Mini-Mental State Evaluation

<sup>a</sup> Glomerular filtration rate < 60ml/min

<sup>b</sup> Including only angioplasty and/or coronary stenting

Table 2

Procedural and CT- angiography characteristics aggregate to vascular complications

Characteristics	Vascular complication			p-value
	No VC n = 354	Minor VC n = 111	Major VC n = 14	
<i>Urgent procedure</i> <sup>a</sup>	19 (5.4%)	2 (1.8)	3 (21.4)	0.547
<i>Local anesthesia</i>	314 (88.9%)	98 (88.3%)	8 (57.1%)	0.222
<i>Conversion to general anesthesia</i>	1 (0.3%)	6 (1.3%)	5 (35.7%)	<0.001
<i>Technical success</i>	347 (98.2%)	109 (98.2%)	14 (100%)	1
<i>True femoral percutaneous</i>	300 (84.7%)	103 (92.8%)	13 (92.9%)	0.034
<i>Radial secondary puncture</i>	112 (32.5%)	25 (22.7%)	1 (7.2%)	0.016
<b>Valve type</b>				0.864
<i>CoreValve EVOLUTR</i>	134 (37.9%)	46 (41.4%)	7 (50%)	
<i>Edward SAPIEN 3</i>	215 (60.7%)	64 (57.6%)	7 (50%)	
<i>Portico</i>	3 (0.9%)	0	0	
<i>Minimal iliofemoral diameter (mm)</i>	6.7±1.3	6.3±1.2	5.8±1.5	0.002
<i>Sheath-to-iliofemoral ratio</i>	0.91±0.2	0.98±0.2	1.1±0.3	<0.001
<b>Primary puncture closure device</b>				0.07
<i>Perclose Proglide</i>	133 (37.6%)	42 (37.8%)	6 (42.9%)	
<i>Prostar</i>	158 (44.6%)	60 (54%)	7 (50%)	
<b>Secondary puncture closure device</b>				0.642
<i>Femoseal</i>	191 (54%)	62 (55.8%)	12 (85.7%)	
<i>Manual compression</i>	117 (33%)	40 (36%)	2 (14.3%)	
<i>Others systems</i>	24 (6.7%)	6 (5.4%)	0	
<i>Irradiation time (mn)</i>	14.9±7	15.1±8.3	19.2±10.3	0.444
<i>Radiation dose (cGy.m<sup>2</sup>)</i>	3967.1±2910	4078.5±2894.5	4616.2±3976.6	0.170
<i>Contrast volume (mL)</i>	104.3±48.9	97.6±37.3	102.9±49.8	0.239

<sup>a</sup> : Cardiogenic shock or acute decompensated heart failure

Closure device primary puncture was missing in 14 patients

Closure device secondary puncture was missing in 25 patients

Table 3

Predictors of **all vascular complications** in multivariate analysis

	Adjusted OR (95% CI)	p-value
<i>Age</i>	1.02 (0.99-1.06)	0.221
<i>Female</i>	1.16 (0.76-1.78)	0.497
<i>BMI</i>	0.99 (0.95-1.03)	0.662
<i>Diabetes</i>	0.87 (0.54-1.42)	0.579
<i>Peripheral artery disease</i>	0.87(0.53-1.42)	0.528
<i>Chronic renal failure</i>	1.12 (0.72-1.72)	0.628
<i>Logistic Euroscore</i>	1.01 (0.99-1.03)	0.355
<i>Anticoagulant use</i>	1.41 (0.90-2.20)	0.135
<i>OADs use</i>	1.02 (0.55-1.91)	0.949
<i>Femoral secondary puncture</i>	0.61 (0.37-1.01)	0.054
<i>IMS score</i>	1.25 (1.08-1.46)	<b>0.003</b>
<i>SIFAR</i>	6.52 (1.19-21.34)	<b>0.002</b>
<i>Moderate/severe calcification</i>	2.00 (1.29-3.10)	<b>0.002</b>
<i>Moderate/severe tortuosity</i>	2.36 (1.48-3.76)	<b>&lt;0.001</b>

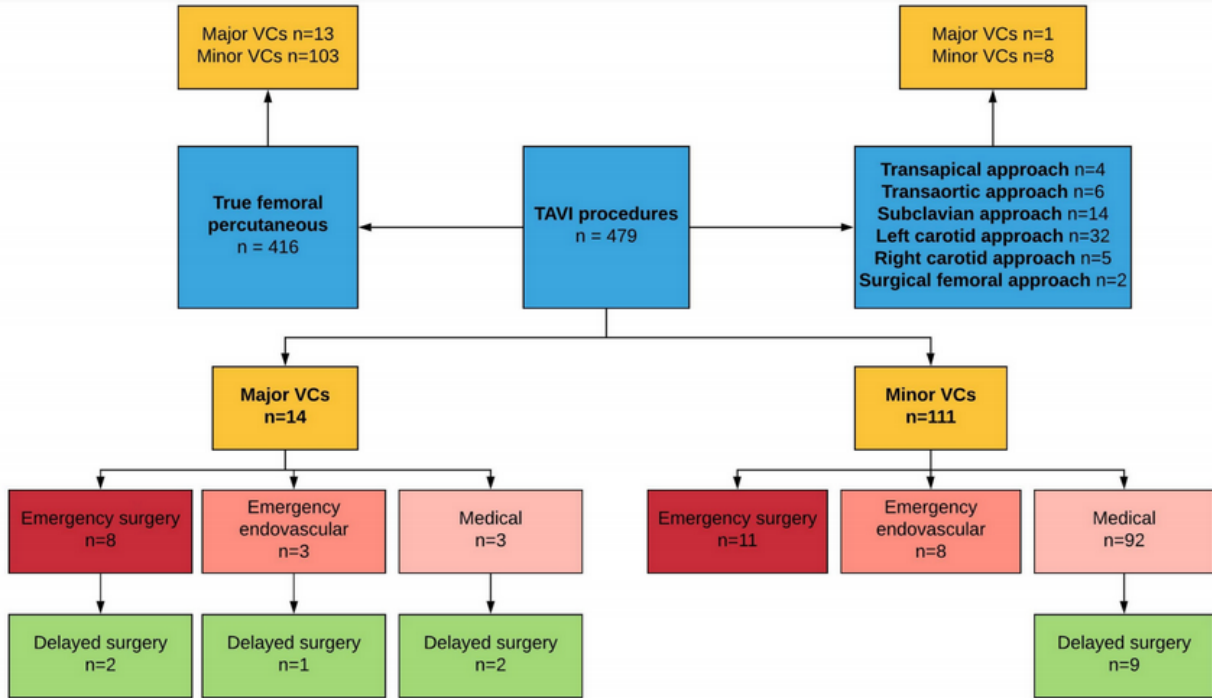
Predictors of **major vascular complications** in multivariate analysis

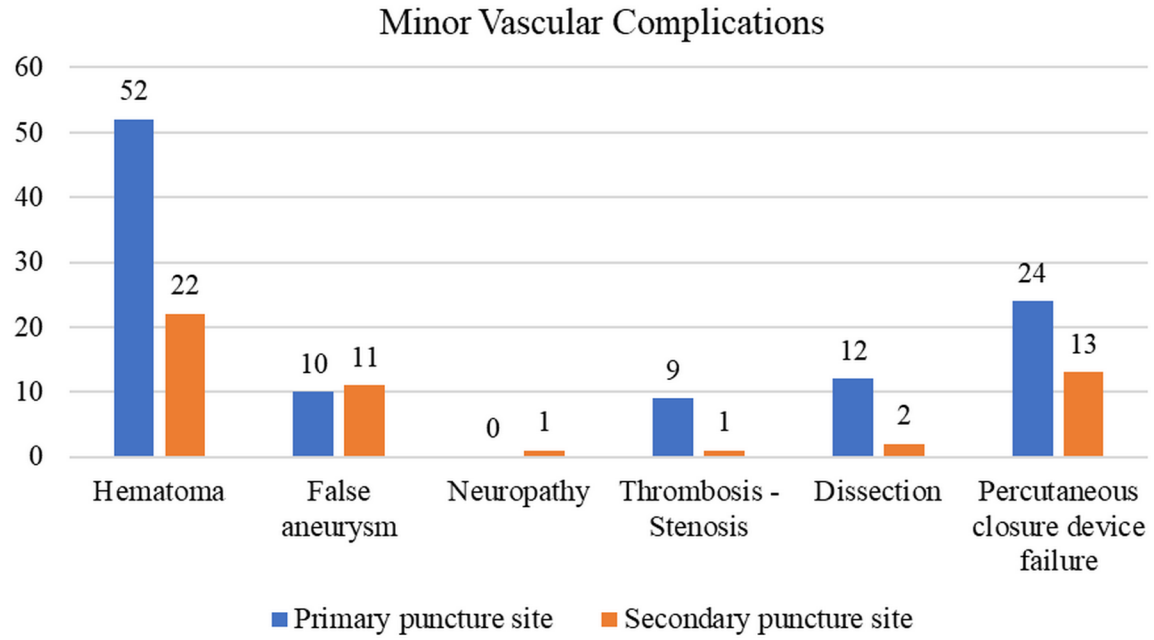
	Adjusted OR (95% CI)	p-value
<i>Age</i>	0.99 (0.92-1.07)	0.835
<i>Female</i>	2.29 (0.75-6.95)	0.146
<i>BMI</i>	0.87 (0.76-0.99)	0.040
<i>Diabetes</i>	0.70 (0.19-2.58)	0.596
<i>Peripheral artery disease</i>	1.64(0.36-7.49)	0.523
<i>Chronic renal failure</i>	0.87 (0.29-2.66)	0.813
<i>Logistic Euroscore</i>	0.98 (0.92-1.05)	0.611
<i>Anticoagulant use</i>	1.34 (0.44-4.08)	0.612
<i>OADs use</i>	0.50 (0.06-3.93)	0.512
<i>Femoral secondary puncture</i>	0.16 (0.02-1.24)	0.079
<i>IMS score</i>	1.33 (0.92-1.91)	0.134
<i>SIFAR</i>	31.02 (4.03-238.61)	<b>0.001</b>
<i>Moderate/severe calcification</i>	0.32 (0.09-1.17)	0.084
<i>Moderate/severe tortuosity</i>	1.57 (0.52-4.78)	0.426

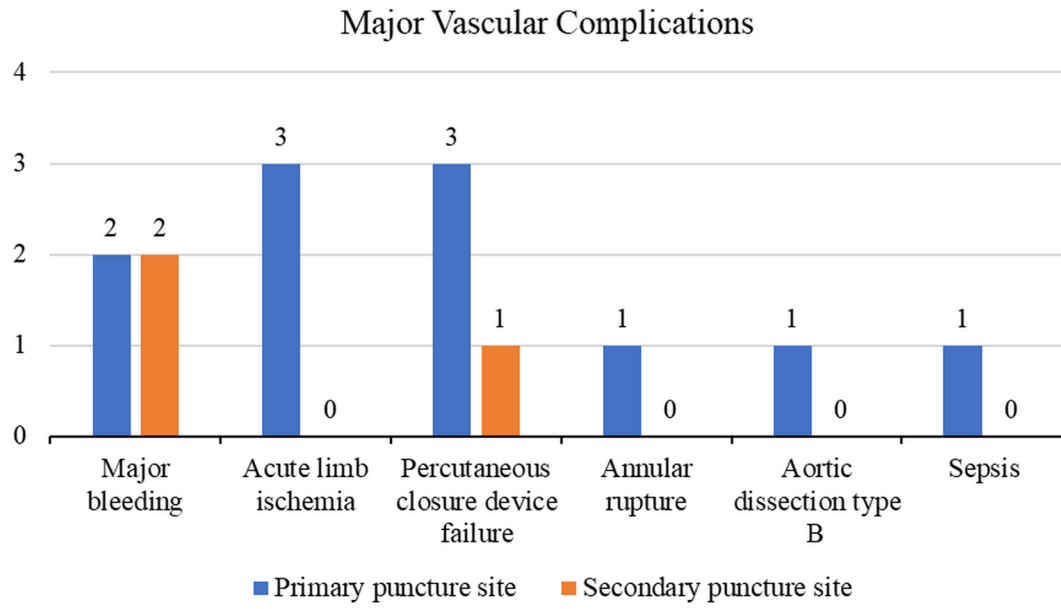
**Table 4**

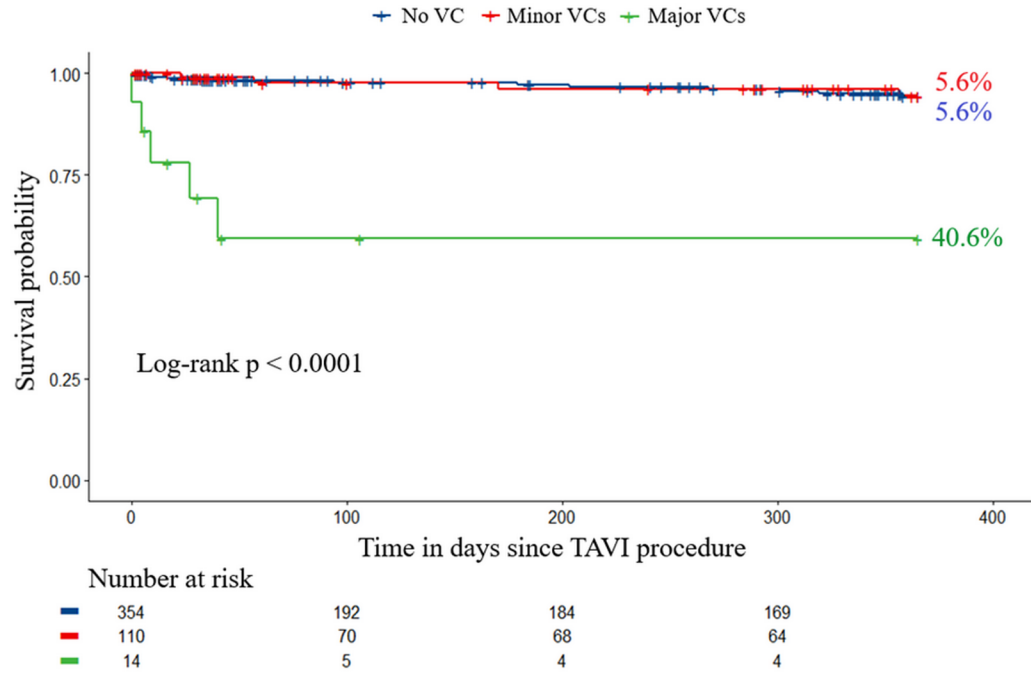
Univariate and multivariate analysis with hazard ratio of survival curves at one year

<i>1-year survival</i>	<b>Univariate model</b>		<b>Multivariate model</b>	
	<b>Unadjusted HR (95% CI)</b>	<b>p-value</b>	<b>Adjusted HR (95% CI)</b>	<b>p-value</b>
<i>Minor VC</i>	0.69(0.23-2.04)	p=0.49	0.91(0.28-2.93)	p = 0.87
<i>Major VC</i>	14.19(5.17-38.94)	p<0 .001	18.69(5.72-61.13)	p<0.0001





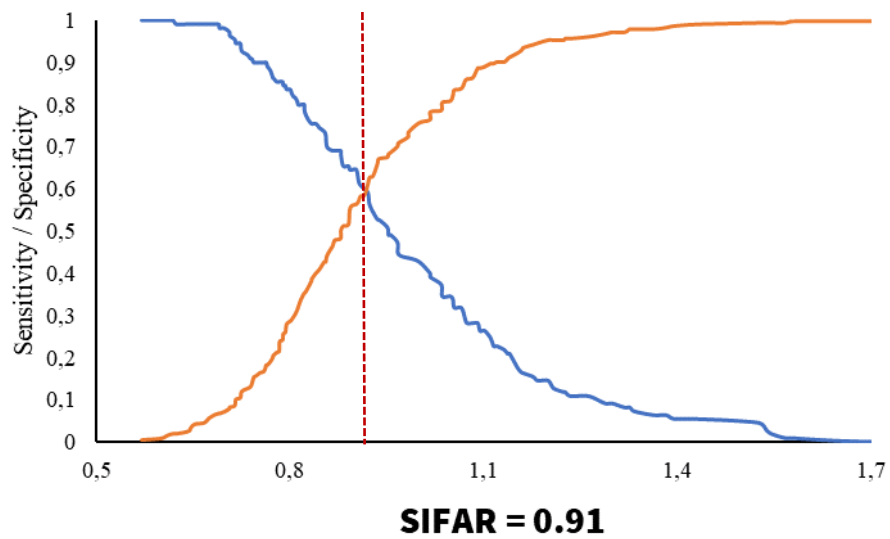






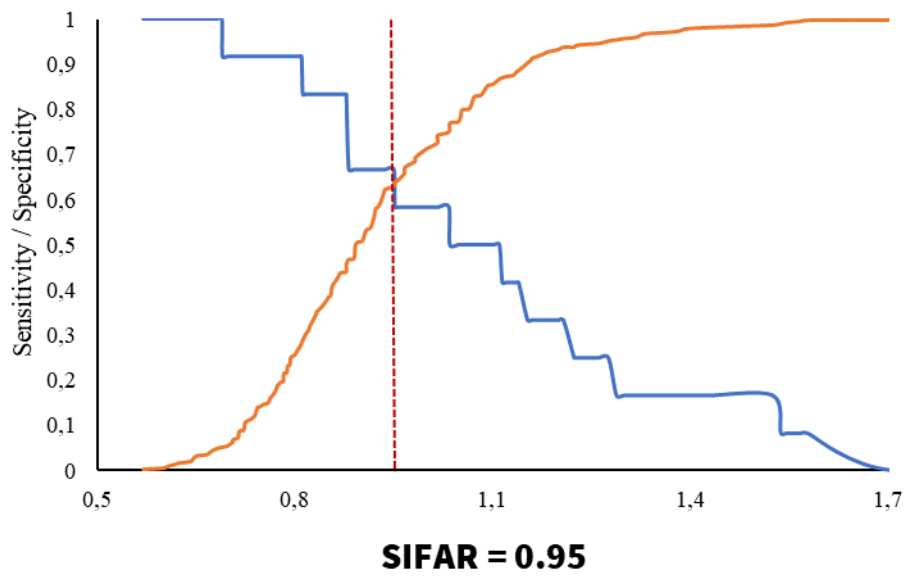
**SUPPLEMENTARY FILES****Supplementary figure 1**

Sensitivity/specificity curves for prediction of all vascular complications by SIFAR.



**Supplementary figure 2**

Sensitivity/specificity curves for prediction of major vascular complications by SIFAR.



**Supplementary table 1**

In-hospital outcomes for every three groups

	Vascular complications			p-value
	No VC n = 354	Minor VC n = 111	Major VC n = 14	
<b>Bleeding</b>				
Major/Life threatening	2 (0.6%)	0	6 (42.8%)	<b>0.001</b>
Minor	8 (2.3%)	50 (14.1%)	2 (14.3%)	<b>&lt;0.001</b>
Decrease haemoglobin (g/dL)	0.69 ± 0.87	0.91 ± 0.91	1.67 ± 1.07	<b>0.003</b>
Transfusion <sup>a</sup>	0.01 ± 0.2	0.06 ± 0.31	0.69 ± 1.2	<b>&lt;0.001</b>
<b>Stroke</b>				
Disabling	3 (0.8%)	1 (0.9%)	4 (28.6%)	<b>0.018</b>
Non-disabling	0	2 (1.8%)	1 (7.1%)	<b>0.003</b>
Acute Kidney Injury <sup>b</sup>	4 (1.12%)	1 (0.9%)	0	0.76
Myocardial infarction	3 (0.85%)	1 (0.9%)	3 (21.4%)	0.06
Delayed surgery	3 (0.85%)	9 (8.1%)	5 (35.7%)	<b>&lt;0.001</b>
<b>Length of hospital stay</b>				
ICU (days) <sup>c</sup>	0.9 ± 1.57	1.2 ± 1.89	2.8 ± 3.98	<b>0.013</b>
LOS (days) <sup>d</sup>	6.5 ± 3.8	6.8 ± 3.43	14.6 ± 8.21	<b>0.004</b>

<sup>a</sup> In number of units of packed cells transfused<sup>b</sup> Acute Kidney Injury stage 2 and 3 were included according to AKIN classification<sup>c</sup> Length of stay in the intensive care unit<sup>d</sup> Total length of hospital stay

p-values are for comparison in two groups: without VCs and with VCs.

Definitions of bleeding, stroke, acute kidney injury, myocardial infarction are according to VARC-2 definitions.