Effect of oral anticoagulation on clinical outcomes and haemodynamic variables after successful transcatheter aortic valve implantation

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Impact du traitement anticoagulant oral dans le devenir clinique et l'évolution des paramètres hémodynamique après un remplacement valvulaire aortique percutanée

Abbreviated title: Effect of antithrombotic treatment after TAVI

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Summary

Background. – The effect of oral anticoagulation on clinical and haemodynamic outcomes following successful transcatheter aortic valve implantation is unclear.

Aims. – To evaluate the effect of oral anticoagulation within the first year after transcatheter aortic valve implantation.

Methods. – All patients undergoing transcatheter aortic valve implantation in two French tertiary centres from 2010 to 2016 were included prospectively. The composite outcome of death, stroke, readmission for heart failure or major/life-threatening bleeding according to Valve Academic Research Consortium 2 criteria within 1 year was evaluated. Valvular haemodynamic deterioration was defined as mean transprosthetic gradient ≥ 20 mmHg or an increase of ≥ 10 mmHg during echocardiographic follow-up.

Results. – Of the 1139 patients included, 400 (35.1%) were discharged on oral anticoagulation. The primary endpoint was more frequent in the group with versus without oral anticoagulation (29.4% vs 17.3% 21.5%; hazard ratio 1.83, 95% confidence interval 1.42–2.35). Composite endpoint risk factors were chronic pulmonary and kidney diseases, previous atrial fibrillation, left ventricular ejection fraction ≤ 30% at discharge and no femoral vascular approach, but not oral anticoagulation prescription at discharge. Conversely, 58 patients were identified with valvular haemodynamic deterioration, including 11 (19%) in the group with oral anticoagulation and 47 (81%) in the group without oral anticoagulation. Valvular haemodynamic deterioration risk factors were absence of oral anticoagulation exposure, increased body mass index, use of a balloon-expandable bioprosthesis and use of a bioprosthesis with diameter ≤ 23 mm. Antithrombotic treatment crossover (i.e. oral anticoagulation interruption or introduction during follow-up) occurred in 9.6% of patients, and was a risk factor for death (adjusted hazard ratio 3.39, 95% confidence interval 1.63–7.07).

Conclusions. – Baseline characteristics, rather than oral anticoagulation prescription at discharge, were associated with adverse outcomes following successful transcatheter aortic valve implantation. Conversely, oral anticoagulation was associated with reduced valvular haemodynamic deterioration.

Résumé

Contexte. – L'impact du traitement anticoagulant oral (TAO) sur les paramètres cliniques et hémodynamiques après TAVI demeure incertain.

Objectifs. – Evaluer l'impact du TAO dans l'année suivant un TAVI.

Méthodes. – Tous les patients traités par TAVI dans deux centres français entre 2010 et 2016 furent prospectivement inclus. Le critère de jugement principal (CJP) était composé de la mortalité, accident vasculaire cérébrale, hospitalisation pour insuffisance cardiaque ou hémorragie sévères, défini selon les critères VARC-2. Une détérioration hémodynamique valvulaire prothétique (DHV) était définie par un gradient moyen transprothétique ≥ 20 mmHg ou par une majoration ≥ 10 mmHg durant le suivi échocardiographique.

Résultats. – Un TAO fut prescrit à 400 patients soit 35,1 % des 1139 patients inclus dans le registre. Le CJP est survenu plus fréquemment en cas de TAO post-TAVI qu'en son absence (29,4 % vs 17,3% % ; HR 1,83, IC à 95 % 1,42–2,35). Les facteurs de risque (FdR) du CJP étaient une pneumopathie chronique, une insuffisance rénale chronique, une fibrillation atriale, une FEVG ≤ 30 % après TAVI et un abord vasculaire extrafémoral. La prescription de TAO après un TAVI n'était pas un FdR indépendant du CJP. Une DHV fut relevée chez 58 patients, dont 11 (19 %) traités par TAO et 47 (81 %) non traités par TAO. Les FdR de DHV étaient l'absence de TAO après TAVI, un IMC augmenté, l'utilisation de bioprothèse expansible au ballon et un diamètre de bioprothèse ≤ 23 mm. Un crossover de TAO (défini comme un arrêt ou une initiation de TAO au cours du suivi) survenu chez 9,6 % des patients et était associé à la mortalité (HR ajusté 3,39, IC à 95 % 1,63–7,07).

Conclusions. – Les antécédents médicaux et non la prescription de TAO sont associés au devenir clinique après un TAVI. A l'inverse, la prescription de TAO est associée à une moindre survenue de DHV.

KEYWORDS

Transcatheter aortic valve implantation;

Valvular haemodynamic deterioration;

Oral anticoagulation therapy

MOTS CLÉS

Remplacement valvulaire aortique percutané ;

Détérioration hémodynamique valvulaire ;

Traitement anticoagulant oral.

Abbreviations: AF, atrial fibrillation; CI, confidence interval; NOAC, non-vitamin K antagonist oral anticoagulation; OAC, oral anticoagulation; TAVI, transcatheter aortic valve implantation; VHD, valvular haemodynamic deterioration.

Background

Transcatheter aortic valve implantation (TAVI) is a validated therapeutic alternative for patients with severe aortic valve stenosis who are at moderate-to-high risk of surgical aortic valve replacement (SAVR) [1]. The effect of antithrombotic strategy after TAVI on clinical outcome is unclear. The target population is frail and at high risk of both ischaemic and haemorrhagic complications [2, 3]. In the absence of an established indication for oral anticoagulation (OAC), lifelong aspirin and clopidogrel for 1–6 months is currently recommended [1, 4]. OAC alone is recommended when there is an underlying indication, such as atrial fibrillation (AF), and single antiplatelet therapy may be combined in case of recent coronary stenting or acute coronary syndrome. According to the American College of Cardiology/American Heart Association update on valvular heart disease, OAC may also be considered after TAVI when the bleeding risk is low [4]. Recent studies have focused mainly on the benefits of dual versus single antiplatelet therapy or OAC and antiplatelet therapy compared with OAC alone [5-7]. A consistent worse outcome in OAC-treated patients was demonstrated [8], but whether this was driven by AF (the major reason for OAC exposure) or OAC *per se* is unknown. In addition, the rising issue of valvular haemodynamic deterioration (VHD), defined according to mean transprosthetic gradient using transthoracic echocardiography (TTE) or reduced prosthetic leaflet motion on computed tomography scan [9-11], was not addressed in these studies. The main cause of VHD is subclinical valve thrombosis, which has been associated with an increased rate of transient ischaemic attack, and may be prevented or treated by OAC [12, 13].

The purpose of this retrospective analysis was to evaluate the effect of antithrombotic regimen on both clinical outcome and occurrence of VHD in all-comers after successful TAVI.

Methods

Study design

All patients enrolled in the nationwide FRANCE-TAVI or FRANCE-2 registries who were discharged alive after successful TAVI at Pitié-Salpêtrière and Nantes University Hospitals were considered. Decision for the intervention and vascular access were determined at each centre by the local heart team. Antithrombotic strategy after TAVI was left at the discretion of the physicians. Clinical follow-up at 1 year was performed by clinical interviews, and face-to-face meetings were entered in the

nationwide database. Each patient provided informed consent according to institutional standard practice.

Transthoracic echocardiogram evaluations were performed at hospital discharge (baseline) and during the first year of follow-up, and the mean transprosthetic gradient was determined after measurement of the peak transprosthetic flow velocity by continuous-wave Doppler imaging. Mean gradient from baseline to the last known measurement was used to define valve haemodynamic dysfunction.

Study objectives and endpoints

Our primary objective was to evaluate clinical outcome according to the antithrombotic regimen after TAVI. The primary composite endpoint was a composite of all-cause death, ischaemic stroke, hospitalization for worsening heart failure, or major or life-threatening bleeding at 1-year follow-up, defined according to the Valve Academic Research Consortium 2 criteria [14]. The second objective was to evaluate the effect of antithrombotic regimen after TAVI on the occurrence of VHD, defined as either a mean gradient ≥ 20 mmHg after discharge or an absolute increase of ≥ 10 mmHg for procedure on native valve and a mean gradient ≥ 40 mmHg and/or an absolute increase ≥ 20 mmHg in case of valve-in-valve procedure, 1 year after the TAVI procedure [9]. The third objective was to describe antithrombotic treatment crossover, defined as an interruption to or the introduction of OAC in patients initially discharged with or without OAC, and to evaluate its effect on death within 1 year of the index hospitalization.

Statistical analyses

Continuous variables are reported as means ± standard deviations or medians (interquartile ranges) and were compared using Student's *t* test or the Wilcoxon rank-sum test, as appropriate. Categorical variables are reported as numbers and percentages (percentages were calculated excluding missing data) and were compared using the χ^2 test or Fisher's exact test, as appropriate. Missing data were not handled. Time to clinical event (first event that occurred) after hospital discharge was analysed using the Kaplan-Meier method. Estimate rates at 1 year and their 95% confidence intervals (CIs) are presented. Patients without an event at 1 year or lost to follow-up were censored. Determinants of the primary clinical endpoint and of VHD were assessed using the Cox proportional hazards model and

the logistic regression model, respectively. The effect of antithrombotic treatment crossover on death was explored in a dedicated Cox proportional hazards model. Univariate analyses ($P < 0.2$) were first performed to select potential explanatory variables, which were then tested in the multivariable model (stepwise method). Of note, both OAC status at discharge and history of AF were entered in the multivariable models assessing the primary clinical endpoint and VHD; however, given its clinical relevance, OAC was included as a forced variable in the multivariable model evaluating determinants of the primary clinical endpoint. The results are interpreted in terms of adjusted hazard ratios or adjusted odd ratios with their associated 95% CIs. A P value < 0.05 was considered significant, unless otherwise specified. All statistical analyses were performed with SAS statistical software package, release 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

From February 2010 to December 2016, 1219 patients underwent TAVI at both centres; a total of 1139 (93%) were discharged alive after a successful procedure and were considered for the present analysis (Fig. 1). Complete 1-year follow-up was obtained for 1133 (99.5%) patients. Baseline characteristics of the study population (all-comers undergoing TAVI) are shown in Table 1. The Edwards SAPIEN™ (Edwards Lifesciences, Irvine, CA, USA) balloon-expandable prosthesis was used predominantly. One-third of the patients were discharged on OAC; these patients were older and had more frequent comorbidities (Table 1). Non-vitamin K antagonist oral anticoagulants (NOACs) were used in 50 (13%) patients in the OAC group. Procedural characteristics did not differ according to OAC status at discharge, but a balloon-expandable valve was used more frequently in patients with OAC than in those without OAC. Dual antiplatelet therapy was the predominant antiplatelet regimen among patients who did not receive OAC.

Outcomes and independent correlates of the primary endpoint

The primary endpoint at 1-year follow-up occurred in 21.5% (95% CI 19.3–24.1%) of the participants, with a twofold increase in patients discharged with OAC versus those discharged without OAC (Table 2 and Fig. 2). Death was of cardiovascular or unknown origin in 60.3% of cases. Death and major life-threatening bleeding were twice as likely among those discharged with versus without OAC (Figs.

A.1–A.4). A similar trend was observed for readmission for heart failure. No major or life-threatening bleeding occurred in patients treated with NOACs.

Independent correlates of the primary endpoint were chronic pulmonary disease, chronic kidney disease, history of AF, left ventricular ejection fraction ≤ 30% at hospital discharge, and non-femoral vascular approach (Fig. 3). Conversely, the association between OAC and the primary composite endpoint was no longer significant in the adjusted model.

Effect of antithrombotic treatment crossover

Analysis of antithrombotic regimens during follow-up was available in 939 (82.4%) patients, of whom 90 (9.6%) underwent treatment crossover. OAC was initiated or interrupted in 50 (5.3%) and 40 (4.3%) participants, respectively. Baseline and procedural characteristics according to treatment crossover are detailed in Table A.1. Antithrombotic treatment crossover was associated with more frequent adverse outcomes (Table A.2), and remained an independent risk factor for death after multivariable adjustment (adjusted hazard ratio 3.39, 95% CI 1.63–7.07; $P = 0.001$).

Independent correlates of VHD

Bioprosthetic gradient was available in 746 (66%) participants, 58 of whom were identified with VHD (8%; 95% CI 6–10%), including 11 (19%) patients discharged with OAC and 47 (81%) patients discharged without OAC. Baseline and procedural characteristics according to the availability of echocardiographic follow-up are detailed in Table A.3. The time delay from the TAVI procedure to the echocardiographic evaluation did not differ according to the presence or absence of VHD: 365 (180–416) and 338 (98–385) days, respectively ($P = 0.07$). Independent correlates of VHD were increased body mass index, use of a bioprosthesis with a diameter ≤ 23 mm, use of a balloon-expandable bioprosthesis and discharge without OAC (Fig. 4).

Discussion

The use of OAC after aortic valve replacement with a bioprosthesis for aortic stenosis remains a matter of debate given the frailty of the treated population and the lack of proven benefit when there is no other established indication for OAC. In the present analysis, we first demonstrated that patients discharged on OAC after successful TAVI have an increased rate of adverse outcomes. Second, the

use of OAC was not an independent correlate of worse outcome, as opposed to AF, the driving indication for OAC exposure. Of importance, antithrombotic treatment crossover during follow-up was an independent correlate of death, while the lack of OAC exposure was independently associated with the occurrence of VHD.

OAC is mainly prescribed to prevent AF-related thromboembolic complications in one-third of patients after TAVI [15, 16]. More patients ought to be treated with OAC, given the frequent occurrence of new-onset AF after TAVI, a condition associated with increased adverse events, including stroke or death [17, 18]. In addition, the native valve and the created neosinus represent prothrombotic niches where low shear stress blood flow may activate the coagulation pathway, promoting thrombus formation and potentially VHD [19]. Finally, OAC prevents subclinical leaflet thrombosis, especially when using a prosthesis with a diameter ≤ 23 mm, which has been associated with the occurrence of stroke/transient ischaemic attack [12, 13, 20]. Nonetheless, a recent large analysis from the FRANCE-TAVI registry found OAC exposure to be an independent risk factor for long-term death [8]. It is unclear whether this association reflects a detrimental effect of the drug exposure or the numerous comorbidities in this frail population. In this regard, the present study confirmed that patients' comorbidities, rather than the type of antithrombotic treatment at discharge, led to the risk of adverse events following TAVI.

Another interesting finding of the present study was the strong association between antithrombotic crossover (OAC interruption or introduction during follow-up) and death. In the frail TAVI population, the need for antithrombotic treatment crossover reflects poor outcome as a result of the occurrence of new-onset AF or ischaemic/haemorrhagic complications, or is motivated by a perceived high risk of complications by the treating physician. This finding emphasizes the need for a safer therapeutic alternative to vitamin K antagonists after TAVI, to reduce the need for OAC interruption during follow-up.

In the present analysis, the use of NOACs was low, but safe and consistent with previous pivotal trials demonstrating better safety for the preventive effect of NOACs versus vitamin K antagonists in patients with AF [21]. This finding is also aligned with early reports on the use of NOACs after TAVI [22, 23]. However, these data are exploratory, and the strategy of systematic OAC after TAVI using direct factor Xa inhibitors is currently being investigated in the ATLANTIS (NCT02664649), ENVISAGE-TAVI AF (NCT02943785) and the prematurely interrupted GALILEO trial [24, 25]. Trial

designs and dosing regimens differ in these trials according to exclusions or AF stratification and concomitant use of antiplatelet therapy. The primary endpoint definitions of these trials are similar, and comprise valve thrombosis.

The rate of VHD in our analysis was similar to that reported previously with echocardiography evaluation [26], but lower than the leaflet thrombosis reported with computed tomography scan evaluation [27, 28]. Our findings are also consistent with respect to the preventive effect of OAC use on the occurrence of VHD [12, 26, 29], but other potential determinants remain a matter of debate, such as the diameter of the bioprosthesis. We demonstrated an independent association between increased rate of VHD assessed by echocardiography and a bioprosthesis with a diameter ≤ 23 mm, whereas some computed tomography scan studies have reported that larger bioprostheses are associated with transcatheter heart valve thrombosis [11]. The type of bioprosthesis used is also under debate. We found self-expanding bioprostheses to be protective against VHD, a finding that is consistent with an increased rate of subclinical bioprosthesis thrombosis with balloon-expandable valves, using both transoesophageal echocardiography and computed tomography evaluation [20]. Sustained reduction in the mean aortic valve gradient with self-expanding TAVI compared with surgical aortic valve replacement at 3-year follow-up in the CoreValve US trial (CoreValve™; Medtronic Inc., Minneapolis, MN, USA) is another intriguing observation that supports our findings [30]. Many factors are key players in the occurrence of valve thrombosis, including the geometry of the deployed device and the implant depth [31]. In addition, supra-annular valves may allow improved haemodynamic conditions compared with intra-annular valves, and the creation of a supra-annular neosinus may reduce the thrombosis risk because of reduced flow stasis, a finding that is more frequent with the self-expanding valve [19, 32, 33]. These latter arguments should also be considered as potential confounders when assessing the effect of the antithrombotic regimen on the occurrence of VHD.

Study limitations

We acknowledge several limitations. Not all patients underwent echocardiographic evaluation at 1 year, which may have led to an underestimation of VHD. Moreover, patients with VHD did not undergo systematic transoesophageal echocardiography or computed tomography scan during follow-up. Therefore, a change in antithrombotic treatment strategy could not be evaluated, although crossover

was frequent. Echocardiography evaluation did not always coincide with the occurrence of adverse events, while the accurate timing of the antithrombotic treatment crossovers within 1 year were unknown; as a consequence, their clinical effect could not be evaluated. New-onset AF was not collected, and was not included in the multivariable model. The duration of antiplatelet prescription was not available. There was no central core laboratory for blinded evaluation of VHD, although this is representative of the real-life situation. Available follow-up was limited to 1 year, and late adverse outcomes were not evaluated. Finally, this was an observational study, and unaccounted cofounders may have persisted, despite the multivariable model. As a consequence, our results should be considered as hypothesis generating.

Conclusions

The use of OAC after TAVI is frequent and is associated with worse outcomes. However, 1-year clinical outcome was mainly driven by the patients' baseline characteristics, whereas the occurrence of VHD was driven by the procedure and the antithrombotic treatment after the procedure. Treatment crossover is another important independent correlate of survival. Randomized trials with different antithrombotic strategies are ongoing and should answer these challenging questions.

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Disclosure of interest

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Figure legends

Figure 1. Study flow chart. OAC: oral anticoagulation; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

Figure 2. Kaplan-Meier curves of survival free from death, stroke, hospitalization for heart failure, and major or life-threatening bleeding. OAC: oral anticoagulation.

Figure 3. Independent correlates of the primary composite endpoint. aHR: adjusted hazard ratio; CI: confidence interval; LVEF: left ventricular ejection fraction.

Figure 4. Independent correlates of valvular haemodynamic deterioration. aOR: adjusted odds ratio; CI: confidence interval; VHD: valvular haemodynamic deterioration.

Table 1 Baseline characteristics.

	Overall (*n* = 1139)	No OAC (*n* = 739)	OAC (n = 400)	*P*
Baseline characteristics				
Age (years)	82.4 ± 7.7	81.9 ± 8.1	83.2 ± 6.8	0.009
Male sex	594 (52.2)	381 (51.6)	213 (53.3)	0.59
Body mass index (kg/m²)	26.7 ± 5.4	26.6 ± 5.4	26.8 ± 5.5	0.4
Severe dyspnoea[a]	630 (55.3)	405 (54.8)	225 (56.3)	0.64
Angina pectoris[b]	154 (13.5)	114 (15.4)	40 (10.0)	0.01
EuroSCORE II	5.2 ± 4.5	4.9 ± 4.1	5.6 ± 5.0	0.054
STS score	4.3 ± 3.1	4.2 ± 3.0	4.4 ± 3.3	0.42
Previous non-CABG cardiac surgery	78 (6.8)	42 (5.7)	36 (9.0)	0.03
Coronary artery disease	512 (45.0)	347 (47.0)	165 (41.3)	0.065
Peripheral artery disease	309 (27.1)	201 (27.2)	108 (27.0)	0.94
Chronic pulmonary disease	224 (19.7)	137 (18.5)	87 (21.8)	0.19
Diabetes mellitus	304 (26.7)	198 (26.8)	106 (26.5)	0.92
Insulin-dependent diabetes	101 (8.9)	76 (10.3)	25 (6.3)	0.02
Systemic hypertension (*n* = 1133)	894 (78.9)	589 (80.2)	305 (76.4)	0.13

Chronic kidney disease	617 (54.2)	382 (51.7)	235 (58.8)	0.02
History of AF	422 (37.1)	93 (12.6)	329 (82.3)	< 0.001
CHA_2DS_2-VASC score	4.0 ± 1.3	3.9 ± 1.3	4.1 ± 1.3	0.035
HAS-BLED score	2.9 ± 1.0	2.8 ± 1.0	2.9 ± 1.0	0.07
Baseline echocardiogram characteristics				
LVEF (%)	54.8 ± 12.4	55.1 ± 12.4	54 ± 12.3	0.14
LVEF ≤ 30%	58 (5.1)	37 (5.0)	21 (5.3)	0.86
Mean aortic gradient (mmHg) (*n* = 1108)	48.6 ± 16.2	50.1 ± 16.3	45.8 ± 15.5	< 0.001
Aortic regurgitation (*n* =1089)	693 (63.6)	460 (65.5)	233 (60.2)	0.08
Pulmonary arterial pressure > 30 mmHg (*n* = 1031)	550 (53.3)	310 (47.4)	240 (63.7)	< 0.001
Procedural characteristics				
PCI before TAVR	156 (13.7)	115 (15.6)	41 (10.3)	0.01
Vascular approach				0.44
Transfemoral approach	939 (82.4)	602 (81.5)	337 (84.3)	
Transapical approach	68 (6.0)	45 (6.1)	23 (5.8)	
Other approach	132 (11.6)	92 (12.4)	40 (10.0)	
Prosthesis type				0.051
Edwards SAPIEN	691 (60.7)	433 (58.6)	258 (64.5)	
CoreValve	448 (39.3)	306 (41.4)	142 (35.5)	

Valve-in-valve procedure (*n* = 1138)	54 (4.7)	35 (4.7)	19 (4.8)	0.99
Prosthesis diameter > 23 mm	903 (79.3)	584 (79.1)	319 (79.8)	0.81
Hospital discharge				
Echocardiogram characteristics				
LVEF (%)	55.4 ± 10.5	55.8 ± 10.4	54.5 ± 10.6	0.047
LVEF ≤ 30%	46 (4.0)	29 (3.9)	17 (4.3)	0.79
Mean gradient (mmHg) (*n* = 1065)	10.6 ± 5.4	10.9 ± 5.6	10 ± 5	0.009
Severe aortic regurgitation (*n* = 1105)	7 (0.6)	4 (0.6)	3 (0.8)	0.7
Antiplatelet therapy at discharge				< 0.001
Single antiplatelet therapy	389 (34.2)	264 (35.7)	125 (31.3)	
Dual antiplatelet therapy	488 (42.8)	464 (62.8)	24 (6.0)	
None	262 (23.0)	11 (1.5)	251 (62.8)	

Data are expressed as mean ± standard deviation or number (%). AF: atrial fibrillation; CABG: coronary artery bypass graft; CHA_2DS_2-VASC: Congestive heart failure, Hypertension, Age ≥ 75 years (Doubled), Diabetes, Stroke/transient ischaemic attack/thromboembolism (Doubled) – Vascular disease, Age 65–74 years and Sex category (Female); HAS-BLED: Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile international normalized ratio, Elderly and Drugs/alcohol; LVEF: left ventricular ejection fraction; OAC: oral anticoagulant; PCI: percutaneous coronary intervention; STS: Society of Thoracic Surgeons; TAVR: transcatheter aortic valve implantation.

[a] Class III or IV according to the New York Heart Association.

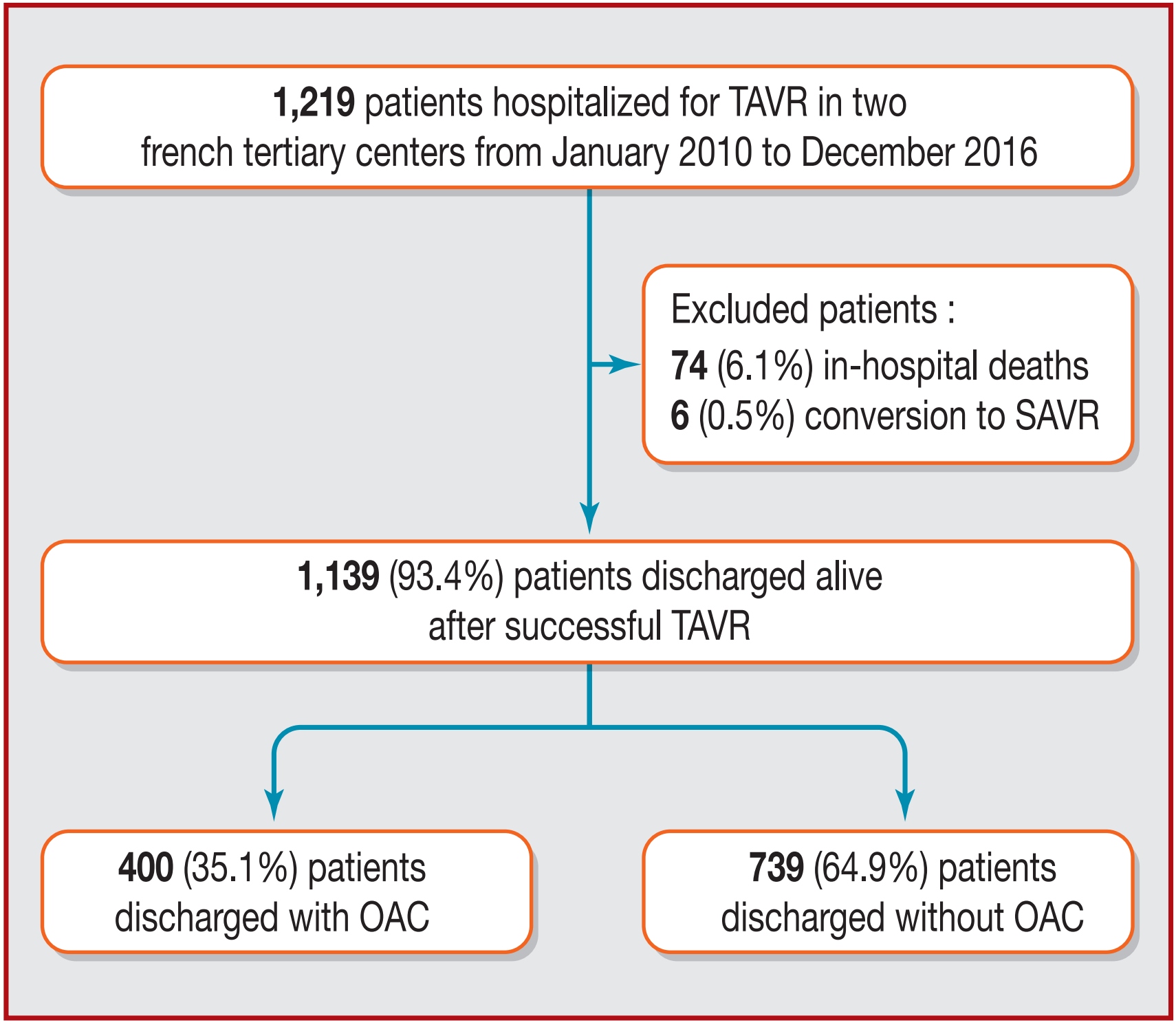
[b] Class II or above according to the Canadian Cardiovascular Society score.

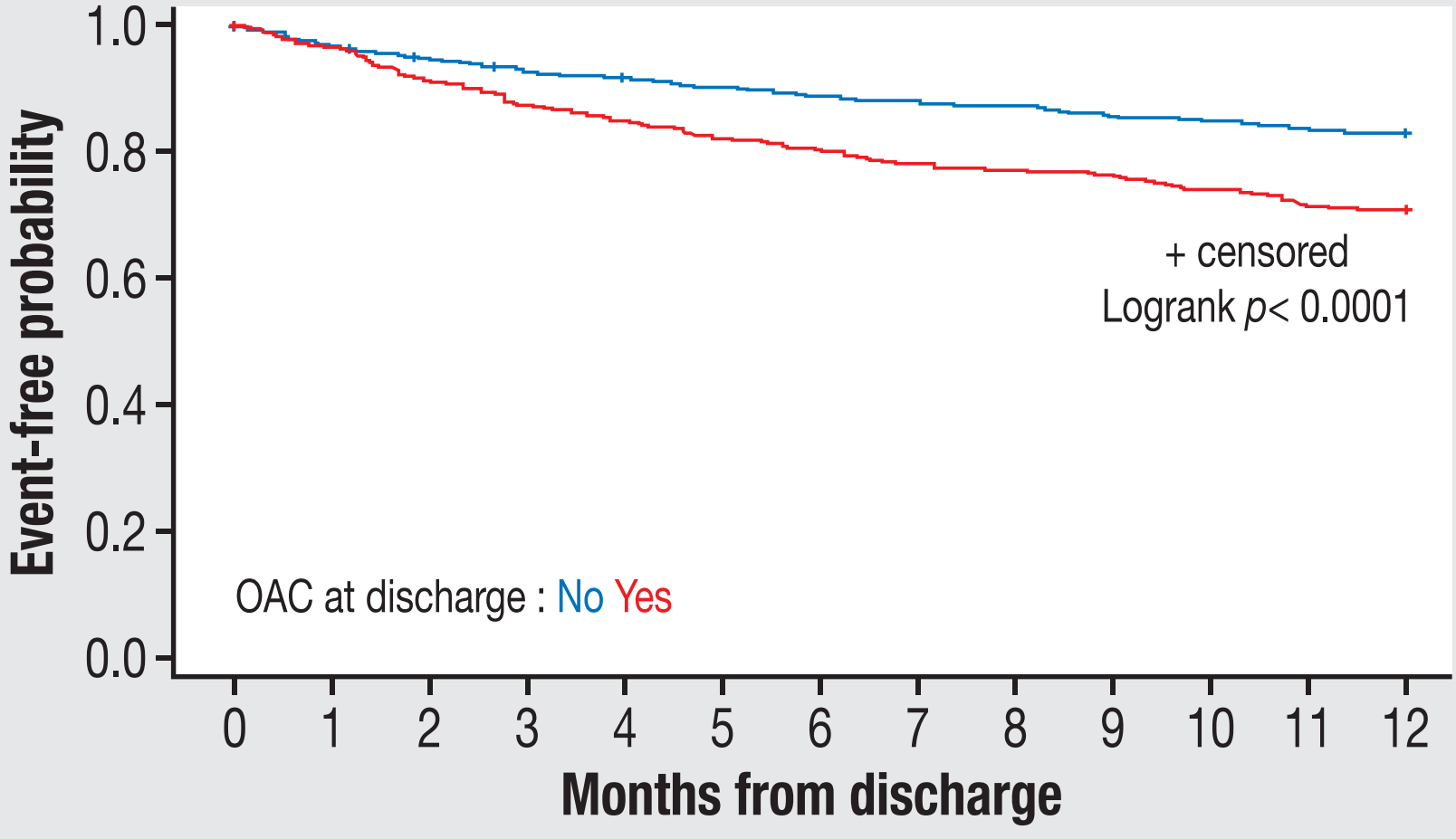
Table 2 One-year clinical outcomes according to antithrombotic treatment at discharge.

Clinical outcome	Overall (n = 1139)	OAC at discharge (n = 400; 35.1%)	No OAC at discharge (n = 739; 64.9%)	HR (95% CI)	P
Death, stroke, hospitalization for heart failure and severe bleeding	21.5 (19.3–24.1)	29.4 (25.2–34.1)	17.3 (14.7–20.2)	1.83 (1.42–2.35)	< 0.001
Death	12.9 (11.0–15.0)	18.8 (15.3–23.0)	9.6 (7.7–12.0)	2.07 (1.49–2.87)	< 0.001
Stroke[a]	1.6 (1.0–2.6)	2.0 (0.9–4.1)	1.4 (0.8–2.6)	1.35 (0.51–3.55)	0.54
Hospitalization for heart failure[a]	9.2 (7.6–11.1)	12.4 (9.4–16.2)	7.5 (5.8–9.7)	1.70 (1.14–2.52)	0.008
Major or life-threatening bleeding[a]	3.7 (2.7–5.0)	5.3 (3.4–8.1)	2.8 (1.8–4.3)	1.9 (1.02–3.5)	0.041

Data are expressed as Kaplan-Meier estimate (95% CI). CI: confidence interval; HR: hazard ratio OAC: oral anticoagulation.

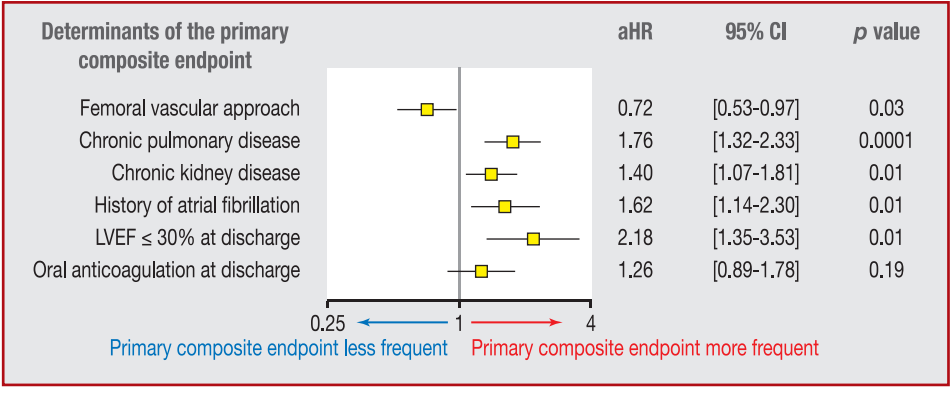
[a] Patients who died without an event were censored at the date of death.


1,219 patients hospitalized for TAVR in two french tertiary centers from January 2010 to December 2016
Excluded patients :
74 (6.1%) in-hospital deaths
6 (0.5%) conversion to SAVR
1,139 (93.4%) patients discharged alive after successful TAVR
400 (35.1%) patients discharged with OAC
739 (64.9%) patients discharged without OAC



At-risk patients

No	739	710	692	676	669	657	648	641	636	624	619	610	603
Yes	400	384	363	348	338	327	320	311	307	304	295	284	281


Determinants of the primary composite endpoint
aHR
95% CI
p value
Femoral vascular approach
0.72
[0.53-0.97]
0.03
Chronic pulmonary disease
1.76
[1.32-2.33]
0.0001
Chronic kidney disease
1.40
[1.07-1.81]
0.01
History of atrial fibrillation
1.62
[1.14-2.30]
0.01
LVEF ≤ 30% at discharge
2.18
[1.35-3.53]
0.01
Oral anticoagulation at discharge
1.26
[0.89-1.78]
0.19
0.25
1
4
Primary composite endpoint less frequent
Primary composite endpoint more frequent

Determinants of valvular hemodynamic deterioration	aOR	95% CI	*p* value
Increased body mass index	1.12	[1.07-1.17]	< 0.0001
Valve diameter ≤ 23mm	3.10	[1.75-5.39]	< 0.0001
Self-expanding bioprosthesis	0.42	[0.21-0.85]	0.016
Oral anticoagulation at discharge	0.33	[0.17-0.65]	0.0014