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# **Oral anticoagulation continuation throughout transcatheter aortic valve replacement: high risk-high reward or marginal gains?**

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Within the past decade, the performance of transcatheter aortic valve replacement (TAVR) swiftly evolved towards a streamlined and straightforward procedure with predictable outcomes. Major complications, which would have jeopardized the worldwide adoption of the technique such as surgical conversion, annulus rupture, device embolization or coronary obstruction, were quickly circumvented, and can now be anticipated, thus being seldom encountered in clinical practice (1). Increased operator experience, continuous decline in TAVR candidate risk profile, device iterations, and increasing availability of several differing transcatheter heart valves designs allowed TAVR operators greater choice in selecting “the right valve for the right patient” to optimize both procedural safety and longer-term durability. Nonetheless, vascular complications still routinely ensue in up to 20% of cases according to recent reports (2,3). Albeit rarely of major importance, these complications may in turn lead to clinically relevant bleeding, which negatively affects short-term survival, especially among patients requiring oral anticoagulants (OAC), which account for 25-45% of TAVR candidates (1,4). Therefore, in the current setting of an optimized TAVR approach aiming at minimizing procedural burden and promoting early recovery (5), the perioperative management of OAC is a relevant issue. Of particular interest is the continuation of OAC throughout the procedure, which has already been the focus of small sample size studies suggesting its potential safety (6,7).

Building upon those reports, in this issue of *JACC: Cardiovascular Interventions*, Brinkert et al. performed the largest analysis to date comparing the safety and efficacy of OAC continuation vs. interruption throughout transfemoral TAVR procedures (8). Among 4459 patients treated at 5 European centers from 2011 to 2019, 1317 (median age: 82 years, 51% women) on OAC were included in this retrospective study. A total of 584 and 733 patients underwent TAVR with continuation and interruption of OAC, respectively. Atrial fibrillation (AF) was the indication of OAC in 95% of patients. Direct-acting oral anticoagulants (DOAC)

were more often prescribed in the continuation group (50% vs. 30%,  $p < 0.001$ ). Following adjustment on pre-specified covariates (age, body mass index, previous stroke, peripheral arterial disease, and center), 30-day major or life-threatening bleeding, the primary outcome of the present study, were not significantly different between groups (odds-ratio [OR]: 0.86, 95% confidence interval [CI]: 0.61-1.21;  $p = 0.39$ ). Secondary outcomes included the 30-day rate of major vascular complications, stroke, and mortality, which were comparable between the continuation and interruption groups. Furthermore, need for red blood cell transfusion was significantly lower in the continuation group. Results were consistent in multiple sensitivity analyses. In one particular sensitivity analysis further adjusting for TAVR date, device success, pre-TAVR antiplatelet therapy, minimal artery diameter, sheath size, and closure device, the OR for the primary outcome was 1.01 (95%CI: 0.67-1.53,  $p = 0.95$ ). The authors concluded that based on these results OAC continuation throughout transfemoral TAVR appears safe and effective.

Although these data appear sound (whilst harboring the known limitations of a retrospective design), a deeper dive into the analysis is required to better place the results in clinical context. First, can we be confident that these results represent the true treatment effect of OAC continuation? Only prospective randomized trials can properly inform the medical community regarding the efficacy and safety of a particular treatment or a strategy. Approximately 80% of patients in the continuation group were included after 2015 compared with 65% of their interruption group counterparts. A trend towards increased inclusion in the continuation group over time was observed in most centers and was even more pronounced in the center accounting for 45% of the study population. Consequently, these patients likely represented lower risk TAVR recipients benefiting from the numerous factors, which contributed to improved TAVR outcomes during the last decade, representing just as many confounders impossible to adequately adjust for. Aside from possible procedural-related

confounders, it should also be highlighted, that over the study period, OAC prescription vastly evolved with an increasing proportion of patients receiving DOAC, three of which, apixaban, edoxaban, and dabigatran at the 110mg bid regimen, contributing towards a significant reduction in major bleeding compared with warfarin (9). Patients in the continuation group were more likely DOACs.

Another question arising from the study concerns OAC management. Do the interruption and continuation strategies truly represent what we expect from these designations? Patients treated with vitamin K antagonists (VKA) either continued their treatment with a targeted INR the day of the procedure in the therapeutic range depending on VKA indication or stopped their medication 2-4 days before the procedure with or without heparin bridging at the operator's discretion. Among patients treated with a DOAC, treatment was either omitted the morning of the procedure or stopped 2-4 days before TAVR. OAC was restarted 24-48h after TAVR regardless of the type of OAC. The proportion of patients who were bridged with heparin in the interruption group reached 66%, actually representing 90% of VKA-treated patients in this group. Therefore, two-thirds of the interruption group did not adequately represent patients who genuinely interrupted their anticoagulant treatment, who were subjected to a higher risk of major periprocedural bleeding (10). The Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery (BRIDGE) randomized trial demonstrated heparin bridging in AF patients interrupting OAC for a planned invasive procedure resulted in an increased 30-day major bleeding rate without benefit on systemic thromboembolism compared with no bridging (10). Regarding patients on DOACs, who accounted for 40% of the study population, the safety of a 24-48h interruption before and after an invasive procedure has already been demonstrated in the prospective Perioperative Anticoagulation Use for Surgery Evaluation (PAUSE) cohort with almost 99% of patients showing minimal residual levels of anticoagulants prior to high

bleeding risk procedures (11). In the study by Brinkert et al., the continuation strategy allowed for a 12 to 24h withdrawal of the OAC treatment before TAVR, treatment being restarted 24-48h afterwards. As such, it represents a short “PAUSE-like” interruption rather than a true continuation. For some patients with a once daily DOAC, this practice is essentially aligned with European guidelines prior to low-risk procedures (12). These guidelines even allow for a “true” OAC continuation with the performance of procedures “without an important bleeding risk and/or allowing adequate local haemostasis” 12-24h after the last OAC intake, and recommend restarting OAC 6-8h after complete hemostasis. Current TAVR procedures in contemporary candidates may well fall within this category with rates of major vascular complications and life-threatening/major bleeding below 5% (13,14). Therefore, future studies evaluating this strategy are required to accurately assess the safety and efficacy of OAC continuation throughout a TAVR procedure.

Overall, the potential benefit of OAC continuation remains elusive (**Figure**) as, in addition to the previous limitations, the exact role of some factors mitigating the peri-procedural risk of bleeding and thromboembolic events could not be adequately assessed in the present study. Cerebral embolic protection devices were used in a minority of patients. Protamine administration at the end of the procedure was also limited although it may be associated with a reduced rate of major bleeding without increasing the risk of stroke or myocardial infarction (15). As the optimal antithrombotic treatment in TAVR recipients continues to be debated, a potential major advantage of OAC continuation may be a reduction in peri-procedural stroke/systemic embolism events related to early valve thrombosis or aortic plaque disruption. Nonetheless, this hypothesis warrants further research. On the contrary, stopping OAC before TAVR may be an opportunity for clinicians to easily switch AF patients from VKA to the safer DOACs. In conclusion, even if the robustness of the data presented by Brinkert et al. falls short of convincing us that OAC continuation is safe and effective throughout TAVR, the data

nevertheless are important and hypothesis generating. Their merit perhaps are to remind us that TAVR is continuously evolving, and that we need to question and challenge our old habits and strive to design meaningful clinical trials to benefit patients.

## References

1. Auffret V., Lefèvre T., Van Belle E., et al. Temporal Trends in Transcatheter Aortic Valve Replacement in France: FRANCE 2 to FRANCE TAVI. *J Am Coll Cardiol* 2017;70:42–55.
2. Batchelor W., Patel K., Hurt J., et al. Incidence, prognosis and predictors of major vascular complications and percutaneous closure device failure following contemporary percutaneous transfemoral transcatheter aortic valve replacement. *Cardiovasc Revasc Med* 2020. Doi: 10.1016/j.carrev.2020.01.007.
3. Ruge H., Burri M., Erlebach M., Lange R. Access site related vascular complications with third generation transcatheter heart valve systems. *Catheter Cardiovasc Interv* 2020. Doi: 10.1002/ccd.29095.
4. Lothar A., Kaier K., Ahrens I., et al. Bleeding Complications Drive In-Hospital Mortality of Patients with Atrial Fibrillation after Transcatheter Aortic Valve Replacement. *Thromb Haemost* 2020. Doi: 10.1055/s-0040-1715833.
5. Ichibori Y., Puri R., Taramasso M., et al. An optimized approach for transfemoral transcatheter aortic valve implantation: A comprehensive review and current evidence. *Cardiovasc Revasc Med* 2020. Doi: 10.1016/j.carrev.2019.12.032.
6. Brinkert M., Keller LS., Moriyama N., et al. Safety and Efficacy of Transcatheter Aortic Valve Replacement With Continuation of Oral Anticoagulation. *J Am Coll Cardiol* 2019;73:2004–5
7. Mangner N., Crusius L., Haussig S., et al. Continued Versus Interrupted Oral Anticoagulation During Transfemoral Transcatheter Aortic Valve Implantation and Impact

- of Postoperative Anticoagulant Management on Outcome in Patients With Atrial Fibrillation. *Am J Cardiol* 2019;123:1134–41.
8. Brinkert M., Mangner N., Moriyama N., et al. Safety and Efficacy of Transcatheter Aortic Valve Replacement with Continuation of Vitamin K Antagonists or Direct Oral Anticoagulants. *JACC Cardiovasc Interv* 2020.
  9. Ruff CT., Giugliano RP., Braunwald E., et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;383:955–62.
  10. Douketis JD., Spyropoulos AC., Kaatz S., et al. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. *N Engl J Med* 2015;373:823–33.
  11. Douketis JD., Spyropoulos AC., Duncan J., et al. Perioperative Management of Patients With Atrial Fibrillation Receiving a Direct Oral Anticoagulant. *JAMA Intern Med* 2019;179:1469-1478.
  12. Steffel J., Verhamme P., Potpara TS., et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J* 2018;39:1330–93.
  13. Mack MJ., Leon MB., Thourani VH., et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med* 2019; 380:1695-1705..
  14. Popma JJ., Deeb GM., Yakubov SJ., et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *N Engl J Med* 2019; 380:1706-1715.
  15. Al-Kassou B., Kandt J., Lohde L., et al. Safety and Efficacy of Protamine Administration for Prevention of Bleeding Complications in Patients Undergoing TAVR. *JACC Cardiovasc Interv* 2020;13:1471–80.

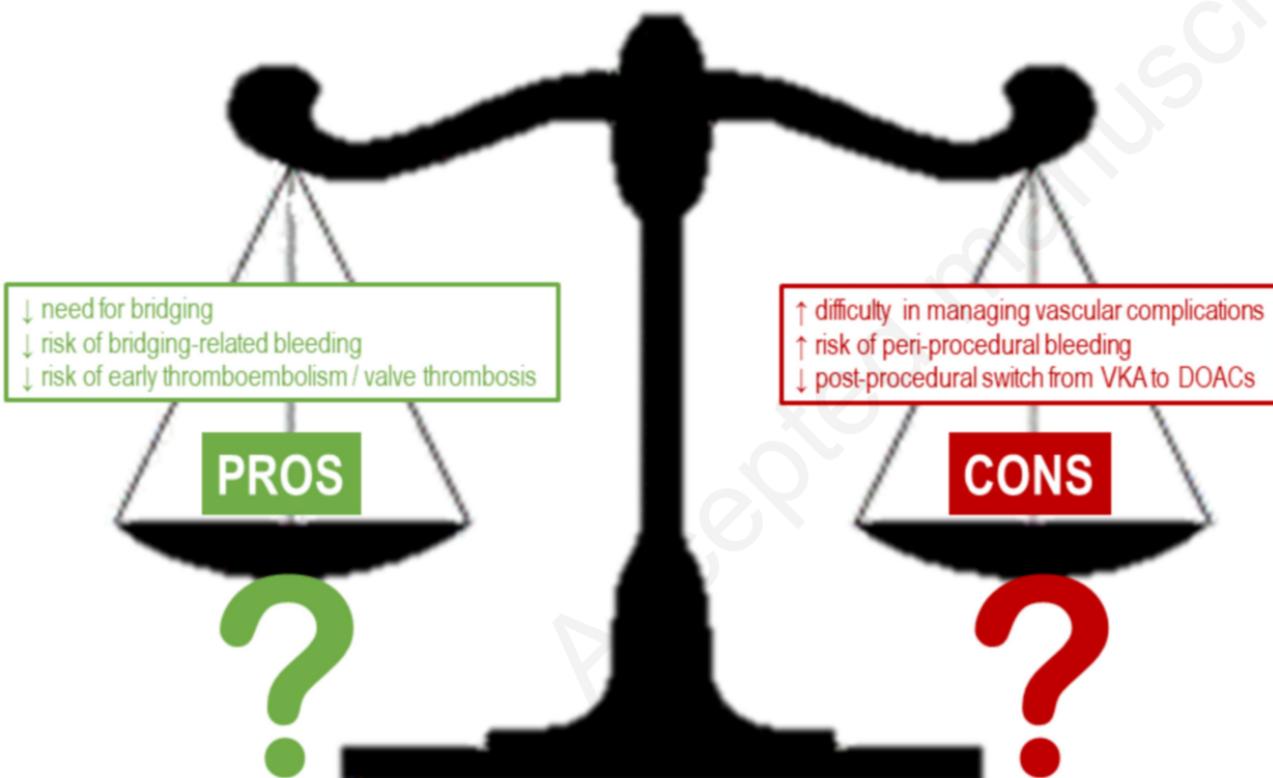
**Figure legend – Potential risks and benefits associated with OAC continuation throughout transfemoral transcatheter aortic valve replacement**

\* denotes a statistically significant difference between groups.

DOAC: Direct acting oral anticoagulant; OAC: oral anticoagulant; TAVR: transcatheter aortic valve replacement; VKA: Vitamin K antagonist

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# Balancing the risks and benefits of OAC continuation throughout transfemoral TAVR



Brinkert et al. JACC Cardiovasc Interv 2020

OAC continuation	Variable/ 30-day outcomes	OAC interruption
584	Patients	733
-	Heparin bridging	66%
11.3%	Major or life-threatening bleeding	14.3%
11.0%	Major vascular complications	12.3%
13.7%	Need for transfusion*	17.7%
2.9%	Cerebrovascular events	5.2%
2.4%	Mortality	2.9%