or surgery, and 30-day HF readmissions did not differ among the 4 groups.

In this observational analysis, we evaluated the association of BMI with clinical outcomes in patients who underwent treatment for MR with TMVr. Our findings indicate that BMI does not significantly influence rates of in-hospital mortality, stroke/transient ischemic attack, AMI, pericardial effusion/tamponade requiring treatment, and 30-day HF readmissions. Patients with BMI < 20 kg/m^2 were more likely to develop AKI and those with BMI ≥ 25.0 to 29.9 kg/m^2 had higher rates of bleeding/transfusion.

In a previous study from the German TRAnscatheter Mitral valve Interventions registry of 799 patients, in-hospital mortality did not differ across the 4 BMI caregories.[6] Further, patients with BMI < 20 kg/m^2 had higher rates of postprocedure bleeding/transfusion and increased mortality at a median follow-up of 1 year. There is mounting evidence that frailty is associated with increased morbidity and mortality after cardiac surgery and percutaneous cardiac interventional procedures. Hence, BMI < 20 kg/m^2 is considered as an important marker of frailty according to the Valve Academic Research Consortium 2 criteria.[7] In our study, rates of AKI were higher in patients with BMI < 20 kg/m^2, but no significant difference was found for other outcomes.

This study is limited by database, which lacks information on laboratory variables, medications used, procedural details/success, and etiology of MR (degenerative vs functional) which may have affected outcomes. In addition, the NRD lacks long-term follow-up.

In conclusion, our study showed no significant association of BMI with short term outcomes in patients who underwent TMVr. Further studies are needed to determine long-term influence of BMI on outcomes of TMVr.

Disclosures

The authors have no conflicts of interest to disclose.

Acknowledgments

None.

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17 August 2020
27 August 2020

1. Sharma A, Lavie CJ, Elmariah S, Borer JS, Sharma SK, Vemulapalli S, Yerokun BA, Li Z, Matsouaka RA, Marmur JD. Relationship of body mass index with outcomes after transcatheter aortic valve replacement: results from the National Cardiovascular Data-STS/ACC TVT Registry. *Mayo Clin Proc.* 2020;95:57–68.
2. Johnson AP, Parlow JL, Whitehead M, Xu J, Rohland S, Milne B. Body mass index, outcomes, and mortality following cardiac surgery in Ontario, Canada. *J Am Heart Assoc* 2015;4:e002140.
3. Rapetto F, Bruno VD, King M, Benedetto U, Caputo M, Angelini GD, Ascione R, Ciulli F, Vohra HA. Impact of body mass index on outcomes following mitral surgery: does an obesity paradox exist? *Interact Cardiovasc Thorac Surg* 2018;26:590–595.
4. Anon. NRD Overview. Available at: https://www.hcup-us.ahrq.gov/nrdoverview.jsp. Accessed August 17, 2020.
5. Quan H, Li B, Duncan Saunders L, Parsons GA, Nilsson CI, Alibhai A, Ghali WA. Assessing validity of ICD-9-CM and ICD-10 administrative data in recording clinical conditions in a unique dually coded database. *Health Serv Res* 2008;43:1424–1441.
6. Kalbacher D, Tigges E, Boekstegers P, Puls M, Plicht B, Eggebrecht H, Nickenig G, von Bardeleben RS, Zuern CS, Franke J, Sievert H, Ouarrak T, Senges J, Lubos E. Underweight is associated with inferior short and long-term outcomes after MitraClip implantation: Results from the German TRAnscatheter mitral valve interventions (TRAMI) registry. *Am Heart J* 2020;222:73–82.
7. Stone GW, Adams DH, Abraham WT, Kappetein AP, Généreux P, Vranckx P, Mehran R, Kuck K-H, Leon MB, Piazza N, Head SJ, Filippatos G, Vahanian AS, Mitral Valve Academic Research Consortium (MVARC). Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: Part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. *J Am Coll Cardiol.* 2015;66:308–321.

https://doi.org/10.1016/j.amjcard.2020.09.001

Network Meta-Analysis Comparing Apixaban Versus Rivaroxaban in Morbidly Obese Patients With Atrial Fibrillation

The efficacy and safety of DOACs in morbidly obese patients have been well investigated over the last few years.[1–4] Our recent meta-analysis showed that the Direct oral anticoagulants (DOAC) group did not increase stroke or systemic embolism (SE) event rate compared with the warfarin group and the DOAC use was significantly associated with a lower major bleeding event rate compared with the warfarin group.[5] However, it is still unknown which DOAC is more appropriate than others. Apixaban and rivaroxaban are the 2 most common DOACs prescribed in the United States but there is no guidance on which agent should be selected in morbidly obese patients with AF.[6] Traditional meta-analyses cannot be used this time because no study directly compared apixaban with rivaroxaban. In addition, it is not feasible to conduct clinical studies directly comparing DOACs in real-world setting. Thus, we conducted a network meta-analysis (NMA) to indirectly compare apixaban and rivaroxaban and address which direct oral anticoagulant should be used.

Cochrane Library, Embase, Google Scholar, MEDLINE, and Web of Science database searches for relevant articles through December 23, 2019 were performed. The keywords used were (rivaroxaban OR apixaban OR warfarin) AND (obese OR obesity). The study selection was independently performed by 2 investigators (KK and MH) based on the pre-specified inclusion and exclusion criteria. This NMA included studies if patients are aged >18 years old with BMI >40 kg/m^2 or weight >120 kg receiving apixaban, or rivaroxaban who are diagnosed as AF. The NMA excluded studies if they included pregnant, dialysis or mechanical heart valve recipients. Case series, case-control studies and non-English articles were excluded. Conference abstracts were also excluded because Enough data were not provided for study quality assessment.

Two investigators independently extracted the following data from the

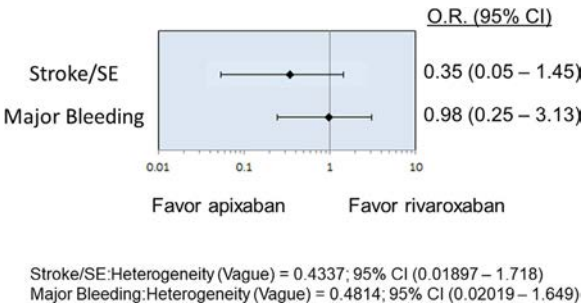

Figure 1. Forest plots of enrolled studies for the stroke or systemic embolism and major bleeding event rate in morbidly obese patients receiving apixaban, rivaroxaban or warfarin. Forest plot shows relative effect of each drug. Diamond is the summary estimate from the pooled studies. 95%. CI = credible interval; SE = systemic embolism.

included studies: baseline characteristics, follow-up period, and efficacy and safety outcome results, number of included patients, and study design. Primary efficacy outcome is the composite outcome of stroke or SE and primary safety outcome is the major bleeding event rate.

Odds ratios (OR) and 95% credible interval (CI) were calculated for stroke or SE as a primary efficacy outcome and major bleeding as a primary safety outcome using Microsoft-Excel-based network meta-analysis software (NetMetaXL).[7] Our NMA applied the random effects models because we assumed that the included studies would have a variety of effect sizes due to heterogenous populations included in the studies and random effects models fit the data better than fixed effects model. Bayesian network meta-analysis was described with 95% CI. The NMA followed Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.[8]

Five retrospective studies were included for our NMA.[1–3,9,10] The flow diagram and details in literature search results have been published elsewhere.[5] Key baseline characteristics and quality assessment results of the included studies have been reported previously.[5] In brief, four studies were retrospective cohort studies and one study was a post-hoc study of the randomized controlled trial. The network plot showed that similar number of studies compared between the apixaban (3 studies for both efficacy and safety outcomes) or rivaroxaban (4 studies for efficacy outcome and 3 studies for safety outcome) and warfarin groups but more subjects in the warfarin group (n = 4,311 for efficacy outcome and 4,281 for safety outcome) were included more than the rivaroxaban group (n = 3,799 for efficacy outcome and 3,762 for safety outcome) than apixaban group (n = 602 for efficacy and safety outcomes).

There was no statistically significant difference in stroke or SE event rate between the apixaban and rivaroxaban groups (OR 0.35; 95% CI 0.05, 1.45; Figure 1). Four studies reported the major bleeding event rate and were included for this NMA. There was no significant difference in major bleeding event rate between apixaban and rivaroxaban groups (OR 0.98; 95% CI 0.25, 3.13; Figure 1).

To our knowledge, this is the first NMA study comparing apixaban with rivaroxaban in morbidly obese patients with AF. Our NMA showed there was no significant difference in both the event rates of stroke or SE and major bleeding between the apixaban and rivaroxaban groups with atrial fibrillation. It is reasonable to consider either apixaban or rivaroxaban in morbidly obese patients with AF. A randomized controlled trial directly comparing apixaban with rivaroxaban is needed to confirm our NMA results in morbidly obese patients with AF.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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22 August 2020

1. Kido K, Ngorsuraches S. Comparing the efficacy and safety of direct oral anticoagulants with warfarin in the morbidly obese population with atrial fibrillation. *Ann Pharmacother* 2019;53:165–170.
2. Peterson ED, Ashton V, Chen YW, Wu B, Spyropoulos AC. Comparative effectiveness, safety, and costs of rivaroxaban and warfarin among morbidly obese patients with atrial fibrillation. *Am Heart J* 2019; 212:113–119.
3. Kushnir M, Choi Y, Eisenberg R, Rao D, Tolu S, Gao J, Mowrey W, Billett HH. Efficacy and safety of direct oral factor Xa inhibitors compared with warfarin in patients with morbid obesity: a single-centre, retrospective analysis of chart data. *Lancet Haematol* 2019; 6:e359–e365.
4. Spyropoulos AC, Ashton V, Chen Y-W, Wu B, Peterson ED. Comparative effectiveness, safety, and costs of rivaroxaban and warfarin treatment among morbidly obese patients with venous thromboembolism. *Blood* 2018; 132:2537.
5. Kido K, Shimizu M, Shiga T, Hashiguchi M. Meta-analysis comparing direct oral anticoagulants versus warfarin in morbidly obese patients with atrial fibrillation. *Am J Cardiol* 2020;126:23–28.
6. Barnes GD, Lucas E, Alexander GC, Goldberger ZD. National trends in ambulatory oral anticoagulant use. *Am J Med* 2015; 128:1300–1305. e2.
7. Brown S, Hutton B, Clifford T, Coyle D, Grima D, Wells G, Cameron C. A microsoft-excel-based tool for running and critically appraising network meta-analyses—an overview and application of NetMetaXL. *Syst Rev* 2014;3:110.
8. Moher D, Liberati A, Tetzlaff J, Altman DG. The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLOS Med* 2009;6:e1000097.
9. Hohnloser SH, Fudim M, Alexander JH, Wojdyla DM, Ezekowitz JA, Hanna M, Atar D, Hijazi Z, Bahit MC, Al-Khatib SM, Lopez-Sendon JL, Wallentin L, Granger CB, Lopes RD. Efficacy and safety of apixaban versus warfarin in patients with atrial fibrillation and extremes in body weight: insights from the ARISTOTLE trial. *Circulation* 2019;139:2292–2300.
10. Perales IJ, San Agustin K, DeAngelo J, Campbell AM. Rivaroxaban versus warfarin for stroke prevention and venous thromboembolism treatment in extreme obesity and high body weight. *Ann Pharmacother* 2019. 1060028019886092.

https://doi.org/10.1016/j.amjcard.2020.09.003