comorbidities was significantly higher in the HFpEF group. On propensity score matching + multivariate logistic regression, HFpEF group had higher VT odds (2.1% vs 1.9%; OR, 1.06; 95% CI, 1.03 to .10; p <0.001) and higher length of stay (6.41% vs 5.92%; p <0.001). Nonetheless, VF and in-hospital mortality were surprisingly higher in the non-HFpEF group. No difference in QTc prolongation between both groups was noted. A subgroup analysis of the VT prevalence revealed that the female gender and age of 65 or higher carried the highest risk in the HFpEF cohort.

Our finding is consistent with the findings of McHugh et al who studied the HFpEF with DM in THE GWTG-HF REGISTRY,[2] and supported by an earlier report by Jae Hyung Cho et al showing that HFpEF predisposed to VA in rats.[7] To our knowledge, this is the first retrospective analysis that evaluated this association, utilizing such a large patient sample. Our study failed to depict the association between DM and QTc prolongation, likely owing to the paucity of data describing QTc prolongation in the retrieved sample for both groups. Our analysis is subject to the inherent limitations associated with retrospective studies as well as the nature of the national inpatient sample database itself. Although our findings are consistent with other database-based work, further prospective studies in settings of more controlled confounding factors are needed to explore this relation further and examine interventions that are likely to mitigate morbidity associated with this synergism.

Disclosures

All authors declare that they have no conflicts of interest to disclose.

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Myocardial Contractile Reserve and Mortality in Patients With Severe Aortic Stenosis With Impaired Left Ventricular Function Who Underwent Transcatheter Aortic Valve Implantation

Low-flow, low-gradient aortic stenosis (LFLG AS) with reduced left ventricular ejection fraction (LVEF) remains a challenging subgroup of severe AS. In these patients, dobutamine stress echocardiography (DSE) is routinely used to establish the diagnosis of true severe AS. The 2014 ACC/AHA Valve Guidelines endorse a class IIa recommendation for low−dose DSE in AS patients with LVEF <50% to confirm AS severity and to assess myocardial contractile reserve (CR), which is defined as stroke volume increase of ≥20%. Earlier studies have shown that patients with LFLG AS and no CR have increased mortality with conservative management as well as with surgical aortic valve replacement (SAVR).[1] However, it is not known if CR portends similar prognostic significance in patients who underwent transcatheter aortic valve implantation (TAVI). Hence, we performed a meta-analysis to systematically review the impact of the presence or absence of CR on all-cause mortality in patients with LFLG AS who underwent TAVI.

We conducted a systematic literature search of PubMed, Scopus, Embase, and Cochrane Library, from 2002 to October 31, 2020. We used the following key words and Medical Subject Headings: "contractile reserve," "flow reserve," "dobutamine stress echocardiography," "DSE," "transcatheter aortic valve replacement," "transcatheter aortic valve implantation," "TAVR," "TAVI," "aortic

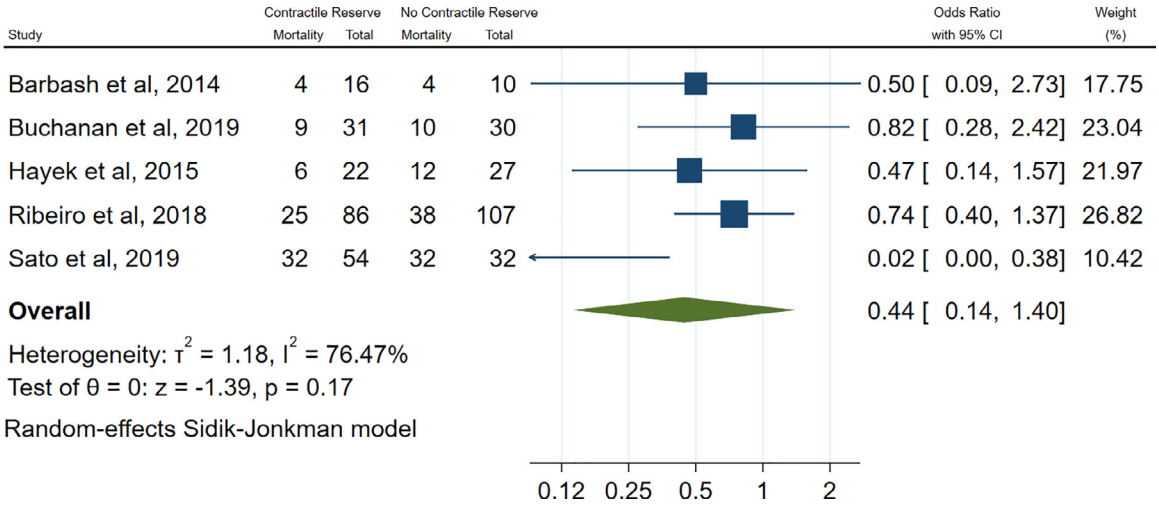

Figure 1. Forest plot of studies comparing all-cause mortality by contractile reserve in patients with low-flow low-gradient severe aortic stenosis with reduced ejection fraction undergoing TAVI. Figure shows odds ratios of outcomes (boxes) with 95% confidence limits (bars) for each study selected; pooled odds ratio is represented by a diamond in this forest plot.

stenosis." We selected studies that, (1) included patients with LFLG AS. (2) reported data in patients who underwent TAVI, and, (3) reported mortality outcomes stratified by CR groups. Two physician reviewers (C.B. and V.T.) independently reviewed originally identified titles and abstracts. The quality of each study was assessed using the Newcastle-Ottawa scale. For outcome, we evaluated all-cause mortality at the longest reported follow-up. Considering that heterogeneity of the studies might influence the treatment effects and small number of included studies, we used a Hartung-Knapp-Sidik-Jonkman random-effects model to estimate pooled odds ratio and confidence intervals.[2] We conducted this meta-analysis in accordance with the recommendations from the PRIMA and MOOSE guidelines.[3]

A total of 5 observational studies[4–8] met our inclusion criteria and were included in the analysis. Of the 415 patients with LFLG AS, 209 (50%) had CR, whereas 206 patients had no CR. In all the studies, DSE was used to assess for CR. The follow-up for all-cause mortality ranged from 1 to 5 years. All studies were of good quality signifying low-bias risk. The estimated baseline mean LVEF was 31± 8%. There was no difference in all-cause mortality between patients with CR and without CR (pooled odds ratio 0.44, 95% CI 0.14 to 1.40, p = 0.17; Figure 1). High heterogeneity was observed in the analysis (I^2 76%), which was predominantly due to study by Sato et al.[8] On excluding that study, the heterogeneity I^2 was 4% and pooled odds ratio was 0.68, (95% CI 0.42 to 1.11, p = 0.13).

Our meta-analysis involving 415 patients with LFLG AS with impaired LVEF suggests that there is no impact of CR in this high-risk group who underwent TAVI. Absence of CR has traditionally been considered a marker of worse prognosis for SAVR. Although the underlying mechanism for this finding is not clearly understood, cardiopulmonary bypass and cardioplegia may result in further myocardial injury (in an already compromised left ventricle) and need for increased inotropic and mechanical support, thus potentiating worse short and long-term outcomes. In addition, patients with LFLG AS also have increased burden of co-morbidities making TAVI an attractive option for management of severe AS.[9] TAVI is certainly a less invasive procedure and better tolerated in patients with reduced LVEF.[10] Our review of available literature supports the use of TAVI in patients with reduced LVEF irrespective of CR. Further dedicated randomized controlled trials on comparative effectiveness of TAVI and SAVR in LFLG severe AS patients are needed.

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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A Meta-analysis of Intravenous Iron Therapy for Patients With Iron Deficiency and Heart Failure

Iron deficiency is highly prevalent among heart failure patients and is associated with worse quality of life and a higher risk of hospitalizations and mortality. Early randomized clinical trials (RCTs)[1–4] evaluating the efficacy of intravenous iron replacement in heart failure patients with iron deficiency showed promising results in improving objective clinical outcomes, including heart failure hospitalizations and cardiovascular mortality. However, they were not explicitly powered for these outcomes. The 2017 ACC/AHA/HFSA focused guideline update provides a IIb recommendation for intravenous iron repletion in NYHA class II and III heart failure patients and iron deficiency to improve functional status and quality of life.[5] Most recently, the results of the AFFIRM-AHF (A Randomized, Double-blind Placebo-Controlled Trial Comparing the Effect of Intravenous Ferric Carboxymaltose on Hospitalisations and Mortality in Iron Deficient Subjects Admitted for Acute Heart Failure) was presented in the American Heart Association Scientific Sessions and has refueled the interest regarding the utility of intravenous iron therapy in patients with heart failure.[4] We aimed to pool results from all randomized controlled trials evaluating the efficacy of intravenous iron in improving cardiovascular outcomes in patients with heart failure with reduced ejection fraction (HFrEF).

We performed a comprehensive electronic database search for RCTs comparing the outcomes of intravenous iron therapy to standard of care in patients HFrEF who were diagnosed with iron

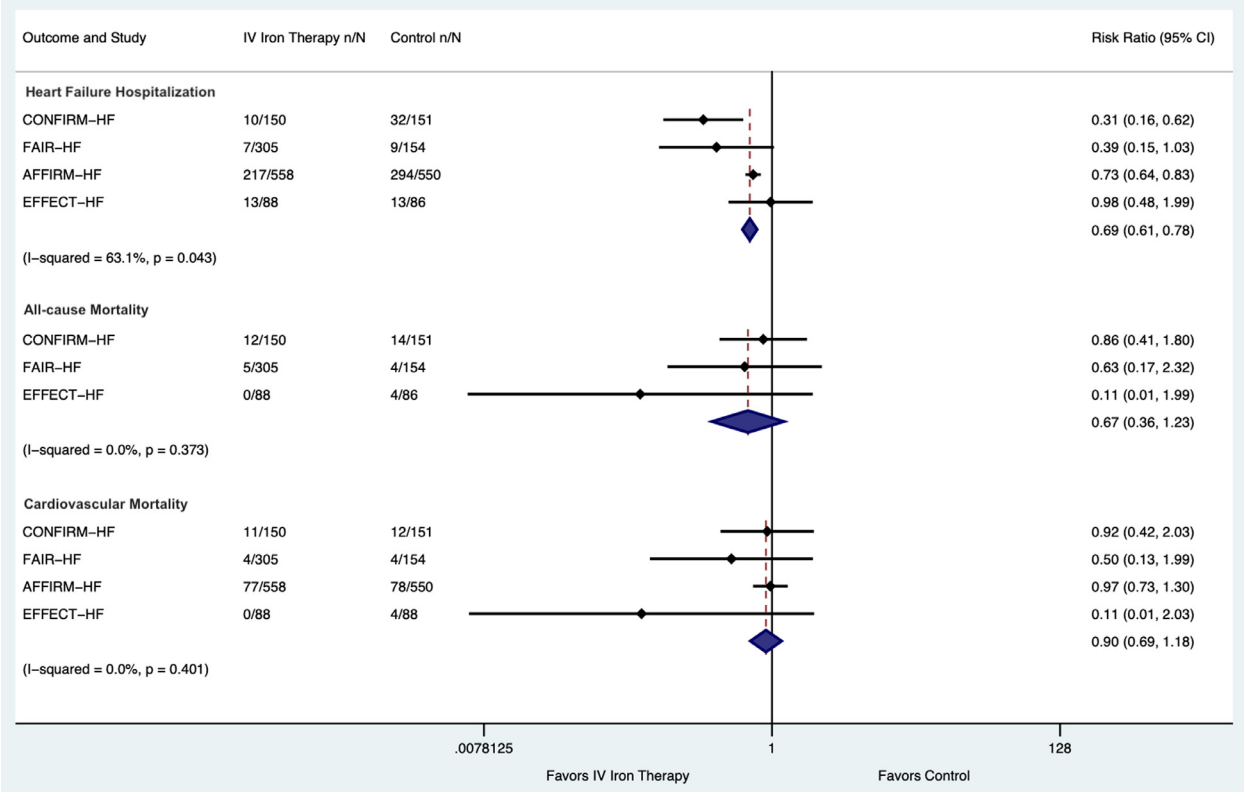

Figure 1. Forest plot summarizing the main findings from the meta-analysis.