論　文　内　容　要　旨

Left-atrial volume reduction reflects improvement of cardiac sympathetic nervous function in patients with severe aortic stenosis after transcatheter aortic valve replacement

（左房容積縮小は重症大動脈弁狭窄症患者における経カテーテル的大動脈弁置換術後の心臓交感神経機能改善を反映している）

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Introduction

Aortic stenosis (AS) is the most common valvular heart disease in the elderly population and increasing morbidity worldwide. It is known that cardiac sympathetic nervous (CSN) function is impaired and left atrium dilatation in patients with severe AS. Transcatheter aortic valve replacement (TAVR) improves CSN function immediately and induces left atrial volume (LAV) reduction; both are outcome predictors after TAVR. The relationship between these two outcome predictors is unknown. Therefore, we conducted this retrospective observational study to evaluate the correlation between CSN function and LAV in patients with AS before and after TAVR.

Methods

We recruited symptomatic patients with severe AS who underwent TAVR at Hiroshima University Hospital between February 2016 and August 2021. Severe AS was defined as (1) an aortic valve area (AVA) < 1.0 cm^2 (or AVA indexed by body surface area < 0.6 cm^2/m^2) or (2) a resting or inducible peak transaortic velocity > 4.0 m/s or (3) a resting or inducible mean pressure gradient (MPG) > 40 mm Hg. We used ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy for the assessment of CSN function. Delayed heart-to-mediastinum ratio (dHMR) was calculated semi-automatically, and the change between baseline and 6 months after TAVR was calculated using the following formula: $\Delta dHMR = (post\text{-}procedural\ dHMR) - (baseline\ dHMR)$. In transthoracic echocardiography (TTE), LAV was measured by the biplane Simpson method and indexed according to the body surface area (LAV index [LAVI]). We calculated the LAVI reduction rate (ΔLAVI%) between baseline and follow-up echocardiography as follows: $\Delta LAVI\% = ([LAVIfollow\text{-}up - LAVIbaseline] / LAVIbaseline) \times 100$.

The correlation between ΔLAVI% and ΔdHMR was assessed by Pearson's method. We performed multiple linear regression analyses using fixed adjustment for age and sex to evaluate the independent association of ΔLAVI% with ΔdHMR; model 1 was performed with covariates that reached $p < 0.05$ in univariate analysis, and model 2 was adjusted by the previously reported variables associated with improvement in the MIBG parameters after TAVR such as baseline estimated glomerular filtration rate (eGFR), clinical frailty scale ≥6, baseline AVA, baseline dHMR.

Results

283 patients underwent TAVR during this period, and 67 underwent MIBG scintigraphy at baseline and 6 months after TAVR. After exclusion, 48 patients treated with TAVR (median age 85 years, IQR 82–88 years; 81% female) were included in the study analyses. Among the 48 patients, 31 (65%) showed improved dHMR, defined as Δ dHMR > 0, after TAVR. There was no significant difference in baseline patient characteristics with

or without dHMR improvement: demographic data, symptom, frailty, surgical risk, comorbidities, and medications. The severity of AS was more severe in patients with dHMR improvement (AVA 0.58 cm^2 [IQR 0.49–0.72] vs. 0.70 cm^2 [0.64–0.90], p = 0.0270).

TAVR improved the dHMR, WR, and LA volume index (LAVI) (dHMR: 2.89 [2.62–3.23] vs. 2.98 [2.49–3.25], p = 0.0182; WR: 28% [24–38] vs. 23% [16–32], p < 0.0001; LAVI: 47.7 mL/m^2 [37.8–56.3] vs. 41.2 mL/m^2 [33.7–56.1], p = 0.0024).

There was a significant correlation between ΔLAVI% and ΔdHMR (r = −0.35, p = 0.0139). In multiple linear regression analyses, ΔLAVI% had an inverse correlation with ΔdHMR independently (β = −0.35, p = 0.0110 in model 1; β = −0.32, p = 0.0471 in model 2).

Discussion

This retrospective observational study revealed that LA volume reduction reflected CSN functional recovery in patients treated with TAVR.

The relationship between LA reverse remodeling and sympathetic nervous functional recovery has been reported. In patients with atrial fibrillation who underwent catheter ablation (CA), it has been reported that the percentage change in LAVI was correlated with the percentage change in muscle sympathetic nervous activity (MSNA) before and at 12 weeks after CA. In our study, we performed MIBG scintigraphy to evaluate the sympathetic nervous function, which focused on the “cardiac” sympathetic nerve; this is an advantage over MSNA in the analysis of CSN function.

It is well established that LA volume is related to the severity of left ventricular diastolic dysfunction (LVDD), and it is an essential component of LVDD diagnosis in TTE. LVDD is present in 30%–40% of patients with AS who underwent TAVR and is associated with long-term outcomes after TAVR. It is known that LVDD impairs CSN function. LA volume and CSN function might be interrelated through LVDD coexisting with AS. After TAVR, which contributes to release of aortic obstruction, persistent LVDD represented by LA volume could disturb the recovery of CSN function.

It has been reported that LA reverse remodeling following TAVR is associated with an improved prognosis. Although the mechanism is unknown, it might be related to the CSN improvements reported in this article, but future research is necessary to confirm this hypothesis.

Conclusion

We found that LA reverse remodeling was correlated with CSN functional recovery after TAVR in patients with symptomatic severe AS. Our results indicated that the ΔLAVI% might be a useful variable reflecting CSN functional improvement after TAVR.