Impact of Prosthesis-Patient Mismatch After Transcatheter Aortic Valve Replacement on Changes in Cardiac Sympathetic Nervous Function: Assessment by 123I-Metaiodobenzylguanidine Myocardial Scintigraphy

Kazuhiro Nitta,[1] MD, Yukihiro Fukuda,[1] MD, Hitoshi Susawa,[1] MD, Hiroki Ikenaga,[1] MD, Hiroto Utsunomiya,[1] MD, Ken Ishibashi,[1] MD, Satoshi Kurisu,[1] MD, Shinya Takahashi,[2] MD, Yukiko Nakano,[1] MD, Kazuo Awai,[3] MD, Taijiro Sueda,[2] MD and Yasuki Kihara,[1] MD

[1]Department of Cardiovascular Medicine, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan

[2]Department of Cardiovascular Surgery, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan

[3]Department of Diagnostic Radiology, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan

Introduction

Aortic stenosis (AS) is a cardiovascular disease which is common among elderly patients. Transcatheter aortic valve replacement (TAVR) has recently emerged as a minimally invasive therapeutic option. However, prosthesis-patient mismatch (PPM)—which occurs when the effective orifice area of the implanted prosthetic valve is too small in relation to the patient's body surface area—is an important potential complication of TAVR. Several studies have shown PPM to be associated with increased mortality after TAVR. 123I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy has been widely used for the assessment of CSN activity and represents a useful prognostic marker in patients with heart failure. However, the impact of PPM after TAVR on changes in CSN function remains unclear. The present study aimed to investigate the impact of PPM after TAVR on CSN activity using 123I-MIBG scintigraphy.

Methods

Study Population

We recruited a total of 117 patients with symptomatic severe AS who

underwent TAVR between February 2016 and May 2019 at the Hiroshima University Hospital. Severe AS was defined as an aortic valve area (AVA) of <1.0 cm^2 and a resting or inducible peak transaortic velocity >4 m/s or mean pressure gradient of ≥40 mmHg. Of these, 58 underwent 123I-MIBG scintigraphy at baseline and at about 9 months after TAVR. Exclusion criteria were as follows: (1) prior cardiac surgery (n = 2), (2) presence of unstable pre-procedural conditions (n = 2), (3) undergoing TAVR with the trans-apical or trans-aortic approach (n = 3), and (4) permanent pacemaker implantation (n = 6) or hemodialysis (n = 1) after TAVR. Finally, 44 patients were enrolled in this study.

Transcatheter Aortic Valve Replacement

The procedure was performed using either a balloon-expandable Edwards Sapien XT/Sapien 3 or self-expandable Medtronic CoreValve Evolut R device. All patients were treated using a transfemoral approach under general anesthesia.

123I-Metaiodobenzylguanidine Scintigraphy

123I-MIBG was administered intravenously at a dose of 111 MBq. Anterior planar images were obtained at 15 min (early image) and 210 min (delayed image) after injection using a dual-detector 90° γ-camera with a medium-energy general collimator. Images were analyzed based on the region of interest determined using dedicated software (Jetpack, Hitachi) by an experienced radiology technician who was blinded to the clinical status of the patients. The Jetpack software was able to semi-automatically determine heart-to-mediastinum (H/M) ratios and correct them to standard medium-energy collimator conditions. Early and delayed H/M ratios were calculated by measuring the average counts in each region. The washout rate (WR) was calculated by: [(H−M) early − (H−M) delayed/k] × 100/(H−M) early, with background subtraction and time-decay correction (k = time-decay coefficient). Changes between pre- and post-procedural 123I-MIBG parameters were calculated using the following formulae: (1) ΔH/M ratio = (post-procedural H/M ratio) − (baseline H/M ratio) and (2) ΔWR = (baseline WR) − (post-procedural WR).

Transthoracic Echocardiography

We obtained echocardiographic data at baseline and at 7 days and 9 months after TAVR. Comprehensive echocardiographic assessments were performed by three experienced sonographers, who had no knowledge of the patients' clinical statuses. The severity of PPM was classified using an indexed effective orifice area, with moderate defined as $\geq$0.65 and $\leq$0.85 cm^2/m^2 and severe defined as <0.65 cm^2/m^2, and this was assessed by echocardiogram at 7 days after TAVR.

Results

Patient Characteristics Before Transcatheter Aortic Valve Replacement in Relation to Patient-Prosthesis Mismatch

There were 9 male and 35 female patients with a mean age of 84 ± 4 years. There were no significant differences in terms of age, sex, body surface area, body mass index, past medical history, serum creatinine, medications, and transthoracic echocardiographic data between patients with PPM and those without PPM before TAVR. As for 123I-MIBG parameters before TAVR, patients without PPM had higher early H/M ratio and WR than those with PPM.

Patient Characteristics Before and After Transcatheter Aortic Valve Replacement in Relation to Patient-Prosthesis Mismatch

The rate of overall and severe PPM among the study population was 39% (n = 17) and 11% (n = 5), respectively. Significant improvements in AVA, peak pressure gradient, and mean pressure gradient after TAVR were observed in patients with and without PPM. Those without PPM exhibited significant regression in LVMI after TAVR, whereas those with PPM did not. Patients without PPM exhibited significant improvements in delayed H/M ratio and WR after TAVR, while those with PPM did not.

Factors Associated with Improvements in 123I-Metaiodobenzylguanidine Parameters

Multivariable linear regression analysis revealed PPM was a negative predictor of improvement in delayed H/M ratio. Furthermore, PPM and baseline WR were independent predictors of improvement in WR.

Discussion

This investigation of the impact of PPM after TAVR on changes in CSN function using 123I-MIBG scintigraphy demonstrates the following: (1) delayed H/M ratio and WR improve significantly after TAVR for patients without PPM, whereas patients with PPM do not experience these improvements, and (2) PPM is a negative predictor of improvements in delayed H/M ratio and WR in patients undergoing TAVR.

Although the use of TAVR is expanding rapidly, the risk of PPM remains a potential limitation of the procedure.

Although previous studies have reported the early effects of TAVR on CSN function using 123I-MIBG scintigraphy, the impact of PPM after TAVR on changes in CSN function is not well established.

Our findings of the impact of PPM after TAVR on changes in CSN function may be explained by the association between PPM and reduced hemodynamic improvement after TAVR. We found that patients with PPM experienced less favorable changes after TAVR compared to those without PPM including lower AVA, higher peak and mean pressure gradients, and limited LVMI regression. Similar findings have been reported in previous studies. The small indexed effective orifice area and its residual high pressure gradient may

suppress improvements in 123I-MIBG parameters.

In conclusion, our findings suggest that delayed H/M ratio and WR improve significantly after TAVR for patients who do not experience PPM. Because of the negative effects in terms of improvement in 123I-MIBG parameters, strategies to prevent or minimize PPM are important, especially for patients with CSN overactivation.