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Original Research

Comparison of Intracardiac Echocardiography Versus Transesophageal Echocardiography for Guidance During Transcatheter Aortic Valve Replacement

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AUTHOR'S SUMMARY

Although transcatheter aortic valve replacement (TAVR) has become a mainstream strategy for symptomatic severe aortic stenosis, transesophageal echocardiography (TEE) remains the standard intraprocedural echocardiographic modality for TAVR. Recently intracardiac echocardiography (ICE) provides real-time high-resolution images during procedure and widely used for structural cardiac interventions. This study demonstrated the comparable efficacy of ICE to TEE regarding 1-year composite of all-cause mortality, rehospitalization for cardiovascular cause, or stroke without increasing the risk of significant paravalvular regurgitation, new permanent pacemaker implantation, or major bleeding. This result may support that ICE could be a safe and effective alternative to TEE for TAVR guidance.

ABSTRACT

Background and Objectives: Evidence regarding the efficacy and safety of intracardiac echocardiography (ICE) for guidance during transcatheter aortic valve replacement (TAVR) is limited. This study aimed to compare the clinical efficacy and safety of ICE versus transesophageal echocardiography (TEE) for guiding TAVR.
Methods: This prospective cohort study included patients who underwent TAVR from August 18, 2015, to June 31, 2021. Eligible patients were stratified by echocardiographic modality (ICE or TEE) and anesthesia mode (monitored anesthesia care [MAC] or general anesthesia [GA]). Primary outcome was the 1-year composite of all-cause mortality, rehospitalization for cardiovascular cause, or stroke, according to the Valve Academic Research Consortium-3 (VARC-3) definition. Propensity score matching was performed, and study outcomes were analyzed for the matched cohorts.

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The authors have no financial conflicts of interest.

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The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions
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Results: Of the 359 eligible patients, 120 patients were matched for the ICE-MAC and TEE-GA groups, respectively. The incidence of primary outcome was similar between matched groups (18.3% vs. 20.0%; adjusted hazard ratio, 0.94; 95% confidence interval [CI], 0.53–1.68; p=0.843). ICE-MAC and TEE-GA also had similar incidences of moderate-to-severe paravalvular regurgitation (PVR) (4.2% vs. 5.0%; adjusted odds ratio, 0.83; 95% CI, 0.23–2.82; p=0.758), new permanent pacemaker implantation, and VARC-3 types 2–4 bleeding.
Conclusions: ICE was comparable to TEE for guidance during TAVR for the composite clinical efficacy outcome, with similar incidences of moderate-to-severe PVR, new permanent pacemaker implantation, and major bleeding. These results suggest that ICE could be a safe and effective alternative echocardiographic modality to TEE for guiding TAVR.

Keywords: Transcatheter aortic valve replacement; Aortic valve stenosis; Cardiac imaging techniques; Conscious sedation

INTRODUCTION

Rigorous randomized studies have demonstrated the safety and efficacy of transcatheter aortic valve replacement (TAVR) for patients with symptomatic severe aortic stenosis considered at low risk to those considered at high risk.[1-7] Accordingly, contemporary guidelines recommend TAVR as a preferred treatment for symptomatic severe aortic stenosis in patients aged ≥75 years, regardless of surgical risk,[8][9] and it is expected that the indications for TAVR will be expanded to younger, lower-risk patients in the near future.[10]

Intraprocedural echocardiography is used to assess procedural results and detect immediate post-procedural complications. Transesophageal echocardiography (TEE) was the standard modality for echocardiographic guidance during the era of TAVR performed under general anesthesia (GA).[11-13] However, as confidence in the safety of TAVR increased with accumulating experience and the use of recent-generation devices has reduced procedural complications, such as paravalvular regurgitation (PVR), annular rupture, conduction disturbances, or coronary access impairment, anesthesia for TAVR shifted from GA to monitored anesthesia care (MAC) with conscious sedation, and TEE was replaced with transthoracic echocardiography (TTE).[14]

Recently, due to inherent limitation of TTE, intracardiac echocardiography (ICE) emerged as an imaging tool for guidance during various structural heart and electrophysiology procedures.[15-17] ICE provides high-resolution images and continuous monitoring during procedures, without the need for GA. Nevertheless, there are limited data regarding the efficacy and safety of ICE for guidance during TAVR. In the current study, we compared the clinical efficacy and safety of ICE versus TEE as an intraprocedural echocardiographic modality for guidance during TAVR.

METHODS

Ethical statement

Our Institutional Review Board approved the study protocol (Yonsei University Health System, 1-2011-0099), and all patients provided informed consent for the procedure and data collection.

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Study population

This prospective cohort study included patients who underwent transfemoral TAVR at Severance Cardiovascular Hospital in Seoul, Korea, between August 2015, and June 2021. All patients received a recent-generation transcatheter heart valve (THV): SAPIEN III balloon-expandable THV (Edwards, Irvine, CA, USA), or Evolut R or Evolut Pro self-expandable THV (Medtronic, Minneapolis, MN, USA). The key exclusion criteria were 1) previous aortic valve replacement, 2) previous permanent pacemaker implantation, 3) emergency procedure, 4) TTE-guided procedure, and 5) missing pre-procedural computed tomography (CT) data. Eligible patients were stratified into two groups according to the intraprocedural echocardiographic modality and anesthesia mode (ICE-MAC or TEE-GA).

Transcatheter aortic valve replacement procedures

All TAVR procedures were performed by highly experienced operators who had previously performed >100 TAVR procedures. All procedures were discussed in advance by a heart team consisting of interventional cardiologists, imaging cardiologists, cardiovascular surgeons, and a cardiac anesthesiologist. The type and size of THV and anesthesia mode were determined by the heart team. The procedures followed the usual standards and detailed techniques for the specific implanted valves. A temporary pacemaker was routinely inserted via right internal jugular vein, and if not accessible, left common femoral vein was used. ICE was performed using an AcuNav ICE catheter (Siemens-Acuson, Mountain View, CA, USA) or a ViewFlex Xtra catheter (Abbott Vascular, St. Paul, MN, USA). The ICE catheter was introduced via right common femoral vein into right atrium and manipulated by the operator. In addition to the monitoring of position and implantation depth during procedure, the echocardiography in use provided information regarding immediate post-procedural complication, appropriateness of the THV position, and the degree of PVR after deployment of THV. Post-dilation was performed at the discretion of operators only when moderate-to-severe PVR was noted in echocardiography or underexpnaded THV was observed in fluoroscopy. In case that significant PVR or underexpanded THV still remained after post-dilation, additional post-dilation could be performed at the discretion of operators with consideration for complications, such as annular rupture or conduction disturbance. Aortography was performed at the discretion of the operators, depending on the patient's renal function. The doses of anesthesia-related drugs were left to the discretion of the cardiac anesthesiologist.

Definitions of study outcomes

The primary outcome was a composite of all-cause mortality, rehospitalization for cardiovascular cause, or stroke within 1 year after TAVR. The following early post-procedural outcomes were also assessed: technical failure, device failure, and early safety outcome. Technical failure was defined as a composite of the following outcomes assessed at the time of exit from the procedure room: mortality; failure to deliver the transcatheter device, to retrieve the delivery system, or to adequately deploy a single THV at the intended position; or the need for surgery or intervention because of a device-related reason or a major vascular or cardiac structural complication.[18] Device failure and early safety outcome were assessed at 30 days after the index procedure. Device failure was defined as a composite of technical failure, mortality, need for surgery or intervention because of a device-related reason or a major vascular or cardiac structural complication, or failure to achieve adequate performance of the THV. Adequate THV performance was defined as meeting three following criteria: mean pressure gradient across the THV <20 mmHg; peak velocity across the THV <3.0 m/s; and less than moderate PVR.[18] Early safety outcome was defined as a composite of mortality, stroke, Valve Academic Research Consortium-3 (VARC-3) types 2–4 bleeding, need for surgery or

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intervention because of a major vascular or cardiac structural complication, moderate-to-severe PVR, stage 3 or 4 acute kidney injury, or new permanent pacemaker implantation for a conduction disturbance related to the procedure.[18] The hospital and intensive care unit (ICU) lengths of stay were calculated as the time from the day of the index procedure until the day of hospital discharge and transfer to a general ward, respectively.

In addition, serial echocardiographic parameters including left ventricular ejection fraction, mean systolic pressure gradient, and effective orifice area were obtained after the procedure by TTE. Each parameter was obtained at early post-procedural period, which assessed within 7 days of the procedure, and at 1 year after the procedure.

Statistical analyses

Continuous variables were reported as mean with standard deviation or median with interquartile range, according to normality assessed by Shapiro–Wilk test. Categorical variables were reported as numbers with proportions. Continuous variables were compared by Student's t-test or Mann–Whitney U test and categorical variables were compared by Chi-square test or Fisher's exact test.

Propensity score matching (PSM) was used to adjust possible confounding factors. The propensity score indicating the probability of each patient being allocated to the ICE-MAC group was calculated using a logistic regression model including these variables: age, sex, diabetes mellitus, atrial fibrillation, chronic kidney disease, stroke, bundle branch block, prior percutaneous coronary intervention, New York Heart Association functional class (class I–II vs. class III–IV), Society of Thoracic Surgeons (STS) score, left ventricular ejection fraction, aortic valve area, mean systolic pressure gradient on pre-procedural TTE, annular diameter on pre-procedural CT, type of THV (balloon-expandable vs. self-expandable), and pre-dilation during the procedure. Matching was conducted using the nearest neighbor protocol with a 1:1 ratio and a caliper width of 0.2 standard deviations of the logit of the propensity score. Standard mean difference (SMD) between groups was calculated for each variable in both unmatched and matched cohorts. The variables for PSM were chosen among those considered to affect the physicians' decision on echocardiographic modality and mode of anesthesia to make all SMDs be <10%, which considered appropriately balanced.

Time-to-event data were presented as Kaplan–Meier curves and compared using log-rank test. The study outcomes were estimated using Cox proportional hazard or logistic regression models and presented as hazard ratio (HR) or odds ratio (OR) with a 95% confidence interval (CI), as appropriate. $p<0.05$ was considered statistically significant. All statistical analyses were performed using R statistical software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study population baseline characteristics

The CONSORT flow diagram of the study is presented in **Figure 1**. Of the 359 eligible patients, 172 (47.9%) underwent TAVR under MAC and ICE guidance (ICE-MAC group), while 187 (52.1%) underwent TAVR under GA and TEE guidance (TEE-GA group). After PSM, each matched group included 120 patients. Baseline characteristics of the unmatched and matched cohorts are presented in **Table 1**. In the unmatched cohort, the ICE-MAC group

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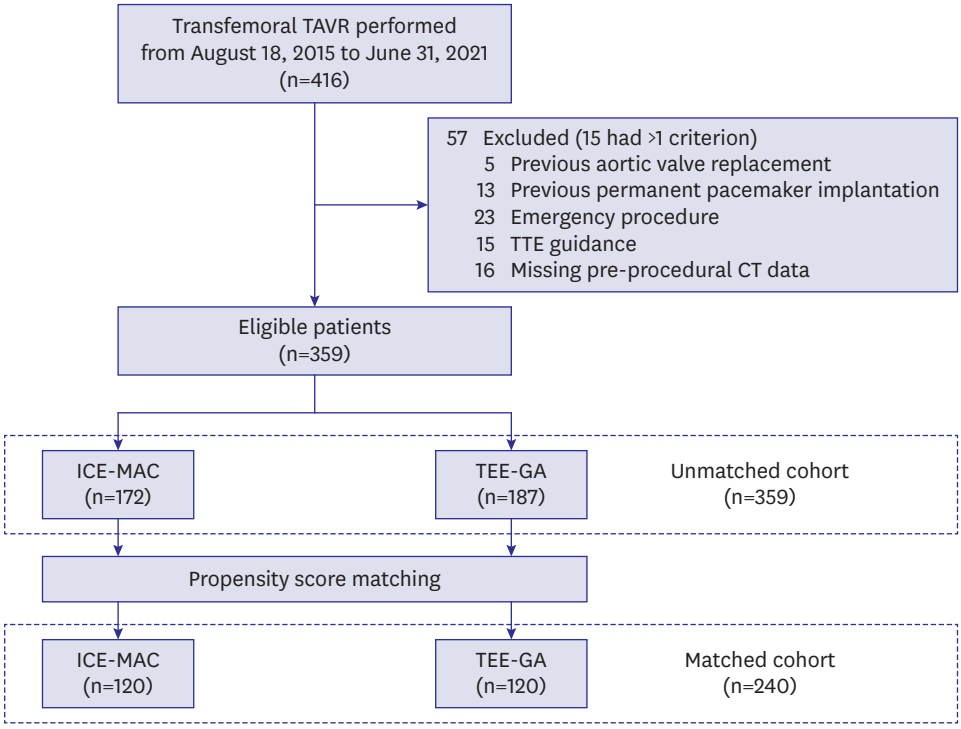

Figure 1. CONSORT flow diagram.
Patients undergoing transfemoral TAVR from August 18, 2015, to June 31, 2021, were included. Among 359 patients eligible for the study, 120 patients were included in each of the matched ICE-MAC and TEE-GA groups based on propensity score matching.
CT = computed tomography; GA = general anesthesia; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

had a lower proportion of chronic kidney disease (33.7% vs. 52.9%), lower median STS score (3.32% vs. 4.70%), and higher median left ventricular ejection fraction (67% vs. 63%), compared with the TEE-GA group. In the matched cohort, adequate balance was achieved for all variables (all SMDs <10%). Distributions of propensity scores of the unmatched and matched cohorts are shown in **Supplementary Figure 1**.

Procedural data and early post-procedural outcomes

The proportion of patients who received a balloon-expandable THV was not different in the two matched groups (40.0% vs. 37.5%; p=0.791) and that of pre-dilation also did not differ between the two matched groups (54.2% vs. 55.8%; p=0.897). However, post-dilation was performed less frequently in the ICE-MAC group (25.8% vs. 40.0%; p=0.028) (**Table 1**). Procedural data and early post-procedural outcomes are summarized in **Table 2**. The incidence of technical failure did not differ between the two matched groups (5.8% vs. 10.0%; adjusted OR, 0.56; 95% CI, 0.20–1.44; p=0.237).

Of note, only 1 patient in this study required emergent open-heart surgery. This patient was in the TEE-GA group and required emergent surgery because of a Type A aortic dissection after self-expandable Evolut R valve implantation. Surgical aortic valve replacement and graft replacement of the ascending aorta and hemiarch were performed, after which the patient recovered uneventfully. Mechanical circulatory support was required in only 1 patient, who was in the ICE-MAC group. Extracorporeal membrane oxygenation (ECMO) was initiated

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Table 1. Baseline characteristics of unmatched and matched cohorts

Characteristic	Unmatched cohort				Matched cohort			
	ICE-MAC (n=172)	TEE-GA (n=187)	p value	SMD (%)	ICE-MAC (n=120)	TEE-GA (n=120)	p value	SMD (%)
Age (years)	81 (79–84)	82 (79–85)	0.226	8.6	81 (79–84)	82 (79–84)	0.993	0.2
Male sex	82 (47.7)	82 (43.9)	0.535	7.7	53 (44.2)	52 (43.3)	>0.999	1.7
Body surface area (m^2)	1.60±0.19	1.59±0.19	0.500	7.1	1.60±0.19	1.59±0.18	0.677	5.4
Hypertension	134 (77.9)	158 (84.5)	0.143	16.9	95 (79.2)	96 (80.0)	>0.999	2.1
Diabetes mellitus	61 (35.5)	79 (42.2)	0.227	13.9	45 (37.5)	44 (36.7)	>0.999	1.7
Atrial fibrillation	39 (22.7)	47 (25.1)	0.673	5.8	25 (20.8)	22 (18.3)	0.745	6.3
Chronic kidney disease*	58 (33.7)	99 (52.9)	<0.001	39.5	48 (40.0)	48 (40.0)	>0.999	<0.1
Prior stroke	22 (12.8)	39 (20.9)	0.058	21.7	16 (13.3)	19 (15.8)	0.715	7.1
Chronic lung disease	21 (12.2)	17 (9.1)	0.431	10.1	16 (13.3)	14 (11.7)	0.845	5.0
Prior myocardial infarction	10 (5.8)	15 (8.0)	0.540	8.7	8 (6.7)	6 (5.0)	0.783	7.1
Coronary artery disease	90 (52.3)	111 (59.4)	0.217	14.2	66 (55.0)	64 (53.3)	0.897	3.3
Prior percutaneous coronary intervention	42 (24.4)	61 (32.6)	0.110	18.2	30 (25.0)	32 (26.7)	0.883	3.8
Prior coronary artery bypass graft surgery	7 (4.1)	13 (7.0)	0.338	12.7	6 (5.0)	6 (5.0)	>0.999	<0.1
Bundle branch block			0.101	23.0			0.838	7.7
None	154 (89.5)	155 (82.9)			105 (87.5)	102 (85.0)		
Left bundle branch block	2 (1.2)	8 (4.3)			2 (1.7)	2 (1.7)		
Right bundle branch block	16 (9.3)	24 (12.8)			13 (10.8)	16 (13.3)		
NYHA fc III–IV	102 (59.3)	115 (61.5)	0.751	4.5	69 (57.5)	71 (59.2)	0.896	3.4
STS (%)	3.32 (2.27–5.31)	4.70 (3.19–7.04)	<0.001	55.3	3.80 (2.41–5.67)	3.86 (2.82–5.81)	0.561	9.3
Low risk†	102 (59.3)	76 (40.6)	0.001	38.0	64 (53.3)	65 (54.2)	>0.999	1.7
Intermediate-to-high risk†	70 (40.7)	111 (59.4)			56 (46.7)	55 (45.8)		
Bicuspid aortic valve	11 (6.4)	10 (5.3)	0.843	4.5	9 (7.5)	7 (5.8)	0.796	6.7
Left ventricular ejection fraction (%)	67 (58–72)	63 (48–70)	0.014	29.0	65 (55–72)	66 (50–71)	0.907	6.1
Aortic valve area (cm^2)	0.74 (0.63–0.85)	0.74 (0.58–0.85)	0.629	7.1	0.74 (0.60–0.86)	0.74 (0.58–0.86)	0.898	3.8
Indexed aortic valve area (cm^2/m^2)	0.46 (0.38–0.54)	0.46 (0.39–0.52)	0.676	5.5	0.45 (0.38–0.54)	0.46 (0.38–0.53)	0.863	3.1
Mean systolic pressure gradient (mmHg)	48 (38–58)	46 (39–58)	0.944	3.4	49 (39–58)	48 (39–62)	0.888	4.2
Annular diameter of aortic valve (mm)	23.8 (22.4–25.1)	23.8 (22.5–25.4)	0.444	7.3	23.4 (22.4–24.7)	23.6 (22.2–25.4)	0.687	4.9
Annular perimeter of aortic valve (mm)	76.0 (71.8–80.0)	75.9 (72.2–80.5)	0.766	1.8	74.6 (71.3–79.3)	75.3 (71.8–80.9)	0.661	1.3
Type of THV			<0.001	39.4			0.791	5.1
Balloon-expandable valve	86 (50.0)	58 (31.0)			48 (40.0)	45 (37.5)		
Self-expandable valve	86 (50.0)	129 (69.0)			72 (60.0)	75 (62.5)		
Pre-dilation	71 (41.3)	123 (65.8)	<0.001	50.7	65 (54.2)	67 (55.8)	0.897	3.4
Post-dilation	40 (23.3)	77 (41.2)	<0.001	39.1	31 (25.8)	48 (40.0)	0.028	30.5

Data are presented as number (%), median (interquartile range), or mean ± standard deviation. Propensity score matching was performed using these variables: age, sex, diabetes mellitus, atrial fibrillation, chronic kidney disease, prior stroke, bundle branch block, prior percutaneous coronary intervention, NYHA fc (class I–II vs. class III–IV), STS score, left ventricular ejection fraction, aortic valve area, mean systolic pressure gradient, annular diameter of the aortic valve, type of THV (balloon-expandable vs. self-expandable), and pre-dilation.

GA = general anesthesia; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; NYHA fc = New York Heart Association functional class; SMD = standardized mean difference; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography; THV = transcatheter heart valve.

*Chronic kidney disease was defined as an estimated glomerular filtration rate of <60 mL/min/1.73 m^2 body surface area or requiring renal replacement therapy.

†Surgical risk was stratified by STS score (low risk, <4%; intermediate-to-high risk, ≥4%).

for this patient because of sudden hypotension with a new-onset left bundle branch block immediately after balloon-expandable SAPIEN III valve implantation. After stabilization of the blood pressure, ECMO was successfully removed the next day. THV malposition was observed in 3 patients (2 in the ICE-MAC group and 1 in the TEE-GA group), with 1 patient in each group requiring a second THV.

The incidence of device failure did not differ between matched groups (15.8% vs. 20.0%; adjusted OR, 0.75; 95% CI, 0.38–1.46; p=0.401). The incidence of the early safety outcome also did not differ between groups (25.8% vs. 33.3%; adjusted OR, 0.70; 95% CI, 0.40–1.21; p=0.204). There was no difference between groups for the rate of moderate-to-severe PVR (4.2% vs. 5.0%; adjusted OR, 0.83; 95% CI, 0.23–2.82; p=0.758) or VARC-3 types 2–4 bleeding (9.2% vs. 10.8%; adjusted OR, 0.83; 95% CI, 0.35–1.94; p=0.667). Gastrointestinal bleeding occurred in 5 patients, all of whom were in the TEE-GA group. The rate of new

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Table 2. Early post-procedural outcomes of unmatched and matched cohorts

Post-procedural outcomes	Unmatched cohort				Matched cohort			
	ICE-MAC (n=172)	TEE-GA (n=187)	Unadjusted OR (95% CI)	p value	ICE-MAC (n=120)	TEE-GA (n=120)	Adjusted OR (95% CI)	p value
Technical failure	10 (5.8)	14 (7.5)	0.76 (0.32–1.75)	0.527	7 (5.8)	12 (10.0)	0.56 (0.20–1.44)	0.237
Device failure	26 (15.1)	35 (18.7)	0.77 (0.44–1.34)	0.365	19 (15.8)	24 (20.0)	0.75 (0.38–1.46)	0.401
Early safety outcome	37 (21.5)	63 (33.7)	0.54 (0.33–0.86)	0.011	31 (25.8)	40 (33.3)	0.70 (0.40–1.21)	0.204
Major vascular complication	6 (3.5)	13 (7.0)	0.48 (0.17–1.25)	0.151	5 (4.2)	9 (7.5)	0.54 (0.16–1.60)	0.277
Major cardiac structural complication	4 (2.3)	3 (1.6)	1.46 (0.32–7.50)	0.623	3 (2.5)	2 (1.7)	1.51 (0.25–11.6)	0.653
Moderate-to-severe PVR*	6 (3.5)	10 (5.3)	0.64 (0.21–1.76)	0.397	5 (4.2)	6 (5.0)	0.83 (0.23–2.82)	0.758
VARC-3 types 2–4 bleeding†	12 (7.0)	21 (11.2)	0.59 (0.27–1.23)	0.167	11 (9.2)	13 (10.8)	0.83 (0.35–1.94)	0.667
Gastrointestinal bleeding†	0 (0.0)	5 (2.7)	-	-	0 (0.0)	5 (4.2)	-	-
Stage 3 or 4 acute kidney injury‡	1/163 (0.6)	3/173 (1.7)	0.35 (0.02–2.76)	0.365	1/111 (0.9)	2/112 (1.8)	0.50 (0.02–5.29)	0.574
New permanent pacemaker implantation	18 (10.5)	25 (13.4)	0.76 (0.39–1.44)	0.398	14 (11.7)	15 (12.5)	0.92 (0.42–2.02)	0.843

Data are presented as number (%). Technical failure was assessed at the time of exit from the procedure room. Device failure and the early safety outcome were assessed at 30 days after the index procedure.
CI = confidence interval; GA = general anesthesia; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; OR = odds ratio; PVR = paravalvular regurgitation; TEE = transesophageal echocardiography; THV = transcatheter heart valve; VARC = Valve Academic Research Consortium.
*PVR was estimated by transthoracic echocardiography within 7 days after the index procedure.
†Bleeding events were assessed within 48 hours after the index procedure, and gastrointestinal bleeding was confirmed by esophagogastroduodenoscopy.
‡Acute kidney injury within 7 days after the index procedure. Data are presented as n/N (%), after excluding patients with end-stage renal disease receiving renal replacement therapy before the index procedure.
§Standardized mean differences for the type of THV and use of pre-dilation were 5.1% and 3.4%, respectively.

permanent pacemaker implantation did not differ between matched groups (11.7% vs. 12.5%; adjusted OR, 0.92; 95% CI, 0.42–2.02; p=0.843).

Hospital length of stay and proportion of patients requiring ICU for >1 day are shown in **Supplementary Figure 2**. Compared with the TEE-GA group, the ICE-MAC group had a shorter median hospital length of stay (4 [3–7] days vs. 5 [3–8] days; p=0.014) and a lower proportion of patients requiring ICU for >1 day (18.3% vs. 35.8%; p=0.004).

Clinical and echocardiographic outcomes at 1 year

Individual components of the primary outcome are presented in **Table 3**. Although the rate of the primary outcome was lower in the ICE-MAC group than the TEE-GA group among the unmatched cohort (12.8% vs. 20.9%; unadjusted HR, 0.59; 95% CI, 0.35–0.99; p=0.043), those did not differ between matched groups (18.3% vs. 20.0%; adjusted HR, 0.94; 95% CI, 0.53–1.68; p=0.843) (**Figure 2**).

Serial echocardiographic data before and after TAVR are shown in **Figure 3** and **Supplementary Table 1**. The rate of moderate-to-severe PVR did not differ between matched groups on the early post-procedural TTE (performed within 7 days of the procedure), as well on the 1-year follow-up TTE (4.8% vs. 6.0%; p=0.746) (**Figure 3A**). Left ventricular ejection

Table 3. Incidence of the clinical outcomes in unmatched and matched cohorts

Outcomes	Unmatched cohort				Matched cohort			
	ICE-MAC (n=172)	TEE-GA (n=187)	Unadjusted HR (95% CI)	p value	ICE-MAC (n=120)	TEE-GA (n=120)	Adjusted HR (95% CI)	p value
Primary outcome	22 (12.8)	39 (20.9)	0.59 (0.35–0.99)	0.043	22 (18.3)	24 (20.0)	0.94 (0.53–1.68)	0.843
All-cause mortality	4 (2.3)	13 (7.0)	0.33 (0.11–1.01)	0.053	4 (3.3)	8 (6.7)	0.52 (0.16–1.72)	0.274
Cardiovascular mortality	1 (0.6)	4 (2.1)	0.27 (0.03–2.41)	0.208	1 (0.8)	2 (1.7)	0.50 (0.04–5.47)	0.559
Rehospitalization for cardiovascular cause	19 (11.0)	28 (15.0)	0.71 (0.39–1.27)	0.241	19 (15.8)	18 (15.0)	1.09 (0.57–2.08)	0.793
Stroke	3 (1.7)	4 (2.1)	0.80 (0.18–3.59)	0.775	3 (2.5)	3 (2.5)	1.00 (0.20–4.94)	0.998

Data are presented as number (%). The primary outcome was the clinical efficacy outcome, defined as a 1-year composite of all-cause mortality, rehospitalization for cardiovascular cause, or stroke.
CI = confidence interval; GA = general anesthesia; HR = hazard ratio; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; TEE = transesophageal echocardiography.

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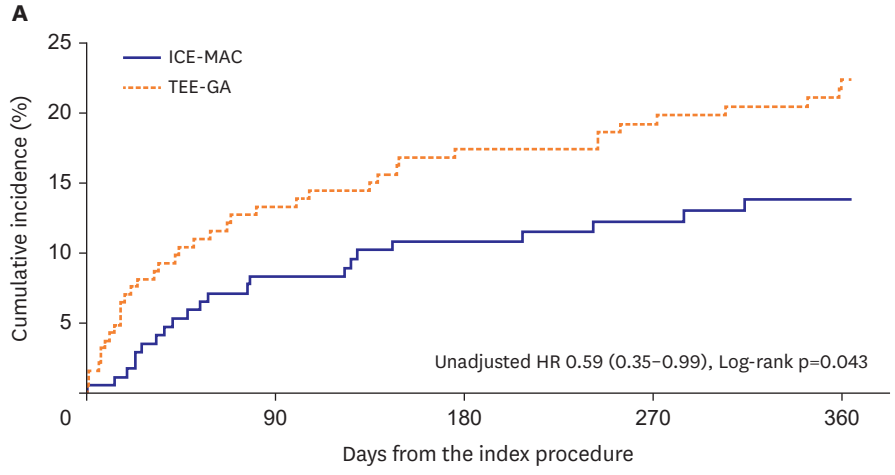
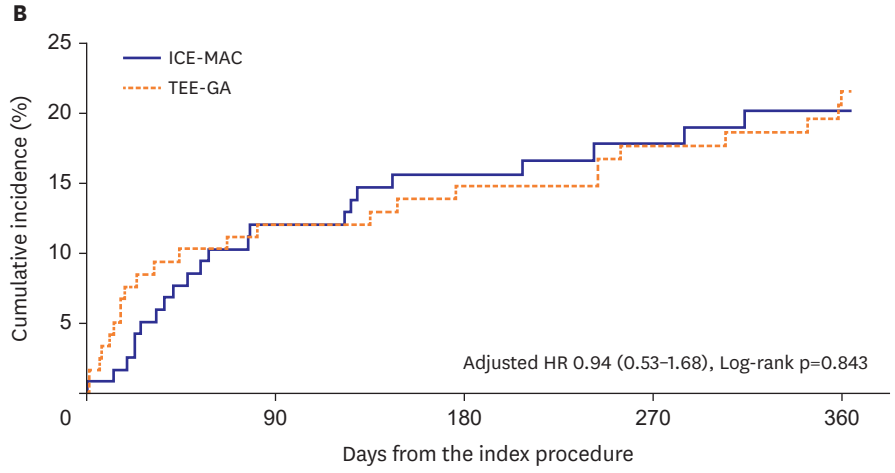


Number at risk					
ICE-MAC	172	153	138	116	96
TEE-GA	187	150	140	132	122



Number at risk					
ICE-MAC	120	102	88	70	61
TEE-GA	120	98	93	87	82

Figure 2. Time-to-event curves for the primary outcome.
Kaplan–Meier curves of the primary outcome for the unmatched groups (A) and matched groups (B) (ICE-MAC vs. TEE-GA).
GA = general anesthesia; HR = hazard ratio; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; TEE = transesophageal echocardiography.

fraction (**Figure 3B**), mean systolic pressure gradient (**Figure 3C**), and effective orifice area of the aortic valve (**Figure 3D**) were also similar between the two matched groups, regardless of the time point (**Supplementary Table 1**).

DISCUSSION

In the present study, early post-procedural outcomes and 1-year composite clinical outcomes did not differ between ICE-MAC and TEE-GA groups. Additionally, the incidences of moderate-to-severe PVR and the values of hemodynamic parameters in the early post-

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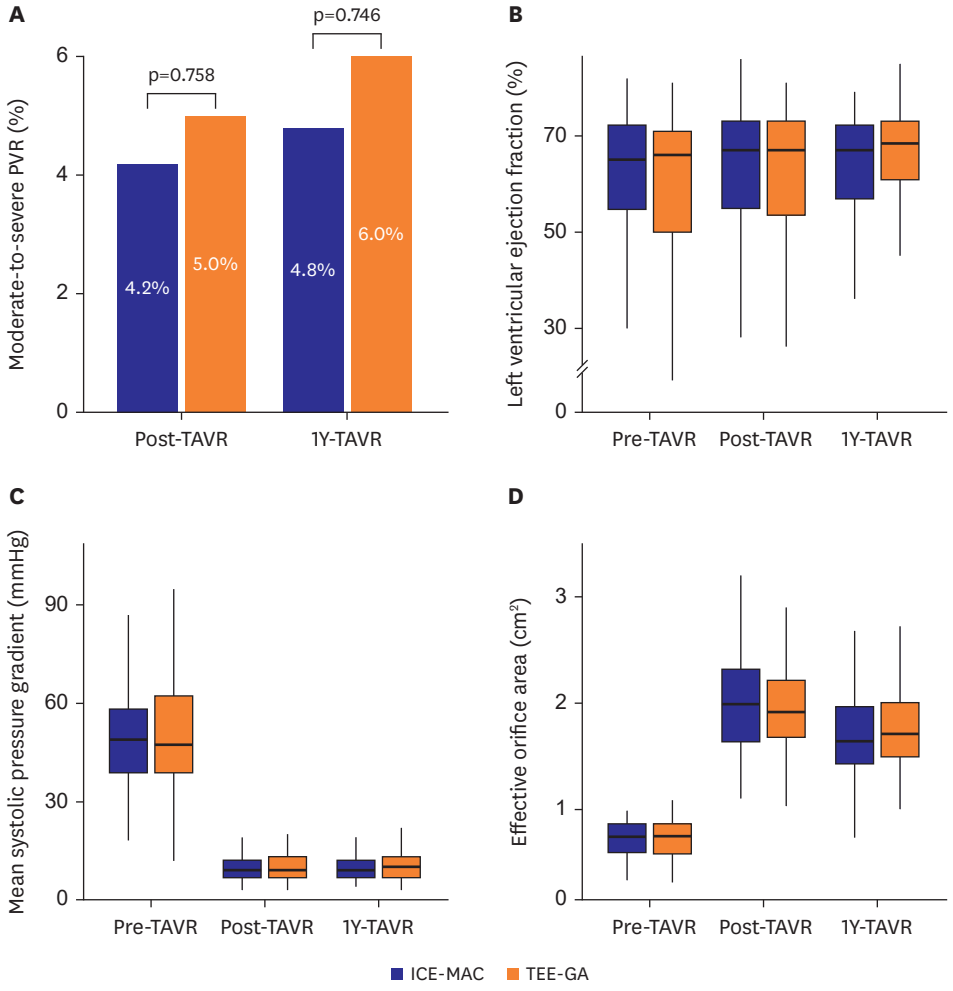

Figure 3. Serial echocardiographic assessment before and after TAVR.
(A) Bar plots of the incidences of moderate-to-severe PVR assessed by early post-procedural TTE (Post-TAVR; TTE performed within 7 days of the procedure) and 1-year follow-up TTE (1Y-TAVR), with p values for the comparison between the matched ICE-MAC and TEE-GA groups. (B–D) Boxplots of the median values with interquartile ranges before TAVR (Pre-TAVR), at early post-procedural period (Post-TAVR), and at 1-year after the procedure (1Y-TAVR) for left ventricular ejection fraction (B), mean systolic pressure gradient (C), and effective orifice area (D) for the matched ICE-MAC and TEE-GA groups.
GA = general anesthesia; ICE = intracardiac echocardiography; MAC = monitored anesthesia care; PVR = paravalvular regurgitation; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography.

procedural period and at 1-year follow-up also did not differ between groups. These findings suggest that ICE and TEE had similar safety and efficacy when used for guidance during TAVR.

The major roles of echocardiographic guidance during TAVR are to assess the function of the implanted valve and to detect potential post-procedural complications.[13] Currently, TTE is commonly used for TAVR performed under conscious sedation. However, TTE has several limitations, such as suboptimal image quality (especially in patients with obesity or chest deformity) and risk of contamination of the sterile operating field. In addition, TTE cannot provide continuous echocardiographic monitoring throughout TAVR procedure. Furthermore, TTE could underestimate PVR.[19][20] A registry study reported that intraprocedural TTE can miss nearly half of ≥mild PVR or underestimated PVR by ≥1 grade.[19] Another retrospective study comparing intraprocedural TEE and TTE reported that TTE-TAVR was associated with increased PVR-related events, leading to a concern regarding post-

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procedural PVR.[20] Since PVR can increase late mortality and morbidity, precise estimation of PVR is of considerable importance for long-term clinical outcomes after TAVR.[21] Thus, use of optimal intraprocedural echocardiographic guidance is essential, especially in patients at high risk of PVR, such as those with heavily calcified or bicuspid aortic valves.[22][23]

ICE can provide high-resolution real-time echocardiographic images without interrupting fluoroscopy, even during deployment of the THV. In contrast to TTE, ICE can be used under MAC, does not risk contamination of the operating field, and can avoid the limitations of image quality. In a small randomized clinical trial comparing ICE versus TEE in patients undergoing TAVR, ICE-derived annular measurements were closely correlated with pre-procedural TEE-derived measurements, and ICE reflected pre-procedural transvalvular pressure gradient better than TEE. Furthermore, probe repositioning during the procedure was required less frequently with ICE than with TEE, although the severity of PVR detected by intraprocedural ICE was comparable to that detected by TEE.[15] Our current findings of similar rates of significant PVR in the early post-procedural period and at 1-year after the procedure between groups despite less frequent post-dilation in the ICE-MAC group suggest that ICE guidance have avoided overestimation of post-procedural PVR and reduced balloon dilation after THV implantation, while not failing to detect significant PVR and achieving similar clinical outcome.

ICE catheter which has a diameter of 8–9 Fr inserted through venous system and manipulated inside cardiac chambers. For this reason, there is a potential risk of complications, such as vascular injury or pericardial effusion, which can result in cardiac tamponade. The incidence of these severe complications has been reported as 1–2%,[16] however, we observed none of these ICE-related complications in the current study. On the contrary, TEE can cause gastrointestinal bleeding secondary to mechanical injury. In a small prospective study of patients undergoing structural heart interventions using TEE, routine post-procedural esophagogastroduodenoscopy found a new injury in 86% of patients, of whom 40% had complex lesions.[24] Bleeding from esophageal injury is important, as it can be life-threatening in patients receiving antithrombotic agents. In a large retrospective study of patients undergoing transcatheter left atrial appendage closure procedures, ICE and TEE guidance were associated with similar rates of major complications.[25] However, ICE guidance was associated with a significantly lower rate of gastrointestinal bleeding (2.1% vs. 3.5%; p=0.02), while incidences of peripheral vascular complications were not different (2.8% vs. 1.8%; p=0.06). In the current study, post-procedural gastrointestinal bleeding was observed in 5 patients in the TEE-GA group and no patients in the ICE-MAC group. Thus, despite the invasive nature of the ICE device, complications do not seem to be increased by using ICE instead of TEE.

The ICE-MAC group in this study had a shorter hospital length of stay and a lower proportion of patients requiring ICU for >1 day, compared with the TEE-GA group. Likewise, the efficacy and safety of MAC during TAVR have been investigated in previous studies.[14][26-28] These studies consistently demonstrated that MAC is associated with a shorter procedural time, shorter hospital and ICU length of stay, and similar clinical outcomes, when compared with GA in patients undergoing TAVR. Accordingly, the shorter hospital and ICU stay of the ICE-MAC group observed in this study might be resulted from the difference in mode of anesthesia and patient factor affecting the selection of mode of anesthesia rather than the difference in echocardiographic modality.

Despite the apparent advantages of ICE, it has some drawbacks. First, ICE catheters are expensive and approved for only single use. The cost-effectiveness of ICE for TAVR should

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be assessed in future studies. Second, as with any new procedure, there is a learning curve for using ICE during TAVR. Operators must learn to maneuver the ICE catheter freely and to obtain optimal views.

This study has several limitations. First, it was a non-randomized study based on a single-center registry, resulting in an inherent risk of selection bias. The distribution of propensity score was largely skewed, which might result that about one-third of whole eligible patients were dropped out during PSM. Although the distribution of propensity score was almost identical after PSM, residual imbalances between matched groups for unassessed confounding factors may have affected our study results. Second, due to the limited number of patients included, the statistical power was not sufficient to discriminate the difference in clinical efficacy and safety between the two therapy strategies. Especially regarding the mortality outcome, a wide range of effects was observed, which was compatible with unclear clinical efficacy of ICE over TEE in terms of mortality. Third, the outcomes observed in the ICE-MAC group may reflect combined effects of both ICE and MAC. To investigate independent effects of ICE versus TEE, studies comparing ICE-guided and TEE-guided TAVR under the same mode of anesthesia are required. Fourth, the degree and distribution of calcification around the aortic valve were not evaluated in our analyses. Because the extent of calcification is one of the most important predictors of post-procedural complications and significant PVR, future studies considering the effects of calcification are warranted.

ICE was comparable to TEE in terms of the composite clinical efficacy outcome for guidance of TAVR, with similar incidences of moderate-to-severe PVR, new permanent pacemaker implantation, and major bleeding events. Our results suggest that ICE could be a safe and effective alternative echocardiographic modality to TEE for guiding TAVR procedures.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1
Serial echocardiographic parameters of the matched cohort before and after TAVR

Supplementary Figure 1
Distribution of propensity scores for the unmatched and matched cohorts.

Supplementary Figure 2
Hospital length of stay and proportion of patients requiring ICU for more than 1 day.

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