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ORIGINAL ARTICLE

Utility of preprocedural multidetector computed tomography in alcohol septal ablation for hypertrophic obstructive cardiomyopathy

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Abstract

Preprocedural computed tomography (CT) imaging appears to provide an advantage in localization of the appropriate septal branch targeted for alcohol septal ablation (ASA). The objective of this study was to compare the clinical backgrounds, procedural characteristics, and outcomes of patients who underwent ASA with preprocedural CT assessment against those without CT assessment. Thirty consecutive patients with obstructive hypertrophic cardiomyopathy who underwent ASA were retrospectively included. Patients who underwent preprocedural CT (CT-guided ASA group, $n=11$) were compared with patients who underwent ASA without CT (traditional ASA group, $n=19$). The CT-guided ASA group had a significantly lower number of approached target vessels (1 [interquartile range {IQR}, 1–2] vs. 2 [IQR, 2–3], $P=0.036$) and non-ablated target vessels (0 [IQR, 0–1] vs. 1 [IQR, 0–2], $P=0.031$) than the traditional ASA group. There were no differences between the two groups in total fluoroscopy time, the amount of delivered radiation dose, and the volume of contrast medium used during the procedures. There were also no differences between the two groups in procedural success rate and improvement of left ventricular outflow tract gradient and New York Heart Association functional class at 1 month follow-up. CT had a significant impact on the ASA procedure diminishing the number of target vessels, and could be a reliable assessment modality to build its procedural strategy.

Keywords Alcohol septal ablation · Computed tomography · Hypertrophic cardiomyopathy · Left ventricle outflow tract obstruction

Introduction

Alcohol septal ablation (ASA) is commonly performed as an alternative to surgical myectomy in patients with hypertrophic cardiomyopathy to reduce left ventricular outflow tract (LVOT) obstruction [1]. ASA has been shown to reduce the LVOT gradient by widening the outflow tract and to improve symptoms and long-term survival rates [1–5]. With this technique, alcohol is injected into the septal perforator, providing perfusion to the region of the basal septum at the point of mitral valve contact, which relieves left ventricular (LV) obstruction [6]. However, infarcts that are too small or are located outside the target myocardial territories may be predisposed to residual obstruction [7], and reintervention may be needed after ASA in about 9% of cases [2]. In contrast, a larger infarct size may be predisposed to complications such as arrhythmias, including complete heart block and ventricular tachycardia, or mitral insufficiency due to papillary muscle dysfunction [8, 9]. One of the keys to success of the procedure is to identify the appropriate target septal artery and to limit the area of myocardial necrosis to minimize the potential for undesired outcomes.

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Echocardiography with intracoronary contrast injection is commonly used during the procedure to explore the appropriate septal branch, but with this technique, it may be necessary to try many septal branches, resulting in more time spent and increased contrast volume and radiation dose [10]. The addition of preprocedural computed tomography (CT) imaging to conventional myocardial contrast echocardiography appears to provide an advantage in determining the appropriate septal branch targeted for ASA by providing details of the anatomy of the coronary arteries and the myocardial territories supplied; however, detailed data describing the advantages of CT-guided ASA are still limited [11, 12].

The purpose of the present study was to compare the demographic data, cardiovascular risk factors, medications, procedural characteristics, and outcomes of patients who underwent ASA with preprocedural CT assessment against those of patients without CT assessment.

Methods

Patient selection

Thirty consecutive symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM) who underwent a first ASA in the Sendai Kousei Hospital between November 2011 and December 2016 were included. Patients who had undergone ASA previously with unsatisfactory outcomes were excluded. Hypertrophic obstructive cardiomyopathy (HCM) was clinically diagnosed in the absence of any other cardiac or systemic disease that could produce a similar degree of hypertrophy such as hypertension, valve disease or restrictive cardiomyopathy, showing thickness of the LV septal wall (> 15 mm) in one or more LV myocardial segments on M-mode or 2D echocardiography and asymmetrical septal hypertrophy (septum to LV posterior wall thickness ratio > 1.3). However, patients with well-controlled hypertension were included in the present study. The indication of ASA was retained according to the European Society of Cardiology guidelines in patients with symptoms and LVOT obstruction of 50 mmHg at rest or after exercise despite optimal medical treatment. All patients provided written informed consent prior to undergoing any study procedures.

CT image acquisition and analysis

Coronary computed tomography angiography (CTA) was performed using a 320-detector row CT system (Aquilion ONE VISION edition, Toshiba Medical Systems, Tokyo, Japan). Electrocardiography (ECG)-gated volume scanning was performed using the following scanning parameters: tube voltage, 120 kV; tube current (modulated using volume EC), 10–750 ± 20 mA; rotation time, 0.275 s; slice thickness, 0.5 mm. By reconstructing the volumetric dataset every 10% of the cardiac cycle in ZIOSTATION 2 (Ziosoft, Tokyo, Japan), we could document systolic anterior motion of the mitral valve (SAM) throughout mid-to-late systole and the target myocardium for ASA at the mitral valve leaflet–septal contact in the LVOT view (Fig. 1a–f). Then, the fusion of two images, a three-dimensional volume rendering image of the coronary artery and a two-dimensional image of the myocardium, was reconstructed to assess septal arteries perfusing the target myocardium (Fig. 1g, h). To allow identification or rejection of a target vessel, all potential target vessels were followed, and the ultimate distribution was noted.

ASA procedure

A guiding catheter was engaged in the ostium of the left main coronary artery, and a coronary wire was passed into the target branch of the septal vessel, which was identified by CT in the CT-guided ASA group (Fig. 2). A 1.5–2.0-mm over-the-wire balloon was inflated in the ostium of the target vessel with subsequent agitated contrast injection for contrast myocardial echocardiographic studies. If the target cardium was contrasted, ethanol injection was started. If contrast was seen to travel to unexpected septum or untargeted territories, such as the right ventricular (RV) cavity or the LV papillary muscles, alcohol was not injected [13], and reselection of a target subbranch of the septal vessel or another septal branch was considered. Ethanol of 1–5 mL was injected into the artery supplying the culprit septal segments slowly at a rate of 0.3 mL/min and left in place for 5 min. If there was < 50% gradient reduction or if an LVOT gradient < 50 mmHg measured by transthoracic echocardiography (TTE) was not achieved, ablation of another septal perforator branch was considered. If complete heart block was present 48 h after the procedure, a permanent dual-chamber pacemaker was implant.

"Approached vessels" were defined as target vessels, wherein we tried to cross a guidewire or perform contrast myocardial echocardiography. We decided to approach the vessels referring the preprocedural CT assessment in the CT-guided ASA group (Fig. 2) and the intra-procedural angiography in the traditional ASA group. When we approached the same vessel twice, it was counted only once. "Non-ablated vessels" were defined as vessels technically inaccessible or supplying untargeted territories found by myocardial contrast echocardiography among the approached vessels. "Ablated vessels" were defined as vessels ethanol injection was performed. Therefore, the number of approached vessels was the sum of the number of non-ablated vessels and that of ablated vessels.

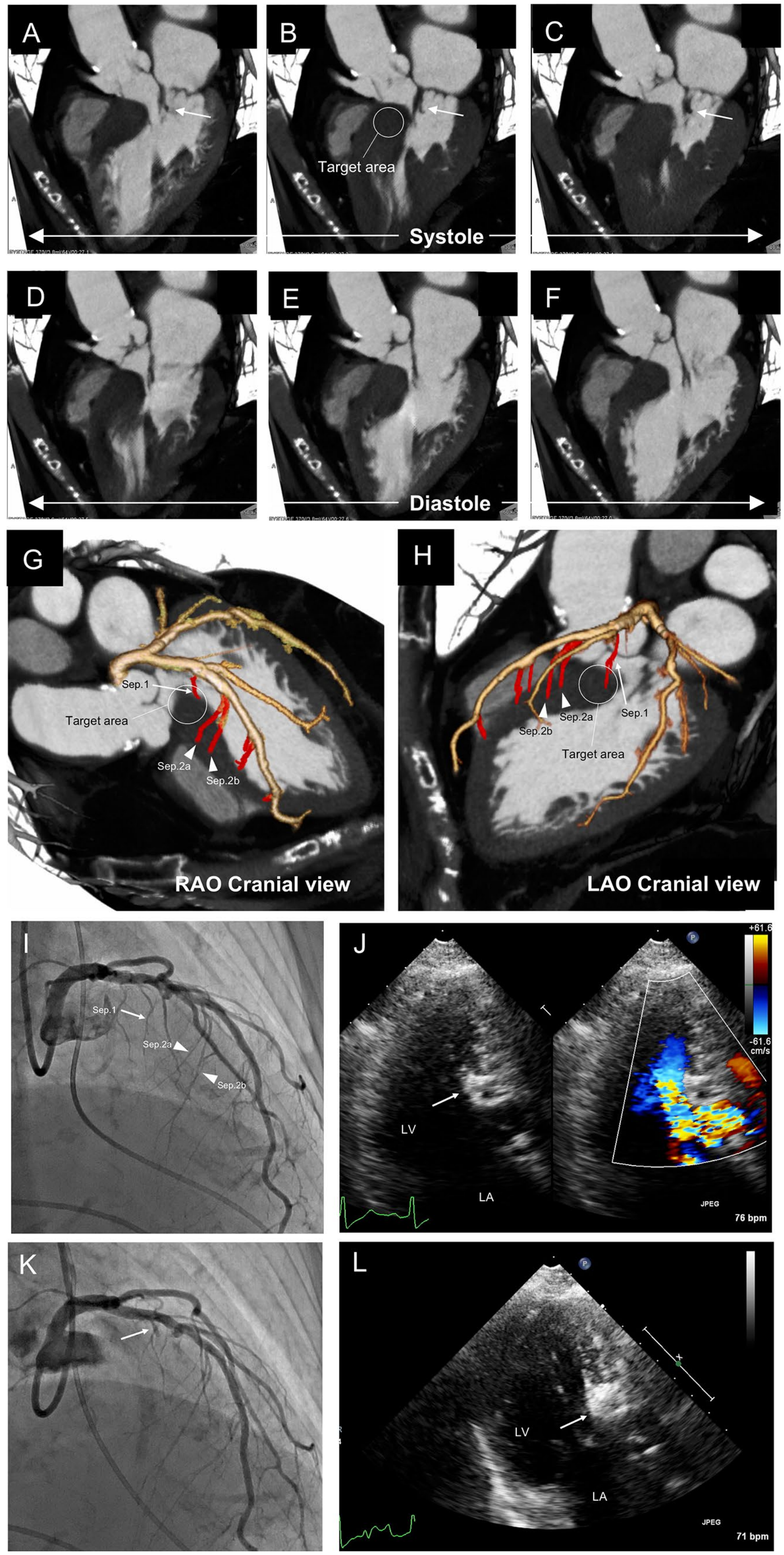
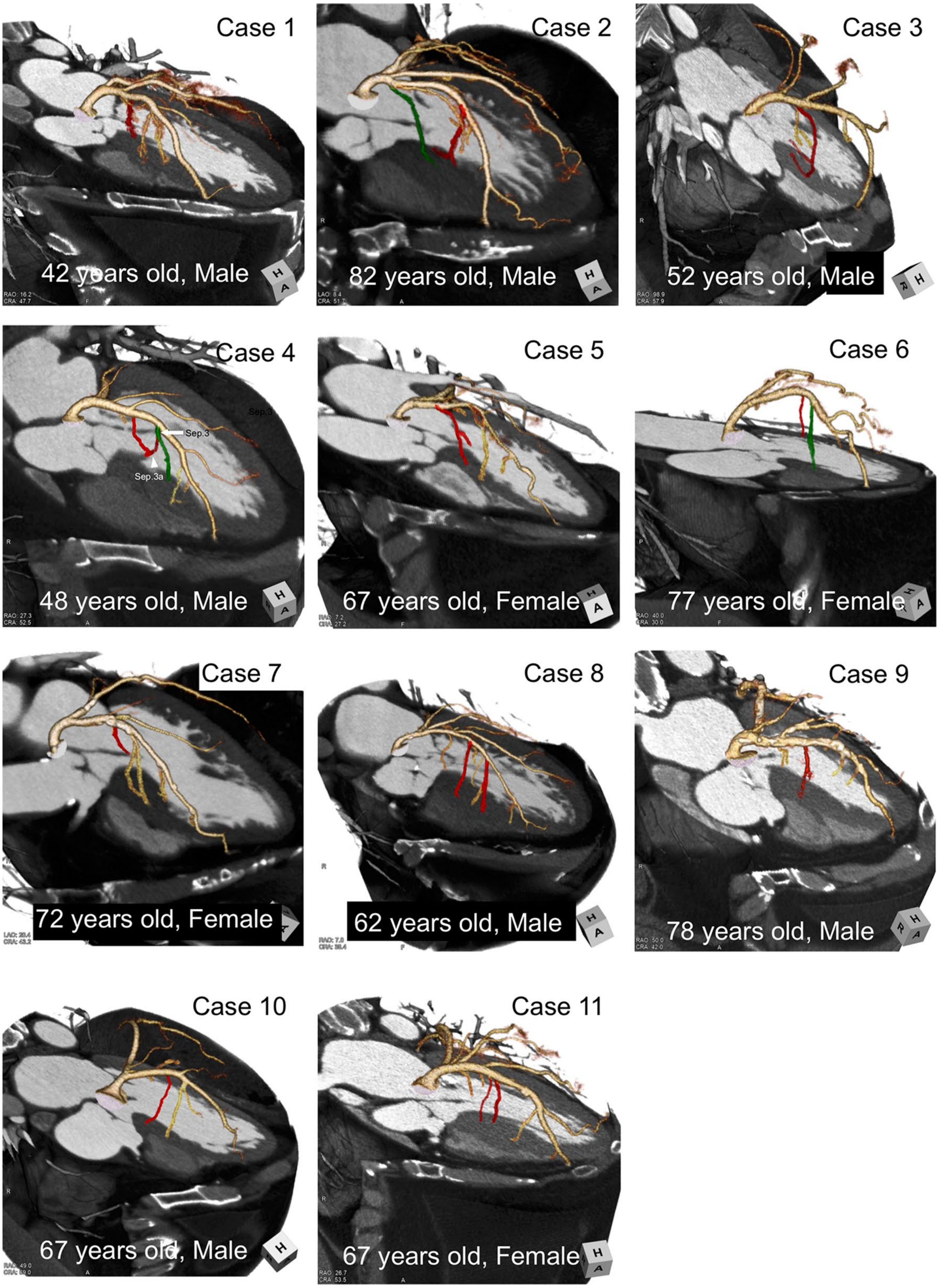


Fig. 1 Computed tomography-guided alcohol septal ablation procedure. **a**–**f** Moving image of mitral valve and LV myocardium throughout systole (**a**–**c**) and diastole (**d**–**f**) obtained by reconstructing the ECG-gated volumetric data set. We could document SAM of the mitral valve throughout mid-to-late systole (arrows in **a**–**c**) and the target myocardium at the mitral valve leaflet–septal contact (white circle in **b**). **g**, **h** Fusion of the three-dimensional volume rendering of the left coronary artery and the two-dimensional image of the myocardium in diastole. The target area of myocardium in the basal septum (white circles in **g**, **h**) was mainly perfused from the first septal artery (arrows in **g**, **h**), whereas it appeared that the second septal branch perfused the right-sided septal muscles or the LV papillary muscles (arrowheads in **g**, **h**). **i** Left coronary artery angiography showing the target first septal branch for alcohol septal ablation (arrow). **j** Myocardial contrast echocardiography study. Apical long-axis echo view just after contrast injection into the first septal artery; myocardial contrast was seen predominantly in the target septal myocardium (arrow). Then, 1.7 mL of alcohol was injected. **k** Final angiography showing disappearance of the target septal branch (arrow). **l** Transthoracic echocardiography just after alcohol was injected into the first septal artery; the target septal myocardium (arrow) was correctly ablated and the LVOT gradient decreased significantly (the pre- and postprocedural peak systolic gradients were 99 and 9 mmHg). *Sep. 1* first septal branch, *Sep. 2* second septal branch, *RAO* right anterior oblique position, *LAO* left anterior oblique position, *LV* left ventricle, *LA* left atrium



Follow-up

Procedural success was defined as the following composite endpoint: successful over-the-wire balloon delivery and ethanol infusion to any of the targeted septal perforators and achieving a resting LVOT gradient < 50 mmHg by TTE at discharge. Follow-up consisted of a functional and

◂**Fig. 2** Computed tomography images of all cases in the CT-guided ASA group. Fusion of the three-dimensional volume rendering of the left coronary artery and the two-dimensional image of the myocardium in diastole. "Ablated vessels" were marked red, and "non-ablated vessels" were marked green. The green-marked non-ablated vessels were dismissed as serving the right ventricle and the left ventricular papillary muscle found by myocardial contrast echocardiography in cases 2 and 6, respectively. In case 4, a 1.5-mm over-the-wire balloon was inflated in the ostium of the third septal branch with subsequent myocardial contrast echocardiography (Sep. 3: arrow); however, contrast traveled to not only the target myocardium but also the right ventricle. Thus, alcohol was not injected, and the target sub-branch of the septal vessel (Sep. 3a: arrow head) was reselected. *CT* computed tomography, *ASA* alcohol septal ablation, *Sep. 3* third septal branch

echocardiographic assessment and was performed 1 month after ASA.

Statistical analysis

Nominal variables were expressed as numbers and percentages. Continuous variables were expressed as mean ± standard deviation for non-skewed data and medians (interquartile range [IQR]) for skewed data. Binary variables were compared with the use of the Pearson Chi-square test or Fisher's exact test, as appropriate. Comparisons of continuous and ordinal variables were performed by two-sample *t* tests for non-skewed continuous data and Mann–Whitney *U* tests for skewed continuous or ordinal data. All statistical analyses were performed with JMP version 13.1 (SAS Institute, Cary, NC, USA), and $P < 0.05$ was considered to indicate statistical significance.

Results

From November 2011 to December 2016, a total of thirty patients with HOCM underwent a first ASA procedure in the Sendai Kousei Hospital. We performed ASA without CT assessment in the first 19 patients. Thereafter, we applied preprocedural CT assessment in the next 11 patients. We retrospectively compared patient characteristics, procedural data, and clinical and echocardiographic data at 1 month follow-up between the patients who underwent ASA with preprocedural CT assessment (CT-guided ASA, $n = 11$) and those of patients without CT assessment (traditional ASA, $n = 19$).

Patient characteristics

The demographic and echocardiographic characteristics of the two groups are summarized in Table 1. There were more males in the CT-guided ASA group (64% vs. 21%, $P = 0.047$), and patients in this group were taller compared with patients in the traditional ASA group (1.66 ± 0.11 vs. 1.56 ± 0.11 m, $P = 0.022$). Despite previous medical treatment, all patients had symptoms, with a balanced distribution of poor dyspnea (New York Heart Association [NYHA] class II) and severe dyspnea (NYHA class III and IV), with no difference between the two groups. Echocardiographic characteristics, including maximum LV wall thickness, LV ejection fraction, and LVOT obstruction at rest, did not differ between the two groups.

Procedural characteristics and outcomes

The CT-guided ASA group had a significantly lower number of approached vessels (1 [IQR, 1–2] vs. 2 [IQR, 2–3], $P = 0.036$) and non-ablated vessels (0 [IQR, 0–1] vs. 1 [IQR, 0–2], $P = 0.031$) than the traditional ASA group, whereas there was no difference between the traditional ASA and the CT-guided ASA group in the number of ablated vessels (1 [IQR, 1–2] vs. 1 [IQR, 1–2], $P = 1.000$) (Fig. 3). Of the 17 non-ablated vessels in the traditional ASA group, 5 vessels were not technically accessible, and 12 vessels were dismissed as supplying the RV or the LV papillary muscles, whereas all of the 3 non-ablated vessels in the CT-guided ASA group were dismissed as serving an incorrect area of myocardium.

There were no differences between the two groups in total fluoroscopy time, the amount of delivered radiation dose, and the volume of contrast medium used during the procedures (Table 2). The CT-guided ASA group had significantly lower peak creatine kinase (CK) levels than the traditional ASA group (552 ± 291 vs. 1012 ± 499 U/L, $P = 0.004$), while the total volume of injected alcohol did not differ between the two groups. Procedural success was achieved in 9 patients (82%) and 17 patients (89%) in the CT-guided ASA and the traditional ASA group, respectively ($P = 0.558$). Delivery of both over-the-wire balloons and alcohol infusion was successful in all cases, but two patients (18%) in the CT-guided ASA group and two patients (11%) in the traditional ASA group failed to achieve a pressure gradient < 50 mmHg at discharge. There was no difference between the two groups in the maximum LVOT gradient at 1 month follow-up: 24 mmHg (IQR, 14–43) in the CT-guided ASA group and 18 mmHg (IQR, 12–26) in the traditional ASA group ($P = 0.405$). All patients in the two groups achieved improvement in at least one NYHA functional class. No patients in the CT-guided ASA group and four patients (21%) in the traditional ASA group developed heart block requiring permanent pacemaker implantation ($P = 0.268$). No patients died or had any severe complication after procedures in both groups.

Table 1 Patient characteristics at baseline

Characteristic	CT-guided ASA ($n=11$)	Traditional ASA ($n=19$)	*P* value
Age (years)	67 (52–77)	71 (63–76)	0.464
Male sex—no. (%)	7 (64)	4 (21)	0.047
Weight (kg)	66 (58–77)	57 (50–70)	0.126
Height (m)	1.66 ± 0.11	1.56 ± 0.11	0.018
Body surface area (m^2)	1.75 (1.64–1.91)	1.53 (1.45–1.76)	0.058
Hypertension—no. (%)	9 (82)	15 (79)	1.000
Diabetes mellitus—no. (%)	1 (9)	4 (21)	0.626
Dyslipidemia—no. (%)	5 (45)	11 (58)	0.510
Current smoking—no. (%)	3 (27)	2 (11)	0.327
eGFR (mL/min)/1.73 m^2	63 ± 9.9	60 ± 14.0	0.521
CKD—no. (%)	4 (36)	10 (53)	0.466
Previous pacemaker or ICD—no. (%)	0 (0)	2 (11)	0.520
Medications—no. (%)			
Bisoprolol fumarate	7 (64)	8 (44)	0.450
Carvedilol	1 (9)	3 (17)	1.000
Atenolol	1 (9)	6 (33)	0.202
Verapamil hydrochloride	5 (45)	8 (42)	0.859
Cibenzoline succinate	9 (82)	14 (74)	1.000
Amiodarone hydrochloride	0 (0)	1 (6)	1.000
NYHA functional class—no. (%)			
II	7 (64)	12 (63)	0.979
III/IV	4 (36)	7 (37)	
Chest pain—no. (%)	1 (9)	4 (21)	0.626
Syncope—no. (%)	2 (18)	3 (16)	1.000
Maximum LV wall thickness (mm)	18 ± 3	19 ± 3	0.681
LV ejection fraction (%)	84 (76–89)	83 (76–86)	0.682
LVDD—mm	43 ± 6	41 ± 5	0.269
LVOT gradient at rest (mmHg)	81 ± 38	95 ± 42	0.359
LVOT gradient > 50 mmHg at rest—no. (%)	8 (73)	16 (84)	0.641

Obesity was defined as a body mass index (BMI) of 25 or above. Resting gradient was determined by echocardiography

ASA alcohol septal ablation, *CKD* chronic kidney disease, *CT* computed tomography, *eGFR* estimated glomerular filtration rate, *ICD* implantable cardioverter–defibrillator, *LV* left ventricular, *LVDD* left ventricular end-diastolic dimension, *LVOT* left ventricular outflow tract, *NYHA* New York Heart Association

Discussion

This report documents the use of ECG-gated multidetector CT in noninvasive dynamic evaluation of HOCM patients prior to ASA. The major findings of the study are as follows: the CT-guided ASA group had a significantly lower number of approached vessels and non-ablated vessels than the traditional ASA group (Fig. 3); the CT-guided ASA group had significantly lower peak CK levels than the traditional ASA group; and there were no differences between the two groups in the procedural success rate and improvement of the LVOT gradient and NYHA functional class at 1-month follow-up.

Preprocedural CT assessment: how to identify the target septal artery

We propose a two-staged approach to identifying the target septal artery for ASA using CT. First, ECG-gated CT enables us to create the moving image of mitral valve and LV myocardium throughout cardiac cycle, and we can document the degree and exact location of interventricular septal hypertrophy, SAM, and mitral valve leaflet–septal contact (Fig. 1a–f). This allows us to determine the target myocardial territories for ablation. Then, a three-dimensional volume rendering image of the coronary arteries and a two-dimensional image of the myocardium in diastole are fused

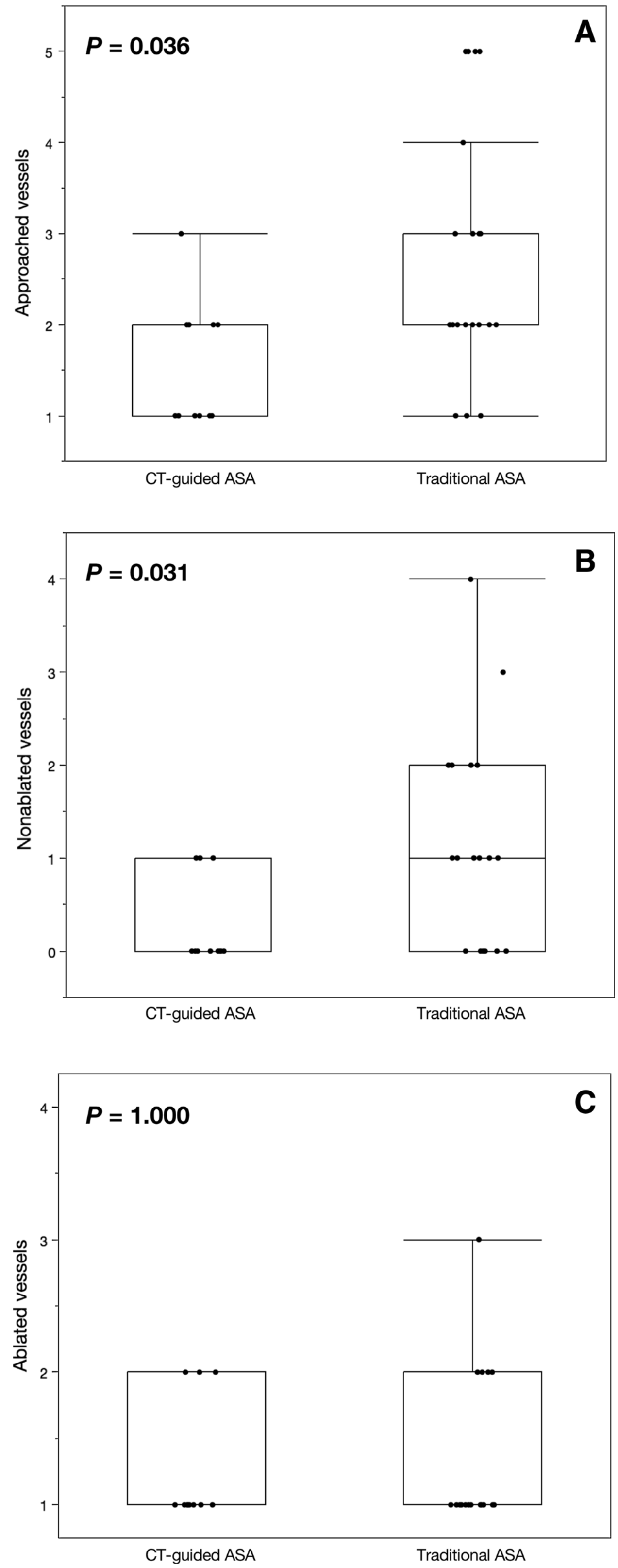


Fig. 3 Box-and-whisker plot of numbers of approached vessels, non-ablated vessels, and ablated vessels in the two groups. The CT-guided ASA group had a significantly lower number of approached vessels (1 [interquartile range {IQR}, 1–2] vs. 2 [IQR, 2–3], $P=0.036$) (**a**) and non-ablated vessels (0 [IQR, 0–1] vs. 1 [IQR, 0–2], $P=0.031$) (**b**) than the traditional ASA group. There was no difference between the two groups in the number of ablated vessels (1 [IQR, 1–2] vs. 1 [IQR, 1–2], $P=1.000$) (**c**). CT = computed tomography; ASA alcohol septal ablation

into a single image to assess the spatial relationship between the septal branches and the target myocardial territories. Thus, we can select the target septal artery and determine the feasibility of ASA (Fig. 1g, h). In this study, we ascertained whether all the target septal arteries selected by the preprocedural CT assessment actually perfused the target myocardial territories or not, using intraoperative contrast echo studies.

The left anterior descending (LAD) coronary artery does not always supply the target basal septum. The circumflex artery, the intermediate artery, and the right coronary artery can be parent vessels for the appropriate septal arteries. A previous study reported that the target vessel did not originate from the LAD in 5 of the 59 patients [14]. Using CT, we can also track the appropriate vessel for ASA back to its parent artery, whereas these patients may be dismissed as not having an appropriate artery with the use of traditional ASA.

CT assessment diminishes the number of approached vessels

Traditional teaching for alcohol ablation is to site an over-the-wire balloon at the ostium of the septal artery with subsequent contrast injection and echocardiographic studies. A septal artery may have many branches involving both targeted and untargeted ventricular myocardium. If contrast is seen to travel to untargeted myocardial territories, including the RV cavity or the LV papillary muscles, reselection of the subbranch of the septal vessel that supplies the target myocardial area or another septal branch is considered [13]. The addition of preprocedural CT assessment to conventional echocardiography provides an advantage in reselection of the appropriate target subbranch. Moreover, ECG-gated CT enables adequate delineation of the origin of the angulated vessel, and preprocedural assessment of whether the target vessel is technically accessible. If the target vessel was extremely angulated, we did not try to approach the vessel. Thus, in the present study, we could reduce the number of approached vessels and non-ablated vessels in the CT-guided ASA group compared with the traditional ASA group. However, there were no differences between the two groups in total fluoroscopy time, the amount of delivered radiation dose, and the volume of contrast medium used during the procedures. Such parameters may be affected by interoperator variability and the single-operator learning curve, and further prospective multicenter studies in a larger population comparing CT-guided ASA with traditional ASA

Table 2 Procedural characteristics and outcomes

Characteristic	CT-guided ASA ($n=11$)	Traditional ASA ($n=19$)	P value
Total fluoroscopy time (min)	31.9 (26.2–64.5)	28.8 (18.5–49.9)	0.242
Delivered radiation dose (mGy)	1170 (609–1707)	908 (610–1354)	0.731
Volume of contrast medium used (mL)	221 (196–373)	200 (155–255)	0.217
Total volume of injected alcohol (mL)	1.4 (1.2–2.7)	1.6 (1.2–2.7)	0.488
Peak CK (U/L)	552 ± 291	1012 ± 499	0.004
Peak CK/septal thickness (U/L per cm)	278 (207–492)	476 (338–740)	0.031
Hospital stay period (days)	7 (6–8)	8 (6–11)	0.175
Procedural success—no. (%)	9 (82)	17 (89)	0.611
Permanent pacemaker requirement—no. (%)	0 (0)	4 (21)	0.268
LVOT gradient at 1-month follow-up (mmHg)	24 (14–43)	18 (12–26)	0.405
LVOT gradient > 50 mmHg at 1-month follow-up—no. (%)	2 (18)	2 (11)	0.611
NYHA class improvement at 1-month follow-up—no. (%)	11 (100)	19 (100)	–

Procedural success was defined as the following composite endpoint: successful ethanol infusion to targeted septal perforators and achieving a resting LVOT gradient < 50 mmHg by transthoracic echocardiography (TTE) at discharge. NYHA class improvement was defined as improvement in at least one NYHA functional class

ASA alcohol septal ablation, *CK* creatine kinase, *CT* computed tomography, *LVOT* left ventricular outflow tract, *NYHA* New York Heart Association

are needed. Furthermore, we should take into consideration the radiation exposure dose and the amount of contrast medium used in preprocedural CT imaging, when deciding the indication of CT-guided ASA. The present CT-guided ASA group ($n=11$) revealed a median dose-length product (DLP) of 1794 mGy × cm [IQR, 1670–2443 mGy × cm], which corresponds with an estimated effective radiation dose of 25 mSv [IQR, 23–34 mSv], applying the conversion factor of 0.014 $\text{mSv} \times (\text{mGy} \times \text{cm})^{-1}$ for dose estimation, and a contrast medium volume of 64 mL [IQR, 63–76 mL].

The CT-guided ASA group had lower peak CK levels than the traditional ASA group

One possible explanation for the lower peak CK levels in the CT-guided ASA group is improvement of the accuracy of iatrogenic infarct location. A previous study from Willem and colleagues evaluating myocardial infarction after ASA using contrast-enhanced magnetic resonance imaging pointed out that cardiac enzyme release was correlated with the quantified infarction size and septal mass reduction [15]. This finding indicates that in our present study, the size of the infarct was smaller in the CT-guided ASA group than in the traditional ASA group, whereas the procedural success rate and the amount of LVOT gradient reduction did not differ between the two groups. Thus, in the CT-guided ASA group, more targeted ablation of the LV myocardium might create significant reductions in the LVOT gradient and SAM with minimal change in the size of the septum. However, we considered that this was not only by virtue of the CT assessment because we ascertained whether all the target septal arteries selected by the preprocedural CT assessment actually perfused the target myocardial territories or not using intraoperative contrast echo studies, and finalized the target septal artery to be ablated not by CT but by myocardial contrast echocardiography.

Notably, four patients (21%) in the traditional ASA group developed heart block requiring permanent pacemaker implantation, whereas no patient in the CT-guided ASA group required permanent pacemaker implantation. The difference between the groups does not reach statistical significance, but we considered that the reduction in the incidence of heart block requiring permanent pacemaker implantation might also be indicative of the selective ablation.

Study limitations

Our data should be interpreted in light of the study limitations. First, this is a small, nonrandomized, observational, single-center study with a short follow-up duration. Second, strategic decision making in the procedure (such as changing the target vessel) depended on the subjective feelings of the operators. Inter-operator variability and the single-operator learning curve for the ASA were not taken into consideration, while the procedures were performed by one of the several interventional cardiologists with over 10 years of experience with percutaneous coronary intervention. Third, we did not have adequate detailed data regarding the CK isoenzyme MB value. The peak CK value may not precisely reflect the amount of myocardial necrosis. At last, we cannot exclude completely the possibility that this study includes LVOT obstruction due to long-standing hypertension or sigmoid septum, because the mean age of the study patients is relatively high compared to those of previous studies and patients with well-controlled hypertension were included in the present study.

Conclusion

The present study implies that pre-procedural CT assessment improves the ASA procedure, diminishing the number of target vessels. Although the small sample size of our report is a major limitation and a larger study should be performed to confirm our findings, CT could be a reliable assessment modality to build procedural strategy for ASA.

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