




openheart Individualised left anterior oblique projection for lead implantation into interventricular septum

Taro Narumi , Yoshihisa Naruse , Yutaro Kaneko, Tomoaki Sakakibara, Makoto Sano, Satoshi Mogi, Kenichiro Suwa , Hayato Ohtani, Tsuyoshi Urushida, Masao Saotome, Yuichiro Maekawa

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/openhrt-2022-002009>).

To cite: Narumi T, Naruse Y, Kaneko Y, *et al.* Individualised left anterior oblique projection for lead implantation into interventricular septum. *Open Heart* 2022;**9**:e002009. doi:10.1136/openhrt-2022-002009

Received 5 March 2022

Accepted 25 July 2022

ABSTRACT

Objective We sought to investigate whether it is possible to obtain individualised left anterior oblique (LAO) by preprocedural electrocardiographic parameters and, if so, whether these parameters can help to improve the success rate of right ventricular (RV) lead implantation into the interventricular septum.

Methods In this observational study, we assessed the relationship between preoperative electrocardiographic parameters and the angle of the interventricular septum obtained using thoracic CT. The participants were divided into two groups: a retrospective derivation cohort to derive the optimal formula for the individual septum axis, and a prospective internal validation cohort to which we applied the optimal formula and implanted using the new method.

Results In the retrospective derivation cohort (n=39), the mean angle of individualised LAO assessed by thoracic CT was $53.1^{\circ} \pm 8.9^{\circ}$, and the preoperative ECG QRS axis was strongly correlated with the interventricular septum axis ($R^2=0.490$). LAO projection derived from the preoperative ECG QRS axis confirmed that the RV lead was placed in the interventricular septum during the pacemaker procedure in the prospective internal validation group (n=30). The success rate for placing the RV lead into the interventricular septum was significantly improved in the internal validation cohort (93% vs 64%, $p<0.05$). In addition, the N-terminal pro-brain natriuretic peptide level decreased significantly after surgery in the interventricular septal indwelling group.

Conclusions Individualised LAO angle derived from the preoperative ECG QRS axis is a new useful and simple method for RV lead implantation into the interventricular septum.

Trial registration number UMIN000045741.

INTRODUCTION

Some clinical studies have reported that dyssynchronous contraction related to right ventricular (RV) apex pacing aggravates left ventricular (LV) function and leads to pacing-induced heart failure.^{1 2} These results have led to the development of an alternate pacing site (non-RV apex) for the RV apex.^{3 4} These include the interventricular septum (upper septum, middle septum and lower septum)

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ The interventricular septum is preferred to the apex for the placement of right ventricular (RV) leads, as it results in a better prognosis with fewer complications; however, with the conventional method, the success rate of RV leads implanted into the septum is low.
- ⇒ Individualised left anterior oblique (LAO) has been reported to improve the success rate of RV lead placement in the interventricular septum; however, there are concerns regarding the complexity of the procedure.

WHAT THIS STUDY ADDS

- ⇒ Prediction of individualised LAO using the QRS axis of the preoperative ECG dramatically increased the success rate of interventricular septal placement of RV leads, without any complexity.
- ⇒ The cardiac load was significantly reduced in the group in which the RV lead was implanted into the interventricular septum.

HOW THIS MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ With the results of this study, it is hoped that patients undergoing new pacemaker implantation procedures in the future will be able to have the lead safely and non-invasively implanted in a precise position.

and RV outflow. The RV lead is commonly placed in the interventricular septum with a spread of screw-in lead.

Several methods have been used to place leads in the RV septum. One method is to confirm the presence of the interventricular septal lead implantation by ECG.^{5 6} When a lead is implanted in the inferior septum or RV free wall, the QRS width on the ECG is narrower than that resulting from RV apex pacing but wider than the QRS width via the normal conduction pathway. The QRS width during interventricular septal pacing is around 150 ms. It is also reported that the QRS waveform in ECG I lead appears positive.



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Department of Internal Medicine III, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan

Correspondence to

Dr Yoshihisa Naruse; ynaruse@hama-med.ac.jp

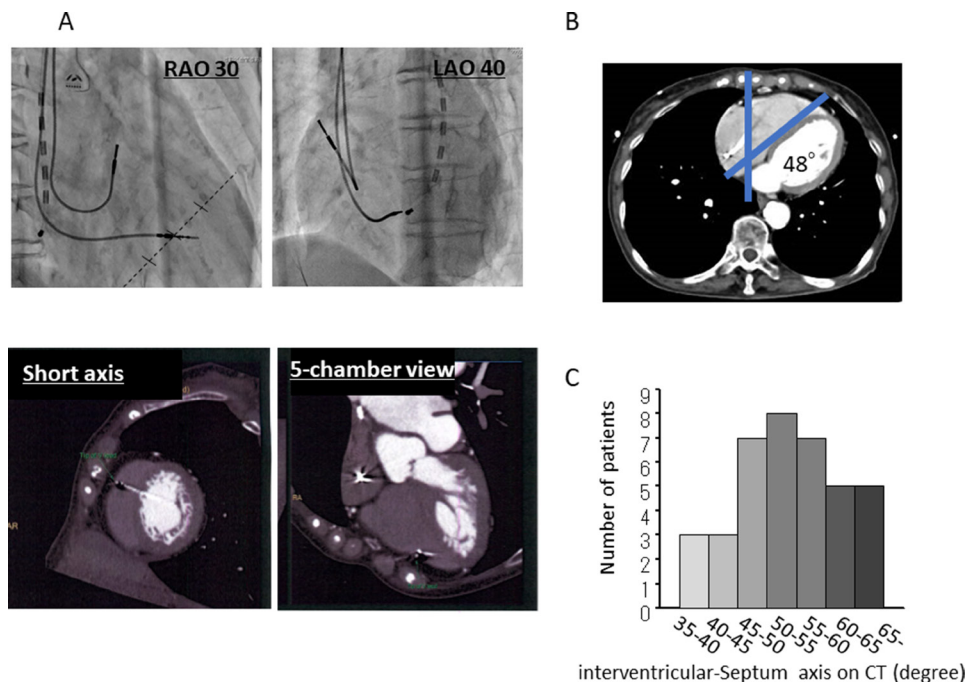


Figure 1 Representative non-septum RV lead implantation and interventricular septum angle on CT. (A) Representative figure of non-septum RV lead implantation. Fluoroscopic images make it seem that RV lead is implanted in the interventricular septum. However, postoperative thoracic CT confirmed that the RV lead is placed in the RV free-wall. (B) In the slice image showing the interventricular septum, a perpendicular line was drawn towards the spine, and the angle of intersection with the straight line drawn towards the interventricular septum was defined as the angle of the individualised LAO. (C) The distribution of degree of individualised LAO, assessed by thoracic CT. LAO, left anterior oblique; RAO, right anterior oblique; RV, right ventricle.

Therefore, this method may be used to confirm whether the QRS waveform is isoelectric or negative in ECG I lead guidance during interventricular pacing. However, the fact that the waveform is not isoelectric or negative does not mean that the RV lead has not been implanted in the interventricular septum.⁵ This is not a reliable method of RV lead implantation. Another method is to use conventional fluoroscopic guidance. Previous reports have shown that the RV lead is accurately placed in the interventricular septum in only 16%–48% of cases when using conventional fluoroscopic guidance.^{4–7} Although the use of right anterior oblique (RAO) projection in addition to the left anterior oblique (LAO) projection helps to distinguish the RV septum from the non-septum,⁵ we experienced a case of RV lead on the RV free wall, despite confirmation of lead implantation into the interventricular septum by both RAO and LAO projections (figure 1A). Recently, Squara *et al* reported the importance of individualised LAO to improve the success rate of RV lead placement in the interventricular septum.^{8,9} Individualised LAO can be calculated using the superior vena cava (SVC)-inferior vena cava (IVC) guidewire and apical RV lead during the pacemaker implantation procedure or by thoracic CT. We hypothesised that preprocedural electrocardiography could be a useful tool to predict individualised LAO.

By assessing the relationship between the preoperative electrocardiographic parameters and the angle of the interventricular septum obtained by CT, we examined whether it is possible to obtain individualised LAO by

preprocedural electrocardiographic parameters and, if so, whether these parameters can help to improve the success rate of RV lead implantation into the interventricular septum.

METHODS

Patient and public involvement

Between January 2016 and April 2021, 181 consecutive patients were admitted to the Hamamatsu University Hospital for treatment of complete atrioventricular block, advanced atrioventricular block, sick sinus syndrome and/or brady-atrial fibrillation to implant a pacemaker. The diagnosis and indication of pacemaker implantation were determined by at least two board-certified cardiologists. The participants were divided into two groups according to the period of admission, from 2016 to 2019 (n=147) and from 2020 to 2021 (n=54). The first group was a retrospective derivation cohort group to derive the optimal formula for the individual septum axis. The other group was a prospective internal validation cohort to which we applied the optimal formula and implanted using the new method. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Electrocardiographic analysis

Patients with a wide QRS complex on ECG were excluded from the analysis. Every patient whose ECG on

admission had wide QRS complex was asked for ECGs recorded before admission. Junctional escape beats with a narrow QRS complex were considered acceptable for analysis of the QRS axis and transition zone. We evaluated the last 12-lead ECG recorded before pacemaker implantation with a narrow QRS complex, and the QRS axis was calculated using the following equation: $QRS\ axis = \tan^{-1} [3(II+III)/(2I+II-III)]$. The I, II and III in the equation are the sum of the maximum amplitudes of the Q, R, S, R' and S' waves for each induction. The transition zone was scored based on previous reports.^{10,11} Additionally, we evaluated the paced QRS duration 1 week after pacemaker implantation.¹²

Retrospective derivation cohort and prospective internal validation cohort

In the retrospective derivation cohort group, 47 patients had no preoperative ECG with a narrow QRS complex, and 61 patients did not undergo thoracic CT after pacemaker implantation. The remaining 39 patients were included in this study. In the internal validation cohort group, preoperative ECG with sinus rhythm and postoperative thoracic CT were not available in 10 and 14 patients, respectively. The remaining 30 patients were included in this study.

Evaluation of lead location and axis of the septum using thoracic CT

Thoracic CT was performed using a 128-slice CT scanner (SOMATOM Definition Flash, Siemens, Tokyo, Japan). A total of 51–100 mL of contrast media (Iopamidol, Bayer, Leverkusen, Germany) was injected at a flow rate of 3.04.6 mL/s depending on the patient's body weight. The interventricular septum axis was measured using thoracic CT after pacemaker implantation (figure 1B). In the slice image showing the interventricular septum, a perpendicular line was drawn towards the spine, and the angle of intersection with the straight line drawn towards the interventricular septum was defined as the angle of the individualised LAO (figure 1B; Ziostation 2, Ziosoft Japan, Tokyo, Japan).

Pacemaker operation

Pacemaker implantation was performed by a board-certified cardiologist. In the retrospective derivation cohort group identification of the location of the RV lead was performed according to conventional methods.^{4,5} In brief, the position of the RV lead was the LAO projection 30°–40° fluoroscopic view, which is thought to show the heart along its long axis and thus offers a profile view of the interventricular septum, and RAO projection of 30° to avoid placement near the anterior edge of the RV, divide the cardiac shadow into four equal parts and avoid placing the lead in the upper 1/4.⁵ In contrast, in the prospective internal validation cohort group, only individualised LAO, the previously reported CT findings and calculations from SVC-IVC guidewire and apical RV lead intraoperatively were not used, and RAO projections of

30° were used. The generator was connected, inserted in a pocket, and the skin was sutured to complete the procedure. Lead placement was performed with a guide sheath in some cases and a stylet in others (tables 1 and 2). The stylet was manually shaped by the surgeon, and no preshaped or steerable stylet was used.

Short-term efficacy of true interventricular septum RV lead implantation

To investigate the effect of interventricular septum RV lead placement on cardiac load assessed by serum N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, complete atrioventricular block patients were extracted from all participants to eliminate the effect of cumulative percent ventricular pacing. NT-proBNP was measured along with other biomarkers on admission, the day before surgery. It was measured again 5–7 days after surgery. Briefly, serum NT-proBNP was measured using a commercially available electrochemiluminescence assay (Elecys, Roche Diagnostics, Tokyo, Japan).

Statistical analysis

Data are presented as the mean±SD. If the data were not normally distributed, they are presented as the median and IQR. The unpaired Student's t-test and the χ^2 test were used for between-group comparisons for continuous and categorical variables, respectively. The Mann-Whitney U test was used when the data were not normally distributed. A paired t-test was used for comparison between the two corresponding groups. Correlations were assessed using the Pearson's product-moment correlation coefficient. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using a standard statistical programme package (JMP V.10; SAS Institute, Cary, North Carolina, USA).

RESULTS

Retrospective derivation cohort characteristics

The baseline characteristics of the patients are shown in table 1. There were 26 men (68%), and the mean age was 72±10 years. The median serum NT-proBNP level was 395 pg/mL (IQR –143–1334 pg/mL). During the procedure, 24 cases were implanted with LAO projection of below 40°, and 15 cases were implanted with LAO projection of 40°. In all these cases, interventricular septal placement was confirmed using fluoroscopy. However, postoperative assessment by thoracic CT showed a success rate of septal placement of 64% (25 cases). There was no significant difference in the utilisation rate of the delivery catheter (SelectSecure MRI SureScan, Medtronic Japan, Tokyo, Japan; 8% vs 7%, $p = 0.87$). The mean degree of individualised LAO assessed by thoracic CT was 53.1°±8.9°. LAO of 40° was insufficient in 32 (84%) patients with respect to the individualised LAO obtained from postoperative thoracic CT. The distribution of the degree of individualised LAO assessed by thoracic CT is shown in figure 1C. The difference in the angle of the interventricular septum measured by thoracic CT and LAO angle

Table 1 Retrospective derivation cohort characteristics

	All patients (n=39)	Septum group (n=25)	Non-septum group (n=14)	P value
Age, years	72±10	74±9	69±11	0.13
Male, n (%)	26 (68)	15 (71)	9 (81)	0.22
Body mass index, kg/m ²	22.2±4.1	22.4±4.3	21.8±3.9	0.65
Aetiology, n (%)				0.45
Sick sinus syndrome	15 (38.5)	9 (36)	6 (43)	–
Advanced atrioventricular block	5 (13)	4 (16)	1 (7)	–
Complete atrioventricular block	15 (38.5)	10 (40)	5 (36)	–
Brady-atrial fibrillation	4 (10)	2 (8)	2 (14)	–
Blood biomarkers				
Blood urea nitrogen, mg/dL	19.1±6.3	18.3±6.8	20.6±5.2	0.29
Creatinine, mg/dL	0.93 (0.76–1.12)	0.89 (0.73–1.08)	0.99 (0.86–1.19)	0.62
Haemoglobin, g/L	129.5 (116.0–140.0)	127.0 (113.0–139.3)	139.0 (114.3–145.5)	0.58
NT-proBNP, pg/dL	395 (134–1334)	362 (142–1200)	428 (205–1991)	0.56
Echocardiographic data				
Left ventricular ejection fraction, %	63±12	62±15	65±6	0.49
LVDd, mm	47±6	47±5	48±7	0.56
LVDs, mm	31±7	31±7	31±7	0.85
Paced QRS duration, ms	133±22	120±6	157±24	<0.05
Utilisation of delivery catheter, n (%)	3 (8)	2 (8)	1 (7)	0.87
LAO angle confirmed septal placement by procedure, LAO 40°/LAO under 40°	15/24	7/18	8/6	0.77
Deviation between the confirmation angle at the time of surgery and the actual angle on thoracic CT, degrees	10 (6–17)	8 (5–13)	19 (16–22)	<0.05

Data are presented as the mean±SD, median (IQR) or %.

LAO, left anterior oblique; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; NT-proBNP, N-terminal pro-brain natriuretic peptide.

during pacemaker implantation surgery was significantly different between the septum and non-septum groups ($p<0.05$; [table 1](#)).

Correlation between preoperative ECG QRS axis and interventricular septum angle

The preoperative ECG QRS axis was strongly correlated with the interventricular septum axis detected by cardiac CT ($R^2=0.490$, $p<0.05$; [figure 2](#) and online supplemental figure 1). The formula for calculating one's individualised LAO was LAO (degrees) = $56.96 - 0.121 \times$ preoperative ECG QRS axis (degrees). In contrast, the preoperative electrocardiographic transitional zone was not associated with the interventricular septum axis ($R^2=0.041$, $p=0.78$, online supplemental figure 2).

Internal validation cohort

To examine whether the interventricular septum angle derived from the preoperative ECG QRS axis is useful, an internal validation cohort was designed ([table 2](#)). As shown in [figure 3](#), pacemaker surgery was performed using the interventricular septum angle derived from

the preoperative ECG as the intraoperative individualised LAO projection (online supplemental figure 3 shows examples of various axes and corresponding changes in the septal angulation). Although the use of the delivery catheter system did not increase, the success rate for RV lead implantation into the interventricular septum was significantly improved in the internal validation cohort compared with the retrospective derivation cohort (93% vs 66%, $p<0.05$, [figure 4](#)). The difference between the angle of the interventricular septum measured by thoracic CT and the individualised LAO obtained from the preoperative ECG QRS axis in the internal validation cohort group was -1.5° (IQR: -5.3° – 2.4°). Interventricular septal placement was impossible in two cases in which the RV lead operation was difficult due to the severe meandering of the innominate vein, and the interventricular septal LAO confirmed by postoperative thoracic CT had an error of 10° or more from the individualised LAO.

Table 2 Internal validation cohort characteristics

	All patients (n=30)
Age, years	78±13
Male, n (%)	18 (60)
Body mass index, kg/m ²	22.1±3.6
Aetiology, n (%)	
Sick sinus syndrome	14 (47)
Advanced atrioventricular block	10 (33)
Complete atrioventricular block	6 (20)
Brady-atrial fibrillation	0 (0)
Blood biomarkers	
Blood urea nitrogen, mg/dL	21.7±13.9
Creatinine, mg/dL	0.97 (0.73–1.13)
Haemoglobin, g/L	120.5 (109.0–132.0)
NT-proBNP, pg/dL	356 (125–936)
Echocardiographic data	
Left ventricular ejection fraction, %	62±9
LVDd, mm	47±7
LVDs, mm	31±6
Paced QRS duration, ms	123±24
Utilisation of delivery catheter, n (%)	3 (10)
Deviation between the ECG-derived individualised LAO and the actual interventricular septum angle on thoracic CT, degrees	-1.5 (-5.3–2.4)

Data are presented as the mean±SD, median (IQR) or %. LAO, left anterior oblique; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Short-term effect of true interventricular septum RV lead implantation

Of the cases analysed in this study, 24 had complete atrioventricular block. Of these, 18 cases had the RV lead implanted into the interventricular septum, and 6 into the non-interventricular septum. There was no significant difference in the use of diuretics between the septal and non-septal groups (33% vs 28%, $p=0.88$) and in the distribution of New York Heart Association functional classes I/II/III and IV (16 (64)/7 (28)/2 (8) vs 8 (57)/4 (29)/2 (14), $p=0.63$). In the septal indwelling group, postoperative NT-proBNP levels were significantly reduced (538 (133–2907) pg/mL to 323 (160–721); [figure 5](#), $p<0.05$). Conversely, postoperative NT-proBNP levels were significantly increased in the non-septal indwelling group (871 (320–1860) pg/mL to 1507 (597–4088); [figure 4](#), $p<0.05$). Although preoperative NT-proBNP levels did not differ between the two groups, the per cent change in NT-proBNP level was significantly reduced in the group in which the RV lead was implanted into the interventricular septum (50.5% vs 210%, $p<0.05$).

DISCUSSION

In the present study, we clearly demonstrated that the interventricular septum angle derived from the preoperative ECG dramatically improved the success rate of RV lead implantation into the interventricular septum compared with the conventional method of fluoroscopic guidance. In addition, the NT-proBNP level decreased significantly after surgery in the interventricular septal indwelling group.

Although ventricular septal pacing is widely performed with fluoroscopic guidance, the success rate of septal placement is not high when verified by CT. Moreover, unexpected free wall pacing worsens the prognosis,⁶ placement outside the ventricular septum increases the risk of perforation of the RV free wall,¹³ and it is therefore important to establish a methodology for reliable interventricular septal lead placement. One report has claimed that the conventional LAO projection of 40° is not sufficient and the cut-off value of LAO projection is 80°.¹⁴ However, since a large LAO angle could reduce the negative predictive value, an LAO projection of 80° appears to be unsuitable. The concept of individualised LAO projection was first proposed in 2018, and the method of determining individualised LAO projection according to the positional relationship between the SVC and IVC guidewire and the apical RV lead during pacemaker implantation is a logical method.⁸ Hence, the use of individualised LAO projection improves the success rate of interventricular septal RV lead implantation compared with the classical method (89% vs 40%).⁸ That said, it is necessary to place the wire in the IVC during the operation and temporarily place the RV lead in the apex, which is a complicated procedure that could result in a long procedural and fluoroscopic time. A complicated procedure is a risk factor for cardiovascular implantable electronic device infections.¹⁵ In contrast, the new procedure

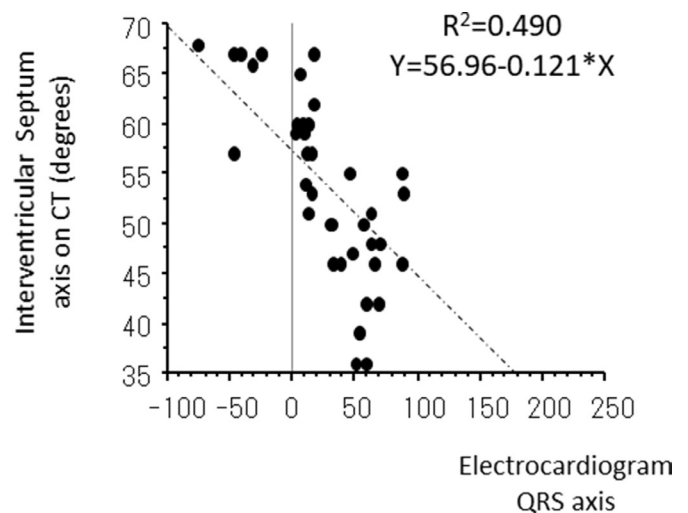


Figure 2 The association between preoperative ECG QRS axis and interventricular septum angle on cardiac CT. The preoperative ECG QRS axis and interventricular septum angle measured by CT showed a strong correlation.

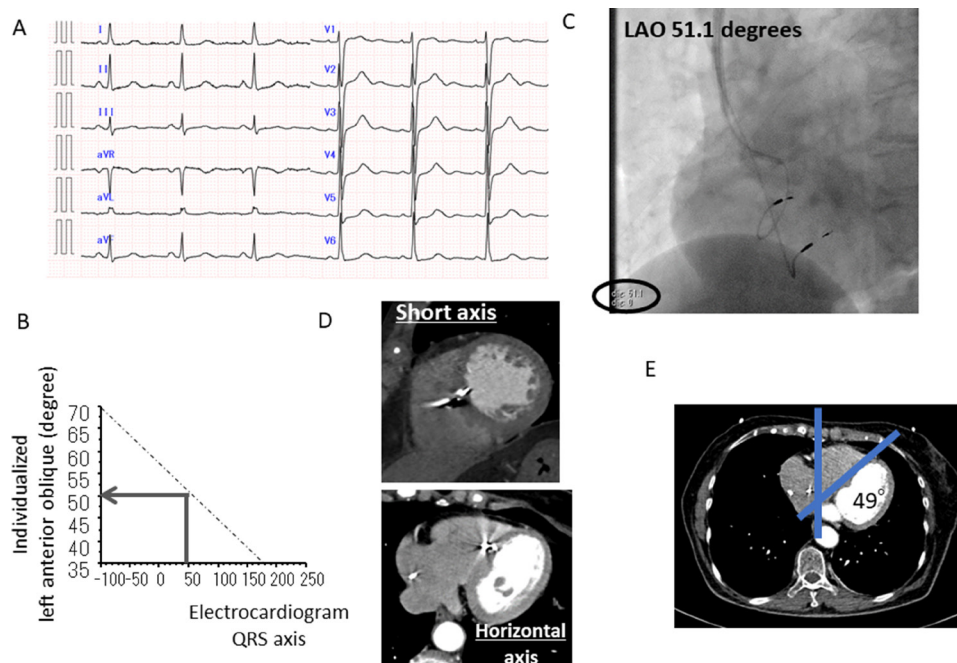


Figure 3 Representative figure of preoperative ECG QRS axis guide pacemaker implantation. (A) Preoperative ECG showed the QRS axis of 48°. (B) Since the preoperative ECG QRS axis was 48°, it was judged to be an individualised LAO of 51°. (C) Intraoperative fluoroscopic image. LAO projection 51° was used for implanting the RV lead. (D) After performing the procedure using the individualised LAO projection, postoperative thoracic CT confirmed that it was accurately placed in the interventricular septum. (E) Measurement of individualised LAO by thoracic CT. The actual interventricular septum axis was 49°. LAO, left anterior oblique; RV, right ventricle.

we propose is uncomplicated because an individualised LAO can be inferred from the preoperative ECG.

In the present study, the success rate of interventricular septal RV lead implantation improved dramatically (93% vs 64%, $p < 0.05$) by using preoperatively estimated ECG-derived individualised LAO. The success rate of septal placement in our cohort tended to be higher than in previous reports.^{4–7} Assessing the RAO projection in addition to the LAO projection could contribute to the increased success rate. However, there was no significant difference in the usage rate of delivery catheters. In addition, the RV lead could not be placed in the interventricular septum using our method because of the severe meandering of the innominate vein, which led to an uncontrolled RV lead. However, we previously reported the usefulness of delivery catheters in interventricular septal placement of RV leads.⁷ In the future, such an indwelling method may be considered for RV leads in patients with complicated vascular anatomy.

The present study found that the preoperative ECG QRS axis was strongly related to the interventricular septum axis detected by thoracic CT. The cardiac electrical axis indicates the direction of the cardiac electrical axis at the front-face value. Generally, the QRS axis is called the cardiac electrical axis because ventricular excitement is the largest electromotive force, and it has great clinical significance. In some animals, it has been found that the QRS electrical axis almost coincides with the anatomical axis.¹⁶ In humans, based on Einthoven's theory of equilateral triangles, it has been reported that

if the electromotive force of the heart is considered as a vector, the vector can be drawn at each moment of the QRS, and the direction of the vector almost coincides with the anatomical axis. To draw the electromotive force of the heart, it is necessary to draw and average the QRS vector at each moment, which is the QRS electric axis.^{17,18} Thus, the preoperative ECG QRS axis was strongly related to the interventricular septum axis detected by thoracic CT.

Our findings showed that cardiac load, which was assessed by serum NT-proBNP levels, was significantly reduced in the septum group compared with that in the non-septum group. It is possible that placement into the interventricular septum reduced the cardiac load, even if it was limited to a short period of 1 week after pacemaker implantation. As a result of excitement that is different from the physiological conduction pattern in non-septum RV lead placement, asynchrony of contraction between the LV and RV can occur, which leads to haemodynamic deterioration and LV remodelling.^{19,20} In the mode selection trial in the sinus-node dysfunction (MOST) study, patients with a QRS complex of 160 ms or more were reported to have a higher hospitalisation rate due to heart failure. In addition, the risk of heart failure increased by 17% for every 10ms extension of the QRS complex.²¹ In the present study, the paced QRS complex in the septum and non-septum groups was 121 ms vs 157 ms, which is consistent with our previous report.⁷ It is possible that the QRS complex would be closer to normal without extension, and that the cardiac load would be reduced by accurate placement in the septum.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The protocol was approved by the Standards of Official Conduct Committee of Hamamatsu University School of Medicine (20-005). All procedures were performed in accordance with the Declaration of Helsinki. The written informed consent was waived owing to the observational nature of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The data that support the findings of this study are available from the corresponding author or first author on reasonable request.

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ORCID iDs

Taro Narumi <http://orcid.org/0000-0001-6466-9457>

Yoshihisa Naruse <http://orcid.org/0000-0001-9630-951X>

Kenichiro Suwa <http://orcid.org/0000-0001-6934-7932>

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