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Can QRS morphology be used to differentiate between true septal vs. apparently septal lead placement? An analysis of ECG of real mid-septal, apparent mid-septal, and apical pacing

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The location of the pacemaker lead is based on the shape of the lead on fluoroscopy only, typically in the left and right anterior oblique positions. However, these fluoroscopy criteria are insufficient and many leads apparently considered to be in septum are in fact anchored in anterior wall. Periprocedural ECG could determine the correct lead location. The aim of the current analysis is to characterize ECG criteria associated with a correct position of the right ventricular (RV) lead in the mid-septum. Patients with indications for a pacemaker had the RV lead implanted in the apex (Group A) or mid-septum using the standard fluoroscopic criteria. The exact position of the RV lead was verified using computed tomography. Based on the findings, the mid-septal group was divided into two subgroups: (i) true septum, i.e. lead was found in the mid-septum, and (ii) false septum, i.e. lead was in the adjacent areas (anterior wall, anteroseptal groove). Paced ECGs were acquired from all patients and multiple criteria were analysed. Paced ECGs from 106 patients were analysed (27 in A, 36 in true septum, and 43 in false septum group). Group A had a significantly wider QRS, more left-deviated axis and later transition zone compared with the true septum and false septum groups. There were no differences in presence of q in lead I, or notching in inferior or lateral leads between the three groups. QRS patterns of true septum and false septum groups were similar with only one exception of the transition zone. In the multivariate model, the only ECG parameters associated with correct lead placement in the septum was an earlier transition zone (odds ratio (OR) 2.53, $P = 0.001$). ECGs can be easily used to differentiate apical pacing from septal or septum-close pacing. The only ECG characteristic that could help to identify true septum lead position was the transition zone in the precordial leads. ClinicalTrials.gov identifier: NCT02412176.

Introduction

Right ventricular (RV) apical pacing produces a pathological ventricular activation pattern, resulting in inter/intraventricular electrical and mechanical dyssynchrony. It is associated with reduced cardiac output, increased myocardial

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workload and ventricular remodelling, which can lead to dysfunction of the left ventricle (LV), heart failure, or new-onset atrial fibrillation.[1-4] It is assumed that non-apical pacing (e.g. His bundle, RV septum, and RV outflow tract—RVOT) can produce more physiological contraction pattern because of its proximity to the conduction system. The main focus of non-apical pacing sites has been on the mid-septum due to the relative technical ease of lead implantation. Studies comparing RV apical to RV septal pacing have yet to draw any firm conclusions. Comparing long-term LV systolic function and clinical outcomes, studies have yet to show a clear clinical benefit for septal pacing.[5-9] However, short term, echocardiographic parameters of synchronization and related QRS duration were significantly better during septal stimulation compared to apical stimulation.[3,8,10] In one randomized study of patients with reduced ejection fraction (<45%), septal pacing was associated with better preservation of systolic function compared to apical pacing.[10]

The major criticism of these studies was that the exact position of the leads was often undetermined, i.e. the only method used for lead determination was fluoroscopy. The septum is not visible by fluoroscopy, therefore the location of the lead in the septum was based on the shape of the lead, typically only in the left anterior oblique (LAO) 40° position. For years, the position of the lead as seen in the LAO was considered sufficient. Recently it has been shown that such an assumption is unjustifiable. Few studies have focused on verification of the actual site of lead placement by using more exact imaging methods, e.g. echocardiography, cardiac computed tomography (CT). Those studies found that only about half of the leads was actually situated in the septum, while the other half was implanted in adjacent areas, e.g. anterior or free wall, or anteroseptal groove.[6,11-13] The pattern of paced QRS complexes on a 12-lead ECG was proposed as an additional tool to define the exact position of the lead. Multiple criteria, especially q or negative QRS in lead I,[5,14] have been described as being associated with septal stimulation. Most of these criteria were obtained by comparing stimulation from the RVOT septum and RVOT anterior wall using electrophysiological (EP) catheters.[12,15,16] However, criteria obtained from RVOT cannot necessarily be easily interpreted to mean mid-septal lead placement.

The aim of the current analysis was to verify all described ECG criteria and find the optimal combination of those ECG elements that can indicate the exact location of the lead in the septum.

Methods

Patients

Patients with an indication for pacemaker implantation, according to the current ESC guidelines, were studied. In all patients considered to have been implanted in the septum, the exact position of the RV lead was assessed using cardiac CT.

The anatomy of RV and selective pacing sites has yet to be united. In previous studies, RVOT septal pacing and mid-septal pacing were often considered the same.[5,16] Right ventricular outflow tract is defined by its borders: in the anteroposterior projection, the superior border is the pulmonary valve and the inferior border is the plane of the tricuspid valve. The septal part of the right ventricle below the RVOT septum was considered to be mid-septal in our study.

Patients were recruited from two studies. The first study was performed to assess the best fluoroscopic criteria for septal lead placement, the study has been published elsewhere.[11] In that study, 51 patients were implanted into the septum using standard fluoroscopy criteria. The location of the RV lead after implantation was verified using cardiac CT. In 21 patients, the lead was found to be in the septum (true septum, true septum), and in the remaining 30 patients in the nearby areas (false septum, false septum). In all patients, ECGs with paced QRSs were obtained. The other pool of patients comes from an ongoing randomized study comparing apical, true septal, and apparently septal pacing (i.e. thought to be septal at the time of implantation); the protocol of the study has been published elsewhere.[17] In brief, patients with a standard indication for pacemaker implantation were randomized to apical pacing and septal pacing (2:1 ratio). In the apical group (A), the correct position of the lead in the apex was assessed using only fluoroscopy criteria during implantation [anteroposterior view, LAO, and right anterior oblique (RAO) view]. In the septal group, the location of the RV lead was verified using cardiac CT. Based on the exact location of the RV lead, the septal group was further divided into a 'true septal' (true septum) and 'false septal' (false septum, i.e. the lead was found in the adjacent areas, such as the anteroseptal groove, the anterior or free wall) subgroups. The endpoints of the study were changes in LV volumes, echocardiography dyssynchrony markers, and myocardial extracellular matrix markers. The study is ongoing, an ECG with paced QRSs has already been obtained in most of the enrolled patients.

For the current analysis, two main groups of patients were analysed: patients with apical pacing (Group A, all of whom were recruited from the second randomized study). The other group were patients with septal pacing (MS group), regardless of the exact location of the lead (i.e. patients with attempted septal pacing during implantation using established fluoroscopic criteria, consisted of all patients from the first study and patients randomized to septal pacing from the second randomized study). The MS group was further divided into two subgroups based on the result of cardiac CT, 'true septum' and 'false septum' patients.

Patients in both studies signed informed consent. Both studies were approved by local ethics committee.

Implantation procedure

Pacemaker implantation was done under local anaesthesia, mild sedation, and prophylactic intravenous antibiotics. The RV lead was inserted via the right cephalic or subclavian venous approach. Commercially available 58 or 60 cm bipolar active fixation (Biotronik Siello S 60, Vitatron ICQ09B, Boston Scientific Ingevity™) leads with steroid-eluting electrodes were used for the RV septal implants.

Apical position of the lead was assessed in the anteroposterior and RAO view. Septal position of the lead was assessed using the LAO40 and RAO30 views. First, a lead with a J-shaped angulated stylet was inserted into the pulmonary trunk. The positioning of the ventricular leads into the pulmonary trunk was guided by the posterior–anterior fluoroscopic view. The other stylet was hand prepared for correct placement into the mid-septum. Initially, a generous curve was created using the distal 5–6 cm of wire. Then, the last 2 cm was slightly bent posteriorly to create a swan neck deformity similar to the design suggested by Mond *et al.*[16] On the LAO40 view, the lead was withdrawn across the pulmonary valve back into the mid-RV until the desired LAO40 position was achieved (i.e. the tip of the lead faced the spine and the angulation between horizontal plane and the axis of the distal part of the lead was between 0° and 60°). The position of the lead was checked in the RAO position. In the RAO30, the heart was divided into four quadrants perpendicular to the cardiac silhouette. The lead should be in the second or third quadrant. After that, a standard measurement of the amplitude of the QRS complex and threshold were carried out. Only in cases with markedly insufficient pacing parameters (pacing threshold $>$ 1.5 V) was the lead repositioned to a different location.

Cardiac computed tomography

Computed tomography was performed 1–5 months after the implantation using a 256-detector-row CT scanner (Brilliance iCT 256; Philips, Best, The Netherlands) with a tube voltage of 100 kV, a tube current of 200–300 mAs (depending on the patient's body mass index), collimation of 2 mm $\times$ 128 mm $\times$ 0.625 mm, a pitch of 0.18, a rotation time of 0.27 s, and a slice thickness of 0.9 mm. Additionally, triphasic injection of 60 mL of contrast media (Ultravist 370; Bayer Healthcare Pharmaceuticals, Montville, NJ, USA) was injected. The first 50 mL of contrast agent was administered at a flow rate of 4.0 mL/s, followed by 20 mL of 50% contrast/saline. Subsequently, a saline flush of 30 mL was administered at a flow rate of 3.0 mL/s. Bolus tracking was used for synchronization of the contrast medium injection with scanning. The region of interest was positioned over the descending aorta. After enhancement reached 140 HU, there was 3 s post-threshold delay before the scan commenced. Prospective ECG-triggered dose modulation (mode step and shoot) was used, scanning 70–80% of the relative risk interval. After examination, the displayed dose-length product was recorded to evaluate the radiation dose. The mean dose-length product was 412 $\pm$ 74 mGy cm^2. The mean effective dose was calculated using a weighting factor of 0.14 and was 6.0 $\pm$ 1.1 mSv.

Image post-processing

Data sets were transferred to an external workstation (Comprehensive Cardiac Analyses, Brilliance Workspace v. 4.0; Philips Healthcare, Cleveland, OH, USA) for offline analysis. Axial slices, oblique reconstructions, and maximum-intensity projection images were used for precise localization of the RV lead. All evaluations were carried out by two experienced readers, who were blinded to the other's results. Disagreement between readers was resolved by consensus.

ECG analysis

The 12-lead surface ECGs with standard parameters (paper speed of 25 mm/s, gain of 10 mm/mV) were analysed. ECGs were recorded during the first outpatient check-up. In pacemaker-dependent patients, in whom no sensing was measured while stimulated at VVI 40 b.p.m., ECGs were recorded at standard pacemaker settings (i.e. DDD 60/min or VVI 60–70/min). In patients with spontaneous AV conduction, the pacemaker was programmed to VVI 90–100/to achieve a paced QRS and avoid fusion.

The measurements were analysed by a single observer, who was blinded to the CT results, using ECG analysis software on ECG machines and software for on-screen ECG measurements (Cardio Calipers, Iconico, NY, USA). Among several reports, the presence of a negative QRS or q might be associated with septal stimulation. The presence of notching in the inferior leads, on the other hand, has been described in association with pacing from anterior wall/anteroseptal groove.[5,12,14–16] Based on previously published studies, the following parameters were analysed:

(1) QRS duration—measured using CardioCalipers software.
(2) QRS axis—manually estimated.
(3) Presence of q-wave or negative QRS in lead I.
(4) Notching in the limb leads (II, III, aVF), i.e. the presence of notched QRS complex in any of the inferior leads.
(5) Notching in the lateral leads (I, aVL, V6), i.e. the presence of notched QRS complexes in any of the lateral leads.
(6) QRS transition in the precordial leads, i.e. the first lead, in which the 'R' is taller than the 'S' (i.e. sum of positive deflections is higher than the sum of negative deflections). If the R wave was less than the height of the S wave, even on lead V6, the transition zone was considered to be on lead V7 (i.e. no more precordial leads, like V7, V8, etc. were connected, but the absence of the transition zone in V6 was generally considered as being V7).

Statistical analysis

Continuous data are presented as means plus standard deviation for normally distributed variables or as medians with percentiles for log-normally distributed variables. Normality was tested using the Shapiro–Wilk test. Categorical data are given as absolute and relative frequencies (percentages). Comparison between all three groups was initially done using the Kruskal–Wallis (for continuous variables) or Fisher's test (for categorical variables). If the differences were found significant, *post hoc* comparison between particular groups was done respecting three measured groups. The multivariate analysis between Group 1 and 2 used a stepwise backward logistic regression model. Initially, a univariate logistic regression analysis was performed using all measured ECG variables. All univariate predictors with *P*-values $<$0.1 were included in the multiple logistic regression model with the goal of

identifying those that were independently related to the position of the lead in the septum. Statistical analysis was performed using statistical software Stata (Stata Corp LP, College Station, TX, USA) and SPSS (SPSS, College Station, TX, USA). *P*-values <0.05 was considered significant.

Results

One hundred and six patients were enrolled in the study. Twenty-seven patients had a lead implanted in the apex (Group A). Seventy-nine underwent mid-septal implantation. Based on the position of the lead on the cardiac CT (performed 39.3 ± 40.5 days after implantation), mid-septal patients were divided into the true septum group ($n = 36$) and false septum group ($n = 43$). The clinical characteristics of all groups are shown in *Table 1* and the ECG characteristics in *Table 2*. Examples of patient's ECGs and CTs with the lead located in the apex, true septum, and septum-adjacent areas are shown in *Figures 1-3*.

Procedural complications

There was one pericardial effusion in a patient in the false septum group (2.3%), the patient was treated conservatively without need for pericardiocentesis or surgery with good outcome. No pericardial effusion were in either the true septum or the A groups. There was one dislodgement of the ventricular lead requiring reimplantation in the MS group (2.8%), three in the false septum group (7%), and two in the group A (7.4%).

QRS complex duration

The width of the QRS was significantly different between all three groups ($P = 0.003$). The apical group had a significantly wider QRS compared with true septum group (A: 155.1 ± 15.6 ms, true septum: 138.1 ± 20.0 ms, $P = 0.006$) and with false septum group (false septum: 138.4 ± 21.3 ms, $P = 0.007$). There was no significant difference in the QRS duration between the true septum and false septum groups ($P = 1.0$).

QRS axis

The QRS axis was significantly different between all three groups ($P < 0.001$). The axis was significantly left deviated in the apical group. The apical group had a significantly more leftward deviated axis in comparison to the true septum group (A: $-58.5 \pm 18.1^\circ$, true septum: $11.6 \pm 54.5^\circ$,

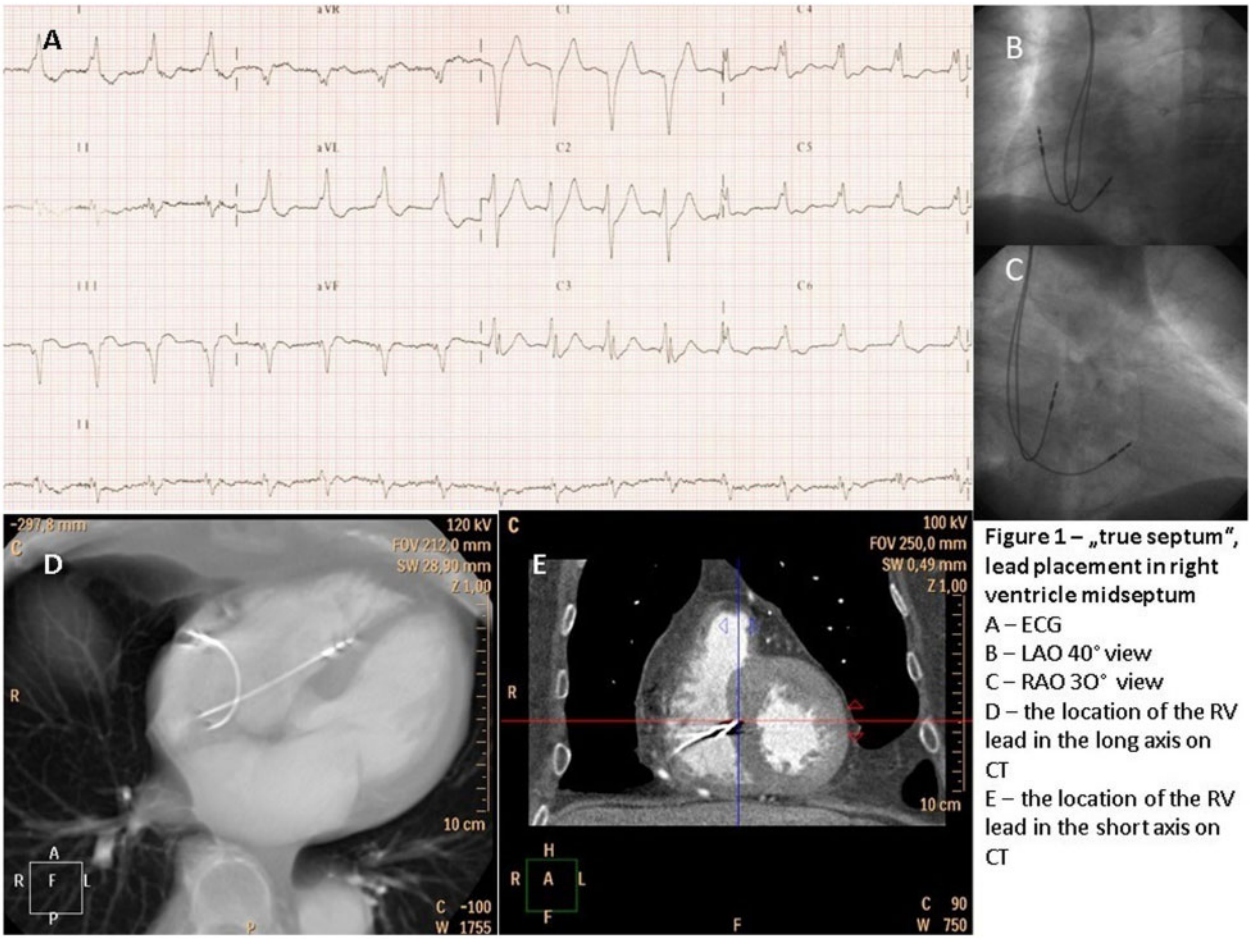

Figure 1 – „true septum", lead placement in right ventricle midseptum
A – ECG
B – LAO 40° view
C – RAO 30° view
D – the location of the RV lead in the long axis on CT
E – the location of the RV lead in the short axis on CT

Figure 1 Example of paced ECG and computed tomography scans of true mid-septal pacing. (*A*) ECG of a patient with lead implanted in the septum, (*B*) the position of the right ventricular lead in the left anterior oblique projection 40° on fluoroscopy during the implant, (*C*) the position of the right ventricular lead in the right anterior oblique projection 30° on fluoroscopy during the implant, (*D*) the location of the right ventricular lead in the long axis on computed tomography, and (*E*) the location of the right ventricular lead in the short axis on computed tomography.

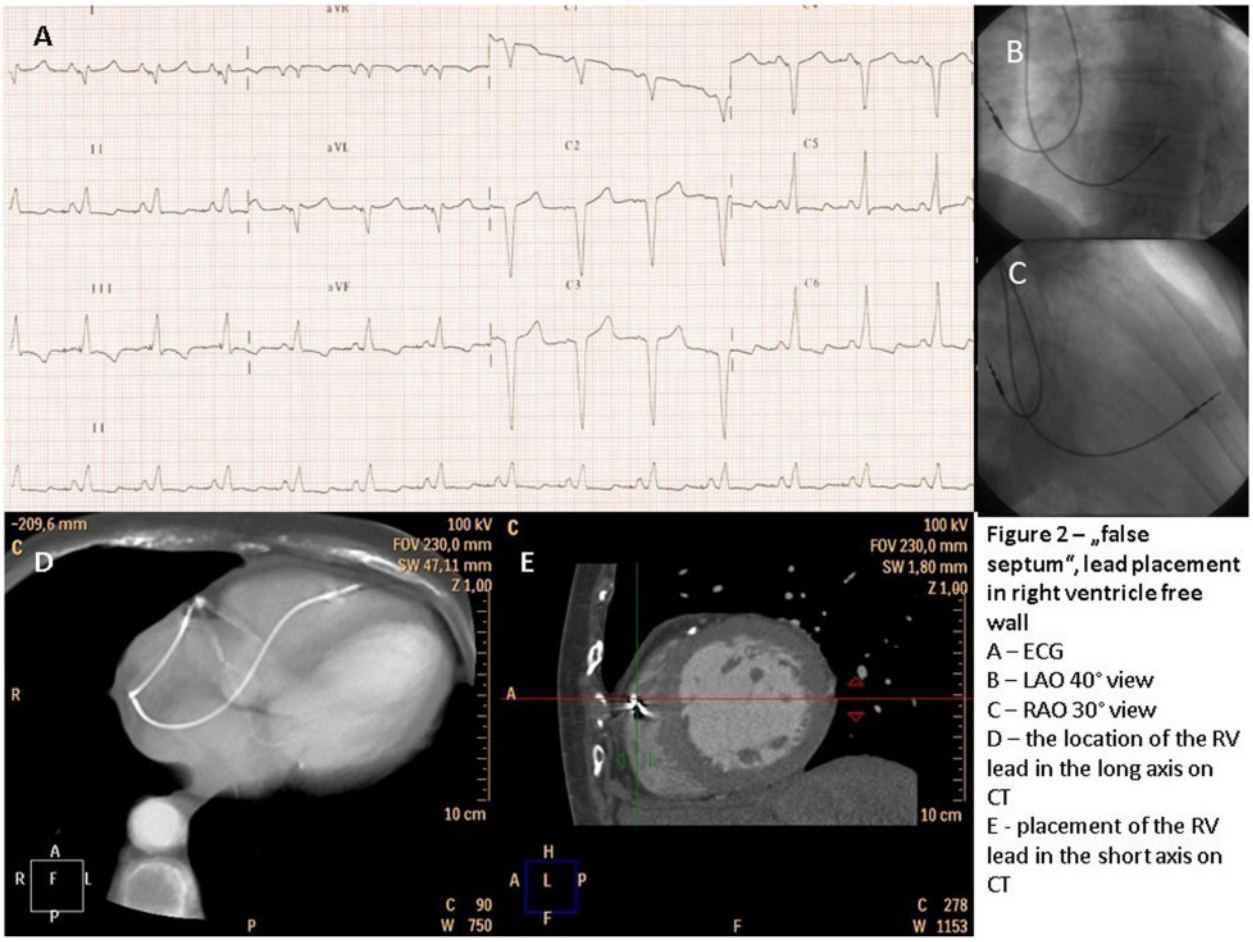

Figure 2 – „false septum", lead placement in right ventricle free wall
A – ECG
B – LAO 40° view
C – RAO 30° view
D – the location of the RV lead in the long axis on CT
E - placement of the RV lead in the short axis on CT

Figure 2 Example of paced ECG and computed tomography scans of 'false' septal pacing (i.e. anterior wall). (*A*) ECG of a patient with lead implanted in the anterior wall of the right ventricle, (*B*) the position of the right ventricular lead in the left anterior oblique projection 40° on fluoroscopy during the implant, (*C*) the position of the lead in the right anterior oblique projection 30° on fluoroscopy during the implant, (*D*) the location of the right ventricular lead in the long axis on computed tomography, and (*E*) the location of the right ventricular lead in the short axis on computed tomography.

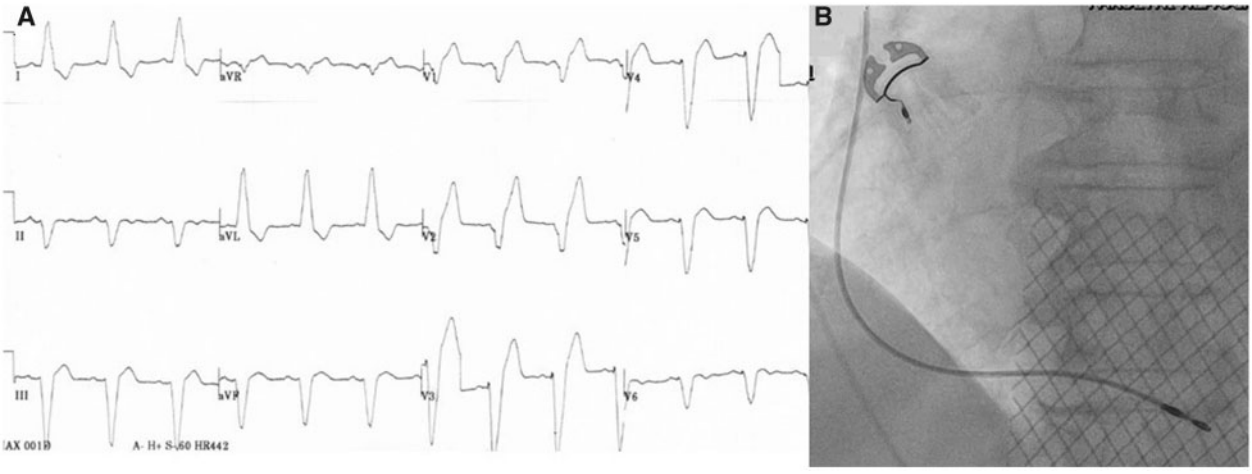

Figure 3 Example of paced ECG and fluoroscopy of apical pacing. (*A*) ECG of a patient with lead implanted in the apex and (*B*) the position of the lead in the anteroposterior projection on fluoroscopy during the implant.

$P < 0.001$), as well as with the false septum groups (false septum: $34.2 \pm 51.9°$, $P < 0.001$). The difference in axis deviation between true septum and false septum did not reach statistical significance ($P = 0.365$).

Negative QRS/q in lead I

The presence of q-waves or negative QRS complexes in lead I was not significantly different between the three groups ($P = 0.21$).

Notching in the inferior (II, III, aVF) leads

The presence of notching in the inferior leads was not significantly different between the three groups ($P = 0.532$).

Notching in the lateral (I, aVL, V6) leads

The presence of notching in lateral leads was not significantly different between the three groups ($P = 0.580$).

QRS transition zone in the precordial leads

The transition zone was significantly different between all three groups ($P < 0.001$). The transition zone was latest in the apical group, followed by false septum and true septum groups. Regarding the transition zone, there was a significant difference between the apical and true septum groups [A: 6.7 ± 0.5 (number 7 got every patient without transition zone in the precordial leads), true septum: 4.3 ± 1.3, $P < 0.001$], as well as between the apical and false septum group (false septum: 5.2 ± 1.0, $P < 0.001$). The difference between the true septum and false septum group had borderline significance ($P = 0.07$), with transition zone showing up on V4 in the true septum group and on V5 in the false septum group.

Multivariate logistic regression (all three groups)

For the purpose of analysing an unknown paced ECG, a multivariate analysis of all ECGs (including apical group) was done. In the univariate regression model, the QRS axis and the transition zone were associated with the true septum position and were further used in a multivariate model. In the multivariate model, the parameters associated with correct lead location (i.e. in the septum) were a shorter QRS duration [OR 0.96 (0.93–0.99), $P = 0.02$], and an earlier transition zone (i.e. before V5) for the QRS complex in the precordial leads [OR 1.7 (1.1–2.7), $P = 0.02$].

Multivariate logistic regression (true septum and false septum groups only)

Furthermore, a multivariate logistic regression run separately only for true septum and false septum groups (i.e. apical patients were not included in this analysis) was also carried out. While the position of the lead in the apex, during the implantation, can only be reliably recognized with fluoroscopy using the AP view, this kind of analysis could be valuable during implantation, when both LAO40 and RAO30 criteria are fulfilled, and additional criteria are needed to confirm the position of the lead in the septum (i.e. to use an ECG as an additional criterion, since many leads fulfilling both LAO40 and RAO30 are actually found to be off-septum). In the univariate regression model, only the QRS axis and transition zones were associated with the true septum position and were further used in the multivariate model. In the multivariate model, the only parameter associated with correct location lead in the septum was an earlier transition zone of the QRS complex in the precordial leads [OR 2.53 (1.44–4.43), $P = 0.001$].

Early and late transition zone as markers of true septal placement of the right ventricular lead

The distribution of the transition zone in all three groups is shown in *Figure 4*. Specificity and sensitivity of the transition zone as a predictive marker of septal location was calculated in two different settings of the test. In both tests, the location of the lead was dichotomized to be in the true septum (true septum patients), or be outside the septum (i.e. all patients in the false septum and A groups). Furthermore, for the purpose of these statistical analyses, the transition zone had to be dichotomized to be in V2–V3 or later (i.e. from V4 up to V7, in the first analysis), or to be from V2 to V5, or later (V6–V7, in the second analysis).

The presence of the transition zone in V2–V3 had a high positive predictive value for the lead being in the true septum, however, its sensitivity was low (sensitivity 25%, specificity 98.6%, positive predictive value 90%, and negative predictive value 71.9%). On the other hand, the absence of

Table 1 Basic clinical characteristics

	A ($n = 27$)	true septum ($n = 36$)	false septum ($n = 43$)	*P*-value
Gender (male)	20 (74%)	21 (58%)	19 (45%)	0.38
Age (years)	70.9 ± 8.7	70.9 ± 8.9	71.2 ± 9.0	n.s.
LV EF (%)	60.56 ± 3.7	61.7 ± 2.4	63.8 ± 2.9	n.s.
LA size (mm)	45.1 ± 5.5	37.7 ± 4.7	41.9 ± 4.6	n.s.
LV EDD (mm)	52.2 ± 5.3	48.3 ± 4.7	49.6 ± 5.8	n.s.
Hypertension	24 (88.9%)	13 (36%)	9 (21%)	<0.001
Diabetes mellitus	3 (11%)	5 (14%)	1 (2.4%)	0.16
DDD pacemaker	20 (77%)	23 (64%)	31 (72%)	n.s.
VVI pacemaker	7 (23%)	13 (36%)	12 (28%)	n.s.

DDD, dual chamber pacemaker; false septum, false septal; n.s., not significant; LA, left atrial, LV EDD, left ventricular end-diastolic dimension; LV EF, left ventricular ejection fraction; true septum, true septal; VVI, single chamber ventricular pacemaker.

Table 2 ECG characteristics of apical, true septal, and false septal pacing

	A ($n = 27$)	true septum ($n = 36$)	false septum ($n = 43$)	*P*-value (MS vs. A)
QRS width (ms)	155.1 ± 15.6	138.1 ± 20.0	138.4 ± 21.3	0.003
QRS axis (°)	-58.5 ± 18.1	11.6 ± 54.5	34.2 ± 51.9	<0.001
q-Wave or negative QRS in lead I	7 (26.3%)	12 (33.3%)	22 (52.3%)	0.21
Inferior notching (leads II, III, aVF)	11 (42.1%)	8 (22.2%)	16 (38.0%)	0.53
Lateral notching (leads I, aVL, V6)	12 (45.6%)	16 (45.5%)	19 (44.4%)	0.58

Statistical analysis was done using Kruskal–Wallis test, or Fisher's exact test, as appropriate.

the transition zone up to lead V5 showed that the location of the lead was outside the septum (sensitivity 86.1%, specificity 60%, positive predictive value 52.5%, and negative predictive value 89.4%). It means, the presence of the transition zone in V2 or V3 can be a useful marker for prediction of true septal lead placement, and the presence of the transition zone in V6 or later can be a useful marker that the lead is located outside the septum.

Discussion

ECG criteria have been proposed as auxiliary methods for lead placement verification. In our study, six criteria suggested to be specific for non-apical lead placement were analysed, e.g. negative QRS/q in lead I and notching in the inferior or lateral leads. Since CT scans with lead placement verification were available in all our patients, the position of the RV lead was exactly known. The number of 106 patients makes our series the largest, in which the precise validation of the position of RV lead was performed. Based on the lead location, patients were enrolled in three groups—apical (A), true septal (true septum), and false septal (false septum, i.e. anterior/free wall, anteroseptal groove) pacing.

A negative initial deflection in lead I

Based on results of two small studies (published by Lieberman *et al.*, and McGavigan *et al.*), a negative deflection in lead I (initial q or negative QRS complex) has been considered an indicator of septal pacing.[5,14] However, both studies were comparing stimulation from the RVOT septum and RVOT anterior wall. These two studies are cited as the source of information in the majority of later articles on this topic,[11,12,15,16] and in recent reports, these sources are cited without further detailed validation. Fluoroscopy was the only method used for verification of lead position, and

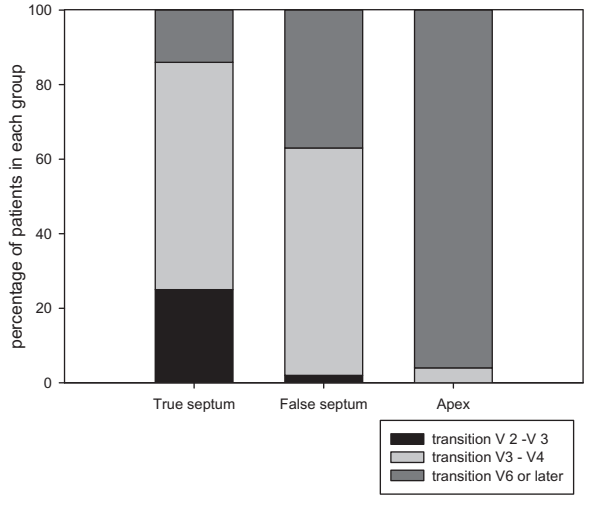

Figure 4 Figure plot of the distribution of transition zones in each group. Each column represents a patient group (i.e. true septum, false septum, A) as 100% of patients. The different coloured bars of the plot shows the percentage of patients with a particular transition zone. Black = transition zone in V2 or V3, dark grey = transition zone in V4 or V5, and light grey = transition zone in V6 or later (V7).

other difficulties in the interpretation of the results are present: McGavigan *et al.*[14] showed that a negative or isoelectric QRS complex is more often found in RVOT septal pacing; however, from 81 patients, this pattern was present in only 46% of them.

Recently, Burri *et al.*[15] created a three-dimensional (3D) anatomical reconstruction of the right ventricle using the NavX system and studied ECG criteria from mid-septal, anterior, and free wall pacing in 31 patients. The verification of the position of the catheter was done using a 3D mapping system, and pace-mapping was done in multiple locations. In that study, the presence of a negative initial deflection in lead I was not associated with septal pacing; moreover, q-waves or a negative QRS in lead I were more frequently present in anterior RV pacing.[15] Similarly, Pang *et al.*[12] used cardiac CT in 23 patients to validate lead locations in the RV (e.g. septum, anterior wall, anteroseptal junction) that had been placed using ECG and fluoroscopic criteria. They found a higher prevalence (100%) of negative or isoelectric QRS complexes in lead I in the RV anteroseptal junction (i.e. anteroseptal groove) compared to the septum (40%) or the anterior RV wall (56%). Both these findings support our observations: the presence of an initial negative deflection in lead I in our patients was more common (52%) in the false septum group then in the true septum group (33%).

Paced QRS duration

In our patients, QRS duration was significantly longer in the apical group compared with septal group; however, no difference was present between the true septum and false septum groups (138 ms on average in both). Wide QRSs have been associated with apical pacing for many years. As shown by Pang *et al.*,[12] there is a significant negative linear relationship between the paced QRS duration and the percentage distance from the RV apex to the base. However, and as with our patients, Pang *et al.* did not find any significant difference in paced QRS duration between septal and non-septal (anterior or anteroseptal groove) sites. Additionally, the QRS width was not able to differentiate true septum and false septum pacing. Recently, Rowe *et al.*[18] studied the paced ECGs of 18 patients: 8 were implanted in the apex and 10 in the septum based on fluoroscopy criteria. However, CT later revealed that only 1 of the 10 patients actually had the lead in the septum, the rest were in the adjacent anterior or free wall. In the report, the QRS duration was non-significantly shorter in patients with apparent septal implantation (168 ms in the apex vs. 160 ms in the septum) with the shortest QRS duration found in the one patient with the lead actually in the septum (130 ms); however, statistical analysis was impossible in such small group.

QRS axis

A morphology like left bundle branch block and left-deviated QRS axis has been associated with RV apical pacing.[12] In the above-mentioned Burri report, mid-septal pacing had a more leftward calculated axis compared with pacing from the para-Hissian or anterior sites; however, axis values had very broad range, and no single cut-off was

able to accurately differentiate pacing sites. Hillock *et al.*[19] described a significant leftward shift in the mean frontal axis if paced from the RV free wall ($43.4 \pm 7.6^{\circ}$), anterior wall ($54.5 \pm 8.2^{\circ}$), and from the septum ($82.8 \pm 2.3^{\circ}$, $P < 0.001$); however, in that report, the position of the leads was verified only by fluoroscopy and pacing was conducted from the RVOT. It has been shown that we cannot simply transfer the parameters from the RVOT to the septum and fluoroscopy in not sufficient to accurately show the position of the lead. In agreement with Burri, in our patients with RV leads implanted in the mid-septum, QRS axis tended to be slightly more horizontal compared to placement in adjacent areas, however, there was a wide range and the differences did not reach statistical significance ($P = 0.07$).

The presence of notching in inferior and lateral leads

Theoretically, septal pacing is closer to the conduction system, therefore septal pacing should have less notching compare to anterior or free wall pacing. McGavigan *et al.*[14] found that notching in the inferior leads was significantly more common in free wall pacing compared to septum pacing (41.2% vs 13.6%); however, in that report, pacing of the RVOT, not the septum was analysed (see the above-mentioned implications), and only fluoroscopy was used to validate lead position. The presence of notching in the limb leads was associated with shorter QRS duration in a report by Pastore *et al.*;[20] however, whether the lead was positioned exactly in the septum, or adjacent anterior wall (which can have similar QRS durations, as shown in our study) was not analysed.

In Burri's report, QRS notching was only marginally more frequent when pacing from the mid-septum compared to pacing from an anterior site, which was true in lead I and all inferior leads.[15] The absence of notching in the inferior leads was only partially supported (35%) by CTs in the report by Pang *et al.*[12] The same was true of our patients, i.e. no clear and significant differences in inferior or lateral notching was found between septal and non-septal QRS pacing.

Precordial QRS transition

As mentioned above, the transition zone was represented by the first precordial lead in which the 'R' was taller than 'S', and a number from 1 to 6 was assigned. If the R was not taller than S, even in V6, the transition zone was assigned as being in V7. Precordial transition was significantly later in apically paced RV compared to septal pacing. The precordial transition was also significantly later in false septum patients (in lead V5) compared to true septum patients (in lead V4). Burri *et al.*[15] reported that pacing from the mid-septum was associated with QRS transition that was intermediate between pacing from the para-Hissian region and anterior sites. In this report, QRS transition at >V4 was present in 94% (29/31) of cases during mid-septal pacing and in all cases during anterior pacing. The difference between the transition zone in true septal and false septal pacing in our patients was greater compared to that reported by Burri. This difference could be explained by slightly different methodology: in Burri's report, anterior pacing involved only pacing of the anteroseptal groove, i.e. an area very close to the septum. In our report, some 'false septal' leads were found also in the anteroseptal groove, while others were anchored more laterally in the 'true' anterior wall (as visualized in patients after implantation); thus, the differences could have been a function of the greater distance between lead locations.

As it is known, ablation procedures of ventricular extrasystoles have shown that a later transition zone in ventricular extrasystole of right origin compared to a left origin. However, it is difficult to translate directly these findings into an ability to recognize septal vs. non-septal pacing, however, in accordance with our multivariate analysis, an ECG with an earlier transition zone was twice as likely to have come from a lead implanted in the septum compared to an ECG with a later transition zone.

Practical consideration

The key finding of our report is that a transition zone in the precordial leads can be used as an additional tool in the effort to insure that the lead is correctly placed in the true septum. Recently, the use of a double-curved stylet and the combination of RAO with the traditional LAO40 projection was found to be associated with higher probabilities of getting the lead implanted in the septum.[21] However, despite recent progress in fluoroscopy criteria for septal lead position, many leads are still implanted in the anterior wall. To increase the likelihood of achieving a true septal position during implantation, the anatomical (fluoroscopy) criteria could be combined with ECG criteria, which have been previously suggested by others. Pastore *et al.*[20] showed that a delay from the QRS onset to the intracardiac signal on the RV electrode, and the absence of notching in limb leads on a paced QRS, are predictive of shorter QRS complex durations. The advantage of this technique is the use of limb leads only, however, whether the lead was in the septum or in the adjacent anterior wall (which has similar QRS durations) was not analysed. The use of precordial leads during implantation can further enhance the technique and increase the likelihood of implanting the lead in the true septum. Using chest lead V3–V6, the transition zone of the paced QRS can be detected. Radiologically neutral electrodes V2–V5 can be placed on the chest at the beginning of the procedure before local disinfection of the operating field under sterile draping. After positioning based on LAO and RAO, the presence of very early transition zones in V2 or V3 becomes suggestive of proper septal lead placement (positive predictive value of 90%). On the other hand, very late transition zones (in V6 or later) are very suggestive (predictive value 90%) that the lead is not in the septum. Unfortunately, specificity is high at the expense of low sensitivity (<25%). However, further studies on this topic are needed to confirm this finding and to further improve implantation techniques.

All the lead used in our study were active fixation leads. Passive fixation lead could be used for the apical position, however, the use of passive fixation leads is difficult for mid-septal placement, and the results of the present study should not be considered for this kind of leads.

Conclusion

Based on our results, ECGs can be used to easily differentiate apical pacing from septal pacing or septum pacing from septal proximity pacing; however, the differences between true mid-septal and septal proximity pacing are minimal. Nonetheless, very early or very late transition zones could help distinguish true septal lead placement from placement in adjacent areas of the anterior wall.

Study limitations

Although the methodology of the RV lead assessment was the same and the study team including two independent readers of cardiac CT results investigator was the same, patients were recruited from two studies (one prospective observational, the other prospective randomized) which presents a limitation of the study.

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