PACED P WAVE MORPHOLOGY TEMPLATES TO GUIDE ATRIAL TACHYCARDIA LOCALIZATION

Ahmed El Damaty, MD PhD[1], Dhaifallah Y. Yahya, MD PhD[1], Mahmoud Abouelatta MD MSc[1], Hussien H. Rizk, MD PhD[1], Amir M. AbdelWahab, MD PhD[1]

(1) Electrophysiology and Pacing Service, Department of Cardiovascular Medicine, Cairo University, Cairo, Egypt.

Corresponding Author: Ahmed El-Damaty:

Ahmed.damaty@kasralainy.edu.eg

16 Oroba street, new Maadi, Cairo, Egypt, 11435.

+2010923452229

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INTRODUCTION

Atrial tachycardia (AT) is a relatively uncommon arrhythmia in the adult population (0.34% and 0.46% of asymptomatic and symptomatic patients, respectively). It accounts for approximately five percent of paroxysmal supraventricular tachycardia (PSVT).[1]

AT originates from atrial tissue and does not require participation of either the sinus node or the AV node for maintenance. AT could be present in normal individuals, and in general, manifestations and prognosis are usually related to underlying cardiovascular status. The mechanism of focal AT is attributed to enhanced automaticity, triggered activity or microreentry.[2,3]

Identifying the AT origin based on the surface 12-lead electrocardiogram (ECG) P wave morphology can be challenging. Different ECG algorithms have been proposed using data from patients who underwent successful ablation for focal AT. [4,5,6] These studies are limited by the small number of studied P wave morphologies at each anatomic site.

Pace-mapping is useful in identifying the source of focal tachycardias in structurally normal hearts. The principle of the technique is that the cardiac activation sequence generated by the arrhythmia will be reproduced by pacing at its focal origin and at a similar cycle length. Although there are some limitations to this technique, several studies have demonstrated efficacy using pace mapping to choose ablation target sites for idiopathic VT. [7,8] In the case of an atrial tachycardia, the tachycardia P wave morphology on the surface ECG will be reproduced by such pacing.

Pace-mapping in the atrium is hampered by the inaccurate discrimination of P wave morphology in the 12-lead ECG. However, it allows investigating P wave morphologies in many anatomic sites within a smaller number of patients.

We thought to construct 12-lead ECG templates for P wave morphology during endocardial pacing from different sites in both atria. These templates can be used to localize focal atrial tachycardias in structurally normal heart.

PATIENTS AND METHODS

Study population

We prospectively enrolled consecutive patients who underwent a clinically indicated electrophysiologic study/ablation procedures at the Cardiology department, Cairo University, School of Medicine over the period from February 2013 to June 2014. Patients with structural heart disease, those who presented with atrial fibrillation or atrial flutter and those who refused to sign a consent form were excluded from the study. All subjects underwent a clinical evaluation, 12-lead ECG and echocardiography prior to their procedure.

Electrophysiologic study

After informed consent, patients were studied in the post-absorptive state. All antiarrhythmic drugs were withdrawn at least 5 half-lives before the study (3-4 weeks in case of amiodarone). Patients were prepped and draped in the usual fashion under complete local aseptic condition then the right groin was infiltrated with 2% lidocaine without epinephrine.

Two 6 F (French) and one 7 F venous sheaths were introduced percutaneously via the right femoral vein. A 6 F quadripolar catheter was advanced

to the right ventricular (RV) apex. A decapolar catheter was advanced to the coronary sinus (CS). A standard 4-mm tip ablation catheter was initially positioned at the His bundle region. All catheters were positioned under fluoroscopic guidance. Intracardiac bipolar electrograms along with the 12- lead surface ECG were recorded and stored digitally on a computerized multichannel system (Cardiolab-Prucka-GE).

Cardiac pacing was performed with a programmable stimulator (Micropace EP Inc. - United States) at twice the diastolic threshold and with a pulse width of 2 ms. A transseptal puncture was performed using SL-1 (St. jude Medical) or Preface (Biosense Webester) sheath and Brockenbrough needle (18G×71cm, Medtronic-USA) for patients requiring left atrial mapping/ablation. Heparin IV bolus was administered for left sided procedures. Atrial and ventricular pacing and extra-stimuli were performed for routine EP study and induction of tachycardia. Ablation was performed as indicated based on the clinical arrhythmia. All measurements were made at a screen speed of 100 mm/sec using onscreen digital calipers.

Atrial pacing

Atrial pacing was carried out at different atrial sites during the usual 30 minute waiting time after successful ablation. The paced chamber was dictated by the clinical arrhythmia e.g. LA pacing was only performed for those patients who underwent access to the left side of the heart to cure their clinical arrhythmia. Pacing was done at twice the diastolic threshold to reduce the captured surface area. Pacing was done at the following anatomical sites (Figure 1):

Right atrium:

- Crista terminalis (CT), (high, mid and low): Ablation catheter was directed to CT based on visualized double potential along the lateral RA.

- Tricuspid annulus (TA), (superior, medial, lateral and inferior): Where equal atrial and ventricular electrogram amplitudes were recorded.
- Right atrial appendage (RAA).
- Superior vena cava (SVC).
- Right side of inter-atrial septum (high septum, fossa ovalis (Fo) and low septum): Defined as the region of the fossa ovalis and septum primum.
- Perinodal region: His bundle electrogram was recorded, pacing without capturing His or ventricle.
- Coronary sinus ostium (CS os).

Left atrium:

- Pulmonary veins (right superior pulmonary vein (RSPV), right inferior pulmonary vein (RIPV), left superior pulmonary (LSPV), left inferior pulmonary vein (LIPV)): Where pulmonary vein potentials were recorded.
- Mitral annulus (MA), (superior, medial, lateral and inferior): Where equal atrial and ventricular electrogram amplitudes were recorded.
- Left atrial appendage (LAA).
- Left side of inter-atrial septum.
- Coronary sinus (CS, mid and distal).

Analysis of P-wave morphology (PWM), duration (PWD) and amplitude (PWA):

Surface 12-lead ECG recordings obtained during atrial pacing were analyzed. P waves were included for analysis only if preceded by an isoelectric interval (there was no fusion with the preceding QRS or T-wave). Measurements were performed with adjusted gain to standardize the analysis, in limb leads: gain was at 2500 with

scale 1/8 and in chest leads: gain was at 1000 with scale 1/4. The P waves were classified into four types: **1**) positive = P waves with deflections above the isoelectric line (the T-P segment); **2**) negative = P waves with deflections below the isoelectric line; **3**) biphasic = P waves having either positive/ negative or negative/positive deflections; and **4**) isoelectric (flat) = low-amplitude P waves; arbitrarily defined as no deviation from a baseline of >0.03 mV. P wave duration was calculated from the spike of pacing to the end of widest P wave. The maximum amplitude of the P-wave in the 12-leads, whether positive or negative was measured (Figure 2). In patients with manifest pre-excitation, P wave measurements were obtained after successful ablation of the accessory pathway was performed to avoid distortion of the terminal portion of the P wave by the delta wave.

Statistical analysis

Data were statistically described in terms of range, mean ± standard deviation (SD), frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparisons between groups were performed with either an unpaired Student *t* test or the Mann-Whitney *U* test, where a normal distribution could not be assumed. Categorical variables expressed as numbers and percentages were compared with a Pearson's chi-square test. A P value < 0.05 was considered significant for all tests. Receiver operating characteristic (ROC) curves were used to determine the accuracy of different P wave duration and amplitude variables and the threshold values that separated patients with different pacing sites. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY and USA), SPSS (Statistical Package for the Social

Science; SPSS Inc., Chicago, IL, USA) version 16 for Microsoft Windows and Arcus QuickStat (Biomedical), Arcus statistical software, Research Solutions, Addison Wesley Longman Ltd. USA.

Results

We prospectively enrolled 64 consecutive patients (mean age 37±13 years and BMI 24 ± 4), 25 of them were men (39%). Clinical tachycardia was diagnosed as AVNRT in 27 patients (42%), AVRT in 31 patients (48%), atrial tachycardia (AT) in one patient, right ventricular outflow tract PVCs in one patient, SNRT in one patient, idiopathic VT in one patient and two patients had negative EP study. ECG examination during sinus rhythm revealed manifest pre-excitation in thirty (46.8%) patients. Thirty-four (53.1%) patients had documented regular short RP tachycardia on the 12-lead ECG with a mean heart rate of 202±33 bpm. Echocardiographic data of the study population was as follows: mean left atrial size 3.2+/-0.3 cm, mean left ventricular end-diastolic dimension 4.7+/-0.5 cm, mean left ventricular end-systolic dimension 3.1+/-0.4 cm and mean left ventricular ejection fraction was 65+/-5%. We were able to pace at 1025 pacing sites in this population. Distribution of the anatomic sites of successful atrial pacing is shown in figure 3.

Analysis of P wave morphology (PWM):

RA versus LA:

To assess the utility of the 12-lead ECG in differentiating left from right atrial origin of pacing, we analyzed leads I, aVL, and V1, which have been previously considered to be most useful for this purpose.[9]

A negative (46%) or isoelectric (39%) P wave in V1 was seen with 85% of right atrial pacing sites. A positive P wave in V1 was seen with 71% of left atrial pacing sites. In aVL, PWM was isoelectric (46%) or positive (51.4%) at 98% of right atrial pacing sites, and negative at 44% of left atrial pacing sites. In lead I, PWM was isoelectric (37%) or positive (62%) at 99% of right atrial pacing sites, and negative at 37% of left atrial pacing sites. (table 1)

Localization based upon P wave frontal plane axis:

P wave axis in frontal plane, utilizing lead AVR, was used to differentiate various groups of pacing sites in both atria. In the right atrium, p wave was negative in lead AVR (91%) in pacing sites that were referred to as superior RA pacing sites as they mostly involved superior anatomical location including high CT, high septum, superior TA, RAA and SVC. On the other hand, pacing sites rendering pos/Iso morphology in AVR (88%) were mostly inferiorly located including medial, lateral and inferior TA and perinodal area. Table 2

In the left atrium, p wave was neg/Iso in lead AVR (95%) in pacing sites that were referred to as superior LA pacing sites as they mostly involved superior anatomical location including LAA, superior MA and pulmonary veins (inferior PVs showed the same P wave axis, although they are not anatomically superior). On the other hand, pacing sites rendering positive morphology in AVR (90%) were mostly inferiorly located including Medial, lateral and inferior MA and Cs ostium. Table 2

Anatomical locations within the RA

CT: At high CT, PWM was positive in I (95%), and aVF (97%), while negative in aVR (98%) and V1 (67%). (figure 4) At mid CT, PWM was positive in I (90%), and aVF (75%), while negative in aVR (84%) and V1 (60%). While at low CT, PWM was positive in leads I (72%) and aVF (45%), while negative in aVR (51%), and V1 (31%). Lead AVR was used to localize pacing sites that rendered Table 2 summarizes value of lead AVR in localizing different pacing within both atria.

TA: At the superior TA, PWM was negative in lead V1 (85%), positive (36%) or isoelectric in aVL (60%) and positive in aVF (70%). At medial TA, PWM was isoelectric in V1 (65%) and lead I (82%), while negative in aVF (84%). At the lateral TA, PWM was negative in lead V1 (64%), positive in lead I (59%) and negative in aVF (73%). At the inferior TA, PWM was isoelectric in V1 (72%) and lead I (79%) and negative (89%) in aVF. The lead aVF significantly differentiated superior TA pacing from other TA locations (table 3, Figures 4),

Right atrial appendage, high septum and SVC:

RAA: PWM at the right atrial appendage (RAA), high septum, high CT and SVC demonstrated a similar PWM to the superior location of TA in limb leads. However, in precordial leads PWM showed early transition when pacing at high septum, high CT and SVC in contrary to late transition at RAA. Superior TA showed negative concordance along the precordial leads. (Figure 5)

Perinodal region and right side of inter-atrial septum: At perinodal region, PWM was isoelectric in V1 (72%) and lead I (80%), and negative in aVF (80%). At high

right septum, PWM was negative in V1 (46%) and positive in aVF (94%). At fossa ovalis, PWM was isoelectric in V1 (64%) and negative in aVF (44%). At low septum, PWM was isoelectric in V1 (64%) and negative in aVF (40%). Pacing at perinodal, fossa ovalis and low septum produced similar PWM but in precordial leads there was negative concordance at perinodal region.

CS: At CS os, PWM was positive in lead V1 (70%), negative in aVF (95%), and positive in aVL (97%). No significant difference was seen between CS os and mid CS regarding PWM. The lead I was significantly negative at distal CS (89.5) and isoelectric at mid CS and CS os (91.5%).

Anatomic locations within the LA

PVs: At the right-sided PVs, PWM was positive in lead V1 (70%) and lead I (100%). PWM was isoelectric in lead I (71%) and positive in lead V1 (82%) at left sided PVs. Lead aVL was isoelectric (65.4%) or positive (15.3%) at RPVs and negative (85.2%) at LPVs (figure 4). PWM in lead aVR was negative in all PVs (88.7%).

MA: At superior MA, PWM was positive in lead V1 (80%) and aVF (67%), while negative in aVL (80%), lead I (74%). At medial MA, PWM was positive in V1 (72%), while negative in lead I (65%) and aVF (79%). At the lateral MA, PWM in lead V1 was positive (80%), while negative in lead I (94%) and aVF (67%). At the inferior MA, PWM was positive in V1 (87%), while negative in lead I (74%) and aVF (87%). Lead aVF was significantly differentiated the superior MA from other MA locations (table 3,

figure 4). PWM in lead aVR was positive (66.1%) at all locations of MA except for superior MA.

LAA: At LAA, PWM was positive in V1 (80%), negative in lead I (87%) and isoelectric in V6 (80%). At LAA, PWM in lead I and V6 were significantly different in comparison to PWM at LPVs (isoelectric 70.4 % and positive 92.6%, respectively). The same leads had PWM that were significantly different at superior MA in comparison to LPVs (negative in lead I (73.3%) and isoelectric in V6 (60%) vs isoelectric and positive in LPVs, respectively) (figure 4). There was positive precordial concordance when pacing from the left pulmonary veins in contrast with late positive to isoelectric transition when pacing from the LAA and superior MA (Figure 6).

Left septum: At LS, the PWM was positive in V1 (62%) and aVL (70%), and negative in aVF (77%).

Analysis of the P wave duration (PWD):

We compared the mean PWD between different anatomical atrial sites. PWD at the lateral atrial sites was significantly longer than those at medial sites. Mean PWD at SVC, lateral TA and RAA was compared to high septum, medial TA and perinodal locations respectively [(130+/-9 vs 95+/-10), P<0.001, (136+/-12 vs 99+/-10), P<0.001, (127+/-10 vs 93+/-8), P<0.001]. PWD was significantly wider at high CT when compared to high septum (125+/-10 vs 95+/-10), P<0.001. Mean PWD was significantly wider at LPVs, lateral MA and LAA compared to RPVs, medial MA and

left side of the interatrial septum, respectively [(155+/-12 vs 137+/-10), P=0.001, (140+/-10 vs 118+/-10), P=0.001, (145+/-8 vs 109+/-22), P<0.001].

Receiver Operator Characteristic (ROC) curves analysis showed the highest sensitivity and specificity for differentiation lateral MA, lateral TA and high septum from medial MA, medial TA and SVC with a cutoff of 140, 130 and 110 msec respectively. Figure 7 shows an example for ROC curve differentiating high septum from SVC with sensitivity 93% and specificity 88% (P<0.001).

Analysis of the P wave amplitude (PWA)

The mean value of the maximum P wave amplitudes was compared between superior and inferior anatomical atrial pacing sites. Superior atrial pacing sites showed significantly larger maximum P wave amplitude, for example superior TA and superior MA was compared to inferior TA and inferior MA respectively [(0.09 +/-0.04 vs 0.08+/-0.03),P=0.001, (0.09 +/-0.02 vs 0.08+/-0.03),P=0.002]. Using Receiver Operator Characteristic (ROC) curves analysis (Figure 7), the optimum point for separation of maximum P wave amplitude arising from superior PVs from those arising from inferior PVs was 0.1mV with a sensitivity of 95% and specificity of 56% (P<0.001).

P-wave morphology algorithm

Based on our results, a proposed P-wave morphology algorithm was developed to allow prospective identification of the likely pacing site according to P wave morphology, duration and amplitude (Figure 8).

Discussion

Major findings

This study demonstrated that simple pacing during sinus rhythm carried out at different atrial anatomic sites in a structurally normal heart could generate a characteristic PWM that may help to guide in localization of the origin of atrial depolarization. We constructed an algorithm based on our results to guide localization of origin of P waves based on PWM. Several algorithms have been previously generated utilizing correlation between successful ablation sites and the surface 12 lead ECG of the AT. Uhm et al.[10] tested the accuracy of these algorithms in a population of 194 patients and reported overall accuracy rates of 78, 60 and 55% for Kistler et al.[5], Tang et al.[4] and Qian et al.[6] respectively.

First step: RA versus LA

We found that PWM in lead V1 was the most useful in differentiating right (negative/isoelectric in 85%) from left (positive in 71%) atrial locations. Tang et al.[4] found that a positive P wave in lead V1 can predict a left atrial origin with a sensitivity of 93%, specificity of 88%, positive predictive value (PPV) of 87%, and negative predictive value (NPV) of 94%. Kistler et al.[5] also developed an algorithm to localize focal AT in which positive or negative–positive biphasic P-wave in V1 had 100% sensitivity, 81% specificity, 76% PPV, and 100% NPV for left atrial locations. Qian et al.[6] also reported that a positive P wave in lead V1 was associated with a sensitivity of 95% for a left AT with a high sensitivity of 95% and relatively low specificity of 64%.

Second step: Localization based upon P wave frontal plane axis

We found that PWM in lead aVR was useful in differentiating superior (negative in 91% RA and 95% LA) from inferior (positive in 88% RA and 90% LA) atrial locations. Also, the lead aVF significantly differentiated superior TA pacing from other TA locations with all other superior RA locations demonstrating PWM similar to that of superior TA pacing. The same was also demonstrated for pacing around the mitral annulus.

Qian et al.[6] reported that a negative P wave in lead aVR and positive in inferior leads has a sensitivity of 95%, specificity of 90%, a PPV of 83% and a NPV of 97% for high atrial areas including high CT, superior PVs, and RAA. On the other hand, a positive P wave in lead aVR and negative in inferior leads has a sensitivity of 88%, specificity of 89%, a PPV of 84% and a NPV of 92% for low septal origins, including CS os and inferior TA. Tang et al.[4] and Kistler et al.[5] reported similar findings regarding the P wave polarity in inferior lead, but they didn't use the lead aVR for such differentiation.

Third step: specific locations

Superior locations within the RA **(CT, SVC, RAA, High septum and High TA)**

This group of locations demonstrated a similar PWM in the limb leads with the P wave negative or isoelectric in V1, positive in aVF and negative in aVR. However, we found that the precordial transition was earlier at high CT, high septum and SVC and late transition from negative to positive PWM at RAA and a negative concordance at superior TA. In our algorithm, a cutoff point at 110 msec of P wave

duration could differentiate between SVC & CT (>110 msec) and High septum (<110 msec).

Kistler et al.[5] reported that a PWM positive in lead II, negative in aVR, and biphasic in V1 was associated with a sensitivity of 93%, a specificity of 95%, a PPV of 84%, and an NPV of 98% for foci at the CT.

ATs originating from TA often has a characteristically negative P wave in lead V1, and deeply negative inferior leads except for superior TA that usually shows a positive, or biphasic PWM with low amplitude.[11] ATs from RAA has PWM negative in lead V1, becoming progressively positive across the precordial leads and in the inferior leads these p waves are low amplitude positive in the majority of patients.[4]

Qian et al.[6] reported that the negative P wave in lead V1 became progressively positive from V1 to V6 with predictive accuracies over 90% for RAA ATs. Several studies reported the difficulty in differentiating PWM between RAA and sup. TA.[5,6]

Inferior locations within the RA (med., Lat., inf. TA and perinodal region)

This group of locations demonstrated a similar PWM in the limb leads with the P wave negative or isoelectric in V1, negative in aVF and positive in aVR. In our algorithm, a cutoff point at 130 msec of P wave duration could differentiate between inferolateral TA (>130 msec) and inferomedial TA & CS os (<130 msec).

Kistler et al.[5] showed that an isoelectric P-wave in lead V1 had a specificity and a PPV of 100% and an NPV of 97% for perinodal and right septal tachycardias, but the sensitivity was only 50% as there was significant overlap between perinodal and left septal sites.

Anatomical locations within the LA

Superior locations within the LA (PVs , LAA and High MA)

This group of locations demonstrated a similar PWM in the limb leads with the P wave positive in V1, positive in aVF and negative in aVR. PWM in leads I & V6 could differentiate between pacing from these locations being negative (73.3% & 68.7%) and isoelectric (60% & 80%) in LAA and superior MA, respectively, compared to isoelectric 70.4 % and positive 92.6% in LPVs, respectively. PWM in RPVs was positive in 100% in lead I and V6. P wave amplitude could differentiate between superior and inferior PVs with a cutoff point at 0.10 mv.

Kistler et al.[5] reported that a PWM positive in leads V1 to V6 and positive in lead I had a sensitivity of 87%, specificity of 94%, PPV of 65%, and NPV of 100% for RPV. For LPVs, a PWM that was isoelectric or negative in lead I and positive in lead II & V1 had a sensitivity of 82%, specificity of 98%, PPV of 88%, and NPV of 97%. They also reported P-wave for AT arising from inferior PVs was low-amplitude compared to superior PVs.

Yamane et al. reported that positive P waves in I and aVL had high specificity, but moderate sensitivity for RPVs and a Superior PV origin could be distinguished from inferior by amplitude in lead II of >100 microV.[12]

Kristler et al.[5] reported that PWM from RAA ATs was similar to LPVs with deeply negative P-waves in lead I suggesting an origin in the LAA. While those from superior MA showed a negative, then positive PWM in lead V1 and isoelectric or negative in lead aVL with a sensitivity of 88%, a specificity of 99%, a PPV of 88%, and an NPV of 99%. Another study observed that a negative P-wave in leads I and

aVL predicted an LAA focus with a sensitivity and specificity of 92% and 97%, respectively.[13]

Qian et al.[6] stated that a negative or low-amplitude positive P waves in leads I & aVL has a sensitivity of 79% and a specificity of 94% for the extreme left foci, including LAA, left PVs, and superior MA. They also reported that PV P waves were always positive in precordial leads but progressively flattened with a predictive accuracy over 90%.

Inferior locations within the LA (med., Lat., inf. MA and CS)

This group of locations demonstrated a similar PWM in the limb leads with the P wave positive in V1, negative in aVF and positive in aVR. PWM in the lead I was significantly negative at distal CS and MA locations and isoelectric at mid CS and CS os. In our algorithm, a cutoff point at 140 msec of P wave duration could differentiate between inferolateral MA (>140 msec) and medial MA (<140 msec).

Kistler et al.[5] reported that, at CS ostium, a PWM neg/pos or iso/pos in lead V1, negative in leads II, III, and aVF, and positive in aVL had a sensitivity of 86%, a specificity of 98%, a PPV of 86%, and an NPV of 98% with significant overlap was seen with AT foci at the left septum. Qian et al.[6] also reported that migration of PWM from positive to negative in precordial leads was a specific feature of CS ostium-originated AT.

The P wave duration

We found that the P wave duration (PWD) at the lateral atrial sites was greater than those at the medial or septal sites. The PWD was greater at lateral TA, RAA, SVC and high CT in contrary with the medial TA and right atrial septal sites. The PWD was greater at LAA, LPVs and lateral MA in comparison to RPVs, medial MA and left septum.

Qian et al.[6] reported that P waves associated with parahisian AT were narrower in most of the 12 leads. Compared with that of CS ostium, lead aVL showed the most significant difference (49.6 +/- 8.8 ms vs 71.8 +/- 6.9 ms, P = 0.005). They suggested that P-wave duration in lead aVL less than 60 ms predicted parahisian origin with an accuracy of 74% (P = 0.008).

Limitations

Our study population was small and was performed over a relatively short time period. However, despite the small patient population, more than 1000 P wave morphologies were obtained from different anatomic locations in the atria. Our template is only valid in structurally normal heart which may limit its generalizability for patients who have structural heart disease. Finally, this is considered a derivation study that needs further validation in patients with atrial tachycardia.

Conclusion

P-wave morphology and duration derived from templates generated through atrial pace-mapping can help localize sites of origin of pacing and thus could be used to guide localization of focal atrial tachycardia.

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List of abbreviations

AT: Atrial tachycardia

AVNRT: Atrioventricular Nodal Re-entrant Tachycardia

AVRT: Atrioventricular Re-entrant Tachycardia

BPM: Beat per minute

CS: Coronary Sinus

CS os: Coronary Sinus ostium

CT: Crista terminalis

ECG: Electrocardiogram

EPS: Electrophysiological study

F: French

FO: Fossa ovalis

ISO: Isoelectric

LA: Left Atrium

LAA: Left atrial appendage

LIPV: left inferior pulmonary vein

LS: Left septum

LSPV: left superior pulmonary vein

MA: Mitral annulus

NEG: Negative

NPV: Negative predictive value

POS: Positive

PPV: Positive predictive value

PSVT: Paroxysmal supraventricular tachycardia

PVs: Pulmonary veins

PVC: Premature Ventricular Contraction

PWA: P-wave duration amplitude

PWD: P-wave duration

PWM: P-wave morphology

RA: Right atrium

RAA: Right atrial appendage

RIPV: Right inferior pulmonary vein

ROC: Receiver operating characteristic

RSPV: Right superior pulmonary vein

RV: Right ventricle

SD: Standard deviation

SNRT: Sinus node Re-entrant Tachycardia

SPSS: Statistical Package for the Social Science

SVC: Superior Vena Cava

TA: Tricuspid annulus

VT: Ventricular Tachycardia

Figures:

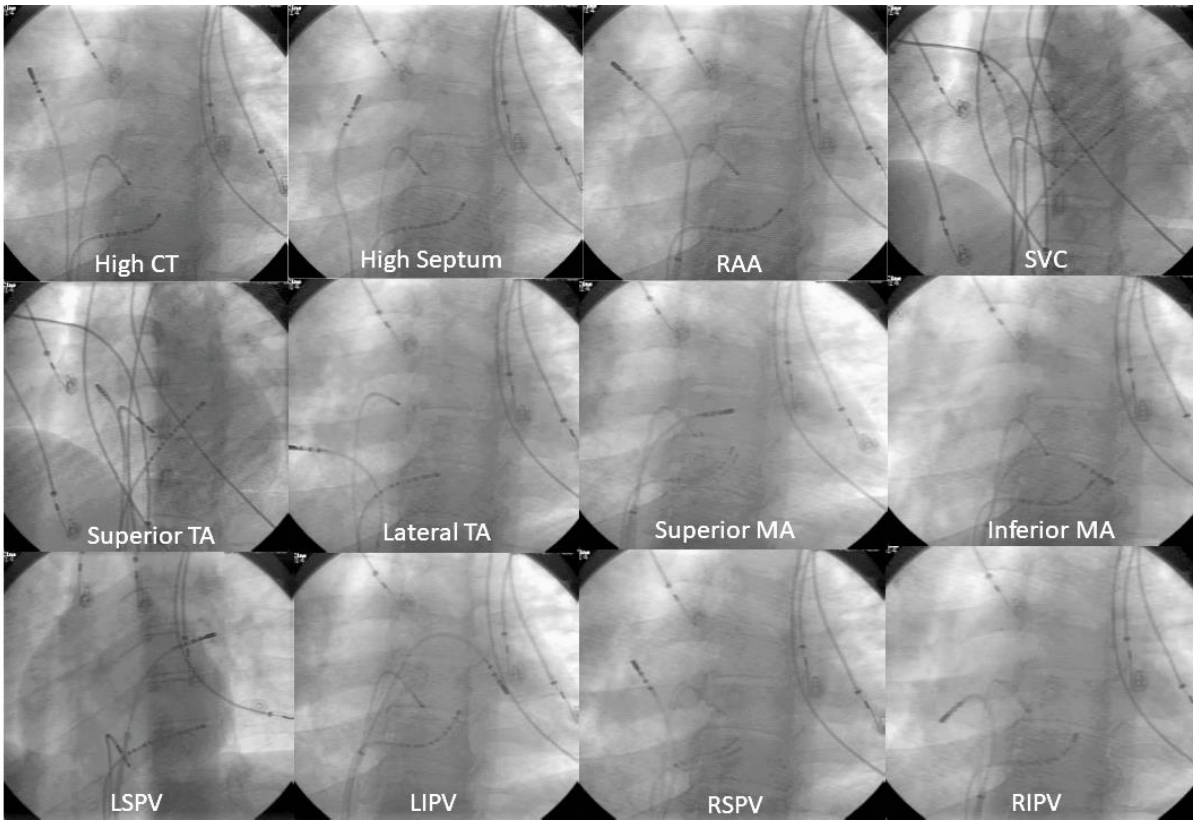

Figure 1. An LAO 30^{o} fluoroscopic views of catheter positions for atrial pacing sites. Top panel (from left to right): high CT, high septum and RAA and SVC. Middle panel (from left to right): Bottom: SVC, superior TA, lateral TA, superior MA and inferior MA. Top panel (from left to right) : LSPV, LIPV, RSPV and RIPV.

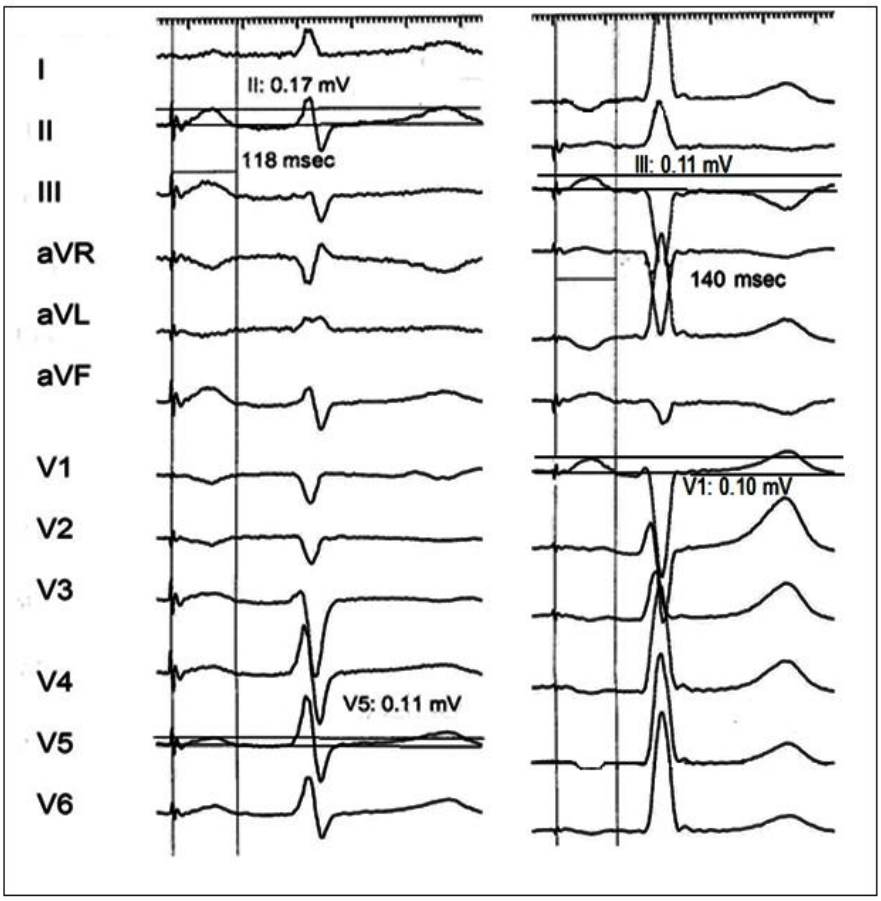

Figure 2: Examples of how P wave duration and amplitude were calculated. Left: 12-lead ECG recording from high crista terminalis with a P wave duration of 118 ms and a P wave amplitude of 0.17 mV in lead II and 0.11 mV in lead V5, P wave morphology was isoelectic in lead aVL and negative in lead V1. Right: 12-lead ECG recording from superior mitral annulus with a P wave duration of 140 ms and a P wave amplitude of 0.11 mV in lead III and 0.10 mV in lead V1, P wave morphology was negative in lead aVL and positive in lead V1.

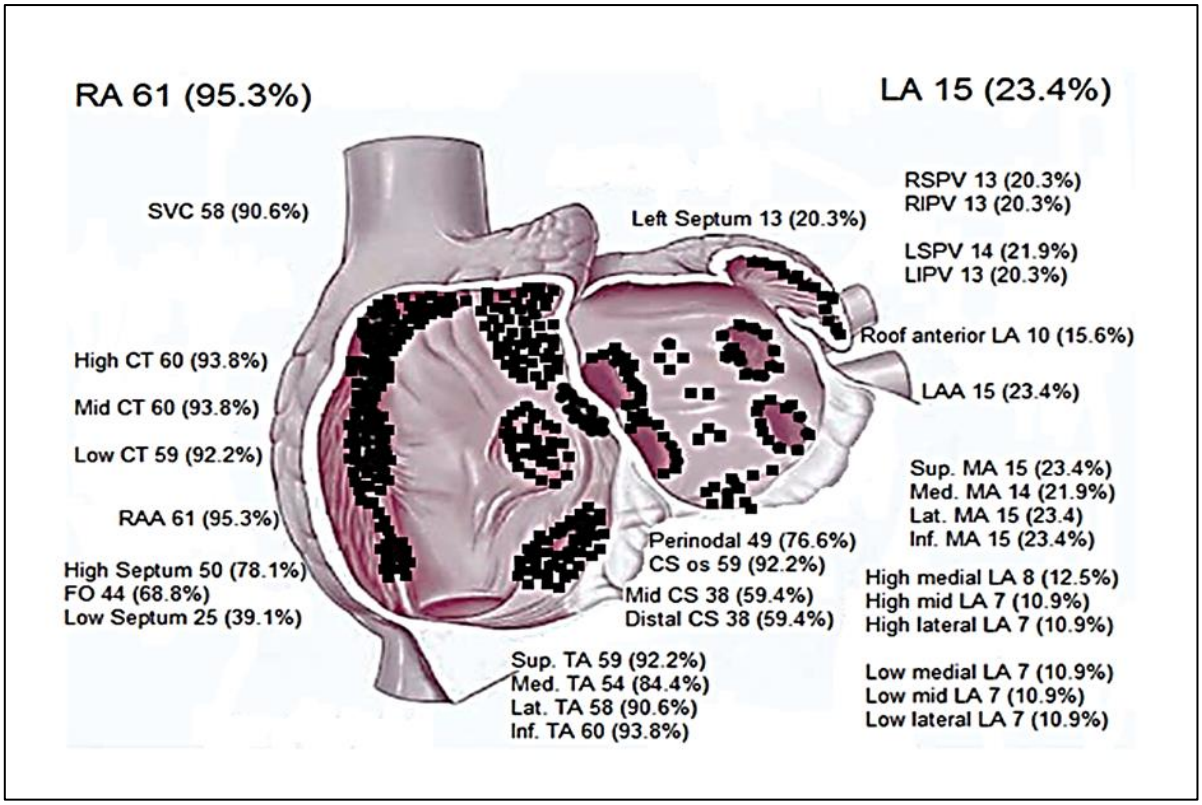

Figure 3: A schematic representation of the anatomic distribution of the atrial pacing sites. RA: right atrium, SVC: superior vena cava, CT: crista terminalis, RAA: right atrial appendage, FO: fossa ovalis, Sup.: superior, Med.: medial, Lat.: lateral, Inf.: inferior, TA: tricuspid annulus, LA: left atrium, RSPV: right superior pulmonary vein, RIPV: right inferior pulmonary vein, LSPV: left superior pulmonary vein, LIPV: left inferior pulmonary vein, LAA: left atrial appendage, CS: coronary sinus, MA: mitral annulus. The number of pacing sites with percentage to total number of subjects of studied population was shown. (adapted from Kistler et al).

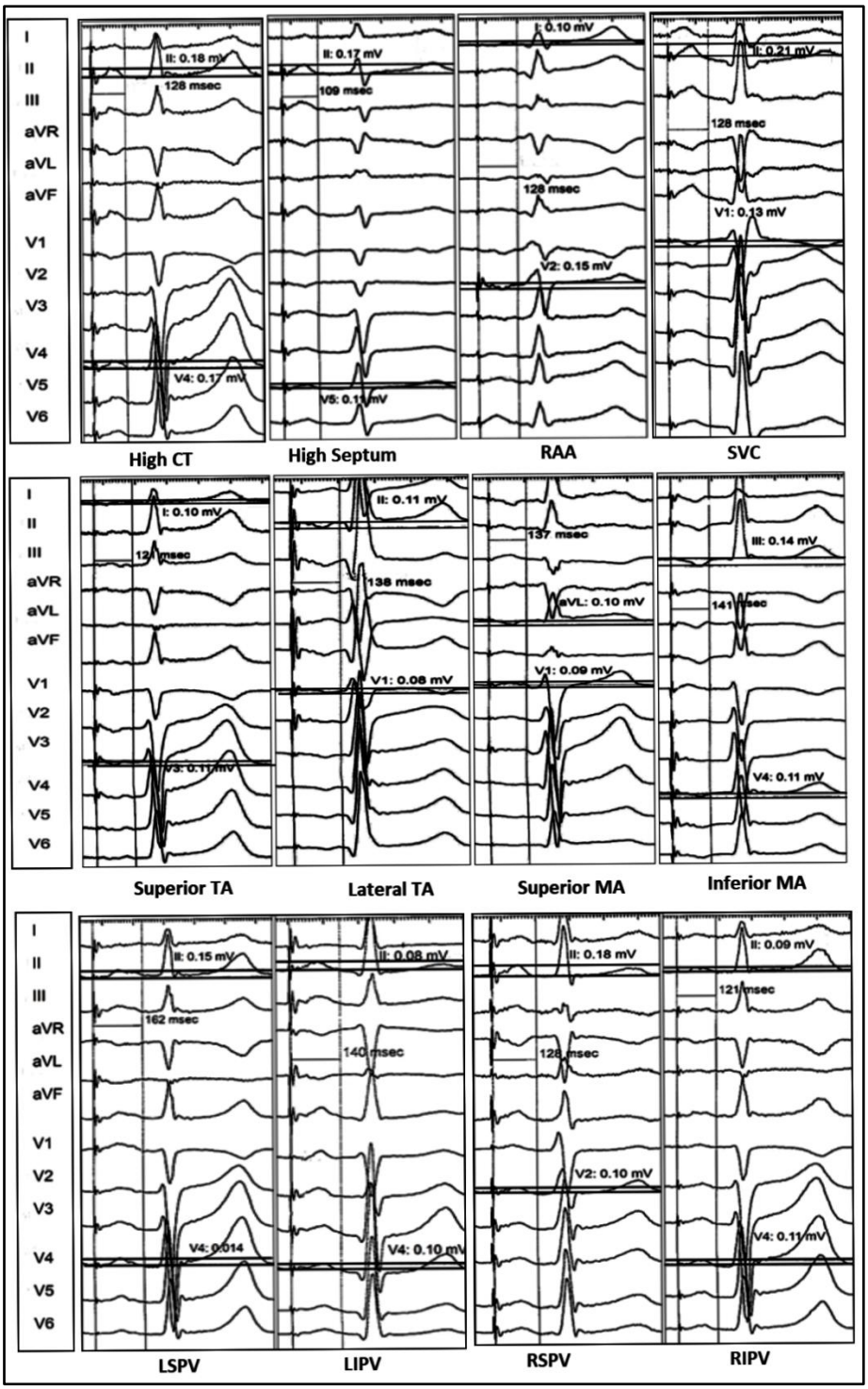

Figure 4: Examples of the paced P-wave morphology for atrial pacing sites. . Top panel (from left to right): high CT, high septum and RAA and SVC. Middle panel (from left to right): Bottom: SVC, superior TA, lateral TA, superior MA and inferior MA. Top panel (from left to right) : LSPV, LIPV, RSPV and RIPV.

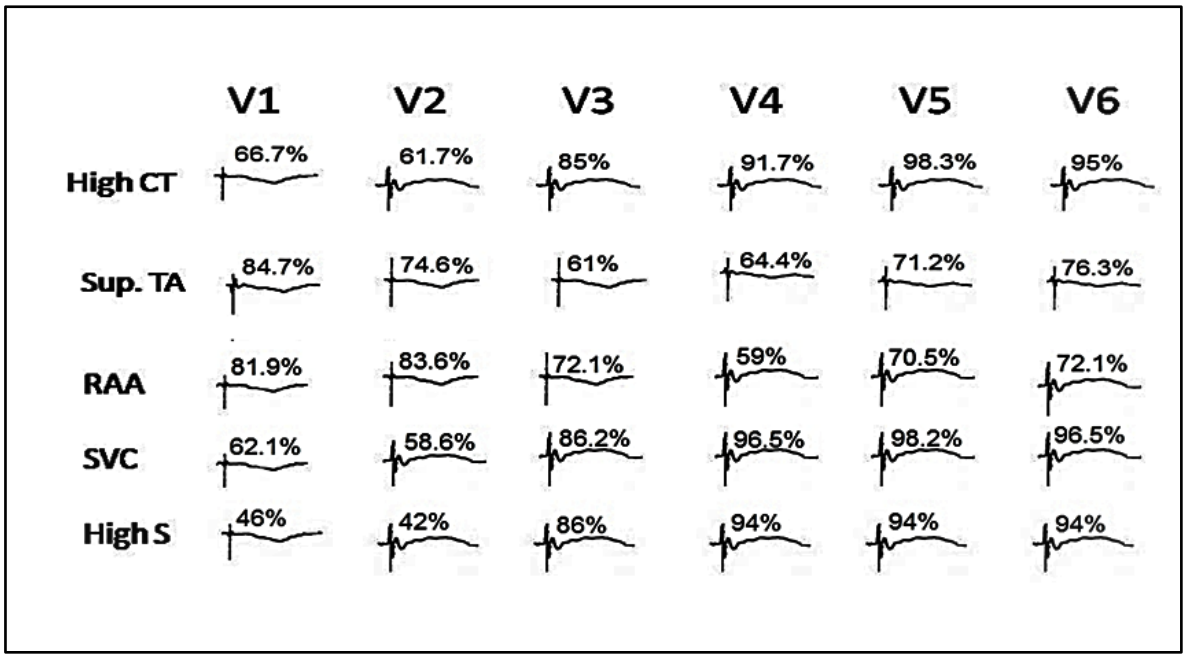

Figure 5: Diagram showing the pattern of precordial transition during pacing at high CT, SVC and high right septum with early transition from negative to positive between V1 and V2 (61.7%, 58.6% and 42% respectively). RAA pacing showed late transition from negative to positive between V3 and V4 (59%), while pacing at superior TA showed negative concordance with shallow negative at V5,6(76.3%) across precordial leads.

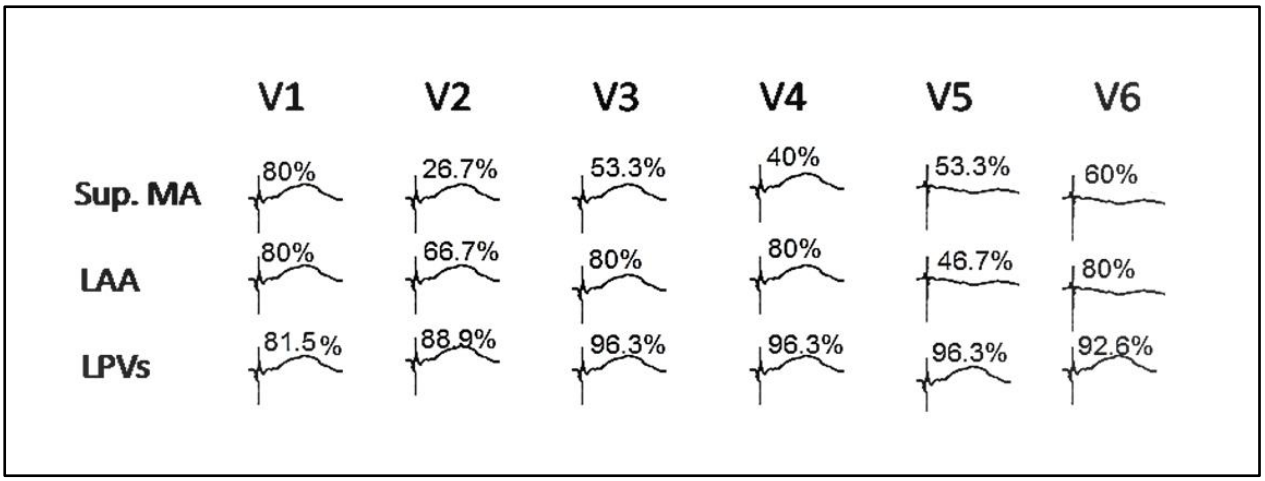

Figure 6: Diagram showing the precordial transition of PWM from positive to isoelectric when pacing at superior MA between V4 and V5 (53%) and LAA (46.7%). LPVs showed positive precordial concordance of PWM.

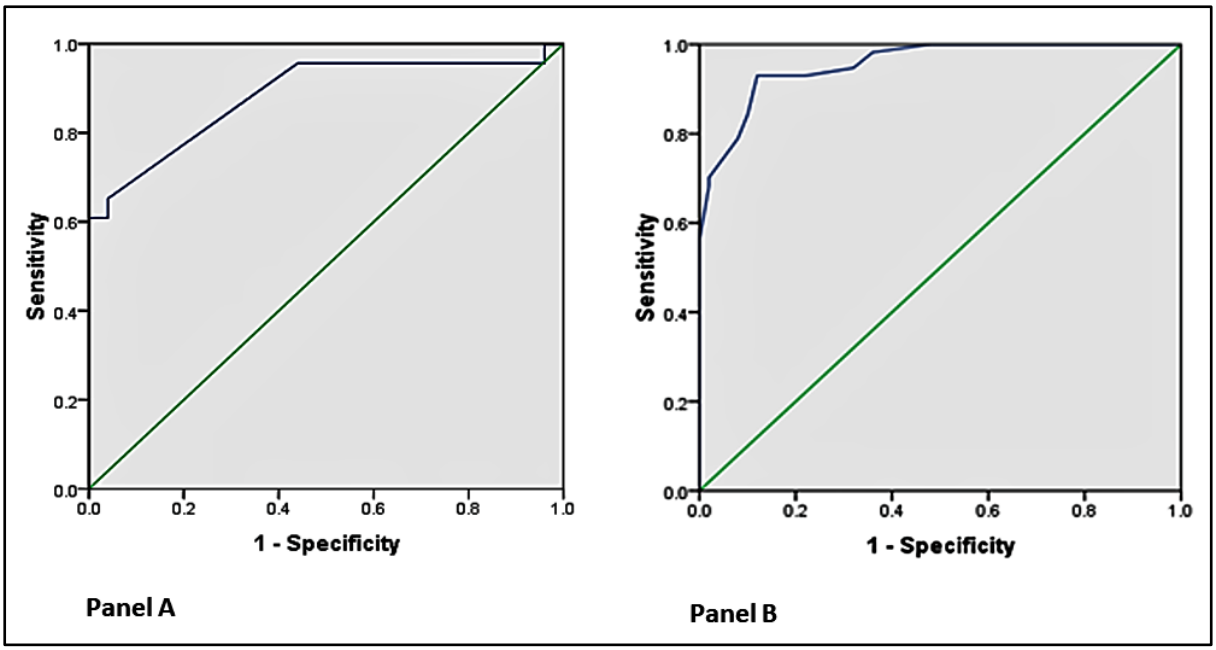

Figure 7: Panel A: ROC curve of P wave duration< 110msec predicting high septal pacing in comparison with SVC pacing. **Panel B:** ROC curve of maximum P wave amplitude >0.1mV to predict superior PVs in comparison with inferior PVs.

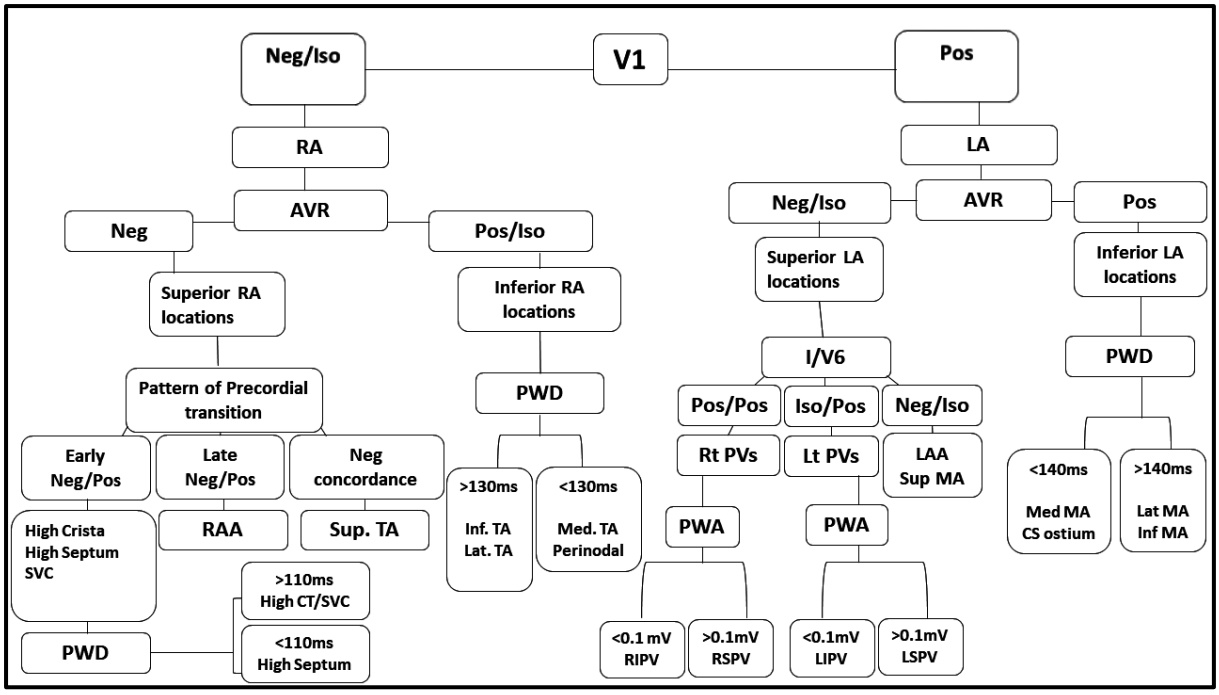

Figure 8: A proposed algorithm for predicting atrial site on the bases of PWM. LA: left atrium, RA: right atrium, CT: crista terminalis, SVC: superior vena cava, RAA: right atrial appendage, Sup. TA: superior tricuspid annulus and High Septum, Inf. TA: inferior, Med. TA: Medial, Lat. TA: lateral tricuspid annulus and Perinodal, PVs: pulmonary veins, LAA: left atrial appendage and Sup. MA: superior mitral annulus, Inf. MA: inferior, Med. MA: Medial, Lat. MA: lateral mitral annulus, CS ostium: coronary sinus ostium, RIPVs: right inferior pulmonary veins, RSPVs: right superior pulmonary veins, LIPVs: left inferior pulmonary veins, LIPVs: left superior pulmonary veins. Pos: positive, neg: negative, iso: isoelectric, PWD: P wave duration, PWA: P wave amplitude.

Tables

Table 1: Comparison of the PWM between RA and LA pacing sites using leads **V1, aVL** and **I**.

PWM/V1	**RA (n= 756)**	**LA (n= 269)**	***P- value***
po	76 (10.2%)	190 (**71%**)	
ne	346 (**46%**)	3 (1 %)	
iso	290 (**39%**)	75 (28%)	**0.049**
po/ne	27 (4%)	0 (0%)	
ne/po	6 (0.8%)	0 (0%)	
PWM/aVL			
po	388 (**51.4%**)	77 (28.7%)	
ne	15 (1.8%)	118 (**44%**)	
iso	346 (**46%**)	73 (27.3%)	**0.041**
po/ne	0 (0%)	0 (0%)	
ne/po	6 (0.8%)	0 (0%)	
PWM/I			
po	467 (**61.8%**)	67 (25%)	
ne	7 (0.8%)	99 (**37%**)	
iso	277 (**36.7%**)	102 (**38%**)	
po/ne	0 (0%)	0 (0%)	
ne/po	5 (0.7%)	0 (0%)	

RA: right atrium, LA: left atrium, PWM: P wave morphology, po: positive, ne: negative, iso: isoelectric.

Table 2: Comparison of PWM in lead **aVR**

PWM	**RA (superior)* (n= 288)**	**RA (inferior)* (n= 221)**	***P- value***
po	9 (3.1**%**)	165 (**74.7**%)	
ne	262 (**91**%)	25 (11.3**%**)	**0.041**
iso	14 (4.9%)	30 (13.6%)	
po/ne	2 (0.7%)	0 (0%)	
PWM	**LA (superior)"** (n= 83)	**LA (inferior)"** (n= 179)	
po	4 (4.8**%**)	161 (**89.9**%)	
ne	55 (**66.3**%)	4 (2.2**%**)	**0.043**
iso	24 (28.9%)	14 (7.8%)	
po/ne	0 (0%)	0 (0%)	

PWM: P wave morphology, RA: right atrium, ne: negative, po: positive, LA: left atrium

*(Superior RA: high crista terminalis, high septum, superior TA, RAA, and SVC, inferior RA: Medial, lateral, inferior TA and perinodal)

"(Superior LA: Pulmonary veins, superior MA and LAA, inferior LA: Medial, lateral, inferior MA and CS)

Table 3: Comparison of the PWM in the lead **aVF** across tricuspid and mitral annuli

PWM/aVF	**Sup.TA (n= 59)**	**Inf.TA (n= 60)**	**Med.TA (n= 54)**	**Lat.TA (n= 58)**
po	41 (**69.5%**)	3 (5%)	4 (7.4%)	4 (6.9%)
ne	3 (5.1%)	53 (**88.3%**)	45 (**83.3%**)	42 (**72.4%**)
iso	14 (23.7%)	3 (5%)	5 (9.3%)	11 (19%)
po/ne	1 (1.7%)	1 (1.7%)	0 (0%)	1 (1.7%)
P value **(Each group compared to the sup TA)**		**<0.001**	**0.001**	**0.001**
PWM/aVF	**Sup.MA (n= 15)**	**Inf.MA (n= 15)**	**Med.MA (n= 14)**	**Lat.MA (n= 15)**
po	10 (**67.7%**)	0 (0%)	1 (7.1%)	1 (6.7%)
ne	3 (20%)	13 (**86.7%**)	11 (**78.6%**)	10 (**66.7%**)
iso	2 (13.3%)	2 (13.3%)	2 (14.3%)	4 (26.7%)
po/ne	-	-	-	-
P value **(Each group compared to the sup MA)**		**0.001**	**0.002**	**0.001**

TA: tricuspid annulus, Sup.:superior, Inf.: inferior, Med.: medial, Lat.: lateral, PWM: P wave morphology, po: positive, ne: negative, iso: isoelectric. MA: mitral annulus, Sup.:superior, Inf.: inferior, Med.: medial, Lat.: lateral, PWM: P wave morphology, po: positive, ne: negative, iso: isoelectric.