Al-Azhar Med. J. *Vol. 49(3), July, 2020, 1173-1184*
DOI : 10.12816/amj.2020.91637
https://amj.journals.ekb.eg/article_91637.html

NONINVASIVE LOCALIZATION OF ACCESSORY PATHWAYS IN WOLFF–PARKINSON–WHITE SYNDROME BY TWO-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY

By

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ABSTRACT

Background: Two-Dimensional Speckle Tracking Echocardiography (2D-STE) is a non-Doppler echocardiographic modality that allow quantification of myocardial deformity and its timing in 2D grey scale images, and was proved to be beneficial in assessment of dyssynchrony (STAR trial).

Objective: To investigate the capability of 2D-STE for localizing Accessory Pathways (APs) in patients with Wolf-Parkinson-White (WPW) Syndrome.

Patients and Methods: The prospective study included 15 patients with manifest AP indicated for invasive endocardial mapping and ablation. All patients were assessed by twelve-lead ECG, 2D-STE for the earliest activated site and invasive Electrophysiology study (EPs).

Results: Out of the 15 patients with left-sided APs, 2D-STE was able to accurately localize the site of AP in 10 patents (66.6%), while electrocardiogram (ECG) was able to localize the site of AP in 12 patients (80%).

Conclusion: 2D-STE has the ability to approximate the location of AP without the pitfalls of Doppler methods. However, ECG still more accurate and reproducible tool.

Keywords: Speckle Tracking Echocardiography, Accessory Pathway, Wolf-Parkinson-White Syndrome.

INTRODUCTION

The hallmark of Wolff–Parkinson–White (WPW) syndrome is early depolarization and thereby contraction of part of the ventricles at the site of atrioventricular APs *(Delelis et al., 2012)*. In patients with Wolff–Parkinson–White (WPW) syndrome, ventricles are electrically and mechanically pre-excited through an accessory pathway, which cause eccentric ventricular activation and an asynchronous spread of ventricular depolarization *(Park et al., 2013)*. LV wall motion abnormality was reported in patients with WPW syndrome, and some studies have suggested that presence of abnormal interventricular septal wall motion could be one of the causes of LV dyssynchrony and hence LV dysfunction that is reversible and not attributed to tachyarrhythmia *(Dai et al., 2013)*. Whereas numerous body surface electrocardiogram algorithms have been described, the invasive electrophysiological study remains the gold standard method for localizing the site of the AP, hence allowing its catheter ablation *(Delelis et al., 2012).*

In myocardium with intact excitation-contraction coupling, electrical and mechanical events are tightly linked. Therefore, determining the site of first systolic motion is the basis of usage of different echocardiographic modalities in localization of accessory pathway *(Cai et al., 2012).* In the STAR study, the utility of speckle-tracking strain to quantify LV dyssynchrony was proven with the advantage of differentiating active motion from passive motion independent of Doppler angle *(Tanaka et al., 2010).* 2D-STE is a promising imaging modality which is reflected by the increasing number of publications focusing on its great potential clinical utility. Some have already heralded STE as 'the next revolution in echocardiography *(Blessberger and Binder, 2010).* 2D-STE modality is a non-Doppler method that allows the quantification of the myocardial deformation and its timing on 2D greyscale images without the potential pitfalls of Doppler-dependent methods *(Delelis et al., 2012).*

PATIENTS AND METHODS

Ethical approval was obtained from the medical ethical and research committee, Faculty of Medicine, Al-Azhar University. Written informed consent was obtained from each patient.

The study population consisted of 15 patients with manifest WPW syndrome, who were collected from the Cardiology Clinic of Al-Azhar University Hospitals, based on resting ECG findings, clinical history of frequent palpitation and/or documented ECG with attacks of atrioventricular reentrant tachycardia (AVRT). All enrolled patients were indicated for invasive endocardial mapping and radiofrequency catheter ablation (RFCA). The study was performed at Cardiology Department, Faculty of Medicine, Al-Azhar University between June 2019 and March 2020.

Patient's selection:

Inclusion criteria:

Patients with manifest WPW syndrome, with left-sided AP, who were indicated for invasive endocardial mapping and ablation.

Exclusion criteria:

Presence of structural heart disease such as coronary artery disease, congestive heart failure, valvular or congenital heart disease. Any rhythm other than sinus rhythm or AVRT. Presence of chronic systemic, inflammatory or neoplastic disease. Patients with right-sided AP as predicted from surface ECG was excluded after confirmation by endocardial mapping, due to unavailability of right ventricular speckle tracking echocardiography system.

The surface ECG of each subject was assessed to estimate the location of APs according to the criteria of Arruda algorithm *(Arruda et al., 1998).* Briefly, it is based on classifying the initial 20 ms of the delta wave in leads I, II, aVF and V1 as positive, negative or isoelectric, and assessment of the ratio of R and S wave amplitude in leads III and V1. Accordingly, the diagnostic flow chart of Arruda algorithm was followed to determine one of 10 possible locations around mitral and tricuspid annuli. Patients with right-sided AP were excluded after confirmation by EP study.

All subjects underwent a comprehensive transthoracic echocardiography before the planned invasive endocardial mapping using Philips Affinity 50 Ultrasound system with an S4-2 (2-4 MHz) cardiac sector transducer. With simultaneous ECG recording and over three cardiac cycles, all standard views were obtained including parasternal long-axis view, parasternal short-axis views (basal, mid and apical), apical 4-chamber view, apical 2-chamber view and apical long-axis view. All measurements were according to the guidelines of American Society of Echocardiography (ASE). The physician analyzer was unaware of clinical data or ECG data.

Standard echocardiographic measurements were obtained including aortic root diameter (AoD), left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum thickness (IVST), and left ventricular posterior wall thickness (LVPWT). Left ventricular ejection fraction (LVEF) was assessed by modified Simpson method, while cardiac valves and diastolic function were assessed by a comprehensive Doppler study.

For left ventricular 2D-STE, the ECG-gated 2D data over three cardiac cycles were stored and transferred to a computer for offline analysis. Six sectors were used including the three parasternal short axis views (basal, mid and apical) and the three aforementioned apical views. The images were analyzed for 2D-STE using 2D wall motion tracking software named Automated Cardiac Motion Quantification AI (aCMQAI). The automatic tracking of the myocardial contour on an end-systolic frame was carefully verified with manual correction if necessary, to ensure optimal tracking and to cover the entire thickness of LV myocardium. Using the time to peak tool in the aCMQAI software, the LV myocardial segmental deformational timing were computed and automatically represented in a single bull's eye depiction divided into 17 segments identical to the 17 segments ASE model *(Cerqueira et al., 2002)*. The segment with the shortest estimated time represented the earliest activated site and hence the location of the AP.

All WPW patients underwent an invasive electrophysiological study for radiofrequency catheter AP ablation. The ablation procedure was considered successful if anterograde and retrograde conduction of the AP was completely abolished. This was associated with inability to induce AVRT. Endocardial mapping was considered the gold standard reference for localization the AP and was compared with the 2D-STE-derived location *(Issa et al., 2019)*.

Statistical analysis:

Data were analyzed using Statistical Package for the Social Science (SPSS) version 20. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done: The relationship between the ACP site determined by endometrial mapping, and either ECG or 2D-STE were determined by Cramer's V test which was based on Pearson’s chi-squared statistics. P-value < 0.05 was considered significant.

RESULTS

The study group included 15 patients, 7 males and 8 females. The mean age was 34.87 ± 7.909 years (range = 21 – 51 years), while the Body Mass Index (BMI) mean was 24.20 ± 1.935 Kg/m^2 (range = 21 – 27 Kg/m2). Subject characteristics were summarized in **Table (1)**.

Table (1): Subjects Characteristics

Parameters		Patients (N = 15)	
Age (years)	**Mean ±SD**	**34.87± 7.909**	
	Median	**36**	
Sex (No & %)	**Male**	**7**	**46.7%**
	Female	**8**	**53.3%**
BMI (kg/m^2)	**Mean ±SD**	**24.20± 1.935**	
	Median	**24**	

Table (2) demonstrated the data of all patients regarding localization of their APs, with comparison between the accurate site as derived from the EP study and the predicted sites from ECG Arruda algorithm and 2D-STE. It’s obvious that many of ECG potential sites can cover two echo potential sites. The difference between the modalities regarding nomenclature was obvious. Therefore, agreement between modalities was not always reflected by the modality-specific names.

Table (2): Comparison between ECG, 2d-STE and EP study regarding location of AP in each patient

WPW Subjects	Sex	Age Years	Prediction From Arruda Algorithm	Prediction From 2D-STE	EP study (Gold Standard)
1	M	51	LP / LPL	Infero-Lateral	LPL
2	M	21	LL / LAL	Antero-Lateral	LAL
3	F	43	LPS	Inferior	LP
4	M	36	RPS	Inferior	RPS
5	F	28	LL / LAL	Anterior	A
6	F	26	LPS	Infero-Septum	LPS
7	F	29	LL / LAL	Antero-Lateral	LAL
8	M	33	LL/ LAL	Antero-Lateral	LAL
9	F	39	LP / LPL	Infero-Lateral	LPL
10	M	43	LP / LPL	Infero-Lateral	LPL
11	F	27	LP / LPL	Antero-Lateral	LPL
12	F	36	LL / LAL	Infero-Septum	LPS
13	M	37	LL / LAL	Infero-Lateral	LAL
14	M	33	LL / LAL	Antero-Lateral	A
15	F	41	LP / LPL	Infero-Septum	MS

A: anterior, AL: antero-lateral, IL: infero-lateral, I: inferior, IS: infero-septum, AS: antero-Septum, LAL: left antero-lateral, LPL: left postero-lateral, LP: left posterior, LPS: left postero-septum, RPS: right postero-septum, MS: mid septum.

Perfect agreement was achieved in 10/15 (66.6%) patients, with significant P value = 0.038, but all the remaining five patients demonstrated adjacent agreement on either side of the perfect agreement site **(Figure 1)**.

EPS \ STE	A	AL	IL	I	IS	AS
A	1	1				
LAL		3	1			
LPL		1	3			
LP				1		
LPS/ RPS				1	2	
MS					1	

Figure (1): Correlation between predicted accessory pathway location by 2D- STE and the actual location based on EPS. Green cell indicates a perfect match between echo-predicted site and the EPS Localization site. pale green cell indicates Non-perfect but adjacent localization. Numbers indicate numbers of patients. A: anterior, AL: antero-lateral, IL: infero-lateral, I: inferior, IS: infero-septum, AS: antero-Septum, LAL: left antero-lateral, LPL: left postero-lateral, LP: left posterior, LPS: left postero-septum, RPS: right postero-septum, MS: mid septum.

Perfect agreement was achieved in 12/15 (80%) of patients, with P value = 0.001, and adjacent agreement within a range on either side of the perfect agreement site was observed in one patient. The remaining two patients demonstrated disagreement (Figure 2).

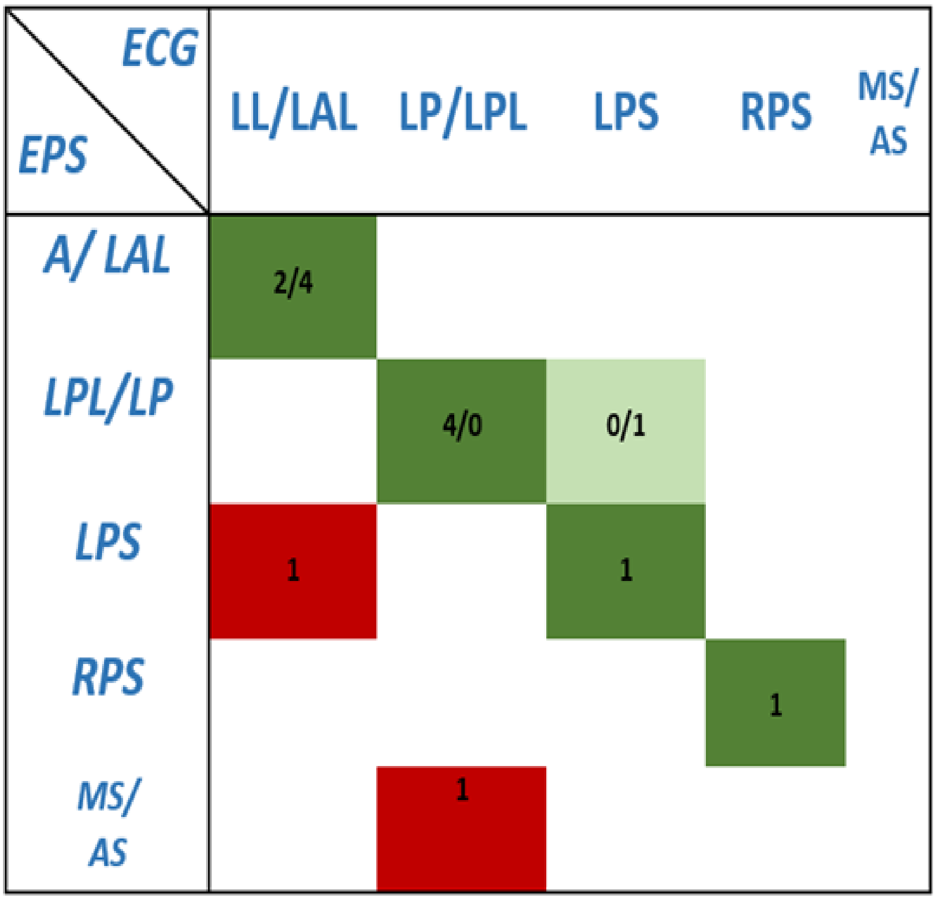

Figure (2): **Correlation between predicted accessory pathway location by ECG and the actual location based on EPS. Green cell indicates a perfect match between echo-predicted site and the EPS Localization site. pale green cell indicates Non-perfect but adjacent localization. Red cell indicate disagreement. Numbers indicate numbers of patients.LL/LAL: left-lateral/left antero-lateral, LP/LPL: left posterior/left postero-lateral, LAL: left antero-lateral, LPL: left postero-lateral, LP: left posterior, LPS: left postero-septum, RPS: right postero-septum, MS: mid septum.**

In comparison with EP study as the gold standard for localizing APs, ECG was superior to 2D-STE, 80% and 66.6% respectively. However adjacent agreement within a range on either side of the accurate site was in favor of the 2D-STE **(Figure 3)**.

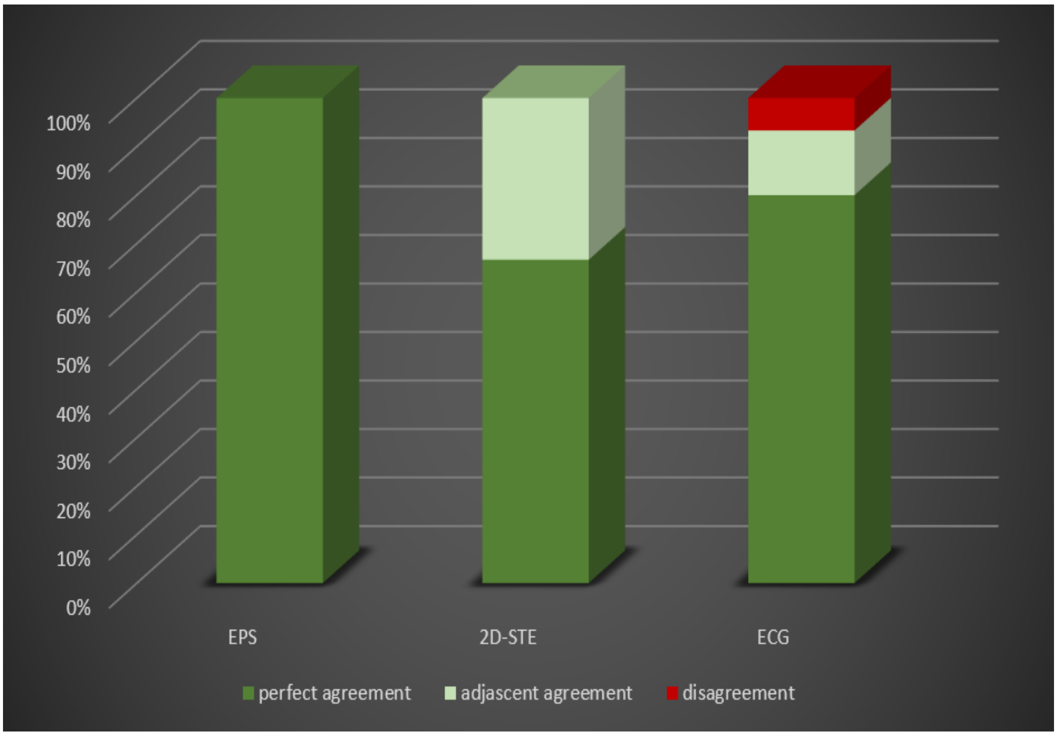

Figure (3): Comparison between 2D-STE and ECG regarding accuracy of AP localization with EP study as the gold standard

DISCUSSION

The present study demonstrated clear superiority of ECG over 2D-STE regarding approximation of the location of APs. However, the accuracy of ECG algorithms in recent studies has not reached the accuracy that was previously reported by their designers *(Maden et al., 2015)*. In a study that tested seven different ECG algorithms in localizing APs, all algorithms were less accurate in predicting APs location than expected from data from their original authors *(Wren et al., 2012)*. 3D-STE was found superior to ECG in localizing APs with regard that EP study as the gold standard *(Ishizu et al., 2016)*. It was concordant with the results of *Esmaeilzadeh et al. (2013)* which showed superiority of strain imaging parameters over ECG prediction. Other echocardiographic conventional modalities including M-Mode and Trans-Esophageal Echocardiography (TEE) were inferior to ECG *(Cai et al., 2012)*.

The capability of 2D-STE for localizing APs was confirmed in the present study. It is concordant with the results of *Delelis et al. (2012)* who concluded that 2D-STE has the ability to approximate the location of APs in addition to its ability to assess myocardial dyssynchrony. The 2D-STE potential abilities regarding APs location was confirmed by the study of *Ishizu et al. (2016)*, a noninvasive isochrone activation imaging (AI) system with 3D-STE was developed which showed matching results with our study. Tissue Doppler (TD) myocardial imaging has higher accuracy (80–90%) than conventional M-mode and 2-D imaging in localizing left-sided accessory pathways. However, it is still not ideal or right-sided pathways *(Cai et al., 2012)*. However, the clinical utility of TDI-derived strain has been limited by artefacts caused by myocardial translational motion, requirement for optimal Doppler alignment, poor reproducibility, time consuming off-line analysis and angle dependency. In contrast, 2D-STE is a non-Doppler method that allows quantification of the myocardial deformation and its timing on 2D greyscale images without the potential pitfalls of tissue Doppler *(Delelis et al., 2012)*.

LIMITATIONS

The number of patients was relatively small. The unavailability of right ventricular STE software excluded right sided AP cases. Echocardiograph has an inherent limitation of interpersonal as well as intrapersonal variations.

An important fundamental limitation was that 2D-STE dealt with mechanical activation and not electric activation. We assumed that electromechanical coupling is well preserved in the normal heart such that the mechanical activation pattern seems to reflect the electric phenomenon of the myocardium. Each electric activation is followed by an electromechanical one, that is, the depolarization of a cardiac muscle cell is followed by an uptake of calcium, which triggers contraction after a certain electromechanical delay of a few milliseconds.

The clinical role of noninvasive diagnosis of location of the AP with speckle-tracking may be limited, as it does not alter the therapeutic plan, and as ablation is based on the localization by the electrophysiological testing. However, the present findings in the setting of WPW syndrome, highlights the accuracy of speckle-tracking imaging in the assessment of pre-systolic contractile events and hence myocardial dyssynchrony.

CONCLUSION

In concordance with its proved utility in assessment of myocardia dyssynchrony, 2D-STE has the ability to approximate the location of AP without the pitfalls of Doppler methods. However, ECG still more accurate and reproducible tool. Practically, since invasive EP study is irreplaceable, either ECG or 2D-STE should be used as an orientation rather than precise localizing tools.

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تحديد مكان الضفيرة الكهربية الزائدة عن طريق إستخدام التتبع النقطي بواسطة الموجات فوق الصوتية في الحالات التي تعاني من متلازمة وولف-باركنسون-وايت

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خلفية البحث: يعد التتبع النقطي ثنائي الأبعاد بواسطة الموجات فوق الصوتية للقلب مقياس كمي فعال ومثبت لدرجة وتوقيت الإنحراف الإنقباضي لأجزاء عضلة القلب.

الهدف من البحث: التحقق من مدي قدرة التتبع النقطي ثنائي الأبعاد بواسطة الموجات فوق الصوتية للقلب على تحديد مكان الضفيرة الكهربية الزائدة عند مرضي متلازمة وولف-باركنسون-وايت.

المرضى وطرق البحث: تضمنت الدراسة خمسة عشر مريضا يعانون من ضفيرة كهربية زائدة جلية في تخطيط القلب الكهربي ويحتاجون جميعا إلي دراسة كهربيه فسيولوجية تداخلية وكي إذا لزم الأمر. وقد تم تقييم جميع المرضي بتخطيط قلبي كامل بالإضافة إلي التتبع النقطي ثنائي الأبعاد بواسطة الموجات فوق الصوتية للقلب.

نتائج البحث: تمكنت تقنية التتبع النقطي ثنائي الأبعاد من تحديد مكان الضفيرة الكهربية بدقة في عشرة مرضي بنسبه تقترب من سبع وستون بالمائة، في حين تمكن تخطيط القلب الكهربي من تحديدها بدقة في إثنا عشر مريضا بنسبة ثمانون بالمائة.

الإستنتاج: تقنية التتبع النقطي ثنائي الأبعاد لديها القدرة على تقريب مكان الضفيرة الكهربية الزائدة متجاوزا مزالق تقنية الدوبلر، ومع ذلك يظل تخطيط القلب الكهربي أداه أدق وأسهل.