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Different patterns of pre-excitation in a large Italian cohort of asymptomatic non-competitive athletes evaluated by telecardiology screening: Prevalence and ECG features

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ABSTRACT

Background: Telecardiology has proven to be a useful and cost-effective tool for ECG screening in several contexts, allowing the evaluation of large cohorts of subjects in a short time, even for non-competitive athletes (NCA).

Aim of the study: To evaluate and detail the prevalence of the Wolff-Parkinson-White (WPW) syndrome in a large Italian cohort of young NCA.

Methods: In a 4-year period 216,424 consecutive NCA (118,851 males; 55%) underwent preparticipation ECG screening through a Telecardiology System. ECGs were recorded and sent by a network of 'spoke' centers located all over Italy; a 'hub' center, located in Genoa, received and reported back on ECGs, digitally stored and analyzed. Only asymptomatic NCA were included in the study.

Results: Out of 216,424 NCA 88 (mean age: 14 ± 8) presented a WPW pre-excitation at ECG analysis (55 males, 62.5 %); the prevalence of WPW pre-excitation in this population was 4.1 per 10,000 NCA. No significant sex-related differences were found. The highest incidence (29 WPW patterns) was observed in the 10–15 year group with an equal sex ratio (M/F:16/13).

Intermittent pre-excitation was found in 8 NCAs. The most frequent accessory pathway locations were right antero-septal (25.0%), mid-septal (21.6%) and postero-septal (13.6%).

Conclusions: In a large population of young NCA the prevalence of ECG pre-excitation at telemedicine remote screening was 4.1 per 10,000; intermittent pre-excitation was found in 9% of NCA with ECG pre-excitation.

1. Introduction

Wolff–Parkinson–White (WPW) syndrome is characterized by electrical impulse conduction via an accessory pathway between the atria and ventricles, which bypasses the physiological delay of the A–V node [1]. The three main electrocardiogram (ECG) features of WPW syndrome are a short PR interval (< 0.12 s), a prolonged QRS-complex (> 0.10 s), with an initial slurring upstroke ("delta" wave) in the presence of sinus rhythm, caused by the fusion of ventricular preexcitation through the accessory pathway and normal electrical conduction. [1 2 3].

Sudden cardiac death can be the first presentation of [Wolff-Parkinson-White (WPW) syndrome] and the overall risk of sudden cardiac death in WPW syndrome is estimated at 0.1 % in asymptomatic [pre-excitation] and 0.3 % in symptomatic patients per year [4 5]. WPW syndrome accounts for 1.6 % of all sudden cardiac death among young athletes in the USA [6]. Early diagnosis of WPW can lead to timely catheter ablation, which is now considered a safe and curative procedure [7].

To date, the role of ECG screening in competitive athletes is still debated, with some major organizations supporting ECG use, and others recommending against widespread ECG-inclusive screening [8 9 10 11].

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Since 1982, in Italy pre-participation screening is mandatory and requires physician-led screening with history, physical, and ECG examination for competitive athletes. Furthermore, since 2013, all subjects involved even in recreational physical activities should have an ECG recorded and analyzed.

Telecardiology has proven to be a useful and cost-effective tool for applying ECG screening in any context, allowing the evaluation of large cohorts of subjects in a short time, even for non-competitive athletes (NCA) [12 13 14 15].

The purpose of this retrospective cohort study was to evaluate and detail the prevalence of the WPW syndrome in a large Italian cohort of young NCA.

2. Methods

2.1. Data collection

Data were derived from NCA aged ≤ 35 years and referred for ECG analysis as a pre-participation screening at Telemedico Srl-Telecardiology Center (Genoa, Italy) between September 1^{rst}, 2018 and August 31^{rst}, 2022, digitally stored and analyzed. ECGs were recorded and sent by a network of 'spoke' centers located all over Italy; a 'hub' center, located in Genoa, received and reported back on ECGs, as previously reported [15]. Only asymptomatic NCA were included in the study.

The study was performed in accordance with the Declaration of Helsinki and approved by an ethical committee.

2.2. ECG recording and measurements

A multi-vendor system compatible with various digital acquisition units of the ECG signal that allows secure transmission of the acquired exam for viewing and reporting by the cardiologist in a certified web-based platform (TeleCardioCalm Telecardiology System) was used.

The devices used for the acquisition of the ECGs allow the recording of a simultaneous 12-lead ECG signal of high diagnostic quality with a lead DII duration of 10 s. Technical characteristics of the devices were:

- Spaulding 2100iQ by Spaulding Clinical Research, LLC, Sampling Rate: 500 s/sec/channel, Frequency Response: 0.05 to 250 Hz, Filtering: High Pass Filter to remove baseline wander, Low Pass Filter to remove high frequency noise.
- ECG Expert by Custom Software & Electronics, SL, Sampling rate: 500 s/sec/channel, Frequency response: From −3dB@ 0.02 to 150 Hz, Filter: High Pass Filter to remove baseline wander, 40 Hz Low Pass filter to remove high frequency noise.

For remote ECG viewing and reporting, the system integrates the web-based software WebCor, a certified medical device that automatically measures ECG time intervals, QRS axis and allows Cardiologist to analyze and measure the traces by creating a digitally signed report with a strong signature.

2.3. Identification of intermittent WPW pre-excitation

In the considered 4-years period most NCA underwent ECG pre-participation screening every year.

We considered intermittent WPW pre-excitation the NCA as it follows:

- having at least a normal ECG before the pathological one;
- evidence of intermittent pre-excitation on the same ECG.

2.4. Localization of WPW accessory pathway

An accurate and detailed ECG analysis of the delta wave orientation in the precordial leads was essential to establish the right or left ventricular origin of the accessory pathway. We also calculated the direction of the delta wave vector in the frontal plane to find out the anterior, lateral or posterior origin of the pre-excitation, and analyzed QRS axis position to assess the appearances of the latest ventricular activity.

2.5. Statistical analysis

Continuous variables are reported as means ± standard deviation or 95 % confidence intervals (CIs) and median (with interquartile range or 5th and 95th percentiles), and dichotomous variables as percentages. Trends and gender differences were analyzed with multiple regression analysis. A p value < 0.05 was considered as statistically significant.

3. Results

In a 4-year period 216,424 NCA (118,851 males; 54.9 %) underwent pre-participation ECG screening through a Telecardiology System. Among these, 88 NCA (mean age: 14 ± 8) presented a WPW pre-excitation at ECG analysis (55 males, 62.5 %); the prevalence of WPW pre-excitation in this population was 4.1 per 10,000 NCA. No significant sex-related differences were found. The highest incidence (29 WPW patterns) was observed in the 10–15 year group with an equal sex ratio (M/F:16/13).

3.1. Intermittent pre-excitation

Two or 3 ECGs, for a total of 167, were available in our database for 62 of 88 NCAs with WPW pre-excitation. The remaining 26 WPW pre-excitations had only 1 ECG. Intermittent pre-excitation was found in 8 NCAs: 5 of them had a previous normal ECG (Fig. 1) and 3 presented the intermittent pattern on the same ECG, also known as WPW alternans' phenomenon (Fig. 2). In our population the prevalence of intermittent pre-excitation was at least of 9 %.

3.2. Accessory pathway

According to Fitzpatrick criteria we detected 63 right sided WPW pre-excitations, characterized by a negative or isoelectric delta wave in the right precordial leads, and 25 left sided WPW pre-excitations, characterized by a dominant delta wave in the right precordial leads.

ECG findings related to the accessory pathway location are displayed in Fig. 3. The most frequent accessory pathway locations were, in decreasing frequency, right antero-septal (25.0 %), mid-septal (21.6 %) and postero-septal (13.6 %).

PR interval was 96.3 ± 15.4 msec for right sided and 101.1 ± 13.4 for left sided ($p = 0.1716$]), QRS interval 118.9 ± 11.0 and 121.5 ± 13.3 ($p = 0.3502$]), and δT corrected interval 419.1 ± 21.9 and 419.6 ± 23.3 ($p = 0.9191$]), respectively.

3.3. Secondary repolarization changes

ST segment/T wave changes (presumably delta-wave related) and QRS complex were detected in 34/88 NCA (38.6 %) presenting WPW pre-excitation. Table 1 shows the clinical characteristics of WPW subjects with and without secondary repolarization changes. When compared, NCA with and without secondary repolarization changes did not show significant differences in terms of age, sex, PR interval, δT and δT corrected interval, and intermittent phenomenon. QRS duration was instead significantly increased in WPW pre-excitation with secondary repolarization changes (125.7 ± 10.6 vs 115.8 ± 10.7, $p = 0.00015$).

4. Discussion

To the best of our knowledge this is the first study assessing the prevalence of ECG pre-excitation in a large population of young NCA by remote telemedicine evaluation: main findings of the study are the following:

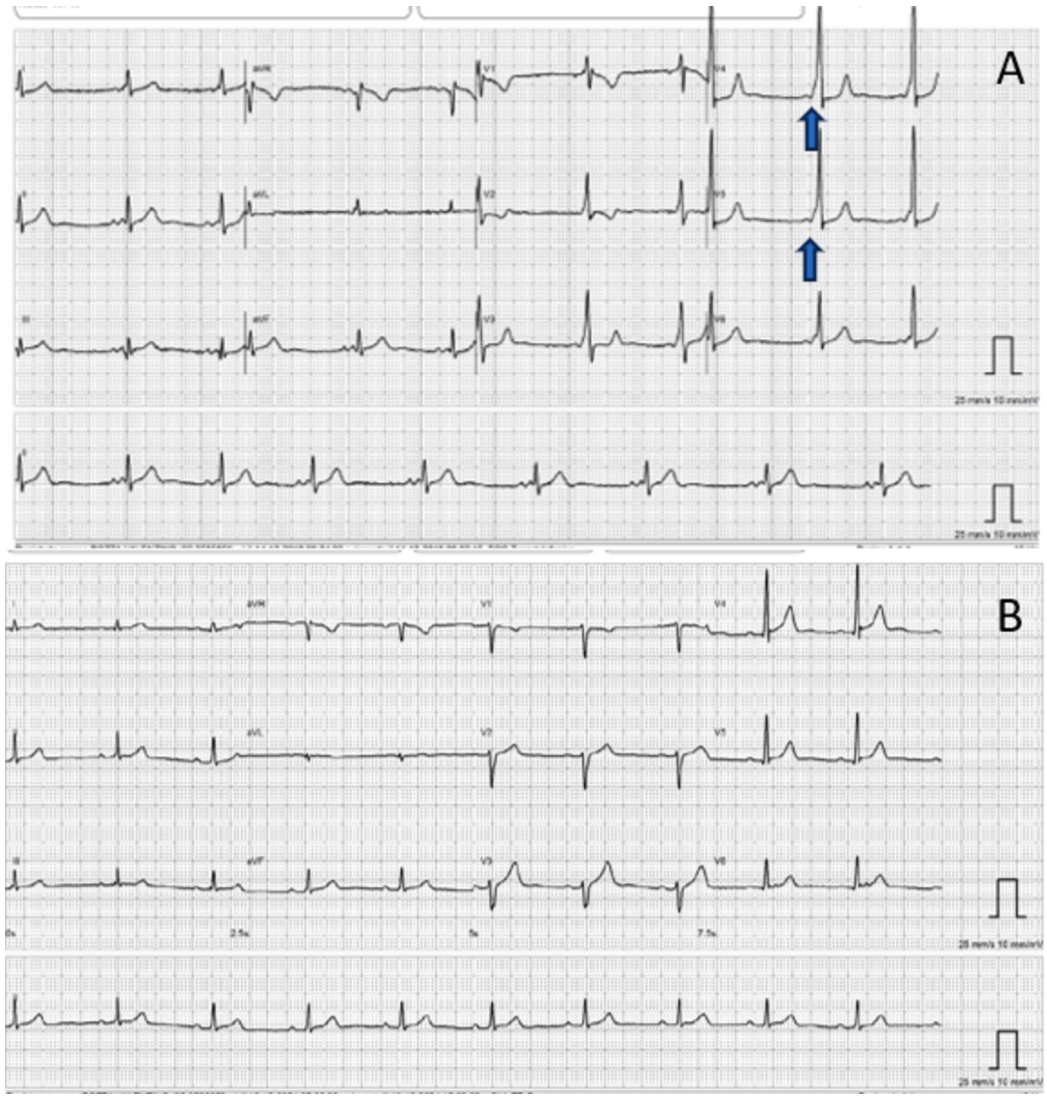


Fig. 1. Intermittent pre-excitation. In panel A, the ECG demonstrates a WPW pattern with right antero-lateral accessory pathway; arrows identify the characteristic delta wave and short PR interval. In panel B, the ECG performed 1 year before shows normal findings.

- telemedicine remote evaluation can be useful in identifying cases of WPW asymptomatic pre-excitation in young NCA
- the prevalence of ECG pre-excitation is 4.1 per 10,000
- the most prevalent accessory pathway locations were right-antero-septal, mid-septal, and postero-septal.

Mortality of WPW syndrome is estimated at 0.1 % in asymptomatic patients and 0.3 % in symptomatic patients per year [4,5]. Accessory pathways are present in 1/300 young individuals. They are often asymptomatic and potentially lethal arrhythmias may be the first presentation [16]. During long-term follow-up, up to 20 % of asymptomatic individuals with pre-excitation go on to develop an arrhythmia and the absence of traditional clinical and electrophysiological (EP) high-risk markers does not guarantee the "safe" nature of an accessory pathway. Either *trans*-esophageal or invasive EP study are usually used to risk stratify asymptomatic patients [17]; evidence of rapid conduction through the accessory pathway is usually considered high risk and prompt sport disqualification. Athletic activity may impose an increased risk of life-threatening arrhythmias in patients with asymptomatic pre-excitation

Prevalence of WPW pre-excitation in young athletes is relatively low. In a report from 2352 Olympic athletes from Athens 2004 to Sochi 2014 there was 1 case of WPW syndrome, even a population of highly screened CA [18]. In American collegiate football athletes, however, prevalence of WPW electrocardiogram was 1/79 over a period of 4 years of observation [19]; in another population of 954 US collegiate athletes 7 showed signs of WPW syndrome (0.72 %) [20].

Even less data are available from populations of young NCA. In 11,487 children consulted for pre-sports participation screening, 15 had WPW syndrome [21]. The remote telemedicine screening with electrocardiogram did not find any case of WPW syndrome in more than 500 young amateur football players in an Italian population [22].

In an observational study on 91 asymptomatic children and adolescents with ventricular pre-excitation 33 patients (36.3 %) had a benign form and were allowed to participate in competitions and 48 patients (52.7 %) showed inducible sustained atrioventricular reentrant tachycardia and/or atrial fibrillation [23]; 45 young athletes underwent transcatheter ablation, without procedure-related complications, and all patients remained asymptomatic during follow-up.

In our population, most prevalent accessory pathways are right-antero-septal, mid-septal, and postero-septal. In a pediatric cohort of 380 patients (mean age 12.4 $\pm$ 3.9 years) treated with catheter ablation most common localization of accessory atrioventricular pathways was at the left lateral mitral valve annulus, followed by the posteroseptal region [24]. Distribution between right-sided and left-sided accessory pathways was almost balanced. In a community-based adult and

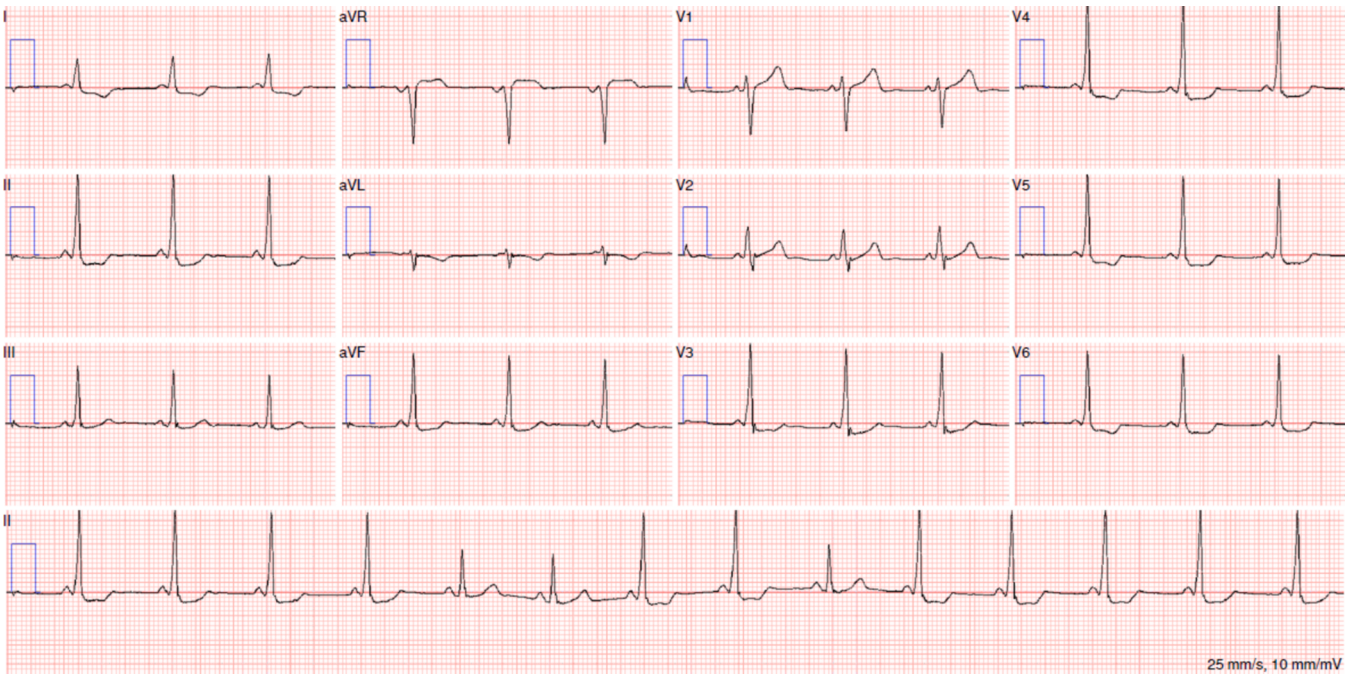


Fig. 2. Intermittent pre-excitation with alternans' phenomenon in a WPW NCA with right antero-septal accessory pathway. In lead II three beats (arrows) show normal conduction and absence of delta wave (the fifth, sixth and ninth beat respectively).

adolescent population, majority of the accessory pathways were found in the left freewall and posteroseptal region and tend to be more easily ablated [25]. Accessory pathways were in left freewall (61.6 %), posteroseptal (24.6 %), right freewall (9.6 %), and anteroseptal (4.3 %) locations. Acute success was highest for left freewall pathways (97.1 %) with lowest case times and fluoroscopy times, longest procedure time parameters were seen with anteroseptal, left anterolateral, epicardial-coronary sinus, and right anterolateral pathway ablations. In another very young population (120 patients. mean age 12.7 ± 3.6 years) most common location were left lateral wall, right mid-septal, right postero-septal, right antero-septal and left postero-septal [26]. In a study assessing accessory pathway analysis using a multimodal deep learning model more common findings were left lateral (24.8 %), left postero-lateral (10.2 %) and left posterior (10.2 %) [27].

Interestingly, we provide data on intermittent WPW pre-excitation, a phenomenon which can potentially explain the very low diagnosis rates in previous populations. In our WPW population the prevalence of intermittent pre-excitation was at least of 9 %. Intermittent pre-excitation may range according to different studies and populations between 15 % and 50 % of WPW cases [28 29]. Of 328 patients with pre-excitation, those with intermittent pre-excitation were similar in age (12.9 vs 13.0 years) and accessory pathways location (left-sided 54 % vs 50 %; septal 32 % vs 35 %) [30]. In a study comparing intermittent versus persistent WPW syndrome in 295 children, 226 (76.6 %) had persistent, 39 (13.2 %) intermittent, and 30 (10.2 %) loss of pre-excitation during Holter/exercise [31]. There were no differences in symptoms between groups. The low rates of detected intermittent pre-excitation may be probably due to the low number of subjects double checked in our population. Intermittent pre-excitation and alternans' phenomenon do not necessarily indicate a low risk for sudden cardiac death, so such conditions should be promptly diagnosed and adequately managed.

Data provided in this study come from approximately 700 "spoke" centers located throughout Italy: cardiologist reporting telemedicine electrocardiograms are not involved in the clinical management of subjects diagnosed with an arrhythmia or WPW pre-excitation, except for possible temporary disqualification pending further clinical investigations.

However, considering possible positive impact of this study on clinical practice and health policy, we may assume that telemedicine may enable large swaths of NCA to be easily screened with an electrocardiogram, and that is true also for WPW syndrome and even more for intermittent pre-excitation. Furthermore, this large population of NCA provides updated and real-world data on the true prevalence of the disease, described with its different pathways. Such epidemiology data may support further studies for the clinical management of WPW pre-excitation.

ECG screening through telemedicine may be considered an excellent way to detect these conditions in large populations of NCA.

5. Conclusions

In a large population of young NCA the prevalence of WPW pre-excitation on the ECG at telemedicine remote screening was 4.1 per 10,000; intermittent pre-excitation was found in 9 % of NCA with WPW pre-excitation..

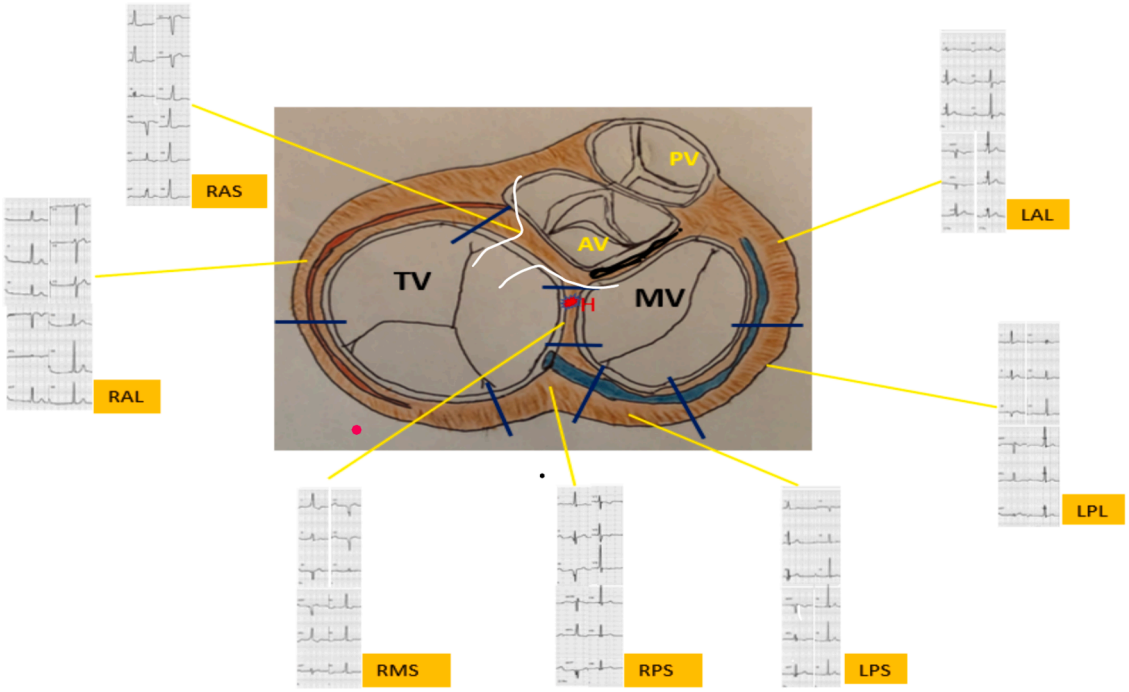
6. Limitations

This is a retrospective, single-center, non-randomized study that only evaluated the presence of fixed or intermittent WPW pre-excitation on the ECG of asymptomatic NCA. Multiple ECG are available only for a small percentage of NCA and this could lead to an underestimation of both the prevalence of WPW pre-excitation and the incidence of intermittent pre-excitation.

Localization of accessory pathway has been detected only on the surface ECG using Fitzpatrick criteria; no EP data were available.

Since the study focuses on asymptomatic NCA, a complete picture of WPW syndrome prevalence in the general population can't be provided.

Clinical follow up of subjects screened by telecardiology remote electrocardiogram is not possible for telecardiology hub cardiologists; subjects diagnosed with preexcitation are usually temporally disqualified from sports pending further clinical investigations. The impact of telemedicine remote screening in preventing sudden cardiac death can be presumed but not adequately quantified.



Accessory Pathway Location	n	%
Right Side	63	71.6
• Anterolateral	10	11.4
• Anteroseptal	22	25.0
• Midseptal	19	21.6
• Posteroseptal	12	13.6
• Posterolateral	0	0
Left Side	25	28.4
• Posteroseptal	9	10.2
• Anterolateral	9	10.2
• Posterolateral	7	8.0

Fig. 3. Location of accessory pathways in the telemedicine population of young non competitive athletes with Wolff-Parkinson-White pattern.

Table 1
Clinical characteristics of WPW subjects with and without secondary repolarization changes.

	SRC (+) (n = 34)	SRC (−) (n = 54)	P value
Age (years)	18.0 ± 8.5	17.9 ± 7.4	n.s.
Male Gender	22 (65 %)	33 (61 %)	n.s.
PR interval (ms)	97.4 ± 15.9	97.8 ± 14.5	0.1716
QRS interval (ms)	125.7 ± 10.6	115.8 ± 10.7	0.00015
δT interval (ms)	389.3 ± 34.3	396.6 ± 34.2	0.3338
δTc interval (ms)	421.7 ± 23.9	417.7 ± 21.1	0.4118
Intermittent pattern	4 (12 %)	4 (7 %)	

SRC = Secondary repolarization changes.

CRediT authorship contribution statement

Martina Molinari: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Sergio Setti:** Data curation. **Natale Daniele Brunetti:** Writing – review & editing, Validation, Methodology, Formal analysis, Data curation. **Nicola Di Nunno:** Data curation. **Maria Alberta Cattabiani:** Data curation. **Giuseppe Molinari:** Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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