Assessing Dynamic Atrioventricular Conduction Time to RR-interval Coupling in Athletes and Sedentary Subjects

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Abstract

Background: Atrioventricular conduction time (AVCT) is influenced by autonomic input and subject to physiological remodeling.

Objective: To evaluate beat-by-beat AVCT and RR-interval variability in athletes and healthy sedentary subjects.

Methods: Twenty adults, including 10 healthy sedentary (Controls) and 10 elite long-distance runners (Athletes), age, weight and height-adjusted, underwent maximal metabolic equivalent (MET) assessment, and 15-min supine resting ECG recording seven days later. The interval between P-wave and R-wave peaks defined the AVCT. Mean (M) and standard deviation (SD) of consecutive RR-intervals (RR) and coupled AVCT were calculated, as well as regression lines of RR vs. AVCT (RR-AVCT). Concordant AV conduction was defined as positive RR-AVCT slope and discordant otherwise. A multivariate linear regression model was developed to explain MET based on AVCT and RR-interval variability parameters. Significance-level: 5 %.

Results: In Athletes, M-RR and SD-RR values were higher than in Controls, whereas M-AVCT and SD-AVCT were not. RR-AVCT slopes were, respectively, 0.038 ± 0.022 and 0.0034 ± 0.017 (p < 0.05). Using a cut-off value of 0.0044 (AUC 0.92 ± 0.07; p < 0.001), RR-AVCT slope showed 100% specificity and 80% sensitivity. In a multivariate model, SD-RR and RR-AVCT slope were independent explanatory variables of MET (F-ratio: 17.2; p < 0.001), showing 100% specificity and 90% sensitivity (AUC 0.99 ± 0.02; p < 0.001).

Conclusion: In elite runners, AVCT to RR-interval dynamic coupling shows spontaneous discordant AV conduction, characterized by negative AVCT vs. RR-interval regression line slope. RR-intervals standard deviation and AVCT vs. RR-interval regression line slope are independent explanatory variables of MET (Arq Bras Cardiol. 2020; 115(1):71-77)

Keywords: Athletes; Adults; Resistance Training; Physical Fitness; Ventricular Remodeling; Sedentarism; Electrocardiography/methods; Heart Ventricles; Ventricular Function.

Introduction

Cardiac adaptation secondary to physical fitness is reflected in mechanical, electrical and autonomic remodeling of the heart, as a consequence of repeated high-demand activities. Well-trained athletes often have slight ventricular mass gain, increased ECG wave amplitude, early repolarization, reduction of resting heart rate and increased heart rate variability, related to the conditioning status.1-7

Particularly, most autonomic heart remodeling in well-conditioned athletes is a consequence of increased vagal tonus and reduced sympathetic stimulation over the sinus and the atrioventricular (AV) nodes.6,16 Although increased vagal tonus may be straightforwardly detected by measuring the resting heart rate, to differentiate between increased parasympathetic activity over the sinus node and the AV node on surface ECG may not be that simple.

Frequently, high-demand athletes have atrioventricular (AV) node remodeling, characterized by several degrees of AV conduction block, non-sinus low atrial or junctional rhythm and, more rarely, complete AV block.8-10 Those AV conduction disturbances depend on physical conditioning status and are related not only to increased parasympathetic activity over the AV node, but also to secondary remodeling of the AV node fibers and cell-to-cell coupling.11-13

Although AV conduction disturbances have been repeatedly documented in athletes, the dynamic AV conduction adaptation to the cardiac cycle in this population still needs clarification. In the general population, AV duration varies dynamically according to RR-interval duration, characterizing a concertina-like effect. However, in athletes, autonomic remodeling may influence dynamic AV conduction to RR-interval adaptation, leading to a distinct behavior of AV conduction, in a time-related response to RR-interval variation.

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The present study evaluated beat-by-beat AV conduction time (AVCT) and RR-interval variabilities in elite runners and healthy sedentary subjects, at rest, aiming at assessing the effect of physical fitness status on spontaneous AVCT to RR-interval duration coupling.

Methods
Detailed information about study protocol, Ethics Committee approval, and ECG data acquisition has been described elsewhere. The present study analyzed raw high resolution ECG data from the ECG data bank of the Biomedical Engineering Program, using a novel technique for extraction of atrioventricular conduction time and RR-intervals. Data sampling procedure was described elsewhere.

The study population comprised 20 volunteers divided in two groups: the ‘Athlete’ group, comprising ten elite long-distance runners (≥ 16.0 maximal metabolic equivalents [MET]) calculated as the maximal oxygen consumption achieved during stress test divided by 3.5 ml·kg⁻¹·min⁻¹, [mean ± SD] 19.5 ± 1.3 MET; aged 25.1 ± 7.1 years), and the ‘Control’ group, comprising ten male healthy sedentary volunteers (≤ 11.5 MET; 8.7 ± 1.9 MET; aged 29.0 ± 5.4 years). It is worth mentioning that the term ‘MET’ is employed throughout the text as the maximal metabolic equivalent achieved during stress test. The athletes’ training program consisted of six to eight training sessions/week; 90 to 120 min/session; 90 to 110 km/week. The waves and fiducial point detection were carried out on ECG acquired using XYZ modified Frank leads, in the resting supine position, using low-pass filter at 15 Hz (Butterworth, 4th order). For the analysis of the RR-interval duration, artefacts and ectopic beats were adequately excluded.

The distance between the peak of the P-wave and the peak of the R-wave in normal beats defined the PR-peak interval and was employed to analyze instantaneous AVCT adaptation over the cardiac cycle. The PR-peak to RR-intervals coupling was assessed in a beat-by-beat basis throughout the whole ECG recording, using the lead showing the tallest P-wave, usually the Y lead. The RR-interval was assessed as the time between the peaks of the R-waves of two consecutive normal beats. The PR-peak interval was assessed immediately before the second beat of the respective RR-interval. For each subject, the mean (M) and standard deviation (SD) of all consecutive normal RR-intervals (M-RR and SD-RR) and respective PR-peak interval (M-AVCT and SD-AVCT) were calculated. PR-peak intervals were correlated to the respective RR-intervals and calculated regression line slopes (RR-AVCTslope).

Statistical Analysis
The variables were expressed as mean ± SD or median and interquartile range, when appropriate. Data normality was assessed using Kolmogorov-Smirnov test, and all analyzed variables had their normality assumption accepted. Variables were compared between groups using non-paired Student’s t-test. To assess the optimal cut-off values, ROC curves were calculated from the regression line slopes (AVCT vs. RR-interval) in both groups. A multivariate linear regression model was developed to explain the MET based on significant AVCT and RR-interval parameters. Pearson’s correlation coefficient r was tested for significance (significance level was set at 5%). A concordant AV conduction was arbitrarily defined as AVCT and RR-interval increased and decreased in the same direction in consecutive cardiac cycles, and discordant otherwise. AVCT was assessed as PR-peak-interval.

A validation bootstrap resampling procedure applied to the multivariate model was carried out using two different approaches. In the first approach, 1100 replications with replacement were carried out in the whole sample of both groups to assess mean and SD estimates of independent variables. In a second approach, both groups were split in a test group, comprising 67% of subjects of each group, and a validation group, with the remaining 33%. The MET estimated by the multivariate model was employed to classify Controls and Athletes in all sets of bootstrap procedures. Raw ECG signals were processed using custom-made programs written in Matlab R2007a (The MathWorks, Inc) language. Statistical analysis was carried out using MS-Excel 360 (Microsoft Corporation) and Medcalc version 11 (Medcalc Software bvba). The significance level adopted in the statistical analysis was 5%.

Results
The Athletes had significantly higher M-RR and SD-RR values than the Controls, whereas there were no significant differences between M-AVCT and SD-AVCT values (Table 1). Examples of subjects from the Control (a) and Athlete (b) groups are shown in Figure 1, where regression lines and respective r of AVCT vs RR-intervals scatterplots are shown. RR-AVCTslope values are positive in Controls (Figure 1-a), whereas they are negative in Athletes (Figure 1-b). Overall, RR-AVCTslope in Controls and Athletes resulted in significant between-groups’ differences (Table 1).

Variables showing significant intergroup differences were entered into a multivariate linear regression model, taking MET as the dependent variable in the bootstrap procedure. SD-RR (p = 0.0099) and RR-AVCTslope (p = 0.006) were independent explanatory variables of MET, showing 90% specificity, 100% sensitivity and 95% total accuracy (Table 2). The average C-statistic in test and validation groups were, respectively, 0.97 ± 0.06 and 0.87 ± 0.13; p < 0.001 for both. The multivariate linear regression analysis and respective bootstrap procedures results are summarized in Table 2.

The RR-AVCTslope values for each group, including interquartile range and 95% confidence intervals (CI) are shown in figure 2-a. Sensitivity, specificity and total accuracy were computed utilizing the optimal cutoff value shown in table 1, and exhibited as inset. To highlight the association between spontaneous decremental conduction and physical status, a regression line of RR-AVCTslope vs. MET is shown in figure 2-a. It shows a significant correlation (r = 0.70; p < 0.05) and a negative slope, demonstrating that RR-AVCTslope decreases as MET increases. An example of a short sequence of sinus beats showing spontaneous decremental conduction, registered during supine rest in a 19 y.o. athlete (MET 16.8 METs) is shown in Figure 2-b.
Discussion

Atrial ventricular conduction is the most important determinant of the PR-interval duration, which undergoes dynamic fluctuations depending on autonomic and health statuses, age, instantaneous HR, medications, stance and respiratory frequency. The evaluation of the PR-interval by using either P wave-onset or P wave-peak approaches as fiducial points has been shown to provide accurate and precise results, and, thus, are both appropriate to assess AVCT inter-beat variations.

In the present study, highly trained longdistance runners and healthy sedentary subjects had their maximal aerobic power assessed, and AVCT coupled to the preceding RR-
interval variability, assessed on resting supine ECG. It was hypothesized that, at rest, AV conduction would be affected by AV remodeling induced by high-end training, causing AVCT to RR-interval coupling to behave differently from sedentary conditions. In a linear model, AVCT to RR-interval coupling showed an average negative regression line slope in the Athlete group and, conversely, an average positive slope in the Control group, indicating that AV node remodeling due to training induces decremental conduction enhancement. A potentially distinguished measure of physical fitness, AVCT to RR-interval regression slope correctly identified 90% all subjects’ related physical fitness status. Although identification of decremental conduction in athletes is a common finding, the application of a linear modeling to quantify AVCT and its relation to RR-interval in highly trained athletes has not been yet reported, to the best of our knowledge.

Previous studies evidenced a high prevalence of Mobitz I 2nd degree AV block in long distance runners at rest. In the present study, the occurrence of spontaneous PR-peak-interval lengthening related to RR-interval shortening was a major finding,
making the average slope negative in the Athletes group (Figure 2b). Conversely to these studies, no blocked P-wave was found after a carefully revision of signals. Spontaneous episodes of decremental conduction were frequent in the Athletes group (57.9% of aggregated ECG recording time of Athletes) and rare in the Control group (7.9% of aggregated ECG time recording of Controls). Furthermore, when the AVCT vs. RR-interval regression slope was plotted against MET, it was observed that the higher the MET, the more negative the RR-AVCT slope, showing that spontaneous decremental AV conduction becomes more frequent as physical conditioning status improves (Figure 2a). Noteworthy was that the decremental conduction was more frequently observed when RR-interval was larger than 1022.0 ms. PR-peak interval reduction related to RR interval increase was also observed in Athletes (Figure 1d). A possible explanation for this latter finding is the common occurrence of vagal-induced spontaneous para-sinus pacing activity.

It has been shown that the resting ECG of endurance athletes may show distinctive features from demographically equivalent healthy sedentary subjects, bearing similarities to those observed in elderly individuals and/or patients with cardiovascular disease. However, in athletes, AV conduction abnormalities have been related to higher parasympathetic activity, differently from the elderly.19 Contemporary studies have shown that athletic training could induce intrinsic physiological adaptations in the conduction system, contributing to the higher prevalence of AV conduction abnormalities. The physiological mechanisms by which endurance training induces those intrinsic changes in the cardiac conduction system are limitedly understood and may be multifactorial, but anatomic changes such as atrial and ventricular dilatation has been shown to create a mechanical-to-electrical remodeling necessary to cause intrinsic AV electrophysiological adaptations.

Limitations of the present study include the sample size of two distinct groups regarding the physical conditioning status. Raw ECG signals were obtained from the ECG database available in the Biomedical Engineering Program (convenience sample). Peak-P to Peak-R interval was employed as a surrogate of conventional PR-interval measurement. Although it has been shown that Peak-P to Peak-R interval appropriately describes PR-interval dynamicity, the duration of the actual PR-interval may be larger than the one observed in the present study. It was observed that both M-AVCT and SD-AVCT were larger among athletes when compared to controls, although statistical significance was not reached. The explanation of this finding may be twofold: i) although AVCT variability was expected to be higher among athletes, no true Mobitz I block was in fact observed after careful signal revision. This indicates that AVCT variability was expected to be increased to a limited extent, and ii) the sample size of the present sample was designed to determine differences related to ventricular activation total energy, thus limiting its statistical power to detect AVCT variation between groups. Subjects were kept on supine rest for 10 minutes before ECG acquisition, aiming at preventing orthostatic memory effect on AV conduction to influence AV conduction to RR-interval coupling dynamicity, in a controlled temperature and acoustically isolated environment. However, it cannot be completely ruled out that some orthostatic memory effect might still be present. In this study, we observed the occurrence of spontaneous PR-peak interval enlargement as RR-interval decreased, and vice-versa. This phenomenon was interpreted as a manifestation of decremental conduction during the transit of the cardiac activation wave-front through the AV node. However, due to the nature of this study, no invasive electrophysiological test was carried out to further characterize decremental conduction or para-sinus pacing activity. It is still necessary to investigate the potential impact of the present findings on clinical settings, such as a marker for supraventricular tachyarrhythmia, particularly AV nodal reentrant arrhythmia and atrial fibrillation.

Conclusion

The atrioventricular node undergoes substantial physiological remodeling in elite long-distance runners, characterized by spontaneous AV decremental conduction at supine rest, rarely observed in healthy sedentary subjects under the same resting conditions. The linear regression line slope of PR-peak to RR-interval coupling is a strong and independent explanatory variable of maximal metabolic equivalent achieved during stress test in this population.

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Author contributions

Conception and design of the research: Benchimol-Barbosa PR, Nasario-Junior O, Nadal J. Acquisition of data: Benchimol-Barbosa PR, Analysis and interpretation of the data: Benchimol-Barbosa PR, Nasario-Junior O, Nadal J. Statistical analysis: Benchimol-Barbosa PR, Nadal J. Obtaining financing: Nadal J. Writing of the manuscript: Benchimol-Barbosa PR, Nasario-Junior O, Nadal J. Critical revision of the manuscript for intellectual content: Benchimol-Barbosa PR, Nasario-Junior O, Nadal J.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Instituto Nacional de Cardiologia under the protocol number 0026/20.02.04. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.
References


