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# Synopsis of Most Relevant Articles on Cardiac Arrhythmias

*Sinopse de Artigos Mais Relevantes em Arritmias Cardíacas*

**Section Editor:** Bruno Papelbaum
Papelbaum B https://orcid.org/0000-0001-7154-7001
**1.**Centro Avançado de Ritmologia e Eletrofisiologia – São Paulo/SP – Brazil.
**E-mail:** brpapel@gmail.com

## Diurnal, Seasonal and Monthly Variations of Ventricular Arrhythmias in Patients with Implantable Cardiac Defibrillators*

Evolutionarily, the understanding of the incidence of therapies and, mainly, the damaging effects of short and long term shocks in patients with implantable cardiac defibrillators (ICD) has improved. Although changes in the programming of the devices have improved the outcomes, it is necessary an understanding of when tachyarrhythmia events occur, to optimize the programming of the devices and avoid unnecessary and inappropriate therapies. Six prospective studies were grouped to evaluate the frequency of ventricular arrhythmias (VA): PainFree Rx II, EMPIRIC, WAVE, EnTrust, MVP, and OMNI. All the episodes of VA ≤ 500 ms were included. The VA distribution in function of time, day, month, the season was evaluated through the construction of four negative bionominal models, for each model the outcome was the number of VA episodes in a given period. A total of 3.969 matters were included in the analysis, the mean age of the patients was of 65 ± 12.5 years, and the mean ejection fraction was of 28 ± 10.2%. The occurrence of VA was higher in the spring than in the summer (0.86% vs. 0.70%; p = 0.009), but not significantly different in the autumn (0.74%; p = 0.069) or in the winter (0.84%; p = 0,732). The estimated probability of occurring at least one VA episode in each block of one hour during the period of eight in the morning to ten at night in 365 days (0.10% to 0.12%) was higher (35% estimated to 63% higher) than in the period of mid-night to one in the morning (0.07%), not being found significant statistical differences according to days of the week or individual months throughout the year. The authors discuss that there should be variations in the autonomic tonus, adrenergic stimulation, or other modulating factors by the circadian cycle. It is also possible that factors such as air pollution, barometric pressure or humidity that differ throughout the seasons of the year may have either direct or indirect role in the occurring of ventricular ectopias. The results were similar to the TEMPEST (*temperature-related Incidence of Electrical Storm*) study, in which most episodes occurred in association to temperature rise compared to the previous month. In conclusion, there are periods of VA occurrence, and additional studies should be performed in order to understand the real reasons for that, as well as enabling better programming of the devices.

*Maan A, Sherfesee L, Lexcen D, Heist EK, Cheng A. Diurnal, seasonal, and monthly variations in ventricular arrhythmias in patients with implantable cardioverter-defibrillators. J Am Coll Cardiol EP. 2019;5(8):979-86. https://doi.org/10.1016/j.jacep.2019.05.014

## "Omission" of Ergometric Test Loses and Delays the Diagnosis of Polymorphic Ventricular Tachycardia in Young Survivors of Sudden Cardiac Death*

Polymorphic Catecholaminergic Ventricular Tachycardia (PCVT) is a hereditary illness that affects 1 in 10.000 individuals and manifests itself clinically as syncope. Without treatment, the general mortality varies from 30 to 50% at 35 years of age. Unfortunately, the diagnosis may not be identified through a resting electrocardiogram, echocardiogram, or invasive electrophysiologic study. Therefore, the ergometric test (ET), or the provocative catecholaminergic test (CPT) is critical in the diagnosis of PCVT. The purpose of this study was to determine the number of diagnoses lost/delayed of PCVT in a coorte of young survivors of sudden cardiac death (CSD). After the analysis of 3.194 consecutive patients and the appropriate exclusions (congenital cardiopathy, coronary disease, myocarditis, etc.) a retrospective review of 101 survivors of (< 35 years of age at the moment of CSD) with structurally normal heart was used to identify those with lost or delayed diagnosis due to the neglected evidence or lack of ET/CPT. Among the 101 survivors , 41/101 (41%), experienced a CDS related to exercise or emotion (EECSD), being significantly (16.6 ± 8.2 years vs. 20.4 ± 11,0 years; p = 0.02) and had more events in pubic (34/41; 83% vs. 26/60.43%; p < 0001). The PCVT diagnosis was more common in EECSD survivors (8/41; 20% vs. 2/60; 3.3%; p = 0.01). Collectively, 15/101 patients (15%) presented a diagnosis of PCVT, the genetic diagnosis was the more common (13/41, 32%), and was lost/delayed in a third (5/15, 33%) the diagnostic time of the survivors with PCVT (mean delay of 15.8 ± 16.6 months). In conclusion, among the 15 patients diagnosed with PCVT, one third had a delay in the diagnosis by not performing an ET, being that an important exam to become standardized in the investigation of CSD in young people, especially if CSD occurring during exercise/emotion.

*Giudicessi JR, Ackerman MJ. Exercise testing oversights underlie missed and delayed diagnosis of catecholaminergic polymorphic ventricular tachycardia in young sudden cardiac arrest survivors. Heart Rhythm 2019;16(8):1232-239. https://doi.org/10.1016/j.hrthm.2019.02.012

## Electronic Implantable Cardiac Devices in Elderly Population*

The number of electronic implantable cardiac devices (EICD) has increased, being added to higher longevity/life expectancy. However, most studies include few elderly patients (> 80 years), being the results extrapolated to this age group. The purpose of the revision was to analyze the different types of EICD and discuss approaches for the population > 75 years, besides the guidelines recommendations. Elderly patients have a higher chance of syncope by bradyarrhythmia, which could manifest by falls. The implant of *a loop recorder* may act in this profile of the patient for a possible electric diagnosis related to syncope. Around 80% of pacemakers (PM) are implanted in elderly patients, which are more susceptible to complications, mainly pneumothorax, and electrode displacement, implying in higher morbidity due to prolonged hospitalization. In fragile elderly patients with a total atrioventricular block (TAVB), the implant of a mono chamber PM may seem reasonable. The evidence of an implantable cardiac defibrillator (ICD) in elderly patients is not right in the main studies from the device since the mean age was of 63 years. Besides, this profile of patients presents a higher incidence of non-arrhythmic deaths, and the studies counted with 252 elderly patients (≥ 75 years). In the elderly population, a rational approach is to discuss together with the patient and family members, the device may modify the type of death, from sudden to long and more stressful, not impacting on the quality of life. Cardiac resynchronization therapy with (CRTD) or without (CRT) defibrillator is well-established in patients with heart failure; its use in elderly patients is rising, with implants in 40% of patients > 80 years Most studies have included mainly young patients, being the results in elderly not representative. Martens et al. investigated the impact in this population, with the improvement of functional class and ejection fraction compared to young. However, the use of ICD does not bring additional benefits to the

elderly population. The authors concluded that guidelines should not separately drive the implant of devices in the elderly population; these patients have complex comorbidities and personal desires, being fundamental a discussion regarding the offered therapy so that the purposes of both parties can be achieved.

*Lim W-Y, Prabhu S, Schilling RJ. Implantable Cardiac Electronic Devices in the Elderly Population. Arrhythm Electrophysiol Rev. 2019;8(2):143-46. https://doi.org/10.15420/aer.2019.3.4

## Incidence and Predictors of Clinically Essential and Dangerous Arrhythmias During Effort Test in Pediatric Patients with Congenital Heart Disease*

Effort test (ET) is a crucial modality commonly used by pediatric heart centers to evaluate the functional capacity and effort-induced arrhythmias to guide the safe participation in physical activities and to help the decisions of handling medicament therapy. Data of EF in young and adult population with congenital heart disease (CHD) are limited and extrapolated in the adult population with cardiovascular disease. In a review of a single-center, the incidence of clinically essential arrhythmias was of 3%. The purpose of the present study was to quantify the incidence of arrhythmias in the pediatric population during EF and identify patients at risk. This was a retrospective study from *Boston Children's Institutional Research Board* from January 2013 to December 2015. A total of 5.307 EF, with a mean age of 16 years (variation of 13 to 24 years), is 20% with CHD.were analyzed. The exams were interrupted if there was the development of symptomatic supraventricular tachycardia, hemodynamic instability, pre-syncope or syncope, chest pain with progression, ventricular ectopias or elevation of the ST segment (> 2 mm) with chest pain or history of ischemia. The presence of CHD was of 49%, being Fallot's tetralogy the most prevalent (555 tests; 10%) were considered, according to the study, some high-risk criteria. The most common criteria were the presence of implantable cardio defibrillator (ICD) in 198 tests and cardiomyopathy in 186 tests. Some arrhythmias, classified in different degrees, were identified (46%), but only 33 events (0.6%) needed interruption of the exam. The absence of high risk criteria had 99.7% of negative predictive value (NPV) for an arrhythmia that needed interruption of the exam (95% confidence interval from 99.5% to 99.8%) and 99.96% of NPV to arrhythmia that needed intervention beyond to the exam interruption (95% confidence interval: 99.85% to 9999%). The authors pointed out that the incidence of arrhythmias in EF in the pediatric population, even with CHD, is low; using pre-defined criteria such as high risk, it was able to identify the patients with more adverse events (class IV or who needed electric external or internal cardioversion by the ICD). In conclusion, these data allowed better options in terms of supervising performed exams.

*Barry OM, Gauvreau K, Rhodes J, Reichman JR, Bourette L, Curran T, O'Neill J, Pymm JL, Alexander ME. Incidence and Predictors of Clinically Important and Dangerous Arrhythmias During Exercise Tests in Pediatric and Congenital Heart Disease Patients. J Am Coll Cardiol EP. 2018;4(10):1319-327. https://doi.org/10.1016/j.jacep.2018.05.018

## Periodic Dynamic Repolarization as a Risk Factor After a Myocardium Heart Attack: Prospective Validation Study*

Patients after a myocardium heart attack (HA) present higher cardiovascular risk, including malignant arrhythmia, cardiac insufficiency, recurrent HA, thromboembolism, and death, being necessary the risk stratification. Periodic dynamic repolarization (PDR) is a new electrocardiographic phenomenon related to sympathetic activity associated to low-frequency oscillations (≤ 0,1 Hz) in repolarization and, therefore, promotes important notions

over the sympathetic regulation level in the left ventricular myocardium. Analysis of the studies ART (*Autonomic Regulation Trial*) and MADIT-II (*Multicenter Automatic Defibrillator Implantation Trial II*) showed an increase of PDR after HA strongly predicts subsequent death, but there was a limitation due to retrospective data. The study in question proposes analysis the results in prospective form patients under medicament therapy after HA. A total of 455 surviving patients of HA (≤ 80 years of age) in sinus rhythm were included. The primary and secondary outcomes were total and cardiovascular mortality after three years. In all patients, a high-resolution digital electrocardiogram was performed (2,048 Hz) during 20 minutes, in the morning period and upright position. According to mathematics calculation, the final step was the calculus of the PDR as mean of the wave coefficient corresponding to frequencies ≤ 0,1 $Hz^3$ after the transformation of the sign; the cut value was of ≥ 5,75 $deg^2$. A total of 754 patients were analyzed with the inclusion of 455 patients; during mean follow up of 27.25 months, 47 patients died, being 23 classified as cardiovascular. The increase in the PDR was significantly associated to both outcomes, with areas below the ROC curve of 69.3% (60.2-77.8%) and 79.1% (69.7-86.7%) to total and cardiovascular mortality, respectively. Patients with PDR ≥ 5,75 $deg^2$ presented total and cardiovascular mortality of 22.9 and 14.85%, respectively when compared to 6.82 and 0.87% in patients with PDR ≤ 5,75 $deg^2$. Multivary analysis showed that PDR ≥ 5,75 $deg^2$ was the independent risk factor, including score GRACE > 140, ejection fraction ≤ 35%, and the presence of diabetes mellitus. Higher PDR, however, indicated risk 2.2 and 9.5 times higher for total and cardiovascular mortality ($p = 0.024$ and $p = 0.003$, respectively). The exact mechanisms still need to be clarified, but previous data suggest that PDR reflects the dynamic effects of sympathetic activation in cardiac repolarization; it is known that sympathetic activity occurs in the range of low frequency and that in normal conditions the sympathetic activation causes differential effects in cellular layers of the ventricular myocardium, shortening the duration fo the potential of action. This could lead to the appearance of transmural dispersion of repolarization after sympathetic outbreaks, which could be captured by PDR. Sympathetic denervation, induced ischemia, and sympathetic hyperinervation after HA contribute to the increasing of transmural dispersion, resulting in higher PDR. The authors concluded that PDR promotes additional information as a non-invasive methodology over the sympathetic tonus, and that also has a great prognostic impact.

*Rizas KD, Doller JA, Hamm W, Vdovin N, Stuelpnagel LV, Zuern CS, Bauer A. Periodic repolarization dynamics as risk predictor after myocardial infarction: prospective validation study. Heart Rhythm 2019;16(8):123-231. https://doi.org/10.1016/j.hrthm.2019.02.024

## Therapy with Subcutaneous Versus Transvenous Implantable Defibrillator: a Meta-analysis of Case-Control Studies*

Therapy with implantable cardio defibrillator (ICD) is effective for the primary and secondary prevention of sudden cardiac death; its use is associated, however, to short and long term complications, providing morbidity and mortality. Transvenous devices are vulnerable to fracture, and the infection rate of the device itself varies from 0.67 a 1.49%. Subcutaneous ICD (S-ICD) is a recent technology designed to overcome the complications related to transvenous ICD (T-ICD); it presents, however, limitations such as lack of stimulation capacity, not allowing *anti-tachycardia pacing* (ATP). The purpose of the study was, therefore, promote a meta-analysis to summarize and compare the outcomes between S-ICD and T-ICD, including complications regarding the electrode, inappropriate therapies, and appropriate shocks. A study database from PubMed and Embase since the year 2000 was reviewed, identifying six studies for the revision of texts, excluding one study due to the inclusion of the teenage population. The populations were similar regarding age, gender, indications for ICD (primary *versus* secondary prevention), and the proportion of patients with ischemic heart illness, hypertrophy cardiomyopathy (ischemic, non-ischemic and dilated) or hypertrophy cardiomyopathy. The complications with electrode were significant smaller in the Group S-ICD (OR: 0.13; 95% IC:

0.05 to 0.38); the total degree of infection was of 0.35% (8 in 2.269) in S-ICD, similar to T-ICD (OR: 0.75; 95% IC: 0.30 to 1.89). The prevalence of inappropriate therapy (*oversensing* of T-wave, supraventricular tachycardia or inappropriate sensitivity) was similar between the groups (OR: 0.87; 95% IC: 0.51 to 1.49); however, the nature of the therapies was different among them. In the T-ICD group, there was a bigger number of inappropriate therapies due to supraventricular tachycardia; meanwhile, in the S-ICD group, the *oversensing* episodes (sensitivity of noise and T-wave) were more frequent. Only two studies showed data on appropriate shocks, with 17% in S-ICD (95% IC: 6.3% to 26.4%) and 21.3% in T-ICD (95% IC: 12.6% to 27.3%). A study in progress, PRAETORIAN (*Prospective, RAndomizEd comparison of subcutaneous and tRansvenous. ImplANtable cardioverter-defibrillator therapy*), is the most recent randomized, controlled, and multi-centered study, comparing advantages and disadvantages of S-ICD. The current study did not show differences between the infection rate among the two types of device. The authors concluded that the choice of the device, the risk com complications *versus* the rate of inappropriate therapies, as well as the limitations of S-ICD must be individually considered and that S-ICD is safe and effective in properly chosen patients.

*Ray IB-S, Liu J, Jia X, Gold M, Ellenbogen K, Nicolantonio JD, Komócsi A, Vorobcsuk A, Kim J, Afshar H, Lam W, Mathuria N, Razavi M, Rasekh A, Saeed M. Subcutaneous versus transvenous implantable defibrillator therapy: a meta-analysis of case-control studies. JACC: Clinical Electrophysiology 2017;3(13):1475-483. https://doi.org/10.1016/j.jacep.2017.07.017