

Synopsis of Most Relevant Articles on Cardiac Arrhythmias

Sinopse de Artigos mais relevantes em arritmias cardíacas

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Genetic testing and screening cascade for long QT syndrome and hypertrophic cardiomyopathy in pediatric population*

Several of the hereditary cardiovascular conditions, such as long QT syndrome (LQTS) and hypertrophic cardiomyopathy (HCM), are subject to preventive treatments. These conditions usually have autosomal dominant inheritance, with 50% risk for first-degree relatives. Therefore, a screening strategy is the target under these conditions, a process called cascade screening. This study presents the implementation and effectiveness of cascade screening in the United States through: 1) evaluation of the use of genetic tests in index cases; 2) measurement of family participation; 3) identification of barriers to screening; 4) evaluation of utilization and performance by screening method. It was a work of six centers including patients < 21 years with clinical diagnosis and/or positive status for LQTS and HCM from 2008 to 2014. The screening methods were characterized as cardiological only (electrocardiogram, echocardiogram, stress test and/or outpatient monitoring), genetic only (tests aimed at family variants) or combined. A total of 315 patients were identified, 30% of whom were referred by positive family history. The genetic tests were performed in 250 out of 315 (79%). Patients with HCM had lower genetic test rate versus LQTS (65% versus 92%; $p < 0.001$). The number of patients who refused to take the test was significantly higher in cases of HCM ($p < 0.001$), with insurance difficulties as the second largest cause of impediment to genetic testing (28%). The positive test rate was consistent with those expected for LQTS (81%) and HCM (60%). Of the 315 families studied, 234 (74%) participated in the cascade screening. A total of 553 relatives were screened, with a rate of 2.4 per participating family and with higher participation in LQTS families (82% versus 66%; $p = 0.006$). There was a greater influence on screening participation when the index patient had genetic positivity [90% (164/182; $p < 0.001$) positive compared to 67% (38/57) negative]. A total of 874 tests were performed for 553 relatives (588 cardiological and 286 genetic), with an average of 1.6 test per relative; only cardiological method in 46%, combined in 38% and only genetic in 17%. Cascade screening identified 221 affected individuals (40%) among the 553 relatives, with a positive rate for LQTS of 42% and 37% for HCM. The strategy of higher performance in screening was the combined cardiological and genetic (58%) compared with only genetic (34%) and only cardiological (19%); $p < 0.001$. The participation of 74% shows that it is not complete even in tertiary centers with genetic counseling programs; however, this rate is more encouraging than previously published data (39–66%). There has been less acceptance of genetic screening for HCM, which is a particular problem as it is a pathology with a high occurrence of sudden death in young people. Genetic counsellors are important facilitators in the process with communication to family members and psychosocial support. Contrary to expectations, health insurance was not a significant barrier to screening, not even the first barrier. The authors conclude that the data presented promote the following recommendations: 1) to use clear

communication with relatives; 2) to describe the limitations of the tests; 3) to detail the cascade screening, including the results by method, reviewing the classification in return visits; 4) to discuss barriers to communication with the family; 5) to offer letters to families for distribution to relatives; 6) to use noninvasive samples collected at home and submitted by e-mail; and 7) to identify laboratories that offer tiered pricing for patients, free tests for family variants or other financial options.

*Knight LM, Miller MSE, Kovach, MDJ, Arscott MSP, et al. Genetic testing and cascade screening in pediatric long QT syndrome and hypertrophic cardiomyopathy. *Heart Rhythm*, 2019; 7(1):106-112. <https://doi.org/10.1016/j.hrthm.2019.06.015>

Impact of bariatric surgery on the type of atrial fibrillation*

Obesity represents a public health emergency in the United States affecting 93 million adults. Besides its growth, cardiovascular complications have also increased, including atrial fibrillation (AF), which are closely correlated. Obesity is an independent risk factor for AF through several mechanisms including increased blood pressure, left ventricular and atrial remodeling, sleep apnea, insulin resistance, and coronary artery disease (CAD). The study assessed the impact of bariatric surgery (BS) on the type of AF with a retrospective cohort of 440 obese patients with AF (body mass index ≥ 40 kg/m²) in Cleveland Clinic between 2007 and 2013, of which 220 were submitted to BS. Only patients who could perform Holter, ZioPatch (Holter in adhesive form), implantable loop recorder or with implantable cardiac devices were included. All patients were submitted to pre- and postoperative standard management, including psychiatric, nutritional and endocrinological evaluation. The type of BS was documented (Roux-en-Y gastric bypass, sleeve gastrectomy and gastric band), in addition to the type of AF, classified as paroxysmal, persistent, long-standing or permanent. The use of antiarrhythmic before and after BS and systemic anticoagulation were also documented. The average age was 66 ± 9 years and 117 (53%) were male. The patients were followed for a total of 90 ± 47 months; 130 (59%) out of 220 patients underwent Roux-en-Y gastric bypass, 64 (29%) sleeve gastrectomy and 26 (12%) gastric banding. In terms of arrhythmia monitoring, 25 (11%) were monitored with intracardiac devices, 14 (6%) with ZioPatch, 178 (81%) with Holter and 3 (1%) with implantable loop recorder. Global reversion occurred in 92 (71%) patients with *bypass*, 36 (56%) with sleeve gastrectomy and 13 (50%) with gastric banding. There was persistent AF reversal to paroxysmal in 36 (27%) with *bypass*, 16 (25%) with gastrectomy and 6 (23%) with gastric band. Absence of new AF occurred in 56 (43%) with *bypass*, 20 (31%) with gastrectomy and 7 (27%) with gastric band. The AF rate prior to BS was $38.6 \pm 24.5\%$ compared to $19.4 \pm 29\%$ after BS. Antiarrhythmic rescheduling occurred in 58 (45%) patients with *bypass*, 23 (36%) with gastrectomy and 10 (39%) with gastric band. In the control group, i.e., only clinical treatment, there was no AF reversion in any patient, occurring AF progression in 30 (14%) patients versus 7 (3%) in the BS group. The study in question showed significant rates of AF reversal after BS, with the amount of lost weight being a significant predictor for AF reversal. Additionally, BS was associated with reductions in glycated hemoglobin, C-reactive protein, blood pressure, and apnea-hypopnea index. The study has limitations because it is retrospective, requiring prospective analysis, in addition to the exclusion of patients by short follow-up and absence of monitoring pre- and post-BS. However, the results were consistent with previous studies that demonstrated significant substantial weight loss. The authors conclude that bariatric surgery is associated with significant reversion of AF type and weight loss is an independent predictor, besides the effects on inflammatory markers, NT-ProBNP, blood pressure and sleep apnea severity.

*Donnellan E, Wazni OM, Elshazly M, Kanj M, Hussein AA, et al. Impact of bariatric surgery on atrial fibrillation. *Circulation: Arrhythmia and Electrophysiology*, 2020,13:e007626. <https://doi.org/10.1161/CIRCEP.119.007626>.

Oral anticoagulant for patients with atrial fibrillation on long-standing dialysis*

Atrial fibrillation (AF) is common and increasing in patients with end-stage renal disease (ESRD) under long-standing dialysis, with a prevalence of 10%. Oral anticoagulants (OAC) are recommended in patients with AF to reduce the risk of stroke and thromboembolic events. Patients on dialysis are at risk of bleeding (platelet dysfunction), but also of ischemic accident, not knowing precisely the net benefit of OAC in the population with ESRD. The study performed a comparison of OAC versus no anticoagulation for AF patients on dialysis. All studies investigating the impact of OAC for AF on stroke and/or systemic embolism, survival and major bleeding were initially identified by Medline (414) and Embase (1067). The relevant studies were identified through manual research, including 16 articles for data collection. The primary endpoint analyzed was stroke and systemic embolism, followed by major bleeding, defined by the need for hospitalization, transfusion, which led to death, as well as gastrointestinal or intracranial bleeding. There were 71,877 patients with AF on dialysis and mean follow-up of 18 to 52.8 months, all nonrandomized and observational studies. One study compared apixaban 5 mg twice a day versus 2.5 mg twice a day versus warfarin; another study compared bleeding from dabigatran versus rivaroxaban versus warfarin. Regarding the results, OAC had no statistically significant lower rate of thromboembolism and/or stroke compared to nonanticoagulation. Apixaban < 5 mg was associated with lower risk of mortality than other treatments; warfarin was associated with significant risk of bleeding higher than apixaban and not anticoagulation; dabigatran and rivaroxaban were also associated with higher risk of bleeding than apixaban and not anticoagulation. Although results should be interpreted with caution due to high heterogeneity, warfarin, dabigatran and rivaroxaban may not be options due to the high risk of bleeding in AF patients on dialysis. Additional studies are required to establish the risk-benefit ratio of OAC in this patient profile. With respect to limitations, there was little data from observational studies regarding the efficacy and safety of dabigatran, rivaroxaban and apixaban for AF patients on dialysis, so it is not possible to assess why apixaban 5 mg had reduced mortality because there were no data on other cardiovascular events than stroke. There were no studies with information on crossover, which would ensure failure of exposure classification, which would result in truer effects. The authors conclude that OAC was not associated with reduced risk of thromboembolism in patients with AF on dialysis and the risk-benefit ratio must still be validated in randomized clinical trials.

*Kuno T, Takagi H, Ando T, Sugiyama T, Miyashita S, Valentin N, et al. Oral anticoagulation for patients with atrial fibrillation on long-term dialysis, *J Am Coll Cardiol*, 2020;75(3):273–85. <https://doi.org/10.1016/j.jacc.2019.10.059>

Thoracic magnetic resonance imaging safety in patients with pacemakers and defibrillators*

In the last decade the use of cardiac implantable electronic devices (CIEDs) has increased strongly. New conditional nuclear magnetic resonance (NMR) CIEDs have emerged with changes in their design, using minimally ferromagnetic material to prevent internal damage. Moreover, new electrodes became acceptable for conditional use in NMR after extensive investigation; even so, a large proportion of patients have nonconditional CIED. When thoracic NMR is performed, the field is near the device, remaining the doubt if the current is induced in the electrodes, that contains ferromagnetic material, which can generate arrhythmia. More importantly, the magnetic field can generate heat at the electrodes tip resulting in tissue injury and potential elevation of the command thresholds. The study tested the hypothesis that the performance of thoracic NMR in patients with *in situ* nonconditional CIED is associated with a similar incidence of adverse events as previously observed in patients submitted to brain NMR with nonconditional devices. It was a retrospective cohort with data collected prospectively at Mayo Clinic, from January 25, 2008 until February 28, 2017. The term conditional CIED was defined as a system (pulse and electrode generator) with approval by *Food and Drug Administration* under special

conditions. For patients without other imaging alternatives, a standard protocol was followed, including pre- and post-scan evaluation and monitoring during the examination, comparing the results with a control group. All NMRs were performed on 1.5 Tesla (T) machines, specific absorption rate limited to not exceed 1.5 W/kg. The primary outcome was safety observed with no adverse event rate when compared to the control group; events included were death, generator or electrode failure requiring rapid replacement, loss of capture, newly-occurring arrhythmia and system reset. Secondary outcomes included a change in programmed parameters before and after the test; cardiac troponin was measured before and after the test to evaluate possible myocardial damage. All patients with increased command threshold > 1 V, P or R wave drop $> 50\%$ or increased impedance > 50 Ohms were individually followed. Thoracic NMRs were performed in 120 patients (134 MRI procedures); 12 patients received CIED on the right pectoral region, 104 on the left and 4 patients had no generator. Out of 134 procedures, 127 were questioned by CIED before and after the exam. There were no clinical differences between the groups as well as in the number of electrodes. Three patients had a subjective sensation of pain, pulling on the chest or warming at the CIED generator site. Regarding the outcomes, there was no change in the mean follow-up of 7.8 months, with NMR completed in all patients, except one due to inability to lay in pronation during exam. There was no atrial arrhythmia during or immediately after the examination, regardless of the history of paroxysmal atrial arrhythmia. The mean time of device implanted until the NMR was 2.4 years and there were no differences between the groups. Regarding the secondary outcomes, there was no difference in sensitivity, impedance and command thresholds, as well as the changes in battery voltage were similar. Troponin values were recorded before and after NMR in 19 patients (15.8%), no changes were observed when compared to 42 patients (38.5%) of the control group. There were significant alterations in the impedance of the atrial lead (mean variation 10.2 Ohms; $p = 0.01$) and ventricular lead (mean variation 13.1 Ohms; $p = 0.01$) in pacemakers and of the atrial lead (mean variation 10.3 Ohms; $p = 0.04$) in cardioverter-defibrillator (ICD), without clinical correlation. Similarly, there was variation in the amplitude of the R wave (mean variation 0.51 mV; $p = 0.006$) in patients with ICD, and of the P wave (mean variation 0.35 mV; $p = 0.004$) in resynchronizer, also without clinical impact. No impedance elevation > 50 Ohms was observed and the mean variation in the command threshold was < 0.05 V in all devices. In 13 patients, repeated tests were performed with no incidence of adverse effects in this subgroup of patients. The study shows that the incidence of adverse events is no different from those submitted to brain NMR and nonconditional devices. In thoracic NMR there is a higher probability of changes in the CIED due to the system being in the isocenter of the field, having been an initial concern to perform the tests even in conditional devices. The lack of clinical arrhythmias in this and previous studies suggests that the electric field produced may not cause cardiac stimulation under NMR conditions. The common causes of oversensing are radio frequency noise in the magnetic field and the magnetohydrodynamic effect, however some measures can be taken, such as switching off tachycardia therapies in ICDs, programming asynchronous stimulation modes in those dependent on stimulation and disabling any automatic adaptive algorithm. The authors conclude that thoracic NMR performed in nonconditional CIED is not associated with an increase in adverse events compared to brain NMR, and that the risk is low when performed with multidisciplinary protocols focused on patient safety.

*Padmanabhan DMD, et al. Safety of thoracic magnetic resonance imaging for patients with pacemakers and defibrillators. *Heart Rhythm*, 2019,16(11), <https://doi.org/10.1016/j.hrthm.2019.05.031>