Circulation: Arrhythmia and Electrophysiology

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients With Obstructive Sleep Apnea

This study characterizes the atrial substrate, including atrial fibrillation triggers in patients with paroxysmal atrial fibrillation and obstructive sleep apnea. They find that obstructive sleep apnea in patients with paroxysmal atrial fibrillation is associated with biatrial structural remodeling and increased incidence of extrapulmonary vein triggers.

BACKGROUND: Obstructive sleep apnea (OSA) is associated with atrial remodeling, atrial fibrillation (AF), and increased incidence of arrhythmia recurrence after pulmonary vein (PV) isolation. We aimed to characterize the atrial substrate, including AF triggers in patients with paroxysmal AF and OSA.

METHODS AND RESULTS: In 86 patients with paroxysmal AF (43 with ≥moderate OSA [apnea–hypopnea index ≥15] and 43 without OSA [apnea–hypopnea index <5]), right atrial and left atrial voltage distribution, conduction velocities, and electrogram characteristics were analyzed during atrial pacing. AF triggers were examined before and after PV isolation and targeted for ablation. Patients with OSA had lower atrial voltage amplitude (right atrial, *P*=0.0005; left atrial, *P*=0.0001), slower conduction velocities (right atrial, *P*=0.02; left atrial, *P*=0.0002), and higher prevalence of electrogram fractionation (*P*=0.0001). The areas of atrial abnormality were consistent among patients, most commonly involving the left atrial septum (32/43; 74.4%). At baseline, the PVs were the most frequent triggers for AF in both groups; however, after PV isolation patients with OSA had increased incidence of additional extra-PV triggers (41.8% versus 11.6%; *P*=0.003). The 1-year arrhythmia-free survival was similar between patients with and without OSA (83.7% and 81.4%, respectively; *P*=0.59). In comparison, control patients with paroxysmal AF and OSA who underwent PV isolation alone without ablation on extra-PV triggers had increased risk of arrhythmia recurrence (83.7% versus 64.0%; *P*=0.003).

CONCLUSIONS: OSA is associated with structural and functional atrial remodeling and increased incidence of extra-PV triggers. Elimination of these triggers resulted in improved arrhythmia-free survival.

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Circulation: Cardiovascular Genetics

Diminished *PRRX1* Expression Is Associated With Increased Risk of Atrial Fibrillation and Shortening of the Cardiac Action Potential

Atrial fibrillation has a considerable genetic risk component and nearly 30 genetic loci have been identified in genome-wide association studies. These investigators identified a functional genetic variant that alters *PRRX1* expression in atrial myocytes and provides a potential mechanistic link between the genetic association at the 1q24 locus, *PRRX1*, and atrial fibrillation.

BACKGROUND: Atrial fibrillation (AF) affects over 33 million individuals worldwide. Genome-wide association studies have identified at least 30 AF loci, but the mechanisms through which individual variants lead to altered disease risk have remained unclear for the majority of these loci. At the 1q24 locus, we hypothesized that the transcription factor PRRX1 could be a strong candidate gene as it is expressed in the pulmonary veins, a source of AF in many individuals. We sought to identify the molecular mechanism, whereby variation at 1q24 may lead to AF susceptibility.

METHODS AND RESULTS: We sequenced a ≈158 kb region encompassing PRRX1 in 962 individuals with and without AF. We identified a broad region of association with AF at the 1q24 locus. Using in silico prediction and functional validation, we identified an enhancer that interacts with the promoter of PRRX1 in cells of cardiac lineage. Within this enhancer, we identified a single-nucleotide polymorphism, rs577676, which alters enhancer activity in a mouse atrial cell line and in embryonic zebrafish and differentially regulates PRRX1 expression in human left atria. We found that suppression of PRRX1 in human embryonic stem cell–derived cardiomyocytes and embryonic zebrafish resulted in shortening of the atrial action potential duration, a hallmark of AF.

CONCLUSIONS: We have identified a functional genetic variant that alters PRRX1 expression, ultimately resulting in electrophysiological alterations in atrial myocytes that may promote AF.

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Circulation: Cardiovascular Imaging

Ascending Aortic Dimensions in Former National Football League Athletes

The investigators used a sample of 206 former National Football League athletes in comparison with 759 male control subjects from the Dallas Heart Study-2 to find if former athletes have larger ascending aortic dimensions from screening computed tomography scans. After adjusting for their size, age, race, and cardiac risk factors, the ascending aortic dimensions were significantly larger in former National Football League athletes. Further evaluation is required to evaluate whether these changes translate into negative clinical outcomes or are adaptive.

BACKGROUND: Ascending aortic dimensions are slightly larger in young competitive athletes compared with sedentary controls, but rarely >40 mm. Whether this finding translates to aortic enlargement in older, former athletes is unknown.

METHODS AND RESULTS: This cross-sectional study involved a sample of 206 former National Football League (NFL) athletes compared with 759 male subjects from the DHS-2 (Dallas Heart Study-2; mean age of 57.1 and 53.6 years, respectively, *P*<0.0001; body surface area of 2.4 and 2.1 m2, respectively, *P*<0.0001). Midascending aortic dimensions were obtained from computed tomographic scans performed as part of a NFL screening protocol or as part of the DHS. Compared with a population-based control group, former NFL athletes had significantly larger ascending aortic diameters (38±5 versus 34±4 mm; *P*<0.0001). A significantly higher proportion of former NFL athletes had an aorta of >40 mm (29.6% versus 8.6%; *P*<0.0001). After adjusting for age, race, body surface area, systolic blood pressure, history of hypertension, current smoking, diabetes mellitus, and lipid profile, the former NFL athletes still had significantly larger ascending aortas (*P*<0.0001). Former NFL athletes were twice as likely to have an aorta >40 mm after adjusting for the same parameters.

CONCLUSIONS: Ascending aortic dimensions were significantly larger in a sample of former NFL athletes after adjusting for their size, age, race, and cardiac risk factors. Whether this translates to an increased risk is unknown and requires further evaluation.

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Circulation: Cardiovascular Interventions

Efficacy of the RADPAD Protection Drape in Reducing Operators' Radiation Exposure in the Catheterization Laboratory

A Sham-Controlled Randomized Trial

RADPAD radiation shield is used to reduce interventional cardiologists' radiation exposure, although its practical effects are unknown. In this sham-controlled randomized trial, the investigators found that, in comparison with standard treatment (NOPAD) and a sham-shield (SHAMPAD), the standard use of RADPAD is feasible and reduced operator radiation exposure substantially.

BACKGROUND: Interventional cardiologists are increasingly exposed to radiation-induced diseases like cataract and the stochastic risk of left-sided brain tumors. The RADPAD is a sterile, disposable, lead-free shield placed on the patient with the aim to minimize operator-received scatter radiation. The objective of the trial was to examine the RADPAD's efficacy in a real-world situation.

METHODS AND RESULTS: In the current, double-blind, sham-controlled, all-comer trial, patients undergoing diagnostic catheterization or percutaneous coronary interventions were randomized in a 1:1:1 ratio to a radiation absorbing shield (RADPAD), standard treatment (NOPAD), or a sham shield (SHAMPAD). The sham shield allowed testing for shield-induced radiation behavior. The primary outcome was the difference in relative exposure of the primary operator between the RADPAD and NOPAD arms and was defined as the ratio between operator's exposure (E in μSv) and patient exposure (dose area product in mGy·cm^2), measured per procedure. A total of 766 consecutive coronary procedures were randomized to the use of RADPAD (N=255), NOPAD (N=255), or SHAMPAD (N=256). The use of RADPAD was associated with a 20% reduction in relative operator exposure compared with that of NOPAD (P=0.01) and a 44% relative exposure reduction compared with the use of a SHAMPAD (P<0.001). Use of the SHAMPAD was associated with a 43% higher relative radiation exposure than procedures with NOPAD (P=0.009).

CONCLUSIONS: In clinical daily practice, the standard use of the RADPAD radiation shield reduced operator radiation exposure compared with procedures with NOPAD or SHAMPAD. This study supports the routine use of RADPAD in the catheterization laboratory.

CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT03139968.

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Circulation: Cardiovascular Quality and Outcomes

Urban–Rural Comparisons in Hospital Admission, Treatments, and Outcomes for ST-Segment–Elevation Myocardial Infarction in China From 2001 to 2011

A Retrospective Analysis From the China PEACE Study (Patient-Centered Evaluative Assessment of Cardiac Events)

Despite China's recent advances in healthcare reform in the past decade, medical care and patient outcomes between urban and rural areas in China during this period were not available. This study of a nationally representative sample of patients in China found that urban-rural disparities in evidence-based treatment for myocardial infarction have largely been eliminated. However, substantial gaps in quality of care persist in both urban and rural settings.

BACKGROUND: In response to urban–rural disparities in healthcare resources, China recently launched a healthcare reform with a focus on improving rural care during the past decade. However, nationally representative studies comparing medical care and patient outcomes between urban and rural areas in China during this period are not available.

METHODS AND RESULTS: We created a nationally representative sample of patients in China admitted for ST-segment–elevation myocardial infarction in 2001, 2006, and 2011, using a 2-stage random sampling design in 2 urban and 3 rural strata. In China, evidence-based treatments were provided less often in 2001 in rural hospitals, which had lower volume and less availability of advanced cardiac facilities. However, these differences diminished by 2011 for reperfusion therapy (54% in urban versus 57% in rural; *P*=0.1) and reversed for angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (66% versus 68%; *P*=0.04) and early β-blockers (56% versus 60%; *P*=0.01). The risk-adjusted rate of inhospital death or withdrawal from treatment was not significantly different between urban and rural hospitals in any study year, with an adjusted odds ratio of 1.13 (0.77–1.65) in 2001, 0.99 (0.77–1.27) in 2006, and 0.94 (0.74–1.19) in 2011.

CONCLUSIONS: Although urban–rural disparities in evidence-based treatment for myocardial infarction in China have largely been eliminated, substantial gaps in quality of care persist in both settings. In addition, urban hospitals providing more resource-intensive care did not achieve better outcomes.

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Circulation: Heart Failure

Interleukin-1 Blockade in Recently Decompensated Systolic Heart Failure

Results From REDHART (Recently Decompensated Heart Failure Anakinra Response Trial)

This hypothesis-generating study reports results from the REDHART trial (Recently Decompensated Heart Failure Anakinra Response Trial) of interleukin-1 blockade with anakinra in patients with reduced left ventricular ejection fraction and elevated C-reactive protein levels. The investigators hypothesized that interleukin-1 receptor antagonism could inhibit the inflammatory response and improve peak aerobic exercise capacity in patients with recently decompensated systolic heart failure. The results suggest an improvement in peak oxygen consumption after 12 weeks of treatment, although they were not powered to detect between-group differences in comparison with placebo and short-course anakinra. Larger studies evaluating inhibition of the inflammatory response in heart failure are warranted.

BACKGROUND: An enhanced inflammatory response predicts worse outcomes in heart failure (HF). We hypothesized that administration of IL-1 (interleukin-1) receptor antagonist (anakinra) could inhibit the inflammatory response and improve peak aerobic exercise capacity in patients with recently decompensated systolic HF.

METHODS AND RESULTS: We randomly assigned 60 patients with reduced left ventricular ejection fraction (<50%) and elevated C-reactive protein levels (>2 mg/L), within 14 days of hospital discharge, to daily subcutaneous injections with anakinra 100 mg for 2 weeks, 12 weeks, or placebo. Patients underwent measurement of peak oxygen consumption (Vo_2 [mL/kg per minute]) and ventilatory efficiency (the VE/Vco_2 slope). Treatment with anakinra did not affect peak Vo_2 or VE/Vco_2 slope at 2 weeks. At 12 weeks, patients continued on anakinra showed an improvement in peak Vo_2 from 14.5 (10.5–16.6) mL/kg per minute to 16.1 (13.2–18.6) mL/kg per minute (P=0.009 for within-group changes), whereas no significant changes occurred within the anakinra 2-week or placebo groups. The between-groups differences, however, were not statistically significant. The incidence of death or rehospitalization for HF at 24 weeks was 6%, 31%, and 30%, in the anakinra 12-week, anakinra 2-week, and placebo groups, respectively (log-rank test P=0.10).

CONCLUSIONS: No change in peak Vo_2 occurred at 2 weeks in patients with recently decompensated systolic HF treated with anakinra, whereas an improvement was seen in those patients in whom anakinra was continued for 12 weeks. Additional larger studies are needed to validate the effects of prolonged anakinra on peak Vo_2 and rehospitalization for HF.

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