Sat. Jul 10, 2021

Track4

AEPC YIA Session

AEPC YIA Session（ II-AEPCYIA）

Chair: Hiroshi Ono（National Center for Child Health and Development, Japan）
4:30 PM - 5:20 PM Track4 (Web開催会場)

[II-AEPCYIA-1] Atenolol should not be the ß-blocker of choice for symptomatic children with catecholaminergic polymorphic ventricular tachycardia

○Puck J. Peltenburg[1], Krystien V.V. Lieve g[1], Christian van der Werf g[1], Isabelle Denjoy g[2], Guillermo Perez g[3], Carmen Perez[3], Ferran Roses i Noguer[4], Johan M. Bos[5], Connor Lane[5], Vibeke M.Almaas[6], Aurora Djubsjöbacka[7], Sing C. Yap[8], Yuko Wada[9], Thomas Roston[10], Veronica Dusi[11], Takeshi Aiba[12], Maarten van den Berg[13], Thomas Robyns[14], Jason Roberts[15], Esther Zorio[16], Udi Chorin[17], Sally-Ann B. Clur[1], Nico A. Blom[1,18], Martin Borggrefe[19], Andrew M.Davis[20], Jon Skinner[21], Elijah Behr[22], Christopher Semsarian[23], Prince J. Kannankeril[24], Jacob Tfelt-Hansen[25], Frederic Sacher[26], Wataru Shimizu[12], Peter J. Schwartz[11], Shu Sanatani[10], Seiko Ohno[9], Janneke Kammeraad[8], Heikki Swan[7], Kristina Haugaa[6], Vincent Probst[27], Michael J. Ackerman[5], Janice A. Till[4], Ramon Brugada[3], Arthur A.M. Wilde[1], Antoine Leenhardt[2],
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[II-AEPCYIA-2] Contact force guided radiofrequency current application at developing myocardium : lesion size and coronary artery involvement

○David Backhoff[1,2], Matthias Müller[1], Teresa Betz[1], Andreas Arnold[1], Heike Schneider[1], Thomas Paul[1], Ulrich Krause[1]（1.Department of Pediatric Cardiology and Congenital Heart Disease, University Hospital Giessen, Justus Liebig Universität, Germany, 2.Department of Pediatric Cardiology and Congenital Heart Disease, Pediatric Heart Center, Justus-Liebig-University of Giessen, Giessen, Germany.）

[II-AEPCYIA-3] Can regional differences in expression of cardiomyopathy-related proteins explain the clinical phenotype : a pilot study

○Jonathan Searle [1,2], Wendy Heywood [2], Richard Collis [3], Ivan Doykov[2], Michael Ashworth[4], Mathias Gautel[5], Simon Eaton[2], Caroline Coats[3], Perry Elliott[2,6], Kevin Mills[2]
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Introduction
Children with catecholaminergic polymorphic ventricular tachycardia (CPVT) are at risk for malignant ventricular arrhythmias during exercise and emotions, which may lead to arrhythmic events such as sudden cardiac death (SCD). Symptomatic patients are at particular risk for the reoccurrence of arrhythmic events. Beta-blockers are the cornerstone of therapy in patients with CPVT. However, studies comparing the efficacy of different types of betablockers are scarce. We aimed to determine the efficacy of different types of beta-blockers in reducing the risk for recurrent arrhythmic events in a large cohort of symptomatic children with CPVT.
Methods
Data were derived from the International CPVT Registry, a large retrospective observational cohort study. We included symptomatic children aged <19 years who were carrier of a RYR2 variant and who were prescribed a beta-blocker. The primary endpoint was the occurrence of an arrhythmic event (AE), defined as SCD, aborted cardiac arrest, appropriate ICD discharge or syncope. Time-dependent Cox-regression analyses were used to compare the occurrence of AEs between different beta-blockers corrected for possible confounders with nadolol as reference group.
Results
We included 267 children treated with a beta-blocker. One hundred five (39.3%) children were first

treated with nadolol, 64 (24.0%) with propranolol, 43 (16.1%) with atenolol, 26 (9.7%) with metoprolol and 21 (7.9%) bisoprolol. Age at initiation of beta-blocker differed between the groups, with the youngest mean age in propranolol and highest in bisoprolol and metoprolol (10±4 years in propranolol, 13±4 years in bisoprolol and nadolol, overall-p=0.023). Sex, the proportion of probands and the proportion of patients treated with flecainide, left cardiac sympathetic denervation and an ICD were equally distributed among all groups. In total 86 (32.2%) children had an AE. The AE-rate was significantly higher in patients treated with atenolol compared to nadolol (hazard ratio (HR) 2.15, 95% confidence interval (CI) 1.05-4.40, p=0.036, Table). There were no significant differences in the AE-rate in patients treated with bisoprolol (HR 2.08, 95% CI 0.92-4.71), metoprolol (HR 1.79, 95% CI 0.82-3.92), and propranolol (HR 1.55, 95% CI 0.84-2.86) compared with nadolol.

Conclusions

Atenolol is associated with a higher risk for a subsequent arrhythmic event in symptomatic children with CPVT compared to nadolol.

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[II-AEPCYIA-2] Contact force guided radiofrequency current application at developing myocardium : lesion size and coronary artery involvement

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Introduction

Catheter contact is one key determinant of lesion size in radiofrequency catheter ablation (RFA). Monitoring of contact force (CF) during RFA has been shown to improve efficacy of RFA in experimental settings as well as in adult patients. Value of CF monitoring in pediatric patients has not been systematically studied yet.

Methods

RFA with continuous CF monitoring was performed in 24 piglets (median weight 18.5 kg) using a 7F TactiCath Quartz RF ablation catheter (Abott, Abbott Park, Illinois, USA). A total of 7 lesions were induced in each animal applying low (10-20 g) or high (40-60 g) CF. RF energy was delivered with a target temperature of 65 ° C at 30 W for 30 seconds. Coronary angiography was performed prior and immediately after RF application. Animals were assigned to repeat coronary angiography followed by heart removal after 48 h (n=12) or 6 months (n=12). Lesions with surrounding myocardium were excised, fixated and stained. Lesion volumes were measured by microscopic planimetry.

Results

A total of 148/172(86%) of applied lesions were identified in the explanted hearts. Only in the subset of lesions at the AV annulus 6 month after ablation, lesion size and proportion of transmural lesions were higher in the high CF group while CF had no impact on lesion size and extension in all lesions after 48 h as well as in the atrial and ventricular lesions after 6 months. Additional parameters as Lesion-Size-Index and Force-Time-Integral were also not related to lesion size. Coronary artery damage was not related to catheter CF and was present in 2 animals after 48 h and in 1 after 6 months.

Conclusions
In our experimental setting in piglets lesion size was not related to catheter CF. Transmural extension of the RF lesions involving the layers of the coronary arteries was frequently noted irrespective of CF. Coronary artery narrowing was present in 3/24 animals. According to these findings it may be speculated that even lower CF during RF ablation in infants and toddlers may be equally effective and less traumatic than applied in adults. Impact of CF monitoring during conventional RF ablation in children requires further investigations.

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[II-AEPCYIA-3] Can regional differences in expression of cardiomyopathy-related proteins explain the clinical phenotype : a pilot study

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Introduction
Recognised gene mutations poorly explain regional phenotypic differences in the myocardium of patients developing cardiomyopathy. Understanding the mechanisms driving these patterns, which often begin during childhood, may offer clues to innovate new treatment and diagnostic strategies. Previous proteomic studies have typically analysed single, small tissue samples obtained from a cardiac chamber or cell culture. Developing a novel approach, we aim to describe regional differences in the expression of important cardiomyopathy-associated proteins, with high resolution in different axes across each ventricular wall.
Methods
Continuous samples were obtained from 4-chamber cross-sections of bovine myocardium. Proteins from each were solubilised, extracted and digested, before analysis by mass spectrometry using a ‘ hypothesis-free’ approach. Multivariate analysis was applied, to make unbiased comparisons between samples at whole-proteome level. Twenty-eight cardiomyopathy-associated proteins were selected and compared between samples by relative abundance. Multiple correlation analysis described variation from endocardium-toepicardium, apex-to-base and between each ventricular free-wall. Relative intensity maps were additionally generated.
Results
One-hundred and twenty-two samples of ventricular myocardium were analysed over 128 hours, generating 278 GB of data. 1,017 unique proteins were consistently detected among intra-sample repeats. Their relative expression conformed to three distinct regional patterns, varying predominantly from epicardial to endocardial layers. Regional variations in abundance were demonstrated across all selected proteins. Eleven disease-associated proteins, including Myomesin-1 and Actin alpha-1, were enriched within the ventricular septum ($p<0.05$). Likewise, eight proteins were specifically enriched within the right ventricular epicardial wall ($p<0.05$). Interestingly, some proteins were most abundant

within regions associated with their corresponding cardiomyopathy. Mutations in the Desmoglein-2 gene, for example, are associated with a more left-ventricular dominant phenotype of arrhythmogenic cardiomyopathy (AVC). Unlike other AVC-related proteins, Desmoglein-2 was significantly more abundance within the left ventricular free-wall (figure).

Conclusions

This novel approach describes considerable and detailed variation in the regional abundance of 28 proteins implicated in three major cardiomyopathies. Such variation questions the interpretation of previous cardiac proteomic studies, which typically assume random tissue samples to be representative of the wider myocardium. Application of this approach to disease models at different stages, may offer new insights into development of a cardiomyopathy phenotype in populations of genotype-positive children and adolescents.