INCREASING THE DIAGNOSTIC YIELD OF THE 100,000 GENOMES PROJECT FOR PARTICIPANTS WITH CONGENITAL HEART DISEASE

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Congenital heart disease (CHD) is the most common birth defect, affecting approximately 1% of live births globally. The genetic aetiology of CHD is poorly understood: many genetic loci have already been identified which cause CHD either as part of a defined genetic syndrome or as non-syndromic CHD, but the majority of cases remain unexplained. The 100,000 Genomes Project conducted whole genome sequencing for patients with a range of rare diseases and cancers, including a number recruited for CHD. We analysed clinical, phenotypic and genetic data from the 100,000 Genomes Project to identify potentially pathogenic variants in 2638 participants with CHD, including 536 recruited for CHD and 2102 recruited for other conditions who also have cardiac defects. This cohort are primarily composed of individuals with CHD accompanied by additional extra-cardiac abnormalities but without a diagnosis of a recognised syndrome. We estimate that the set of known non-syndromic CHD-causative genes which are routinely screened by Genomics England account for a maximum of 5.6% CHD cases in this cohort. In contrast, expanding screening to include a number of genes associated with CHD as part of a defined genetic syndrome (eg. Noonan, CHARGE or Kabuki syndromes) could increase the diagnostic yield for this cohort by more than two-fold. Analysis of de novo variants in non-familial CHD cases also identified a significant burden of variants in syndromic CHD genes. Copy number variants (CNVs) are known to play a significant role in CHD, especially in cases of CHD with additional abnormalities. Participants with CHD in this cohort have a significantly higher burden of both deletions and duplications than a matched control cohort. However, very few CNVs overlap known CHD-causative regions such as the 22q11.2 or Williams-Beuren syndrome regions indicating novel CNVs are likely to explain a significant number of cases in this cohort. Wider screening of syndromic CHD genes and novel copy number variants could significantly increase the yield of the 100,000 Genomes Project for participants with CHD. Further investigation of rare variants in this cohort, particularly structural variants, will yield additional novel CHD-associated genes and genomic regions to help explain the ‘missing heritability’ of CHD. This research was made possible through access to the data and findings generated by the 100,000 Genomes Project.
ALIVECOR: DETECTING ARRYTHMIAS IN A SINGLE CENTRE ADULT CONGENITAL POPULATION

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Introduction AliveCor ECG tracing, is an established tool for detecting AF (atrial fibrillation) in acquired cardiology patients. It has not yet been assessed in adult congenital cardiology patients (ACHD). 24–48 hour Holter monitor tracing has variable rates of detection in paroxysmal symptoms, therefore newer technology is required to aid diagnosis.

Aim To determine the utility of AliveCor detecting arrhythmias in ACHD patients, with paroxysmal cardiac symptoms.

Methods Retrospective analysis of AliveCor data over a two year period (2019–2021), at a single ACHD centre was performed (Leeds). AliveCor readings were reviewed by cardiologists and followed with a 12-lead ECG.

Results Of the 44 AliveCor devices, 36 (81%) were given for palpitations, 4 for dizziness, 2 for dyspnoea and 2 for syncope. 48% of patients (21) returned readings with palpitations, of which 11 (52%) had arrhythmias detected. Those identified include atrial fibrillation / flutter (6), atrial tachycardia / ectopy (3), PVC (2). 4 had sinus tachycardia only.

Conflict of Interest None