Research Highlights 2016

Inside this issue...
P2 CRY International Conference
P3 European Conferences
P4 Interview with Dr Finocchiaro
P5 Interview with Dr Dhutia
P6 Papers/Articles
P7 Research Fellow Awards
P7 Presentations
P8 CRY’s Research Programme

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The 11th CRY International Medical Conference – and the first to charge for attendance – took place on 14 October 2016, with 88 medical professionals signed up for a day of presentations and case studies delivered by doctors at the frontier of the prevention of young sudden cardiac death. The CRY Conference takes place every year in London after the main British and European cardiology meetings in the summer, and narrows the focus to inherited arrhythmias, cardiomyopathies and other conditions which can cause sudden cardiac arrests in young people.

The meeting is organised by CRY Consultant Cardiologist Professor Sanjay Sharma and myheart Cardiologist Dr Michael Papadakis, who had continued to publish far-reaching papers alongside the CRY Research Fellows throughout 2016. Presenters included current and former CRY Fellows as well as two of their most prominent European colleagues; Professors Domenico Corrado and Mats Börjesson. St George’s Hospital consultant cardiologist Dr Maite Tome, former Real Madrid team physician Dr Luis Serratosa and CRY Chief Executive Dr Steven Cox chaired sessions and helped to field questions throughout.

Dr Papadakis welcomed the attendees and introduced former CRY Fellow Dr Sabiha Gati, who gave an overview of current guidelines for assessing the aortic root of athletes. Departing CRY Fellow Dr Lynne Millar followed with her results on the effectiveness of exercise echocardiography in the diagnosis of athletes with dilated cardiomyopathy. Dr Abbas Zaidi, another former CRY Fellow, moved discussion to the right ventricle with an explanation of his 2015 guidelines to help physicians discriminate between arrhythmogenic right ventricular cardiomyopathy (ARVC) and athlete’s heart. Dr Papadakis chose to give his talk on the markers of hypertrophic cardiomyopathy, which is another of the most common causes of sudden death in sport. To close the session, Professor Domenico Corrado offered his unparalleled experience on interpreting the athlete’s ECG.

After a break, CRY Fellow Dr Gherardo Finocchiaro outlined the problems of ascertaining the scale and causes of sudden death in sport, introducing his 2016 CRY research on the aetiology of these deaths. Professor Sheppard followed by beginning with a full explanation of UK coroners’ referral procedure after a young sudden death and then a presentation on valve disease pathology. CRY Fellow Dr Harshil Dhutia examined ECG screening costs in a crucial study, drawing attention to a 21% reduction in the cost of screening athletes due to the development of new ECG criteria. CRY’s Dr Aneil Malhotra presented on the adolescent athlete’s ECG, suggesting adaptions for ECG guidelines to be adjusted for the juvenile heart, since adolescents make up the biggest group of exercising individuals. Swedish expert Professor Mats Börjesson outlined the practicalities of putting theory into practice when a cardiac arrest spontaneously occurs during a sporting event. In the penultimate presentation, Professor Sharma discussed the shaky evidence that exercise itself can cause cardiac harm.

Case studies on cardiomyopathy and structural disease followed lunch, with two cases of patients showing signs of potential heart muscle disorders from CRY Fellow Dr Keerthi Prakash, and another from CRY’s Dr Stathis Papatheodorou. CRY’s Dr Bode Ensam and Dr Andrew D’Silva, and St George’s fellow Dr Chris Miles, tested the audience with difficult cases of suspected electrical heart disease.

For videos of all the presentations from the CRY Conference 2016 visit www.c-ry.org.uk/cry-international-conference
European Conferences

**BCS Conference**

The BCS Conference, held in Manchester’s ExCeL Centre from 6 to 8 June 2016, was attended by Professor Sharma and myheart Cardiologist Dr Michael Papadakis; Research Fellows Dr Harshil Dhutia, Dr Gherardo Finocchiaro, Dr Tracey Keteepe-Arachi, and Dr Keerthi Prakash; former CRY Fellow Dr Sabiha Gati; Dr Alexandros Steriotis; and collaborating St George’s fellow Dr Yeo Tee Joo.

CRY was also represented by Chief Executive Dr Steven Cox and Azra Loncarevic-Srmic, Director of Research and Screening, who more broadly raised awareness of CRY’s services and objectives at the event.

Dr Finocchiaro won a highest scoring abstract award for his study on the circumstances of sudden death in Wolff-Parkinson-White syndrome, a cardiac rhythm disorder, with the aim of improving doctors’ judgements of risk of cardiac events. He also presented on the relationship between obesity and young sudden death, finding almost one in four cases showed evidence of coronary artery disease. These studies were conducted in collaboration with CRY Consultant Cardiac Pathologist Professor Mary Sheppard.

Dr Steriotis presented an abstract which examined cases of isolated mitral valve prolapse, again working with Professor Sheppard and the valuable data recorded at the CRY Centre for Cardiac Pathology. Two of the heart’s chambers, the left ventricle and left atria, are separated by the mitral valve, which can become leaky and fail to close properly. Dr Yeo presented research led by CRY Fellow Dr Aneil Malhotra investigating the significance of T-wave inversions, a suspicious ECG anomaly which can indicate serious cardiovascular disease, in a large group of athletes and non-athletes.

**ESC Congress**

2016’s ESC Congress was held from 28 August to 3 September at the Fiera di Roma in Rome, Italy – the most proactive nation in Europe for legislating to prevent young sudden deaths in sport, with mandatory cardiac screening for all amateur and professional athletes. Professor Sanjay Sharma was one of several hugely respected cardiologists at the meeting who joined Italian Professor Domenico Corrado in supporting the argument for screening athletes with an ECG. Professor Corrado himself presented a comprehensive rebuttal of articles published in April 2016 in British journal The BMJ, which had criticised the Italians’ evidence demonstrating that their screening programme saves lives.

Some of the most important CRY research delivered at the conference was included in the Highlights from Sports Cardiology session from myheart Cardiologist Dr Michael Papadakis. He explained the significance of a landmark study which had been published that month in the Journal of the American College of Cardiology: CRY Fellow Dr Harshil Dhutia analysed data drawn from 4,925 athletes screened by CRY between 2011 and 2014, comparing three sets of ECG criteria for their cost-effectiveness.

Former CRY Fellow Dr Sabiha Gati delivered findings following 10 years of mandatory cardiac screening of youth academy footballers through the English Football Association (FA). The study, led by CRY’s Dr Aneil Malhotra, included 10,156 adolescents. They were predominantly 16-year-olds, though ages ranged from 14 to 19; 95% were male; 91% were white. As in Dr Dhutia’s study, the ESC guidelines for ECG interpretation were employed, with the Seattle and refined criteria applied retrospectively. All three criteria maintained the same sensitivity to serious cardiac disease. The CRY refined criteria improved specificity (reducing false-positives) from 87% to 97%, indicating their potential suitability for a teenage athletic population.

In another significant CRY contribution, Dr Gherardo Finocchiaro presented his study on hypertrophic cardiomyopathy (HCM), investigating the circumstances of sudden cardiac death for 184 HCM cases from 1994–2014 recorded at the CRY Centre for Cardiac Pathology. Considering HCM’s association with athletic sudden deaths, a major finding was that just over 80% of individuals died at rest or during sleep; young males were found to be the most likely to die during exertion. In almost 80% of cases the disease was only found at post-mortem. To watch his presentation visit bit.ly/esc28816gf
Sudden death in sport and generally in young individuals is a rare event but it’s always tragic – usually with a lot of attention from the media and from the community. When such an event occurs there are many questions: “Why has this happened?” “Could we have prevented this event?” So to understand and to prevent such events we need to understand better the aetiologies, causes, that are underlying sudden cardiac death.

What was the purpose of your study?

Previous findings and reports showed that there are certain diseases that are the main causes of sudden death in sport. Particularly from the United States, studies from 10 and 20 years ago showed that the hypertrophic cardiomyopathy (HCM) accounts for more than one third of the cases of young sudden death in athletes. Other reports from Italy showed that arrhythmogenic right ventricular cardiomyopathy (ARVC) is the main cause of sudden death in sport.

In our cohort of 357 we had 70% competitive athletes engaging in competition in organised sport or individual sport, for example, marathon runners or football players, and then we had another 30% recreational athletes – but all of our sudden death victims were participating in sport for more than 3 hours per week.

What were the main findings of the study?

In our study we had 58% of cases where there was a structural heart disease, so the heart was not normal. There were various structural abnormalities, including cardiomyopathies – which was the most frequent structural abnormality – such as; ARVC, HCM, idiopathic left ventricular hypertrophy, idiopathic fibrosis. And then we had cases of coronary artery abnormalities.

But I think that the most striking finding was that 42% of our cases were characterised by a normal heart at the post-mortem, which is called sudden arrhythmic death syndrome (SADS).

A normal post-mortem examination in a sudden death victim is suggestive of ion channelopathies (inherited cardiac disease which can be detected at the ECG), which are considered to be inherited primary arrhythmias and they can provoke sudden death.

What was the disparity between those who died during exertion and those who died at rest?

Previous reports showed a higher prevalence of athletes dying during exertion. In our cohort we had 61% of athletes dying during exertion, but we had 39% who died at rest, including 11% who died during sleep.

There were some differences between the two subgroups: if you look at the aetiologies you see that patients that died during exertion tend to have ARVC, and left ventricular fibrosis; while patients that died at rest or during sleep tend to have SADS.

Was there a big difference between the ages and the conditions people had when they died?

We divided our cohort into three subgroups: the athletes who died suddenly before the age of 18, so very young; others that died between the ages of 18 and 35; and athletes that died older than 35. And we found some important differences.

The main difference is that athletes that died very young tend to have a normal heart at the post-mortem, so SADS, suggesting possible ion channelopathies. Patients that died suddenly at an older age, after the age of 18, or even more after the age of 35, tend to have structural heart disease, so cardiomyopathies.

What are the implications going forward?

I think that this study has some important findings. The first is that 42% of athletes tend to have a normal heart at post-mortem exam, suggesting SADS.

Second is that there are some differences in the prevalence of aetiologies according to age, so very young athletes more frequently tend to have SADS at post-mortem, older athletes more frequently tend to have structural abnormalities, cardiomyopathies.

Third point is that not all athletes die during exercise; there is a significant 40% who died at rest or even during sleep.

Fourth point is that the main predictor of sudden death during exertion was ARVC. This is very important because if we consider ARVC, which is a disease that can be diagnosed with even a simple baseline ECG, the recommendations to avoid competitive and even possibly recreational sport should be very strong and very definitive.

For the full interview visit www.c-r-y.org.uk/research/research-fellows/dr-gerardo-finocchiaro
Why did you investigate the cost of screening athletes?

Screening and prevention of sudden cardiac death in young athletes has become an important focus of the medical community based on evidence from a large prospective study in Italy, where screening has resulted in a 90% reduction in deaths. Whilst it’s not possible to put a financial value on a life saved, a consideration of cost is important when we are considering large-scale ECG screening of athletes.

One of the concerns of screening with the ECG is the potential for high false-positive rates, because on occasion ECG changes in athletes overlap with those that are seen in patients with cardiac disease. As a consequence, the false-positive rate may make screening difficult because of costs of further investigations required to confirm or refute the underlying cardiac diagnosis. Therefore the aim of my study was to evaluate whether modification of ECG recommendations translates to a cost reduction when athletes are undergoing ECG screening.

What are the main differences between the three criteria you compared?

The 2010 European Society of Cardiology (ESC) recommendations – which were published in the European Heart Journal – provided the first pragmatic approach to interpreting the ECG in athletes, however these criteria were associated with a false-positive rate of between 16% and 25%. In 2013, a group of experts from the United States and Europe developed the Seattle ECG recommendations to try and reduce the false-positive rate. The Seattle criteria were still associated with false-positive rates of between 8% and 15%.

In 2014, research conducted through CRY resulted in the refined ECG criteria. These criteria reduced the false-positive rate to between 5% and 8% without compromising the ability to detect serious cardiac disease.

How did you conduct your study?

This was a prospective study of athletes who were undergoing cardiovascular screening for the first time, through CRY, between 2011 and 2014. 4,925 young athletes were screened nationwide as per the mandatory requirement of their sporting organisation.

What percentage of athletes had follow-up tests?

Nearly 2% of the athletes were considered to have symptoms, a family history of inherited cardiac disease, or an abnormal physical examination. From the ECG point of view, 21.8% of athletes had an abnormal ECG according to the 2010 ESC recommendations.

However the refined criteria, when applied retrospectively to this cohort, reduced the proportion of abnormal ECGs requiring follow-up to 4.3%. This represents an 80% relative reduction in the number of abnormal ECGs, again, without compromising the ability to detect serious cardiac disease.

What was the reduction in the number of follow-up tests?

The refined criteria would have resulted in more than a 50% reduction in the number of echocardiograms required, a 12% reduction in the number of exercise tests required, an 8% reduction in the number of 24-hour ECGs required, and an 18% reduction in the number of cardiac MRI scans that would be required to be performed following screening.

What are the implications of this increased cost-effectiveness?

As a result of this reduction in cost, ECG screening may now be more affordable for less financially endowed sporting organisations to protect their athletes.

In this study, the savings would allow an extra 2,100 athletes to undergo cardiovascular screening or 95 automated external defibrillators to be purchased to further increase the safety margin for our athletes.

For the full interview visit www.c-r-y.org.uk/research/research-fellows/dr-harshil-dhutia
This study highlights sudden cardiac deaths in pregnancy or in the postpartum period, particularly due to SADS with possible channelopathies and cardiomyopathy. We wish to raise awareness of these frequently under-recognized entities in maternal deaths and the need of cardiological screening of the family.

- "Do endurance sports affect female hearts differently to male hearts?" Finocchiaro G, Sharma S. Future Cardiology, March 2016.

- "Although there is only a single chromosome separating the two sexes, females differ from males in several respects including their anthropometric, biochemical, physiological and psychological profile, all of which play a role in their cardiovascular response to athletic training."


- "Although men and women share classic cardiovascular risk factors the relative importance of each risk factor may be gender specific."


- "This article aims to describe the rationale underlying current recommendations and provides guidance for recreational exercise in many asymptomatic individuals. The article concludes with pragmatic recommendations for symptomatic patients with cardiomyopathy in whom physical activity is associated with beneficial effects on the quality and, possibly, the quantity of life."


- "In this review we discuss which ECG patterns can safely be considered benign as opposed to those that should prompt the physician to consider cardiac pathology."


- "This paper discusses the uncertainties about available data and provides comprehensive suggestions for standard definitions and a guide for uniform registration parameters of [sudden cardiac arrest]/[sudden cardiac death]."


- "Conditions predisposing to [sudden cardiac death (SCD)] in sports demonstrate a significant age predilection. The strong association of [arrhythmogenic right ventricular cardiomyopathy] and left ventricular fibrosis with exercise-induced SCD reinforces the need for early detection and abstinence from intense exercise. However, almost 40% of athletes die at rest, highlighting the need for complementary preventative strategies."

- "Pathological remodelling of the athlete’s heart." Kettee-Arachi T, Sharma S. Cardiovascular Medicine, May 2016.


- "New approaches to predicting the risk of sudden death." Behr E, Ensarn B. Clinical Medicine, June 2016.

- "In this review article, we will explore some of the contemporary methods for predicting sudden cardiac death (SCD). These include experimental methods yet to be adopted in the clinical setting, and methods that have been extrapolated from observational data in those with a history of SCD."


- "Preparticipation cardiac screening with 12-lead ECG is feasible. Refinement of the ECG criteria, the use of on-site [transesophageal echocardiogram] and expert setting can minimise the burden of unnecessary investigations and reduce costs."


- "The [early repolarization (ER)] pattern is more common in [sudden arrhythmic death syndrome] family members than controls adjusted in particular for relatedness. [...] ER may therefore represent an underlying heritable arrhythmia syndrome or risk factor for sudden death in the context of other cardiac pathology."


- "Contemporary ECG interpretation guidelines are associated with a cost reduction of up to 21% without compromising sensitivity to detect serious cardiac disease. These results represent a welcome saving for sporting organizations equipped with the infrastructure and expertise for cardiac screening in athletes."


- "There is a positive correlation between higher intensity of sports and increased prevalence of ECG abnormalities. This relationship persists with the use of more restrictive criteria for ECG interpretation, although the number of abnormal ECGs is lower."


- "Preparticipation screening (PPS) is widely used to detect athletes at risk of exercise-related [sudden cardiac death], but the optimal PPS approach remains elusive because of the relatively small number of predisposed individuals, the considerable size of the target population, and the limited sensitivity and specificity of individual screening tools."


- "The data from this meta-analysis support current Task Force criteria for the diagnosis of [arrhythmogenic right ventricular cardiomyopathy (ARVC)]. In addition, other right ventricular measures that reflect the complex geometry and function in ARVC can be differentiated between ARVC and healthy controls and may provide additional diagnostic and management value."


- "Black ethnicity is an important determinant of the phenotypic expression of [hypertrophic cardiomyopathy (HCM)] but does not adversely affect outcomes. Apical and concentric hypertrophy are common in black patients and may hinder the identification of HCM in this cohort."


- "The different patterns of presentation of myocarditis are classified as low-, intermediate-, and high-risk syndromes according to the most recent evidence on prognosis, clinical findings, and both invasive and noninvasive testing, and appropriate management strategies are proposed for each risk class."


"Preventing Sudden Cardiac Death in Athletes: Beyond Pre-participation Screening." Ensam B.

"ECG Phenotypes Suggestive of Cardiac Disease." Finocchiaro G.


In this issue of the BASEM Today, the sports cardiology team of the cardiology clinical academic group at St George’s, University of London, provide an overview of key concepts in sports cardiology. We hope this issue will serve as a reference for the readers when faced with cardiac-related issues in sportspeople and stimulate interest in the expanding field of sports cardiology where the demand for trained healthcare professionals is increasing.”

Dr Michael Papadakis, Guest Editor.


For a full list of CRY’s research visit www.c-r-y.org.uk/research/crys-contribution-to-research
The CRY Research Programme is overseen by Professor Sanjay Sharma, Professor of Inherited Cardiovascular Disease and Sports Cardiology at St George’s Hospital, London; Virgin Money London Marathon Medical Director; and was the London 2012 Olympic Cardiologist.

The CRY Research Fellowship Programme funds doctors for up to three years who choose to specialise in the fields of inherited cardiac diseases, young sudden cardiac death, screening and sports cardiology. It is our unique expertise in sports cardiology and how athleticism, ethnicity and gender affect the ECG that has made CRY a leading international authority on cardiac screening. “Sports cardiology” is cardiac research and clinical practice applied to fit and healthy young people. The knowledge gained from studying athletes better informs the diagnosis and management of all young people at risk from cardiac conditions.

As of January 2017 there are 9 CRY Research Fellows at St George’s Hospital who divide their time between NHS clinics, CRY screenings and research. As well as the Fellows CRY are currently funding, 19 former Fellows have been trained as specialists by CRY and are now working in the NHS throughout the UK.

Professor Sharma oversees the CRY National Screening Programme in which the CRY Research Fellows play a central role. Every person that CRY tests is asked to consent to having their data used anonymously for research purposes. This has developed a symbiotic relationship between research and screening; identifying young individuals at risk whilst learning from our experience and publishing these findings.

CRY's research is preventing tragedies by transforming the way we understand the causes of young sudden cardiac death (YSCD); and the ways we identify, investigate and manage young people with cardiac conditions.

CRY research has shown:

- Every week in the UK at least 12 young people die of undiagnosed heart conditions (Papadakis M et al. 2009)
- 1 in 300 young people that CRY tests will have a potentially life-threatening heart condition (Wilson MG et al. 2008)
- 80% of SADS deaths occur at rest or during sleep (Mellor G et al. 2014)
- ARVC is the cardiac condition most likely to cause sudden death during exercise (Finocchiaro et al. 2016)

CRY’s Research Programme

CRY research grants fund fast-track, expert referral services at the CRY Centre for Cardiac Pathology (CRY CCP) and the CRY Centre for Inherited Cardiovascular Conditions and Sports Cardiology

CRY research grants fund original research using data gathered from the CRY Centres and through the CRY National Screening Programme

CRY research grants fund clinical doctors who are present at every CRY screening event to examine the results of young people tested and provide a consultation on the same day

In 2016 the following ringfenced funds made significant contributions to support CRY’s research team at St George’s Hospital:

- The Nathan Butler Memorial Fund
- The Matthew Cragg Memorial Fund
- The Josh Fell Memorial Fund
- The Stewart Howard Memorial Fund

- The Joe Kellogg Memorial Fund
- The Jannik Lam Memorial Fund
- The Alan Lumley Memorial Fund
- The Andrew Macleod Memorial Fund
- The Lewis Marsh Memorial Fund

- The David Moss Memorial Fund
- The Rebecca Phillips Memorial Fund
- The Hannah Turberville Memorial Fund
- The Northern Ireland Memorial Fund
- The West Midlands ECG Memorial Fund

25% of CRY’s Funding Supports Research