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AUSTRALIAN SCAD STUDY

Update

Dear SCADaddlers:

Apologies, it's been some time since I last provided an update on our work. But firstly, let me extend our most sincere thanks for your support of our research into the genetics and causes of SCAD. Your support is greatly appreciated.

So, despite Covid, we've continued to make good progress. Highlights include a recent paper accepted in the leading cardiovascular genetics journal, *Circulation: Genomic and Precision Medicine*, entitled: "Exploring the genetic architecture of spontaneous coronary artery dissection using whole genome sequencing", which should be coming out very soon. This paper reports on the detailed analysis of gene changes that might predispose to SCAD in 91 unrelated, sporadic SCAD sufferers. The major findings of this work, spearheaded by my colleague, A/Prof Eleni Giannoulatou, are that unfortunately, variations in many different genes might be involved, including those previously associated with connective tissue disorders, albeit that in none of these cases did we find the characteristic features of a connective tissue disorder. Thus, in many instances SCAD may in fact be a subtle and, indeed, the only manifestation of such disorders.

Prior to this study, it was thought that connective tissue disorders are rarely found in SCAD sufferers, but, given that connective tissue, which involves proteins like collagen and elastin, forms an important scaffolding around our cells, it is perhaps not surprising that a weakness in this scaffolding may predispose to a tear in the lining or wall of coronary arteries.

Consistent with SCAD involving many gene variants, that is, having a complex genetic architecture, we also found that SCAD suffers have many more gene variants than people who haven't had a SCAD.

Unfortunately, the implications of this study are that we will need to look at many, many different genes, and their functions, before we can accurately predict, who is at risk of a recurrence, or to predict if your children are at risk of developing a SCAD. So, more work to be done!

Another major study that is currently being written up in a paper, involves our collaboration with other leading SCAD centres worldwide, including in Paris, France; Leicester, UK; Michigan, New York and the Mayo Clinic in the USA, and Vancouver, Canada. Together we have assembled 1,917 SCAD cases and 9,292 controls, which we used to look for common gene variants. While the data is still being analysed, we are very pleased to have identified a number of new locations in our genomes that are associated with SCAD, including many not previously identified.

Recently, I was invited to write an Editorial, which will soon be publish in the journal, *Heart*, commenting on a large study looking at the adverse events associated with SCAD, in some 389 SCAD sufferers in Spain. Reassuringly, this study found that for those patients who are treated in hospital, the prognosis is excellent, with a 98% survival rate, only 6% suffering a major in-hospital adverse cardiovascular problem, and 13% developing a major adverse cardiovascular problem or stroke in the 2 years after their SCAD event. Of interest, this study also found a very low rate (2%) of recurrences in the 2 years after the initial SCAD event. This recurrence rate is much lower than that reported in other studies, so will need to be verified, but overall, I think that these findings should be of some comfort to SCAD sufferers.

Finally, I am very excited about a study we have been involved in together with our colleagues, A/Prof Barbara Murphy and Prof Alan Jackson at the Australian Centre for Heart Health, looking at the psychosocial impacts of SCAD. Specifically, this study involved 30 SCAD sufferers, who took part in focus groups to try and understand the mental and social impacts of SCAD. So, firstly, let me thank all those SCAD sufferers who volunteered their time to be involved in this study, which I think has been extremely informative.

A paper describing these findings has recently been submitted for publication. Once published, I do hope we can disseminate it widely, not only to other SCAD sufferers, but also to both GPs

and specialists looking after SCAD patients, as it's clear from the study that there is both a major lack of knowledge and misinformation about SCAD.

In the future, we will continue working with Barbara and Alun to use the information gained from this study to develop support programs to directly help SCAD sufferers deal with the impacts of SCAD.

So again, many thanks to all of the SCAD community for your support, and let me also take this opportunity to recognise our team, which includes A/Prof Eleni Giannoulatou, Head, Bioinformatics, Victor Chang Cardiac Research Institute (VCCRI); Prof Jason Kovacic, Executive Director, VCCRI; Prof David Muller, Director, Interventional Cardiology, St Vincent's Hospital; Dr Stephanie Hesselson; Dr Siiri Iismaa; Dr Monique Bax; Dr Lucy McGrath-Cadell; Ms Ingrid Tarr, and Ms Keerat Junday.

Kind regards,

Robert M. Graham, AO, MD, FRACP
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