Journal of Affective Disorders 196 (2016) 117–124

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Depression is a risk factor for incident coronary heart disease in women: An 18-year longitudinal study

Adrienne O'Neil [a,b,c,*], Aaron J. Fisher [d], Katherine J. Kibbey [e,f,n], Felice N. Jacka [b,g,j,k], Mark A. Kotowicz [b,e,l], Lana J. Williams [b], Amanda L. Stuart [b], Michael Berk [b,c,g,h,i], Paul A. Lewandowski [b], Craig B. Taylor [l], Julie A. Pasco [b,m]

[a] Melbourne School of Population & Global Health, University of Melbourne, Carlton, VIC, Australia
[b] School of Medicine, Deakin University, Geelong, VIC, Australia
[c] School of Public Health and Preventive Medicine, Monash University, Prahran, VIC, Australia
[d] Department of Psychology, University of California, Berkeley, CA, USA
[e] Barwon Health, Geelong Hospital, Geelong, VIC, Australia
[f] Monash Health, Melbourne, VIC, Australia
[g] Department of Psychiatry, The University of Melbourne, Parkville, VIC, Australia
[h] Orygen Youth Health Research Centre, Parkville, VIC, Australia
[i] Mental Health Research Institute, Parkville, VIC, Australia
[j] Centre for Adolescent Health, Murdoch Children's Research Centre, Parkville, VIC, Australia
[k] Black Dog Institute, Hospital Road, Prince of Wales Hospital, Randwick, NSW, Australia
[l] Department of Psychiatry & Behavioral Medicine, Stanford University & Palo Alto University, CA, USA
[m] Western Medical School, The University of Melbourne, St Albans, VIC, Australia
[n] School of Clinical Sciences, Monash University, Melbourne, Australia

ARTICLE INFO

Article history:
Received 14 September 2015
Received in revised form
12 November 2015
Accepted 6 February 2016
Available online 16 February 2016

Keywords:
Depression
Coronary heart disease
Women
Risk factor
Prevention

ABSTRACT

Background: According to a recent position paper by the American Heart Association, it remains unclear whether depression is a risk factor for incident Coronary Heart Disease (CHD). We assessed whether a depressive disorder independently predicts 18-year incident CHD in women.

Method: A prospective longitudinal study of 860 women enrolled in the Geelong Osteoporosis Study (1993–2011) was conducted. Participants were derived from an age-stratified, representative sample of women (20–94 years) randomly selected from electoral rolls in South-Eastern Australia. The exposure was a diagnosis of a depressive disorder using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders. Outcomes data were collected from hospital medical records: (1) *Primary outcome:* a composite measure of cardiac death, non-fatal Myocardial Infarction or coronary intervention. (2) *Secondary outcome:* any cardiac event (un/stable angina, cardiac event not otherwise defined) occurring over the study period.

Results: Seven participants were excluded based on CHD history. Eighty-three participants (9.6%) recorded ≥ 1 cardiac event over the study period; 47 had a diagnosis that met criteria for inclusion in the primary analysis. Baseline depression predicted 18-year incidence, adjusting for (1) anxiety (adj. OR:2.39; 95% CIs:1.19–4.82), plus (2) typical risk factors (adj. OR:3.22; 95% CIs:1.45–6.93), plus (3) atypical risk factors (adj. OR:3.28; 95% CIs:1.36–7.90). This relationship held when including all cardiac events. No relationship was observed between depression and recurrent cardiac events.

Conclusion: The results of this study support the contention that depression is an independent risk factor for CHD incidence in women. Moreover, the strength of association between depression and CHD incidence was of a greater magnitude than any typical and atypical risk factor.

Abbreviations: CHD, Coronary Heart Disease; OR, Odds ratio; CI, Confidence Intervals; ACS, Acute coronary syndrome; CVD, Cardiovascular Disease; HDL, High density lipoprotein; GOS, Geelong Osteoporosis Study; MI, Myocardial Infarction; STEMI, ST segment elevation MI; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; SCID-I/NP, Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Non-patient edition; MDD, Major Depressive Disorder; BP, Blood pressure; LDL, Low density lipoprotein; BMI, Body mass index; hCRP, High sensitivity C-reactive protein

* Correspondence to: Melbourne School of Population & Global Health – Non Communicable Disease Unit. Level 4, The University of Melbourne, 161 Barry Street, Victoria 3010 Australia.
E-mail address: adrienne.oneil@unimelb.edu.au (A. O'Neil).

http://dx.doi.org/10.1016/j.jad.2016.02.029
0165-0327/

1. Introduction

The medical sub-speciality of psychocardiology (Halaris, 2013; Jordan and Bardé, 2007) has emerged in recognition of the contribution of psycho-social factors including stress, lack of social support and negative emotions to deleterious cardiovascular outcomes (Frasure-Smith et al., 1995a, 1995b). For those with established coronary disease, depression increases the risk of morbidity, mortality (Frasure-Smith et al., 1995a, 1995b), suicide (Larsen et al., 2016), poor risk factor profiles and functional outcomes (Bhattacharyya et al., 2007). Anxiety has also been linked to smoking, hypercholesterolemia and poorer diabetes control (Moylan et al., 2013).

An expert working group was recently commissioned by the American Heart Association to review the evidence and determine whether depression should be elevated to 'risk factor' status for poor prognosis in acute coronary syndrome (ACS) patients (Lichtman et al., 2014). Based on data from 53 individual studies and 4 meta-analyses, the group concluded that depression was predictive of all-cause/cardiac mortality and nonfatal cardiac events in both men and women with established disease. Their primary recommendation was that depression be formally recognized as a risk factor for poor outcomes in ACS populations (Lichtman et al., 2014). The authors highlighted, however, that it remained unclear whether depression was an independent risk factor for incident coronary heart disease (CHD). While there is some evidence that depression increases CHD risk (Lett et al., 2004), it has been argued that, as yet, there is "no convincing evidence that depression is an independent causal risk factor" for CHD (Stampfer et al., 2012).

Given that women have an elevated lifetime risk for depression (and anxiety) (Australian Institute of Health and Welfare, 2010), the relationship between depression and CHD in women is of particular significance. Currently, cardiovascular disease (CVD) is the leading cause of death in women in all major, developed countries including the United States and Australia (Australian Institute of Health and Welfare, 2009). From an etiological perspective, the trajectory of CHD in women is complicated. Women have been considered somewhat protected from CHD due to the effects of estrogen and elevated high density lipoprotein (HDL) cholesterol levels until menopause, after which time their risk of CHD increases with age (Matthews et al., 1989). However, new evidence indicates that the impact of traditional cardiovascular risk factors is greater in women when compared with men (Cheng et al., 2014). Moreover, once CHD manifests, female patients, particularly those of a younger age, are susceptible to adverse CHD outcomes including mortality (Davidson, 2012). While sex-specific differences in pathophysiology are not fully understood, recent data indicate that they may relate to endothelial dysfunction and the involvement of the microvascular system whereby coronary flow reserve is lower in women due to lower resting coronary flow (Kobayashi et al., 2015). Other data have specifically highlighted that the impact of depression on CHD mortality among women with suspected or established coronary disease and that this is most pronounced for those aged 30–55 years (Shah et al., 2014).

From a behavioral perspective, women are less likely to self-identify cardiovascular risk factors (Mosca et al., 2010) or seek help for a cardiac event, holding the view they can self-medicate (Higginson, 2008). From a treatment perspective, the outcomes for women are compromised. They are less likely to be referred for disease assessments (e.g. coronary angiography) (Bougouin et al., 2015), screened for depression following ACS (Smolderen et al., 2011), attend cardiac rehabilitation (Colbert et al., 2013) or benefit from invasive cardiovascular treatment (Lagerqvist et al., 2001). Thus, better understanding how depression contributes to CHD in women is crucial for determining a need to develop sex-specific preventive and therapeutic interventions.

The aim of this study was to address the gaps in the literature as identified by the American Heart Association position statement (Lichtman et al., 2014)-with a focus on how they pertain to women- and provide key data to guide subsequent preventive interventions. Specifically, we sought to examine the role of depression as a risk factor for CHD incidence (and recurrence) in a population-based, random sample of 860 women followed for (up to) 18-years for whom gold standard psychiatric, bio-behavioral and CHD data were available.

2. Method

2.1. Participants

Details of the Geelong Osteoporosis Study (GOS) have been published elsewhere (Pasco et al., 2012). Briefly, the GOS was initiated in 1993, comprising an age-stratified, population-based sample of women (aged 20–94 years) who were randomly selected from electoral rolls of the Barwon Statistical Division, South-Eastern Australia. As voting is compulsory in Australia for adults aged+18-years, this sampling technique provides a random sample of citizens registered with the Australian Electoral Commission. Population characteristics of the Barwon Statistical Division are comparable with national levels. Individuals randomly selected from the electoral roll were mailed an invitation letter, with a request to contact the research centre. Those residing in the area for <6 months or unable to provide informed consent were excluded. During the years 1993–97, 2390 women were invited to participate, of whom 432 lapsed and 444 declined to participate. Personal reasons (53.2%), old age (18%) and illness (12.6%) were the most common reasons. At least 100 women were recruited in each 5-year age group from 20 to 69 years and 200 for both the age groups of 70–79 years and 80+ years. Those eligible were subsequently invited to attend the research centre located at the largest public hospital in the region (Barwon Health; The Geelong Hospital). Participants provided written, informed consent at each assessment. The final sample size at baseline was 1494 participants (overall participation=77%) (Markanday et al., 2013). The Barwon Human Research Ethics Committee approved the study.

2.2. Procedure

While the GOS study comprises ongoing, regular health assessments, this study utilized psychiatric, anthropometric, demographic and other health (non-CHD) data from the major GOS assessments (baseline and 10 years). Trained Research Assistants collected clinical, anthropometric and questionnaire data and those with minimum Honors qualifications in Psychology conducted the psychiatric assessments. In 2011, CHD events data were extracted retrospectively from hospital medical records for the period 1993–2011. Following an overnight fast, blood samples were taken from participants at the time of baseline assessment at a local pathology laboratory and stored at The Geelong Hospital. Bio-specimens were batch analyzed at the Molecular Medicine Research Facility at Deakin University.

2.3. Study measurements

2.3.1. Outcomes

The primary outcome was the occurrence of a CHD event that resulted in hospital presentation over the 18-year follow up period (post baseline assessment), with a formal diagnosis of: cardiac death, non-fatal Myocardial Infarction (MI) based on troponin levels and electrocardiogram reading (ST segment elevation MI;