Journal of Affective Disorders 192 (2016) 34–40

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Depression as a risk factor for fracture in women: A 10 year longitudinal study

Lana J Williams [a,*], Julie A Pasco [a,b], Henry Jackson [c], Litza Kiropoulos [c,d], Amanda L Stuart [a], Felice N Jacka [a,e], Michael Berk [a,e,f,g]

[a] Deakin University, School of Medicine, IMPACT Strategic Research Centre, Geelong, Australia
[b] The University of Melbourne, Department of Medicine, St Albans, Australia
[c] The University of Melbourne, Melbourne School of Psychological Sciences, Australia
[d] Royal Melbourne Hospital, Psychology Department, Australia
[e] The University of Melbourne, Department of Psychiatry, Parkville, Australia
[f] The University of Melbourne, The Florey Institute of Neuroscience and Mental Health, Parkville, Australia
[g] The University of Melbourne, Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, Australia

ARTICLE INFO

Article history:
Received 29 July 2015
Received in revised form
25 November 2015
Accepted 28 November 2015
Available online 10 December 2015

Keywords:
Depression
Fracture
Bone
Osteoporosis
Bone mineral density
Women

ABSTRACT

Background: Previous research has demonstrated deficits in bone mineral density (BMD) among individuals with depression. While reduced BMD is a known risk for fracture, a direct link between depression and fracture risk is yet to be confirmed.
Methods: A population-based sample of women participating in the Geelong Osteoporosis Study was studied using both nested case-control and retrospective cohort study designs. A lifetime history of depression was identified using a semi-structured clinical interview (SCID-I/NP). Incident fractures were identified from radiological reports and BMD was measured at the femoral neck using dual energy absorptiometry. Anthropometry was measured and information on medication use and lifestyle factors was obtained via questionnaire.
Results: Among 179 cases with incident fracture and 914 controls, depression was associated with increased odds of fracture (adjusted odds ratio (OR) 1.57, 95%CI 1.04–2.38); further adjustment for psychotropic medication use appeared to attenuate this association (adjusted OR 1.52, 95%CI 0.98–2.36). Among 165 women with a history of depression at baseline and 693 who had no history of depression, depression was associated with a 68% increased risk of incident fracture (adjusted hazard ratio (HR) 1.68, 95%CI 1.02–2.76), with further adjustment for psychotropic medication use also appearing to attenuate this association (adjusted HR 1.58, 95%CI 0.95–2.61).
Limitations: Potential limitations include recall bias, unrecognised confounding and generalizability.
Conclusions: This study provides both cross-sectional and longitudinal evidence to suggest that clinical depression is a risk factor for radiologically-confirmed incident fracture, independent of a number of known risk factors. If there is indeed a clinically meaningful co-morbidity between mental and bone health, potentially worsened by psychotropic medications, the issue of screening at-risk populations needs to become a priority.

1. Introduction

Depression is a highly prevalent, often chronic condition that imposes a significant health and economic burden worldwide (World Health Organisation, 2008). Cross-national lifetime prevalence figures show that up to 21.4% of the population suffer from depressive symptoms that qualify for a clinical diagnosis (Kessler et al., 2007; Williams et al., 2010). Given that recurrence is common across the lifespan (Andrews, 2001), vulnerability to a range of medical outcomes and risk factors is often increased. The co-

Abbreviations: (BSD), Barwon statistical division; (BMI), Body mass index; (BMD), Bone mineral density; (CI), Confidence intervals; (DXA), Dual energy X-ray absorptiometry; (GOS), Geelong Osteoporosis Study; (HR), Hazard ratio; (MDD), Major depressive disorder; (NHANES I), National Health and Nutrition Examination Survey; (OR), Odds ratios; (p-yrs), Person-years; (SCID-I/NP), Structured clinical interview for DSM-IV-TR research version, non-patient edition

* Corresponding author.
E-mail addresses: lanaw@barwonhealth.org.au (L. Williams), juliep@barwonhealth.org.au (J. Pasco), henryjj@unimelb.edu.au (H. Jackson), litzak@unimelb.edu.au (L. Kiropoulos), amandh@barwonhealth.org.au (A. Stuart), f.jacka@deakin.edu.au (F. Jacka), mikebe@barwonhealth.org.au (M. Berk).

http://dx.doi.org/10.1016/j.jad.2015.11.048
0165-0327/

occurrence of depression and physical illnesses, such as cardiovascular disease, gastro oesophageal reflux disease, asthma, arthritis and cancer is well established (Farmer et al., 2008; Sanna et al., 2013; Scott et al., 2007), with research continually identifying other physical co-morbidities of depression that are underpinned by interconnected biological and behavioural factors.

There is a growing evidence base suggesting that psychiatric illness and the medications used to treat such illnesses modulate bone metabolism (Fernandes et al., 2015; Kishimoto et al., 2012; Williams et al., 2009). Clinical depression, as well as depressive symptoms, anxiety, stress and poorer subjective well-being, have been associated with decreased bone mineral density (BMD) (Cizza et al., 2010; Rauma et al., 2014; Williams et al., 2011); however, whether or not this translates to an increased risk for fracture is uncertain. There is also some evidence from population studies to suggest that self-reported depression is a risk factor for fracture in older women (Forsen et al., 1999; Spangler et al., 2008; Whooley et al., 1999) and possibly in younger women and men (Ahmed et al,. 2006; Mussolino, 2005; Sogaard et al., 2005). A recent meta-analysis of these studies found substantive effect sizes (17% increase risk when outcomes are represented as hazard ratios and 52% increase risk when outcomes are represented as risk ratios) (Wu et al., 2010). However, there is the possibility that observed relationships may have only existed due to a failure to take into account the use of medications known to affect bone and other known risk factors, and it is the case that underlying mechanisms explaining the association between depression and fracture still need to be elucidated.

Overall, this body of research complements the plethora of data suggesting that depression is a common outcome of fracture (Chang et al., 2014; Holmes and House, 2000; Williams et al., 2014), especially among the elderly following hip fracture; this indicates that a bi-directional relationship may exist. Fragility fractures are an escalating public health problem throughout the world, with the estimated number being in excess of 9.0 million and the greatest proportion occurring in women (61.0%) (Johnell and Kanis, 2006). Given that women also have an elevated lifetime risk for depression (Eaton et al., 2007), the relationship between poor mental health and bone is of particular significance. As such, we sought to examine the role of depression as a risk factor for incident fracture, in women spanning the full adult age spectrum. We also aimed to examine the role of demographic, clinical, lifestyle and other heath parameters in accounting for any observed associations.

2. Methods

2.1. Participants

This study examined data collected from women participating in the Geelong Osteoporosis Study (GOS); a large, ongoing, population-based study located in south-eastern Australia (Pasco et al., 2012). Originally, 1494 women (response 77.1%) were randomly recruited between 1993 and 1997 from the Australian Commonwealth electoral rolls for the region known as the Barwon Statistical Division (BSD) and have since been prospectively followed for over a decade. A listing on the electoral roll fulfilled the inclusion criterion for the GOS. Death, inability to provide informed consent and contact failure formed the basis for exclusion. Further details of the study have been published elsewhere (Pasco et al., 2012). Between 2004 and 2008, 881 of the original sample returned for a 10-year follow-up assessment (participation rate for eligible women was 82.1%) and an additional sample of 246 women aged 20–29 years was recruited (participation 70.9%) during this time, allowing for continuing investigation of the full adult age range (Williams et al., 2010). Of the 1127 women who participated in the GOS during 2004–2008, participants for whom psychiatric data were not available were excluded ($n=32$), resulting in a sample of 1095 women aged 20–93 years eligible for this analysis. The Human Research Ethics Committees at Barwon Health, Deakin University and The University of Melbourne approved the study. All participants provided informed, written consent.

2.2. Study designs

2.2.1. Nested case-control

Cases (with fracture) and controls (fracture free) were drawn from the 1095 women who underwent psychiatric assessment at the 10 year follow up. There were 181 cases and 914 controls. Participants were classified as having been exposed to depression if they had experienced depression prior to fracture. Two cases were excluded because it was unclear whether or not depression preceded fracture. Thus, 179 fracture cases and 914 controls were eligible for analysis in the nested case-control study. Exposure data for the cases pertained to the assessment closest to date of fracture; for controls, 10-year follow up data were used.

2.2.2. Retrospective cohort

Over a decade of longitudinal data were available for 858 of the 1095 women who underwent a psychiatric assessment. Participants were classified as having a history of depression if they had experienced an episode prior to or at the time of their baseline appointment ($n=165$), otherwise they were classified as depression-free ($n=693$), then were followed until fracture occurred or until the end of the follow up period. Exposure data for all the participants were the values measured at baseline.

2.3. Data

Study participants who sustained post-baseline incident, clinical fractures during the study period were identified from radiological reports from medical imaging practices servicing the region. This method of fracture ascertainment has been previously validated by comparing hip fracture rates obtained from hospital discharge (ICD-9 codes 820.0-820.9), with rates obtained from radiological reports in the study region (Pasco et al., 1999).

The Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Non-patient edition (SCID-I/NP) was conducted at the 10-year follow-up (First et al., 2002). The use of this tool enabled the identification of those who had ever experienced depression, including major depressive disorder (MDD), minor depression, bipolar disorder, dysthymia, mood disorder due to a general medical condition and/or substance induced mood disorders, as well as age of onset. Participants were classified as having a lifetime history of depression if past or current symptoms met the lifetime and/or current diagnostic criteria for any of the aforementioned DSM-IV depressive disorders. All interviews were conducted by personnel with post graduate qualifications in psychology, who were trained using live and videotaped interviews under the supervision of a psychiatrist.

Data regarding demographic, clinical, lifestyle and other heath parameters were collected at baseline and subsequent follow up assessments (Pasco et al. 2012). Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, and body mass index (BMI) calculated as weight/height^2 (kg/m^2). Education (highest level completed) was self-reported and grouped as primary school, part secondary school, completed secondary school and post-secondary school. Current cigarette smoking was self-reported. Habitual physical activity level was classified as active if vigorous or light exercise was performed regularly; otherwise participants were classified as sedentary. Medication use was classified as