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Research paper

Risk of incident cardiovascular events amongst individuals with anxiety and depression: A prospective cohort study in the east London primary care database

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ABSTRACT

Background: It is unknown how risk of myocardial infarction and stroke differ for patients with and without anxiety or depression, and whether this risk can be explained by demographics, medication use, cardiovascular risk factors. The aim of this study is to quantify differences in risk of non-fatal MI or stroke among patients with anxiety or depression.

Methods: Prospective cohort study examining risk of incident MI and stroke between March 2005 and March 2015 for 524,952 patients aged 30 and over from the east London primary care database for patients with anxiety or depression.

Results: Amongst 21,811 individuals with depression at baseline, 1.2% had MI and 0.4% had stroke. Of 22,128 individuals with anxiety at baseline, 1.1% had MI and 0.3% had stroke. Depression was independently associated with both MI and stroke, whereas anxiety was associated with MI only before adjustment for cardiovascular risk factors. Antidepressant use increased risk for MI but not stroke. Mean age at first MI was lower in those with anxiety, while mean age at first stroke was lower in those with depression.

Limitations: The study was limited to patients currently registered in the database and thus we did not have any patients that died during the course of follow-up.

Conclusions: Patients with depression have increased risk of cardiovascular events. The finding of no increased cardiovascular risk in those with anxiety after adjusting for cardiovascular risk factors is of clinical importance and highlights that the adequate control of traditional risk factors is the cornerstone of cardiovascular disease prevention. Targeting management of classical cardiovascular risk factors and evaluating the risks of antidepressant prescribing should be prioritized.

1. Introduction

The 2010 Global Burden of Disease has identified anxiety and depression as the most prevalent mental health conditions worldwide, contributing significantly to overall global disease burden and years lived with disability. (Ferrari et al., 2013; World Federation for Mental Health, 2012). In the UK, anxiety and depressive disorders affect approximately 15% of the adult population (LSE and The Centre for Economic Performance, 2012).

Patients with psychiatric conditions have an increased risk of cardiovascular disease (CVD), including myocardial infarction (MI) and stroke (De Schutter et al., 2011; Elderon and Whooley, 2013; Hare et al., 2014; Osborn et al., 2007; Tully et al., 2015). Both anxiety and depression are common mental disorders, with high prevalence in the general population. While the relationship between severe mental illness and cardiovascular disease has been widely explored, there is a paucity of evidence around the relationship between anxiety and incident cardiovascular events (Bowen et al., 2000; Chou et al., 2012; Davies and Allgulander, 2013; Lambiase et al., 2014; Osborn et al., 2007). The burden of CVD and CVD risk factors is increasing rapidly amongst young, working-age adults (Lavie and Milani, 2006; Moran et al., 2014; Poisson et al., 2014). Since cardiovascular disease is the leading

Abbreviations: Myocardial Infarction, MI; Cardiovascular Disease, CVD; Egton Medical Information Systems, EMIS; United Kingdom, UK; National Health Service, NHS

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cause of loss of in disability adjusted life-years (DALYs) worldwide, this represents the greatest loss for families and national economies. Accordingly, it is important to know whether individuals with anxiety or depressive disorders are at risk of earlier onset of MI and stroke compared to individuals without these conditions (Murray et al., 2012).

This study aims firstly to quantify the excess risk of non-fatal stroke or MI associated with diagnosed anxiety and depressive disorders and antidepressant use in an unselected primary care population, and secondly, to test the hypothesis that cardiovascular (CV) events may have an earlier presentation in patients with anxiety and depressive disorders compared to those without. We hypothesize that risk will be increased in patients with these psychiatric conditions compared to those without and that the increased risk can be further explained by sociodemographic and cardiovascular risk factors. This work will help to identify groups at higher risk for cardiovascular outcomes and potential areas for focusing preventive interventions.

2. Methods

A prospective cohort study using patients contributing to the east London primary care database held by the Clinical Effectiveness Group at Queen Mary, University of London was undertaken. The database comprises the electronic health records of approximately 950,000 individuals registered with 141 general practices across the east London boroughs of Tower Hamlets, Newham, and City & Hackney, all of which use Egton Medical Information Systems (EMIS) web as their clinical computer system. The population of east London is one of the most deprived in the UK and has high levels of ethnic diversity, with over 50% of the resident population of non-white ethnicity (Hull et al., 2014; Tower Hamlets Council, 2013).

The study sample included all adult patients aged 30 and over in March 2015 who were free from MI or stroke at the start of the study period in March 2005. Anonymised demographic, clinical and prescribing data were extracted for all individuals meeting the study entry criteria.

Read codes are the standard clinical terminology system used in general practice across the UK (Chisholm, 1990). Diagnostic Read codes for anxiety and depressive disorders were selected by the authors, who comprised general practitioners, clinical psychiatrists, and epidemiologists. Diagnoses of diabetes mellitus, before March 2005, and MI and stroke, between March 2005 and March 2015, were defined according the quality and outcomes framework Read code specifications (NHS Employers, 2014). Individuals without a diagnostic Read code for each condition were considered to be free from the disease of interest.

Self-reported ethnicity was recorded at the practice during registration or routine consultation. Ethnic categories were based on the UK census and for this study were condensed into four categories: White (British, Irish, other white), Black (Black African, Black Caribbean, other Black) South Asian (Bangladeshi, Pakistani, Indian, other South Asian) and any other ethnic group. Patients with mixed ethnicity were grouped with their parent ethnic minority. Individuals with missing ethnicity information were grouped into an “unknown” category (results not shown). Deprivation was classified using the Townsend deprivation score, a census-based index of material deprivation calculated by the combination of four variables from the 2001 census: car ownership, overcrowded households, households not owner occupied, and unemployment (Townsend, 1987).

Systolic and diastolic blood pressure, total cholesterol level, tobacco consumption and antidepressant use closest to and before March 2005 were extracted to identify baseline values at study entry. Hypertension was identified using the clinical Read code for hypertensive disease. Obesity was defined as having a body mass index of 30 kg/m^2 or above; Hyperlipidemia was defined as having a total cholesterol value of greater than 5 mmol/L; Tobacco consumption was dichotomized into current smoker vs. not current smoker. Individuals without Read codes for tobacco consumption were considered to be non-current smokers.

Individuals entered the study in March 2005 and were followed up until they experienced an incident non-fatal event of MI or stroke during the ten years of follow-up. Follow-up time was censored at the end of the study period in March 2015 if they did not experience the outcome of interest.

Cox proportional-hazards regression analyses were used to firstly compare the risk of incident MI and stroke in patients with and without depression at baseline and secondly to compare the risk of incident MI and stroke in patient with and without anxiety at baseline. Three regression models were built; The first adjusted for age, gender, and ethnic group, the second additionally adjusted for diabetes, hypertension, hyperlipidemia, and smoking antidepressant prescribing at baseline, obesity, and Townsend deprivation score, and the third additionally adjusted for the presence of co-morbid anxiety or depression. Linear regression models adjusting for gender and ethnicity were used to compare the age at the time of MI and stroke of patients with and without anxiety and depression. All models accounted for clustering of patients within general practices using a shared frailty term for practice, which reflects the non-independence of patients attending the same health care provider (Allison, 2014).

3. Results

A total of 524,952 adults aged 30 and over registered with the east London primary care database in March 2015 were identified. The characteristics of the study sample are presented in Table 1. From the total population, 21,811 individuals had an existing diagnosis of depression at baseline (4.1%) while 22,128 had an existing diagnosis of anxiety (4.2%). Compared to individuals free from psychiatric disorders, individuals with depression or anxiety were older, had a higher proportion of females and a smaller proportion of individuals from ethnic minority groups ($p < 0.001$). Prevalence of all clinical co-morbidities at baseline was higher in those with anxiety or depressive disorders, most notably hyperlipidemia was present in 60% of those with anxiety or depressive disorders and 40% of those without anxiety or depressive disorders ($p < 0.001$). Similarly, 40% of those with anxiety or depressive disorders were identified as current smokers, compared to 27% of the general population. Incidence of both MI and stroke was doubled for those with anxiety or depressive disorders compared to those without ($p < 0.001$).

As all included patients were necessarily registered in the database in March 2015, all were able to contribute a full ten years of follow-up time to the study. Cumulative-hazard curves illustrating the increased cumulative incidence of MI and Stroke in individuals with anxiety or depression compared to those without are shown in Fig. 1.

Cox proportional hazards models for the risk of incident non-fatal MI and stroke for patients with and without anxiety are presented in Table 2. After adjusting for age, gender, and ethnic group (model 1), the risk of MI was raised by 33% in those with anxiety relative to those without (HR 1.33, CI95% 1.17, 1.52). After adjustment for baseline risk factors and deprivation in model 2, the association between anxiety and MI was attenuated, and association did not reach the level of statistical significance (HR 1.10, CI95% 0.96, 1.26). This lack of association remained after, adjustment for co-morbid depression in model 3 (HR 1.08, CI95% 0.94,