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Psychological distress and risk of peripheral vascular disease, abdominal aortic aneurysm, and heart failure: Pooling of sixteen cohort studies

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ABSTRACT

Objectives: Examine the little-tested relation of psychological distress with peripheral vascular disease, abdominal aortic aneurysm, and heart failure.
Methods: Pooling of raw data from 166,631 male and female participants in 16 UK-based cohort studies. Psychological distress was measured using the 12-item General Health Questionnaire. Peripheral vascular disease, abdominal aortic aneurysm, and heart failure events were based on death register linkage.
Results: During a mean follow-up 9.5 years there were 17,368 deaths of which 8625 were cardiovascular disease-related. Relative to the asymptomatic group (0 score), the highly distressed group (score 7–12) experienced an elevated risk of peripheral vascular disease (adjusted hazard ratio; 95% confidence interval: 3.39; 1.97, 5.82) and heart failure (1.76; 1.37, 2.26). Psychological distress was weakly related to the risk of death from abdominal aortic aneurysm. As anticipated, distress was associated with cardiovascular disease, coronary heart disease, and all strokes combined.
Conclusions: In the present study, we provide new evidence of mental health-related cardiovascular disease presentations.

1. Introduction

Meta-analyses of a series of population-based studies demonstrate that psychological distress (depression and anxiety) is related to both coronary heart disease [1] and stroke [2], such that the presence of distress apparently confers as much as twice the risk of these conditions. These associations do not appear to be substantially confounded by conventional risk factors such as socioeconomic deprivation, cigarette smoking, and raised blood pressure. While this evidence base is expanding, little is understood about the link, if any, between psychological distress and other cardiovascular disease presentations. While there has been one study examining the link between depression and heart failure in the general population [3], we are unaware of any investigations linking psychological distress or depression with peripheral vascular disease or abdominal aortic aneurysm. The findings from patient-based cohorts [4,5], although providing important prognostic observations, are not necessarily transportable to people who are disease-free at study induction.

Accordingly, in a large scale pooling of data across 16 cohort studies, we tested the link between psychological distress and a range of cardiovascular disease phenotypes. For the purposes of comparing the magnitude of effects across other cardiovascular disease phenotypes, we also include total cardiovascular disease, coronary heart disease, and stroke as endpoints of interest.

2. Material and methods

Participants were taken from the Health Survey for England [6] and Scottish Health Survey [7], a series of geographically-representative health examinations of people living in private households. Between 1994 and 2008, 16 independent, cross-sectional studies with identical methodologies were conducted

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either on an annual (Health Survey for England; $N = 13$) or intermittent (Scottish Health Surveys; $N = 3$) basis. Ethical approval was obtained from the London Research Ethics Council.

2.1. Measurement of psychological distress

During a household visit, nurse interviewers collected information using computer-assisted personal interviewing modules. Psychological distress was measured using the 12-item version of the General Health Questionnaire (GHQ-12) [8], a widely utilised inventory in population-based studies. Validated against standardised psychiatric interviews [9,10], this unidimensional scale of distress consists of items capturing symptoms of depression, anxiety, social dysfunction, and loss of confidence. We applied existing thresholds to the GHQ-12 data to create categories of clinical relevance: asymptomatic (score 0), subclinically symptomatic (1–3), symptomatic (4-6), and highly symptomatic (7–12) [11].

2.2. Measurement of collateral data

A range of covariate data were collected using standard protocols [6,7]: current occupational social class (professional, managerial or technical, skilled non-manual, skilled manual, partly skilled, and unskilled), age upon leaving full-time education, body mass index (based on directly ascertained height[m] and weight [kg]), smoking status (not a current smoker; or <5, 5–10, 10–15, 15–20, and >20 cigarettes per day), alcohol consumption (frequency of drinking), and the presence of a long-standing illness (yes/no). Diabetes was denoted by one or more of the following: self-report of doctor-diagnosed diabetes, self-report of diabetes as a long-standing illness, hospitalisation for diabetes, or HbA1c $\geq$ 6.5. Hypertension was denoted by one or more of the following: self-report of doctor-diagnosed hypertension, self-report of hypertension as a long-standing illness, and measured systolic blood pressure of $\geq$ 140 mm Hg or a diastolic blood pressure of 90 mm Hg.

2.3. Mortality ascertainment

Consenting study members (166,631 [88.2%]) were linked to UK National Health Service mortality register which provided data on principal and contributing causes of death. In preliminary survival analyses, the use of a narrow, mutually exclusive case definition (i.e., underlying cause of death only) or a broad, non-mutually exclusive (i.e., any mention of the condition on the death certificate) resulted in the same conclusions about the relation of distress with each of the six outcomes under study. We therefore used the latter as this provided the highest number of events and therefore the greatest statistical power. Cardiovascular disease was denoted by any mention of the following codes on death certificates: 390–459 (ICD-9) or I00–I99 (ICD-10). The corresponding codes were 410–414 or I20–I25 for ischaemic heart disease; 430–438 or I60–I69 for stroke; 443 or I73 for peripheral vascular disease; 428 or I50 for heart failure; and 441.3/441.4 or I71.3/I71.4 for abdominal aortic aneurysm.

2.4. Statistical analyses

We used raw data from people aged 16 years and over from all study years, the only exceptions being the surveys years 1996 and 2007 when psychological distress was not measured. In preliminary analyses, we determine that the proportional hazards assumption had not been violated by inspecting the survival curves according to distress categories. Accordingly, we used Cox proportional hazards models [12] to compute study-specific hazard ratios with accompanying 95% confidence intervals for the association of distress score with each cardiovascular disease outcome. We used calendar time (months) as the time scale with study members censored at the date of death or the end of follow-up (15 February 2011) – whichever came first. Hazard ratios were adjusted minimally (age and sex) then maximally (age, sex, occupational social class, smoking status, frequency of alcohol consumption, body mass index, diabetes, hypertension, and self-reported longstanding illness). The I^2 statistic, which quantifies the proportion of the total variation in effect estimates due to between-studies variation, ranged between 0% and 66.8% depending on the mortality outcome used in the analysis. Owing to this heterogeneity, we pooled the study-specific effect estimates and their standard errors in random effects meta-analyses.

3. Results

From an initial sample of 199,504 participants, 32,873 did not consent to record linkage, and/or were missing data on consent, and/or were missing a distress score, giving a maximum analytic sample of 166,631 (55% female, mean age 46.6 years, SD = 18.4, range = 16–102). The characteristics of study members excluded from analyses were similar to those in the included group.

A total of 1.58 million person-years at risk (mean (SD) follow-up of 9.5 (4.3) years) gave rise to 17,368 deaths, 8625 of which were cardiovascular disease-related. The latter comprised the occasionally overlapping causes of ischaemic heart disease ($N = 4519$), stroke (2225), heart failure (1948), peripheral vascular disease (247), and abdominal aortic aneurysm (220). Relative to the group without any such symptoms, the most distressed study members experienced around twice the rate of death due to heart failure (Table 1, Fig. 1). There was almost a four-fold increase in the risk of peripheral vascular disease when the same categories were compared. Notably, both these relationships appeared to occur in a stepwise manner ($p < 0.001$), such that the greater the degree of reported distress, the higher the risk of death ascribed to these cardiovascular disease endpoints. The magnitude of the relationships was partially diminished by statistical control for potential confounding factors. There was a suggestion that abdominal aortic aneurysm was also positively related to psychological distress score, however, the magnitude of this relationship was lower and statistical significance at conventional levels was not apparent; this elevated risk was lost after multiple adjustment. As anticipated, high psychological distress was positively related to mortality ascribed to all cardiovascular disease, coronary heart disease, and stroke, such that around a doubling of death rate was evident in the most distressed individuals relative to those who were symptom-free. Fig. 2, which depicts the association between one standard deviation increase (disadvantage) in psychological distress and mortality from a range of cardiovascular disease phenotypes, provides an at-a-glance summary of our results.

In order to take into account reverse causality – the notion the baseline somatic illness, whether measured or hidden, might be generating the positive relation between distress and the various CVD phenotypes in the present analyses – we carried out some sensitivity analyses. First, we additionally adjusted for self-reported doctor-diagnosed cardiovascular disease (recorded in 11 cohort studies: $N = 82,977$, 3656 CVD deaths). Second, we dropped deaths arising in the first 2 years of follow-up (left censoring: $N = 108,862$, 4764 CVD deaths), reasoning that these would largely be due to baseline illness. In each of these sets of analyses the resulting effects estimates were essentially unchanged.