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Comorbidity and its relevance on general hospital based mortality in major depressive disorder: A naturalistic 12-year follow-up in general hospital admissions

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ABSTRACT

Major depressive disorder (MDD) is associated with physical comorbidity, but the risk factors of general hospital-based mortality are unclear. Consequently, we investigated whether the burden of comorbidity and its relevance on in-hospital death differs between patients with and without MDD in a 12-year follow-up in general hospital admissions. During 1 January 2000 and 30 June 2012, 9604 MDD patients were admitted to three General Manchester Hospitals. All comorbidities with a prevalence ≥1% were compared with those of 96,040 age-gender matched hospital controls. Risk factors of in-hospital death were identified using multivariate logistic regression analyses. Crude hospital-based mortality rates within the period under observation were 997/9604 (10.4%) in MDD patients and 8495/96,040 (8.8%) in controls. MDD patients compared to controls had a substantial higher burden of comorbidity. The highest comorbidities included hypertension, asthma, and anxiety disorders. Subsequently, twenty-six other diseases were disproportionally increased, many of them linked to chronic lung diseases and to diabetes. In deceased MDD patients, chronic obstructive pulmonary disease and type-2 diabetes mellitus were the most common comorbidities, contributing to 18.6% and 17.1% of deaths. Furthermore, fifteen physical diseases contributed to in-hospital death in the MDD population. However, there were no significant differences in their impact on mortality compared to controls in multivariate logistic regression analyses. Thus in one of the largest samples of MDD patients in general hospitals, MDD patients have a substantial higher burden of comorbidity compared to controls, but they succumb to the same physical diseases as their age-gender matched peers without MDD.

1. Introduction

Depressive disorders are characterized by sad, empty, or irritable mood, linked to cognitive and somatic symptoms that affect the individual's capacity to function. Life-time prevalence estimates of major depressive disorder (MDD), the classic condition of clinically relevant depression, vary across countries (Kessler and Bromer, 2013). The WHO predicted MDD to be the 2nd leading cause for "years of healthy life loss" by 2020 (WHO, 2004). Its complexity in treatment is partly caused by higher mental and physical morbidity compared to the general population as well as of poor adherence to medical treatment and self care for diabetes and cardiovascular disease (CVD), modifiable health risk behaviors, excessive alcohol consumption, and cognitive impairment (Hirschfeld, 2001; Sato and Yeh, 2013; Gallo et al., 2013). The likelihood of having MDD via a screening instrument increases with each additional chronic physical disease in the general population (Egede, 2007). Especially physical conditions like chronic lung diseases and type-2 diabetes mellitus (T2DM) confer increased risks of long-term organic lesions that can worsen MD episodes and increase the non-suicide related mortality risk (Black et al., 2003; Park et al., 2013; Atlantis et al., 2013; Holt et al., 2013; Van Dooren et al., 2013). Diabetic depressed individuals have a 36% increased risk of microvascular complications such as end-stage renal disease and a 25% higher risk of macrovascular complications with a widespread impact on pneumonia and CVD related mortality compared to diabetic

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individuals without depression (Lin et al., 2010). Knowledge of the specific diseases or disease cluster that are risk factors for hospital-based mortality in MDD patients is of clinical relevance to intensify efforts that aim at the long term effect of depression care management and reduction of avoidable mortality.

1.1. Aim of study

The aims of this study are to evaluate in a hospital-based sample with up to 12.5-year follow-up in general hospital admissions if the prevalences of specific diseases and their impact on in-hospital death differ between MDD patients and hospital controls. Four specific hypotheses were tested: (1) MDD patients have a more severe course of disease during the observation period than controls: MDD patients are more often than controls admitted as emergencies at their initial hospitalization; MDD patients compared to controls have an extended length of hospital stay at their initial hospitalization, have a higher total number of hospital admissions over 12.5 years, and have a shorter survival after their initial hospitalization. (2) The prevalences of mental and physical comorbidities are increased in MDD patients compared to controls. (3) Some, but not all comorbidities contribute to the prediction of hospital-based mortality in MDD patients and controls. (4) The impact of particular physical comorbidities on in-hospital death is higher in MDD patients than in controls.

2. Methods

2.1. Study population

The initial study population consisted of all adults ($n = 369{,}488$) that were admitted for hospital treatment in three General Manchester Hospitals for at least 24 h or elective day patient care between January 1, 2000, and June 30, 2012. For patients with several hospitalizations the first hospitalization was chosen as initial admission. The target population consisted of all 9604 depressed patients (2.6%) that were consecutively hospitalized during the observation period. The inclusion criteria were diagnosis of MDD, age 18 years or above and hospital care for at least 24 h. The exclusion criteria were outpatient care or partial hospitalization for less than one day. The sub-population of deceased patients included all 997 MDD patients that had died in any of the three hospitals during the observation period. The sub-population of survivors included those 8607 MDD patients that had not died in any of the three hospitals during the observation period. A control population was identified to equalize age and gender distributions by matching each depressed patient at initial admission with ten randomly selected hospital controls of the same age (+/− 1 year) and gender ($n = 96{,}040$, Table 1), using SPSS version 20.0. The sub-population of deceased controls included the 8495 subjects that had died in any of the three hospitals during the observation period. The sub-population of survivors included the 87,545 controls that had not died in any of the three hospitals during the observation period.

2.2. Sampling strategy and definitions of clinical course parameters

Anonymous information of discharge diagnoses were received from the computerized hospital activity analysis register. Vital status on June 30, 2012 was determined by record linkage to the National Health Tracing Services. The general hospital mortality data were crosschecked against the hospital case records and patient information system. For each patient, follow-up was commenced at the beginning of the initial hospitalization continuing until June 30, 2012. A distinction was drawn between an admission to general hospital treatment as an emergency case or other at initial hospitalization within the observation period, i.e. elective admission for more than 24 h inpatient care and elective day admission. The length of hospital stay was defined as the number of inpatient days at initial hospitalization during the observation period. Readmissions occurring within one day after discharge were counted to the corresponding hospitalization. The number of hospital stays was defined as the total number of hospitalizations within the observation period. The hospitalization during which a patient died was counted as last hospitalization. Length of survival was defined as days from initial hospitalization until the day of in-hospital death in the subgroups of deceased patients respectively until the end of the observation period in the subgroups of surviving patients. Confidentiality of information was maintained in accordance with the UK Data Protection Act. The patient information was anonymous and non-identifiable when received by the authors. Local research approval was obtained.

2.3. Recording of diagnoses

MDD was diagnosed according to the ICD-10 categories F32.x and F33.x by senior physicians responsible for the formulation of

Table 1
Sociodemographic and clinical characteristics of the study population subdivided into MDD population and control population. Stars indicate in the first column group comparisons between all MDD patients and all controls, in the second column group comparisons (1) between deceased MDD patients and MDD survivors and (2) between deceased MDD patients and deceased controls, in the fifth column group comparisons between deceased controls and control survivors. $^{***}p \leq 0.001$, $^{**}p \leq 0.01$, $^{*}p \leq 0.05$.

Characteristics	Study population					
	MDD population			Control population		
	All	Deceased	Survivors	All	Deceased	Survivors
Sociodemographic description						
Number, *N* (%)	9604 (100)	997 (10.4)	8607 (89.6)	96,040 (100)	8495 (8.8)	87,545 (91.2)
Mean age, years ± SD	47.6 ± 0.2	67.3 ± 0.5 (1)***	45.3 ± 0.2	47.6 ± 0.1	68.3 ± 0.2***	45.6 ± 0.1
Female gender, N (%)	5775 (60.1)	567 (56.9) (1)*	5208 (60.5)	57,750 (60.1)	4839 (57.0)***	5,2911 (60.4)
Marital status, married, N (%)	2527 (26.3)***	278 (27.9) (1)*** (2)***	2249 (26.1)	36,718 (38.2)	3012 (35.5)***	33,706 (38.5)
Caucasian ethnicity, N (%)	7668 (79.8)***	834 (83.7) (1)***	6834 (79.4)	68,340 (71.2)	6967 (82.0)***	61,373 (70.1)
South Asian ethnicity, N (%)	555 (5.8)***	31 (3.1) (1)***	524 (6.1)	7755 (8.1)	259 (3.0)***	7496 (8.6)
Afro-Caribbean ethnicity, N (%)	295 (3.1)***	19 (1.9) (1)***	276 (3.2)	4824 (5.0)	225 (2.6)***	4599 (5.3)
Unknown ethnicity, N (%)	1086 (11.3)	113 (11.3)(2)**	969 (11.2)	15,121 (15.7)	1044 (12.3%)**	14,077 (16.1)
Clinical description						
Initial admission (emergency), N (%)	6058 (63.1)***	665 (66.7) (1)* (2)***	5393 (62.7)	43,020 (44.8)	4212 (49.6)***	38,808 (44.3)
Length of hospital stay at initial hospitalization during 2000–2012, days ± SD	6.2 ± 0.2***	17.8 ± 1.2 (1)*** (2)***	4.8 ± 0.2	3.1 ± 0.0	9.7 ± 0.2***	2.5 ± 0.0
Mean number of admissions, N	9.0***	11.0 (1)*** (2)***	8.7	6.3	8.7***	6.1
Average length of survival, days ± SD	1876 ± 13.2***	1178 ± 35.3 (1)*** (2)***	1957 ± 13.9	2176 ± 4.5	1030 ± 11.1***	2287 ± 4.6