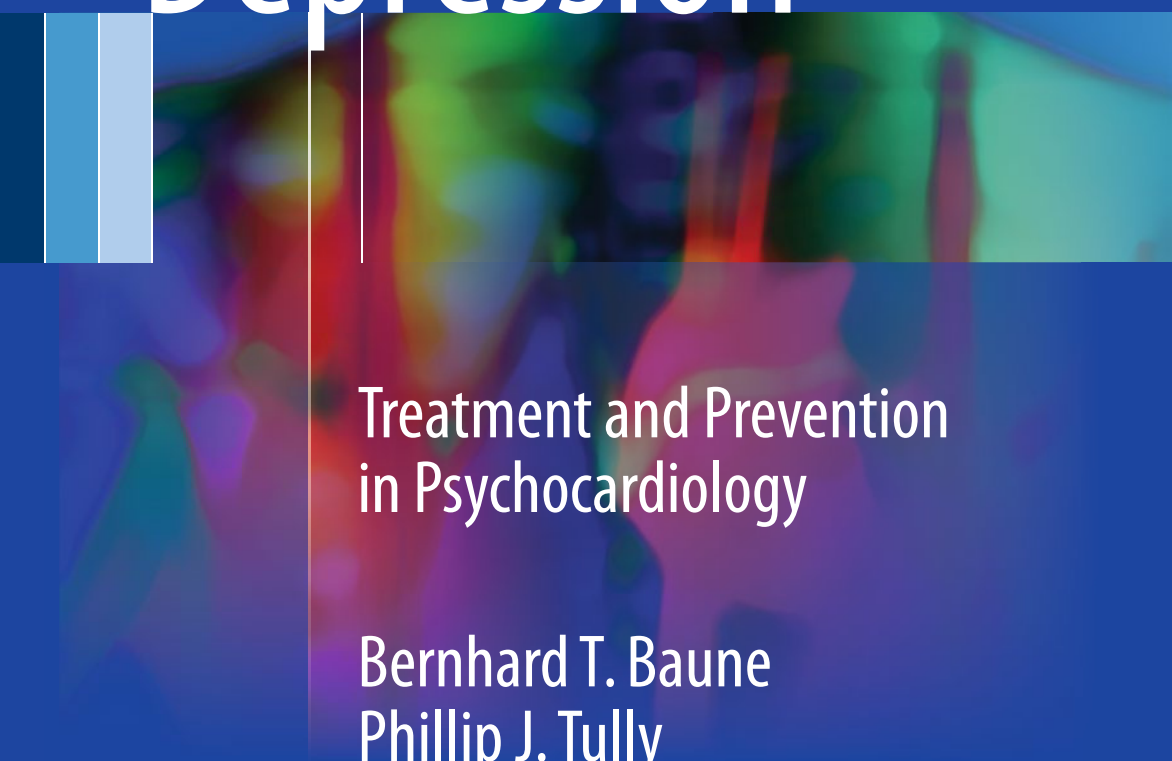
Cardiovascular Diseases and Depression



Treatment and Prevention in Psychocardiology

Bernhard T. Baune
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Editors

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Introduction

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Bernhard T. Baune and Phillip J. Tully

Content

The association between cardiovascular diseases (CVDs) and depression has long been recognized. Reports as early as 1937 suggested that institutionalized psychiatric patients had an eight times higher mortality rate than the general population and "diseases of the heart" accounting for almost 40 % of these deaths (Malzberg 1937).

In the following decades, the comorbidity of depression and CVDs has been rigorously investigated in many cross-sectional and longitudinal studies pointing to an important clinical and societal burden. Current literature suggests that the relationship between CVD and depression is bidirectional. Numerous clinical and epidemiological studies investigating the association between depression and cardiovascular disease have suggested that depression increases the risk of subsequent CVD 1.5-fold on average (Grippo and Johnson 2002; Thombs et al. 2006; Lippi et al. 2009; Nicholson et al. 2006) and that patients with coronary artery disease and depression have a two- to threefold increased risk of future nonfatal and fatal cardiac events compared to those cardiac patients without depression (Goldston and Baillie 2008; Kooy et al. 2007; Rudisch and Charles 2003; Frasure-Smith and

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Lesperance 2010). Moreover, depression has been found to be an independent predictor of a poorer health outcome after an ischemic event (Nicholson et al. 2006; Barth et al. 2004; Meijer et al. 2011).

While the etiology and pathophysiology of the relationship between depression and CVD have been heavily related to various biological mechanisms relating to the hypothalamic-pituitary-adrenal (HPA) axis, pro-inflammatory cytokines, increased sympathetic tone, platelet dysfunction, changes in arterial vessel elasticity, and endothelial function, other reports support important contributions of clinical characteristics of depression (e.g., severity of depression, number of episodes, duration of depression, depression subtype) and sociodemographic factors (marital status, education, and income) to the bidirectional relationship between depression and cardiovascular disease. Whether screening for and treatment of depression are effective in reducing the clinical comorbidity and in improving health outcomes in affected patients, e.g., by using antidepressants, psychotherapy, or anti-inflammatories, became of increasing interest in recent years.

In this most comprehensive book on the topic of cardiovascular disease and depression, expert authors from around the world focus on novel aspects of the clinical and biological etiology and pathophysiology of the comorbidity by extending into new frontiers such as the role of anxiety, neuropsychological and cognitive impairment, emotion processing, and stress and into the underlying neurobiology of the cardiovascular disease and depression comorbidity. To extend the more established knowledge on biological mechanisms of the cardiovascular and depression comorbidity as reviewed here, the book will go beyond in order to review neuroimaging findings, metabolic-inflammation aspects, and the possibility of a genetic overlap between the two conditions. The second main focus of the book is on the topics of treatment and prevention. State-of-the art psychological (e.g., behavioral activation, cognitive training, mobile-app technologies) and pharmacological (e.g., antidepressants, anti-inflammatory agents) as well as complementary alternative and integrative medicine approaches carry promise to improve the short-term and long-term outcomes of this comorbid condition. Finally, the critical topics of screening and prevention will be given extensive consideration.

The broad concept and the comprehensive topics of this book make it a unique reference for the interested student, clinician, and researcher across medical, psychological, public and allied health, and complementary medicine disciplines to better understand the foundations and to clinically improve the conditions of people with cardiovascular and depression comorbidity.

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Epidemiology of Cardiovascular Disease and Depression

2

Tracy Air, Phillip J. Tully, Shaun Sweeney, and John Beltrame

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Abstract

Depression is common in cardiac patients, with 20 % of patients meeting the criteria for major depressive disorder or experiencing depressive symptoms. The relationship between cardiovascular diseases is likely to be bidirectional: people with depression are more likely to develop cardiovascular disease, while patients

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with cardiovascular disease and co-morbid depression have worse cardiac outcomes than those who are not depressed. The influence is not only restricted to cardiovascular outcomes; however, the impact upon psychosocial outcomes such as quality of life and social participation can be just as deleterious. This relationship can also be moderated by socio-demographic and psychosocial risk factors, including gender, age, previous history of depression, social isolation and functional impairment. This chapter will focus on the epidemiology and relationship between depression and cardiovascular disease, the effects on psychiatric and cardiac outcomes and the known risk factors.

2.1 Introduction

Cardiovascular disease (CVD) and depression are significant public health concerns. Both have significant impact with respect to key health system indicators, such as service utilisation and medical costs (Baumeister et al. 2015). More importantly, they also have a profound impact on the quality of life of afflicted individuals.

2.1.1 Cardiovascular Disease

CVD is a collective term for diseases of the heart and blood vessels. The term can refer to a group of disorders, such as coronary heart disease, heart failure, peripheral vascular disease and stroke. CVD is the leading cause of death worldwide, causing more than 17 million deaths per year in 2013, up from 12 million in 1990 (Naghavi et al. 2015). CVD can also result in severe disability. One measure of overall disease burden, disability-adjusted life years (DALYs), combines both mortality and morbidity into a single measurement. Results from the Global Burden of Disease Study report that between 2005 and 2013, DALYs for CVD increased by 6.7 % (Murray et al. 2015). The 2010 Global Burden of Disease Survey estimated that depression accounted for 8.2 % of global years lived with disability (YLD) and 2.5 % of global DALYs (Ferrari et al. 2013). By 2013, ischemic heart disease and cerebrovascular disease were two of the five leading causes of disease burden (Murray et al. 2015).

2.1.2 Depression

Depression (also known as major depressive disorder (MDD), clinical depression or unipolar depression) is a common psychiatric disorder, characterised by a persistent low mood that is accompanied by anhedonia, fatigability and low self-esteem. It has been linked to diminished quality of life, medical morbidity and mortality.

2.2 Depression and Cardiovascular Disease as Co-morbidities: Cause and Effect?

Depression commonly afflicts patients with CVD and contributes to poor cardiovascular and psychosocial outcomes. Two major findings have emerged from the literature: firstly, that depression is associated with an increased risk of development of CVD and other vascular disorders such as vascular dementia. Secondly, depression predicts increased morbidity and mortality in patients with CVD, including those with HF, in individuals following MI or who have undergone coronary artery bypass graft (CABG) surgery. Despite this, depression remains underdiagnosed and undertreated in cardiac populations, even with the availability of safe and effective treatments. The effects of CVD and depression are widespread and harmful, impacting quality of life (Djarv et al. 2012; O'Neil et al. 2013), health service utilisation (Egede 2007), medical costs (Sullivan et al. 2002) and day-to-day functioning (Dickson et al. 2012; Mensah and Brown 2007).

2.2.1 Prevalence of Depression in Cardiovascular Disease Patients

Globally, the lifetime prevalence of depression varies widely, ranging from 1.0% in the Czech Republic to 17% in the United States according to the DSM-IV criteria, while the 12-month prevalence can range between 0.3% (Czech Republic) and 10% (United States) (Kessler and Bromet 2013). Prevalence estimates of depression in the general population also vary by sex with estimates between 5–9% for females and 2–3% among males (American Psychiatric Association 2000). Compare these prevalence estimates to those in cardiovascular populations, and it is clear that the latter chronic disease population are disproportionately affected. Specifically, the prevalence of major depression is most widely documented in coronary heart disease with strikingly similar prevalence rates across CVD subtypes. Thombs et al. showed a 20% prevalence in persons with a recent myocardial infarction (Thombs et al. 2006). Other estimates in acute CVD populations are very similar. Between 15 and 20% major depression prevalence is reported in coronary artery bypass graft (CABG) surgery patients though estimates tend to increase when dysthymia is taken into account (Tully and Baker 2012). Also approximately 20% depression prevalence is evident in heart failure patients (Rutledge et al. 2006). Persons receiving implantable cardioverter defibrillator are an exception, and depression estimates vary considerably 11–26% and may be less reliable since fewer studies have adopted structured clinical interviews to diagnose depression (Magyar-Russell et al. 2011). Putting these collective findings in a clinical context, it can be reliably expected that at least one in five persons with CVD will meet the criteria for major depression.

2.2.2 Prevalence of Cardiovascular Disease in Depressed Patients

People with severe mental illness, including depression, have an increased risk of physical illness, especially CVD. For example, Carter et al. (2014) reported that, in a study of 74,734 psychiatric patients admitted to hospital in the Greater Manchester

region between 2001 and 2012, 9.63 % were diagnosed with ischemic heart disease, 6.63 % were diagnosed with atrial fibrillation, 4.6 % had heart failure and 2.31 % reported having an MI. Not surprisingly, similar prevalence rates have been found in samples with major depression. Results from the Medical Outcomes Study (Wells et al. 1989a), in a sample of 11,242 outpatients who either had been diagnosed with depression or reported depressive symptoms, found that 5 % also had current CAD while 4 % currently reported having angina. Other studies have reported a prevalence of 12 % and 5 % of CAD and CHF, respectively, in depressed patients (Lyness et al. 1993), while Diminić-Lisica and colleagues (2010) reported 10.85 % of their depressed sample also had cardiovascular disease. In US adults who reported a diagnosis of depression during their lifetime, the age-standardised prevalence of myocardial infarction, angina and stroke was around 30 %, compared to around 15 % for those who did not (Zhao et al. 2009).

2.2.3 Depression as a CVD Risk Factor

The role of depression in the development of CVD has been examined in numerous studies. In the Baltimore cohort of the Epidemiologic Catchment Area (ECA) Study, patients with a history of dysphoria or depression had 4.5 times the risk of having experienced an acute MI at follow-up when compared to nondepressed patients (Pratt et al. 1996). Rugulies (2002) determined that the risk of developing CVD was approximately 60 % higher in depressed patients, while Wulsin and Singal (2003) reported that MDD was a better predictor for the development of CVD in initially healthy people (Relative risk = 2.69; CI: 1.63–4.43) than depressive symptoms (Relative risk 1.49; CI 1.16–1.92). Furthermore, Rafanelli et al. (2010) reported that patients with dysthymia had a significantly higher risk of developing a cardiac event than patients without dysthymia, while depression has also been found to increase the risk of CVD by 1.5–3 times in otherwise physically healthy individuals (Lett et al. 2004; Xian et al. 2010).

Several population-based studies have also linked MDD in children and young adults to increased risk of premature CVD. A Taiwanese national health insurance study investigated the association of MDD (and other psychiatric disorders) with risk of CVD involving more than one million participants of all age groups including young adults (Huang et al. 2009). The relative risk for CVD among patients less than 20 years old was 2.19 for MDD. Although the prevalence of CVD increased with increasing age, the excessive relative risk for CVD among patients with MDD was greatest among those 20 years old or younger. These results have also been supported by data from meta-analyses. The largest published meta-analysis to date (21 studies N = 124 5,098 participants) indicated that depression was consistently predictive of incident cardiac events in individuals free of CVD (Nicholson et al. 2006), though smoking and exercise were infrequently adjusted for.

Given that depression is associated with major cardiac risk factors, this relationship should be no surprise. For example, numerous cross-sectional and longitudinal studies have found a significant relationship between MDD and smoking (Bakhshaie

et al. 2015; Boden et al. 2010; Grant et al. 2004; Hughes et al. 1986; Kinnunen et al. 2006; Lasser et al. 2000). Hypertension is also more prevalent in depressed patients (Adamis and Ball 2000; Kahl et al. 2012; Nakagawara et al. 1987; Wells et al. 1989b, 1991), and MDD has also been associated with reduced physical activity (Aihara et al. 2011; Biddle and Asare 2011; Gallegos-Carrillo et al. 2013; Lampinen et al. 2000; Overdorf et al. 2016).

2.2.4 Risk Factors for Depression in CVD Patients

Determinants of health associated with the development of depression in CVD patients have been identified and aid the recognition of people at high risk of depression. Numerous predictors of depression in physically healthy cohorts can also be a predictor of the development of depression in patients with CVD. These include female gender, age, previous history of depression, social isolation and functional impairment.

2.2.5 Gender

In recent years researchers have made considerable effort to investigate gender differences in CVD. This research recognises the need to improve our understanding of heart disease in women. As in the general population, depression has also been associated with similar increases in cardiovascular risks in both genders with established CVD (Barefoot et al. 1996). Women with CVD are more likely to experience depression when compared to men (Wiklund et al. 1993; Frasure-Smith et al. 1995; Balog et al. 2003; Vaccarino et al. 2003). It has been contended that this partly explains why women face higher mortality rates after MI (Mallik et al. 2006). Smolderen et al. (2015) established a much higher prevalence of prior depression and concurrent depressive symptoms among young women with acute MI than among young men. Even after adjusting for numerous socio-demographic, clinical and disease severity characteristics, young women with an acute MI had 60% greater odds of having significant depressive symptoms compared with young men.

Numerous studies have found women report more severe and persistent depressive symptoms compared with men (Stern et al. 1977; Drory et al. 2003) with prognosis found to be poorer (Carney et al. 1991; Greenland et al. 1991). Additionally, gender differences in depressive symptoms are greatest among younger female patients (Mallik et al. 2006; Uuskula 1996). In the prospective Community Mental Health Epidemiology Study of Washington County, depression increased cardiovascular risk in women younger than 40 years more than sixfold, while no association was found among men (Wyman et al. 2012).

Even when baseline differences in history of hypertension, congestive heart failure and diabetes are adjusted for, the gender differences in mortality for women persist in some studies (Greenland et al. 1991). This suggests that the reason for these differences may not be entirely due to co-morbidity. Similarly, research by Vaccarino

et al. (1999) suggests that depressed women with acute MI may experience an increased risk for adverse outcomes even after adjustment for prognostic variables.

Even though the presence and severity of depressive symptoms following a cardiac event seem to have similar risk factors to depression as in the general population, it should be noted that gender is not always a predictor of depression in these studies. For example, Doyle et al.'s (2015) recent study utilising Cox regression analyses for all-cause mortality demonstrated that the interaction between sex and depression was statistically significant (HR for interaction = 1.12, 95 % CI = 1.05–1.19, $p < 0.001$). This may signify that the association between depression and mortality was stronger for men than for women. The HR associated with depression was 12 % higher in men compared with women (men: HR = 1.38, 95 % CI 1.30–1.47; women: HR = 1.22, 95 % CI 1.14–1.31). Bjerkeset et al. (2005) reported that men and women differed in their long-term outcome after MI. Women showed a higher risk for depression in the first 2 years subsequent to an MI, whereas, in men, the risk for depression increased after 2 years post-MI. This could suggest a difference between the genders in the aetiology for depression in CVD patients.

2.2.6 Age

Studies have found that younger patients are more likely to have depression in the context of CVD. For example, in ACS, age has been identified as a risk factor for the development of depression (Lesperance et al. 1996; Dickens et al. 2004; Schrader et al. 2004; van Melle et al. 2006). In a prospective study of 648 patients at 14 Veterans Affairs (VA) hospitals, Ho and colleagues (2005) established that following cardiac valve surgery, depressed patients were significantly more likely to be younger. In a recent study by Shah et al. (2014), women less than 55 years of age emerged as the group with the highest risks associated with depressive symptoms. Of additional concern (Baumeister et al. 2015), this group also had the highest burden of depression as well, with 27 % exhibiting at least moderate depressive symptoms or higher. Additionally, in the Heart and Soul Study, Whooley and colleagues (2007) found that depressed patients with coronary heart disease were significantly more likely to be younger. Hamo and colleagues (2015) found that in patients with heart failure with preserved ejection fraction and who were also depressed were more likely to be younger than those without depression. Andrikopoulos et al. (2007) reported that the risk ratio in women for in-hospital death was exaggerated among younger patients, aged less than 55 years (RR = 3.84, 95 % CI 1.07–13.74).

However, like gender, not all studies have found age to be a significant risk factor in the development of depression in CVD patients. Doyle and colleagues (2015) determined that age did not have an effect on the prevalence of depression. Given that sex differences between depression and cardiac prognosis may be dependent on postmenopausal status (Vaccarino et al. 2013, 2014), Doyle and colleagues also scrutinised their data to determine if there was a sex-by-age interaction effect in the influence of depression on mortality. The interaction was found to not be significant (HR = 1.00, 95 % CI 0.99–1.01). Supporting this, Krannich et al. (2007) did not find a significant relationship between age and the change in depression pre- and post-CABG surgery.

2.2.7 Prior History

The chronicity of depressive symptoms may be especially relevant considering the onset and progression of CVD during the life course. Smolderen et al. (2015) found that at the time of their acute MI, women with a history of clinical depression were particularly vulnerable to experiencing depressive symptoms when compared with men with a history of depression. Approximately 25 % of women with a history of depression reported current depressive symptoms versus 10 % of men with a history of depression. Lesperance and colleagues' (1996) landmark paper investigated the impact of prior depressive history on 222 acute MI patients. Compared with those without a history of depression, patients with a previous history of depression were more likely to become depressed at some time during the year post discharge. When the data were examined on the basis of whether the depression was a recurrent episode or a first depression, they determined that patients with a recurrent depression were at significantly increased risk of 18-month mortality (40.0 %) when compared with patients who were depressed for the first time in their lives during their index admission.

Leung and colleagues (2012) performed a systematic review and examined the timing of the onset of depression relative to the onset of the CVD. They established that when compared to people who reported never experiencing depression, the risks of poor outcomes (all-cause mortality, cardiac mortality or cardiac morbidity) were increased. This increase was evident in both individuals whose first episode of depression started after the onset of CHD (RR = 2.11) and among those whose depression was a recurrence of a previous episode of depression (RR = 1.59). Carney and colleagues (1999), in a sample of medically stable patients with coronary artery disease (CAD), found that a higher proportion of depressed subjects experienced a prior history of depression than those who were not depressed.

2.2.8 Functional Impairment

The relationship between depression and functional impairment has been well established in community samples. Depression has been shown to be a strong predictor of difficulties in performing activities of daily living (ADLs) in community-dwelling adults (Mehta et al. 2002; Covinsky et al. 2010). Thus, it is no surprise that similar associations are evident in cardiac populations, specifically HF. For example, in a group of outpatients attending a community heart failure chronic disease management programme, Haworth et al. (2005) established that greater functional impairment as measured by the New York Heart Association (NYHA) classification could predict depression. Sin (2012) reported that high classification on the NYHA at baseline also significantly predicted depression at 6 months. She concluded that people with functional impairment may have slower recovery resulting in less improvement in depression scores at 6 months. Gottlieb and colleagues (2004) also reported a relationship between major depression and functional impairment as measured by NYHA class and also on the physical functioning subscale of a quality of life scale. Several other studies have also employed the NYHA classification as a

measure of functional impairment and have found similar results. For example, in a sample of 839 symptomatic HF patients free of depression at baseline, Lossnitzer et al. (2013) found that NYHA class again was a strong predictor of incident depression. Additionally, Freedland et al. (2003) also reported the relationship between MDD and functional impairment.

Similar findings have also been reported in MI populations. Depression following an acute MI has also been shown to correlate with decreased overall functional status (Griego 1993). de Jonge et al. (2006) reported that patients with post-MI depression demonstrated significantly poorer health status on all indicators at 12 months as well as a fourfold increased risk of disability following the MI compared with patients without a post-MI depression.

A possible explanation for these findings could be that increased functional disability may result in reduced activity and social contact. This allows for more time for patients to ruminate about their health conditions and may lead to increased feelings of alienation, helplessness and loneliness (Haworth et al. 2005).

2.2.9 Social Isolation/Participation

An extensive literature has examined the relationship between depression and perceived social support in CVD populations (Krishnan et al. 1998; Bosworth et al. 2000; Horsten et al. 2000; Brummett et al. 2001; Raynor et al. 2002; Bucholz et al. 2014). Prospective studies have provided evidence that low perceived social support can place CVD populations at risk for the development or worsening of MDD (Bucholz et al. 2014; Holahan et al. 1997; Barefoot et al. 2000; Frasure-Smith et al. 2000; Welin et al. 2000). Research has suggested that it is critical to consider the combined effect of depression and social support in predicting CVD prognosis. For example, social support in conjunction with depression has been associated as a predictor. Horsten et al. (2000) reported that CVD patients with high depression scores and who also lacked social support were at the greatest risk for subsequent cardiac events and death. Furthermore, Frasure-Smith and colleagues (2000) found that depressed patients with low perceived social support were at the greatest risk for mortality during the first year following an acute MI. Patients with greater levels of perceived social supports were not at increased risk compared to nondepressed patients given that high perceived social support appeared to buffer the effects of depression on 1-year mortality.

2.2.10 Impact of Depression on CVD Patients

Depression also predicts cardiac morbidity among patients with established CVD. Depression is a particularly significant risk factor for CVD morbidity following acute MI (Tully and Baker 2012; Frasure-Smith et al. 1995; Leung et al. 2012; van Melle et al. 2004; Freedland and Carney 2013). Depressed patients with CVD are at greater risk for readmission or nonfatal cardiac events than

nondepressed patients (Barefoot et al. 1996; Carney et al. 1988; Connerney et al. 2001; Tully et al. 2008). Additionally, depression has been shown to predict declines in health status and is associated with worse cardiovascular-specific morbidity. In a study of 460 outpatients with a history of HF and left ventricular ejection fraction, depression was found to be the strongest predictor of decline in health status over a 6-week follow-up period (Rumsfeld et al. 2003). Similarly, Vaccarino and colleagues (2001) also found a graded relationship between the severity of depressive symptoms and a combined end point of functional decline among HF patients.

Numerous studies have demonstrated that the presence of depression predicts all-cause and cardiac mortality following hospitalisation for cardiovascular events (Frasure-Smith et al. 1993; Denollet and Brutsaert 1998; Irvine et al. 1999; Romanelli et al. 2002; Wheeler et al. 2012). For example, Frasure-Smith and colleagues (1993) assessed outcomes following an acute MI in depressed and nondepressed patients. In patients with MDD, the 6-month mortality rate after an MI was 17 %, compared with 3 % among nondepressed patients (HR = 3.44, 95 % CI 2.25–4.63). Similar findings have been reported in larger cohorts of acute coronary syndrome (ACS) patients (Frasure-Smith et al. 1999; Lesperance et al. 2000), as well as in other ischemic heart disease patient cohorts (Barth et al. 2004; Parashar et al. 2006). Depression has also been associated with an increased risk of heart failure readmission and death among HF patients (Jiang et al. 2001; Sherwood et al. 2011). It has also been associated with and increased risk of mortality among patients with prior stoke (Williams et al. 2004; Pan et al. 2011).

Meta-analyses have also found similar results. Barth and colleagues (2004) reported that depressed patients with histories of cardiovascular events were 1.7 times as likely to die within 2 years of initial assessment when compared to nondepressed patients in broad range of CVD conditions (including MI and CABG). In their evaluation of MI patients, van Melle and colleagues (2004) found that post-MI depression was associated with a 2- to 2.5-fold increase in risk of cardiac or all-cause mortality. Finally, in their study of 16,889 MI patients, Meijer and colleagues (2011) reported that post-MI depression was associated with an increased risk of all-cause mortality (OR = 2.25; 95 % CI 1.73–2.93) and cardiac mortality (OR = 2.71; 95 % CI, 1.68–4.36).

Furthermore, a dose-response relationship has been observed between the severity of depression and cardiovascular outcomes. Using data from the Framingham Heart Study, Wulsin and colleagues (2005) also reported a dose-response relationship between severity of depressive symptoms and all-cause mortality. When compared with scores from the lowest tertile of the Center for Epidemiologic Studies Depression Scale (CES-D), the risk of death in the second and third tertiles were 33 % and 88 % higher, respectively. Of course not all findings suggest a positive association (Parashar et al. 2006; Strik et al. 2003; Drago et al. 2007; Thombs et al. 2008). Nicholson et al. showed most studies insufficiently adjusted for confounding variables. For example, left ventricular ejection fraction reduced the purported depression-CVD morbidity link by 65 % (Nicholson et al. 2006).

2.2.11 Impact of CVD on Depressed Patients

The relationship between antecedent depression and subsequent cardiovascular morbidity was investigated in the 1930s, when Malzberg (1937) reported a higher incidence of CVD-related death when compared to control groups. He found the death rates due to cardiac disease were approximately eight times higher in involutional melancholia (depression beginning in midlife or later) than in the general population. In the decades following, numerous studies have observed similar results. For example, Dreyfuss and colleagues (1969) reported the rate of MI was about six times higher among inpatients with depression than among all other inpatients. Prospective studies such as the National Health Examination Follow-Up Study (Anda et al. 1993) found that self-reported depressed mood was associated with a significantly increased risk of fatal ischemic heart disease. In another prospective cohort, Penninx and colleagues (1998) reported that newly depressed older men were approximately twice as likely to have a fatal CVD event than those who were never depressed. Surtees and colleagues (2008) found that participants diagnosed with MDD in the year preceding baseline assessment were 2.7 times more likely to die from IHD in participants free of established heart disease. The severity of depression symptoms has also been found to be an independent risk factor for CVD mortality in prospective cohorts free of CHD at baseline (Ahto et al. 2007; Brown et al. 2011; Whang et al. 2009).

Conclusion

It is important to acknowledge that the association between MDD and CVD is complex and likely bidirectional (Teismann et al. 2014). It should also be considered that the aetiology of depression may differ in certain subgroups within the CVD population (Baune et al. 2012) and that traditional classifications of depression such as melancholia or dysthymia may not be applicable; however, further research is needed to ascertain this.

Given that CVD and depression are among the leading causes of death, disability and disease burden in the developed world, there is the potential for significant harm in ignoring the relationship between the two. The presence of co-morbid CVD and depression not only has the potential to change the prognosis of both clinical and psychosocial outcomes, but it can impact the pathways and responses to treatment.

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