DEPRESSION IN HEART FAILURE

COMMENTARY

Sad hearts in heart failure patients

A cardiologist's perspective on depression in heart failure by Shirley Middlemost.

Address for correspondence:
Dr S Middlemost
Vergelegen Mediclinic
Main Road
Somerset West
7130

Email:
shirley@helderbergheart.co.za

ABSTRACT **Heart failure is a common clinical entity. Because patients with heart failure face high rates of debilitation and mortality, the study of depression characteristics in this population is a critical research area in the pursuit of improved quantity and quality of their lives. Studies have shown that depression is common in heart failure and, interestingly, that both conditions share similar pathobiological mechanisms. Depression in heart failure is a serious co-morbidity. It is a strong predictor of short-term worsening of heart failure symptoms, a decline in health status, mortality and re-hospitalization, independent of baseline ventricular function and severity of cardiovascular disease. Depression remains poorly recognized and under-treated in heart failure. The presence of depression is not random. It is disproportionately diagnosed amongst patients who are female, those suffering more advanced disease, those who are socially isolated and those of low socioeconomic status. Patients should be screened regularly for symptoms of depression. Although effective treatment is available, no studies have been done to show that treatment of depression has a positive impact on heart failure outcome.**

Research conducted over the last two decades has provided strong evidence for an association between depression and the incidence of coronary artery disease,[1, 2] between depression and premature mortality among patients with documented coronary artery disease [3,4] and between depression and all-cause mortality in populations with and without coronary artery disease.[5] The recent INTERHEART study confirmed that psychosocial factors were stronger risk factors for myocardial infarction than diabetes, smoking, hypertension and obesity.[6]

About 4-10% of the general population in the United States and Europe meet diagnostic criteria for depressive disorders using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) and International Statistical classification of diseases and related health problems (ICD-10) criteria.[7,8] Depression is even more prevalent in patients with cardiovascular disease. Abundant evidence suggests that depression is under-recognized and under-treated in cardiac patients. Depression has been reported in about 20% of outpatients with coronary heart disease, 30- 40% of patients with heart failure,[9-11] and up to 50% of patients recently hospitalized for bypass surgery or acute coronary syndrome.[12] The prevalence of depression in patients with heart failure has varied in different studies. This is likely due to the use of different diagnostic instruments and the inclusion of different patient populations in terms of age, gender and disease severity.

The relationship between depression and heart failure is a relatively new but rapidly expanding area of interest in cardiology research. Because patients with heart failure face high rates of debilitation and mortality, the study of depression characteristics in this population is a critical research area in the pursuit of improved quantity and quality of their lives.[13-15] Depression may even be associated with the development of heart failure. For example, in the Systolic Hypertension in the Elderly Program (SHEP Study), 16% of patients who were depressed developed heart failure compared to 7% in the non-depressed group.[16] Depression remained an important variable after adjustments for traditional risk factors, confirming an overall increased relative risk of 2.6.

Why is depression common in heart failure?

The explanation for the elevated incidence of depression in heart failure is uncertain. Various genetic, pathophysiologic and psychosocial factors have been postulated. Recent studies have identified the same genetic polymorphisms to be associated with the development of both depression and cardiovascular disease.[17] Gene-gene interactions as well gene-environment interactions have also been identified.[18, 19] Some have attributed the markedly elevated prevalence of depression in patients with heart failure, to the fact that both heart failure and depression share similar pathophysiology.[20] Neurohumeral activation, alterations in cardiac autonomic tone, inflammation, increased levels of circulating catecholamines, greater platelet activation and elevated levels of cytokines may all play a role in the development, progression

and outcomes in heart failure.[12] Each of these pathophysiological states has also been seen in depression.[21-23] Psychosocial factors, such as stressful life events, have been shown to precipitate depression. Also, depression-generating stressors such as the threat of death and loss of autonomy that accompanies heart failure can precipitate depression.

Depression increases morbidity and mortality in heart failure

Depression in patients with heart failure is a strong predictor of short-term worsening of heart failure symptoms, a decline in health status, and mortality and re-hospitalization, independent of baseline ventricular function and severity of cardiovascular disease.[11, 24, 25] A link between depressive symptoms and the course of heart failure may be expected, because depressed individuals have elevated sympathoadrenal activation, a response that may be deleterious for patients with heart failure.[26, 27] Jiang et al. found that mortality and repeat hospitalization for decompensated heart failure, was 2.5 times higher in heart failure patients with major depression than in those without depression.[11] The incidence of repeat hospitalization followed a similar pattern. Depression is associated with medical non-compliance, a higher prevalence of smoking, and lower levels of social support, each of which have been correlated with negative outcomes in patients with heart failure.[20]

Depression is under-diagnosed in heart failure

Although addressing depression in heart failure patients provides a prime opportunity to really improve the patient's quality of life, heart failure patients are not often treated for depression. Depression commonly is undiagnosed. Physicians may not address depression because they have not been adequately trained to recognize both typical and atypical depressive symptoms because of time constraints or because they don't know how to best treat the condition. In addition, patients may be unwilling to disclose feelings of depression in order to avoid being stigmatized with the label of mental illness. The poor recognition rate of depression might be partly explained by the symptom overlap of the two disorders. These include fatigue, loss of energy, poor appetite, sleep disturbance, psychomotor agitation/retardation and concentration deficit.[28] Due to substantial overlap of somatic symptoms between depressive disorders and heart failure, depression may often be dismissed as the somatic symptom burden of heart failure. In order to improve the diagnosis of depression in heart failure patients, an awareness of the specific symptom profile of depression as presented in heart failure patients is necessary. One study compared depression symptoms in depressed patients with and without heart failure.[29] This study found no difference between patients with regard to somatic symptoms of depression such as sleep disturbance, change in appetite, poor concentration and psychomotor agitation/retardation. However, they did find that depressed patients without heart failure experienced more cognitive-emotional symptoms related to depression compared to depressed patients with heart failure. These symptoms included a sense of hopelessness and feelings of worthlessness or guilt. Similar findings were confirmed in two other studies.[28, 30]

This finding may partially explain the lower recognition rate of depression in patients with heart failure. Given their specific depression profile, heart failure patients might report fewer feelings of depression, hopelessness, worthlessness and guilt in their medical history, so that their clinicians may not consider the presence of a depressive co-morbidity. It has been suggested that patients with medical conditions may attribute their depression to their physical illness as an external, non-controllable factor. This might prevent these patients from self-reproaches, feelings of worthlessness and guilt. Recent studies have also confirmed that depression prevalence is unrelated to the etiology of heart failure.[31, 32]

The presence of depression in patients with heart failure can be assessed in the outpatient scenario by the use of rating scales such as the 9-Item Patient Health Questionnaire (PHQ-9).[33] The following should alert the physician to the presence of possible depression: the symptom burden is out of keeping with the objective measures of heart failure severity; heart failure remains stable, but the symptom burden increases; or the patient does not complain of anything or even hardly talks anymore. All of the above can be an indication that the patient simply is not well. The PHQ-9 is a self-report questionnaire that patients can fill out in the waiting room, taking less than 2 minutes to complete (see Figure 1). If the patient scores 10 or higher, this has a

FIGURE 1: The 9-item Patient Health Questionnaire Depression Screening Instrument.[33]

Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself - or that you are a failure or have let your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Add columns Total				

90% specificity and high positive predictive value, making it a good screening test to identify those at risk for depression. These patients should be referred to a psychiatrist to confirm the diagnosis. If there are time constraints, patients can complete a 2-item screen, which takes less than a minute to complete.[34] Patients should have a follow-up clinical interview for depression if an affirmative answer is given to either of two following questions:

- During the past month, have you often been bothered by feeling down, depressed or hopeless?
- During the past month, have you been bothered by little interest or pleasure in doing things?

In assessing patients, it is important to remember that some medication, such as corticosteroids, opioids and benzodiazepines, can induce depression. In a meta-analysis of 15 trials involving more than 35 000 cardiac patients, the absolute annual increase in risk of reported depressive symptoms was 6 per 1 000 patients which, contrary to popular belief, was not significant.[35]

Predictors of the onset of depressive symptoms in heart failure patients

A greater awareness of which heart failure patients may be at increased risk for the development of depression, may aid in earlier diagnosis and intervention. The presence of depression is not random. It is disproportionately diagnosed amongst patients who are female, those suffering more advanced disease, those who are socially isolated and those of low socioeconomic status.[29] Certain psychosocial factors may contribute to the high prevalence of depression. These include medical non-compliance, high prevalence of smoking and lower levels of social support, each of which has been correlated with worse outcomes in heart failure.[20]

One study evaluated the factors associated with the onset of depression in patients with heart failure.[36] This study used the Medical Outcome Study – Depression questionnaire (MOS-D), a screening tool used in case-finding studies of depression.[37] Patients also completed the Kansas City Cardiomyopathy Questionnaire (KCCQ), which is a 23-item, disease specific, health status instrument for patients with heart failure. The KCCQ measures symptoms, physical functioning, social functioning, self-efficacy and quality of life. The KCCQ has been shown to predict mortality and cardiac events, such as hospitalization in heart failure patients.[24, 38, 39] In a multivariate analysis, the study showed that living alone, alcohol abuse, the perception that medical care has been a substantial economic burden and health status, as measured by the KCCQ, were independent predictors of developing depressive symptoms.

For patients without these factors, about 8% developed depression by one year of follow-up in the study. At one year, 16%, 36% and 69% of those with one, two or three of these risk factors, respectively, developed depression. There was also a gradient relationship between poor health status and increased risk of developing depression. The authors concluded that social factors and health status are predictive of the risk of development of depression in outpatients with heart failure. Clinicians should be aware of which patients are at risk for the development of depression, so that these patients can be screened and evaluated more fully. Since 8% of those without any of these risk factors developed depression over the ensuing year, clinicians should screen patients regularly over time for depression.[36]

Gottlieb et al. demonstrated that depression was more common in younger patients with heart failure.[40] Depression was also more commonly reported in women than in men. Depressed patients scored significantly worse than non-depressed patients on all components of questionnaires measuring quality of life. However, they did not differ in ejection fraction or treatment, except that depressed patients were significantly less likely to be receiving beta-blockers.

Treatment of depression in heart failure

Efficacious treatments for depression are still lacking, despite the development of state-of-the-art pharmacotherapy. A substantial patient population does not respond to treatment and / or maintains clinically significant symptoms despite treatment attempts.[41] Responsiveness may itself have prognostic importance.[42] Studies describing depression treatments among heart failure patients rely on too small and heterogeneous samples to permit definitive conclusions regarding intervention effectiveness. No studies have, to date, investigated the effects of depression intervention on objective clinical outcomes such as survival or secondary cardiac events in a heart failure population. Despite these limitations, a general pattern of decreased depressive symptoms and increased physical activities, as measured by the standard 6-minute walk test, has been observed across the treatment studies.

When discussing treatment with patients, it is important to emphasise the biological etiology of depression, because many patients see depression as a character weakness or personality flaw. Social stigma against mental health diagnoses can make patients reluctant to acknowledge and report depressive symptoms. It may also be helpful to inform patients that depression is very common, affecting 1 out of 5 patients with heart disease. An experienced clinical psychologist can administer cognitive behavioral therapy, which helps patients develop new ways of thinking and behaving, minimizing symptoms of depression. The addition of interpersonal and problem-solving therapy can also be effective in treating depression.[43] Interpersonal therapy addresses social and interpersonal stress that can contribute to depression, whilst

problem-solving therapy helps patients identify specific problems that may be contributing to their depression.

Pharmacotherapy for depression

As far as pharmacotherapy is concerned, little is known about treatment options for depression in patients with heart failure. The selective serotonin reuptake inhibitors (SSRI), such as sertraline, are safe and effective medication for treating depression in patients with heart disease such as acute coronary syndrome.[44] Drugs such as citalopram and sertraline are the least likely to inhibit cytochrome p-450 enzymes, thus minimizing exposure to pharmacokinetic interactions in cardiac patients taking multiple drugs.[45]

It is important that the dose of these drugs should be modified in elderly patients or in those with hepatic or renal disease. If the patient does not respond to one SSRI at an optimal therapeutic dose, an alternative one should be prescribed. Most commonly recorded side effects of these agents include insomnia or somnolence, nausea, diarrhoea and sexual dysfunction. Most of these effects disappear within the first month of treatment, so it is important to encourage the patient to continue with the medication. However, sexual dysfunction occurs in about 60% of patients treated with SSRIs and is the least likely adverse effect to resolve over time.[46] Some patients with SSRI-induced sexual dysfunction derive benefit from sildenafil.[47]

Other antidepressant medication such as mirtazapine is generally safe for patients with heart disease, but not as first-line therapy, as it is associated with weight gain.[48] Tricyclic agents should not be used as first-line, because of their association with adverse cardiovascular events.[49]

In managing depression in heart failure, it is important to know which patients need to be referred to a psychiatrist. Patients who report manic symptoms, delusions or hallucinations and those who have suicidal thoughts, should be referred for further evaluation. Once pharmacotherapy has been instituted, the patient should be advised that it would take at least four weeks to feel better, with the majority recovering after six months of treatment. Once the patient has responded to pharmacotherapy, treatment should be continued for at least another six to twelve months to avoid relapse. Once the decision has been made to discontinue drug therapy, it should be weaned over a period of time.

Palliative care in patients with heart failure

Spiritual well-being, an important coping resource in patients with terminal cancer, is associated with less depression. This relationship has only recently been studied in patients with heart failure. Spirituality is defined as "the way in which people understand their lives in view of their ultimate meaning and value."[50] Bekelman et al. identified the relationship between spiritual well-being and depression in an elderly heart failure population, in the context of other common risk factors for depression, including low social support, poor health status and number of physical symptoms.[52]

In this study, greater inner peace was shown to be significantly associated with less depression when adjusted for other variables such as better health status, fewer physical symptoms, gender and income, which were also associated with less depression. Whether enhancing a patient's sense of meaning/peace might reduce or prevent depression and thus improve quality of life in patients with heart failure, has thus far been untested. One approach to address the multiple factors associated with depression and poor quality of life in heart failure patients may be the early incorporation of palliative care.[53, 54] Palliative care addresses spiritual well-being and may be an under-utilized resource in caring for patients with heart failure.

CONCLUSIONS

The increased prevalence of depression seen in patients with heart failure is now well established. What remains is to determine why this is the case, in the hope of eventually being able to target treatment at the true root of the problem. In the meantime, heart failure patients should be screened for depression and treated when depression is found to be present. This may help to improve the patient's quality of life and potentially improve long-term outcomes.

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