

Depression, cardiovascular disease and stroke

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Abstract

Depression is common in patients with cardiovascular disease and following stroke. It is associated with poorer outcomes, including higher mortality. Treatment of post-stroke and post-myocardial-infarction depression is associated with better outcomes, including lower mortality rates. Despite this, depression is often unrecognised and untreated. The aim of this paper is to assist the clinician in the assessment and treatment of depression in the context of stroke and cardiovascular disease.

Introduction

Depression has been found to have a high comorbidity with both cardiovascular disease (CVD) and stroke. Despite this, depression is often undiagnosed and untreated, in these groups (1, 2).

Depression in cardiovascular disease

Following myocardial infarction (MI), two-thirds of patients develop mild forms of depression (3) and 15% have major depression (4). The prevalence of depression in patients with chronic heart failure (CHF) is > 20% (5).

The association between depression and CVD is pertinent for several reasons. Depression has been identified as a risk marker for the development of new CVD and is also associated with poorer outcomes in pre-existing CVD (4, 6). Notably, depression post-MI is associated with a three-fold increase in mortality (7), and depression is a predictor for lower survival rates in patients with CHF (8) and post-MI (6). Furthermore, the presence of depression in patients with CVD is associated with an increased rate of non-adherence with medications, possibly double that of non-depressed patients (9), and poorer quality of life (10).

Several mechanisms have been suggested to explain the relationship between CVD and depression, including alterations in platelet function, endothelial function, autonomic nervous system function, coagulative factors, neurohormonal factors and cytokines (11).

Post-stroke depression

Approximately 40% of patients who survive a stroke develop depression (12). The presence of depression post-stroke has been associated with impairment in activities of daily living (13), slower functional rehabilitation (14), residual motor impairment (15) and significantly lower MMSE scores, indicating cognitive impairment (16). Furthermore, the mortality of patients in the 10 years following stroke is 3.4 times higher in those with depression (17). Conversely, depression has been identified as a risk factor for stroke (18).

Several mechanisms have been suggested in the pathophysiology of depression post-stroke. Studies have suggested an association between lesion location and post-stroke depression, particularly the left frontal region of the brain (19). It has also been suggested that stroke results in the release of pro-inflammatory cytokines and tumor necrosis factor (TNF), which lead to reduced serotonin (20).

Depression in patients with CVD or stroke should be assessed and managed in accordance with the NICE guidelines: Depression in adults with a chronic physical health problem: recognition and management. However, these guidelines make few specific recommendations with regard to CVD or stroke. This article, therefore, focuses on elements of assessment and management particular to depression in CVD and stroke, in the context of the NICE guidelines.

Screening

Depression in cardiovascular disease

It is recommended that all patients are screened for depression following Acute Coronary Syndrome (ACS) and screened again two months after the event (11). This second screening is required as patients have been noted to be in denial in the initial period following an MI (21). The same review recommends that all patients with CHF should be screened for depression at least annually (11).

Several screening tools for depression are available. An American Heart Association Science Advisory has recommended the use of the Patient Health Questionnaire-2 (PHQ-2) which asks two questions, assessing mood and anhedonia, over the previous two weeks (22). If the answer to either question is “yes”, it recommends further assessment using the Patient Health Questionnaire-9 (PHQ-9), which includes a further seven DSM-IV depression symptoms, and formal assessment by a clinician.

The European guidelines on CVD prevention have suggested the following two questions in screening for depression (23).

1. Have you lost interest and pleasure in life?
2. Do you feel down depressed or hopeless?

Post-stroke depression

The NHS Guidelines on Psychological Care after Stroke (24) recommend assessment, as opposed to screening, of mood at the following time points: 1 month post-stroke or prior to discharge or at six week follow-up; 3 months post-stroke, following discharge; 6 months post-stroke; and at six month and annual reviews and at any other times where concerns are raised. They recommend the use of a variety of standardised measures and specifically mention the 12-item General Health Questionnaire (GHQ-12), the Brief Assessment Schedule Depression Cards (BASDEC), Hospital Anxiety and Depression Scale (HADS) and PHQ-9 as suitable examples. They recommend that an interview should also be conducted to enquire about emotional state and assess for distress.

Diagnosis

In keeping with general guidelines for depression, the diagnosis of depression in CVD and stroke should be made through a structured interview to cover diagnostic criteria, such as the ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision) or DSM-IV (Diagnostic and Statistical Manual of Mental Disorders 4th Edition).

Assessment for depression may be complicated by the presence of physical symptoms following both MI and acute brain injury, independent of depression, which may mimic the somatic symptoms of depression.

In post-stroke patients with fluent aphasia, global aphasia or cognitive impairment, obtaining reliable verbal responses may not be possible. In such cases, the clinician should communicate with family, carers and other professionals to obtain information on observed measures, including changes in sleep pattern, early morning waking, changes in weight or appetite, loss of interest, distress, self-harm and social withdrawal (20). The Stroke Aphasic Depression Questionnaire (SAD-Q), a questionnaire of observed behaviours which is completed by the patient's carer, may be of use. The Depression Intensity Scale Circles (DISCs) uses a visual rating scale of circles with increasing amounts of grey to represent severity of depression, and has been found to have acceptable validity and reliability in patients with disability following acquired brain injury (25).

The Cardiac Depression Scale (CDS) can be useful in assessing change in symptoms and response to interventions in cardiac patients (26).

Management

i. Rehabilitation

Cardiac rehabilitation programmes utilise a combination of education and exercise to promote secondary prevention and minimise the physical and emotional consequences of CVD. Although the value of these programmes in reducing cardiovascular events is unclear (27), they have been shown to reduce depression when focused on exercise in groups (28). It is not clear whether the benefits in mood originate from the exercise or the psychological support derived from the group. Aerobic exercise has been shown to have a similar effect on reducing depression as antidepressants in coronary heart disease patients (29).

Stroke rehabilitation utilises a multidisciplinary team to optimise physical function (notably mobility and activities of daily living) and independence. There have been fewer studies on the effects of stroke rehabilitation on post-stroke depression. A population-based cohort study has suggested that stroke rehabilitation significantly lowers the risk of developing depression post-stroke (30). A meta-analysis of exercise programmes in post-stroke depression found a significant improvement in depressive symptoms with higher intensity exercise protocols (31).

ii. Cognitive behavioural therapy (CBT)

The results for CBT in depression in patient with CVD are variable. Meta-analysis has suggested a small treatment effect with CBT and problem solving (32).

The use of CBT in post-stroke depression is also under scrutiny, with studies suggesting its effects are comparable with placebo (33).

iii. Medication

When prescribing antidepressants following a stroke or MI, potential adverse effects, worsening of physical symptoms and interactions with medications should be considered.

Depression in cardiovascular disease

Research suggests that selective serotonin reuptake inhibitors (SSRIs) may have a protective effect against MI (34) and have a neutral or positive effect on mortality post-MI (35). However, antidepressants have been associated with arrhythmias, cardiac conduction disturbances and alterations in QTc interval, blood pressure and heart rate. The Maudsley Prescribing Guidelines in Psychiatry have summarised the cardiac effects of the widely used antidepressants and make recommendations for treatment of depression in patients with CVD, which have been summarised below (36).

- SSRIs are recommended in the treatment of depression in CVD (36). The guidelines particularly recommend the use of sertraline as first-line treatment post-MI. Other relatively safe options are the other SSRIs and mirtazapine. Although relatively safe, SSRIs have several potential adverse effects, notably increased risk of upper GI bleed through antiplatelet action (37) and interactions with cardiac drugs via the cytochrome system (36).
- In patients at risk of arrhythmia (i.e. history of arrhythmia, previous MI, left ventricular hypertrophy or heart failure), citalopram, escitalopram, bupropion, moclobemide, venlafaxine and lofepramine should either not be prescribed or prescribed with caution. When prescribed, an ECG should be obtained prior to starting treatment and should be repeated one week following any dose increase.
- Tricyclic antidepressants (TCAs) have been associated with arrhythmogenic activity (including PR, QRS and QT prolongation) via cardiac ion channel blockade, with the exception of lofepramine. Therefore, patients at risk of arrhythmia should not be prescribed TCAs (except lofepramine). When, for clinical reasons, prescription of TCAs is unavoidable, an ECG should be obtained prior to starting treatment and should be repeated one week following any dose increase. ECG should also be repeated intermittently throughout the duration of treatment, in discussion with a cardiologist.

Post-stroke depression

Antidepressants are effective in reducing depression following stroke (38). Furthermore, they have been associated with significant recovery of activities of daily living (39) and reduced mortality rates (40). The Maudsley Prescribing Guidelines make several recommendations in the treatment of post-stroke depression which have been summarised below (36).

- The use of SSRIs (notably citalopram and fluoxetine) and nortriptyline in the treatment of post-stroke depression is recommended, due to studies supporting their safety and efficacy.
- SSRIs have been noted to elevate the risk of *de novo* haemorrhagic stroke when given in combination with antiplatelet treatment or warfarin (41). As a result of this, there have been concerns that the use of SSRIs in the treatment of post-stroke depression may increase the risk of further stroke. The Maudsley guidelines suggest that SSRIs may reduce the risk of embolic stroke and increase the risk of haemorrhagic stroke (42, 43) and suggest caution when prescribing SSRIs in post-haemorrhagic stroke.
- In patients prescribed anticoagulants or aspirin, who are also prescribed an SSRI, the addition of a proton pump inhibitor should be considered to reduce risk of bleeding complications.
- In patients prescribed warfarin, citalopram or escitalopram should be considered as first-line treatments for post-stroke depression.

Referral

Local referral pathways to specialists vary. Rehabilitation services will often have a specialist psychologist as part of the multidisciplinary team. Referral to the local Community Mental Health Team should be considered on an individual basis but would be appropriate when depression is severe, has not responded to treatment, is significantly impacting on the patient's ability to participate in rehabilitation, or is associated with suicidal ideation, psychotic phenomena, significant neglect, psychiatric comorbidity, or psychosocial issues.

Generic

As with all patients with depression, there should be a clear assessment of degree of functional impairment and risk, which should include risk of suicide and neglect.

There should be provision of written information about depression and support services, including emergency contacts.

Carers should be offered a carer assessment and offered information about carer support services. With patient consent, carers should be regularly updated as to the patient's progress and management plan; they should be offered written information about depression and management.

Patients should have regular follow-up appointments to assess treatment response and monitor adherence and adverse effects.

Conclusion

Depression is common in patients with cardiovascular disease and following stroke. It is associated with poorer outcomes, including higher mortality. Treatment of post-stroke and post-MI depression is associated with better outcomes, including lower mortality rates. Despite this, depression is often unrecognised and untreated. Patients should be routinely screened for depression following stroke or cardiac events and should be treated appropriately.

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