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HOW TO DO

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Treating depression: Psychiatric consultation in cardiology

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Abstract

Depression is the most common psychiatric disorder in coronary artery disease, and it can worsen cardiac outcomes. Also, cardiac disease predisposes patients to the development of depression. Assessment of depression is an important part of ongoing patient contacts. It can be easily done through the regular use of a self-report screening tool and the clinical interview. Treatment can consist of antidepressant use, psychotherapy and mindfulness-based group therapy. The antidepressants known as the selective serotonin reuptake inhibitors can generally be used safely in cardiac patients. They are a mainstay in the treatment of moderate to severe depression. Individual cognitive-behavioral therapy can treat milder forms of depression and can augment antidepressant use in more severe cases. Mindfulness-based group therapy can provide patients with additional means of handling distress while offering social contact and support, both of which are important in the treatment of depression. The use of consulting psychiatric services offers the cardiologist a collaborative team approach when treating patients with depressive illnesses. (Cardiol J 2009; 16, 3: 279–293)

Key words: depression, psychiatric consultation, cardiac outcomes

Case vignette

Steve is a 57 year-old married, white male recently hospitalized for an acute myocardial infarction (MI). About a week after discharge he saw his cardiologist. During that visit, he expressed feelings of sadness and hopelessness. His cardiologist gave him the Patient Health Questionnaire-9 (PHQ-9), a nine-item self-report depression questionnaire [1], on which Steve scored 23, suggesting severe depressive symptoms. Steve's cardiologist referred him for mental health care. The patient was seen within a week of his referral.

In the initial mental health appointment, the clinician gathered information about Steve's current symptoms, his psychiatric and medical history, his social and family history, and did a mental status exam. Steve reported a high level of hopelessness. He also reported a three-week history of early morning awakening, low energy, poor appetite, difficulty concentrating, and irritability. He expressed decreased interest in activities he used to enjoy, and had passive suicidal ideation ("I would be better off dead"). He denied any plan or intent for suicide and denied any previous attempts. He had no prior psychiatric treatment but noted mild depressive symptoms started in adolescence. There was no family psychiatric history. Steve reported a high level of stress associated with his job as a supervisor at an electrical company. He described his work environment as "demanding and stressful". He reported being "obsessive" at his job and not being able to delegate because he felt he could do a better job. He could at times lash out at employees. He reported frequent arguments with his wife, which he attributed to being overwhelmed. He felt unable to

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express his anger without yelling, and had difficulty communicating his thoughts and feelings. Steve reported a low level of social support, having few friends and a sedentary lifestyle. He reported a long history of poor self-image and low self-esteem. He denied nicotine, alcohol or drug use. On examination, Steve presented a disheveled appearance, slowed speech, low mood, constricted affect, and tearfulness when discussing his health. There were no hallucinations or delusions, and aside from negative distortions about his life circumstances, he was logical in his thinking. He had passive thoughts of suicide but no active ideation, intent or plans. Steve met the criteria for a diagnosis of major depression. Treatment is imperative both for the depression and for his cardiac outcome.

Introduction

Stress, anxiety and depression can have significant impacts on the heart. They can increase the likelihood of developing cardiac problems, or worsening cardiac outcomes in patients who already have cardiac problems. Stress can give rise to arrhythmias [2]. Anger can lead to increased risk of coronary heart disease (CHD) [3–7]. 30–50% of patients with coronary artery disease (CAD) who experience mental stress can have transient symptomatic ischemia, left ventricular dysfunction, and even fatal arrhythmias [8–10]. Heart failure (HF) patients are at increased risk of MI following episodes of anger or anxiety [11]. In fact, psychological distress confers a greater risk of acute MI than hypertension, obesity or diabetes [12]. Both depression and anxiety can increase the risk of CHD in a graded fashion [13]. There is ample evidence for the significant prevalence of depression in congestive heart failure (CHF) patients [14, 15]. Depression increases the risk of developing CHF in patients with risk factors for it [16], and is a strong predictor of worsening HF in patients who already have CHF [17]. Depression can decrease adherence to medical regimens in cardiac patients [18, 19], further complicating health issues and contributing to distress. HF patients with depression are more likely to die from cardiac events or be medically rehospitalized, even when controlling for left ventricular ejection fraction and brain natriuretic peptide levels [20]. Morbidity and mortality are known to worsen if depression occurs after myocardial infarction [21, 22], and in patients with CHF [20, 23]. Major depression can worsen cardiac outcomes [14], and depression and social isolation increase mortality by 2.2–5.4 times over those without depression [24].

Social factors also play a role in cardiac difficulties. Social isolation and living alone increase the risk of recurrent coronary events in cardiac patients, and can lead to worse cardiac outcomes [25]. The fewer support people available to HF patients, the greater the risk of increased mortality at one year [26]. Limited social supports can have an indirect negative impact on cardiac outcomes: living alone and having fewer supports point toward the possibility of poorer adherence to medical regimens, which in turn predicts worse cardiac outcomes [27].

Stress, anxiety and depression can adversely impact the heart, but it is also possible that heart problems give rise to stress, anxiety and depression.

Patients with HF are more likely to develop depression or experience anxiety and psychosocial distress as a result of their heart disease. Further, living with HF challenges coping abilities, and can lead to diminished job function, worse stamina, changes in household roles/duties, and more social isolation. As a result, patients can experience a loss of control and increased frustration. This can adversely impact cardiac function, and deepen the cycle of distress and cardiac dysfunction.

It is important to address these issues in the service of improving cardiac outcomes in cardiac patients. This paper will focus specifically on depression and interventions for it, as well as describing a model of collaborative care between the disciplines of Cardiology and Psychiatry used at the University of Rochester Medical Center.

Depression and the heart

Major depression is the most common psychiatric disorder in coronary artery disease [28]. A study of point prevalence of depression in acute MI, CAD and unstable angina showed a rate of 15–20% [29]. Another study of CAD patients post-angiography showed rates of 16% major depression and 17% minor depression [30]. CHF patients showed a point prevalence of about 20% [20, 31]. In a hospitalized population with CHF, 14% met criteria for major depression, and 35% showed significant levels of depression when screening for it using the Beck Depression Inventory (BDI) [32]. In addition to the greater likelihood of depression in cardiac patients, depression is also known to worsen the outcomes of many general medical conditions. Depression increases the risk of mortality in nursing home patients [33], increases morbidity post-stroke [34], and worsens outcomes in diabetes, cancer, AIDS and other illnesses [35]. The risk of having an MI

Table 1. Diagnostic criteria for major depression [DSM-IV-TR. American Psychiatric Association, Washington, DC 2000].

≥ 5 symptoms in the same two-week period
Sleep: insomnia or hypersomnia
Interest: depressed mood*, loss of interest or pleasure*
Guilt: feelings of worthlessness
Energy: fatigue
Concentration: diminished ability to think or make decisions
Appetite: weight change
Psychomotor: psychomotor retardation or agitation
Suicidality: preoccupation with death, hopelessness

*Must include 1 of these

Table 2. Complexities of assessment.

Complexity #1 (stigma)
'Fallacy of good reasons'
— 'I have good reasons to be depressed…'
— 'who wouldn't be depressed? I would be, too'
Complexity #2 (multi-determined symptoms)
'Confound of overlapping etiologies'
— signs/sxs may be caused by depression, co-morbid physical illness, or both:
• fatigue/low energy
• loss of appetite
• trouble sleeping
• slowing of motor movements

is increased in patients with at least two weeks of major depression symptoms [12].

Depression is a systemic disease showing increased neurophysiologic kindling, increase of locus ceruleus firing rate, causing downstream effects of increased heart rate, increased blood sugar, increased blood pressure, and decreased gastrointestinal blood flow. Increases in corticotropin releasing factor increases ACTH secretion with the effect of increasing glucocorticoids, in turn causing increased lipolysis, increased gluconeogenesis, proteolysis, increased insulin resistance and decreased inflammation [36]. Physiologically, during depressive episodes, increased platelet aggregation and thrombus formation occur and there is decreased heart rate variability [37–39].

The diagnosis of Major Depression per Diagnostic and Statistical Manual IV (DSM-IV-TR) [40] requires ≥ 5 symptoms over a two week period (Table 1). However, it can be challenging to detect and distinguish these symptoms in the midst of many other medical issues. Complexities of assessment include: 1) the fallacy of good reasons: "I have good reasons to be depressed"…"who wouldn't be depressed?"."I would be, too, if…"; and 2) multi-determined symptoms — that is, whether the symptoms are 'caused' by depression or by the co-morbid physical illness (Table 2). Four models have been examined in an effort to obtain the best diagnostic sensitivity and specificity. They are the Inclusive, Etiologic, Substitutive and Exclusive models (Table 3) [41]. DSM-IV-TR simplifies this issue to a degree by recommending 'Count all physical symptoms unless they are clearly and fully accounted for by the physical illness'.

For the busy clinician, the bottom line is that one or both of the following must be present to make the diagnosis of major depression: depressed mood or anhedonia (lack of, or diminished, capacity to enjoy). If one or both of these symptoms are present, then look for other symptoms to make the diagnosis.

Recognition of major depression can be complicated by vague physical complaints, which can be the presenting feature. The greater the number of vague physical complaints, the greater the chances a mood disorder exists. For example, with four to

Table 3. Confound of overlapping etiology diagnostic models [Cohen-Cole and Stoudemire Psychiatric Clinics of North America 1987].

	Model	Projected Pos/Neg
Inclusive	Count all symptoms regardless of etiology	High sensitivity Low specificity
Etiologic	If 'etiology' is physical, do not count	High face validity ? Inter-rater reliability
Substitutive	Substitute physical sxs with psychological sxs	?
Exclusive	Exclude common physical symptoms	High specificity Low sensitivity

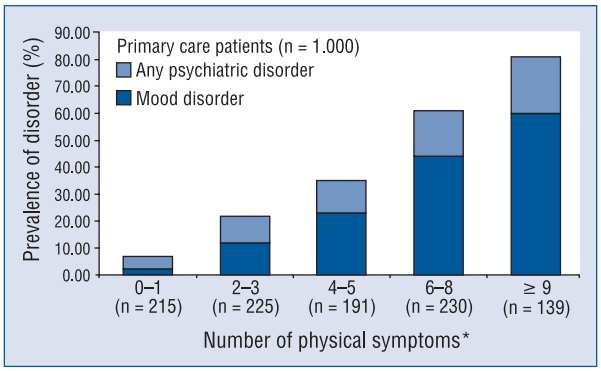

Figure 1. Multiple physical symptoms may indicate depression. *Physical symptoms included fatigue; disturbed sleep; menstrual problems; dizziness; GI complaints (nausea, vomiting, gas, constipation, diarrhea); headache; joint or limb pain; back pain; abdominal pain; chest pain; sexual dysfunction/apathy; and others [Kroenke K et al. Arch Fam Med, 1994; 3: 774–779].

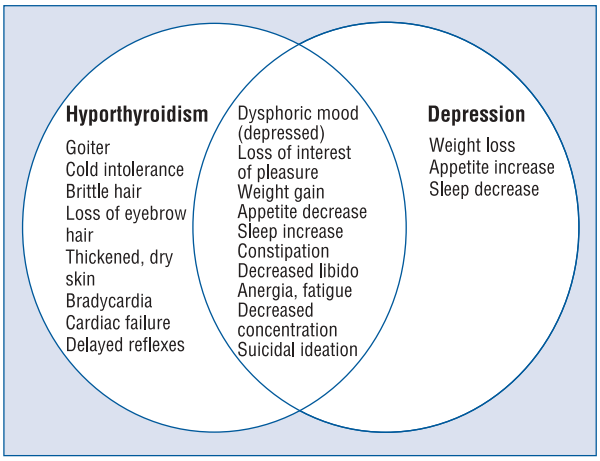

Figure 2. Signs and symptoms of hypothyroidism and depression [Extein I, Gold MS eds. Medical Mimics of Psychiatric Disorders Progress in Psychiatry, American Psychiatric Press 1986; 101].

five physical symptoms, there is an approximate 20% chance that the patient has depression. When there are nine or more physical complaints, the chance is about 60% (Fig. 1) [42].

When patients present with depressive symptoms, it is important to consider whether the depression is part of bipolar disorder. In bipolar disorder, patients have a history of episodes not only of depression, but also of mania. This is important when using antidepressants because their use can precipitate hypomania or mania in bipolar patients. It is also important to consider the possibility that medical problems can mimic depression. Symptoms often seen in depression, such as trouble sleeping, low energy or fatigue, loss of appetite, or slowing of motor movements, can also be seen in medical conditions. One of the common mimics is hypothyroidism. Clinicians should routinely check a thyroid stimulating hormone (TSH) level (Fig. 2). Other medical mimics are extensive and beyond the scope of this paper [43].

The use of a screening tool can facilitate the diagnosis of depression. Self-report instruments can easily be given to patients in the waiting room. In fact, the use of self-report questionnaires given in waiting rooms may be the preferred method for screening [44]. One tool that may be helpful to the busy clinician is the PHQ-9, mentioned in the case vignette. This self-rating form for depression can be completed by patients in a few minutes, and scored easily and quickly by clinicians (Fig. 3).

Steve's clinical history and PHQ-9 score clearly indicate he has a severe depression, and needs treatment. Antidepressants are warranted as part of the treatment, and can be started in the cardiologist's office. The patient should also be referred for psychiatric consultation.

Treatment

Antidepressants

There are many classes of antidepressants (Table 4) based upon molecular structure and mechanism of action. These include the selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), the Norepinephrine and Specific Serotonin Antidepressant (NaSSA) mirtazapine, the dopamine norepinephrine reuptake inhibitor (DNRI) bupropion, monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs). The first factor to consider in choosing which antidepressant to use is safety. The treatment of depression in cardiac patients, and especially post-MI patients, was an area of particular concern in the era of tricyclic antidepressants. However, this changed with the advent of the SSRIs. SSRIs can generally be used safely in cardiac patients; howerer see below regarding drug–drug interactions to be considered. Glassman et al. [45] studied the SSRI sertraline in post-MI or unstable angina patients. The study found that sertraline was safe and effective in the treatment of depression in this group. It was not powered enough to determine if treatment of depression made a statistical difference in cardiac outcome post-MI or unstable angina (Table 5).

Side effects are also part of the selection process. The SSRIs are relatively well-tolerated.

A

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ **DATE:** _____

Over the *last 2 weeks,* how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	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 yourself or 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:		+	+
(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card.)	**TOTAL:**			

10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	**Not difficult at all**	_____
	Somewhat difficult	_____
	Very difficult	_____
	Extremely difficult	_____

Figure 3. Patient health questionnaire (PHQ-9) (**A**) and instructions for use (**B**).

B

Fold back this page before administering this questionnaire

INSTRUCTIONS FOR USE

for doctor or healthcare professional use only

PHQ-9 QUICK DEPRESSION ASSESSMENT

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment on accompanying tear-off pad.
2. If there are at least 4 ✓s in the blue highlighted section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.
3. ***Consider Major Depressive Disorder***
   — if there are at least 5 ✓s in the blue highlighted section (one of which corresponds to Question #1 or #2)

   Consider Other Depressive Disorder
   — if there are 2 to 4 ✓s in the blue highlighted section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician and a definitive diagnosis made on clinical grounds, taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient. Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying PHQ-9 Scoring Card to interpret the TOTAL score.
5. Results may be included in patients' files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

PHQ-9 SCORING CARD FOR SEVERITY DETERMINATION

for healthcare professional use only

Scoring — add up all checked boxes on PHQ-9

For every ✓: Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1–4	Minimal depression
5–9	Mild depression
10–14	Moderate depression
15–19	Moderately severe depression
20–27	Severe depression

Figure 3. Patient health questionnaire (PHQ-9) (**A**) and instructions for use (**B**).

Table 4. Antidepressants.

TCA	SNRI	SSRI	5HT-2 Antag	DNRI	MAOI	NaSSA
Amitriptyline Nortriptyline Desipramine Imipramine	Venlafaxine (IR/XR) Duloxetine	Fluoxetine Sertraline Paroxetine Citalopram Fluvoxamine Escitalopram	Trazodone Nefazodone Isocarboxazid	Bupropion (IR, SR, XL)	Tranylcypromine Phenelzine	Mirtazapine

Table 5. Antidepressant safety [SADHART Trial, Glassman et al. 2002].

369 patients with major depression after myocardial infarction or unstable angina — randomized to sertraline 50–200 mg, or placebo.
Primary goal was to assess safety.
Secondary goal was to assess effect on cardiac outcomes.
Not powered to adequately test effect on morbidity or mortality (7 deaths occurred in the follow-up period). However, sertraline in absolute numerical terms was superior to placebo in rate of recurrent myocardial infarction, mortality, heart failure, and angina. Suggested need for larger study.
At least sertraline safe and effective in treatment of depression post-myocardial infarction.

Among the more commonly reported side effects are nausea, diarrhea, constipation, lethargy, activation, headache and sexual side effects. The antidepressant classes that effect norepinephrine have a small risk of increasing blood pressure. However, in most cases the effectiveness of these drugs in the treatment of depression far outweighs the possibility of increased blood pressure. Should that occur, and the patient is already on antihypertensive medication, the blood pressure increase may be handled simply by adjusting those medications. Monoamine oxidase inhibitors are excellent medications for the treatment of depression, but have strong logistical limitations. Oral forms in the United States require dietary limitations of tyramine to prevent acute hypertensive reactions. MAOIs also have the risk of hypertensive crisis if patients use sympathomimetic drugs like decongestants. The most common side effect of MAOIs is hypotension. The relatively new MAOI, the selegiline skin patch, avoids the need for dietary tyramine restriction at low dose, but carries the same risks as the oral forms regarding drug-drug interactions of hypertensive crisis or serotonin syndrome. The serotonin syndrome is a condition of excessive serotonin action manifested by a wide variety of findings that can include tachycardia, shivering, diaphoresis, mydriasis, myoclonus, overreactive reflexes, hypertension, hyperthermia, agitation and hypervigilance.

The selection of antidepressants should also take into consideration drug-drug interaction (DDI) risks. Some of the SSRIs can inhibit P450 isoenzyme systems, whereas others are far less likely to. (Tables 6, 7). For example, although fluoxetine and paroxetine may be effective antidepressants, they are potent inhibitors of multiple P450 isoenzyme systems and could elevate serum levels of beta blockers and warfarin above what would be expected for the oral dose given. In this era of multiple specialist care, with the potential for multiple handoffs of patient care, initial safe selection of an antidepressant is important.

The mechanism of action of the antidepressants can also somewhat guide the selection of medication. While all antidepressants can theoretically improve or remit the entire constellation of depressive symptoms, these different mechanisms of action might preferentially impact certain symptoms more than others. For example, the patient with significant problems with energy, motivation and drive may do well with the DNRI bupropion or an SNRI such as venlafaxine; patients with anxiety, impulsivity and aggression could perhaps do better with an SSRI (Fig. 4).

Knowledge of how the different antidepressants work on the neurophysiology (Table 8) also helps inform selection, especially of second or third choice antidepressants. For example, it does not make clinical sense to use a third SSRI antidepressant if two thus far have not been helpful. Knowledge of the mechanisms of action can be important in treatment-resistant cases that have not had

Table 6. P 450 Isoenzyme inhibition.

	3A4	2D6	2C19	2C9	1A2
Escitalopram	0	0	0	0	0
Citalopram	0	X	0	0	X
Sertraline	X	X	XX	X	X
Paroxetine	X	XXX	X	X	X
Fluoxetine	XX	XXX	XX	XX	X
Fluvoxamine	XXX	0	XXX	0	XXX
Venlafaxine	0	X	0	0	0
Mirtazapine	X	X	0	0	0
Duloxetine	0	XX	0?	0	0/X
Desvenlafaxine	0	0	0	0	0
Bupropion	0	XXX	0	0	0
Nefazodone	XXX	0	0	0	0

X — low, XX — moderate, XXX — strong

Table 7. Metabolic pathways of some common medications.

3A4	3A4	2D6	2C19	2C9	1A2
Dextromethorphan	**Diltiazem**	Codeine	Lansoprazole	Diclofenac	Amitriptyline
Erythromycin	**Nifedipine**	Dextrometh orphan	Omeprazole	Ibuprofen	Imipramine
Haloperidol Imipramine Methadone Prednisone	Verapamil Indinavir Nelfinavir	Desipramine Perphenazine Risperidone	Rabeprazole	Naproxen	Clomipramine
Sertraline	Ritonavir	Nortriptyline	Citalopram	Piroxicam	Clozapine
Tamoxifen	Saquinavir	Fluoxetine	Diazepam	Tolbutamide	Caffeine
Alprazolam	Carbamazepine	Fluvoxamine **Timolol**	Imipramine	Amitriptyline	Cyclobenzaprine
Diazepam	Cisapride	Venlafaxine	Mephenytoin	Celcoxib	Estradiol
Midazolam	Citalopram	**Propranolol** **Metoprolol**	**R-warfarin**	Fluoxetine	Haloperidol
Triazolam	Clomipramine	Thioridazine		Phenytoin	Acetaminophen
Amiodarone	Clonazepam Cyclobenzaprine Cyclosporine	Tramadol **Captopril** **Mexiletine**		Sulfamethoxazole Tamoxifen **S-warfarin**	Propranolol Theophylline

adequate results often with multiple antidepressants with or without augmentation strategies.

The cost of medications is playing an increasingly important role for patients. Generic forms often have substantially lower co-pays. This of course varies by insurance carrier. Since many patients need to remain on antidepressants for long periods of time, cost factors to the patient will greatly affect compliance, and hence need to be a factor in the medication choice.

SSRIs are considered typical first-line antidepressants in depressed cardiac patients. Among them, good options include sertraline or citalopram, both of which have favorable side effect and DDI profiles, and also have generic forms. Escitalopram can also be used, having a favorable side effect and drug-drug interaction profile but it currently does not have a generic equivalent. While mild levels of depression can respond favorably to non-medication interventions such as counseling, moderate to severe forms of depression are best treated with antidepressants; psychotherapy alone will not be sufficient. However, the addition of psychotherapy can further improve response rates.

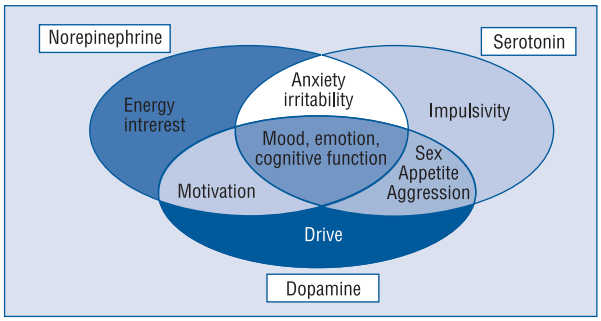

Figure 4. Several neurotransmitters are involved in regulating mood [Stahl SM. Essential psychopharmacology: Neuroscientific basis and practical applications. 2nd Ed. Cambridge University Press, Cambridge, UK 2000; 152].

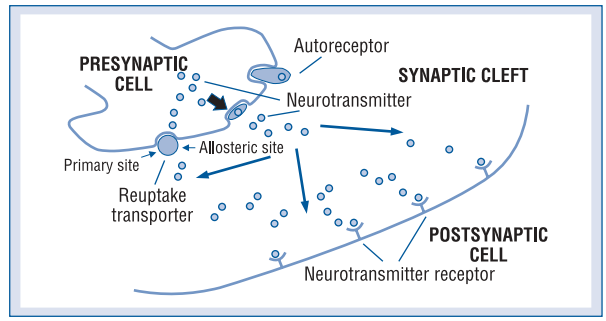

Figure 5. Neurotransmitters: mechanism of action [Nemeroff CB. Sci Am, 1998; 43–49 (with sub-site addendum)].

Steve's severe major depression warrants use of an antidepressant and referral for psychotherapy. Steve's cardiologist referred him quickly to the consulting mental health team. The consulting psychiatrist assessed his case and determined that sertraline was a reasonable choice. Antidepressants should be initiated promptly for two reasons: the full onset of action in major depression is typically four to six weeks; and the greatest impact of depression on the cardiac patient is within several weeks after the acute MI. The patient was started on sertraline 50 mg, and was increased in two 25 mg increments each over a week to a total daily dose of 100 mg. The consulting psychiatrist referred Steve back to the cardiologist for ongoing medication management, and also made a referral for the patient for psychotherapy. The consulting psychiatrist remained available to the cardiologist as needed and also saw the patient four and eight weeks after starting the sertraline to assess medication tolerability and to monitor symptoms.

Most guidelines recommend a duration of antidepressant use of about a year. This covers the acute phase, which is approximately 12 weeks when symptoms typically go into remission, and the continuation phase, approximately the next six to nine months when the major depressive episode is considered recovered. Discontinuing the antidepressant too soon risks symptoms returning before the depressive episode is fully treated. At the point of recovery, it is necessary to decide whether to taper off slowly over weeks to months and watch for signs of relapse or to continue longer. The consulting psychiatrist will take into consideration whether this is a first episode or a recurrent one, the severity of the symptoms, the nature of the patient's circumstances, and the patient's awareness of signs of relapse, all of which can impact the decision of how long to use the antidepressant. Patients with three or more previous depressive episodes should remain on antidepressants indefinitely.

When the time comes to discontinue the antidepressant, patients fare better when medication is tapered off. Patients who stop antidepressants abruptly risk acute SSRI Discontinuation Syndrome. This is a syndrome of acute depletion of serotonin in the synapse brought about when the serotonin reuptake inhibition is abruptly stopped, causing the flow of neurotransmitter, in this case serotonin, into the presynaptic cell, depleting the synapse of neurotransmitter (Fig. 5). Symptoms can include severe flu-like symptoms: headache, diarrhea, dizziness, chills, nausea, vomiting and fatigue. There may be insomnia, agitation, impaired concentration, vivid dreams, depersonalization, irritability and suicidal ideation. These symptoms can persist for up to three weeks.

Table 8. Clinically significant consequences of stimulating post-synaptic neurotransmitter receptors.

5 HT 1D	5 HT 1A	5 HT 2	5 HT 3
Antimigraine actions	Antidepressant actions Anti-obsessive compulsive properties Anti-panic and anti-social phobia properties Anti-bulimia properties	Agitation Akathisia Anxiety Panic attacks Insomnia Sexual dysfunction	Nausea Gastrointestinal distress Diarrhea Headache

In addition to the risk of the discontinuation syndrome, abruptly stopping the antidepressant poses a greater risk of relapse of depression, by not allowing the brain to readjust to neural mechanisms affected by the drug. At times, it can be difficult to distinguish SSRI Discontinuation Syndrome from a recurrence of depression. A clinically useful way to do so is to reinstitute the antidepressant. If the patient's symptoms remit in hours, up to a day or two, it is likely to be SSRI Discontinuation Syndrome. If it takes several days or even weeks to get better, it is probably a true recurrence of depression.

Individual counseling/therapy

Research suggests it is important for the initial mental health (MH) referral to be made quickly, especially after MI, as depression appears to have the greatest negative impact on the cardiac patient within weeks of the acute event [46]. Additionally, during the initial critical period, the patient's treating MH team has the best opportunity to engage the patient and establish a strong connection.

In Steve's initial therapy session, special attention was paid to his emotional and cognitive symptoms. Research has shown that patients meeting the criteria for major depression based on emotional/ /cognitive symptoms alone were at greater risk of mortality compared to those meeting diagnostic criteria based on somatic symptoms [46, 47]. Feelings of hopelessness are associated with risk of fatal and nonfatal cardiac events [48] and predict later CHD mortality in initially healthy individuals [49]. Steve was provided with the rationale for cognitive-behavioral treatment (CBT), a specific form of psychotherapy found to be highly efficacious in the treatment of depression. The Enhancing Recovery in Coronary Heart Disease (ENRICHD) trial, funded by the National Heart Lung and Blood Institute (NHLBI), found that up to six months of individual CBT (with up to three months of group therapy where feasible) significantly reduced depressive symptoms in patients versus a care-as-usual group [50]. Additionally, a recent meta-analysis on psychological treatment of cardiac patients found that adding treatment such as CBT to usual care reduced mortality in patients for at least the first two years [51]. Benefits were greater for men than for women. Individual therapy can help patients adhere to treatment recommended by the cardiac team and increase maintenance of healthy behaviors to reduce future risk. Steve was made aware that psychotherapy with patient's post-MI can be challenging. This is because a key component of treatment for depression is often behavioral activation, which involves getting patients to engage in activities that get them moving and have previously brought them joy or satisfaction, such as exercise. It was important that Steve agreed to be upfront about his limitations and for the clinician to discuss recommendations with his cardiologist to determine appropriate activity levels. Other elements of CBT were then explained to Steve, including the assignment of homework to encourage the continuation of treatment outside of sessions [52]. Steve was informed that treatment would involve approximately 15 weekly sessions, with follow-ups as appropriate. The treatment would utilize three main techniques: 1) behavioral activation, within the confines of activity restrictions post-MI; 2) active problem-solving to improve skill deficits, such as interpersonal communication and coping with stress; and 3) cognitive restructuring to challenge negative thoughts that may be maintaining depression and poor self-care.

At the start of each psychotherapy session, Steve completed a measure of depressive symptoms and reported any change in mood or activity over the past week. Steve and his therapist reviewed the previous session and went over any questions. Homework was reviewed, such as weekly activity logs, thought records and readings. Together, they then set the session's agenda and prioritized agenda items. The next steps involved tackling the agenda items, assigning new homework, and recapping the session. Steve and his therapist worked on building a strong rapport, which helped engage Steve in treatment and reinforced his completion of homework on time. Several techniques were applied to build skills and reduce depressive symptoms. These included:

- role playing;
- self monitoring;
- behavior chains to reduce risky behaviors;
- challenging negative thoughts about self, world, and the future;
- identifying negative automatic thoughts that give rise to feelings of depression and examining evidence for and against those thoughts and providing ways to reframe them into positive thoughts;
- relaxation training to reduce stress and anxiety;
- assertiveness training to increase ability to express anger and irritability in a healthy, productive way;
- active problem solving.

Feedback was provided every few weeks to Steve's referring cardiologist.

At the end of 15 sessions, Steve reached his goals of reporting a significant reduction in symptoms, a significantly lower PHQ-9 score, re-engaging in activities and reporting increased pleasure in those activities, and following a healthier diet. Collateral information from his wife was helpful in knowing his irritability at home decreased and he was able to communicate more effectively. A relapse prevention plan was made, in which Steve listed triggers for negative mood (e.g. decreased socialization, increased stress at work) and the coping strategies implemented during the course of treatment that he found effective. Steve was encouraged to schedule a follow-up appointment in three months. Red flag symptoms i.e. those that would herald recurrence of the depression, were identified. Steve expressed an understanding of his high risk symptoms, and that if they returned, he should resume therapy.

Mindfulness-based group therapy

A timely and targeted mindfulness-based group therapy is another intervention that can be of value for Steve's presenting symptoms of hopelessness, irritability, and his report of experiencing high levels of stress.

Mindfulness-based treatment practices have been a significant innovation in Western health care since the 1970s. One of the first scientific papers describing mindfulness was co-authored by the cardiologist, Herbert Benson MD [53]. Benson followed this with his book entitled The Relaxation Response [54]. Fellow New Englander Jon Kabat-Zinn PhD established the Center for Mindfulness in 1979 at the University of Massachusetts Medical Center. He described the practice of Mindfulness Based Stress Reduction (MBSR), which has subsequently been extensively reviewed [55]. Kabat-Zinn says: "Mindfulness means paying attention in a particular way: on purpose, in the present moment, and non-judgmentally." Such an intentional wakeful state is experienced in a variety of mindfulness meditation practices that are taught to patients. Steve can be taught a systematic way of observing his own affect, stepping back so that his emotions do not 'hijack' his brain. Instead of becoming a human pressure cooker, unable to delegate, unable to express his anger without escalating and yelling, Steve can learn to accept the moment as it is, with a minimum of harsh self-judgment, which in turn can allow him to use newly learned behavioral skills to communicate and problem-solve the issues at hand.

Whether Steve knows it or not, newly learned behavioral changes result in a helpful feedback loop of experience, changing the brain even as the brain changes the experience.

Findings in this area of mind-body/body-mind work highlight the neuroplasticity and neurogenesis capabilities of the brain. Significant increases in left frontal brain activation have been demonstrated with mindfulness training. This shift in brain activity is a pattern associated with positive affect [56]. Such increases in neural activity have the potential to create new synaptic connections. Research reveals that experience may stimulate the growth of new neurons [57].

Mental health theorists and practitioners in the 1980s and 1990s began to combine CBT interventions with the well-documented benefits of Kabat-Zinn's work in Mindfulness Based Stress Reduction. Marsha Linehan PhD developed dialectic behavior therapy [58]. Dialectic behavior therapy is a skills-based CBT model that incorporates brief practices of mindfulness. This approach has been helpful particularly with a population of patients who struggle with rapidly shifting affect, feelings of abandonment and who present at high risk for self harm behaviors. Zindel Segal and others have created the approach known as mindfulness based cognitive therapy, particularly for patients who have had more than three episodes of depression and are now in remission [59]. Steven Hayes and others have developed an approach to therapy referred to as acceptance and commitment therapy [60].

One of the common denominators in these various applications of CBT and mindfulness is the importance of accepting the present moment for what it is, even with its problems. In this case, Steve can learn that his experience of hopelessness, low self esteem, anger or whatever distress he experiences exists in just *this* moment, a moment that then continually changes. As Steve improves his ability to accept the present moment, he is simultaneously better able to move toward change, similar to the pitcher in an important baseball game who walks in the tying run, and who can accept the reality of this unwanted event, is able to let it go and be ready for the next pitch.

A beneficial way of teaching mindfulness and CBT skills is to use the modality of a time-limited structured group therapy setting. In such a group of six to 12 patients, meetings are held weekly for several weeks. Patients focus on individually defined goals. Daily home practice of skills is encouraged between sessions. The group also offers the

benefits of social support and social acceptance. Being with others who are also managing the challenges of illness can normalize one's experience of emotional pain, cardiac disease and other illness. This is a well known effect in group psychotherapy. Humans are constitutionally built as relational beings, and are profoundly affected by the experience of relationship. Woody Allen was not alone in describing our need for relationship [61]. With the exquisite intimacy of experience changing the brain, we are beginning to understand the deep nature of how relationships shape our lives and brains. This has led some researchers to describe an interdisciplinary field of interpersonal neurobiology [57].

Emotional health depends in many ways on the presence of community (which can be present in group therapy), one's ability to use the power of thoughts to effect mood and behavior (cognitive therapy), how we subsequently act (behavior therapy) and being able to 'stop and smell the roses', or at least notice from time to time that there are roses right in front of us (mindfulness).

Collaborative care for cardiac patients

It is vitally important to address the psychiatric issues in the course of treating patients with heart disease. While cardiologists can, and routinely do, address some of these issues, the availability of a consultation psychiatrist or mental health practitioner can provide expertise in the care of these patients. Collaborative care between medical providers and psychiatric providers is well known to result in better patient outcomes. This effect is particularly important in cardiac patients, given the link between cardiac outcomes and emotional issues. Behavioral interventions in patients with chronic illness can result in better psychosocial outcomes [62]. Gilbody et al. [63] conducted a meta-analysis of 37 randomized control trial studies covering 12,355 patients, and clearly found that collaborative care for depression produced better health outcomes, even five years later. The authors attribute the results to better patient compliance and the active involvement of MH providers, often case managers. Katon and Unützer [64] in an editorial on the Gilbody study emphasize how collaborative care results in better clinical outcomes. Beyond the clinical outcomes, collaborative care can be helpful to primary physicians in deciding on the next steps of antidepressant use or other treatment strategies, and it can result in neutral or positive healthcare cost-offset as well [65–67].

Commonly, cardiologists refer to available mental health clinicians in their local area, subject to the availability of those clinicians. This is considered a coordinated relationship. Blount outlines three types of collaborative care links between medical physicians and mental health providers [68]. The coordinated relationship is one in which providers who practice in different geographical locations refer patients to one another. This is a common type of linkage. A second model is that of co-located care. In this type of link, different specialists work in the same practice setting, for example within the same office building. This arrangement reduces the geographical distance and thereby reduces some barriers to coordination of care in specific patient cases. It also helps medical and MH providers become accustomed to the different 'cultures' and 'languages' of the different specialties. The third model is that of integrated healthcare. In this model, the MH provider is embedded within the practice of the medical provider. This model has the benefits of the co-located model plus it further reduces geographical barriers and greatly enhances coordination of care. For example, providers can informally consult one another about specific patient issues regularly. It also increases familiarity and further minimizes the specialty-specific cultural differences, and can minimize patient compliance problems when cardiologists make mental health referrals.

All models of collaborative care rely on specific clinicians working with each other. Good collaboration requires several key ingredients, among them a good working relationship between providers, regular communication and a degree of geographic proximity [69]. The University of Rochester collaborative care model incorporates ingredients of the coordinated and co-located models. The outpatient psychiatric consultation program is located within the University of Rochester Medical Center, a tertiary care and regional referral facility. Regulatory and staffing issues limit using an integrated model at this point, (that is, being in the same office suite), but the Cardiology and Psychiatry practices remain within the Medical Center. The University of Rochester model uses a team of three specific MH clinicians, a psychiatrist and two mental health clinicians, dedicated to working with the cardiology practices. This facilitates development of an interactive treatment team, which in turn enhances ongoing collaboration and coordination of care. In addition to a dedicated team of psychiatric providers, the psychiatric team uses a dedicated secretary. In the same way that relationships are

built between the cardiologists and mental health providers, the use of a dedicated secretary facilitates coordination between the psychiatry front office and front office personnel of the cardiology practices. This can smooth the referral process and help resolve communication or coordination issues. The Department of Psychiatry retains the specialized mental health insurance and billing functions.

Psychiatrists and MH providers who are certified or trained in consultation work, or who are comfortable dealing with medically ill patients often on various medications, may offer additional advantages in collaborative care arrangements. The skills traditionally important in inpatient consultation/liaison psychiatry work are also important in outpatient collaborative care settings: medical-psychiatric differential diagnosis, ability to address unexplained physical symptoms and pain, psychopharmacological expertise in medically ill patients and a high degree of knowledge in secondary psychiatric disorders [70]. The University of Rochester model of collaborative care utilizes such MH clinicians.

The University of Rochester model uses a consultative format when seeing patients. This means referred patients are seen in consultation to the cardiologists, to whom treatment recommendations are given. The patients are then referred back to the cardiologists who provide the ongoing care for the patients. In this regard, patients are co-managed. This process ensures the psychiatric clinicians can remain regularly available to see new patients promptly, a very important factor for referring cardiologists. Were the mental health clinicians to fill their caseloads with patients requiring ongoing mental health care, there would be little if any time for new cases, or waiting times for new patients could be prolonged. When the consulting psychiatrist identifies referred patients as being in need of ongoing or more intensive psychiatric care, the psychiatrist can refer such patients into appropriate MH care. Thereafter, the psychiatrist acts as a liaison as necessary between the cardiologist and the specialized MH clinicians. This liaison function offers the cardiologist ease of access to MH information about their patients, utilizing their collaborative link with their psychiatric consultant.

Ease of access for the cardiologist is crucial. We use a dedicated phone number for referrals, given only to referring providers. This phone number is different from the number of the general MH clinic. Finally, patient-specific communication, which occurs regularly, involves clinical notes contained in an electronic medical record, and e-mail and phone contacts between providers.

Summary

The treatment of stress, anxiety and depression in cardiac patients can improve cardiac outcomes.

Psychotropic medications, including antidepressants, have an important place in the treatment armoury. In addition, CBT and group-based mindfulness interventions have a role in treating cardiac patients and improving cardiac outcomes. The use of a collaborative model, which maximizes communication and contact and minimizes geographic distance between cardiac and psychiatric providers, can also improve cardiac outcomes and can be of significant value to cardiologists in managing psychiatric aspects in their patients.

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