The Epidemiology, Pathophysiology, and Management of Psychosocial Risk Factors in Cardiac Practice

The Emerging Field of Behavioral Cardiology

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Observational studies indicate that psychologic factors strongly influence the course of coronary artery disease (CAD). In this review, we examine new epidemiologic evidence for the association between psychosocial risk factors and CAD, identify pathologic mechanisms that may be responsible for this association, and describe a paradigm for studying positive psychologic factors that may act as a buffer. Because psychosocial risk factors are highly prevalent and are associated with unhealthy lifestyles, we describe the potential role of cardiologists in managing such factors. Management approaches include routinely screening for psychosocial risk factors, referring patients with severe psychologic distress to behavioral specialists, and directly treating patients with milder forms of psychologic distress with brief targeted interventions. A number of behavioral interventions have been evaluated for their ability to reduce adverse cardiac events among patients presenting with psychosocial risk factors. Although the efficacy of stand-alone psychosocial interventions remains unclear, both exercise and multifactorial cardiac rehabilitation with psychosocial interventions have demonstrated a reduction in cardiac events. Furthermore, recent data suggest that psychopharmacologic interventions may also be effective. Despite these promising findings, clinical practice guidelines for managing psychosocial risk factors in cardiac practice are lacking. Thus, we review new approaches to improve the delivery of behavioral services and patient adherence to behavioral recommendations. These efforts are part of an emerging field of behavioral cardiology, which is based on the understanding that psychosocial and behavioral risk factors for CAD are not only highly interrelated, but also require a sophisticated health care delivery system to optimize their effectiveness. (J Am Coll Cardiol 2005;45:637–51) © 2005 by the American College of Cardiology Foundation

Various lifestyle behaviors promote the development and clinical manifestations of coronary artery disease (CAD), including an unhealthy diet, physical inactivity, and smoking. Emotional factors and the experience of chronic stress also promote atherosclerosis and cardiac events, as previously reviewed (1). However, although cardiologists are accustomed to managing lifestyle behaviors such as overeating and physical inactivity, they are less likely to assess and treat psychosocial risk factors, perhaps because of their limited familiarity with effective strategies and recommendations. A potential dilemma is that, on the one hand, it is not the function of cardiologists to serve as mental health professionals; on the other hand, the strong and robust relationship between psychosocial risk factors and CAD suggests that cardiologists need to be proactive in addressing this important aspect of patient care. What then should the cardiologist’s role be? Herein, we address the question of the role of the cardiologist by exploring various ways for effective clinical involvement. We also provide an update on the epidemiologic and pathophysiologic evidence linking psychosocial factors and the progression of CAD, emphasizing recent select studies rather than providing a comprehensive review, and suggesting areas for future research. Thus, this review is designed to provide an integrated understanding of how psychosocial risk factors influence the current and future practice of cardiology.

EPIDEMIOLOGY

Psychosocial factors that promote atherosclerosis and adverse cardiac events can be divided into two general categories: emotional factors and chronic stressors. Emotional factors include affective disorders such as major depression and anxiety disorders as well as hostility and anger. Chronic stressors include factors such as low social support, low socioeconomic status, work stress, marital stress, and caregiver strain.
Emotional factors. Among emotional factors, depression has been studied in recent years. Depressive disorders vary from mild (subclinical) depressive symptoms to classic major depression. According to the Diagnostic and Statistical Manual of Mental Disorders–4th edition, depression is characterized by severely depressed mood and/or anhedonia (inability to take pleasure in life) that lasts for two weeks or more and is accompanied by significant functional impairment and somatic complaints. Research in this area has evaluated the effects of depression in both initially healthy individuals and in patients with known CAD. Depression plays a role in promoting CAD events in both cohorts (1). Most epidemiologic studies have primarily assessed depressive symptoms rather than major depression. Data indicate the presence of a strong consistent gradient between the level of depressive symptoms and the likelihood of adverse cardiac events, beginning at relatively low levels of depressive symptoms (2) (Fig. 1). Such data suggest that the pathophysiologic effects of depression may be triggered by even mild subclinical symptoms.

Major depression has been studied less commonly, partly because its identification requires a formal interview performed by trained professionals. However, consistent with the evidence derived from assessing symptom measures, major depression has also been found to be associated with a highly significant increase in adverse cardiac events, over and above that observed for the presence of depressive symptoms alone (3).

Epidemiologic studies have also considered two other emotional factors relative to prognosis: anxiety and anger/hostility. Those that have examined the risk of cardiovascular outcomes associated with anxiety disorders are limited. Three large studies have shown a significant relationship between phobias and sudden cardiac death (1), but data linking other forms of anxiety to CAD are relatively scant or conflicting and more work is needed. Although hostility and chronic anger have been linked to cardiovascular outcomes in a number of studies, results have been generally mixed. Several factors may contribute to inconsistent findings in this area. Measures used to assess anger and hostility have varied widely, making it difficult to compare results. A recent study suggests that there is some self-denial and lack of self-awareness associated with self-reported hostility (4). This may be overcome by using a structured interview approach (4), but the approach has not been widely tested. Interestingly, a number of recent studies have demonstrated a relationship between hostility or anger and measurements of subclinical atherosclerosis (5–8) and also have linked hostility to progression of atherosclerosis during serial coronary angiography (9). Such findings suggest that hostility and chronic anger merit further study as potential psychosocial risk factors.

Chronic stressors. A variety of adverse life circumstances that promote chronic stress have been evaluated for their relationship to adverse cardiac outcomes. For instance, whereas the presence of high levels of social support is known to promote psychologic and physical well being, a consistent literature indicates that low levels of social support are health damaging. Although historically there has been little integration of differing theories of social support, there is increasing agreement that social support can be divided into two broad categories: social networks, which describe the size, structure, and frequency of contact with the network of people surrounding an individual; and functional support, which may be further divided into received social support, which highlights the type and amount of resources provided by the social network, and perceived social support, which focuses on the subjective satisfaction with available support or the perception that support would be available if needed. Received and perceived social support are often further delineated by type, including instrumental (e.g., help getting tangible tasks done), financial (economic support), informational (providing needed information), appraisal (help evaluating a situation), and emotional support (e.g., providing emotional support, feelings of being loved). The term “tangible support” also is used to describe types of support that are readily seen or quantified, such as instrumental or financial support. Both inadequate structural and functional support have been consistently linked to the occurrence of cardiac death and all-cause mortality in many studies (1). For example, low structural support has been associated with increased mor-
characterizes job imbalance. High demand but low decision latitude characterizes job strain. In the effort-reward imbalance model (right), increased job effort may result from either extrinsic demands or personal overcommitment, and “reward” may occur in the form of money, recognition, prestige, security, or career opportunities. High effort with low reward characterizes job imbalance.

Marital stress also represents a chronic stressor with apparent pathophysiology effects (27,32,33). For instance, Ort-Gomer et al. (32) reported that following myocardial infarction (MI), women with concomitant marital stress had a higher frequency of recurrent cardiac events during a five-year follow-up compared to those with less marital stress. These data are supported by a recent study that found a higher prevalence of subclinical atherosclerosis, and accelerated progression over time, among healthy women reporting marital dissatisfaction (Fig. 3) (34), supporting the assertion that marital stress is atherogenic.

Caregiving strain is an increasingly prevalent stressor that has recently been studied for potential cardiovascular sequelae (35,36). In the Nurses’ Health Study, caregiving for an ill or disabled spouse was associated with a nearly twofold adjusted risk ratio for experiencing an adverse cardiac event during a four-year follow-up period (35). However, this report did not stratify patients based on the emotional appraisal of their caregiving experience. Because other research indicates that highly meaningful and altruistic experiences can be of psychologic benefit (37), it is possible that the effects of caregiving are dependent on the meaning...
attached to such activities. In support, another study observed that when caregivers were divided into those with and without a sense of emotional strain during caregiving, only those reporting strain had an increased death rate during follow-up (36).

**Clustering of psychosocial risk factors.** Although we have discussed emotional factors and chronic stressors as separate entities, they frequently cluster. For example, individuals who experience job strain tend to have higher rates of depression compared to those who do not report strain (38). The strong overlap between chronic stress and emotional factors suggests that any life situation that has the capacity to evoke chronic negative emotional responses may promote heart disease. For instance, a recent study found that childhood maltreatment (39) was associated with a significant increase in both depression and cardiovascular disease among adult women. Similarly, exposures ranging from the death of a child to adverse wartime experiences may potentially affect the risk of CAD development and should be candidates for study.

**Comparison of psychosocial risk factors with traditional CAD risk factors.** The characterization of psychosocial risk factors as “major” CAD risk factors has been debated. However, more consistent and reproducible outcome studies confirm that psychosocial risk factors such as depression, poor social support, and low SES represent potent CAD risk factors. Furthermore, many reported studies now link psychosocial risk factors to the presence of subclinical atherosclerosis or its progression, as measured by carotid ultrasonography (5–8,29–31,34,40,41). Meta-analyses of psychosocial studies have been limited by the use of varying measures and inconsistent methods for calculating risk ratios. However, a recent meta-analysis of outcomes associated with depressive symptoms indicates a relative risk that is comparable to those noted for traditional CAD risk factors reported from the Framingham study (Fig. 4) (3,42).

This observation is supported by the recently reported INTERHEART case-control study, which uniquely assessed eight coronary risk factors and a composite index of psychosocial factors within a single standardized international population of 12,461 acute post-MI patients and 14,637 matched controls gathered from 52 countries (43). The psychologic index was necessarily limited by the study’s design to either brief or even single-item assessments of depression, locus of control, perceived stress at home or...
work, moderate to severe financial stress, and experience of adverse life events. Nevertheless, the odds ratios and population-attributable risk for acute MI by this limited subjective measure of psychosocial stress was substantial, comparable to those noted for other major CAD risk factors (Fig. 5). In addition, this psychosocial index remained a robust predictor of MI independent of geographic or ethnic context (26).

Moreover, for a variety of reasons, the risk associated with psychosocial factors may actually be greater than such statistical evidence suggests. First, behavioral and metabolic risk factors tend to aggregate disproportionately among individuals with psychosocial stress (1). However, this potentially powerful effect is reduced because of the statistical convention to adjust psychosocial risk ratios for behavioral and metabolic risk factors. Second, because measures of psychosocial stress may be imprecise, they may underestimate the relationship between psychosocial stress and CAD outcomes. For example, although depressive disorders are generally episodic, the scales used to measure self-reported depressive symptoms assess only the presence of relatively current depressive symptoms. Thus, it is not surprising to find that the chronicity and level of depressive symptoms are together more strongly associated with measures of atherosclerosis compared with symptom levels alone (40). Third, psychosocial risk factors tend to aggregate. Such clustering is associated with an increased likelihood of cardiac events (1) and more subclinical atherosclerosis (8,9).

Future epidemiologic directions. In contrast to the data linking negative emotional states and chronic stress to CAD, the potential protective effect of positive psychologic factors has not been extensively investigated. Building on work in other areas, we suggest that one potential direction for clinical investigations in this neglected area could be to explore the notion of flexibility as it relates to mental health (44). In the physical domain, the ability to demonstrate variability in response to stressors may be associated with better clinical outcomes (45). Similarly, having the capacity to respond to situations in a variety of different ways (i.e., to flexibly adapt one’s emotional and coping responses to any given situation) may be associated with better mental health. We consider three psychologic components that may be central to developing emotional and coping flexibility (Fig. 6). One key component is “vitality,” which refers to the presence of energy and enthusiasm and a sense of aliveness (46). It is characterized by two positive emotions, joy and interest, and is fueled by both a sense of purpose and a sense of self-worth. Vitality may be considered both restorative and regenerative and, as such, connotes a sense of freshness and positive excitement. Conversely, when someone lacks vitality, the likelihood of becoming excited and investing energy toward goals and in interactions with others is...
diminished. The availability of this energy promotes two key adaptive responses (which may in turn promote vitality): development of various positive response mechanisms (such as patience, discipline, and maintaining friendships) and emotional competence, or the ability to regulate emotions across a range of situations (47). An important aspect of emotional competence is the ability to either enhance or suppress emotional expression, a trait that may be termed “emotional flexibility,” as discussed by Bonanno et al. (48) and others.

From this perspective, depression and various exhaustive states can be viewed as a long-term deficit in vitality and an escalating inability to be flexible and responsive to life and daily challenges. Anxiety and anger can also be viewed as emotionally inflexible responses, with the constant negative emotions dissipating energy and taxing positive coping mechanisms. Job strain is also an excellent example of a situation that can drain energy and vitality. For example, a recent study has demonstrated that chronic job strain can lead to exhaustion and an inability to unwind after work (28). Such sequelae can increase the risk for adverse cardiac events (49). By contrast, professional, marital, interpersonal, and avocational activities that require effort but that also promote joy and interest serve to preserve vitality and flexibility.

Early emotional theorists suggested that positive emotions such as joy might provide recuperative power. Support for this concept is provided by recent data showing that positive psychologic factors can dampen physiologic reactivity to negative emotional stimuli (50). Similarly, individuals who score high on the trait of forgiveness (51) or who are provided with social support (52) demonstrate lower heart rate and blood pressure elevations during laboratory mental stress. Other data indicate that positive emotions can enhance immune function (53). Evaluation of the impact of positive psychologic factors upon clinical outcomes is also limited and recent. In the largest study to date, Kubzansky et al. (54) conducted a 10-year follow-up study of 1,306 men from the Normative Aging Study, who were assessed for optimistic versus pessimistic “explanatory style” (i.e., how one explains the causes of bad events). Stratification of individuals according to optimistic, neutral, and pessimistic explanatory styles revealed a gradient relationship between levels of optimism and cardiac outcomes, with optimism halving the risk for cardiac events. A separate measure of dispositional optimism has been linked to more favorable outcomes following bypass surgery (55). A strong relationship has also been noted between positive emotions and longevity in the long-term follow-up of nuns whose diaries in early adult life were assessed for positive emotional content (56). Such findings suggest the value of further exploring positive psychologic factors that may promote health or protect against disease.

**PATHOPHYSIOLOGY**

Emotional disturbance and chronic stress can have a profound impact on the central nervous system, including increased output from the sympathetic nervous system and the HPA axis. Chronic stimulation from these central outputs can induce a wide variety of pathophysiologic responses, as displayed in Figure 7. Depression has been particularly studied in this regard. Chronic stimulation of the HPA axis by depression frequently results in hypercortisolism, blunted HPA activity, and diminished feedback control, as evidenced by nonsuppression of cortisol secretion.
following dexamethasone suppression. When present, hypercortisolemia is associated with suppression of growth and sex hormones. Heightened stimulation of the sympathetic nervous system is also common in depression and is associated with higher concentrations of circulating plasma norepinephrine and an increase in total body sympathetic activity (57). As a consequence, depressed patients commonly manifest higher resting heart rates than healthy controls and exhibit autonomic nervous system dysfunction, including diminished heart rate variability, baroreflex dysfunction, and increased QT variability (57).

Hypercortisolemia, in association with blunted growth and sex hormones, promotes central obesity (58), which may occur despite overall weight loss, and an increase in peripheral and portal fatty acids. These metabolic changes also contribute to more insulin resistance and diabetes among depressed subjects, and a higher frequency of diabetic complications (59). Depressed patients manifest substantial platelet abnormalities, including increased concentrations of beta-thromboglobulin and platelet factor 4 and increased concentration of functional glycoprotein IIb/IIIa receptors. In addition, there is evidence that depression is associated with increases in C-reactive protein, interleukin-6, tumor necrosis factor, and other inflammatory proteins (61). The potential mechanism for this association may be complex, involving not only stimulation of the HPA axis and the sympathetic nervous system but also potential synergy induced by peripheral effects, such as hyperglycemia (62). More recent data indicate that depression is associated with a heightened incidence of endothelial dysfunction among various cohorts, including young and otherwise healthy depressed patients (63). Finally, depression is also associated with decreased bone mineralization, which is the result of increased cortisol and decreased concentrations of growth and sex hormone concentrations, and probable interaction with local inflammatory proteins. Thus, depression is capable of inducing virtually the full spectrum of pathophysiologic effects noted in Figure 6.

**Future research directions.** Because other psychosocial risk factors have not yet been investigated as extensively as depression, the full spectrum of their pathophysiologic effects requires further study. In addition, we highlight three areas where clinical observations provide new research directions. First, the observation that cardiac event rates increase when psychosocial risk factors cluster has focused interest on explanatory mechanisms. Whether this increase is due to greater overall stress or the synergistic effects of stressors that evoke different pathophysiologies needs to be determined. The latter possibility is supported by recent data indicating distinct pathophysiologic differences according to the exposure of Watanabe Heritable Hyperlipidemic rabbits to two different chronic stressors: an unstable social environment versus social isolation. Both forms of stress produced more atherosclerosis compared to a control group, but the groups exposed to different forms of stress exhibited different metabolic consequences and patterns of accrued atherosclerosis (64).

Second, various data suggest links between chronic psychologic distress and certain adverse behaviors, such as overeating (65,66). New technologies that study brain function suggest that such links may be centrally mediated. Immunohistochemistry has been used to identify an anatomic chronic stress response network, localized to several specific brain centers, in a rat model of chronic stress (67). Whereas glucocorticoids help end acute stress responses by exerting negative feedback upon the HPA axis, glucocorticoids occupy central glucocorticoid receptors during chronic stress, with resultant activation of the chronic stress response network, including continued glucocorticoid production, in these experimental animals (66,67). This combination of chronic stress and high glucocorticoid levels appears to stimulate a preferential desire to ingest sweet and fatty foods (66). Further study indicates that glucocorticoids affect dopaminergic transmission in areas of the brain associated with motivation and reward (68). Positron emission tomography (PET) has been used to identify the presence of diminished dopamine D2 binding potential within midbrain systems under conditions of chronic stress in the cynomolgus monkey (69). In humans, PET studies have revealed that this area is involved specifically in food motivation (70), and that, like stressed monkeys, obese individuals also have decreased D2 receptor function in this same reward area of the brain, varying inversely with body mass index (71).

Third, data suggest that enhanced physiologic reactivity to acute stress is clinically important, linked to subclinical atherosclerosis (72,73) and interacting with known psychosocial risk factors to produce greater degrees of subclinical atherosclerosis (41). Clinical observations suggest that chronic stress, per se, may be an important cause for such enhanced physiologic reactivity (as exemplified in Fig. 7). For instance, depressed (57), hostile (74), and low-SES subjects (19) all manifest exaggerated physiologic responses to acute stressors. These observations are complemented by experimental animal studies that indicate that repeated exposure to a chronic stressor results in increased adrenal and pressor responses to acute novel stressors (66,75). Other animal research indicates that the mimicking of chronic stress by experimentally elevating glucocorticoids within the brain produces enhanced adrenocorticotropic hormone responses (76) and increases in both baseline arterial blood pressure (77) and blood pressure and heart rate responses to an acute novel stressor (78). Research that further elucidates the neurophysiology of the chronic stress circuitry, and the mechanisms of neuroplasticity that produce long-term stress-induced changes in the control of physiologic functions, could pave the way for understanding
and mitigating the adverse effects of chronic stress in cardiovascular disease.

**FACTORS LINKING PSYCHOSOCIAL RISK FACTORS AND CARDIAC PRACTICE**

As illustrated in Figure 8, there are important reasons that cardiologists should be interested and skilled in recognizing and managing psychosocial risk factors in practice. We have already discussed two compelling reasons: psychosocial risk factors are strongly linked to the development of adverse cardiac events and cluster with adverse behaviors that promote CAD. We now discuss four additional factors that link psychosocial risk factors to cardiac practice.

First, psychosocial risk factors are highly prevalent within cardiac populations. For instance, the National Comorbidity Survey (79) assessed the frequency of serious psychiatric illness and found that the 12-month and lifetime prevalence rates of certain depressive and anxiety disorders, as well as serious substance abuse, were remarkably high, with 48% reporting at least one of these disorders in their lifetime. To compare these prevalence rates with those noted in general medical and CAD populations, it is also useful to examine point prevalence rates, the percentage of persons with psychiatric disorders at a specific point in time. For example, the prevalence rate of major depression disorder in the National Comorbidity Survey was approximately 5%, compared with a prevalence of 15% or greater in populations with CAD (1). In addition, at least another 15% to 20% of patients with cardiac disease exhibit depressive symptoms that do not necessarily meet criteria for major depressive disorder (1). Similarly, anxiety disorders, such as phobic anxiety or panic disorder, are relatively common among patients with CAD. As a consequence, cardiologists are likely to encounter a significant number of psychologically distressed patients in clinical practice.

Second, psychologic distress commonly presents as symptoms of cardiac disease in clinical practice. Notably, whereas certain psychosocial risk factors such as depression and anxiety can present with either psychologic and/or somatic manifestations, it is those with primarily somatic symptoms, such as chest pain or palpitations, who seek medical evaluation preferentially, thus exacerbating this tendency. In fact, estimates indicate that more than three-fourths of patients with major depression or panic disorder seen in primary care settings present with somatic complaints only (80,81). Because chest pain and palpitations are common somatic complaints, a high proportion of patients presenting with such symptoms in medical settings have psychologic distress in the absence of objective evidence of organic heart disease. For instance, whereas panic disorder occurs in <4% of the general population (79), it occurs in more than 15% to 20% of patients presenting with chest pain complaints in emergency departments, reflecting the high rate of medical care use by these patients (82). Physician awareness of these relationships is important, because psychologic distress is frequently underdiagnosed in medical evaluations of cardiac symptoms. For example, in a prospective evaluation of 441 patients presenting to a cardiac care emergency department with chest pain and evaluated blindly for psychiatric diagnosis, approximately 25% had panic disorder, but in 98% of the patients with panic disorder, the diagnosis was missed by the cardiologists in the cardiac care emergency department (83).

Third, psychosocial risk factors can adversely affect treatment adherence. For instance, a meta-analysis has demonstrated that patients with depression were three times more likely to be nonadherent with treatment recommendations (84). Similarly, a recent meta-analysis of 122 social support studies (85) has revealed that patient adherence is strongly influenced by the magnitude of adequate functional or structural social support. However, although it seems intuitively reasonable, it has not yet been conclusively demonstrated that alleviation of psychologic distress improves treatment adherence.

Fourth, acute psychologic stress shapes the course of cardiac disease in both positive and negative fashion. On the one hand, acute emotional stress represents an important trigger for exacerbating pathophysiologic processes, ranging from the induction of endothelial dysfunction to the precipitation of myocardial ischemia. The latter occurs during laboratory mental stress in approximately 50% of patients with exercise-induced ischemia (1). On the other hand, patients’ experience of acute cardiac events and premonitory symptoms, such as angina pectoris, is itself a form of acute psychologic stress that can sometimes transform patients’ lives by signaling a need for personal reflection, inducing a reappraisal of values and/or shifting the perspective of time from “years since birth” to “years remaining” (86). Such events may cause patients to be more receptive to adopting new attitudes and be more successful in altering unhealthy behaviors, as indicated by various studies. Because cardiologists commonly treat patients who experience acute life-threatening events and who may be more receptive to...
physician advice, cardiologists may be ideally positioned to initiate these interventions.

IDENTIFICATION AND MANAGEMENT OF PSYCHOSOCIAL RISK FACTORS

Given that psychologic distress is often first detected in clinical health care settings, the cardiologist can play a critical role in the identification and management of psychosocial risk factors. This role can be divided into three broad categories: screening for psychosocial risk factors, referring of appropriate patients to behavioral health care providers, and managing milder forms of psychologic distress in the context of clinical practice.

Screening for psychosocial risk factors. Cardiologists can increase the detection of psychosocial risk factors by systematically screening for them. Querying patients about psychosocial risk factors conveys the message that these factors are important and relevant to providing optimal care. Screening can be accomplished by structured interviews and/or by validated questionnaires. Although questionnaire measures are easily administered and objectively scored, interviews allow greater flexibility and offer richer clinical information than that provided by written inventories. Because cardiologists are accustomed to obtaining medical histories through a brief review of systems, additional questions about psychosocial risk factors could easily be incorporated into such assessment. These questions should cover three kinds of experiences that may help to identify psychologic distress: 1) emotional factors, such as depression, anxiety, and anger; 2) chronic stressors, such as work strain and home stress; and 3) somatic complaints that may be stress-related, such as fatigue and disrupted sleep. Some questions for screening patients’ psychosocial status are suggested in Table 1.

The identification of emotional distress can often be challenging in the medical setting. Hallmarks of disorders such as depression (e.g., changes in appetite and/or significant changes in weight) and panic disorder (e.g., palpitations, and/or shortness of breath) can indicate either a cardiac or psychiatric condition. Inaccuracy in determining the cause of such symptoms can result in misdiagnosis and mistreatment. Moreover, because physicians’ time is often limited, psychosocial problems need to be assessed relatively quickly and efficiently. However, research suggests that such skills can be learned and effectively implemented. Finally, following acute events or surgical interventions, cardiac patients may feel especially vulnerable and helpless. During such times, inquiries about mental health and psychosocial functioning can be perceived as highly threatening, and may elicit defensiveness, resentment, and denial. The cardiologist can help preempt this response by openly addressing the patient’s concerns and establishing rapport.

Referring patients to behavioral health care providers. The benefits of screening for psychosocial risk factors will be realized only if proper identification leads to appropriate intervention and follow-up. Patients with apparently significant psychologic distress or behavioral maladjustment should be referred to appropriate specialists for counseling and/or psychiatric treatment (87). Thus, part of the cardiologist’s role in managing psychologic distress may be the development of a referral network of specialists. However, close follow-up of patients even after referral is highly advisable because early dropout from both pharmacotherapy and psychotherapy is common (87).

Managing psychologic distress in clinical practice. Subclinical presentations of psychologic distress, such as minor depression, work stress, inability to relax, and difficulty sleeping, may be appropriately handled in routine cardiac practice. Tools that are readily available to cardiologists for direct management of psychosocial risk factors are practical behavioral interventions, as outlined in Table 2. Cardiologists are familiar with some of these interventions, such as exercise and nutritional counseling, but physicians may underestimate the potential effectiveness of such counseling techniques (88) and the other tools listed in Table 2.

As for the treatment of obesity, poor nutritional habits, smoking, and sedentary lifestyles, patient non-adherence can complicate physician attempts to modify psychosocial risk factors. Helping patients to initiate behavior change is challenging, requiring mastery of techniques and approaches derived from psychology and the behavioral and social sciences, and recommendations stemming from the American Heart Association’s Expert Panel on Compliance (89). Representative techniques that cardiologists can use to promote patient adherence are summarized in Table 3. For example, the use of “micro goals” for poorly adherent patients, such as those who may claim to not have the time, willingness, or belief that they can exercise, can be applied. In such patients, initiating a modest exercise program requiring only 5 to 10 min of walking per day may be useful, increasing exercise at a measured pace. All new behaviors represent transitional intentional practices that initially require more intense physician monitoring and personal feedback before becoming more automatic and habitual. Because no single approach is effective for all patients, mastery of multiple approaches and diverse strategies may improve behavioral adherence rates typically reported in clinical practice.

Although mastery of techniques to promote adherence may be highly desirable, these add to the time, diligence,
training, and complexity required to manage multiple risk factors in cardiac practice. As a consequence, cardiologists may rely on a nurse or other qualified office personnel, an organized community or hospital program, and/or complementary instructional material to assist them in managing psychosocial risk factors, particularly for the more intense interventions noted in Table 3.

Table 3. Steps to Promote Effective Adherence to Behavioral Suggestions

1. Use clear and effective communication, including making recommendations that are as specific and simple as possible.
2. Schedule follow-up visits to check adherence, especially during the early practice phase, as opposed to the later, more ingrained habit phase.
3. Provide a motivating rationale for the patient’s treatment regimen, with consideration of explanations that befit the patient’s health literacy.
4. Follow oral suggestions with written ones to reinforce the cardiologist’s message and aid memory and concentration.
5. Begin with “micro” goals for patients who are resistant to behavior change or who have fewer available personal resources.
6. Help patients establish realistic goals and expectations.
7. Involve patients in tailoring behavioral suggestions rather than dictating change.
8. Suggest activities that are commensurate with patients’ abilities and that provide positive feedback (factors that tend to promote a sense of pleasure).
9. Openly and candidly explore potential patient barriers to adherence (such as lack of personal motivation, time, family support, facilities, or knowledge; fears; job, home or other pressures; and cultural issues) and assist patients with problem-solving and developing strategies (e.g., self-monitoring approaches, written agreements, and relapse prevention) at the time of recommendations.
10. Refer patients with poor structural or functional social support to programs or activities that will enhance adherence by providing social support.

Results of behavior and psychopharmacologic intervention trials. A variety of behavioral and psychosocial interventions have been implemented in cardiac patients, including exercise training, psychosocial interventions as part of multifactorial risk factor modification, organized psychosocial interventions designed to reduce psychosocial risk factors, and psychopharmacotherapy. The results of cardiac outcome studies involving these approaches are reviewed here.

Exercise is commonly recommended by cardiologists to promote both primary and secondary CAD prevention, but evidence suggests that exercise may also modify psychosocial risk factors, including depression. For instance, cross-sectional studies of both medical populations and healthy cohorts have consistently demonstrated lower depression scores among those who are most active. The ability of exercise to reduce depression also has been demonstrated in randomized controlled trials, although many of these studies have had methodologic limitations (90). More recently, a randomized controlled comparison between antidepressant medication versus exercise was performed in a group of 156 men and women with depression (91). After 16 weeks, exercise was just as effective as sertraline hydrochloride in reducing depressive symptoms. Follow-up of these patients after six months revealed a low rate of relapse in the exercise group (92). Although the study may have had some methodologic limitations, these intriguing data suggest the need for additional prospective trials.

The utility of organized psychosocial interventions has been most commonly assessed by evaluating their incremental impact upon prognosis among patients referred to formal cardiac rehabilitation programs. For instance, Linden et al. (93) performed a meta-analysis of 23 randomized controlled...
trials that evaluated the impact associated with adding psychosocial interventions to standard cardiac rehabilitation regimens. During the first two years of follow-up, lack of psychosocial intervention was associated with greater rates for mortality and recurrent infarction. In a separate meta-analysis of psychosocial interventions and cardiac rehabilitation, Dusseldorp et al. (94) observed differential effects depending on the efficacy of the psychosocial intervention. When psychologic distress was reduced, the odds ratio for mortality and recurrent MI also was reduced, but when no reduction in psychologic stress occurred, mortality was higher in intervention than in control rehabilitation patients. Along these lines, recent data suggest that the failure to respond to psychosocial interventions may identify a subgroup of patients who are particularly susceptible to adverse clinical events (95).

The utility of stand-alone psychosocial interventions has also been evaluated in five large-scale behavioral intervention trials in cardiac patients, with mixed results. The Recurrent Coronary Prevention Project Study was a group therapy behavior modification program that succeeded in decreasing both Type A behavior and negative affect and also reduced the rates of cardiovascular mortality and nonfatal MI (96). The Ischemic Heart Disease study was a second successful intervention trial, using a unique home-based stress-reduction program to reduce cardiac events (97). Two other large trials did not reduce subsequent cardiac events in the treatment groups, but neither intervention successfully reduced psychosocial distress (98,99). In fact, one of these trials was a follow-up of the approach used in the Ischemic Heart Disease trial, and secondary analysis of the data from this trial revealed that the results could be attributed to inadequate psychologic intervention in the experimental group (100). Indeed, cardiac mortality was significantly reduced at one year among the subgroup of experimental treatment patients who experienced an early reduction in psychologic distress. The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) study was the fifth and largest stand-alone psychosocial intervention trial to date. It evaluated the effect of psychologic treatment on the composite end point of all-cause mortality and nonfatal MI in post-MI patients who were either depressed and/or who reported low perceived social support (101). Patients were randomized within four weeks of the index MI, and treatment consisted of individual cognitive therapy and, when possible, group therapy supplemented by the use of a selective serotonin reuptake inhibitor (SSRI) for severe or unremitting depression. Primary analyses found no treatment differences in event-free survival (101). However, analyses suggested only a modest difference in psychosocial functioning between the treatment and control groups. Psychosocial functioning was better than anticipated in the control group, perhaps due to aggressive treatment as part of routine medical care, including participation in cardiac rehabilitation and psychologic therapies, thereby reducing treatment group differences.

Figure 9. Proposed three-stage approach for developing behavioral intervention trials. Stage 1 consists of a single-center evaluation of a specific behavioral intervention. If successful, this intervention would be repeated at multiple centers to assess the reproducibility of findings (stage 2). In both stages, intermediate end points, such as change in carotid intimal wall thickening or plaque size during carotid ultrasonography, would be used to minimize necessary sample size and follow-up time. If reproducible results are obtained during stage 2, a multicenter intervention trial would be performed in stage 3, during which subjects would be observed for the occurrence of hard cardiac events. IMT = intima media thickness.

The paucity of stand-alone behavioral intervention trials is partly due to the large sample sizes, long follow-up, and high costs required of such trials. One way to reduce this problem would be to use a three-stage approach for developing future interventions (Fig. 9) based on initial evaluations of surrogate end points, such as measures of subclinical atherosclerosis, myocardial ischemia, or flow-mediated dilation in smaller samples. Although there are limitations to the use of surrogate end points, they can be effective for developing new and innovative interventions for CAD before launching large multicenter randomized trials.

The impact of psychopharmacologic therapies upon cardiac outcomes represents an area of new interest. An initial trial in this arena, the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART), demonstrated that an SSRI (sertraline) could be safely prescribed for the treatment of clinical depression in patients with known CAD (102). However, this trial was not powered to evaluate the influence of sertraline use on adverse cardiac events, as it was a safety study. Cohen et al. (103) assessed antidepressant use in a large group of union health plan members divided into those who were taking antidepressants and those who were not. Participants using tricyclic antidepressants had a more than a twofold increased risk of subsequent MI, but there was no increase in adverse cardiac events among the patients taking SSRIs. A recent case-control study suggests that the protective effect of SSRIs may be related to their degree of serotonin transporter affinity (104). If confirmed, these findings suggest that SSRIs with high serotonin transporter affinity may be the preferred pharmacologic means for treating depression in CAD patients because of a biologic antiplatelet effect. A biologic protective
effect for depressed patients also may be introduced by the use of statin therapy, as suggested by preliminary data indicating that statin therapy lowers the high levels of C-reactive protein associated with depression (105).

**Future directions in behavioral interventions.** Although clinical practice guidelines advocate psychosocial interventions in the context of cardiac rehabilitation programs, there are no existing recommendations to guide the delivery of psychosocial interventions in cardiac practice. Cardiac rehabilitation programs are widely recognized as effective in providing multifactorial multidisciplinary treatment for cardiac patients (106), but these programs are geographically limited and third-party reimbursement policies may limit patient participation. Overall, only 10% to 20% of eligible cardiac patients are referred to cardiac rehabilitation programs (106). Thus, these programs represent an incomplete delivery system for behavioral health care in cardiac practice. Moreover, because of time constraints and lack of formal training in behavioral techniques, many cardiologists may find it difficult to provide psychosocial interventions to their patients. In addition, even though cardiologists commonly manage behavioral risk factors, such as physical inactivity, poor diets, and smoking, lack of patient adherence to their behavioral recommendations remains an important problem (89) for which there is no easy solution. For all these reasons, development of effective models for the provision of psychologic and behavior services for cardiologists is needed.

Accordingly, programs of various complexities have been examined for their ability to improve physician management of behavioral risk factors. These programs include providing brief targeted physician training, monitoring patients by telephone follow-ups, using nurse managers in cardiology practice, and involving patients’ primary care physicians in collaboration with mental health professionals such as psychologists and psychiatrists. This latter approach has shown promise for optimizing primary care physician management of serious psychologic illnesses such as depression (107) and panic disorder (108). Although critical assessment of these approaches is beyond the scope of our review, a conceptual approach for organizing behavioral health care interventions for cardiac patients, based on the collective experience garnered from these approaches, is shown in Figure 10. In this approach, guidelines would be developed for stepped collaborative care interventions for cardiac patients, based on the complexity of patients’ psychosocial and behavioral problems and their ability to adhere to behavioral recommendations.

The difficulty in maintaining long-term behavioral change among cardiac patients, coupled with the growing epidemic in obesity and type 2 diabetes, makes it imperative to develop more effective adherence strategies. Bellg (109) suggests that standard efforts to optimize treatment adherence most commonly view nonadherence as a form of patient deficit that can be overcome by using external forms of behavioral regulation, such as use of incentives or structured provider support (Fig. 11). Such controlled behavior regulation may be very effective in eliciting short-term behavioral change, but fostering patient autonomy is critical to maintain long-term change (110). Conversely, lack of internal motivation is a primary reason why patients continue to engage in unhealthy shortsighted behaviors after being informed about the long-term adverse consequences. Approaches for fostering internal motivation are suggested in Figure 11. An approach that incorporates many of these principles is “motivational interviewing,” which is designed to enhance patients’ intrinsic motivation to change unhealthful behaviors by exploring and resolving ambivalence.

**Figure 10.** Stepped collaborative care for cardiac patients depending on the degree of psychological distress. Patients with mild psychologic distress (step 1) would generally be treated by cardiologists without additional collaborative intervention. The greater the degree of psychosocial distress, the greater the need for collaborative intervention.

**Figure 11.** Approaches to promoting treatment adherence commonly make use of techniques that involve external regulation, such as the use of incentives or external network support. An alternative motivational paradigm to such controlled behavior regulation focuses on attempting to promote autonomy by fostering greater intrinsic motivation. Health providers can foster this motivational process through a variety of steps, including promoting patient ownership over recommended behavioral changes (i.e., getting patients to voice their own reasons for initiating change), helping patients to find a meaningful purpose for suggested changes, formatting the specifics of behavior recommendations in a manner most consistent with patients’ personal preferences, and recognizing what coping mechanisms were best served by the old adverse behaviors (e.g., eating to decrease a sense of tension) and finding alternative solutions. At the same time it is important to avoid ignoring a sense of conflict (which can occur if behavioral recommendations are made without considering the relationship of physician advice to patients’ internal values and preferences), fostering a sense of coercion, or setting goals that are not readily achievable.

<table>
<thead>
<tr>
<th>STEPPED INTERVENTIONS</th>
<th>DEGREE OF PSYCHOSOCIAL DISTRESS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 3</td>
<td>SEVERE</td>
<td>ADD mental health care specialist</td>
</tr>
<tr>
<td>Step 2</td>
<td>MODERATE</td>
<td>ADD nurse manager, and adherence promotion (e.g., telephone follow-up, group exercise, etc.)</td>
</tr>
<tr>
<td>Step 1</td>
<td>MILD</td>
<td>M.D. supervision and close follow-up</td>
</tr>
</tbody>
</table>

**TRADITIONAL PERSPECTIVE**

**USE OF INCENTIVES**

(e.g., fear, rewards, nagging)

**USE OF NETWORK SUPPORT**

(e.g., nurse manager, telephone follow-up, etc.)

**MOTIVATIONAL PERSPECTIVE**

FOSTER AUTONOMY

Promote

Ownership over goals
Sense of purpose
Personal preferences
Alternative coping strategies

Avoid

Ignoring conflicting feelings
Fostering a sense of coercion
Setting unrealistic goals
to change (111). In this approach, the interviewer uses empathy to help patients focus on discrepancies between present behavior and long-term aspirations and values, and avoids confrontation or playing an authoritarian role. This approach has been applied to various behavior settings (99), and is promising for treating cardiac patients. Other novel strategies also may be used to create “teachable moments,” for example, by showing patients personally relevant clinical images of calcium deposits in their coronary arteries (112). To date, this motivational approach has not yet been tested in a sufficiently broad spectrum of patient populations.

THE EMERGING FIELD OF BEHAVIORAL CARDIOLOGY

Behavioral cardiology is an emerging field of clinical practice based on the recognition that adverse lifestyle behaviors, emotional factors, and chronic life stress can all promote atherosclerosis and adverse cardiac events. In recent years, the pathophysiologic understanding of how psychosocial risk factors contribute to atherosclerosis and adverse cardiac events has broadened substantially. By contrast, the development of effective therapeutic interventions both for modifying high-risk lifestyles and behaviors and for reducing psychosocial risk factors for CAD patients remains a challenge. There have been few large-scale psychosocial intervention trials, and the design of future trials is under debate. Moreover, the lack of patient adherence to behavioral interventions remains a significant problem. Nevertheless, there is increasing evidence that interventions such as exercise training, multifactorial secondary prevention efforts that incorporate psychosocial interventions, and antidepressant medication may be effective in treating psychologic distress and improving outcomes among patients with cardiac disease. Other preliminary evidence suggests that stress management programs can improve surrogate markers for CAD. Prospective investigations are needed to determine which patients may respond best to specific forms of behavioral interventions and also define how cardiologists can best collaborate with other health care providers and health care delivery systems to reduce psychologic distress in a cost-effective and practical manner. The field of behavioral cardiology requires the development of such practical solutions because the etiologic links among psychosocial risk factors, behavioral risk factors, and atherosclerosis suggest that cardiologists will consistently encounter many patients with psychologic distress and unhealthy behaviors in clinical practice.

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REFERENCES

28. Suadipani C, Heo HN, Gyntelberg F. Are social inequalities associated with the risk of ischemic heart disease a result of psychosocial working conditions? Atherosclerosis 1993;101:165–75.


