Section 6: Nonpharmacologic Management and Health Care Maintenance in Patients With Chronic Heart Failure

Overview

Nonpharmacologic management strategies represent an important contribution to heart failure (HF) therapy. They may significantly impact patient stability, functional capacity, mortality, and quality of life. Most of the recommendations that follow derive from consensus expert opinion or are based on theory extrapolated from limited trial data in the elderly or chronic disease populations.

Diet and Nutrition

Recommendations

6.1 Dietary instruction regarding sodium intake is recommended in all patients with HF. Patients with HF and diabetes, dyslipidemia, or severe obesity should be given specific dietary instructions. (Strength of Evidence = B)

6.2 Dietary sodium restriction (2-3 g daily) is recommended for patients with the clinical syndrome of HF and preserved *or* depressed left ventricular ejection fraction (LVEF). Further restriction (<2 g daily) may be considered in moderate to severe HF. (Strength of Evidence = C)

Background

Excessive dietary sodium intake is a common proximate cause of worsening symptoms and hospitalization for HF exacerbation.[1–3] Furthermore, dietary sodium restriction typically results in a decrease in the diuretic dose required for maintenance of a euvolemic state and clinical stability. This is important because loop diuretics increase plasma renin activity and may adversely impact clinical outcomes through neurohormonal stimulation.[4] Studies of sodium restriction indicate an impact on such parameters as quality of life and even functional status,[5] but not mortality. Despite limited clinical trial data, sodium restriction remains an important and common component of HF disease management programs.[6]

The ''average'' American diet contains between 8,000 and 10,000 mg sodium; certain ethnic diets are typically several-fold higher. (See Table 3.3 in Section 3 for salt-sodium equivalents.) A ''low-sodium'' or ''no added salt diet'' as defined by the American Heart Association is 4000 mg sodium. The current recommendation from the American Heart Association and the United States Department of Agriculture (USDA) for the general population is to limit sodium intake to 2300 mg per day, while the current USDA recommendation for those with hypertension, blacks and middle-aged and older people is 1500 mg per day for hypertension prevention.[7] Thus, although there remains no evidence about the ideal level of sodium restriction in patients with HF because of lack of studies on this topic, it is reasonable to recommend that sodium intake be limited to 2000−3000 mg per day.

Because following a low sodium diet is a specific activity, greater patient success can be expected when the clinician provides the patient with a daily sodium intake target and the knowledge and skills to reach that target. It is not enough to simply ask patients to follow a low salt diet. Nor is it sufficient to advise not salting food at the table or while cooking as most (~70%) of our daily sodium intake comes from processed and pre-packaged foods. Appropriate education and counseling regarding the 2000−3000 mg sodium diet recommendation is covered in Section 8.

Additional dietary instruction should be provided to all patients with HF who have comorbid conditions, including arteriosclerosis, diabetes, renal insufficiency, or obesity. Patients with hyperlipidemia or known underlying coronary or peripheral arteriosclerosis should be given specific instruction regarding dietary fat and cholesterol restriction according to national guidelines, such as the National Cholesterol Education Program. Diabetics exhibiting poor glycemic control or with significant albuminuria should receive individualized nutritional counseling regarding protein and carbohydrate consumption and caloric constraints as indicated to reduce risk for morbidity and mortality. Aggressive management of hyperglycemia diminishes osmotic forces leading to water retention and glomerular hyperfiltration, while reducing infection risk and the long-term risk of additional end-organ damage.[8] Patients with significant underlying renal insufficiency may require individualized instruction regarding protein, potassium, phosphorus, or other dietary constraints to preserve electrolyte and acid-base homeostasis.

Obesity is independently associated with HF and contributes to the development of additional HF risk factors, including hypertension, LV hypertrophy and diastolic filling abnormalities. Obesity is linked to insulin resistance and glucose intolerance, hyperaldosteronism, salt sensitivity, and plasma volume expansion, creating both pressure and volume overload stressors with increased systemic vascular resistance. The metabolic demand of excessive adipose tissue increases cardiac output requirements, making cardiomyopathy with HF the leading cause of death in patients with severe obesity. Arrhythmia risk is increased in association with prolongation of the QT interval frequently seen in the setting of morbid obesity. Sleep-disordered breathing is linked to pulmonary hypertension, right ventricular failure, and hypoxemia. For both obesity-cardiomyopathy and obesity-hypoventilation syndromes, weight loss and sodium restriction are effective measures to improve symptoms and prognosis.[9]

A number of recent studies evaluating the relationship between body mass index (BMI) and mortality have suggested that overweight (BMI 25−29.9 kg/m^2) and obese (BMI ≥30 kg/m^2) people with HF have a better survival

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than healthy weight people (BMI 18.5−24.9 kg/m^2) with HF.[10−13] Reasons for this ''obesity paradox'' remain unexplained. Low BMI (<18.5 kg/m^2) subjects with HF appear to have the highest mortality.[11−14] At least one study suggests that severely obese subjects (BMI ≥35 kg/m^2) also have a higher mortality than normal weight or mild to moderately obese people with HF, resulting in a ''J'' shaped curve for the BMI-mortality relationship.[14]

When risk of death was assessed in 359,387 people from the general population using BMI, waist circumference and waist-hip ratio, general and abdominal obesity were associated with risk of death.[15] In patients with HF, central adiposity, assessed by waist-hip ratio, but not BMI, was predictive of all-cause mortality independent of age and gender.[16] Of note, waist-hip ratio was more strongly associated with LV diastolic function as well. After adjustment for LVEF and diastolic function, waist-hip ratio was no longer a risk factor for mortality. Thus, ventricular dysfunction may be an important mediating factor between waist-hip ratio and mortality.[16] Another explanation for the ''obesity paradox'' may be that it is the change in weight over time, not the specific weight at any given time, that predicts mortality. Normal weight people with HF may have been overweight or obese and are actively losing weight.[11] It is also possible that HF is detected earlier in overweight and obese people due to symptom exacerbation caused by excess weight.[12] Other explanations include the use of higher doses of beneficial medications or the benefits of elevated TNF-α receptor levels in the obese.[17,18] Although it seems unlikely that there is a beneficial effect of obesity in people with HF, the explanation for the ''obesity paradox'' remains uncertain. Until further data are available, caloric restriction as part of the treatment of the severely obese patient with HF and weight stabilization or reduction in overweight and mildly obese patients seems reasonable.

There are defined risks of extreme calorie and carbohydrate restriction that may be increased in patients with HF. Electrolyte abnormalities and ketosis may occur with these diets and require frequent monitoring and physician oversight.

For HF patients with a BMI >35, gastrointestinal surgery is an option, with operative risk dependent on clinical symptoms, hemodynamic stability, and stability of coronary artery disease.[19] Surgical intervention is the only weight loss therapy with reasonable long-term result maintenance, although operative morbidity and mortality are substantial.[20] One recent study found that weight reduction after bariatric surgery in subjects with morbid obesity may reverse LV hypertrophy.[19] Preliminary data also suggest that in subjects with morbid obesity and reduced systolic function, bariatric surgery may lead to improvements in cardiac function.[21−23] It is therefore a consideration in morbidly obese patients for whom all other weight loss measures have failed.

Recommendation

6.3 Restriction of daily fluid intake to <2 L is recommended in patients with severe hyponatremia (serum sodium <130 mEq/L) and should be considered for all patients demonstrating fluid retention that is difficult to control despite high doses of diuretic and sodium restriction. (Strength of Evidence = C)

Background

Fluid restriction is indicated in the setting of symptomatic hyponatremia (serum sodium <130 mEq/L), whether or not it is precipitated by pharmacologic therapy. Concomitant dietary sodium restriction facilitates maximal diuresis and may reduce hospital length of stay. In the outpatient setting, fluid restriction generally is reserved for advanced HF refractory to high doses of oral diuretic agents. Fluid restriction in the outpatient setting has many inherent logistical difficulties, often leading to increased stress, anxiety, and poor adherence with therapy. Most disease management programs monitor patient volume status reliably and effectively through the attainment of daily morning weight, rather than through patient measurement of daily intake and output.[24]

Apparent diuretic refractoriness is most often a reflection of nonadherence with dietary sodium restriction or prescribed pharmacologic therapy, unrecognized drug interactions (eg, nonsteroidal anti-inflammatory agents [NSAIDs] and glitazones) or the uncommon patient with excessively high fluid intake (>6 L/day). Physiologic diuretic refractoriness can be observed with chronic loop diuretic administration, primarily from distal renal tubular hypertrophy that facilitates enhanced sodium reabsorption. On the other hand, ''true'' diuretic refractoriness may reflect underlying disease progression with reduced cardiac output and effective renal plasma flow, development of significant intrinsic renal insufficiency, or nephrosis.

Recommendation

6.4 It is recommended that specific attention be paid to nutritional management of patients with advanced HF and unintentional weight loss or muscle wasting (cardiac cachexia). Measurement of nitrogen balance, caloric intake, and prealbumin may be useful in determining appropriate nutritional supplementation. Caloric supplementation is recommended. Anabolic steroids are not recommended for cachexic patients. (Strength of Evidence = C)

Background

Cardiac cachexia is a well-described phenomenon that is associated with intense activation of the cytokine, tumor necrosis factor-α, or chronically low cardiac output states. Similar features are observed in patients with terminal cancer, acquired immunodeficiency syndrome (AIDS), and chronic inflammatory diseases. Such patients are at extremely high risk for serious morbidity, such as infection, hospitalization and impaired wound healing.

In HF patients with reduced LVEF, tumor necrosis factor-α, levels are highest in advanced disease and correlate with the highest risk of mortality. Formal metabolic evaluation and determination of minimal nutritional requirements should be strongly considered for patients demonstrating this muscle-wasting syndrome. Specific recommendations have been made for these patients, including altering the size and frequency of meals and ensuring a high-energy diet.[25]

There are no data to support the use of anabolic steroids or human growth hormone supplementation in patients with cardiac cachexia and skeletal muscle wasting. Initial enthusiasm for this approach was based on data suggesting that small doses of testosterone have a beneficial effect on dysfunctional myocardium.[26] However, long-term exposure to these compounds has been reported to increase ischemia risk and to promote adverse ventricular remodeling risk. Fluid retention and electrolyte abnormalities are frequently observed with the use of this therapy. Additional serious risks include increased thrombogenicity and erythrocytosis, as well as benign prostatic hypertrophy and prostate cancer.

Recommendation

6.5 Patients with HF, especially those on diuretic therapy and restricted diets, should be considered for daily multivitamin-mineral supplementation to ensure adequate intake of the recommended daily value of essential nutrients. Evaluation for specific vitamin or nutrient deficiencies is rarely necessary. (Strength of Evidence = C)

Background

Based on research, dietary guidelines for individuals at risk for developing HF are more established than for those who already have the condition.[27] Balanced nutrition with multivitamin/mineral supplementation to fulfill the recommended daily value of essential nutrients is prudent for persons with any chronic disease, including HF. Multivitamin/mineral supplementation may offset nutritional imbalances from early satiety and altered digestive efficiency related to decreased absorption, enhanced water-soluble vitamin and mineral loss from diuretic administration, and increased utilization due to oxidative stress.[28] It should also be recognized that population-related issues, such as old age or other chronic conditions, rather than HF itself, can be responsible for nutritional deficiencies in patients with HF.[29]

In general, for most patients with HF, a prudent diet providing adequate protein, carbohydrate, and calories according to age, gender, and activity level is advisable. Dietary supplementation consisting of a daily multiple-vitamin should be considered, given that most American diets are inadequate in providing the recommended basic nutrient requirements.

Studies estimate that approximately 50% of patients with HF consume herbal, megavitamin, or other dietary supplements.[30] The likelihood of an adverse reaction or vitamin toxicity increases with consumption of multiple supplements, the safety and efficacy of which are not well documented. It is therefore important to ask patients with HF about supplements they are already taking before recommending a daily multiple vitamin.

Recommendation

6.6 Documentation of the type and dose of naturoceutical products used by patients with HF is recommended. (Strength of Evidence = C)

Naturoceutical use is not recommended for relief of symptomatic HF or for the secondary prevention of cardiovascular events. Patients should be instructed to avoid using natural or synthetic products containing ephedra (ma huang), ephedrine, or its metabolites because of an increased risk of mortality and morbidity. Products should be avoided that may have significant drug interactions with digoxin, vasodilators, beta blockers, antiarrhythmic drugs, and anticoagulants. (Strength of Evidence = B)

Background

Naturoceutical use cannot be recommended for the relief of HF symptoms or for the secondary prevention of cardiovascular events. Given the paucity of efficacy data about naturoceutical products, reporting suspected adverse effects or drug interactions to the Food and Drug Administration is strongly encouraged.

There are several agents with documented potential to do harm. Natural or synthetic catecholamine-like products containing ephedra (ma huang), ephedrine metabolites, or imported Chinese herbs are specifically contraindicated in HF. Hawthorne (Cratageus) products appear to have inodilator activity, increasing the risk of orthostatic hypotension and possibly arrhythmia. Hawthorne potentiates the action of vasodilator medications and increases serum digoxin levels. One recent long-term placebo-controlled trial failed to show any incremental benefit when hawthorn extract was given with standard drug therapy to patients with chronic HF. It did show, however, that the drug appeared safe to use with angiotensin converting enzyme (ACE) inhibitors, beta blockers, and other standard HF medications.[31] Many other naturoceutical products, including garlic, gingko biloba, and ginseng, have antiplatelet effects or potential anticoagulant interactions.[32]

Other Therapies

Recommendation

6.7 Continuous positive airway pressure to improve daily functional capacity and quality of life is recommended in patients with HF and obstructive sleep apnea documented by approved methods of polysomnography. (Strength of Evidence = B)

Background

Sleep-disordered breathing is highly prevalent in HF patients.[33–35] Formal sleep evaluation is therefore recommended for patients who remain symptomatic despite

optimal HF therapy. Testing should be considered for patients with a positive screening questionnaire or whose sleep partner reports signs suggesting apnea or periodic breathing. Whether clinical outcome is favorably affected by treatment of sleep-disordered breathing is unclear, but patient quality of life and functional capacity is increased by treatment when the respiratory disturbance index is at least moderately elevated, and individual studies have shown that use of continuous positive airway pressure (CPAP) reduces edema, daytime muscle sympathetic nerve activity, systolic blood pressure, frequency of ventricular premature beats during sleep, and improves LV function.[36–40] Concomitant treatment for restless leg syndrome may be reduced when the patient is treated for associated sleep-disordered breathing.

The other component of sleep-disordered breathing, central sleep apnea, was studied in a large-scale trial that tested the hypothesis that CPAP would improve the survival rate without transplantation for patients with central sleep apnea and HF. The Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure trial (CANPAP) of 258 patients found that those patients randomized to CPAP had attenuated central sleep apnea, improved nocturnal oxygenation, increased LVEF, and improved 6-minute walk distances, but did not survive longer.[41]

Recommendation

6.8 Supplemental oxygen, either at night or during exertion, is not recommended for patients with HF in the absence of an indication of underlying pulmonary disease. Patients with resting hypoxemia or oxygen desaturation during exercise should be evaluated for residual fluid overload or concomitant pulmonary disease. (Strength of Evidence = B)

Background

Pulmonary vascular congestion creating resting or exertional hypoxemia requires aggressive diuretic therapy, rather than supplemental oxygen. Oxygen supplementation is a useful therapeutic adjunct in hospitalized patients during acute decompensation or with coronary ischemia. Patients with residual resting hypoxemia or exertional arterial oxygen desaturation after optimization of intravascular volume should be evaluated for concomitant pulmonary disease, pleural effusion, pulmonary emboli, pulmonary hypertension, silent myocardial ischemia, obesity-hypoventilation syndrome, and sleep-disordered breathing.

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Recommendation

6.9 The identification of treatable conditions, such as sleep-disordered breathing, urologic abnormalities, restless leg syndrome, and depression should be considered in patients with HF and chronic insomnia. Pharmacologic aids to sleep induction may be necessary. Agents that do not risk physical dependence are preferred. (Strength of Evidence = C)

Background

Chronic insomnia is associated with a risk of psychological instability and impaired cognitive function. After metabolic, physiologic, pharmacologic, and dietary causes are excluded, screening should be considered for urologic abnormality, sleep-disordered breathing, restless leg syndrome, depression, and anxiety disorders. Nocturnal anxiety may be a manifestation of paroxysmal nocturnal dyspnea. Sedatives can worsen apnea and should be initially eliminated. Paradoxical agitation from the use of antihistamine products or benzodiazepine preparations is not uncommon. For these reasons, the use of medication to aid sleep induction should be undertaken only when necessary, and then with caution and careful monitoring.

Specific Activity and Lifestyle Issues

HF is a syndrome with an enormous impact on the quality of life of patients and families. HF can affect employment, relationships, leisure activities, eating, sleeping, and sexual activity-to name just a few critical areas. Physicians have a significant opportunity to improve their patients' quality of life by initiating discussion regarding these issues and providing education, feedback, and support.

Recommendation

6.10 It is recommended that screening for endogenous or prolonged reactive depression in patients with HF be conducted following diagnosis and at periodic intervals as clinically indicated. For pharmacologic treatment, selective serotonin reuptake inhibitors are preferred over tricyclic antidepressants, because the latter have the potential to cause ventricular arrhythmias, but the potential for drug interactions should be considered. (Strength of Evidence = B)

Background

Depression is common in both elderly and HF populations and has an enormous impact on quality of life and functional capacity.[42–44] It is an independent risk factor for coronary heart disease and is associated with increased morbidity and mortality.[43,45] In a recent prospective cohort

study in outpatients with HF and LVEF <40%, living alone, alcohol abuse, perception of medical care as being a substantial economic burden, and health status were independent predictors of developing depressive symptoms.[46] Clinicians should be aware of patients at risk for the development of depression so that they may be targeted for screening and psychosocial intervention, as needed. Several screening questionnaires for depression are available.

Selective serotonin reuptake inhibitors (SSRI) are effective and generally safe in patients with HF. Tricyclic antidepressants have anticholinergic that increase heart rate, promote orthostatic hypotension, and alter ventricular repolarization. A recent study evaluating the association of long-term mortality with antidepressant use versus depression in patients with HF found that depression, but not the use of an SSRI, was associated with a 33% increased mortality risk in 1006 patients followed up over a mean of 972 days (HR 1.33, 95% CI 1.07−1.66).[47]

Recommendation

6.11 Nonpharmacologic techniques for stress reduction may be considered as a useful adjunct for reducing anxiety in patients with HF. (Strength of Evidence = C)

Background

Anxiety is commonly associated with depression, and often manifests as the inability to adjust to stressful situations. Although it is depression that is predictive of a worse prognosis,[48] anxiety should be taken seriously and reduced as much as possible. An assessment of intrinsic coping skills may be useful. Relaxation techniques such as meditation and biofeedback may improve patient daily functioning.[49] In one small study, researchers found that acupuncture inhibited sympathetic activation during mental stress in patients with advanced HF.[50]

Effective communication skills can reduce anxiety. The diagnosis of HF and its prognosis are likely to provoke anxiety. Anxiety, in turn, may contribute to a patient's inability to comprehend or follow a treatment plan. In discussing recommendations regarding end-of-life issues, including advance directives, care should be taken to avoid inducing excessive anxiety.

Recommendation

6.12 It is recommended that treatment options for sexual dysfunction be discussed openly with both male and female patients with HF. (Strength of Evidence = C)

The use of phosphodiesterase-5 inhibitors such as sildenafil may be considered for use for sexual dysfunction in patients with chronic stable HF. These agents are not recommended in patients taking nitrate preparations. (Strength of Evidence = C)

Background

Sexual dysfunction is common in patients with heart disease and should be discussed openly with all patients, male and female. Standard HF therapy may worsen sexual dysfunction in some patients, leading to nonadherence and worsening of HF symptoms.[51] Use of phosphodiesterase-5 inhibitors generally is safe when HF symptoms are compensated and there is no concomitant use of nitrate medications. In fact, a number of studies showed a positive impact of sildenafil on cardiac performance, particularly exercise capacity, in patients with HF.[52−54]

Many other nonpharmacologic aids exist for erectile dysfunction, impotence, and other forms of sexual dysfunction. Patients reluctant to initiate discussion regarding sexuality or who are unaware of treatment options may be intentionally noncompliant with HF medications to determine their influence on sexual dysfunction. A proactive discussion may therefore alleviate some risk of adherence-related clinical instability.

Health Care Maintenance Issues

Routine health care maintenance is often neglected by patients with HF, who are consumed with cardiovascular issues. Access to care may be an additional problem among the elderly and those with limited socioeconomic means. General health measures are at least as important in patients with HF as they are in other populations.

Recommendation

6.13 It is recommended that patients with HF be advised to stop smoking and to limit alcohol consumption to ≤2 standard drinks per day in men or ≤1 standard drink per day in women. Patients suspected of having an alcohol-induced cardiomyopathy should be advised to abstain from alcohol consumption. Patients suspected of using illicit drugs should be counseled to discontinue such use. (Strength of Evidence = B).

Background

All patients with the clinical syndrome of HF who abuse tobacco, alcohol, or illicit drugs should be counseled to stop. For such patients, these recommendations carry even greater potential benefit than they do in the general population.[55] Nicotine has vasoconstrictor activity, which can worsen hemodynamics and antagonize vasodilator effect. Transdermal nicotine preparations do not appear to significantly increase cardiovascular risk, even in high-risk patients, although physician-monitored use is advisable. Additional pharmacologic aids for tobacco withdrawal, such as bupropion, have not been associated with exacerbation of HF.

Alcohol-induced dilated cardiomyopathy is generally associated with chronic daily consumption of at least 70 g of

ethanol. Alcohol alters myocardial metabolism in many ways, significantly affecting fatty acid composition of the sarcolemma. Confounding nutritional and vitamin deficiencies coexist in chronic alcoholism and may adversely affect ventricular function. Renal magnesium and potassium wasting are enhanced. In the Studies of Left Ventricular Dysfunction (SOLVD) trials, a positive relationship was found between light to moderate alcohol intake and significant increases in serum markers of inflammation, shown to correlate with adverse clinical outcome.

The potential for reversal of ventricular remodeling and normalization of LVEF with cessation of alcohol ingestion are well recognized and correlate with improved prognosis. For patients who are not suspected of having an alcohol-induced cardiomyopathy, there is controversy regarding the impact of small amounts of alcohol. Light to moderate alcohol consumption (1−2 drinks per day) does not appear to alter the risk for HF in patients with LV dysfunction after myocardial infarction or to alter outcomes in patients with HF.[56,57]

Recommendations

6.14 Pneumococcal vaccine and annual influenza vaccination are recommended in all patients with HF in the absence of known contraindications. (Strength of Evidence = B)

6.15 Endocarditis prophylaxis is not recommended based on the diagnosis of HF alone. Consistent with the AHA recommendation, 'prophylaxis should be given for only specific cardiac conditions, associated with the highest risk of adverse outcome from endocarditis.' [58] These conditions include: 'prosthetic cardiac valves; previous infective endocarditis; congenital heart disease (CHD)' such as: unrepaired cyanotic CHD, including palliative shunts and conduits; completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure; repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization) cardiac transplantation recipients who develop cardiac valvulopathy. (Strength of Evidence = C)

Background

Pulmonary congestion and pulmonary hypertension increase the risk of lung infection. Therefore, administration of pneumococcal vaccine and annual influenza vaccines is highly recommended in HF patients, as is counseling patients to seek early evaluation for potentially serious infections. Additional vaccines, such as hepatitis and specific immunization matching foreign travel standards, should be given if appropriate. Maintenance of tetanus toxoid vaccination is prudent in all patients with HF.

There are few indications for infective endocarditis (IE) prophylaxis because the risk of IE due to dental or other procedures is quite low compared to the prevalence of bacteremia due to activities of daily living, such as chewing and teeth brushing.[58] Prophylaxis should follow American Heart Association/American College of Cardiology (AHA/ACC) guidelines in the setting of valvular heart disease when applicable. [58] Whether functional mitral regurgitation resulting from LV chamber and valve ring dilation carries the same attributable risk as that of primary valvular disorders is unclear from available data, although most experts would recommend treatment. When a patient has an implanted intravascular device, such as a pacemaker or automated internal cardiac defibrillator, most electrophysiologists recommend antibiotic prophylaxis under the same conditions as valvular heart disease, at least for the first 3 months after implantation.

Recommendation

6.16 Nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors, are not recommended in patients with chronic HF. The risk of renal failure and fluid retention is markedly increased in the setting of reduced renal function or ACE-inhibitor therapy. (Strength of Evidence = B)

Background

The need for analgesic medication for musculoskeletal complaints is common in HF patients, partially because HF is predominantly a disease of the elderly.[59] Unsuspected use of NSAID products may explain worsening renal function, hyperkalemia, fluid retention, or hypertension among HF patients. NSAID use has been implicated in the onset of HF symptoms in the elderly, perhaps unmasking underlying ventricular dysfunction.[60] The use of cyclooxygenagase-2 inhibitors has been associated with a higher risk of hospitalization for HF, although some studies indicate that celecoxib appears safer than rofecoxib.[61,62] All patients should be instructed to avoid the use of these products, unless all other treatment modalities have been exhausted. When these agents are prescribed, there should be careful clinical monitoring and laboratory assessment of renal function.

The risk of gout is increased in HF patients. Diuretic use, obesity, renal impairment, and alcohol consumption are additional risk factors. Colchicine and corticosteroids are preferred to NSAIDs as initial therapy for acute attacks.

Recommendations

6.17 It is recommended that patients with new- or recent-onset HF be assessed for employability following a reasonable period of clinical stabilization. An objective assessment of functional exercise capacity is useful in this determination. (Strength of Evidence = B)

6.18 It is recommended that patients with chronic HF who are employed and whose job description is compatible with their prescribed activity level be encouraged to remain employed, even if a temporary reduction in hours worked or task performed is required. Retraining should be considered and supported for patients with a job demanding a level of physical exertion exceeding recommended levels. (Strength of Evidence = B)

Exercise Rehabilitation as Therapy for HF

Recommendation

6.19 It is recommended that patients with HF undergo exercise testing to determine suitability for exercise training (patient does not develop significant ischemia or arrhythmias). (Strength of Evidence = B)

If deemed safe, exercise training should be considered for patients with HF in order to facilitate understanding of exercise expectations (heart rate ranges and appropriate levels of exercise training), to increase exercise duration and intensity in a supervised setting, and to promote adherence to a general exercise goal of 30 minutes of moderate activity/exercise, 5 days per week with warm up and cool down exercises. (Strength of Evidence = B)

Background

Cardiac/exercise rehabilitation offers a potential therapeutic approach in the management of patients with HF. The HF-ACTION trial (A Controlled Trial Investigating Outcomes of Exercise Training), a large, multicenter, randomized controlled study, failed to show significant improvement in all-cause mortality or all-cause hospitalization in patients who received a 12-week (3 times/week) exercise training program followed by 25−30 minute, 5 days/week home-based, self-monitored exercise workouts on a treadmill or stationary bicycle.[63] However, after controlling for HF etiology, atrial fibrillation, exercise duration and depression, patients who exercised had an 11% risk reduction in the primary endpoint ($P=0.03$). Additionally, cardiovascular mortality or HF hospitalization was reduced by 15% after adjustment ($P=0.03$), and at three months after enrolment, quality of life was significantly improved in the exercise group.[64] In HF-ACTION, exercise was safe and may be effective in improving clinical outcomes in patients not at highest prognostic risk. Additionally, functional status was significantly improved in patients receiving usual care plus exercise training in HF-ACTION. Distance walked at 3 months was higher and cardiopulmonary exercise time and peak oxygen consumption were improved at both 3 and 12 months in the exercise training group.[63]

HF-ACTION investigators found that many participants were non-adherent to the prescribed exercise program. In the first three months after enrolment, about 40% of patients fully adhered to the exercise duration goal and an additional 15% partially adhered, but in the last year of enrollment, less than 30% of participants were fully adherent and overall adherence had dropped below 45%.[65] In a sub-analysis of HF-ACTION, researchers found that participants in the exercise training group with a higher volume of exercise per week had a reduction in all cause death or hospitalization, cardiovascular death or cardiovascular hospitalization and cardiovascular death or HF hospitalization at 90 days. Moreover, peak oxygen consumption, six-minute walk distance and quality of life all significantly improved in participants who exercised at a higher volume.[65] HF-ACTION results provide further evidence beyond the many single center, short-term studies that showed that supervised exercise training improved quality of life and exercise capacity in patients with HF.[66−78]

Exercise training was found to have physiological benefits in patients with HF. Exercise training improved autonomic dysfunction and heart rate variability and was associated with a fall in resting plasma norepinephrine levels.[67,79−82] It was found to improve exercise cardiac output, decrease peripheral vascular tolerance, and produce favorable changes in skeletal muscle metabolism and structure.[83,84] Exercise training has been demonstrated to improve endothelium-dependent vasodilatation and coronary blood flow reserve in epicardial coronary vessels of patients with coronary artery disease, which may account for the observation that exercise training improves myocardial perfusion without reducing coronary obstruction or enhancement of collateral blood flow.[85−89] Despite the favorable mechanistic studies, HF-ACTION is the only definitive study conducted to test whether exercise training for patients with HF can improve survival or reduce risk of hospitalization. The available trial data, from studies underpowered to provide definitive results had mixed results.[89,90]

Exercise Intolerance in HF. Exercise intolerance is an important adverse effect of HF and contributes significantly to the poor quality of life experienced by patients suffering from this syndrome. Impaired exercise capacity is an independent predictor of survival, and progressive loss of functional capacity is characteristic as HF worsens clinically.[91−94] Intense investigation has focused for the past 2 decades on the potential mechanisms responsible for exercise intolerance in patients with HF. Interestingly, the degree of LV systolic dysfunction has been found to be poorly correlated with the degree of exercise intolerance.[95−97] In contrast, the importance of reduced blood flow to exercising muscle is apparent from the closer relationship between exercise capacity and exercise cardiac output.[98−111]

Summary. Clinical studies support the concept that exercise training is safe and may be beneficial in patients with HF from LV systolic dysfunction. Evidence for benefit is derived both from mechanistic studies, short-term clinical

trials that show physiologic improvement and benefits on exercise capacity following exercise training, and a large, multicenter study of long term benefits.[63,64,112] The possibility exists that exercise training could be harmful to patients with HF, especially if it is applied in a population not consistent with those participating in completed studies. At present, exercise training cannot be recommended in patients with LV systolic dysfunction who had a major cardiovascular event or procedure within the last six weeks, in patients receiving cardiac devices that limit the ability to achieve target heart rates, and in patients with significant arrhythmia or ischemia during baseline cardiopulmonary exercise testing.

Potential Pathophysiologic Role of Hemoglobin in HF: An Unresolved Issue

Anemia and reduced hemoglobin have been associated with HF for decades. Until recently the assumption was that the observed reduction in hemoglobin was consistent with ''anemia of chronic disease,'' was not of prognostic significance and did not need to be treated. A number of recent studies demonstrated a significant association between reduced hemoglobin and a number of adverse outcomes, including exercise capacity, quality of life, and risk of death or hospitalization.

Prevalence and Pathogenesis. The prevalence of reduced hemoglobin and anemia in HF varies widely. Depending on the anemia criterion used and patient population studied, from 10% to 70% of HF patients meet criteria for anemia.[113] Reduced renal function is increasingly common in patients with HF and is a well-documented cause of anemia.[114] Anemia is common in elderly patients with HF, especially those with a history of hospitalization for HF, and patients with advanced clinical class are more likely to have reduced hemoglobin. A prospective ongoing study of patients with HF seen in specialty clinics and community cardiology practices suggests approximately 30 percent of patients with HF are anemic.[115,116]

The pathogenesis of anemia in patients with HF is uncertain. Several potential mechanisms have been proposed, including impaired renal function, malabsorption, nutritional deficiency and cytokine activation.[114,117–120]

Morbidity and Mortality. Preliminary analysis of the results of prospective quality of life measurements in unselected outpatients with HF seen in specialty clinics or community cardiology practices suggests that reduced hemoglobin is associated with poorer quality of life.[121] Reduced hemoglobin has been shown to be a risk factor for hospitalization for HF. A retrospective study of Medicare patients reviewed the association between outcome and hemoglobin in 665 patients admitted to community hospitals for HF.[122] The risk of hospitalization was significantly increased in patients who also had anemia and was nearly doubled among those patients with anemia and chronic kidney disease (defined as a serum creatinine >1.4 mg/dL for women and >1.5 mg/dL for men).

A number of retrospective database studies have demonstrated that reduced hemoglobin is significantly associated with increased mortality in patients with HF.[123–125] Early work in a high-risk subset of patients with HF suggests that dilutional anemia, even more than true anemia, is associated with a poor prognosis. Hemodilution can worsen HF by impairing peripheral oxygen delivery, and the volume overload that occurs with hemodilution increases pulmonary capillary wedge pressure. As a result, survival in patients with HF and dilutional anemia is decreased compared with that of patients with HF and true anemia.[126]

Therapeutic Experience. There are very preliminary data to suggest that increasing hemoglobin may have beneficial effects in patients with HF. A recent single-center, small-scale randomized, single-blind, placebo-controlled study evaluated the effect of 3 months of erythropoietin treatment on exercise capacity in 26 patients with anemia and New York Heart Association (NYHA) class III-IV HF.[127] Significant improvement in peak oxygen consumption (VO_2 max) occurred with erythropoietin treatment versus no significant change in the control patients. In the and Ferinject Assessment in Patients with Iron Deficiency and Chronic Heart Failure (FAIR-HF) trial, 200 mg of intravenous iron improved symptoms, functional capacity, and quality of life in patients with chronic heart failure, reduced LVEF, and iron deficiency.[128]

Possible Adverse Effects. Although the association studies and the preliminary clinical investigations suggest potential benefit from augmenting hemoglobin in patients with HF, there are theoretical concerns about this form of therapy. Erythropoietin therapy has been associated with worsening hypertension in 20% to 30% of patients on hemodialysis.[129] Raising the hemoglobin level could adversely affect viscosity, which could lead to increased risk of thrombosis. Increased risk of thrombosis also could occur as a result of increased platelet activation, increased blood viscosity, or effects on the levels of proteins C and S.[130–135]

Summary. Retrospective analysis of database and early interventional studies raises the possibility that augmenting hemoglobin concentration may benefit patients with HF. However, given the risk carried by higher hemoglobin levels, more definitive data on the clinical benefits of anemia therapy in HF are needed. Several important questions remain unanswered concerning the ideal implementation of this therapy, including the optimal hemoglobin level and the appropriate rate of rise of hemoglobin when therapy is initiated. Randomized placebo controlled trials in patients with HF, including Reduction of Events with Darbepoetin alfa in Heart Failure (RED-HF), and IRON-HF are underway to establish the safety and efficacy of this and other treatment strategies.

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