Denton A. Cooley's 50th Anniversary in Medicine

Cardiac Rehabilitation, Exercise Training, and Preventive Cardiology Research

at Ochsner Heart and Vascular Institute

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We review data from our institution demonstrating the benefits of cardiac rehabilitation and exercise training on coronary risk factors, exercise capacity, behavioral characteristics, and quality of life in various subgroups of patients. In addition, we discuss our research in several other areas of preventive cardiology, including lipid disorders, hypertension, left ventricular hypertrophy, fish oils, and antioxidants. We believe that we are now in a very exciting era in which a multifactorial approach to the primary and secondary prevention of coronary artery disease is needed in order to further reduce morbidity and mortality rates. ***(Tex Heart Inst J 1995;22:44-52)***

During the past decade, extensive strides have been made in establishing both the importance of various coronary heart disease (CHD) risk factors and a multifactorial approach to preventing and reducing the progression of atherosclerotic CHD. In this review, we emphasize the research done in these areas, particularly cardiac rehabilitation and exercise training, exercise testing, lipid disorders, hypertension, omega-3 fatty acids, and antioxidants, at the Ochsner Heart and Vascular Institute.

Cardiac Rehabilitation and Exercise Training

Substantial evidence has demonstrated the benefits of phase II cardiac rehabilitation and exercise training programs in patients after major CHD events.[1,2] Significant improvements in exercise capacity and in risk-factor reduction—such as increasing high-density lipoprotein cholesterol (HDL-C) and reducing triglycerides, low-density lipoprotein cholesterol (LDL-C), and obesity indices—have produced psychosocial benefits, reduced subsequent hospitalization costs, and reduced CHD morbidity and mortality and all-cause mortality.[1,2] In this era of increased emphasis on cost-effectiveness, greater scrutiny should be applied to cardiac rehabilitation and exercise training programs, in order to ensure that they are indeed of benefit to patients in various subgroups. Recently, we analyzed a large number of patients in our phase II cardiac rehabilitation and exercise training programs to evaluate the benefits obtained in several subgroups, particularly elderly patients, women, patients with high baseline exercise capacity, obese patients, and patients with abnormal baseline psychosocial and behavioral characteristics.

Elderly Patients. Despite the well-known benefits of cardiac rehabilitation and exercise training, elderly patients are frequently not referred to these programs or given strong encouragement to attend these programs.[3,4] Therefore, we recently compared the benefits of cardiac rehabilitation and exercise training in 92 elderly (≥65 years of age) coronary patients with the benefits in 182 younger (<65 years of age) patients.[3] At baseline, the elderly patients had less obesity, lower hostility scores, lower body mass index (BMI), lower triglyceride levels, and higher levels of HDL-C. In addition, they had significantly lower exercise capacity (Table I). After the cardiac rehabilitation and exercise training program, elderly patients had significant improvements in lipid values, particularly in HDL-C (+6%; $p < 0.001$) and in the LDL-C/HDL-C ratio (-8%; $p < 0.01$). In addition, elderly patients had

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TABLE I. Coronary Risk Profile in Elderly Coronary Patients*

- Lower body mass index
- Higher percent body fat
- Lower triglycerides
- Higher HDL-C levels
- Markedly reduced exercise capacity
- More hypertension
- More diabetes
- Less smoking
- Lower overall functional scores
- Less hostility

*Note: Total cholesterol levels, LDL-C levels, LDL-C/HDL-C ratios, and most behavioral characteristics and parameters of quality of life are similar in elderly and younger coronary patients.

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol

modest improvements in obesity indices (BMI -1.5%, p <0.01; percent body fat -6%, p <0.0001) and fairly marked improvements in estimated exercise capacity (+34%; p <0.0001). Improvements in lipid levels, obesity indices, and exercise capacity were statistically similar in the older and younger patients. We concluded that despite the baseline differences, improvements in exercise capacity, body fat, BMI, and lipid levels were statistically similar in older and younger patients after cardiac rehabilitation and exercise training.

More recently, we have observed a larger cohort of 199 elderly coronary patients and 259 younger patients and have extended our assessment to include behavioral characteristics and quality of life (QOL) parameters, both before and after our cardiac rehabilitation and exercise training program.[5] Again, we found significant baseline differences between the 2 age groups: elderly patients had significantly lower exercise capacity, triglyceride levels, BMI, hostility scores, and overall function scores, and had higher levels of percent body fat and HDL-C. The 2 groups were statistically similar in regard to triglyceride levels, LDL-C levels, LDL-C/HDL-C ratios, and most behavioral characteristics and QOL parameters. After cardiac rehabilitation and exercise training, this large elderly cohort had significant improvements in lipid levels, including modest reductions in total cholesterol and LDL-C levels (-2% and -3%, respectively), an increase in HDL-C levels (+3%,; p = 0.03), and improvement in the LDL-C/HDL-C ratios (-5%; p = 0.05). The elderly patients also had quite dramatic improvements in exercise capacity (+43%; p <0.0001), with modest improvements in obesity indices. Unfortunately, there were no significant improvements in glucose or glycosylated hemoglobin values.

After cardiac rehabilitation and exercise training, elderly patients had quite dramatic improvements in most of their behavioral characteristics, including anxiety, depression, and somatization scores, but did not have a significant improvement in hostility scores. All QOL parameters significantly improved in elderly patients after cardiac rehabilitation and exercise training programs. When we compared the relative improvements in elderly coronary patients with those in younger patients, we found that improvements in most parameters, including lipid levels, obesity indices, and most behavioral characteristics and QOL parameters, were statistically similar in the older and younger patients. However, elderly patients had *greater* relative improvements in estimated exercise capacity (+43% vs +32%; p <0.01) and in mental health (+5% vs +2%; p = 0.05) than younger coronary patients. Therefore, we concluded from this study that despite baseline differences, elderly patients showed improvement in most CHD risk factors, including lipid levels, obesity indices, exercise capacity, behavioral characteristics, and QOL parameters, after cardiac rehabilitation and exercise training. The elderly patients, in fact, had relatively greater improvements than did younger patients in both exercise capacity and mental health after cardiac rehabilitation.

In an analysis of 54 very elderly patients (≥75 years of age), we again demonstrated quite significant improvements in CHD risk factors and in all behavioral characteristics and QOL parameters.[6] Compared with younger coronary patients (<60 years of age), the very elderly had greater relative improvements in exercise capacity, total QOL, well-being, and hostility, and had statistically similar improvements in all other parameters. These data together support the idea that elderly coronary patients, even those ≥75 years of age, should be vigorously encouraged to pursue formal cardiac rehabilitation and exercise training programs after major cardiac events.

Women. On the average, women develop CHD 10 years later than men, yet the disease remains the leading cause of morbidity and mortality in women, and there is substantial evidence that women coronary patients, particularly older women, often are not referred to cardiac rehabilitation and exercise training programs, or are not vigorously encouraged to attend these programs. However, we recently have demonstrated quite significant improvements in CHD risk factors, exercise capacity, behavioral

characteristics, and QOL parameters after cardiac rehabilitation and exercise training in women.[7,8]

Even more recently, we determined the effects of cardiac rehabilitation and exercise training in a cohort of 83 women and 375 men. At baseline, women with CHD had lower exercise capacity, lower LDL-C /HDL-C ratios, and lower scores for energy, function, and total QOL (Table II). The women, however, had higher levels of total cholesterol and LDL-C, higher percent body fat, and higher HDL-C values than their male counterparts. After cardiac rehabilitation and exercise training, women had significant improvements in exercise capacity and lipid levels. Improvements in anxiety scores and somatization scores were statistically significant in women, but improvements in depression and hostility scores did not reach statistical significance. In fact, male coronary patients appeared to have 2 times greater improvements in both depression and somatization scores than did women, although these relative differences were not statistically significant. With the exception of mental health scores, all QOL parameters improved significantly in women after cardiac rehabilitation and exercise training, including total QOL scores. We concluded from these data that women also have significant benefits from cardiac rehabilitation and exercise training programs and, therefore, should be routinely referred to these programs after major CHD events and vigorously encouraged to pursue them.

Patients with High Baseline Exercise Capacity. Some experts have suggested that patients with high baseline exercise capacity may not obtain significant benefits from cardiac rehabilitation and exercise training programs, and could quite possibly be enrolled in less aggressive (and less costly) programs. Therefore, we recently reviewed our experience with 163 patients with a high baseline functional capacity (arbitrarily defined as ≥6 estimated metabolic equivalents [METs]), in comparison with 125 patients with a low baseline exercise capacity (arbitrarily defined as <6 estimated METs).[9] After cardiac rehabilitation and exercise training, patients with high baseline functional capacity had significant improvements in lipid testing, including reductions in total cholesterol (-2%), LDL-C (-4%), triglycerides (-10%), and LDL-C/HDL-C ratios (-10%), and increases in HDL-C (+7%). Patients with high exercise capacity also demonstrated a 22% improvement in estimated exercise capacity (8.8 METs at baseline to 10.7 METs after cardiac rehabilitation; $p < 0.0001$), as well as significant improvements in BMI and percent body fat. When the relative improvements of the 2 groups were compared after cardiac rehabilitation and exercise training, the group of patients with the low baseline exercise capacity had significantly greater improvements in exercise capacity (+48% vs +22%; $p < 0.0001$), but the group with high baseline exercise capacity actually had significantly greater improvements in both LDL-C (-4% vs no change; $p < 0.05$) and in LDL-C/HDL-C ratios (-10% vs -4%; $p < 0.04$). Therefore, we concluded that patients with high baseline exercise capacity have quite significant improvements in exercise capacity, obesity indices, and lipid levels after cardiac rehabilitation and exercise training. In fact, they have relatively greater improvements in both LDL-C levels and LDL-C/HDL-C ratios, suggesting that these patients also should be referred to cardiac rehabilitation and exercise training programs, and encouraged to attend.[9,10]

TABLE II. Coronary Risk Profile in Women with Coronary Heart Disease

Lower in Women	Higher in Women
• Exercise capacity	• Hypertension
• LDL-C/HDL-C ratio	• Diabetes
• Energy scores	• Total cholesterol
• Functional scores	• LDL-C
• Total quality of life scores	• Percent body fat
	• HDL-C

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol

Obese Patients. Numerous studies indicate that obesity is an independent risk factor for CHD events, in addition to its adverse effects on other CHD risk factors, including unfavorable plasma lipid levels, insulin resistance, sedentary lifestyle, elevated arterial blood pressure, and the development of left ventricular hypertrophy.[11,12] We recently assessed the benefits of cardiac rehabilitation and exercise training programs in 116 obese coronary patients (defined as BMI ≥27.3 kg/m^2 in women and ≥27.8 kg/m^2 in men). Unfortunately, the prevalence of obesity did not change significantly after the rehabilitation program (37% to 33%), and the prevalence of severe obesity (BMI ≥35 kg/m^2) also improved only slightly (3.5% to 2.5%).[13] However, the obese patients did show significant improvements in lipid readings, including reductions in total cholesterol levels (-2%), LDL-C levels (-4%), triglyceride levels (-6%), and LDL-C/HDL-C ratios (-10%), and increases in HDL-C levels (+6%). In addition, the obese individuals had improvements in BMI (-3%; $p < 0.0001$) and in percent body fat (-5%; $p < 0.001$), and had a significant improvement in estimated exercise capacity (+24%; $p < 0.001$). However, when the relative benefits of the cardiac rehabilitation and exercise training were

compared, the obese individuals had significantly less improvement in exercise capacity than did nonobese coronary patients.

Although these data support the benefits of cardiac rehabilitation and exercise training in obese individuals, the overall improvements, at least with regard to reducing obesity and improving exercise capacity, were disappointing in the obese patients. Therefore, we concluded that physicians and exercise therapists need to make considerably greater efforts to reduce weight and increase exercise in obese patients.

Patients with Abnormal Psychosocial and Behavioral Characteristics. We have reported that baseline psychological factors help predict improvement in exercise capacity after cardiac rehabilitation and exercise training programs.[14-19] Recently, in a large cohort of Ochsner patients, we demonstrated quite significant improvements in behavioral characteristics, including significant reductions in anxiety, somatization, and depression, and modest improvements in hostility. In subgroups of patients who had high levels of depression, hostility, or both, significant improvements in exercise capacity, obesity indices, lipid levels, behavioral characteristics, and QOL parameters were noted after cardiac rehabilitation and exercise training. In general, those patients with higher depression and hostility scores actually had greater relative improvements in behavioral characteristics after cardiac rehabilitation and exercise training programs.[20]

We strongly believe that depression and hostility significantly improve after cardiac rehabilitation and exercise training, and result in significant improvements in QOL and other behavioral characteristics in these patients. In addition, we feel strongly that greater emphasis should be placed on ensuring that depressed patients and patients with high hostility scores are referred to formal cardiac rehabilitation and exercise training programs after major CHD events. Finally, greater attention in general should be directed at behavioral characteristics, to enhance the secondary prevention of CHD.

Exercise Testing

Although we have substantial evidence that exercise capacity improves significantly after cardiac rehabilitation and exercise training programs (discussed above), most of our earlier studies were performed by estimating exercise capacity on the basis of time and workload on the treadmill. However, we recently demonstrated a significant discrepancy between simply estimating exercise capacity, and precisely measuring exercise capacity by cardiopulmonary exercise testing.[21] Although, nationally, most exercise treadmill tests are performed using the Bruce protocol, we demonstrated in our coronary patients that the Bruce protocol overestimated exercise capacity by approximately 44%, whereas ramping protocols overestimated exercise capacity by only 22%.[21] More recently, we also have demonstrated that use of standard recommended formulas grossly overestimates not only exercise capacity, but particularly the change in exercise capacity after exercise training.[22] This further emphasizes that precisely measuring exercise capacity with cardiopulmonary assessment is crucial in determining the true work capacity and in assessing the response to various therapeutic modalities.

We and others are also quite interested in the use of cardiopulmonary exercise assessment in patients with significant congestive heart failure (CHF). In fact, other investigators have indicated that measuring peak oxygen consumption is very useful in differentiating patients with severe cardiomyopathy (who have a very high mortality rate and urgently need cardiac transplantation) from cardiomyopathy patients with a relatively good short- and medium-term prognosis. However, many patients with severe CHF cannot attain maximal oxygen consumption with treadmill testing. We recently demonstrated that a lack of reduction in VE/VCO_2 with early exercise predicts a low maximal oxygen consumption in patients with CHF and, therefore, can be used as a surrogate in patients who do not achieve the peak oxygen consumption.[23] Finally, we have recently assessed improvements in maximum oxygen consumption and functional measurements of QOL after a 3-month exercise training program in 35 patients with mild to moderate CHF.* In general, changes in measured exercise capacity correlated poorly with most measures of QOL, although there was a quite excellent correlation between improvement in maximal oxygen consumption and one QOL parameter (i.e., role limitation due to physical health) ($r = 0.65$; $p < 0.05$).

Lipids

Considerable evidence during the past decade has indicated the importance of lipids, including LDL-C, HDL-C, and triglycerides, in contributing to the atherosclerotic process.[24-27] Several years ago, the National Cholesterol Education Program (NCEP) made firm recommendations regarding lipid assessment and treatment, which were aimed mostly at reducing LDL-C levels.[28] Although we strongly believe that the NCEP should be applauded for increasing the attention that both physicians and the lay public pay to lipids, we feel that the program's original recommendations strongly underemphasized the role of HDL-C levels.[27,29-31] In fact, in a review of 238 patients with CHD, we demonstrated that nearly half had

*Milani RV, Lavie CJ; unpublished observations; July 1994.

ideal levels of total cholesterol (<200 mg/dL) and LDL-C (<130 mg/dL).[30] Furthermore, less than 25% of our patients had high-risk LDL-C, which was originally defined as LDL-C >160 mg/dL. Nearly 50% of our patients, however, had high-risk HDL-C values of <35 mg/dL, and 25% of our coronary patients had extremely low HDL-C (<30 mg/dL).[30] Although, as mentioned above, elderly patients have higher HDL-C levels than do younger patients, low HDL-C levels were considerably more prevalent than high LDL-C levels both before and after a cardiac rehabilitation and exercise training program, even in the elderly patients.[32] Therefore, we concluded several years ago that the NCEP should reassess the pivotal role of HDL-C levels for its assessment and treatment guidelines, particularly in patients with established CHD, since emphasis on both LDL-C and HDL-C levels is needed for optimal prevention of CHD. While we are delighted that recent recommendations by both the National Institutes of Health Consensus Conference[33] and NCEP II[34] have increased the emphasis on HDL-C, particularly in their assessment guidelines, we still believe that the NCEP II recommendations underestimate the importance of HDL-C. Although the major emphasis in the new recommendations in coronary patients is to achieve a goal LDL-C level of <100 mg/dL and to institute drug treatment for LDL-C levels ≥130 mg/dL, a very high number of coronary patients (approximately one third) have LDL-C levels between 100 and 129 mg/dL, and more than half of these patients have low HDL-C levels (<35 mg/dL). Therefore, we believe that the current NCEP II recommendations place too little emphasis on improving low HDL-C levels, particularly in the large number of CHD patients with LDL-C levels between 100 and 129 mg/dL.*

Substantial evidence in the literature suggests that patients with "isolated" low levels of HDL-C are extremely resistant to both pharmacologic and nonpharmacologic treatments. We believe that this is of critical importance, since approximately 25% of our patients have isolated low HDL-C levels and relatively normal levels of LDL-C and triglycerides. We recently demonstrated that these patients have quite dramatic responses to vigorous nonpharmacologic therapy, including significant increases in HDL-C levels (+17%; $p < 0.0001$) and LDL-C/HDL-C ratio (-11%; $p < 0.0001$). In fact, patients with isolated low HDL-C levels had relatively greater improvements in both HDL-C levels and LDL-C/HDL-C ratios than did other coronary patients after cardiac rehabilitation and exercise training programs.[35]

In addition, there remains considerable controversy regarding the role that triglycerides play in the atherosclerotic process. Although physicians and other health-care professionals generally believe, without scientific support, that patients with high triglycerides often respond better to vigorous nonpharmacologic therapy than do patients with low baseline triglycerides, our recent data strongly dispute this.[35-38] In fact, in a comparison of patients with hypertriglyceridemia (≥250 mg/dL) and patients with "normal" triglyceride levels (<150 mg/dL), patients with low baseline triglyceride levels had greater relative improvements in both LDL-C levels and LDL-C/HDL-C ratio. In a multivariate analysis, a *low* baseline triglyceride value was one of the strongest independent predictors for improving both LDL-C level and LDL-C/HDL-C ratio after a vigorous nonpharmacologic program. Therefore, we concluded that, contrary to popular belief, patients with hypertriglyceridemia are actually more resistant to nonpharmacologic therapy, at least with regard to improving levels of LDL-C and LDL-C/HDL-C ratios; these patients are, then, more likely than patients with low triglyceride levels to require drug treatment aimed at reducing LDL-C values.[39]

We also have a quite large experience in using sustained-release niacin to treat coronary patients with low HDL-C levels. Using a mean dose of niacin of approximately 2.4 grams/day, we demonstrated that, in patients with very low baseline HDL-C levels (<30 mg/dL), significant improvements in total cholesterol levels (-11%; $p < 0.005$), LDL-C levels (-20%; $p < 0.01$), HDL-C levels (+30%; $p < 0.0001$), and LDL-C/HDL-C ratio (-37%; $p < 0.0001$) occurred after drug treatment. Although patients with hypertriglyceridemia responded better to sustained-release niacin than did patients with normal triglyceride levels, there were still quite significant improvements after niacin therapy in those patients with "isolated" low levels of HDL-C.[40-42]

Despite the beneficial effects of sustained-release niacin preparations, many clinicians are concerned about the potential adverse effects of these preparations (particularly increased liver toxicity), in comparison with the effects of immediate-release niacin preparations. Additionally, we described a clotting factor deficiency (with coagulopathy) that occurred in several patients after sustained-release niacin therapy.[43,44] These patients developed only minimal increases in transaminase values (approximately 1.5 times control), but also developed prothrombin times that were approximately 1.5 to 2 times control, which were associated with low levels of lipids, mildly decreased levels of albumin, and deficiencies in Factor VII and Factor II. This syndrome has recurred after rechallenge with sustained-release niacin preparations, but has not recurred after immediate-release niacin therapy. Although our data and the data from others indicate the need for close monitoring of patients receiving various prepara-

* Milani RV, Lavie CJ; unpublished observations; July 1994.

tions of niacin, particularly sustained-released preparations, we believe that the potential benefits of this therapy strongly outweigh the risks, particularly in patients who are closely monitored and who have known CHD or have a high risk of CHD and low levels of HDL-C.

Hypertension

Considerable research at the Ochsner Heart and Vascular Institute has focused on the importance of left ventricular hypertrophy (LVH) as a CHD risk factor, and substantial work has been directed at determining the risk factors for LVH (Fig. 1), the consequences of LVH, and the implications for reducing LVH. A decade ago, Messerli and colleagues[45] demonstrated that patients with evidence of LVH on their electrocardiograms had 40- to 50-fold increases in the prevalence of ventricular arrhythmias, and also had more complex ventricular ectopic activity. However, we demonstrated that patients with very early concentric LVH did not have significant increases in the prevalence or complexity of ventricular arrhythmias.[46] Obese individuals, particularly those with eccentric LVH, had marked increases in both the prevalence and complexity of arrhythmias.[47]

In addition, we recently demonstrated an increased prevalence and complexity of ventricular arrhythmias and atrial arrhythmias in hypertensive patients with isolated septal hypertrophy.[48] In fact, we have recently pooled data from approximately 300 Ochsner patients that demonstrated that various types of LVH, including significant concentric, eccentric, and isolated septal hypertrophy, are all associated with a significant increased prevalence and complexity of ventricular dysrhythmias.[49] We believe that these data suggest the potential pathophysiologic substrate that may at least partly account for the marked increased risk of sudden death in patients with obesity, hypertension, and LVH, or any combination of these factors.

Many studies indicate that hypertension and LVH are also associated with diastolic ventricular filling abnormalities. Although we too found significant filling abnormalities in patients with hypertension, we demonstrated that lean hypertensive patients have only a mild reduction in diastolic filling, and these diastolic filling abnormalities are considerably more marked in obese normotensive individuals (Fig. 2).[50] However, when obesity and hypertension occur in combination, as is frequent in the population, there is a quite marked reduction in left ventricular diastolic function, which not surprisingly may contribute to symptoms of dyspnea, palpitations, exercise intolerance, and even angina.[11,50] We have also demonstrated significant diastolic filling abnormalities in both patients with concentric LVH and patients with isolated septal hypertrophy.[48]

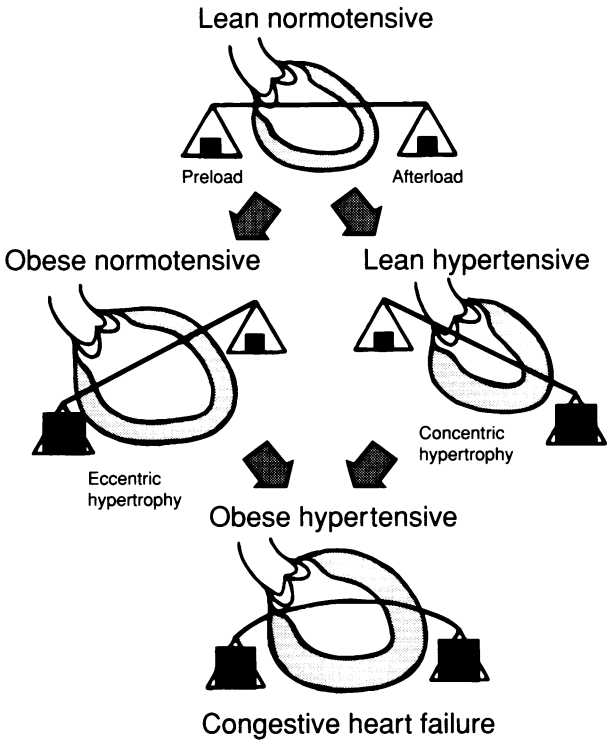

Fig. 1 *Pressure load and obesity indices are important risk factors for left ventricular hypertrophy, because they produce, respectively, concentric hypertrophy (increasing wall thickness without chamber dilatation) and eccentric hypertrophy (mild increase in wall thickness with chamber dilatation).*

(Adapted from: Messerli FH. Cardiovascular effects of obesity and hypertension. Lancet 1982;1:1165-8, with permission. Copyright by The Lancet Ltd.)

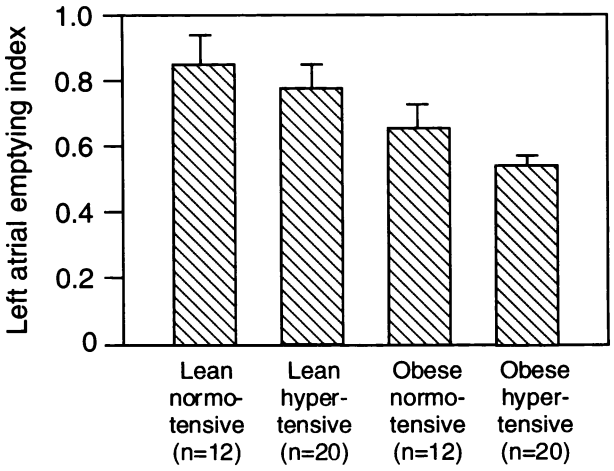

Fig. 2 *Diastolic ventricular dysfunction, as assessed by the left atrial emptying index, in patients with hypertension, obesity, and obesity in combination with hypertension.*

(Adapted from: Lavie CJ, et al.,[50] with permission from Chest.*)*

Moreover, we are studying the effects of cyclosporine-induced hypertension on LVH and concentric remodeling in cardiac transplant recipients.[51] Ventura and colleagues[52] showed that left ventricular concentric remodeling was a predictor of the subsequent development of LVH in cardiac transplant recipients; those patients with concentric remodeling who had elevated pressure and a significantly increased body mass index were particularly prone to developing frank LVH. Studies from our laboratory and elsewhere indicate that various pharmacologic and nonpharmacologic therapies may be associated with significant reductions in LVH (Table III). We recently determined that serotonin uptake inhibition (frequently used to treat depression) was associated with mild reductions in arterial pressure and obesity indices and with modest reductions in LVH in obese hypertensive patients.[53] Ongoing studies will be required in all of these populations to determine if preventing and reducing LVH with various therapeutic modalities reduces cardiac morbidity and mortality beyond reductions achieved with blood pressure control alone.

Other Potential CHD Risk Factors

We have also assessed the effects of cardiac rehabilitation and exercise training on other potential CHD risk factors, including plasma levels of dehydroepiandrosterone sulfate (DHEA-S). Unfortunately, levels of DHEA-S did not increase after cardiac rehabilitation and exercise training.[54] In addition, we are currently assessing the effects of cardiac rehabilitation and exercise training on coagulation factors (e.g., circulatory levels of tissue plasminogen activator, plasminogen activator inhibitor-1, fibrinogen, and von Willebrand factor) and on such other potential CHD risk factors as insulin resistance.

TABLE III. Measures Associated with Reduction of Left Ventricular Hypertrophy

Definite Measures	Possible Measures
• ACE inhibitors	• Weight reduction
• Calcium entry blockers	• Sodium restriction
• β-blockers	• Diuretics with vasodilatory properties (e.g., indapamide)
• Centrally acting agents	• α-blockers
• Immobility	• Serotonin uptake inhibition

ACE = angiotensin-converting enzyme

Omega-3 Fatty Acids

Considerable evidence points to the theoretical benefits of using omega-3 fatty acids (fish oils) in the prevention and treatment of various cardiovascular disorders.[24,55,56] Ventura and colleagues have recently assessed the effects of omega-3 fatty acids in cardiac transplant recipients who had cyclosporine-induced hypertension. In a small cohort of patients, therapy with fish oils resulted in 20% to 25% reductions in both mean arterial blood pressure and systemic vascular resistance, modest reductions in LVH, and modest improvements in left ventricular diastolic filling.[57]

In addition, since omega-3 fatty acids have known immunologic effects, including the potential to reduce levels of tumor necrosis factor, we have recently assessed their effects in patients with end-stage CHF and cardiac cachexia.[58] After fish oil therapy, we noticed improvements in both levels of tumor necrosis factor (-52%) and interleukin-1 (-72%) that were significantly different from the changes noted after placebo administration. Although considerably larger studies are needed for longer time periods, we believe that these preliminary data suggest a potential additional role for fish oils for preventing and treating cardiovascular diseases.

Antioxidants

In common with other investigators, we are very enthusiastic regarding the potential role of antioxidants, particularly antioxidant vitamins (e.g., ascorbic acid, vitamin E, and beta carotene), in preventing and reducing atherosclerotic CHD.[59-62] Although it is clear that more data are needed from large prospective studies, the epidemiologic and experimental evidence for a protective effect of antioxidant vitamins against CHD seems quite strong at present. In addition, therapy with antioxidant vitamins is very inexpensive and seems to be extremely safe, particularly in comparison with other pharmacologic treatments and with invasive interventional treatments for cardiovascular diseases. At this time, we think that the benefits of antioxidant vitamins outweigh the risks, particularly in patients with known CHD or a high risk for CHD.

Conclusion

In this review, we have summarized recent research at the Ochsner Heart and Vascular Institute in various areas related to the prevention and treatment of cardiovascular diseases, particularly CHD. We believe that we are now in a very exciting era, in which a multifactorial approach to the primary and secondary prevention of CHD will best reduce progression and stimulate regression of the disease, thereby lowering morbidity and mortality rates.

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