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Appendix 1. Author Relationships With Industry and Others

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Task Force 6: Coronary Artery Disease

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ATHEROSCLEROTIC CORONARY ARTERY DISEASE

General considerations. Compelling evidence indicates that physical activity reduces cardiovascular events in healthy subjects and cardiac mortality in patients with diagnosed coronary artery disease (CAD) (1). Despite these beneficial exercise effects, vigorous physical activity also transiently increases the risk of both acute myocardial infarction (AMI) (2–4) and sudden cardiac death (SCD) (5–7) with the greatest exercise risk among the most habitually sedentary individuals (2,4,7).

Atherosclerotic CAD is the most frequent cause of these exercise-related cardiac events in adults (8), variously defined as

older than 30, 35, or 40 years of age. Both plaque rupture (9,10) and possibly plaque erosion (11) have been implicated as the immediate cause of exercise-related events in adults, although plaque rupture is more frequent. Several studies over the last decade document that cardiac events frequently occur in coronary arteries that were not previously critically narrowed. This appears to be particularly true for exercise-related cardiac events because angiographic studies of exercise-related AMI in the general population (4) and in sport participants (10) demonstrate less extensive CAD than in comparison subjects. This observation may reflect either selection bias for less severe atherosclerosis in those capable of exercising at high intensity

or the ability of exercise to provoke events in individuals with less severe disease.

Prognosis for diagnosed CAD patients worsens with the extent of disease, left ventricular (LV) systolic dysfunction, inducible ischemia, and electrical instability. Both the recognition that acute cardiac events often occur at the site of previously mild coronary stenoses in the general population and the observation that victims of exercise-related CAD events have less extensive disease than do individuals suffering non-exercise related events reduce the utility of standard CAD risk assessment in evaluating older competitive athletes. Adolescent and young adult athletes also may have variants in their resting electrocardiograms (ECGs) that make the interpretation of their resting and exercise ECGs difficult. In addition, early CAD is increasingly identified by such imaging techniques as coronary artery calcification scoring, further complicating risk assessment because the presence of any coronary artery calcification indicates atherosclerotic disease. Finally, since CAD primarily occurs in adult athletes, the age of the athlete at risk for CAD events complicates the decision process. Older athletes are often engaged in individual competitive pursuits and may not require formal clearance for continued competition. Preparticipation screening guidelines specifically for participants in master's sports have been developed in association with the American Heart Association (AHA) (12).

Diagnosis. The diagnosis of atherosclerotic CAD is established in the presence of any of the following: 1) a history of a myocardial infarction (MI) confirmed by conventional diagnostic criteria; 2) a history suggestive of angina pectoris with objective evidence of inducible ischemia; and 3) coronary atherosclerosis of any degree is demonstrated by coronary imaging studies such as catheter-based coronary angiography, magnetic resonance angiography, or electron beam computerized tomography (EBCT).

CORONARY CALCIFICATION BY COMPUTED TOMOGRAPHY (CT). Since the last version of these guidelines, the widespread dissemination of noninvasive techniques such as EBCT, or even more recently, multi-slice gated CT, has markedly increased the number of individuals, including competitive athletes, who may be diagnosed with atherosclerotic CAD. Although exceedingly rare in young persons (6% of men and 3% of women 20 to 29 years of age), the presence of coronary calcium increases substantially with age, such that for master's athletes, age 40 to 49 years, approximately 41% of men and 13% of women may have measurable coronary calcium (13). Among individuals age 50 to 59 years, 68% of men and 27% of women have documented coronary calcium (13). There is compelling evidence that the presence of any coronary calcium indicates underlying atherosclerosis (14) and that increasing coronary calcium scores are associated with increased CAD risk (15). The coronary calcium score that warrants additional evaluation in asymptomatic competitive athletes is unknown, although scores of more than 100 (15) have been associated

with increased risk for coronary events (16) in the general population compared to patients with no coronary calcium. It is unknown whether the risk of coronary events during intense exercise is increased in the presence of this or lesser amounts of coronary calcium. Nevertheless, for the purpose of the present document, athletes with coronary artery calcification scores more than 100 should undergo the same evaluation as those with more clinically evident CAD.

RISK ASSESSMENT. A paucity of data exists in competitive athletes directly relating the presence and severity of CAD to the risk of athletic participation. This requires that these recommendations for athletes with CAD be based in part on observations obtained from non-athletes with CAD. Nevertheless, it is likely that risk is increased to some degree whenever coronary atherosclerosis is present. It is also likely that the risk of exercise-related events increases with the extent of disease, LV dysfunction, inducible ischemia, and electrical instability, and that the risk increases with the intensity of the competitive sport and the intensity of the participant's effort.

Evaluation.

1. Athletes with CAD diagnosed by any method including coronary artery classification scoring more than 100, coronary angiography, evidence of inducible ischemia, or prior coronary event, and who are undergoing evaluation for competitive athletics, should have their LV function assessed.
2. These athletes should undergo maximal treadmill (or bicycle) exercise testing to assess their exercise capacity and the presence or absence of provokable myocardial ischemia. Exercise testing should approximate as closely as possible the cardiovascular and metabolic demands of the planned competitive event and its training regimen. Despite such simulation, graded exercise testing cannot replicate the cardiovascular stress produced by the sudden bursts of activity, the combination of high dynamic and static exercise, such as rowing, or the sustained bouts of exercise required by athletic training and competition. Therefore, standard clinical exercise tests may not be appropriate for the evaluation of athletes with coronary heart disease.

RISK STRATIFICATION. Two levels of risk can be defined on the basis of testing.

Mildly increased risk. Athletes with CAD diagnosed by any method are judged to be at mildly increased risk if they demonstrate all of the following:

1. Preserved LV systolic function at rest (i.e., ejection fraction greater than 50%).
2. Normal exercise tolerance for age, demonstrated during treadmill or cycle ergometer exercise testing: greater than 10 metabolic equivalents (METs), or greater than 35 O₂/kg-min if less than 50 years old; greater than 9 METs, or greater than 31 ml O₂/kg-min for 50 to 59 years old; greater than 8 METs, or greater than 28 ml

- O₂/kg-min, if 60 to 69 years old; and greater than 7 METS, or greater than 24 ml O₂/kg-min, if greater than or equal to 70 years old. It should be noted that young, highly competitive endurance athletes should have maximal oxygen uptakes far in excess of ranges regarded as normal, which in fact may represent substantial functional impairment in this population.
3. Absence of exercise-induced ischemia and exercise-induced or post-exercise complex ventricular arrhythmias, including frequent premature ventricular contractions (greater than 10% of beats/min), couplets, or ventricular tachycardia.
 4. Absence of hemodynamically significant stenosis (generally regarded as 50% or more luminal diameter narrowing) in any major coronary artery by coronary angiography.
 5. Successful myocardial revascularization by surgical or percutaneous techniques if such revascularization was performed.

Substantially increased risk. Athletes with CAD identified by noninvasive or invasive testing are judged to be at substantially increased risk if they demonstrate *any* of the following:

1. Impaired LV systolic function at rest (i.e., ejection fraction less than 50%).
2. Evidence of exercise-induced myocardial ischemia or complex ventricular arrhythmias.
3. Hemodynamically significant stenosis of a major coronary artery (generally regarded as 50% or more lumen diameter narrowing) if coronary angiography was performed.

The American College of Cardiology/AHA guidelines on exercise testing note that it is not necessary to stop beta-blockers before routine exercise testing, although this practice may reduce the diagnostic and prognostic value of the test (17). The decision whether or not to stop beta-blocker therapy before exercise testing of athletes should be made on an individual basis. Stopping beta-blockers and other anti-ischemic medications before testing may be useful to more closely approximate the probable risk if the athlete either intentionally or unintentionally does not take these medications before competition, or when certain athletic regulatory bodies prohibit beta-blockers. If anti-ischemic medications are stopped, this should be done carefully to avoid a potential hemodynamic rebound effect, which could lead to accelerated angina or hypertension.

Coronary arteriography is not required to determine eligibility for competition in patients with known CAD, and no evidence of inducible ischemia, but is recommended in athletes with exercise-induced ischemia who choose to participate in sports against medical advice. Such studies may identify coronary lesions that may be better managed by percutaneous or surgical myocardial revascularization procedures to relieve exercise-induced ischemia and potentially to reduce exercise-related risk.

The panel wishes to emphasize that the following rec-

ommendations are prepared as a guidelines for permitting participation in *competitive sports*. Restrictions in the following recommendations, therefore, should not be misinterpreted as an injunction against regular physical activity as opposed to athletic competition. Indeed, regular and recreational physical activity and moderate-intensity exercise training are recommended for patients with CAD for its general cardiovascular benefits (1).

Recommendations:

1. **Athletes in the mildly increased risk group can participate in low dynamic and low/moderate static competitive sports (classes IA and IIA—see Fig. 1 in Task Force 8: Classification of Sports) but should avoid intensely competitive situations. We recognize that selected athletes with mildly increased risk may be permitted to compete in sports of higher levels of intensity when their overall clinical profile suggests very low exercise risk. This is particularly true for athletes in whom the only indication that coronary atherosclerosis is present is from an EBCT performed for screening purposes, and in which the total coronary calcium score is relatively low (i.e., less than 15). Increasing amounts of coronary calcium, suggestive of increasing burden disease, should dictate a more cautious approach, particularly if the coronary calcium score is more than 100. All athletes should understand that the risk of a cardiac event with exertion is probably increased once coronary atherosclerosis of any severity is present. Athletes with mildly increased risk engaging in competitive sports should undergo re-evaluation of their risk stratification at least annually.**
2. **Athletes in the substantially increased risk category should generally be restricted to low-intensity competitive sports (class IA).**
3. **Athletes should be informed of the nature of prodromal symptoms (such as chest, arm, jaw and shoulder discomfort, unusual dyspnea) and should be instructed to cease their sports activity promptly and to contact their physician if symptoms appear. Physicians should be aware that competitive athletes may minimize symptoms that occur during exertion.**
4. **Those with a recent MI or myocardial revascularization should cease their athletic training and competition until recovery is deemed complete. This interval varies among patient groups, but depends on the severity of the cardiovascular event and the extent and success of the revascularization procedure. Such patients may benefit from cardiac rehabilitation during the recovery period. No firm guidelines exist for how long patients should avoid vigorous exercise training, but in general, patients post-stent placement for stable CAD symptoms should avoid vigorous exercise training for competition for approximately four weeks. Patients undergoing stent**

placement for unstable disease should wait at least this long. Following coronary bypass surgery, patients should avoid vigorous training until their incisions can tolerate vigorous activity. After recuperation period, the risk and activity level should be defined as in recommendations 1 and 2.

5. All athletes with atherosclerotic CAD should have their atherosclerotic risk factors aggressively treated as studies suggest that comprehensive risk reduction is likely to stabilize coronary lesions and may reduce the risk of exercise-related events.

It must be emphasized that even athletes identified as being at mildly increased risk and permitted to participate in low dynamic and low/moderate static competitive sports (classes IA and IIA) cannot be assured that such participation will not increase the risk of cardiac events because it is probable that any exercise transiently poses some increased exercise risk once CAD is established.

CORONARY ARTERY VASOSPASM

Coronary artery vasospasm classically presents as rest angina associated with ST-segment elevation, but can be provoked by physical exertion on rare occasions (18). Vasospasm is an uncommon cause of chest pain that is evident in 2% to 3% of patients presenting with chest pain undergoing coronary angiography (19). Vasospasm is most frequently observed at coronary sites damaged by atherosclerosis (20), but a substantial cohort may have angiographically normal coronary arteries or minimal angiographic luminal narrowing (18,19). A vasospastic contribution to ischemia should be suspected when there is marked variation in the exercise threshold for angina (18), and when there is evidence of myocardial ischemia with little or no coronary luminal narrowing. Presently, no widely accepted noninvasive test exists for eliciting and quantifying vasospastic angina in the setting of nonobstructive or mildly obstructive coronary arteries. The occurrence of ST-segment elevation during exercise testing appears to correlate with the degree of disease activity (i.e., those with more frequent episodes of angina will more likely have a positive test) (21). Provocative testing with ergonovine-related substances during coronary arteriography is rarely used (22), but remains the only test recommended in current practice guidelines (23). However, forced hyperventilation testing, particularly when combined with nuclear perfusion imaging, may be a useful noninvasive test not requiring the administration of ergonovine (24). The risk associated with participation in sports for athletes with coronary artery spasm is not known, but we recommend a cautious approach to patients with documented coronary vasospasm until the risk of physical exertion for these patients is better defined.

Recommendations:

1. Athletes with CAD as previously defined and clinically important coronary artery vasospasm should follow the

evaluation and risk stratification approach delineated for athletes with coronary atherosclerosis.

2. Athletes with coronary vasospasm documented at rest or with exercise and angiographically normal coronary arteries or without evidence of arterial plaquing should be restricted to low-intensity competitive sports (class IA). This restriction should be re-evaluated at least annually because some patients with coronary vasospasm may experience spontaneous remission.

CAD IN CARDIAC TRANSPLANT RECIPIENTS

Orthotopic transplanted hearts develop an accelerated form of coronary vasculopathy, usually detected by serial coronary angiography or intravascular ultrasound studies, that is a leading cause of death after the first post-transplant year (25,26). The coronary disease is different from that seen in non-transplanted hearts with coronary atherosclerosis; the disease is diffuse and characterized by pronounced intimal thickening and involvement of the entire coronary tree. Discrete stenoses of epicardial arteries can coexist in some instances. Cardiac allografts are denervated, and although some recipients may develop a degree of sympathetic reinnervation, acute coronary syndromes may present with atypical symptoms as opposed to angina (27). Noninvasive testing for CAD is less sensitive in the transplant recipient; many patients do not achieve VO_{2max} , and cardiac denervation can limit peak heart rate response and symptoms. Provocative myocardial perfusion imaging can fail to detect ischemia (25,27) although dobutamine echocardiography has been shown to predict subsequent ischemic cardiac events (26,28–31) after the first three to five years post-transplant. In many cardiac transplant centers, a normal stress echocardiogram justifies postponement of annual coronary angiography (26,28–31). Coronary angiography can also underestimate disease severity because of the diffuse nature of the CAD process; intravascular ultrasound studies increase the sensitivity (26).

Evaluation.

1. Cardiac transplant recipients participating in competitive athletics should undergo yearly maximal exercise testing with echocardiography using a protocol designed to simulate the cardiac and metabolic demands of the competitive event and its training.
2. Additional evaluation, including such procedures as coronary angiography and intravascular ultrasonography (IVUS) should be performed as directed by the transplant center and the transplant cardiologist. Coronary angiography/IVUS should also be performed if the annual exercise test is abnormal and to evaluate unexplained symptoms such as dyspnea or exertional fatigue as these may be the only symptoms of progressive vascular disease.

Recommendations:

1. Because of the special issues involved with transplant patient management, decisions as to the feasibility of athletic competition for cardiac transplant recipients should be made in conjunction with the patient's transplant cardiologist.
2. Athletes with no coronary luminal narrowing, no exercise-induced ischemia, and with normal exercise tolerance for age (as previously defined) can generally participate in all competitive sports as appropriate for their exercise capacity.
3. Athletes with coronary luminal narrowing should be risk stratified as outlined in the section entitled Evaluation with activity recommendations as indicated in the section entitled Atherosclerotic Coronary Artery Disease.

MYOCARDIAL BRIDGING

Myocardial bridging is a condition in which a segment of major epicardial coronary artery (most commonly the left anterior descending) is tunneled within and completely surrounded by LV myocardium. Myocardial bridging is found in approximately 30% of hearts examined at necropsy (32), but is visualized during angiography in less than 5% of patients probably because the thin bridges identified at necropsy cause little anatomic compression during systole (32). Consequently, most tunneled epicardial coronary arteries appear to be of little clinical significance, but this malformation has occasionally been associated with exercise-related sudden death (33,34) and exercise-induced angina pectoris (35). Clinically significant myocardial bridges have a long deeply-tunneled segment and are associated with regional ischemia. Treatment options include medical management with beta-adrenergic or calcium channel-blocking agents, coronary stenting, and surgical resection of the myocardial bridge.

However, coronary stenting has been associated with restenosis and periprocedural complications in 50% of cases (32). Surgical resection in selected symptomatic patients has been shown to reduce angina (35) and improve myocardial blood flow (36). Task Force 4: HCM and Other Cardiomyopathies, Mitral Valve Prolapse, Myocarditis, and Marfan Syndrome provides recommendations for the management of myocardial bridging in patients with hypertrophic cardiomyopathy (HCM).

Recommendations:

1. Athletes with myocardial bridging of an epicardial coronary artery and no evidence of myocardial ischemia at rest or during exercise can participate in all competitive sports as appropriate for their exercise capacity.
2. Athletes with myocardial bridging of an epicardial coronary artery and objective evidence of myocardial

ischemia or prior MI should be restricted to low-intensity competitive sports (class IA).

3. Athletes with surgical resection of the myocardial bridge or stenting should be restricted to low-intensity sports for at least six months after the procedure. Athletes who remain asymptomatic after the procedure should undergo exercise testing. If exercise tolerance is normal for age and gender, and there is no evidence of exercise-induced ischemia, the athlete may participate in all competitive sports.

Finally, recommendations for other congenital coronary artery anomalies, including those originating from the wrong coronary sinus, are provided in Task Force 1: Preparticipation Screening and Diagnosis of Cardiovascular Disease in Athletes.

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Appendix 1. Author Relationships With Industry and Others

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Dr. Luther T. Clark	None	None	None	None	None	None
Dr. Benjamin D. Levine	None	None	None	None	None	None
Dr. Robert J. Myerburg	• Guidant • Procter & Gamble	None	• Procter & Gamble • Reliant Pharmaceutical	None	None	• 2000, Defense, Lewis vs. Mudge • 2002, Defense, Weiner vs. Vitello • 2005, Defense, Ephedra Multi-District Litigation
Dr. Paul D. Thompson	• Astra Zeneca • Bristol Myers Squibb	• Astra Zeneca • Merck • Pfizer • Schering	None	• Astra Zeneca • Merck • Pfizer • Schering	• Pfizer • Schering	• 2005, Plaintiff, Sudden death in college athlete • 2004, Defense, Stress test/recreational sports • 2002, Sudden death, World Gym • 2002, Plaintiff, Sudden death, truck driver • 1998, Plaintiff, Sudden death, recreational sports