38 - 46 Exercise Intolerance

46 Exercise Intolerance

Joseph Loscalzo

Palpitations Palpitations are extremely common among patients who present to their internists and can best be defined as a “thumping,” “pounding,” or “fluttering” sensation in the chest. This sensation can be either inter mittent or sustained and either regular or irregular. Most patients inter pret palpitations as an unusual awareness of the heartbeat and become especially concerned when they sense that they have had “skipped” or “missing” heartbeats. Palpitations are often noted when the patient is quietly resting, during which time other stimuli are minimal. Palpita tions that are positional generally reflect a structural process within (e.g., atrial myxoma) or adjacent to (e.g., mediastinal mass) the heart. Palpitations are brought about by cardiac (43%), psychiatric (31%), miscellaneous (10%), and unknown (16%) causes, according to one large series. Among the cardiovascular causes are premature atrial and ventricular contractions, supraventricular and ventricular arrhythmias, mitral valve prolapse (with or without associated arrhythmias), aortic insufficiency, atrial myxoma, myocarditis, and pulmonary embolism. Intermittent palpitations are commonly caused by premature atrial or ventricular contractions: the post-extrasystolic beat is sensed by the patient owing to the increase in ventricular end-diastolic dimension following the pause in the cardiac cycle and the increased strength of contraction (post-extrasystolic potentiation) of that beat. Regular, sustained palpitations can be caused by regular supraventricular and ventricular tachycardias. Irregular, sustained palpitations can be caused by atrial fibrillation. It is important to note that most arrhythmias are not associated with palpitations. In those that are, it is often useful either to ask the patient to “tap out” the rhythm of the palpitations or to take their pulse during palpitations. In general, hyperdynamic cardio vascular states caused by catecholaminergic stimulation from exercise, stress, or pheochromocytoma can lead to palpitations. Palpitations are common among athletes, especially older endurance athletes. In addi tion, the enlarged ventricle of aortic regurgitation and accompanying hyperdynamic precordium frequently lead to the sensation of palpita tions. Other factors that enhance the strength of myocardial contrac tion, including tobacco, caffeine, aminophylline, atropine, thyroxine, cocaine, amphetamines, and cannabis, can cause palpitations. Psychiatric causes of palpitations include panic attacks or dis orders, anxiety states, and somatization, alone or in combination. Patients with psychiatric causes for palpitations more commonly report a longer duration of the sensation (>15 min) and other accom panying symptoms than do patients with other causes. Among the miscellaneous causes of palpitations are thyrotoxicosis, drugs (see above) and ethanol, spontaneous skeletal muscle contractions of the chest wall, pheochromocytoma, systemic mastocytosis, and postCOVID syndrome. APPROACH TO THE PATIENT Palpitations The principal goal in assessing patients with palpitations is to deter mine whether the symptom is caused by a life-threatening arrhyth mia. Patients with preexisting coronary artery disease (CAD) or risk factors

for CAD are at greatest risk for ventricular arrhythmias (Chap. 253) as a cause for palpitations. In addition, the associa tion of palpitations with other symptoms suggesting hemodynamic compromise, including syncope or lightheadedness, supports this diagnosis. Palpitations caused by sustained tachyarrhythmias in patients with CAD can be accompanied by angina pectoris or dyspnea, and, in patients with ventricular dysfunction (systolic or diastolic), aortic stenosis, hypertrophic cardiomyopathy, or mitral stenosis (with or without CAD), can be accompanied by dyspnea from increased left atrial and pulmonary venous pressure.

Key features of the physical examination that will help confirm or refute the presence of an arrhythmia as a cause for palpita tions (as well as its adverse hemodynamic consequences) include measurement of the vital signs, assessment of the jugular venous pressure and pulse, and auscultation of the chest and precordium. A resting electrocardiogram can be used to document the arrhyth mia. If exertion is known to induce the arrhythmia and accom panying palpitations, exercise electrocardiography can be used to make the diagnosis. If the arrhythmia is sufficiently infrequent, other methods must be used, including continuous electrocar diographic (Holter) monitoring; telephonic monitoring, through which the patient can transmit an electrocardiographic tracing during a sensed episode; loop recordings (external or implantable), which can capture the electrocardiographic event for later review; and mobile (self-monitoring) cardiac outpatient telemetry. Data suggest that Holter monitoring is of limited clinical utility, while the implantable loop recorder and mobile cardiac outpatient telemetry are safe and possibly more cost-effective in the assessment of patients with (infrequent) recurrent, unexplained palpitations. The use of a diary or an electronic marker to indicate the timing of palpitations sensed by the patient is essential for appropriate interpretation of these studies. Exercise Intolerance CHAPTER 46 Most patients with palpitations do not have serious arrhythmias or underlying structural heart disease. If sufficiently troubling to the patient, occasional benign atrial or ventricular premature con tractions can often be managed with beta-blocker therapy. Palpita tions incited by alcohol, tobacco, or illicit drugs need to be managed by abstention, while those caused by pharmacologic agents should be addressed by considering alternative therapies when appropri ate or possible. Psychiatric causes of palpitations may benefit from cognitive therapy or pharmacotherapy. The physician should note that palpitations are at the very least bothersome and, on occasion, frightening to the patient. Once serious causes for the symptom have been excluded, the patient should be reassured that the palpi tations will not adversely affect overall prognosis. ■ ■FURTHER READING Crossland S, Berkin L: Problem based review: The patient with palpitations. Acute Med 11:169, 2012. Jamshed N et al: Emergency management of palpitations in the elderly: Epidemiology, diagnostic approaches, and therapeutic options. Clin Geriatr Med 29:205, 2013. Martson HR et al: Mobile self-monitoring ECG devices to diagnose arrhythmias that coincide with palpitations: A scoping review. Healthcare (Basel) 7:E96, 2019. Sakh R et al: Insertable cardiac monitors: current indications and devices. Expert Rev Med Devices 16:45, 2019. Weinstock C et al: Evidence-based approach to palpitations. Med Clin North Am 105:93, 2021. Joseph Loscalzo, William M. Oldham

Exercise Intolerance Exercise intolerance is defined as the inability to perform physical activity at a level expected for a person of a given age, sex, body mass, and muscle mass. Reduced exercise tolerance is a common symptom of many chronic diseases, including ischemic heart disease, valvular heart disease, heart failure, chronic obstructive pulmonary disease, inter stitial lung disease, cystic fibrosis, pulmonary hypertension, stroke, neuromuscular disorders, and postinfection syndromes, and it reduces

quality of life. While not all patients with these disorders necessarily manifest exercise intolerance, those who do often have an increased rate of disease progression, as well as mortality.

PATHOBIOLOGY The pathobiology of exercise intolerance depends on the specific underlying cause but can be physiologically defined by measuring exercise capacity in terms of the rate of oxygen consumption (V·O2) at peak exercise (V·O2max). Any factor that impairs O2 delivery or utilization can reduce V·O2max and cause exercise intolerance. In natural sequence, reduced inspired O2 concentration, reduced alveolar ventilation, impaired lung diffusion from alveolus to capillary, reduced hemoglobin concentration or transport (loading or release) of O2, decreased cardiac output, impaired diffusion of O2 into (skeletal) muscle, and impaired mitochondrial respiration can each lead to decreased exercise capacity and exercise intolerance (Fig. 46-1). In the absence of clear evidence for a singular cause among these specific pathophysiologic abnormalities (such as decreased cardiac output in a patient with heart failure with reduced ejection fraction) or in the set ting of multiple causes, cardiopulmonary exercise testing (CPET) can serve as an important diagnostic test. CPET typically involves measure ment of breath-by-breath O2 consumption and CO2 production and continuously recording the electrocardiogram during stationary cycle ergometry. In more advanced types of CPET, intracardiac (right-heart) pressures are also measured during exercise, as are arterial blood gases and lactate before, during, and after exercise, providing additional diagnostic information to identify the underlying physiologic etiology of exercise limitation. PART 2 Cardinal Manifestations and Presentation of Diseases SIGNS AND SYMPTOMS The signs and symptoms of exercise intolerance can vary depending on its severity and etiology. For example, patients with heart failure with reduced ejection fraction following an acute myocardial infarction may be unable to walk up a flight of stairs yet feel comfortable at rest, or patients with severe pulmonary arterial hypertension may be short of breath with minimal exertion. In some cases, patients who are quite intolerant of exercise may note unusual breathlessness or dyspnea at rest accompanied by tachypnea, (sinus) tachycardia, muscle fatigue, weakness, or frank myalgias. SPECIFIC DISORDERS Exercise intolerance in patients with heart failure with preserved ejec tion fraction (HFpEF) is a well-recognized feature of the syndrome. The great majority of patients with HFpEF manifest multiple causes, including (in decreasing order of frequency) impaired skeletal muscle diffusion of O2, reduced cardiac output (with exercise), decreased alveolar ventilation, reduced lung diffusing capacity, and anemia. Internal work, a body mass index–related measure of the cost of initiating movement, is higher in patients with HFpEF compared with controls and is associated with rapid increases in cardiac filling pressures (and the pulmonary capillary wedge pressure) early in exercise. Other associated mechanisms for these abnormalities include increased large artery stiffness, chronotropic incompe tence, and microvascular dysfunction (both endothelium-dependent and endotheliumindependent) (Fig. 46-2). Accompanying comorbid conditions may also contribute to these multifactorial drivers of exercise intol erance in HFpEF, including inflammation, adipokine signaling, and insulin resistance in obese diabetics. Ascertaining the set of causes in any individual patient serves as the basis for a precision medicine approach to the treatment of this common symptom in HFpEF, as is the case for other diseases associated with exercise intolerance. Decreased alveolar ventilation Reduced lung diffusing capacity Lung Skeletal Muscle FIGURE 46-2 Determinants of exercise intolerance in heart failure with preserved ejection fraction (HFpEF).

Inspired oxygen Alveolar ventilation Lung diffusing capacity Hemoglobin transport Cardiac output Microvascular perfusion Muscle diffusion Mitochondrial respiration FIGURE 46-1 Oxygen delivery and utilization pathway. A variety of (post)viral syndromes are also associated with exer cise

intolerance, including Epstein-Barr virus infection and postCOVID-19 (long COVID) syndrome. Patients with long COVID often have symptoms that are similar to those of patients with myalgic encephalomyelitis; however, the latter more typically include postex ertional malaise. In patients following recovery from acute COVID, the inability to return to normal activity levels often heralds the devel opment of long COVID. In patients with long COVID, a significant number noted exertional dyspnea, fatigue, and anxiety for up to 3 months after the acute infection, with fatigue remaining as the most common symptom thereafter. Orthostatic intolerance and positional tachycardia are common and reflect autonomic dysfunction. Among the mecha nisms for long COVID–associated fatigue and exercise intolerance are oxidative stress, altered energy metabolism, and dysbiosis of the gut microbiome. Cardiac deconditioning is also believed to play a role in the exercise intolerance of long COVID. Thus, focused exercise pre scriptions guided by patient-specific pathophysiology have been shown to relieve symptoms in many individuals. Heart Increased filling pressures Chronotropic incompetence Increased large artery stiffness Decreased cardiac output Anemia Microvascular dysfunction Impaired skeletal muscle diffusion

---

Revision #1
Created 2026-01-06 16:31:22 UTC by Omar Ayman
Updated 2026-01-06 16:31:22 UTC by Omar Ayman