CARDIOLOGY Rounds®

As presented in the Rounds of the Division of Cardiology, St. Michael's Hospital, University of Toronto

Exercise and Acute Cardiovascular Events

By SEAN JEDRZKIEWICZ, MD, and GORDON MOE, MD

The benefits of regular physical activity in protecting against the manifestations of coronary heart disease (CHD) have been accepted, in part due to data from basic research, as well as from clinical and epidemiologic studies.[1,2,3] As clinicians, we encourage our patients to pursue an exercise regimen with at least 20-30 minutes of moderately intense activity on most, if not all, days of the week.[4] However, it is important to remember that there is an increase in the risk of acute myocardial infarction (AMI) and sudden cardiac death associated with vigorous activity, most pronounced in individuals who are usually sedentary.[5,6] The incidence of and mechanisms for such events vary among young athletes, healthy adults, and adults with known CHD. Strategies are available to help measure this risk and ultimately reduce the incidence of exercise-related events. This issue of *Cardiology Rounds* reviews the incidence and pathophysiology of exercise-related cardiovascular (CV) events in young individuals and adults and explores prediction and prevention strategies. The recent American Heart Association (AHA) Scientific Statement on exercise and acute CV events is also discussed.

Data from epidemiological studies have demonstrated the benefits of regular participation in physical activity, the most notable being a decline in cardiac events such as AMI or sudden cardiac death (SCD).[8] Further studies have illustrated that it is the effect of the activity itself, rather than other factors (eg, an improved lipid profile or dilated epicardial coronaries) that contributes to this benefit.[9] However, vigorous physical exertion, defined historically as an exercise work rate of ≥6 metabolic equivalents (METs), has also been recognized as one of the most common stressors in precipitating cardiac events. The incidence and pathophysiology of exercise-related cardiac events varies among patient groups, including young athletes, healthy adults, and individuals with CHD, and studies have revealed several important risk factors. A clearer understanding of exercise-related cardiac events will enable clinicians to counsel patients on the risk of activity and perhaps identify at-risk patients who require further investigation.

Incidence of cardiovascular events

The incidence of exercise-related cardiac events is very low and, as such, it is difficult to fully characterize these individuals in clinical studies. The social and emotional impact of such events, particularly in young and otherwise healthy athletes, can be devastating. Research in this area has been difficult since most analyses have been retrospective, based on only a few events, and with estimates accompanied by large confidence intervals. The occurrence of adverse CV events during activity may be influenced by the clinical or subclinical characteristics of the population being studied and, in this regard, at least 3 groups may be considered: young athletic individuals, healthy adults, and adults with CHD.

Young individuals: Young athletes are defined in the literature as those aged ≤35 years, who are engaged in regular physical training in preparation for official athletic competitions.[10]

St. Michael's Hospital
30 Bond St.,
Suite 7049, Queen Wing
Toronto, Ont. M5B 1W8
Fax: (416) 864-5941

Competition is either as part of a team or on an individual basis and, at times, it is associated with both extreme physical and emotional stresses during competitions. Data from several recent studies have helped to estimate the absolute rate of exercise-related cardiac events in young athletes. One study indicates that the absolute SCD rate among high school and college athletes varies from 1/133,000 in men and 1/769,000 in women.[14] Data from high school athletes in Minnesota revealed a frequency of sudden death of 1/200 000/year.[15] A large prospective study in Italy reported an incidence of sudden death of 2.1/100 000 athletes per year from CV diseases.[16] Events occur more commonly in males (9:1) versus females, likely because women have a lower participation rate in certain sports. The sports most often cited include football and basketball in the United States (Table 1) and soccer in Europe, likely due to high population rates of participation.

Healthy adults: Vigorous exercise may also induce cardiac events in presumably healthy adults. In the Rhode Island Study, 10 deaths occurred during jogging between 1975 and 1980, for an estimate of 1 death/792,000 person hours jogging or 1 death/15,260 joggers/year.[17] A recent study of exercise-related deaths at a large fitness chain revealed that there were 71 deaths over 2 years, suggesting 1 death/82,000 members and 1 death per 2.57 million workouts.[18] The event rates among the 3,617 male participants with hypercholesterolemia in the Lipid Research Clinics Primary Prevention Trial were 1.7% (62 events): 54 events related to AMI (n=54) and 8 events of SCD. The general estimate from this data is that 0.2%/year of hypercholesterolemic men will sustain a cardiac event related to exercise, suggesting an association with high-risk patients.[19]

Adults with CHD: Data for the incidence of cardiac events during exercise in adults with CHD are derived from events recorded at supervised cardiac rehabilitation programs. Estimates from 2 studies suggest that there is 1 cardiac arrest per 89,501 and 146,127 patient-hours, respectively. The incidence of AMI is similarly low, with 1/268,503 and 1/97,418 patient hours. Patients are supervised by trained healthcare professionals with emergency resuscitation equipment, which possibly results in lower death rates.

Pathophysiology

CV complications associated with vigorous activity and their underlying pathophysiologic mechanisms are unique to each patient group and continued activity presents variable degrees of risk among these patients. The incidence of cardiac events in adults is either occult or documented CHD. Because a continuing exercise regimen likely decreases the incidence of similar events, the weight of evidence is in favour of exercise, even though the incidence of premature CHD is very low in young adults. However, the outcome of sustained exercise regimens may worsen the pathophysiology of hypertrophic cardiomyopathy (HCM) or the ischemic effects associated with anomalous coronaries; therefore, continued exercise increases the overall incidence of SCD known to be associated with these entities.[22]

Table 1: Causes of sudden cardiac death in athletes in the United States

- Hypertrophic cardiomyopathy
- Congenital coronary artery anomaly
- Myocarditis
- Aortic rupture
- Mitral valve prolapse
- Arrythmogenic RV cardiomyopathy
- Atherosclerotic CHD
- Conduction system abnormalities
- Aortic valve stenosis

Adapted from Corrado et al[26]

Young individuals: The structural and functional changes in the CV system of a trained athlete have been systematically defined and, in general, represent adaptations caused by the conditioning required for his/her particular sport. Briefly, athletic conditioning activities may be classified as dynamic (ie, isotonic or endurance) or static (ie, isometric or strength). Endurance training (ie, swimming) involves rhythmic changes in muscle length and joint movement with small muscular force, with a resultant volume load on the left ventricle (LV). Strength training (ie, weightlifting) requires large muscular force with little or no changes in muscle length or joint position, imparting a pressure load on the LV. Changes in cardiac morphology acquired through training can be considered advantageous in competition, but may be adverse in athletes with underlying CV disease. [10, 22]

Sudden death usually occurs with physical exertion during competition, often without prior warning symptoms. Ventricular arrhythmia is most often the cause of death in these individuals. Training may increase the incidence of SCD during periods of non-exertion since repeated training may alter the underlying substrate that is already abnormal because of hereditary/congenital conditions. The single most common cause of SCD in the United States is HCM, which represents about one-third of deaths.[14] In HCM, repeated ischemia from training can produce cell death and myocardial fibrosis. Altered tissue architecture enhances ventricular electrical

instability and sudden death likely results from an electrically-unstable myocardium with re-entrant ventricular arrhythmias.[10]

Another common cause of death among athletes is a congenital coronary anomaly; commonly, it is the left main coronary artery from the right sinus of valsalva. Compression or kinking of these anomalous coronaries with exertion can induce ventricular tachyarrhythmia.[23] Data from Italy, in contrast, suggests arrythmogenic right ventricular cardiomyopathy (ARVC) as the predominant etiologic substrate for SCD among young athletes.[10] This possibly represents a different genetic substrate in this population or the effect of a well-established screening program for Italian athletes that more easily identifies HCM. The 2% of athletes with structurally-normal hearts at autopsy have arrhythmic deaths likely related to either a long-QT, the Brugada or Wolff-Parkinson-White syndromes, or coronary artery vasospasm.[10]

Healthy adults: Acute cardiac events among exercising adults often involve plaque rupture with subsequent thrombotic occlusion resulting in ischemia. This mechanism is considered relevant to individuals with documented CHD or "silent" CHD. The entire mechanism linking physical activity with a coronary event is unclear, but vigorous exercise is considered a common trigger and is associated with 4% to 15% of events.[11]

The physical shear stress from changes in geometry and hemodynamic forces on epicardial coronary arteries during activity may contribute to fissuring and/or plaque rupture. Increased blood pressure and heart rate with hyperdynamic myocardial contraction is associated with increased end-diastolic volume and decreased end-systolic volume, which also contribute to physical stress on the coronaries.[12] An atherosclerotic, less compliant, epicardial vessel is less flexible and more prone to these shear forces. Furthermore, such diseased vessels may show paradoxical constriction during exercise. Alternately, the ischemic effects of spontaneous plaque disruption may be magnified with simultaneous exertion, contributing to a more significant clinical event. Increased platelet activation has also been noted in deconditioned individuals after intense activity.[13]

Adults with CHD: Individuals with documented CHD are subject to thrombotic events (as described) but, given their disease, are also prone to ischemia-induced arrhythmia in the peri-infarct area or scar tissue. A second ischemic mechanism occurs upon cessation of activity, with decreased coronary perfusion due to a drop in venous return, exacerbating any activity-induced ischemia that is already present. The potential for malignant ventricular arrhythmias and subsequent collapse, often at the end of exertion, is possibly due to ischemia-potentiating shifts in myocardial depolarization and repolarization.

Exercise and the risk of acute CV events

While the benefits of regular physical activity have been widely accepted, there are also documented risks associated with exertion. Several published studies have identified physical exertion as a trigger for AMI and SCD and determined that there is a temporal association between activity and cardiac events. In the Determinations of Myocardial Infarction Onset Study[24] (ONSET), a case-crossover comparison with matched controls; 4.5% of patients reported heavy exertion (≥6 METs) within 1 hour of AMI symptoms. The relative risk (RR) of AMI in the first hour post-heavy exertion was 5.9 when compared to mild exertion.

Similarly, the Triggers and Mechanisms of Myocardial Infarction (TRIMM) study[25] demonstrated that there is a short-term increased risk of AMI associated with exertion. The adjusted RR for participating in strenuous activity within 1 hour of AMI was 2.1. Also noteworthy is the lower RR of AMI associated with regular exercise (≥4 times per week; Table 2).

A trend towards increased cardiac events has been shown predominantly during exercise and in the less physically-active population. For example, the Rhode Island study[17] of joggers and the Seattle study[19] reported that the hourly death rate increases 7.6-fold and the rate of AMI increases 25-fold, respectively, during jogging, when compared to rest. Overall, there is a trend towards decreased events in active individuals (only 5/million hours), while the rate is up to 18/million hours in the least-active group.[19] These data, therefore, support the concept that exercise acutely increases the risk of a cardiac event; however, the overall risk of an event – both SCD or an AMI – is lower in more physically-active groups.

The above concept does not hold true for young competitive athletes. While they suffer increased cardiac events during training or competition, there is no benefit and, indeed, they may have increased risk with further

Table 2: RR of AMI in relation to frequency of activity

Frequency of vigorous exertion/week	TRIMM Study RR (±95% CI)	ONSET Study RR (±95% CI)
<1		107 (67-171)
1-2	6.9 (4.1-12.2)	19.4 (9.9-38.1)
3-4		8.6 (3.6-20.5)
>5	1.3 (0.8-2.2)	2.4 (1.5-3.7)

activity. This is illustrated by data collected in Italy over 20 years. In this follow-up, there were 2.3 SCDs per 100 000 athletes assessed both during, and outside, of training, compared to 0.9 SCDs among non-athletes. Therefore, the increased risk of continued training leads to overall increased mortality in younger athletes – even during nontraining periods – who continue to train. This is because the maladaptive changes in cardiac morphology, as outlined above, that develop in at-risk athletes are not easily reversible during nontraining periods.

Reducing exercise-related CV events

Since there are inherent risks in vigorous physical activity that may present rather catastrophically in certain groups, it is important to find strategies to reduce these exercise-related cardiac events. Preparticipation screening of both young athletes and healthy adults presents an opportunity to identify at-risk individuals before they are exposed to the additional risks of exercise. In healthy adults, the clinical guidelines on exercise testing before training reflect expert consensus opinion (because there is a lack of controlled trials). The American College of Cardiology (ACC)/AHA Guidelines on Exercise Testing suggest exercise testing in:

- asymptomatic individuals with diabetes mellitus (Class IIa)
- asymptomatic men aged >45 years and women aged >55 years.

One must, however, remember that there are limitations with exercise testing, since most acute cardiac events during exercise result from acute plaque rupture.

The approach to preparticipation screening in young athletes is somewhat different from that in healthy adults, partly because the unique pathology can easily be overlooked. The AHA recommends that preparticipation screening of young athletes should be repeated at 2- and 4-year intervals. The assessment should involve a review of the family and personal medical history and a physical examination, as outlined in Table 3. Conversely, the European Society of Cardiology (ESC) recommends adding a routine electrocardiogram (ECG) to the history and physical (Table 4).

Table 3: AHA recommendations for preparticipation screening of athletes[27]

Family history
- Premature SCD
- Heart disease in surviving relatives who are <50-years-old

Personal history
- Heart murmur
- Systemic hypertension
- Fatigue
- Syncope/near syncope
- Excessive /unexplained exertional dyspnea
- Exertional chest pain

Physical examination
- Heart murmur
- Femoral arterial pulses
- Stigmata of Marfan syndrome
- Brachial blood pressure measurement

This difference in approach between the AHA and the ESC is based on a recent population-based observational study in Italy of SCD in athletes vs nonathletes, aged 12-35 years, between 1979-2004.[28] The annual incidence of SCD decreased from 3.6 deaths/100,000 person/yrs (1 death/ 27,777 athletes) in 1979 to just 0.4 deaths/100,000 person/yrs (1 death/ 250,000 athletes) in 2004. Of note, there was no change in death rate among nonathletes. While these results may not definitively prove the value of such screening or the relevance of ECGs in this regard, these data are the

Table 4: ESC criteria for abnormal ECG in preparticipation athlete assessment[26]

P wave	QRS complex	Rhythm and conduction abnormalities
• Left/right atrial enlargement	• Left/right axis deviation • Increased voltage • Abnormal Q waves • Right or left bundle branch block • ST-segment depression or T-wave flattening/inversion in ≥2 leads • QT >0.44 s in males/>0.46 s in females	• Premature ventricular beats • Ventricular arrhythmias • Supraventricular tachycardias • Short PR interval (<0.12 s) • Sinus bradycardia with HR <40 bpm • 1st/2nd/3rd degree atrioventricular block

most comprehensive to date. Regardless of the specific approach taken to screen young athletes, it is important to remain vigilant and detailed in their assessment.

Conclusion

Available evidence suggests that there is a benefit of regular physical activity in decreasing CV events, but there are no randomized controlled data. However, vigorous activity causes a transient increase in the risk of MI or SCD, even in trained participants. The incidence and pathophysiology of exercise-related cardiac events varies, depending on patient characteristics. Clinicians can help reduce the morbidity and mortality in these individuals if they accurately assess the risk in each particular patient and if they promptly investigate cardiac-like symptoms, even in highly-active patients. Finally, it is important that clinicians utilize published guidelines to assess, not only athletes for competition, but also asymptomatic "healthy" adults prior to rigorous physical exertion.

Dr. Sean Jedrzkiewicz is a cardiology trainee at St. Michael's Hospital.

References

1. Paffenbarger RS, Jr, Hyde RT, Wing AL, Lee I-M, Jung DL, Kampert JB. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 1993;328:538-545.
2. Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. *Ann Rev Pub Health* 1987;8:253-287.
3. Fletcher GF, Balady G, Blair SN, et al. Statement on exercise: benefits and recommendations for physical activity programs for all Americans: a statement for health professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology, American Heart Association. *Circulation* 1996;94:857-862.
4. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995;273:402-407.
5. Giri S, Thompson PD, Kiernan FJ, et al . Clinical and angiographic characteristics of exertion-related acute myocardial infarction. *JAMA* 1999;282:1731-1736.
6. Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH, Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. *N Engl J Med* 2000;343:1355-1361.
7. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and Acute Cardiovascular Events: Placing the Risks into Perspective: A Scientific Statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation* 2007;115:2358-2368.
8. Powell KE, Paffenbarger RS, Jr. Workshop on epidemiologic and public health aspects of physical activity and exercise: a summary. *Public Health Rep* 1985;100:118-126.
9. Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. *Ann Rev Publ Health* 1987;8:253-287.
10. Maron BJ, Shirani J, Poliac LC, Mathenge R, Boberts WC, Mueller FO. Sudden death in young competitive athletes. Clinical, demographics, and pathological profiles. *JAMA* 1996;276:199-204.
11. Tofler GH, Stone PH, Maclure M, et al. Analysis of possible triggers of acute myocardial infarction (the MILIS study). *Am J Card* 1990;66:22-27.
12. Davies MJ, Thomas AC. Plaque fissuring—the cause of acute myocardial infarction, sudden ischaemic death, and crescendo angina. *Brit Heart J* 1985;53:363-373.
13. Kestin AS, Ellis PA, Barnard MR, Errichetti A, Rosner BA, Michelson AD. Effect of strenuous exercise on platelet activation state and reactivity. *Circulation* 1993;88:1502-1511.
14. Van Camp SP, Bloor CM, Mueller FO, Cantu RC, Olson HG. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exercise*1995;27:641- 647.
15. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *JACC* 1998;32:1881-1884.
16. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *JACC* 2003;42:1959-1963.
17. Thompson PD, Funk EJ, Carleton RA, Sturner WQ. Incidence of death during jogging in Rhode Island from 1975 through 1980. *JAMA* 1982;247:2535-2538.
18. Franklin BA, Conviser JM, Stewart B, Lasch J, Timmis GC. Sporadic exercise: a trigger for acute cardiovascular events? *Circulation* 2005;102:II-612. Abstract
19. Siscovick DS, Ekelund LG, Johnson JL, Truong Y, Adler A. Sensitivity of exercise electrocardiography for acute cardiac events during moderate and strenuous physical activity: the Lipid Research Clinics Coronary Primary Prevention Trial. *Arch Intern Med* 1991;151:325-330.
20. Franklin BA, Bonzheim K, Gordon S, Timmis GC. Safety of medically-supervised outpatient cardiac rehabilitation exercise therapy: a 16-year follow-up. *Chest* 1998;114:902-906.
21. Vongvanich P, Paul-Labrador MJ, Merz CN. Safety of medically supervised exercise in a cardiac rehabilitation center. *Am J Card* 1996;77:1383-1385.
22. Maron BJ, Pelliccia A, Spirito P. Cardiac disease in young trained athletes: insights into methods for distinguishing athlete's heart from structural heart disease, with particular emphasis on hypertrophic cardiomyopathy. *Circulation* 1995;91:1596-1601.
23. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *JACC* 2000;35:1493-1501.
24. Mittleman MA, Maclure M, Tofler GH, et al. Triggering of acute myocardial infarction by heavy physical exertion: protection against triggering by regular exertion. *N Engl J Med* 1993;329:1677-1683.
25. Willich SN, Lewis M, Lowel H, et al. Physical exertion as a trigger of acute myocardial infarction. *N Engl J Med* 1993;329:1684-1690.
26. Corrado D, Pelliccia A, Bjornstad H, et al. for Study Group of Sport Cardiology. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. *Eur Heart J* 2005;26:516-524.
27. Maron BJ, Zipes DP. 26th Bethesda Conference: Eligibility Recommendations for Competitive Athletes with Cardiovascular Abnormalities. *JACC* 2005;45:1313-15.
28. Corrado D, Pavei C, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006;296:1593-1601.

Abstract of Interest

Trends in Sudden Cardiovascular Death in Young Competitive Athletes After Implementation of a Preparticipation Screening Program

CORRADO D, BASSO C, PAVEI A, ET AL, PADUA, ITALY.

CONTEXT: A nationwide systematic preparticipation athletic screening was introduced in Italy in 1982. The impact of such a program on prevention of sudden cardiovascular death in the athlete remains to be determined.

OBJECTIVE: To analyze trends in incidence rates and cardiovascular causes of sudden death in young competitive athletes in relation to preparticipation screening.

DESIGN, SETTING, AND PARTICIPANTS: A population-based study of trends in sudden cardiovascular death in athletic and nonathletic populations aged 12 to 35 years in the Veneto region of Italy between 1979 and 2004. A parallel study examined trends in cardiovascular causes of disqualification from competitive sports in 42 386 athletes undergoing preparticipation screening at the Center for Sports Medicine in Padua (22 312 in the early screening period [1982-1992] and 20 074 in the late screening period [1993-2004]).

MAIN OUTCOME MEASURES: Incidence trends of total cardiovascular and cause-specific sudden death in screened athletes and unscreened nonathletes of the same age range over a 26-year period.

RESULTS: During the study period, 55 sudden cardiovascular deaths occurred in screened athletes (1.9 deaths/100 000 person-years) and 265 sudden deaths in unscreened nonathletes (0.79 deaths/100 000 person-years). The annual incidence of sudden cardiovascular death in athletes decreased by 89% (from 3.6/100 000 person-years in 1979-1980 to 0.4/100 000 person-years in 2003-2004; P for trend < .001), whereas the incidence of sudden death among the unscreened nonathletic population did not change significantly. The mortality decline started after mandatory screening was implemented and persisted to the late screening period. Compared with the prescreening period (1979-1981), the relative risk of sudden cardiovascular death in athletes was 0.56 in the early screening period (95% CI, 0.29-1.15; P = .04) and 0.21 in the late screening period (95% CI, 0.09-0.48; P = .001). Most of the reduced mortality was due to fewer cases of sudden death from cardiomyopathies (from 1.50/100 000 person-years in the prescreening period to 0.15/100 000 person-years in the late screening period; P for trend = .002). During the study period, 879 athletes (2.0%) were disqualified from competition due to cardiovascular causes at the Center for Sports Medicine: 455 (2.0%) in the early screening period and 424 (2.1%) in the late screening period. The proportion of athletes who were disqualified for cardiomyopathies increased from 20 (4.4%) of 455 in the early screening period to 40 (9.4%) of 424 in the late screening period (P = .005).

CONCLUSIONS: The incidence of sudden cardiovascular death in young competitive athletes has substantially declined in the Veneto region of Italy since the introduction of a nationwide systematic screening. Mortality reduction was predominantly due to a lower incidence of sudden death from cardiomyopathies that paralleled the increasing identification of athletes with cardiomyopathies at preparticipation screening.

JAMA 2006;296:1593-1601.

Upcoming meetings

5-8 December 2007
EuroEcho 2007
European Society of Cardiology
Lisbon, Portugal
Contact: www.escardio.org/congresses/EE

16 – 20 March 2008
The 24th Annual Cardiovascular Conference at Lake Louise
Lake Louise, Alberta
Contact: www.acclakelouise.com/
Carol Cox/ Hallmark Meeting Concepts
Tel. (905) 814-1112
carol151@sympatico.ca

29 March – 1 April 2008
American College of Cardiology Annual Meeting ACC.08
Chicago, Illinois
Contact: www.acc.org

1 – 3 May 2008
European Society of Cardiology (ESC) Euro Prevent 2008
Paris, France
Contact: ww.escardio.org/

30 August – 3 September 2008
ESC Congress 2008
Munich, Germany
Contact: www.escardio.org/

Disclosure Statement: *Dr. Jedrzkiewicz and Dr. Moe have stated that they have no disclosures to announce in association with the contents of this issue.*

Change of address notices and requests for subscriptions to *Cardiology Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Cardiology Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an educational grant from

Novartis Pharmaceuticals Canada Inc.