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## Cardiovascular Risk of High- Versus Moderate-Intensity Aerobic Exercise in Coronary Heart Disease Patients

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**Background**—Exercise performed at higher relative intensities has been found to elicit a greater increase in aerobic capacity and greater cardioprotective effects than exercise at moderate intensities. An inverse association has also been detected between the relative intensity of physical activity and the risk of developing coronary heart disease, independent of the total volume of physical activity. Despite that higher levels of physical activity are effective in reducing cardiovascular events, it is also advocated that vigorous exercise could acutely and transiently increase the risk of sudden cardiac death and myocardial infarction in susceptible persons. This issue may affect cardiac rehabilitation.

**Methods and Results**—We examined the risk of cardiovascular events during organized high-intensity interval exercise training and moderate-intensity training among 4846 patients with coronary heart disease in 3 Norwegian cardiac rehabilitation centers. In a total of 175 820 exercise training hours during which all patients performed both types of training, we found 1 fatal cardiac arrest during moderate-intensity exercise (129 456 exercise hours) and 2 nonfatal cardiac arrests during high-intensity interval exercise (46 364 exercise hours). There were no myocardial infarctions in the data material. Because the number of high-intensity training hours was 36% of the number of moderate-intensity hours, the rates of complications to the number of patient-exercise hours were 1 per 129 456 hours of moderate-intensity exercise and 1 per 23 182 hours of high-intensity exercise.

**Conclusions**—The results of the current study indicate that the risk of a cardiovascular event is low after both high-intensity exercise and moderate-intensity exercise in a cardiovascular rehabilitation setting. Considering the significant cardiovascular adaptations associated with high-intensity exercise, such exercise should be considered among patients with coronary heart disease. (*Circulation*. 2012;126:1436-1440.)

**Key Words:** coronary disease ■ death ■ sudden ■ exercise ■ heart arrest

High levels of physical activity and aerobic capacity are associated with low risk of cardiovascular disease and mortality.<sup>1-3</sup> Aerobic exercise is therefore strongly recommended both for healthy individuals and for patients with cardiovascular disease to improve cardiovascular health and reduce risk of premature mortality.<sup>4,5</sup> If the total energy expenditure of exercise is held constant, exercise performed at higher relative intensities has been found to elicit a greater increase in aerobic capacity<sup>6</sup> and greater cardioprotective effects than exercise at moderate intensities.<sup>7,8</sup> An inverse association has also been detected between the relative intensity of physical activity and the risk of developing coronary heart disease, independent of the total volume of physical activity.<sup>9,10</sup> Indeed, when exercise is performed at high intensity, as little as a single weekly bout of exercise seems to be sufficient for reducing the risk of cardiovascular death in a large unselected population,<sup>11</sup> and in subjects with coronary heart disease (CHD), as well.<sup>12</sup>

### Editorial see p 1431 Clinical Perspective on p 1440

Despite that higher levels of physical activity reduce cardiovascular events, it is advocated that vigorous activity could also acutely and transiently increase the risk of sudden cardiac death and myocardial infarction in susceptible persons.<sup>13</sup> Therefore, current guidelines recommend that patients in cardiac rehabilitation or secondary prevention programs perform moderate exercise at between 50% and 90% of peak heart rate ( $HR_{peak}$ )<sup>14,15</sup> Our research group, however, is using an exercise model that incorporates aerobic interval exercise training at 85% to 95% of  $HR_{peak}$ , not only in healthy individuals, but also in CHD patients. The results demonstrate that such high-intensity exercise is superior to moderate intensity for improving both peak oxygen uptake ( $VO_{2peak}$ ) and cardiac function, and reducing the risk factors associated with cardiovascular disease, as well.<sup>16-19</sup> The safety aspect of such high-intensity exercise

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training programs should be evaluated, however, before it is used in large, unselected groups of CHD patients. The aim of this study was therefore to assess if there is an increased risk of cardiovascular events or death during, or immediately after, exercising with high in comparison with moderate intensity in a large group of CHD patients undergoing cardiac rehabilitation.

## Methods

### Subjects

We included 4846 patients (male, 70%; female, 30%) who were referred to an exercise-based cardiac rehabilitation program at 3 different rehabilitation units in Norway between 2004 and 2011. Mean age was 57.8 years. All CHD patients taking part in this survey were enrolled at the rehabilitation units, and the total number of high- and moderate-intensity exercise sessions was registered. The patients were referred to the rehabilitation units by their general practitioner or hospital cardiologist, and their main admission diagnoses included myocardial infarction (7%), angioplasty (40%), coronary surgery (35%), valve surgery (11%), and heart failure (7%).

### Exercise Prescription

Since 2004, we have published several randomized controlled trials with a focus on improving physical capacity after high- versus moderate-intensity exercise in different groups of CHD patients and in individuals at high risk of developing CHD.<sup>17–21</sup> The high-intensity interval training model from these studies has been adopted by several Norwegian cardiac rehabilitation centers and is now a part of their standard rehabilitation procedure. In the current survey, all high-intensity exercise training sessions were performed as interval training with the aim to reach an intensity of 85% to 95% of  $HR_{peak}$ , because this mix of work and rest periods allows for more intense exercise to be tolerated before exhaustion. The moderate-intensity exercise sessions were performed at  $\approx 60\%$  to 70% of  $HR_{peak}$ , and were the typically used intensity involving cardiac patients.<sup>22</sup> All exercise sessions lasted  $\approx 1$  hour.

### Organization of Exercise of at the Rehabilitation Units

The 3 Norwegian rehabilitation units taking part in this survey were located at Ålesund Hospital, Feiring Heart Clinic, and Røros Rehabilitation Center. The patients underwent a medical examination before starting rehabilitation. All rehabilitation centers tested patients for  $VO_{2peak}$  and  $HR_{peak}$  with full-lead ECG before the rehabilitation program for safety reasons, and the results from these tests determined the individual exercise intensity zones for the patients. Both high- and moderate-intensity exercise sessions were conducted throughout a rehabilitation period containing, on average, 37 exercise sessions. All patients in this study participated in the standard rehabilitation given at the institutions, which consisted of separate sessions of high- versus moderate-intensity exercise. The adverse events during or after the exercise sessions were counted and related to the intensity of exercise. The training modality typically consisted of treadmill exercise, but aerobic group training, biking sessions, and outdoor walking and cross-country skiing were also performed.

### Execution of High- and Moderate-Intensity Exercise

The high-intensity interval training sessions were performed as described earlier<sup>17</sup> and typically consisted of warm-up for a minimum of 10 minutes at 60% to 70% of  $HR_{peak}$  before working four 4-minute intervals at 85% to 95% of  $HR_{peak}$ . Each interval was separated by active pauses at 50% to 70% of  $HR_{peak}$ . The training session was terminated by a cool-down period at 50% to 70% of  $HR_{peak}$ . Moderate exercise was simply the intensity one could carry on for a prolonged time period, and the subject should be able to converse in full sentences. During the moderate-exercise sessions, the patients worked continuously, with intensity  $\leq 70\%$  of  $HR_{peak}$ . The subjects wore heart rate monitors in some exercise sessions to ensure that proper intensity was performed according to the initial  $HR_{peak}$  test. Furthermore, high intensity was additionally controlled either by the Borg rating of

**Table 1. The Number of Patients, Exercise-Hours, and the Corresponding Number of Cardiovascular Events Associated With Moderate- and High-Intensity Exercise, Respectively**

Center	Patients, n	Total Training, h	Moderate Intensity, h	High Intensity, h
Ålesund	775	25 720 (1)	15 232	10 488 (1)
Feiring	2629	85 208 (2)	63 032 (1)	22 176 (1)
Røros	1442	64 892	51 192	13 700
Total	4846	175 820	129 456	46 364
Event rates				
Cardiac arrest, fatal			1	0
Cardiac arrest, nonfatal			0	2
Myocardial infarction			0	0
Risk of events		1/58 607	1/129 456	1/23 182

The numbers in parentheses indicate the number of events in each center according to intensity.

perceived exertion (on a scale of 6–20),<sup>23</sup> and by instructing the subjects to exercise at an intensity that brought them to breathe heavily, causing difficulties to speak more than a couple of words. When heart rate monitors were not used, exercise sessions were categorized as moderate-intensity exercise when the perceived exertion was at  $\approx 12$  to 14 on the Borg 6 to 20 scale,<sup>23</sup> and as high intensity when the perceived exertion was  $>15$  to 17 at the high-intensity parts of the session.

### Adverse Events

An adverse event related to exercise training was defined as cardiac arrest or acute myocardial infarction during exercise, or within the first hour afterward. Only events occurring during and after supervised exercise training were included. The emergency response to cardiac arrests was immediate use of defibrillator, and any suspicion of complications during the rehabilitation stay was reported to the individual unit's responsible physician for diagnostic determination.

### Statistical Analysis

Before the collection and interpretation of data, the study was assessed by the regional committee for medical research ethics. Estimation of sample size and power were done by STATA, version 12.

## Results

Among the 4846 patients, a total of 175 820 exercise sessions lasting  $\approx 1$  hour were recorded, distributed on 129 456 hours of moderate-intensity exercise and 46 364 hours of high-intensity exercise. Overall, the incidences included 1 cardiac arrest with fatal outcome during moderate-intensity exercise and 2 nonfatal cardiac arrests during high-intensity exercise (Table 1). There were no myocardial infarctions in the data material. During their stay at the rehabilitation centers, the patients performed an average of 36% high-intensity sessions in comparison with the number of moderate-intensity sessions. Thus, when relating the number of adverse events to the number of patient-exercise hours, the event rates were 1 per 129 456 hours of moderate-intensity exercise and 1 per 23 182 hours of high-intensity exercise. These results indicate that both types of exercise training are associated with low event rates. The types of adverse events related to exercise are presented in Table 2.

**Table 2. Major Cardiovascular Complications During Medically Supervised Exercise in Cardiac Rehabilitation**

Patient	Sex (♂/♀)	Age, y	Rehabilitation Center	Event (Year)	Exercise-Related Complication	Exercise Intensity
1	♂	60	Feiring Clinic	2007	Cardiac arrest, F	Moderate
2	♂	58	Feiring Clinic	2008	Cardiac arrest, NF	High
3	♂	61	Ålesund	2010	Cardiac arrest, NF	High

♂ indicates male; ♀, female; F, fatal; and NF, nonfatal.

## Discussion

Our study is the first to examine the risk of adverse events of combined organized high-intensity interval exercise training and moderate-intensity training in CHD patients. We found 1 fatal cardiac arrest during moderate-intensity exercise and 2 nonfatal cardiac arrests during high-intensity interval exercise. Because the number of high-intensity training sessions was 36% of the number of moderate-intensity sessions, the rates of complications to the number of patient-exercise hours were 1 per 129 456 sessions of moderate-intensity exercise and 1 per 23 182 hours of high-intensity exercise. The absolute event rates were very low after exposure to both types of exercise, and the calculated power to detect such a minor difference was only 23%. A sufficiently powered study with an adequate sample size (power of 0.80 and significance level 0.05) conducted in a similar way to ours would have required close to 21 000 patients to detect differences between groups, and a randomized study with 1:1 randomization would have had to include 10 264 patients in each group. Another challenge is to assess the severity of a death in comparison with a successful resuscitation of 2 cardiac arrests when comparing the risks of the 2 intensity modes. The low event rate after exposure to both types of exercise training may thus be the strongest interpretation of this study. Because of the more extensive use of high-intensity exercise training in cardiac rehabilitation worldwide, we believe that our study provides highly demanded knowledge about the risk of such exercise for secondary cardiac rehabilitation.

At least 5 reports have previously estimated the incidence of exercise-related cardiovascular complications from exercise-based cardiac rehabilitation programs among persons with documented CHD.<sup>24–28</sup> An initial survey involving 30 cardiac rehabilitation programs in Canada and the United States detected 1 nonfatal and 1 fatal cardiovascular complication per 34 673 and 116 402 hours, respectively.<sup>24</sup> Contemporary exercise-based cardiac rehabilitation programs appear to have a lower complication rate, because an analysis of 4 reports estimated 1 cardiac arrest per 116 906 patient-hours, 1 myocardial infarction per 219 970 patient-hours, 1 fatality per 752 365 patient-hours, and 1 major complication per 81 670 patient-hours of participation.<sup>25–28</sup> This low fatality rate applies to medically supervised programs that are run by personnel trained to handle emergencies. It is claimed that the death rate would be 6-fold higher without the successful management of cardiac arrest provided by such specialists.<sup>13</sup> Furthermore, CHD patients are normally medically evaluated before participation in cardiac rehabilitation programs, which typically decreases the event rates even more, supporting the use of supervised exercise-based cardiac rehabilitation programs for patients after cardiac events.<sup>29</sup> In our study, all centers conducted cardiopulmonary testing including 12-lead

ECG before rehabilitation. Exclusion as a result of the stress test on admission was very rare, however. The main reason for exclusion was recurrent ischemia by ECG, chest pain, and low exercise capacity, which resulted in a new examination to decide whether rehabilitation could be initiated. The problem with exclusion of those with the highest risk was thus low in our data set.

We have previously shown that exercise training reduces the risk of cardiovascular and all-cause mortality in both men and women with established CHD, particularly when exercising at moderate or high intensity in comparison with low exercise intensity.<sup>12</sup> However, previous reports also indicate that vigorous exertion increases the likelihood of acute myocardial infarction and sudden cardiac death, especially in sedentary persons with occult or manifested CHD performing irregular vigorous physical activity.<sup>24–28,30–37</sup> Former studies investigating risk of vigorous exercise in general have usually defined strenuous exertion as a metabolic equivalent of 6 or higher.<sup>31,34,35</sup> By using an absolute level of 6 metabolic equivalents, it is hard to assess the relative level of exertion, and an effort close to maximal for 1 individual could be very light for another. Because the myocardial stress among patients is more related to the relative oxygen uptake, it seems more meaningful to assess risk according to relative levels of exertion. All patients in our study exercised according to their relative intensity level determined by individual heart rates and the Borg rating of perceived exertion, which makes the true level of exertion and the associated risk easier to compare.

Long-term aerobic exercise conducted at higher intensities is associated with a reduced risk of future cardiovascular disease in comparison with long-term aerobic exercise conducted at lower intensities,<sup>9</sup> suggesting that the former may confer greater cardioprotective benefits. Despite that randomized controlled trials by now have been underpowered to prove this relationship,<sup>13</sup> Swain and Franklin<sup>7</sup> have addressed this issue in an extensive review with the use of epidemiological studies and smaller clinical trials.<sup>7</sup> They included both epidemiological studies that evaluated the benefits of physical activity of varying intensity levels and clinical trials that trained individuals at different exercise intensities, while controlling for the total energy expenditure. The epidemiological studies consistently found a greater reduction in risk of cardiovascular disease with high- (>6 metabolic equivalents) in comparison with moderate-intensity physical activity and reported more favorable risk profiles for individuals engaged in vigorous, as opposed to moderate-intensity physical activity.<sup>7</sup> Clinical trials generally reported greater improvements after high- (>60%  $\text{VO}_{2\text{peak}}$ ) in comparison with moderate-intensity exercise for diastolic blood pressure, glucose control, and aerobic capacity, but reported no intensity effect on improvements in systolic blood pressure, lipid

profile, or body fat loss. The review concluded that, if the total energy expenditure of exercise is held constant, exercise performed at a high intensity appears to convey greater cardioprotective benefits than exercise performed at a moderate intensity.<sup>7</sup>

It appears that the long-term benefits of moderate physical activity even in those with risk for CHD seem to outweigh the risks.<sup>13</sup> Our research group has, during the past decade, conducted randomized controlled trials among patients with established heart disease such as CHD and post-myocardial infarction heart failure,<sup>17,19,21</sup> in which we have demonstrated that the beneficial cardiovascular effects of aerobic exercise training are intensity dependent, with superiority of high aerobic intensity interval training in comparison with moderate-intensity training. Common for these studies is that, when volume of exercise is controlled for, interval training at 85% to 95% of  $HR_{peak}$  has been even more effective for improving  $VO_{2peak}$  than exercising at 60% to 70% of  $HR_{peak}$ .<sup>38</sup> There thus seems to be a true dose-response relationship regarding exercise intensity for improving  $VO_{2peak}$ , in which high-intensity exercise training confers about twice the benefit of moderate-intensity exercise training.<sup>39</sup> This may be of importance because  $VO_{2peak}$  constitutes an important prognostic parameter for cardiovascular morbidity and mortality.<sup>40–42</sup> High-intensity interval training may also be required for an effect to occur on left ventricular structure and function. We have previously identified several different patterns of response to programs that use high- or moderate-intensity exercise in patients with established heart disease. In patients with CHD and post-myocardial infarction heart failure, a reversal of the pathological remodeling and systolic and diastolic improvements were observed only after high-intensity exercise training.<sup>19,21,38,39</sup> In these randomized studies, both strain rate and tissue imaging echocardiographic evaluation of heart function has suggested that high-, but not moderate-intensity exercise, improved parameters related to both systolic contraction and diastolic relaxation rates.<sup>17,19,21</sup> In fact, 36 sessions of high-intensity interval exercise training in patients with heart failure reduced left ventricular dilatation and mass, increased ejection fraction and systolic and diastolic blood flow, and several systolic and diastolic motion parameters, as well.<sup>19</sup> Favorable intensity-dependent effects of exercise training have also been observed in individuals who have not yet developed cardiovascular disease, but are living with an increased risk of developing such disease because of the presence of risk factors merging into the metabolic syndrome.<sup>18</sup>

The results of the current study indicate that the risk of a cardiovascular event is low after both high-intensity exercise and moderate-intensity exercise in a cardiovascular rehabilitation setting. When considering earlier indications that adaptation in exercise capacity and cardiac function show a dose-response relationship, or display an intensity threshold for adaptation to occur, high-intensity interval training should be considered in future rehabilitation programs among CHD patients.

### Limitations

Because of the low number of casualties the power of the study to detect such a minor difference was only 23%, and a type II error can thus not be ruled out. The absolute event rates, however, were very low after exposure to both types of exercise training, and this fact may thus be the strongest

interpretation of the study. We encourage continuing collection of these types of data to evaluate the safety aspect of high-intensity exercise in future cardiac rehabilitation.

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### Disclosures

None.

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### CLINICAL PERSPECTIVE

High level of physical fitness and regular exercise are closely related to cardiovascular health and reduced risk of cardiovascular disease and mortality. Aerobic exercise is therefore strongly recommended for patients with coronary heart disease. Exercise performed at higher relative intensities has been found to elicit greater increase in aerobic capacity and greater cardioprotective effects than exercise at moderate intensities. Despite that higher levels of physical activity are found to reduce cardiovascular events, it is advocated that vigorous activity could also acutely and transiently increase the risk of sudden cardiac events in susceptible persons. We therefore studied the risk of cardiovascular events during organized high-intensity interval exercise training and moderate-intensity training among 4846 coronary heart disease patients in 4 Norwegian cardiac rehabilitation centers. The event rate after patients were exposed to both types of exercise training was low. In a total of 175 820 exercise training hours where all patient performed both types of training, we found 1 fatal cardiac arrest during moderate-intensity exercise (129 456 exercise hours) and 2 nonfatal cardiac arrests during high-intensity interval exercise (46 364 exercise hours). There were no myocardial infarctions in the data material. Because the number of high-intensity training hours was 36% of the number of moderate-intensity hours, the rates of complications to the number of patient-exercise hours were 1 per 129 456 of moderate-intensity exercise and 1 per 23 182 of high-intensity exercise. We believe that our study provides needed knowledge about the risk of high-intensity exercise training for patients undergoing secondary cardiac rehabilitation.