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

Running title: Rognmo et al.; Risk of high- vs. moderate-intensity exercise

Øivind Rognmo, PhD1; Trine Moholdt, PhD1; Hilde Bakken, BSc2; Torstein Hole, MD, PhD3; Per Mølstad, MD, PhD4; Nils Erling Myhr, BSc4; Jostein Grimsmo, MD, PhD4; Ulrik Wisløff, PhD1

1Dept of Circulation and Medical Imaging, K.G. Jebsen Ctr of Exercise In Medicine, Norwegian University of Science and Technology (NTNU), Trondheim; 2Røros Rehabilitation Ctr, Røros; 3Medical Dept, Ålesund Hospital, Ålesund; 4Feiring Heart Clinic, Feiring, Norway

Address for Correspondence:
Øivind Rognmo
Det medisinske fakultet
NTNU, Institutt for sirkulasjon og bildediagnostikk
Postboks 8905, Medisinsk teknisk forskningsenter
7491 Trondheim, Norway
Tel: +47 72 82 80 80
Fax: +47 72 82 83 72
E-mail: oivind.rognmo@ntnu.no

Journal Subject Codes: [26] Exercise/exercise testing/rehabilitation; [122] Secondary prevention
Abstract:

Background - 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. It has also been detected an inverse association 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 is 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 CHD patients in four Norwegian cardiac rehabilitation centers. Of a total of 175,820 exercise training hours where all patient performed both types of training we found one fatal cardiac arrest during moderate-intensity exercise (129,456 exercise hours), and two non-fatal cardiac arrests during high-intensity interval exercise (46,364 exercise hours). There were no myocardial infarctions in the data material. As 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.

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 CHD patients.

Key words: coronary disease; death, sudden; exercise; heart arrest
Background

High levels of physical activity and aerobic capacity are associated with low risk of cardiovascular disease and mortality. 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. If the total energy expenditure of exercise is held constant, 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. It has also been detected an inverse association between the relative intensity of physical activity and the risk of developing coronary heart disease, independent of the total volume of physical activity. Indeed, when exercise is carried out 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, as well as in subjects with coronary heart disease (CHD).

Despite that higher levels of physical activity reduces 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. Therefore, current guidelines recommend that patients in cardiac rehabilitation or secondary prevention programs perform moderate exercise between 50-90% of peak heart rate (HRpeak). Our research group is however using an exercise model which incorporates aerobic interval exercise training at 85-95% of HRpeak 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 (VO2peak) and cardiac function, as well as reducing the risk factors associated with cardiovascular disease. The safety aspect of such high intensity exercise training programs
should however be evaluated 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- compared to moderate-intensity in a large group of CHD patients undergoing cardiac rehabilitation.

Methods

Subjects

We included 4846 patients (♂ 70%, ♀ 30%) who were referred to an exercise-based cardiac rehabilitation program at three 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%), heart failure (7%).

Exercise prescription

We have from 2004 published several randomized controlled trials with focus on improving physical capacity after high- vs. moderate-intensity exercise in different groups of CHD patients and in individuals at high risk of developing CHD 17-21. 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 85-95% of HRpeak because this mix of work and rest-periods allows for more intense exercise to be tolerated before exhaustion. The moderate-intensity exercise sessions was
performed at approximately 60-70% of $HR_{peak}$, and is the typically used intensity involving cardiac patients. All exercise sessions lasted approximately one hour.

**Organization of exercise of at the rehabilitation units**

The three 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 prior to the rehabilitation program for safety reasons, and the results from these tests determined the individual exercise intensity zone’s 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- vs. 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 also aerobic group training, biking sessions, and outdoor walking and cross-country skiing was performed.

**Execution of High- and moderate-exercise**

The high-intensity interval training sessions were carried out as earlier described 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 peak heart rate. 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 at or below 70% of
HR\textsubscript{peak}. The subjects wore heart rate monitors in some exercise-sessions to control that proper intensity was carried out according to the initial HR\textsubscript{peak}-test. Furthermore, high-intensity was additionally controlled either by the Borg rating of perceived exertion (on a scale of 6 to 20)\textsuperscript{23}, 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 was not employed, exercise sessions were categorized as moderate-intensity exercise when the perceived exertion was approximately at 12-14 on the Borg 6-20 scale\textsuperscript{23}, and as high-intensity when the perceived exertion was above 15-17 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 afterwards. 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 collecting 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 (College Station, Texas).

**Results**

Among the 4846 patients, a total of 175 820 exercise sessions lasting approximately one hour were recorded, distributed on 129 456 hours of moderate-intensity exercise and 46 364 hours of high-intensity exercise, respectively. Overall, the incidences included one cardiac arrest with
fatal outcome during moderate-intensity exercise, and two non-fatal 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 carried out an average of 36% high-intensity sessions compared to 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.

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 one fatal cardiac arrest during moderate-intensity exercise, and two non-fatal cardiac arrests during high-intensity interval exercise. As 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 sufficient 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 21000 patients to detect differences between groups, and a randomized study with 1:1 randomization would had to include 10264 patients in each group. Another challenge is to assess the severity of a death compared to a successful resuscitation of two cardiac arrests when comparing the risks of the
two intensity modes. The low event rate after exposure to both types of exercise training may thus be the strongest interpretation of this study. Due to the more extensive use of high-intensity exercise training in cardiac rehabilitation worldwide, we believe that our study brings highly demanded knowledge about the risk of such exercise for secondary cardiac rehabilitation.

At least five reports have previously estimated the incidence of exercise-related cardiovascular complications from exercise-based cardiac rehabilitation programs among persons with documented CHD\textsuperscript{24-28}. An initial survey involved 30 cardiac rehabilitation programs in Canada and United States detected 1 non-fatal and 1 fatal cardiovascular complication per 34 673 and 116 402 hours, respectively\textsuperscript{24}. Contemporary exercise-based cardiac rehabilitation programs appear to have a lower complication rate as 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\textsuperscript{25-28}. 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\textsuperscript{13}. Furthermore, CHD patients are normally medically evaluated before participation in cardiac rehabilitation programs which typically decrease the event rates even more, supporting the use of supervised exercise-based cardiac rehabilitation programs for patients after cardiac events\textsuperscript{29}. In our study, all centers conducted cardiopulmonary testing including 12-lead ECG prior to rehabilitation. Exclusion as a result of the stress test on admission were however very rare. 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 compared with low-exercise intensity. 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. Former studies investigating risk of vigorous exercise in general have usually defined strenuous exertion as a metabolic equivalent (MET) of 6 or higher. By using an absolute level of 6 METs it is hard to assess the relative level of exertion, and an effort close to maximal for one individual could be very light for another. Since the myocardial stress among patients are 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 compared to lower intensities, suggesting that the former may confer greater cardioprotective benefits. Despite that randomized controlled trials by now have been underpowered to prove this relationship, Swain and Franklin have addressed this issue in an extensive review using epidemiological studies and smaller clinical trials. They included both epidemiologic 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 epidemiologic studies consistently found a greater reduction in risk of cardiovascular disease with high (>6 METs) compared to moderate...
intensity physical activity and reported more favorable risk profiles for individuals engaged in vigorous, as opposed to moderate intensity physical activity \(^7\). Clinical trials generally reported greater improvements after high (>60% \(\text{VO}_2\text{peak}\)) compared to 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 at a moderate intensity\(^7\).

It appears that the long-term benefits of moderate physical activity even in those with risk for CHD seem to outweigh the risks \(^{13}\). Our research group has, during the last decade, conducted randomized controlled trials among patients with established heart disease such as CHD and post-MI heart failure \(^{17, 19, 21}\) where we have demonstrated that the cardiovascular beneficial effects of aerobic exercise training are intensity dependent, with superiority of high aerobic intensity interval training compared to moderate intensity training. Common for these studies is that when volume of exercise is controlled for, interval training at 85-95% of \(\text{HR}_{\text{peak}}\) has been even more effective for improving \(\text{VO}_2\text{peak}\) than exercising at 60-70% of \(\text{HR}_{\text{peak}}\) \(^{38}\). There thus seems to be a true dose-response relationship regarding exercise intensity for improving \(\text{VO}_2\text{peak}\), where high-intensity exercise training conferring about twice the benefit of moderate-intensity exercise training \(^{39}\). This may be of importance since \(\text{VO}_2\text{peak}\) constitutes an important prognostic parameter for cardiovascular morbidity and mortality \(^{40-42}\). 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 utilizing high- or moderate-intensities exercise in patients with established heart disease. In
patients with CHD and post-MI heart failure, a reversal of the pathological remodeling and
systolic and diastolic improvements were observed only after high-intensity exercise training 19,
21, 38, 39. 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 17, 19, 21. In
fact, 36 sessions of high-intensity interval exercise training in heart failure patients reduced left
ventricular dilatation and mass, increased ejection fraction and systolic and diastolic blood flow,
as well as several systolic and diastolic motion parameters19. 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, due to
the presence of risk factors merging into the metabolic syndrome 18.

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 programmes
among CHD patients.

Limitations

Due to 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 were however
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.
**Acknowledgements:** We would like to thank the rehabilitation units at Ålesund Hospital, Feiring Heart Clinic and Røros Rehabilitation Center for providing the data material making up this study.

**Funding Sources:** The study was supported by grants from the K.G. Jebsen Foundation, The Research Council of Norway, and The Norwegian Council of Cardiovascular Disease.

**Conflict of Interest Disclosures:** None.

**References:**


continuous moderate exercise as a treatment for the metabolic syndrome: A pilot study. 


Table 1. The number of patients, exercise-hours and the corresponding number of cardiovascular events associated with moderate- and high-intensity exercise, respectively.

<table>
<thead>
<tr>
<th>Center</th>
<th>Patients (n)</th>
<th>Total training (hours)</th>
<th>Moderate-intensity (hours)</th>
<th>High-intensity (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alesund</td>
<td>775</td>
<td>25 720&lt;sup&gt;1&lt;/sup&gt;</td>
<td>15 232</td>
<td>10 488&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Feiring</td>
<td>2629</td>
<td>85 208&lt;sup&gt;2&lt;/sup&gt;</td>
<td>63 032&lt;sup&gt;1&lt;/sup&gt;</td>
<td>22 176&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Roros</td>
<td>1442</td>
<td>64 892</td>
<td>51 192</td>
<td>13 700</td>
</tr>
<tr>
<td>Total</td>
<td>4846</td>
<td>175 820</td>
<td>129 456</td>
<td>46 364</td>
</tr>
</tbody>
</table>

Event rates:
- Cardiac arrest, fatal: 1 / 0
- Cardiac arrest, non-fatal: 0 / 2
- Myocardial infarction: 0 / 0

Risk of events: 1/58 607 / 1/129 456 / 1/23 182

<sup>1</sup> indicates number of events in each center according to intensity.

Table 2. Major cardiovascular complications during medically supervised exercise in cardiac rehabilitation.

<table>
<thead>
<tr>
<th>Patient (nr.)</th>
<th>Sex (♂/♀)</th>
<th>Age (yr.)</th>
<th>Rehabilitation Center</th>
<th>Event (year)</th>
<th>Exercise-related complication</th>
<th>Exercise intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>♂</td>
<td>60</td>
<td>Feiring Clinic</td>
<td>2007</td>
<td>Cardiac arrest, F</td>
<td>Moderate</td>
</tr>
<tr>
<td>2</td>
<td>♂</td>
<td>58</td>
<td>Feiring Clinic</td>
<td>2008</td>
<td>Cardiac arrest, NF</td>
<td>High</td>
</tr>
<tr>
<td>3</td>
<td>♂</td>
<td>61</td>
<td>Álesund</td>
<td>2010</td>
<td>Cardiac arrest, NF</td>
<td>High</td>
</tr>
</tbody>
</table>

Abbreviations: yr., years; F, fatal; NF, non-fatal
Cardiovascular Risk of High- Versus Moderate-Intensity Aerobic Exercise in Coronary Heart Disease Patients
Øivind Rognmo, Trine Moholdt, Hilde Bakken, Torstein Hole, Per Mølstad, Nils Erling Myhr, Jostein Grimsmo and Ulrik Wisløff

Circulation. published online August 9, 2012;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/early/2012/08/07/CIRCULATIONAHA.112.123117

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2013/05/12/CIRCULATIONAHA.112.123117.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/
L’aldostérone inactive le récepteur à l’endothélaine B par l’intermédiaire d’une substitution redox des cystéinyli-thiols, ce qui diminue la teneur de l’endothélium pulmonaire en monoxyde d’azote et favorise l’hypertension artérielle pulmonaire

Bradley A. Maron, MD ; Ying-Yi Zhang, PhD ; Kevin White, PhD ; Stephen Y. Chan, MD, PhD ; Diane E. Handy, PhD ; Christopher E. Mahoney, BA ; Joseph Loscalzo, MD, PhD ; Jane A. Leopold, MD

Contexte—L’hypertension artérielle pulmonaire (HAP) se caractérise notamment par une diminution de la production endothéliale de monoxyde d’azote (NO) et par une élévation du taux d’endothélaine 1. Sachant que celle-ci stimule la monoxyde d’azote synthétase endothéliale (eNOS) par l’intermédiaire des récepteurs à l’endothélaine B (ETB), il est permis de penser que cette voie de signalisation est altérée dans l’HAP. L’endothélaine 1 stimulate également la synthèse surnéphragmente de l’aldostérone ; au niveau des vaisseaux périphériques, l’hyperaldostéronisme induit une dysfonction vasculaire en augmentant la formation endothéliale d’espèces réactives de l’oxygène et en diminuant les taux de NO. Nous avons donc formulé l’hypothèse selon laquelle l’aldostérone favoriserait l’HAP en perturbant la signalisation de l’ETB et de l’eNOS par un mécanisme consistant à accroître le stress oxydatif au sein de l’endothélium pulmonaire.

Méthodes et résultats—Chez le rat atteint d’HAP, l’élèvement du taux d’endothélaine 1 va de pair avec l’augmentation des concentrations en aldostérone dans le sang et les tissus pulmonaires et avec la diminution des taux pulmonaires de métabolites du NO, cela en l’absence de toute insuffisance cardiaque gauche. Nous montrons que, dans les cellules endothéliales d’artères pulmonaires humaines, l’endothélaine 1 augmente le taux d’aldostérone par un processus de stimulation de l’aldostérone synthétase qui est médial à la fois par le co-activateur 1α des récepteurs gamma activés par les proliférateurs de peroxysomes et par le facteur stéroidal dépendant de type 1. L’aldostérone augmente également la production d’espèces réactives de l’oxygène, ce qui, en oxydant les cystéinyli-thiols au sein de la région de l’ETB qui régit l’activation de l’eNOS, diminue l’activité de cette enzyme médiane par l’endothélaine 1. Le remplacement de la Cys405 de l’ETB par une alanine a amélioré la synthèse du NO dépendante de ce médiateur en situation de stress oxydatif, ce qui confirme que la Cys405 est un thiol redox-sensible qui est indispensable à la voie de signalisation de l’ETB-eNOS. Dans les cellules endothéliales d’artères pulmonaires humaines, l’inhibition des récepteurs aux minéralocorticoïdes par la spironolactone a diminué la libération d’espèces réactives de l’oxygène médiane par l’aldostérone et restauré la production de NO dépendante de l’ETB. Dans deux modèles animaux d’HAP in vivo, l’administration de spironolactone ou d’éplerénone a prévenu ou aboli le remodelage vasculaire pulmonaire et amélioré l’hémodynamique cardio-pulmonaire.

Conclusions—Nos observations démontrent que l’aldostérone induit une modification de la configuration d’oxydréduction des cystéinyli-thiols de l’ETB, qui a pour effet de diminuer la formation de NO à partir de l’endothélium pulmonaire et de favoriser l’HAP. (Traduit de l’anglais : Aldosterone Inactivates the Endothelin-B Receptor via a Cysteinyli Thiol Redox Switch to Decrease Pulmonary Endothelial Nitric Oxide Levels and Modulate Pulmonary Arterial Hypertension. Circulation. 2012;126:963–974.)

Mots clés : endothélaine ■ monoxyde d’azote ■ cardiopathie pulmonaire ■ aldostérone ■ processus biochimiques d’oxydréduction

Risque cardiovasculaire associé à l’éntrainement aérobie chez les patients coronariens associé qu’il est d’intensité élevée ou modérée

Öivind Rognmo, PhD ; Trine Moholdt, PhD ; Hilde Bakken, BSc ; Torstein Hole, MD, PhD ; Per Mølstad, MD, PhD ; Nils Erling Myhr, BSc ; Jostein Grimsmo, MD, PhD ; Ulrik Wisloff, PhD

Contexte—Il a été établi que, lorsqu’il est pratiqué de façon relativement énergique, l’éntrainement physique augmente plus fortement la capacité aérobie et a un effet cardioprotecteur plus marqué que lorsqu’il est effectué à un rythme modéré. Une corrélation inverse a également été mise en évidence entre le risque d’événement coronarien et l’intensité relative de l’activité physique, indépendamment du volume total de cette dernière. Bien que la pratique d’un éntrainement physique d’intensité supérieure constitue un moyen efficace de réduire l’incidence des événements cardiovasculaires, il semblerait toutefois qu’une activité physique trop énergique ait pour effet d’augmenter fortement les risques aigus de mort subite et d’infarctus du myocarde chez les individus prédisposés. Cette éventualité pourrait justifier de reconsidérer les programmes d’éntrainement cardiovasculaire.

Méthodes et résultats—Nous avons évalué le risque d’événement cardiovasculaire encouru du fait de la mise en application d’un programme d’éntrainement fractionné selon qu’il était d’intensité élevée ou modérée chez 4 846 patients coronariens pris en charge dans trois centres de réhabilitation cardiaque norvégiens. Sur une durée totale de 175 820 heures d’éntrainement physique pendant lesquelles tous les patients avaient effectué les deux types d’exercices, nous avons recensé un arrêt cardiaque fatal survenu lors d’une période d’éntrainement d’intensité modérée (129 456 heures d’exercice physique) et deux arrêts
Faut-il instaurer un traitement anticoagulant oral lors de la réalisation d’une coronaroplastie avec pose de stent chez un patient en fibrillation atriale dont le score de risque hémorragique HAS-BLED est élevé ?

Juan M. Ruiz-Nodar, MD, PhD ; Francisco Marín, MD, PhD ; Vanessa Roldán, MD, PhD ; José Valencia, MD, PhD ; Sergio Manzano-Fernández, MD, PhD ; Luis Caballero, MD ; José A. Hurtado, MD ; Francisco Sogorb, MD, PhD ; Mariano Valdés, MD, PhD ; Gregory Y.H. Lip, MD, FACC, FESC

Contexte—Les récentes recommandations européennes en matière de prise en charge de la fibrillation atriale préconisent d’instituer une anticoagulation orale (ACO) chez les patients dont le score CHA2DS2-VASc (insuffisance cardiaque congestive, hypertension artérielle, âge atteignant 75 ans ou plus, diabète, antécédents d’accident vasculaire cérébral, pathologie vasculaire, âge compris entre 65 et 74 ans, sexe féminin) est égal ou supérieur à 1. Certains ont, par ailleurs, proposé d’utiliser le score HAS-BLED (hypertension artérielle, dysfonction rénale hépatique, accident vasculaire cérébral, antécédent ou terrain hémorragique, labilité du rapport international normalisé, âge supérieur à 65 ans, prise concomitante de médicaments et d’alcool) pour évaluer le risque hémorragique chez les patients présentant une fibrillation atriale (un score égal ou supérieur à 3 témoignant d’un risque hémorragique élevé). En dépit des recommandations, cette approche n’a jamais été examinée dans une cohorte de patients en fibrillation atriale relevant d’une angioplastie coronaire percutanée avec pose de stent.

Méthodes et résultats—Notre étude a porté sur 590 patients consécutifs atteints de fibrillation atriale qui devaient faire l’objet d’une coronaroplastie percutanée avec pose de stent et dont le score CHA2DS2-VASc était supérieur à 1 (ce qui, conformément aux recommandations, justifiait l’instauration d’une ACO). Nous avons comparé les patients qui encouraient un risque hémorragique faible à intermédiaire (HAS-BLED compris entre 0 et 2) à ceux exposés à un risque élevé (HAS-BLED ≥3), etudié la relation entre les scores CHA2DS2-VASc et HAS-BLED et confronté les bénéfices et les risques de l’ACO chez les patients présentant un risque hémorragique élevé. Nous avons recensé les épisodes hémorragiques, les événements thromboemboliques, les décès, les événements cardiaques, l’élément composite formé par les événements cardiaques majeurs (décès, infarctus aigu du myocarde et/ou revascularisation d’une lésion cible) et l’élément composite regroupant les événements majeurs (événement cardiaque majeur, hémorragie grave ou événement thromboembolique) survenus au cours d’une période de suivi d’un an. Dans la cohorte de l’étude, 420 (71 %) présentaient un score HAS-BLED égal ou supérieur à 3 ; chez les patients qui étaient sous ACO à leur sortie d’hôpital, la mortalité s’est révélée plus faible (9,3 % versus 20,1 % ; p <0,01), de même que le taux d’événements cardiaques majeurs (13,0 % versus 26,4 % ; p <0,01), alors que le taux d’événements majeurs a été similaire à celui observé dans l’autre groupe (20,5 % versus 27,6 % ; p = 0,11) ; en revanche, l’incidence des hémorragies graves a été plus élevée (11,8 % versus 4,0 % ; p <0,01). L’analyse de Cox multivariée effectuée chez les patients dont le HAS-BLED était égal ou supérieur à 3 a montré que les facteurs prédictifs d’un risque de décès majeur avaient été l’insuffisance rénale chronique et l’insuffisance cardiaque (p <0,05 dans les deux cas), alors que le fait d’avoir été sous ACO à la sortie de l’hôpital avait contribué à diminuer le risque de décès (p <0,01). Les facteurs prédictifs de la survenue d’une hémorragie grave ont été l’insuffisance rénale chronique et la pose de stents à libération de principe actif (p <0,05 dans les deux cas).


Mots clés : fibrillation atriale ■ risque hémorragique ■ anticoagulation orale ■ pose de stent