Relief of Cardiorespiratory Symptoms and Increased Physical Activity After Surgically Induced Weight Loss

Results From the Swedish Obese Subjects Study

Kristjan Karason, MD, PhD; Anna Karin Lindroos, PhD; Kaj Stenlöf, MD, PhD; Lars Sjöström, MD, PhD

Background: Obese people frequently suffer from shortness of breath and chest discomfort on exertion, and they often have a sedentary lifestyle. In the present study of patients with severe obesity, we investigated the effects of surgically induced weight loss on cardiorespiratory symptoms and leisure-time physical activity.

Methods: The Swedish Obese Subjects study is an ongoing intervention trial of obesity consisting of 1 surgically treated group and 1 matched control group. Information on smoking habits, hypertension, diabetes, and sleep apnea was obtained from 1210 surgical cases and 1099 controls who were observed for 2 years. Patients were also asked about symptoms of breathlessness and chest pain and their levels of leisure-time physical activity.

Results: The surgically treated group displayed a mean weight loss of 28 kg (23%) compared with the control group in which the average weight remained unchanged ($P < .001$). The rates of hypertension, diabetes, and apneas during sleep decreased in surgical cases compared with controls ($P < .001$), while smoking habits remained largely the same. The surgical group also displayed highly significant improvements in dyspnea and chest pain and increases in physical activity compared with the control group ($P < .001$). The odds ratio for self-reported breathlessness, chest discomfort, or sedentary behavior after 2 years decreased progressively with the degree of weight loss. Furthermore, patients who recovered from apneas during sleep reduced their odds of having dyspnea and chest discomfort at follow-up, independent of changes in weight.

Conclusions: Surgically induced weight loss in patients with severe obesity is associated with a marked relief in symptoms of dyspnea and chest pain and promotes increased leisure-time physical activity. Sleep-disordered breathing may be involved in the pathophysiology of breathlessness and chest discomfort in obese subjects.

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Obesity has long been associated with disturbances in cardiovascular and pulmonary function. It is strongly related to hypertension and may induce various changes in cardiac structure and function. Obesity also has a significant impact on the respiratory system with alterations in respiratory mechanics, lung volumes, and gas exchange. In addition, people with obesity often suffer from sleep-disordered breathing, in particular obstructive sleep apnea.

The presence of excess body fat, together with related cardiovrespiratory disorders, may give rise to various clinical symptoms. It has been reported that people with obesity experience shortness of breath and chest discomfort on exertion much more frequently than control subjects from the normal population. Such effort-related symptoms limit exercise capacity and may be responsible in part for the low levels of physical activity often observed among obese subjects. Physical inactivity may in turn contribute to further weight gain and maintenance of the obese state.

The optimal treatment of cardiovrespiratory disturbances in obesity is weight loss. However, this is difficult to achieve with conventional methods, and the results are often temporary. Gastric surgery, on the other hand, induces weight losses that are not only large but also sustained over time. The present surgical procedures are not, however, without complications, and it is therefore important to evaluate the overall usefulness of such therapy. Studies have shown that certain features of cardiovrespiratory function may improve following surgically induced weight loss. However, little information is available on the effects of weight
METHODS

THE SWEDISH OBESE SUBJECTS STUDY

The Swedish Obese Subjects study (SOS) is an ongoing nationwide project designed to determine whether the morbidity and mortality rates among obese people who lose weight by surgical means differ from those in a matched obese reference group. The selection criteria and study design have been described. Briefly, the SOS consists of a registry study and an intervention study. The aim of the registry study is to describe the obese state with respect to physical health and psychosocial well-being and to serve as a recruitment base from which eligible patients are enrolled in the intervention study. The criteria for inclusion in the intervention study are age between 37 and 60 years and body mass index (BMI) of 38 kg/m² or higher for women and 34 kg/m² or higher for men.

The intervention study consists of a surgically treated group and a conventionally treated control group. The study is not randomized because the ethics committees in Sweden did not approve of a procedure of this kind. Instead, patients willing to undergo surgical therapy are matched with those preferring conventional treatment with respect to sex and 18 other clinical variables. These are age, height, weight, waist and hip circumferences, waist-hip ratio, systolic blood pressure, cholesterol level, triglycerides level, smoking, diabetes, menopause, and 6 parameters evaluating psychological status: perceived health, psychasthenia, monotony avoidance, available social interaction, availability of attachment, and stressful life events. Several inclusion and exclusion criteria are used, and they are identical in the surgically treated group and the control group. The computerized selection of controls is based on an algorithm that moves the means of as many matching variables as possible in the control group toward the current means of the surgical group and cannot be influenced by the investigators. In these different ways, every possible effort has been made to obtain, in a nonrandomized manner, 2 groups that do not differ at the time of inclusion in the intervention study.

The treatments offered to the surgical group consist of gastric bypass, vertical banded gastroplasty, and gastric banding. These operations, as well as the follow-up of surgically treated patients, are conducted at 25 different surgical departments in Sweden. Control subjects receive conventional dietary recommendations and are observed at 480 primary health care centers throughout the country.

PRESENT STUDY GROUP

For the purpose of the present report, 2-year results for the first 1310 obese patients treated surgically and their 1310 matched controls have been used. Because of mortality, dropouts, and data pending, 2-year data were not available in 100 (7.6%) of the surgically treated patients and 211 (16.1%) of the controls. Table 1 gives the clinical characteristics at baseline and after 2 years for those patients who completed the 2-year examination. Baseline characteristics for the 311 subjects who were not available at follow-up did not differ significantly from those of subjects who completed the study.

CLINICAL CHARACTERISTICS

Body weight was measured with the subjects wearing light clothing and no shoes and rounded off to the nearest 0.1 kg. Height measurements were rounded off to the nearest 0.01 m. Body mass index was calculated as the weight in kilograms divided by the square of the height in meters.

Systolic and diastolic (phase V) blood pressures were measured in the right arm using a mercury sphygmomanometer after 10 minutes of supine rest (single reading). An appropriate cuff, with a width of at least 40% of the circumference of the subject’s arm, was applied. Patients were classified as having hypertension if their systolic blood pressure was 160 mm Hg or greater; if their diastolic blood pressure was 95 mm Hg or greater; or if they were receiving antihypertensive medication.

Blood samples were obtained in the morning after 10 to 12 hours of fasting, and blood glucose levels were measured enzymatically. Patients were classified as having diabetes if their fasting blood glucose level was 6.7 mmol/L (120 mg/dL) or greater or if they were receiving treatment with insulin or an oral antidiabetic agent.

Patients were asked if a family member or other person had observed frequent pauses in breathing during sleep. Subjects reporting a history of observed pauses were regarded as having a high likelihood of sleep apnea, while those not reporting this symptom were classified as having a low likelihood.

CARDIORESPIRATORY SYMPTOMS AND PHYSICAL ACTIVITY

Patients completed a questionnaire at inclusion and again after 2 years of follow-up. They were asked about the occurrence of various types of breathlessness and chest pain using a questionnaire modified from Rose et al (Table 2). Study subjects were also asked to grade their level of physical activity during leisure time using a scale of 1 to 4, where 1 denoted sedentary activity and 4, regular strenuous exercise. In the present study, patients reporting grade 1 were considered physically inactive, while those reporting grades 2 to 4 were classified as physically active.

STATISTICAL ANALYSES

Statistical analyses were performed with SAS version 6.12 (SAS Institute, Cary, NC). Data on clinical characteristics at baseline and follow-up are presented as percentages (categorical variables) or the mean ± SD (continuous variables), and 95% confidence intervals are provided for the differences between groups (Table 1). Differences between groups with respect to 2-year changes in dyspnea, chest pain, and physical inactivity were evaluated with a 2-sample McNemar test (Table 2).

After pooling data from the surgical and control groups, logistic regression was used to determine the independent contribution of changes in weight and occurrence of nightly apneas to the risk of dyspnea, chest pain, and physical inactivity at follow-up (Table 3 and Table 4). The dependent variables in these analyses were dyspnea when climbing 2 flights of stairs, chest pain when walking uphill or climbing stairs, and physical inactivity during leisure time. In each analysis we included only those patients who had reported a history of the individual conditions at baseline. A 2-tailed P value of less than .05 was considered statistically significant.
Table 1. Clinical Characteristics of the Study Groups at Baseline and 2-Year Follow-up*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Surgical Group (n = 1210)</th>
<th>Control Group (n = 1099)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>47 ± 6</td>
<td>49 ± 6</td>
<td>-1.4 (-1.9 to -0.9)</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>67</td>
<td>67</td>
<td>0 (-4 to 4)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169 ± 9</td>
<td>169 ± 9</td>
<td>0 (-0.0 to 0.0)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>121 ± 17</td>
<td>114 ± 16</td>
<td>7 (5.7 to 8.3)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>93 ± 16</td>
<td>114 ± 17</td>
<td>-21 (-23 to -19)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>42.2 ± 4.4</td>
<td>39.7 ± 4.4</td>
<td>2.6 (2.3 to 2.9)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>32.5 ± 4.8</td>
<td>39.5 ± 3.9</td>
<td>-7.0 (-7.4 to -6.6)</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>25</td>
<td>20</td>
<td>5 (2 to 6)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>25</td>
<td>18</td>
<td>7 (4 to 10)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>53</td>
<td>38</td>
<td>15 (11 to 19)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>31</td>
<td>39</td>
<td>-8 (-12 to -4)</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>19</td>
<td>18</td>
<td>1 (-3 to 4)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>10</td>
<td>15</td>
<td>-5 (-8 to -3)</td>
</tr>
<tr>
<td>Sleep apnea, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>23</td>
<td>22</td>
<td>1 (-3 to 4)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>8</td>
<td>20</td>
<td>-12 (-15 to -9)</td>
</tr>
</tbody>
</table>

*Values for continuous variables are given as the mean ± SD. CI indicates confidence interval.

Table 2. Dyspnea, Chest Pain, and Physical Inactivity in Study Groups at Baseline and 2-Year Follow-up*

<table>
<thead>
<tr>
<th>Condition of Interest</th>
<th>Surgical Group (n = 1210)</th>
<th>Control Group (n = 1099)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When climbing 2 flights of stairs</td>
<td>87</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>When walking with people of own age</td>
<td>67</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>When walking on level surface at own speed</td>
<td>15</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>When washing or dressing</td>
<td>24</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When walking uphill or climbing stairs</td>
<td>28</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>In association with anger or anxiety</td>
<td>21</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>46</td>
<td>17</td>
<td>33 29 &lt;.001</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are percentages of patients.
†P values relate to the comparison of 2-year changes between groups.

The clinical characteristics of the study groups at baseline and after 2 years of follow-up are given in Table 1. At baseline, the surgical and control groups were similar with respect to sex, height, diabetes, and apneas during sleep. The average interval between registry examination and baseline examination in the intervention study was 9 months. During this period, between matching and inclusion, the group awaiting surgery gained weight, while the group receiving conventional treatment lost weight, resulting in an average difference in body weight of 7.1 kg. Patients in the surgical group were also slightly younger than those in the control group; they had a higher prevalence of hypertension and were more often smokers.

After 2 years of follow-up, the surgical group displayed significant weight loss of 28 kg (23%), while the average weight in the control group remained essentially unchanged. In the weight loss group, the frequencies of hypertension, diabetes, and nightly apneas decreased by 42%, 47%, and 65%, respectively, and became significantly lower than those in the control group. The difference in smoking habits between the 2 groups remained largely the same.

Although men displayed higher frequencies of hypertension, diabetes, and sleep apnea than women at baseline, the relative changes in these clinical characteristics at follow-up were similar for both sexes (not shown). The prevalence of dyspnea, chest pain, and physical inactivity in the study groups is given in Table 2. At baseline, all 3 conditions occurred more frequently in patients awaiting surgical treatment than in control subjects. At follow-up, the percentage of surgical patients reporting these conditions decreased markedly, and a certain reduction in these symptoms also occurred in the control group. However, when the treatment effect was analyzed, the surgical cases showed a highly significant improvement in all 3 conditions compared with control subjects.

The odds ratios for patients reporting dyspnea, chest pain, or physical inactivity at baseline continuing to have these conditions at follow-up are given in Table 3. The risk of retaining these conditions after 2 years decreased progressively with the degree of weight loss, and these relationships persisted even after adjustments for age, sex, smoking, hypertension, diabetes, height, and baseline weight.

To investigate the possible involvement of sleep-disordered breathing in the pathogenesis of dyspnea and chest pain, we stratified the study sample into 4 groups based on the presence or absence of reported apneas at baseline and whether changes occurred during follow-up (Table 4). When compared with patients with sustained breathing disturbances during sleep, patients who reported recovery from apneas reduced their risk of persistent dyspnea and chest pain, while patients who acquired frequent apneas during sleep increased their odds of retaining chest discomfort after 2 years. These relationships were, or tended to be, independent of weight changes and other confounding factors. Variations in apneas were not associated with changes in physical activity (data not shown).
velops.26 Hemodynamic overload of this kind leads to left hypoxemia.23,24 Ventilation-perfusion mismatch may give rise to arterial owing to airway closure and alveolar collapse and this lung bases in obese patients are often underventilated and cardiac output rise25 and hypertension frequently de-tem. With increasing body weight, both blood volume sociated with several alterations in the circulatory sys-
elevated.21,22 Furthermore, the relatively well-perfused As a result, the work and energy costs of breathing are
dispense17,18 and increases in respiratory resistance.19,20
In addition to respiratory disturbances, obesity is as-
monary venous pressures may further exacerbate breath-
ness, particularly on exertion. Weight loss has favorable effects on pulmonary function and arterial blood gases.5,35 Furthermore, weight reduction is associated with the regression of left ventricular hypertrophy13 and improvements in cardiac function.11 The large decline in body mass, together with these cardiorespiratory improvements, is likely to explain the marked improvement in dyspnea after weight loss in the present study.

Obesity is associated with several cardiovascular risk factors and signs of premature atherosclerosis.29 However, it is unlikely that the high frequency of effort-related chest pain reported by obese patients in the present study is entirely due to underlying coronary heart disease. Left ventricular hypertrophy is prevalent in obese subjects and may give rise to chest pain as a result of an imbalance between oxygen supply and demand.30 Furthermore, the elevation in intra-abdominal pressure associated with visceral adiposity predisposes subjects to gastroesophageal reflux and symptoms of heartburn.31,32 Finally, obstructive sleep apnea has been reported to simulate angina pectoris even in the absence of coronary atherosclerosis.33 All these conditions have been shown to improve following surgically induced weight loss,10,34,35 which might account in part for the considerable relief in chest pain also observed after weight reduction in our patients.

The positive effects of regular leisure-time physical activity on physical health and mental well-being are widely recognized. Physical inactivity, on the other hand, is associated with increased morbidity and mortality, in particular from cardiovascular disease.36-38 More than one third of the obese patients in the present study reported no physical activity during their leisure time, which is similar to the findings in previous surveys in the obese population.5 In contrast, the prevalence of physical inactivity in the normal population in Göteborg, Sweden, is less than 20%.39

### Table 3. Odds Ratios for Patients With Dyspnea, Chest Pain, or Physical Inactivity at Baseline Continuing to Have These Conditions at Follow-up, by Quartiles of Weight Change*

<table>
<thead>
<tr>
<th>Quartile and Mean (Range) Weight Change in Each, kg</th>
<th>No. of Patients With Condition at Baseline</th>
<th>No. of Patients With Condition at Follow-up</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>Adjusted Odds† Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I +4.3 (−0.9 to +23.4)</td>
<td>149</td>
<td>80</td>
<td>1.00‡</td>
<td>1.00‡</td>
</tr>
<tr>
<td>II −6.4 (−14.8 to −1.0)</td>
<td>155</td>
<td>65</td>
<td>0.62 (0.40 to 0.98)</td>
<td>0.64 (0.40 to 1.02)</td>
</tr>
<tr>
<td>III −21.6 (−28.6 to −14.9)</td>
<td>152</td>
<td>32</td>
<td>0.23 (0.14 to 0.38)</td>
<td>0.23 (0.14 to 0.40)</td>
</tr>
<tr>
<td>IV −40.8 (−95.5 to −28.7)</td>
<td>152</td>
<td>12</td>
<td>0.07 (0.04 to 0.14)</td>
<td>0.08 (0.04 to 0.16)</td>
</tr>
<tr>
<td>I +3.5 (−2.9 to +22.1)</td>
<td>224</td>
<td>145</td>
<td>1.00‡</td>
<td>1.00‡</td>
</tr>
<tr>
<td>II −9.4 (−17.0 to −3.0)</td>
<td>231</td>
<td>111</td>
<td>0.50 (0.35 to 0.73)</td>
<td>0.48 (0.33 to 0.70)</td>
</tr>
<tr>
<td>III −23.4 (−29.9 to −17.1)</td>
<td>224</td>
<td>73</td>
<td>0.26 (0.18 to 0.39)</td>
<td>0.25 (0.17 to 0.37)</td>
</tr>
<tr>
<td>IV −42.8 (−123.3 to −30.0)</td>
<td>228</td>
<td>61</td>
<td>0.20 (0.13 to 0.30)</td>
<td>0.18 (0.11 to 0.27)</td>
</tr>
</tbody>
</table>

*The surgical and control groups are pooled in these analyses. CI indicates confidence interval.
†Adjusted for age, sex, smoking, hypertension, diabetes, height, and baseline weight.
‡The reference category is the group that displayed an increase in average weight.

**COMMENT**

This controlled study of severely obese subjects demonstrates that large intentional weight losses are associated with the marked relief of dyspnea and chest discomfort, as well as with an increase in leisure-time physical activity. These findings are in line with the accumulating evidence that surgically induced weight losses in obese subjects are associated with improvements in physical health15 and mental well-being.16

Apart from the increased work of ambulation, exertional dyspnea in obesity may have multifactorial causes related to both respiration and circulation. The accumulation of adipose tissue in the thorax and abdomen changes the properties of the chest wall and diaphragm and affects the mechanics of breathing. These alterations include decreases in chest wall and total respiratory compliance17,18 and increases in respiratory resistance.19,20 As a result, the work and energy costs of breathing are elevated.21,22 Furthermore, the relatively well-perfused lung bases in obese patients are often underventilated owing to airway closure and alveolar collapse and this ventilation-perfusion mismatch may give rise to arterial hypoxemia.21,24

In addition to respiratory disturbances, obesity is associated with several alterations in the circulatory system. With increasing body weight, both blood volume and cardiac output rise25 and hypertension frequently develops.26 Hemodynamic overload of this kind leads to left ventricular hypertrophy,27 which in turn interferes with left ventricular filling.28 The subsequent elevation in pul-

The addition of treatment method (surgical vs conventional) as an explanatory variable to our statistical models did not change the pattern of odds ratios in Table 3 and Table 4, and furthermore, the results remained similar when the data were analyzed separately for men and women.
The relationship between body weight and physical activity is complex, and the directionality of this relationship has not been fully determined. Several investigators have emphasized the primary role of sedentary lifestyle in the development of obesity, while the opposite possibility, that effort-related symptoms in obese subjects might limit exercise performance, has received less attention. In the present study, weight loss was associated with an increase in physical activity, possibly encouraged by the concomitant relief in effort-related symptoms. Our findings thus suggest that sedentary behavior may be secondary to obesity to some extent and support the hypothesis that physical inactivity and the accumulation of body fat reinforce one another in the process of developing and maintaining the obese state. The breaking of this vicious circle with surgical intervention, thereby permitting enhanced leisure-time activity, should be regarded as favorable, not only because it promotes general well-being, but also because improved physical fitness reduces cardiovascular morbidity and mortality.

In a previous report from the SOS study, obese patients with sleep apnea complained more frequently of dyspnea and chest pain compared with patients without sleep-disordered breathing, despite similar degrees of obesity. In the present study, the relief of sleep-disordered breathing was related to improvements in dyspnea and chest discomfort and, correspondingly, the occurrence of apneas during sleep contributed to persistent chest pain. These relationships were or tended to be independent of changes in weight. The results indicate that sleep apnea may be involved in the pathogenesis of daytime breathlessness and chest pain in obese patients and that improvements in these symptoms following weight loss may be dependent on a parallel reduction in sleep-disordered breathing. Potential mechanisms linking breathing disturbances during sleep and cardiorespiratory symptoms could be pulmonary hypertension, left ventricular hypertrophy, or ischemic heart disease, all of which are conditions known to be associated with sleep apnea.

For practical and ethical reasons, the SOS study was not randomized. Despite our efforts to match surgical and control cases, the 2 study groups differed with respect to certain variables at baseline. Although the slightly younger age of surgical cases might favor the reversibility of cardiorespiratory symptoms, the higher prevalence of smoking and hypertension in this group would, on the other hand, tend to produce bias against our findings.

It was not possible to perform sleep studies to evaluate the frequency of sleep apnea owing to the large number and geographical distribution of the SOS study subjects. Instead we used questionnaire data on the occurrence of frequently witnessed apneas during the night to categorize subjects into groups with a high and low risk of sleep apnea. Although this may have limitations in providing accurate prevalence data, apnea is one of the most powerful predictors of sleep-disordered breathing confirmed by polysomnography. One form of bias, however, is that patients living alone may be less aware of sleep apnea than those with a home partner. Nevertheless, misclassification due to underreporting of this kind would tend to underestimate the difference between groups and produce bias against our findings.

Another potential source of error is that patients who choose surgical treatment are likely to differ psychologically from those preferring conventional obesity therapy, which may influence their reporting of cardiorespiratory symptoms and physical activity. Nonetheless, the associations between weight loss and relief of symptoms were of a dose-response nature and were independent of treatment group, which supports our conclusions that improvements in dyspnea, chest pain, and sedentary activity are induced by weight reduction itself.

Surgically induced weight loss in patients with obesity is associated with a marked relief in dyspnea and chest pain on exertion; the severity of these symptoms decreases progressively with the degree of weight reduction. A reduction in sleep-disordered breathing further contributes to recovery from breathlessness and chest discomfort, suggesting that sleep apnea is involved in the pathophysiology of cardiorespiratory symptoms in obese subjects. Finally, weight loss in obese patients promotes increased leisure-time physical activity, supporting the belief that a sedentary lifestyle may be a consequence, as well as a cause, of the obese state.

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Corresponding author: Kristjan Karason, MD, PhD, Department of Cardiology, Sahlgrenska University Hospital, Göteborg, SE-413 45 Sweden (e-mail:kristjan.karason@medfak.gu.se).

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