Lipid, Lipoprotein, and Apolipoprotein Profiles in Active and Sedentary Men With Tetraplegia

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Objective: To investigate whether the risk profile of coronary heart disease (CHD) is more favorable in physically active men with tetraplegia compared with sedentary men with tetraplegia.

Design: Using a cross-sectional design, the lipid and (apo)lipoprotein concentrations of 11 active and 13 sedentary men with tetraplegia were compared. Regression analysis was applied to investigate the influence of subject characteristics and behavioral factors on the risk profile of CHD.

Methods: Subjects: Ten normal men: Two fasting plasma cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides, apolipoprotein-A1 (ApoA1), and apolipoprotein-B (ApoB) concentrations were determined. Low-density lipoprotein cholesterol (LDL-C) and the ratios TC/HDL-C, LDL-C/HDL-C, ApoA1/ApoB, and HDL-C/ApoA1 were calculated.

Results: A significantly higher HDL-C and ApoA1/ApoB and lower TC/HDL-C were found in the active group. Age and body mass index were important determinants of the lipids and (apo)lipoproteins. Sport activity was the only significant determinant of HDL-C.

Conclusions: Results suggest a positive influence of sport activity on HDL-C in men with tetraplegia, which may reduce the risk of CHD.

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In recent years, the life expectancy of persons with a spinal cord injury (SCI) has increased considerably. As a consequence of improved medical care, mortality approximates that in the able-bodied population; renal and pulmonary infections have been reduced considerably and coronary heart diseases (CHD) have become the major cause of death. Compared to the able-bodied population, persons with SCI are at increased risk of CHD, presumably because of a relatively inactive lifestyle. Physical inactivity is also an important risk factor of CHD in able-bodied persons. This is expressed in the level of high-density lipoprotein cholesterol (HDL-C), which correlates positively with physical activity and negatively with the risk of CHD. Accordingly, several studies reported depressed levels of HDL-C in persons with SCI, which suggests an increased risk of CHD due to inactivity. Increasing physical activity may therefore play a major role in reducing the risk of CHD in persons with SCI. Results of two previous studies indeed showed that highly trained persons with SCI had more favorable lipoprotein profiles than inactive subjects. As did other studies that evaluated risk factors of CHD in persons with SCI, these studies focused on total cholesterol (TC) and HDL-C concentrations. Other important indicators for the risk of CHD, such as apolipoprotein-A1 (ApoA1) and apolipoprotein-B (ApoB), have scarcely been studied in persons with SCI, despite their higher power to discriminate between subjects with and without CHD. Furthermore, in persons with tetraplegia, levels of physical activity are assumed to be even lower than in persons with paraplegia, because of the limited muscle mass available for exercise. The lower activity level can result in a lower cardiovascular fitness and inferior lipid and (apo)lipoprotein profiles. Consequently, motivating these subjects to participate in sports activities could benefit them greatly with regard to the risk of CHD.

The objective of this study was to test the hypothesis that physically active men with tetraplegia have a more favorable risk profile of CHD than sedentary men with tetraplegia. For this purpose, the lipid and (apo)lipoprotein concentrations of an active and sedentary group were compared cross-sectionally.

METHODS

Subjects and Procedure

Twenty-four men with tetraplegia, with lesion levels ranging from C5 to C8, participated in this study, after having given their written informed consent. Subjects were divided into an active group (ACT, n = 11), including subjects who were active in regular sport activities for at least 1 month, and a sedentary group (SED, n = 13). In ACT, 4 subjects had an incomplete lesion (ASIA Impairment Scale: D [n = 3] and C [n = 1]), whereas all subjects in SED had a complete lesion. Figure 1 shows the number of subjects per lesion level for each group.

All subjects were participants in a separate study evaluating effects of sport activity on performance capacity. Only subjects without symptoms of cardiovascular diseases or other medical complications were included in the study. Subjects were all living independently and could propel a hand-rim wheelchair.

Blood samples were collected in the morning or early afternoon. Subjects were asked to eat a low-fat breakfast only (bread and tea) at least 2 hours before blood samples were taken. Sports activity was defined as hours of sports participation per week, and ranged in ACT from 1.5 to 6.0 hours per week. All subjects of ACT participated in a weekly quad rugby training (1.5h/wk). Additional sports activities were wheelchair dancing (n = 4), wheelchair basketball (n = 1), and table tennis (n = 1). Smoking behavior was defined as the number of cigarettes smoked per day. Only 4 subjects were smokers (2 in ACT and 2 in SED), and they smoked 2 to 15 cigarettes per day. Alcohol consumption, defined as units alcoholic beverages per week, ranged from 0 (n = 7) to 30 glasses per week. Eight

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subjects (3 in ACT and 5 in SED) had a history of CHD in parents, brothers and/or sisters. Body mass was determined on a hospital scale. Body mass index (BMI [kg/m²]) was defined as body mass divided by the square of self-reported height. Peak oxygen uptake (VO₂peak [mL/kg/min]) was determined as a measure of physical fitness in a separate maximal wheelchair exercise test. Subject characteristics and behavioral factors are summarized in table 1.

Blood Lipids and (Apo)Lipoproteins

Blood samples were drawn by venal puncture into K3EDTA-containing vacutainer tubes. Plasma was isolated within 3 hours for determination of the lipid, lipoprotein, and apolipoprotein levels, and was stored at −80°C until analysis. TC and triglyceride (TG) concentrations were determined by enzymatic, commercially available reagents. LDL-C was determined by the polyethylene glycol 6000 method. Low-density lipoprotein cholesterol (LDL-C) concentration was calculated by the Friedewald formula. Total plasma apoA1 and apoB were determined by immunephelometry. To achieve accurate results in relation to the Centers for Disease Control standardization program, the obtained values were recalculated on the basis of an exchange of sera with Dr. S. Marcovina of the Northwest Lipid Research Laboratory, Seattle WA. The ratios TC/HDL-C, LDL-C/HDL-C, ApoA1/ApoB, and HDL-C/ApoA1 were calculated because these parameters are considered to be relevant indicators of an increased risk of CHD.

Statistics

A Student’s t test for independent samples was applied to detect differences between groups for subject characteristics, behavioral factors, and the lipids and (apo)lipoproteins. To investigate the influence of subject characteristics and behavioral factors on the lipids and (apo)lipoproteins, stepwise multiple regression analysis was applied, using as independent variables age, lesion level, completeness of the lesion (complete lesion = 1, incomplete lesion = 0), time since injury, body mass, BMI, sport activity (sport participation = 1, no sport participation = 0), smoking behavior, alcohol consumption, VO₂ peak and family history of CHD (with family history of CHD = 1, without family history of CHD = 0). Results were considered significant at p < .05.

To determine whether active men with tetraplegia are at increased risk of CHD, the results were qualitatively compared with data from the able-bodied population.

RESULTS

Subjects

There were no significant differences between groups in age, time since injury, body height, smoking behavior, and alcohol consumption. Body mass and BMI were significantly lower, and VO₂ peak was significantly higher, in ACT compared with SED (table 1).

Blood Lipids and (Apo)Lipoproteins

Table 2 summarizes the lipid and (apo)lipoprotein concentrations for both groups. ACT showed a significantly higher value for HDL-C and ApoA1/ApoB, and a lower ratio TC/HDL-C, compared with SED (p < .05). No significant differences were found between groups for TC, LDL-C, LDL-C/HDL-C, TG, ApoA1, ApoB, and HDL-C/ApoA1. Results of the regression analysis, investigating the influence of subject characteristics and behavioral factors (including sport activity) on the lipids and (apo)lipoproteins, are listed in table 3. BMI was the only significant determinant of TC/HDL-C, LDL-C/HDL-C, and HDL-C/ApoA1, explaining 24%, 18%, and 19% of the variance, respectively. These results show that no differences in TC/HDL-C between ACT and SED are found when results are adjusted for BMI. Age was the most important determinant of TC, TG, ApoB, and ApoA1/ApoB. For ApoA1/ApoB this implies that, although a difference was found between ACT and SED, age is a more important determinant than sport activity. Sport activity was the only significant determinant of HDL-C, explaining 17% of the variance, irrespective of the other independent variables (including BMI, age, and lesion level). No significant relationships were found for lesion level, exercise, or family history of CHD.
body mass, family history for CHD, VO2 peak, smoking behavior, alcohol consumption, and sport activity on the lipids and (apo)lipoproteins (n = 24).

Comparing the results of ACT with data from the able-bodied population (TC, 4.7 mmol/L, and HDL-C, 1.15 mmol/L for men aged 25 to 29 yrs; LDL-C, 3.2 mmol/L for men aged 30 to 39 yrs; TG, 1.26 mmol/L for men aged 20 to 34 yrs) revealed normal concentrations for TC, HDL-C, LDL-C, and TG (table 2). The ApoA1 concentration was considerably lower and ApoB was (slightly) higher in ACT, compared with able-bodied subjects (ApoA1, 1.35 g/L; ApoB, 0.92 g/L for men aged 30 to 39 yrs) [table 2]).

**DISCUSSION**

Results of the present study show a more favorable lipid and (apo)lipoprotein profile in a group of active men with tetraplegia, compared to sedentary men with tetraplegia. Lower levels of HDL-C and ApoA1/ApoB and higher levels of TC/HDL-C as found in SED in the present study are associated with a higher risk of CHD.8,19,20 For the other risk profile parameters a tendency was observed for more favorable values in ACT (table 2). The results, therefore, suggest that active persons with tetraplegia are at lower risk of CHD. Because of the cross-sectional design of the study, however, differences in BMI, age, and lesion level between ACT and SED may have influenced the results. Multiple regression analysis, in which the influence of confounding variables was investigated, showed that age and BMI were the most important determinants of most of the lipid and (apo)lipoprotein parameters, including TC/HDL-C and ApoA1/ApoB (table 3). These results imply that BMI and age are more important parameters than sports activity, for predicting TC/HDL-C and ApoA1/ApoB, respectively. However, the lower BMI in ACT can be the result of a higher activity level, influencing the risk profiles indirectly by reducing percentage body fat. It is possible, however, that less obese subjects are more likely to participate in sports activities, and thus a selection bias may be present. Because of the cross-sectional character of the study, these questions remain unanswered. From table 3 it appears that for ApoA1, ApoB, and ApoA1/ApoB, adjusted for age (and completeness of the lesion in ApoA1), no significant association was found with sports activity. Although the relatively small number of subjects, and the variety in hours and intensity of sports activities, may have influenced the results, the hypothesis that apolipoprotein concentrations are more favorable in physically active men with tetraplegia can thus not be confirmed. Future longitudinal research is required to establish the effect of sports activity on apolipoproteins.

Nevertheless, multiple regression analysis showed that, irrespective of BMI, age, lesion level, and the other possible confounding variables, sports activity was the only significant determinant of HDL-C. The higher HDL-C for ACT in the present study is in agreement with previous cross-sectional studies, in which sedentary subjects and wheelchair athletes with SCI were compared.4,5 Longitudinal research is required to establish causal relationships between training and risk factors of CHD in persons with tetraplegia. The absence of a relation between smoking and the lipids and (apo)lipoproteins in the present study is probably the result of the low number of smokers. The significantly higher VO2 peak in ACT might be explained by the higher training status of this group, although the 4 subjects with incomplete lesions in ACT can also account for the higher VO2 peak, due to a larger available muscle mass. This may also explain the nonrelation between VO2 peak, as a measure of physical fitness, and the lipids and (apo)lipoproteins. The results of the present study were comparable to results for persons with paraplegia,9,12,20 which indicates that lesion level is not affecting the lipid and (apo)lipoprotein profiles. Therefore, the assumption that persons with tetraplegia are at higher risk of CHD than persons with paraplegia cannot be confirmed by the present study.

Qualitative comparison with data from the able-bodied population revealed that active men with tetraplegia showed normal levels of HDL-C, whereas for the sedentary subjects lower concentrations were observed. These results suggest that being physically active can increase HDL-C and thus decrease the risk of CHD in men with tetraplegia. Several studies showed depressed levels of HDL-C in persons with SCI4,8-16,20 whereas in another study no differences could be found between able-bodied and subjects with SCI.20 Differences in activity level might therefore be responsible for these contradictory results. In contrast to the normal value for HDL-C in ACT, results showed depressed ApoA1 and elevated ApoB levels for ACT, in comparison with the able-bodied population. Consequently, a depressed ratio ApoA1/ApoB was observed, compared with able-bodied subjects.21 Since ApoA1 concentrations of <1.20 g/L are associated with an increased risk of CHD, the low values for ApoA1 in the present study show that (active) men with tetraplegia have an increased risk of CHD. Furthermore, an increased ApoB level in combination with a normal LDL-C is also associated with a higher risk of CHD, because of an increase of small, dense LDL particles, which contain less cholesterol than normal LDL.13 Future research on the risk profile of CHD in persons with SCI should therefore also include analyses of apolipoproteins.

**CONCLUSIONS**

The results of this study suggest a positive influence of sport activity on HDL-C in men with tetraplegia, which may reduce the risk of CHD. Based on the depressed levels of ApoA1, and an increased level of ApoB, in combination with a normal LDL-C, both active and sedentary men with tetraplegia are at increased risk of CHD.

**Acknowledgment:** We thank Dr. P.N.M. Demaeker, Lab of General Internal Medicine, University Hospital Nijmegen, for his comments and for measurements of the lipids, lipoproteins, and apoproteins.

**Table 3: Results of Multiple Regression Analysis**

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Regression Coefficients + Intercepts</th>
<th>Independent Variables</th>
<th>β Value</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mmol/L)</td>
<td>.053 ± .020</td>
<td>Age (.014)</td>
<td>.24</td>
<td></td>
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<tr>
<td></td>
<td>3.044 ± .888</td>
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<td></td>
<td></td>
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<tr>
<td>HDL-C (mmol/L)</td>
<td>−.174 ± .089</td>
<td>Sport activity (.049)</td>
<td>.17</td>
<td></td>
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<tr>
<td>LDL-C (mmol/L)</td>
<td>.952 ± .056</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TCHDL-C</td>
<td>.123 ± .047</td>
<td>BMI (.16)</td>
<td>.24</td>
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</tr>
<tr>
<td>LDL-C/HDL-C</td>
<td>1.909 ± 1.126</td>
<td></td>
<td>.104</td>
<td></td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>.084 ± .039</td>
<td>BMI (.04)</td>
<td>.18</td>
<td></td>
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<tr>
<td></td>
<td>1.072 ± .926</td>
<td></td>
<td>.28</td>
<td></td>
</tr>
<tr>
<td>ApoA1 (g/L)</td>
<td>−.181 ± .065</td>
<td>Completeness (.01)</td>
<td>.20</td>
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<tr>
<td></td>
<td>.005 ± .002</td>
<td>Age (.04)</td>
<td>.34</td>
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<tr>
<td></td>
<td>1.100 ± .000</td>
<td></td>
<td>.00</td>
<td></td>
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<tr>
<td>ApoB (g/L)</td>
<td>.018 ± .005</td>
<td>Age (.02)</td>
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<tr>
<td></td>
<td>.556 ± .176</td>
<td></td>
<td>.05</td>
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<tr>
<td>ApoA1/ApoB</td>
<td>−.011 ± .004</td>
<td>Age (.02)</td>
<td>.22</td>
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<tr>
<td></td>
<td>1.401 ± .183</td>
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<td>.00</td>
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</tr>
<tr>
<td>HDL-C/ApoA1</td>
<td>−.004 ± .002</td>
<td>BMI (.33)</td>
<td>.19</td>
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<td></td>
<td>.451 ± .042</td>
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Multiple regression analysis investigated the influence of age, level and completeness of the lesion, time since injury, body mass, BMI, V̇Ȯ2 peak, family history for CHD, smoking behavior, alcohol consumption, and sport activity on the lipids and (apo)lipoproteins (n = 24).
CHD RISK PROFILES IN MEN WITH TETRAPLEGIA, Dallmeijer

References


Suppliers
a. Catalogue no. 327574; Boehringer Mannheim GmbH, Santhoferstrasse 116, Mannheim 68298, Germany.

b. Catalogue no. 6639, Sera Pak; Miles, Viale Certosa 210, Milano 20156, Italy.