# **ORIGINAL ARTICLE**



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# Cardiovascular risk factors in adults with coarctation of the aorta

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#### Abstract

**Background:** The aging patient with adult congenital heart disease (ACHD) faces the risk of developing atherosclerotic disease. Patients with coarctation of the aorta (CoA) are especially vulnerable because of an inherent high risk of developing hypertension. However, data on the prevalence of other cardiovascular risk factors are scarce. Therefore, this study aimed to describe the prevalence of traditional cardiovascular risk factors (diabetes, hypertension, hyperlipidemia, smoking, obesity, and sedentary lifestyle) in adult patients with CoA.

**Methods:** Patients with CoA who were registered at the ACHD clinic in Gothenburg were asked to participate in a comprehensive cardiovascular risk assessment. This assessment included a glucose tolerance test, cholesterol profile, ambulatory blood pressure measurements, and a lifestyle questionnaire.

**Results:** A total of 72 patients participated. The median age was 43.5 years and 58.3% were men. Sixty-six (91.7%) patients had  $\geq$ one cardiovascular risk factor and 40.3% had  $\geq$ three risk factors. Three (4.2%) patients were newly diagnosed with diabetes or impaired glucose tolerance. More than half of the patients had hyperlipidemia (*n* = 42, 58.3%) and 35 patients (48.6%) were overweight or obese. Only three (4.2%) patients smoked regularly. Of the 60 patients who underwent 24-hour ambulatory blood pressure measurement, 33 (55.0%) were hypertensive. Of the 30 patients with known hypertension only 9 (30.0%) had well-controlled blood pressure on ambulatory blood pressure measurement.

**Conclusions:** Cardiovascular risk factors among patients with CoA are prevalent. This may indicate a need for more aggressive screening strategies of traditional risk factors to minimize the risk of these patients also developing atherosclerotic disease.

#### KEYWORDS

cardiovascular risk factors, coarctation of the aorta, congenital heart disease, diabetes, hyperlipidemia, hypertension

#### 1 | INTRODUCTION

The number of adults with congenital heart disease (ACHD) is growing and an increasing amount of patients with congenital heart disease reach middle age and even older ages.<sup>1-6</sup> With increasing age, these patients have an increasing risk of developing acquired cardiovascular disease, such as ischemic heart disease and stroke.<sup>7-11</sup>

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Patients with coarctation of the aorta (CoA) have traditionally been assumed to have an increased risk of coronary artery disease, partly due to abnormal vascular reactivity and endothelial dysfunction.<sup>12-15</sup> However, Roifman et al showed that an increased risk of myocardial infarction in patients with CoA was associated with traditional cardiovascular risk factors and not with CoA itself.<sup>16</sup> Further, a large registry study also showed that younger patients with CoA did not have a particularly increased risk of ischemic heart disease compared with patients with other congenital heart conditions.<sup>7</sup>

Patients with congenital heart disease have been reported to have a high prevalence of cardiovascular risk factors,<sup>17,18</sup> with almost 80% of patients having at least one cardiovascular risk factor.<sup>17</sup> Decreased glucose tolerance on oral glucose tolerance test (OGTT) is more common in patients with complex ACHD compared with healthy controls.<sup>19</sup> Furthermore, register studies have reported a higher prevalence of diabetes mellitus in patients with ACHD compared with controls.<sup>20,21</sup> Patients with ACHD have an increased risk of metabolic syndrome compared with controls<sup>22</sup> and obesity is as common in patients with ACHD as in the general population.<sup>23,24</sup> However, patients with ACHD tend to be more physically active and smoke less than controls without congenital heart disease.<sup>17,25</sup>

Almost 50% of patients with CoA are hypertensive from a young age, despite successful surgical repair of the coarctation.<sup>26</sup> However, there are scarce data on the prevalence of other cardiovascular risk factors in patients with CoA. Therefore, the aim of this study was to describe the prevalence of traditional cardiovascular risk factors (diabetes mellitus/impaired glucose tolerance, hypertension, hyperlipidemia, smoking, obesity, and lack of physical exercise) in adult patients with CoA.

# 2 | METHODS

# 2.1 | Study population

Patients  $\geq$ 18 years old who had a diagnosis of CoA as the main congenital heart disease diagnosis and who were registered at the congenital heart outpatient clinic at Östra Hospital, Gothenburg, Sweden, were invited in writing to participate in the study (n = 192). Two reminder letters were sent to patients who did not reply and attempts were also made to reach the patients by telephone. A total of 72 patients agreed to participate in the study.

Figure 1 shows the flowchart of patient recruitment and the geographical data on the location of residence of participants and

nonparticipants in the study. Because our center is a tertiary center, not all patients who were invited to participate were regularly followed at our congenital heart clinics. Most of the patients who participated in the study lived in Gothenburg, in the Västra Götaland region (region where Gothenburg is located), or in the Halland region, which is a geographically neighboring region. Among those who did not respond or who did not wish to participate, 30.0% (n = 36/120) lived in regions that are geographically remote from our center compared with only 11.1% (n = 8/72) of those who participated.

# 2.2 | Study protocol

The patients underwent a clinical examination including measurement of height, weight, body mass index (BMI), waist/hip ratio, and 12-lead electrocardiogram. Blood pressure was measured by a calibrated automated tonometer in the right and left arms, as well as in both legs, in the supine position after at least 5 minute of rest.

The patients underwent venous blood sampling after an overnight fast to assess the lipid profile, including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG) levels. LDL cholesterol was measured by a direct enzymatic colorimetric method. Hemoglobin, electrolytes, liver enzymes, natriuretic brain peptide, and highsensitivity C-reactive protein were measured. The patients underwent an OGTT where plasma glucose levels were measured before and 2 hour after intake of 75 g of glucose dissolved in 200-300 ml of water. Hemoglobin A1c (HbA1c) levels were also measured.

The patients were asked to fill out a lifestyle questionnaire, which included questions on smoking, physical activity, dietary habits, alcohol use, and socioeconomic factors. The patients were asked to estimate their dietary intake. In order to facilitate the estimation, we provided examples of weight of dietary products. The patients were asked to estimate the level of their physical activity (eg, moderate, regular physical activity) according to examples given. Also, the patients were asked to estimate the total number of hours of light, moderate, and intense physical activity per week.

A review of the patients' medical notes was performed to determine any previous diagnosis of hypertension, diabetes mellitus, stroke, transient ischemic attack, or myocardial infarction.

All patients were asked to undergo 24-hour ambulatory blood pressure measurements and 60 patients underwent 24hour blood pressure measurements. For two patients, only daytime measurements were available. The blood pressure cuff was worn on the right arm and set to three measurements per hour during daytime and one to two measurements per hour during night time. We included all ambulatory blood pressure measurements with > 25% problem-free blood pressure measurements and a duration > 10 hours.

The study visits were conducted between April 2013 and February 2015. In some cases, ambulatory blood pressure

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measurements were performed several months after the study visit for practical reasons.

# 2.3 | Definitions

# 2.3.1 | Hypertension

The patients were defined as hypertensive if they had a previously known diagnosis of hypertension (treated or non-treated with medication), if the office blood pressure was  $\geq$ 140/90 mm Hg, or if the patients had any of the following on 24-hour ambulatory blood pressure measurements: mean

24-hour blood pressure of  $\ge$  130/80 mm Hg or mean daytime blood pressure of  $\ge$  135/85 mm Hg, or mean night time blood pressure  $\ge$  120/70 mm Hg.<sup>27</sup>

# 2.3.2 | Diabetes

World health organization definition cut-off values (2006) were used for diabetes, impaired glucose tolerance, and impaired fasting glucose.<sup>28</sup> Diabetes was defined as fasting plasma glucose levels ≥7.0 mmol/l or 2-hour OGTT plasma glucose levels ≥11.1 mmol/l. Impaired glucose tolerance was defined as fasting glucose levels <7.0 mmol/l and 2-hour OGTT glucose levels ≥7.8 and <11.1 mmol/l. - A Congenital Heart Disease

Impaired fasting glucose was defined as fasting plasma glucose levels of 6.1-6.9 mmol/l and 2-hour OGTT plasma glucose levels <7.8 mmol/l. HbA1c alone was not sufficient to diagnose diabetes.

# 2.3.3 | Hyperlipidemia

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Hyperlipidemia was defined as total cholesterol levels  $\geq$ 5 mmol/l (193 mg/dl)<sup>29</sup> or LDL levels  $\geq$ 3 mmol/l (116 mg/dl).<sup>30</sup>

# 2.3.4 | Overweight and obesity

Overweight was defined as a BMI  $\geq 25 \text{ kg/m}^2$  and obesity was defined as a BMI  $\geq 30 \text{ kg/m}^2$ .

# 2.4 | Ethical approval

The study was approved by the Gothenburg Regional Research Ethics Board. All participants gave written informed consent to participate in the study. The study complied with the Declaration of Helsinki.

#### 2.5 | Statistical analysis

Categorical variables are presented as numbers and percentages and continuous variables are shown as means and standard deviations, or medians. Microsoft Excel was used to perform all of the calculations.

# 3 | RESULTS

A total of 72 patients with CoA participated in the study, of whom 58.3% (n = 42) were men. The median age of the participants was 43.5 years (range: 20-71 years). For the 120 patients who did not wish to participate or who did not respond, the median age was 29 years (range: 19-71 years) and 60.0% (n = 72) were men.

The baseline characteristics and socioeconomic data of the study population are shown in Table 1. Most (n = 31, 43.1%) patients had undergone end-to-end surgical correction of the aortic coarctation. Five (6.9%) patients had also undergone surgical correction of a ventricular septal defect and two (2.8%) patients had an atrial septal defect that required surgical correction. Four (5.6%) patients had a prior cardiovascular event, such as myocardial infarction (n = 1), stroke (n = 2), or transient ischemic attack (n = 1).

# 3.1 | Cardiometabolic risk factors and lifestyle

Table 2 shows the lipid profile, HbA1c, fasting, and post-load glucose values and Table 3 shows a summary of cardiovascular risk factors in the study population. Through the OGTT, three (4.2%) patients were diagnosed with diabetes mellitus (n = 2, 2.8%) or impaired glucose tolerance (n = 1, 1.4%). A further two patients had impaired fasting glucose only (but normal OGTT and HbA1c values). None of the patients had a previous diagnosis of diabetes mellitus or impaired glucose tolerance.

More than half of the patients (n = 42, 58.3%) had hyperlipidemia. Approximately one-third (n = 26/72, 36.1%) of the patients had total cholesterol levels  $\geq$ 5 mmol/l and eight (11.1%) patients had total cholesterol levels  $\geq$ 6 mmol/l. More than half of the participants had LDL cholesterol levels  $\geq$ 3 mmol/l (n = 41/72, 56.9%) and 11 (15.3%) patients had LDL levels  $\geq$ 4 mmol/l. Only 23 (31.9%) patients had "ideal" LDL values below <2.6 mmol/l.

A total of 28 (38.9%) patients were overweight (BMI  $\ge$  25 kg/m<sup>2</sup>) and seven (9.7%) patients were obese (BMI  $\ge$  30 kg/m<sup>2</sup>). Only three (4.2%) patients smoked regularly and 29.2% (n = 21/72) had smoked in the past, either regularly or occasionally.

Dietary patterns are shown in Table 4. Unhealthy dietary patterns were common. Approximately half (n = 38, 52.8%) of the patients consumed less than 200 g of vegetables per day and approximately half consumed less than two servings of fruit per day. One-third of the patients consumed 0.3 l or more of soft drinks/juice per day. Additionally, one-third of patients consumed six or more standard drinks per week.

# 3.2 | Blood pressure including 24-hour ambulatory measurements

More than half (n = 37/72, 51.4%) of the participants had a previously known diagnosis of hypertension at baseline. This included seven patients who had previously known hypertension, but who no longer were on any pharmacological treatment because of normalized blood pressure (n = 5) or the patient's preference (n = 2).

A total of 60 patients underwent 24-hour ambulatory blood pressure measurements. A total of 33 (55.0%) patients had high systolic and/or diastolic blood pressure (either at the mean 24-hour measurement, and/or during the day and/or night time). Of these, 12 (36.4%) patients had newly diagnosed hypertension on 24-hour ambulatory blood pressure measurement and 21 (70.0%) patients had increased ambulatory blood pressure, despite a previously known diagnosis of hypertension. Only nine (30.0%) of the 30 patients with known hypertension who underwent ambulatory blood pressure measurements had well-controlled blood pressure on ambulatory blood pressure measurement.

# 3.3 | Physical activity

Most (*n* = 60/72, 86.1%) participants did some type of physical activity in their spare time (Table 5). However, most patients only did light exercise and/or exercised less than three times per week. Only 20 (27.8%) patients participated in regular physical activity of an intense level, such as running, swimming, badminton, and keep-fit exercises, for an average of at least three times a week, or had a level of physical activity that exceeded this. A total of 44 (61.1%) patients met the European Society of Cardiology recommendations on physical exercise (150 minute/week of moderate physical activity or 75 minute/week of intense physical activity, or a combination of these).<sup>30</sup>

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# **TABLE 1** Demographic and socioeconomic characteristics of the study population

| Age, y (median, range)  | 43.5 (20-71) |
|---|--------------|
| Sex   |              |
| Male  | 42 (58.3%)   |
| Female  | 30 (41.7%)   |
| Highest attained education level <sup>a</sup>                     |              |
| Primary school  | 4 (5.7%)     |
| Upper secondary school  | 22 (31.4%)   |
| Occupational training   | 9 (12.5%)    |
| University degree or higher                                       | 36 (51.4%)   |
| Occupational status <sup>b</sup>                                  |              |
| Full-time employment  | 37 (51.4%)   |
| Part-time employment  | 15 (20.8%)   |
| Self-employed   | 8 (11.1%)    |
| On sick leave   | 2 (2.8%)     |
| Student   | 8 (11.1%)    |
| Other   | 10 (13.9%)   |
| Primary surgical corrective procedure of coarctation of the aorta |              |
| End-to-end  | 31 (43.1%)   |
| Subclavian flap   | 19 (26.4%)   |
| Graft   | 4 (5.6%)     |
| Stent/balloon   | 6 (8.3%)     |
| Patch   | 1 (1.4%)     |
| No surgery  | 11 (15.3%)   |
| Any intervention due to recoarctation                             | 7 (9.7%)     |
| Previous diagnosis of hypertension                                | 37 (51.4%)   |
| Use of antihypertensive medication <sup>c</sup>                   | 34 (47.2%)   |
| Use of statins  | 5 (6.9%)     |
| Family history of diabetes mellitus type 1 or 2 (parent/sibling)  | 8 (11.1%)    |

<sup>a</sup>Information on the highest attained education level and occupational status is missing for one patient.

<sup>b</sup>One individual can have several occupational statuses.

<sup>c</sup>Including four patients on beta-blockers because of atrial fibrillation/flutter.

| Cardiovascular risk factor | Mean (±SD) mmol/l | Range mmol/l | Mean (±SD) mg/dl | Range mg/dl |
|----------------------------|-------------------|--------------|------------------|-------------|
| Total cholesterol          | 4.8 (±0.9)        | 2.5-6.7      | 185.6 (±34.8)    | 96.7-259.1  |
| LDL                        | 3.1 (±0.9)        | 1.2-4.9      | 119.9 (±34.8)    | 46.4-189.5  |
| HDL                        | 1.5 (±0.5)        | 0.71-2.8     | 58.0 (±19.3)     | 24.5-108.3  |
| TG                         | 1.0 (±0.5)        | 0.32-0.56    | 88.6 (±19.3)     | 28.3-49.6   |
| Fasting glucose            | 5.1 (±0.7)        | 4.0-8.7      | 91.8 (±27.1)     | 72.0-156.6  |
| Post load glucose          | 5.4 (±2.1)        | 2.5-16.2     | 97.2 (±81.2)     | 45.0-291.6  |
| HbA1c (mmol/mol)           | 32.7 (±4.5)       | 23-55        | 4.2% (±1,4%)     | 3.2%-6.3%   |

**TABLE 2** Lipid profile, HbA1c, and fasting and post-load glucose in the study population

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation; TG, triglycerides.

Data are shown as mean  $\pm$  SD and range (lowest to highest value). Data are shown both in mmol/l and mg/dl.

Data on post-load glucose are missing for two patients.

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 TABLE 3
 Summary of cardiovascular

risk factors in the study population

| Diabetes mellitus2 (2.8%)Impaired glucose tolerance1 (1.4%)Total cholesterol (mmol/l)>68 (11.1%)>526 (36.10%)>526 (36.10%)>526 (36.10%)LDL (mmol/l)>111 (15.3%)LDL (mmol/l)>411 (15.3%)>341 (56.9%)>330 (41.7%)<2.6 <sup>a</sup> 23 (31.9%)HDL (mmol/l)<1 (males)4 (9.5%)<1.2 (females)3 (10.0%)Smoking3BMI (kg/m²)21 (29.2%)<br>occasional)21 (29.2%)<br>occasional)BMI (kg/m²)21 (29.2%)<br>occasional)21 (29.2%)<br>occasional)BMI (kg/m²)37 (51.4%)<br>2.25 to < 3028 (38.9%)<br>2.30Waist circumference (cm)Males89.6 (413.1)<br>Females7.78 (49.5)Waist/hip ratioMales0.89 (40.09)<br>Females0.77 (±0.08) | Risk factor                |                     | Value        |
|---|----------------------------|---------------------|--------------|
| Total cholesterol (mmol/l)       ≥6       8 (11.1%)         ≥5       26 (36.10%)         ≤5       46 (63.9%)         LDL (mmol/l)       >4         ≥4       11 (15.3%)         ≥3       41 (56.9%)         ≤1       ≥3       41 (56.9%)         ≤2.6 <sup>a</sup> 23 (31.9%)         HDL (mmol/l)       <1 (males)  | Diabetes mellitus          |                     | 2 (2.8%)     |
| ≥6       8 (11.1%)         ≥5       26 (36.10%)         <5  | Impaired glucose tolerance |                     | 1 (1.4%)     |
| ≥5       26 (36.10%)         <5   | Total cholesterol (mmol/l) |                     |              |
| <5  |                            | ≥6                  | 8 (11.1%)    |
| LDL (mmol/l)       ≥4       11 (15.3%)         ≥3       41 (56.9%)         ≤3       30 (41.7%)         <2.6 <sup>a</sup> 23 (31.9%)         HDL (mmol/l)       <1 (males)   |                            | ≥5                  | 26 (36.10%)  |
| ≥4       11 (15.3%)         ≥3       41 (56.9%)         <3  |                            | <5                  | 46 (63.9%)   |
| ≥341 (56.9%) $<3$ 30 (41.7%) $<2.6^a$ 23 (31.9%)HDL (mmol/l) $<1$ (males)4 (9.5%) $<1.2$ (females)3 (10.0%)Smoking $<1.2$ (females)3 (4.2%)Current, regular3 (4.2%) $<1.2$ (females)Mell (kg/m²)Current, occasional4 (5.6%)BMI (kg/m²) $<25$ solor37 (51.4%) $<25$ to $<30$ 28 (38.9%) $<30$ $<7(9.7%)$ Waist circumference (cm)Males89.6 (±13.1)Waist/hip ratioMales0.89 (±0.09)   | LDL (mmol/l)               |                     |              |
| $< 3$ $30 (41.7\%)$ $< 2.6^a$ $23 (31.9\%)$ HDL (mmol/l) $<1 (males)$ $4 (9.5\%)$ $<1.2 (females)$ $3 (10.0\%)$ Smoking $<1.2 (females)$ $3 (4.2\%)$ Current, regular $3 (4.2\%)$ $(1.2\%)$ Current, occasional $4 (5.6\%)$ $21 (29.2\%)$<br>occasional)BMI (kg/m <sup>2</sup> ) $<25 $ $37 (51.4\%)$ $< 25 $ $37 (51.4\%)$ $> 230 $ $< 30 $ $7 (9.7\%)$ Waist circumference (cm)Males $89.6 (\pm 13.1)$ Waist/hip ratioMales $0.89 (\pm 0.09)$   |                            | ≥4                  | 11 (15.3%)   |
| <2.6³   |                            | ≥3                  | 41 (56.9%)   |
| HDL (mmol/l)       <1 (males)   |                            | <3                  | 30 (41.7%)   |
| <1.2 (females)  |                            | <2.6 <sup>a</sup>   | 23 (31.9%)   |
| SmokingCurrent, regular3 (4.2%)Current, occasional4 (5.6%)Current, occasional4 (5.6%)Past smoker (regular/<br>occasional)21 (29.2%)BMI (kg/m²)<25   | HDL (mmol/l)               | <1 (males)          | 4 (9.5%)     |
| Current, regular       3 (4.2%)         Current, occasional       4 (5.6%)         Past smoker (regular/<br>occasional)       21 (29.2%)         BMI (kg/m²)       -         <25  |                            | <1.2 (females)      | 3 (10.0%)    |
| Current, occasional4 (5.6%)Past smoker (regular/<br>occasional)21 (29.2%)BMI (kg/m²) $<25$ 37 (51.4%) $<25$ to < 30   | Smoking                    |                     |              |
| Past smoker (regular/<br>occasional)21 (29.2%)BMI (kg/m²)<25  |                            | Current, regular    | 3 (4.2%)     |
| BMI (kg/m²)         <25   |                            | Current, occasional | 4 (5.6%)     |
| <25   |                            | -                   | 21 (29.2%)   |
| ≥25 to < 30   | BMI (kg/m²)                |                     |              |
| ≥307 (9.7%)Waist circumference (cm)Males89.6 (±13.1)Females77.8 (±9.5)Waist/hip ratioMales0.89 (±0.09)  |                            | <25                 | 37 (51.4%)   |
| Waist circumference (cm)         Males         89.6 (±13.1)           Females         77.8 (±9.5)           Waist/hip ratio         Males         0.89 (±0.09)  |                            | ≥25 to < 30         | 28 (38.9%)   |
| Females         77.8 (±9.5)           Waist/hip ratio         Males         0.89 (±0.09)  |                            | ≥30                 | 7 (9.7%)     |
| Waist/hip ratioMales0.89 (±0.09)  | Waist circumference (cm)   | Males               | 89.6 (±13.1) |
|   |                            | Females             | 77.8 (±9.5)  |
| Females 0.77 (±0.08)  | Waist/hip ratio            | Males               | 0.89 (±0.09) |
|   |                            | Females             | 0.77 (±0.08) |

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Data are shown as n (%) or mean ± standard deviation.

<sup>a</sup>Converts to 100 mg/dl.

# 3.4 | Total number of cardiovascular risk factors

Figure 2 shows the number of cardiovascular risk factors in the study population. A total of 66 (91.7%) patients had at least one cardiovascular risk factor of the following: previously known or newly diagnosed hypertension, hyperlipidemia, diabetes mellitus or impaired glucose tolerance, current regular tobacco smoking, overweight or obesity, and a sedentary lifestyle defined as less than 150 minute/week of moderate physical activity or 75 minute/week of intense physical activity, or a combination of these. Half (n = 37, 51.4%) of the patients had one or two cardiovascular risk factors and 11 (15.3%) of the patients had ≥four risk factors. The number of risk factors increased with age as shown in Figure 3.

# 4 | DISCUSSION

In this study of 72 patients with CoA, 91.7% had  $\geq$ one cardiovascular risk factor and 40.3% had  $\geq$ three risk factors (hypertension, hyperlipidemia, diabetes mellitus/impaired glucose tolerance, current smoking, overweight/obesity, sedentary lifestyle). Three patients were newly diagnosed with diabetes mellitus or impaired glucose tolerance. Only 30.0% of patients with a known diagnosis of hypertension had well-controlled blood pressure on ambulatory blood pressure measurement. Unhealthy dietary patterns were common. Cardiovascular risk factors were prevalent in our study, especially considering that our patients were relatively young, with a median age of 43.5 years. There was a trend of an increasing number of cardiovascular risk factors with increasing age (Figure 3), which is in line with studies on cardiovascular risk factors in patients without congenital heart disease.<sup>31</sup>

The participants in our study had a lower BMI, waist circumference, and smoked less compared to participants in an epidemiological study on the prevalence of cardiovascular risk factors in the general population in the Skaraborg region in Sweden (mean age of participants: 46 years).<sup>32</sup> However, the mean systolic blood pressure was higher in our patients. Epidemiological data from northern Sweden and from Finland generally showed a similar comparison trend,<sup>33,34</sup> however, total cholesterol was slightly

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**TABLE 4**Dietary patterns and alcoholintake in the study population

| Product intake/day                                      | ≥500 g    | 300-400 g  | 100-200 g  | 0-100 g    |
|---|-----------|------------|------------|------------|
| Vegetables <sup>a</sup>                                 | 3 (4.2%)  | 29 (40.3%) | 32 (44.4%) | 6 (8.3%)   |
| Meat <sup>b</sup>                                       | 2 (2.8%)  | 17 (23.6%) | 37 (51.4%) | 15 (20.8%) |
| Fish  | 0 (0%)    | 4 (5.6%)   | 31 (43.1%) | 37 (51.4%) |
| Sweets  | 0 (0%)    | 2 (2.8%)   | 8 (11.1%)  | 62 (86.1%) |
| Pasta/potatoes/rice <sup>c</sup>                        | 3 (4.2%)  | 11 (15.3%) | 37 (51.2%) | 18 (25.0%) |
| Fruit intake (number/day) <sup>d</sup>                  | ≥5 pieces | 2-3 pieces | 1 piece    | 0 pieces   |
|   | 1 (1.4%)  | 18 (25.0%) | 32 (44.4%) | 5 (6.9%)   |
| Soft drinks/juice                                       | 1-2 I     | 11         | 0.3-0.5 l  | <0.3       |
|   | 0 (0%)    | 3 (4.2%)   | 17 (23.6%) | 52 (72.2%) |
| Alcohol intake <sup>b,e</sup> (standard<br>drinks/week) | ≥10       | 6-9        | 1-5        | 0          |
|   | 6 (8.3%)  | 18 (25.0%) | 29 (40.3%) | 18 (25.0%) |

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<sup>a</sup>Data are missing for two patients.

<sup>b</sup>Data are missing for one patient.

<sup>c</sup>Data are missing for three patients.

<sup>d</sup>Data are missing for 16 patients.

 $^{\circ}$ A standard drink was defined as follows: two bottles (33 cl) of 2.25% beer, one bottle (50 cl) of 2.25%-3.5% beer, one bottle (33 cl) of 4.5% beer or cider, one glass (15 cl) of wine (7.5%-14%), or one glass (8 cl) of strong wine (15%-22%).

TABLE 5 Level of physical activity in spare time per week

| Level of physical activity                       | Number of patients |
|--|--------------------|
| Sedentary spare time <sup>a</sup>                | 8 (11.1)           |
| Moderate physical activity <sup>b</sup>          | 25 (34.7)          |
| Moderate, regular physical activity <sup>c</sup> | 17 (23.6)          |
| Regular physical activity <sup>d</sup>           | 10 (13.9)          |
| Intensive physical activity <sup>e</sup>         | 8 (11.1)           |
| Very intensive physical activity <sup>f</sup>    | 2 (2.8)            |

Data are shown as n (%).

Data on physical activity in spare time are missing for two patients. <sup>a</sup>Defined as less than 2 hour of walking, cycling, etc per week. <sup>b</sup>Defined as physical activity of light intensity, most often without sweating (eg, walking, cycling to and from work, gardening, fishing, bowling, table tennis).

<sup>c</sup>Defined as regular physical activity one to two times per week at least 30 minute at a time, including activities such as running, swimming, tennis, badminton, and other activities that involve sweating. <sup>d</sup>Defined as physical activity, such as running, swimming, badminton, and keep-fit exercises, at least three times a week. Every occasion lasts at least 30 minute at a time.

<sup>e</sup>Defined as intense physical activity (fitness or strength) >30 minute at a time, including becoming breathless more than three times a week. <sup>f</sup>Defined as very intense physical activity (fitness or strength) for more than 1 hour/time, five to seven times/week.

lower in our cohort and hypertension was more prevalent in our CoA cohort. Comparison of our clinical study with other studies is difficult because of the different methodologies and older age of the participants in the epidemiological studies mentioned above. Furthermore, none of these epidemiological studies assessed the aggregated number of cardiovascular risk factors. The fact that the cardiovascular risk factors were common in our CoA cohort has to be seen in light of the fact that these patients have a congenital aortic pathology and an inherently high prevalence of hypertension, which probably makes a good cardiovascular risk factor control highly important.

Our results are in line with previously published studies on patients with congenital heart disease. Flannery et al reported similar mean total cholesterol (184 ± 31.5 mg/dl or 4.8 ± 0.8 mmol/l) in patients with CoA with mean age of 50 ± 9.2 years,<sup>35</sup> as we found in our study (185.6 ± 34.8 mg/dl or 4.8 ± 0.9 mmol/l). However, in our study, we found a slightly higher mean LDL (119.9 ± 34.8 mg/dl or 3.1 ± 0.9 mmol/l) compared to the study by Flannery et al (mean LDL 103.9 ± 26.3 mg/dl or 2.7 ± 0.7 mmol/l). In a registry study, Roifman et al reported a considerably lower prevalence of hyperlipidemia (4%) in patients with CoA (median age 31.1)<sup>16</sup> compared to our study (58.3%). However, the diagnostic cut-off values for hyperlipidemia were not reported in the registry study where ICD 9 diagnoses were used. These differences between studies are likely explained by different methodologies and diagnostic cut-off values between the studies.

The proportion of overweight and obese patients in our study is consistent with published data on BMI in ACHD in Sweden.<sup>24</sup> In contrast, our study showed a lower prevalence of smoking compared with several other studies on smoking behavior in patients with congenital heart disease.<sup>36-38</sup> In our study, there was a slightly lower prevalence of diabetes mellitus than that previously reported.<sup>16</sup>

Several studies have reported a high burden of cardiovascular risk factors in patients with congenital heart disease, which is in agreement with our study on patients with CoA. Moons et al reported that almost 80% of patients with congenital heart disease had at least one cardiovascular risk factor, despite a young age of the



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**FIGURE 2** Number of cardiovascular risk factors in the study population



patients (median age: 26 years).<sup>17</sup> Additionally, Harris et al reported that only approximately 30% of adolescents and adults with congenital heart disease were in ideal cardiovascular health.<sup>18</sup>

There is a growing body of evidence that patients with congenital heart disease have a higher prevalence of ischemic heart disease compared with controls.<sup>7,39</sup> This is considered to be related to the cardiovascular risk factor burden rather than the congenital heart condition itself.<sup>16,40</sup> Additionally, patients with CoA have their first episode of myocardial infarction 7.2 years earlier than controls without congenital heart disease.<sup>41</sup> Therefore, good cardiovascular risk factor control is of paramount importance in patients with congenital heart disease. This is even more important in patients with CoA because of the high prevalence of hypertension from young age. Potential additional cardiovascular risk factors increase the risk of atherosclerosis and this risk increases further with an increasing number of cardiovascular risk factors.<sup>42</sup>

In our study, 55% of all patients with CoA were hypertensive according to ambulatory blood pressure monitoring. The majority (70%, n = 21/30) of patients had a previous diagnosis of hypertension, but were still regarded as hypertensive. In light of well-known complications during long-term follow-up of patients with CoA, such as progressive dilatation of the ascending aorta and an increased risk

for dissection,<sup>43</sup> well-controlled blood pressure is likely to be very important.

However, there are currently no guidelines on primary prevention of cardiovascular disease that are specifically targeted at patients with CoA or congenital heart disease. Nevertheless, there is evidence that patients with congenital heart disease are less likely to receive statin treatment compared with those without congenital heart disease, despite similar cardiovascular risk scores.<sup>35</sup> A population-based intervention study in Sweden showed that systematic screening for cardiovascular risk factors reduced cardiovascular and all-cause mortality in the general population.<sup>44</sup> Therefore, systematic screening of cardiovascular risk factors (cholesterol profile, fasting glucose/HbA1c, BMI, smoking status, and physical activity level) in CoA patients may be considered in order to identify patients with a high burden of risk factors because these are potentially modifiable. This could also be considered even in younger patients who have several cardiovascular risk factors.

# 4.1 | Strengths and limitations

A strength of this study is that we performed comprehensive and structured assessment of cardiovascular risk factors in patients



with CoA, including lifestyle and physical activity habits. An OGTT was performed to identify patients with decreased glucose tolerance, which is impossible to diagnose only by measuring HbA1c and fasting glucose levels. Additionally, ambulatory blood pressure measurements were performed, which allowed detection of masked hypertension and white coat hypertension.

Limitations of the study include the lack of a control group. However, this study aimed to describe the prevalence of cardiovascular risk factors in patients with CoA and not to compare with other patient groups or controls. Additionally, the data of physical activity and dietary patterns were self-reported by patients, which might have had a risk of overestimation of the hours and intensity of physical activity. Also, approximately 36% of the original cohort participated in the study, however, we do believe that those who participated are representative for the original cohort. The most frequent reason for non-participation was living outside the Gothenburg area. However, most of the area outside, where the nonparticipants came from are likely to be small or moderate size towns. We believe that no truly rural areas have contributed more than one or two occasional patients. Further, because of geographical differences in prevalence of cardiovascular risk factors, our findings may not be generalizable to the patients with CoA who live outside of Sweden.

# 5 | CONCLUSION

Cardiovascular risk factors in patients with CoA are prevalent. Nine of 10 patients with CoA have at least one modifiable cardiovascular risk factor. Our study may indicate a need for systematic screening and development of specific guidelines regarding screening and management of modifiable cardiovascular risk factors, particularly targeting patients with CoA to minimize the risk of atherosclerotic disease.

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# CONFLICTS OF INTEREST

The authors declare that they no conflicts of interest with the contents of this article.

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