ORIGINAL RESEARCH

Interventions in Adults With Repaired Coarctation of the Aorta

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BACKGROUND: Coarctation of the aorta coexists with other cardiac anomalies and has long-term complications, including recoarctation, which may require intervention after the primary coarctation repair. This study aims to clarify the prevalence of and risk factors for interventions related to the coarctation complex as well as late mortality in a large contemporary patient population.

METHODS AND RESULTS: The Swedish National Register of Congenital Heart Disease was used, which comprised 683 adults with repaired coarctation of the aorta. Analysis was performed on freedom from intervention thereafter at the coarctation site, aortic valve, left ventricular outflow tract, or ascending aorta. One hundred ninety-six (29%) patients had at least 1 of these interventions. Estimated freedom from either of these interventions was 60% after 50 years. The risk of undergoing such an intervention was higher among men (hazard ratio, 1.6 [95% CI, 1.2–2.2]). Estimated freedom from another intervention at the coarctation site was 75% after 50 years. In women, there was an increase in interventions at the coarctation site after 45 years. Patients who underwent one of the previously mentioned interventions after the primary coarctation repair had poorer left ventricular function. Eighteen patients (3%) died during follow-up in the register. The standardized mortality ratio was 2.9 (95% CI, 1.7–4.3).

CONCLUSIONS: Interventions are common after coarctation repair. The risk for and time of interventions are affected by sex. Our results have implications for planning follow-up and giving appropriate medical advice to the growing population of adults with repaired coarctation of the aorta.

Key Words: adult congenital heart disease ■ coarctation of the aorta ■ intervention ■ mortality ■ risk factors

Coarctation of the aorta is one of the more common congenital heart defects (5%-10%), first described by Morgagni in 1760. Before modern treatment, the prognosis was poor, with a median survival in the mid-20th century of 31 years. The first surgical repair was performed by Crafoord in 1944 and involved resection of the stenosed segment of the aorta followed by a direct end-to-end anastomosis.

Since then, surgical intervention has been the mainstay of treatment. Several surgical approaches have been introduced, such as subclavian flap aortoplasty, interposition grafts, and more recently catheter-based interventions with angioplasty with or without stenting. The latter has become preferable for coarctation repair in older patients and recoarctations, whereas surgical repair remains the primary modality for native coarctation in neonates, infants, and young children.

Advances in surgical techniques and medical therapy have allowed primary repairs at increasingly younger ages, and today the majority of repairs are performed during the first year of life.

Coarctation of the aorta is often associated with concomitant cardiac lesions, some of which may also require intervention. The most common associated defect is bicuspid aortic valve (detected in 60%-85% of the patients) followed by aortic arch hypoplasia...
(14%–49%) and ventricular septal defects (13%–26%).

Despite successful repair of the coarctation, arterial hypertension is common, and the incidence of myocardial infarction is increased compared with controls without congenital heart disease. Of note, both pre- and postoperative hypertension are independent negative predictors of survival. Furthermore, left ventricular hypertrophy is a common long-term complication and is associated with aortic valve disease as well as arterial hypertension. Patients with bicuspid aortic valves are predisposed to aortic stenosis and regurgitation, as well as dilation of the ascending aorta. Moreover, the site of the coarctation is prone to recoarctation, which exacerbates the hypertension. All of these factors thus intertwined cause an incremental strain on the left ventricle. It is therefore important to find and treat these potential complicating factors as early as possible, and treatment may require surgical or catheter-based intervention.

The need for interventions in adults with repaired coarctation of the aorta is not fully described in a contemporary patient population. Moreover, factors related to the risk of interventions of relevance to the coarctation complex require further investigation. Using data from a national register, this study aims to explore which interventions are performed in these patients and, furthermore, investigate the time of and risk factors for certain interventions related to the coarctation complex. The results have implications for planning follow-up and giving appropriate medical advice to the growing population of adults with coarctation of the aorta.

**METHODS**

**Swedish National Register on Congenital Heart Disease**

The data that support the findings of this study are available from the corresponding author upon reasonable request. This register study is based on data in SWEDCON (Swedish National Register on Congenital Heart Disease; www.ucr.uu.se/swedcon/). Since 1998, the register covers all health care regions in Sweden, although registration was started in 1992 in 2 centers. At the time of data extraction, the register contained data on 14,197 adults (defined as age≥18 years) with congenital heart disease. Longitudinal and serial data are collected by each center and contain information on diagnoses, interventions, patient characteristics, functional class, symptoms, quality of life (EuroQol-5D), social variables, ECGs, exercise tests, self-reported level of physical exercise, medications, pacemakers/implantable cardioverter defibrillators, and echocardiograms. At first entry into the register, information is usually retrospective, for example regarding previous interventions, although it is usually based on access to relevant medical records such as surgical notes. For example, a patient’s first entry in the register may have been in 1992 when seen in a clinic, while the first surgical procedure may have been performed many decades earlier as determined by relevant medical records. The first surgical procedure, registered retrospectively, in this study was in 1950. After the first entry in the database, further data collection from clinic visits and investigations is prospective. All data collected until October 6, 2017, were considered. Patient
Characteristics were obtained from the last available clinic visit. Thus, the present study describes a patient population as seen at the latest clinic visit and vital status at the date of data extraction. The vital status is updated monthly with the Swedish population register.

**Patients**

SWEDCON was searched to identify all patients with repaired coarctation of the aorta who were ≥18 years of age at the time of data extraction (Figure 1). To avoid bias toward repairs performed in older children and adults, patients with a primary repair performed after October 6, 1999 (ie, 18 years before data extraction) were excluded. Patients with coarctation of the aorta in association with chromosomal disorders and severe congenital heart lesions (such as univentricular hearts or transposition of the great arteries) were excluded. The presence of concurrent shunts, such as ventricular septal defects, was accepted.

For analysis based on age at primary coarctation repair, the following age intervals were considered: neonates (0–30 days), infants (31–364 days), younger children (1–5 years), older children (6–17 years) and adults (≥18 years). Coarctation repairs were divided into discrete groups of end-to-end anastomosis, subclavian flap angioplasty, catheter-based repair, interposition graft, patch repair, and other. Hypertension was determined using the standard European Society of Cardiology definition (systolic blood pressure ≥140 or diastolic blood pressure ≥90). The presence of arterial hypertension was thus determined on the basis of absolute blood pressure readings at the clinic visit. All interventions performed in the population were considered and are presented in Figure 2. Patient characteristics and survival analysis was based on 3 different outcomes:

1. Composite event (CE intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract, or ascending aorta).
2. Intervention only at the coarctation site after primary coarctation repair (Reint-CoA).
3. Intervention only at the aortic valve after primary coarctation repair (AVR).

Note that all analyses were on interventions performed after the primary coarctation repair. All survival curves were truncated 50 years after the primary coarctation repair because of few remaining patients at risk.

Data from the most recent registered clinic visit after the primary coarctation repair or, if performed, the first CE thereafter were used for patient characteristics. Patients without such a registered clinic visit were excluded.

The study was approved by the Regional Ethics Review Board in Umeå, Sweden (Dnr 08–218 M

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**Figure 1.** Study flowchart for patient selection.

CE indicates composite event (intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract or ascending aorta); and CoA, coarctation of the aorta.
As this is a register study with approved ethics review, no informed consent was required.

**Statistical Analysis**

All calculations were performed using SPSS version 26 (IBM, Armonk, NY), RStudio version 2021.9.0.351 (Integrated Development Environment for R, RStudio, PBC, Boston, MA) and Excel version 1808 (Microsoft Corp., Redmond, WA). Data were assessed for normality. Continuous data are presented as the mean±SD or median with interquartile range within square brackets, according to normality, and categorical data are expressed as absolute numbers and proportion in percentage. Observed time was defined as the time from primary coarctation repair to CE, death, or censoring. Differences in mean, rank, and ratio between groups were tested with Student’s t test, Mann-Whitney U test or χ²-test as appropriate. The estimated probability of an intervention was described by Kaplan-Meier curves and tested with log-rank statistics. Patients were censored at the time of death or at data extraction.

Variables associated with interventions after the primary coarctation repair were analyzed using univariate Cox proportional hazard regression. These variables (sex, age at primary coarctation repair, type of primary coarctation repair, era of primary coarctation repair) were selected on the basis of their potential relevance for future need of intervention. Ninety-five percent CIs were used for hazard ratios.

The standardized mortality ratio was calculated by the method reported by Finkelstein et al. Reference data were obtained from the Human Mortality Database, using Swedish death rates over the period of 2000 to 2009. Time from the most recent registered clinic visit to death or data extraction was used in calculation of standardized mortality ratio; 95% CIs were used for standardized mortality ratio.

The null hypothesis was rejected for P values <0.05.

**RESULTS**

After application of inclusion and exclusion criteria, 683 patients were identified (Figure 1), 428 (63%) of which were men. All interventions in the order performed are shown in Figure 2. Ten patients had a different intervention (e.g., closure of ventricular septal defect) before their primary coarctation repair. Of all interventions performed after the primary coarctation repair, Reint-CoA was the most common (34%), followed by AVR (24%) and closure of ventricular septal defects/pulmonary artery banding (11%). Closure of ventricular septal defects/pulmonary artery banding occurred early after the primary coarctation repair, that is, 40% within the first 6 months, 55% within the first year, and 82% within the first 2 years.

Further analysis was based on selected interventions after primary coarctation repair analyzed as 3 separate outcomes (CE, Reint-CoA, and AVR). The study comprised 19676 person-years of follow-up. The incidence rate of CE was 10/1000 person-years,
of Reint-CoA 6/1000, and of AVR 4/1000. The median age at primary coarctation repair was 3.6 years [0.1–9.8 years], at first CE thereafter was 18.7 years [5.4–40.4 years] and at data extraction was 37.2 years [28.1–51.0 years] (Table 1). One hundred ninety-six (29%) patients had at least 1 CE after their primary coarctation repair, 74 patients (11%) had 2, and 28 patients (4%) had ≥3 (Table 2).

End-to-end anastomosis constituted the most common technique for primary coarctation repair across all decades investigated (Figure 3). Subclavian flap aortoplasty increased from 4% in the 1970s to 40% in the 1980s. In the 1990s, subclavian flap aortoplasty constituted 23% of all primary repairs, 94% of which were performed in the first half of the decade. Only 2 catheter-based primary coarctation repairs were found, both performed in the latter half of 1999. These 2 patients were 15 and 18 years old, respectively, at the time of the repair.

Concerning Reint-CoA, catheter-based technique was the most common (43%) followed by end-to-end anastomosis (21%). Of all catheter-based repairs in our material, the first was performed in 1986, and 65% were performed after 1999.

### Table 1. Patient Characteristics

| Variables                        | All (683) | No CE performed (487) | CE performed (196) | P value |
|----------------------------------|-----------|-----------------------|--------------------|---------|
| Sex, male, n (%)                 | 428 (63)  | 287 (59)              | 141 (72)           | 0.001*  |
| Age at primary coarctation repair, y | 3.6 [0.1–9.8] (683) | 3.6 [0.2–9.4] (487) | 3.8 [0.1–11.7] (196) | 0.796   |
| Age at first new intervention, y  | N/A       | N/A                   | 18.7 [5.4–40.4] (196) | N/A    |
| Age at clinic visit, y           | 33.8 [25.9–47.9] (683) | 32.8 [25.4–44.6] (487) | 41.1 [27.2–55.4] (196) | <0.001* |
| Age at data extraction, y        | 37.2 [28.1–51.0] (683) | 35.5 [27.7–48.4] (487) | 43.9 [29.1–58.1] (196) | <0.001* |
| Age at death, y                  | 58.1 [43.4–68.3] (18) | 61.0 [43.2–68.3] (14) | 55.2 [46.6–68.6] (4) | 0.915   |
| Height, cm                       | 173.7±9.9 (593) | 173.4±9.8 (425)        | 174.4±10.2 (168)    | 0.249   |
| Weight, kg                       | 76.4±17.2 (534) | 75.2±16.1 (384)         | 79.6±19.5 (150)     | 0.014*  |
| BMI, kg/m²                       | 25.2±4.7 (531) | 24.8±4.4 (382)         | 26.0±5.2 (149)      | 0.009*  |
| Blood pressure gradient, mmHg†   | 0.0 [0.0–8.0] (451) | 0.0 [0.0–8.0] (325) | 0.0 [0.0–10.0] (128) | 0.469   |
| EQ-SD VAS                        | 85.0 [75.0–92.0] (393) | 85.0 [75.0–92.0] (290) | 80.0 [70.0–93.0] (103) | 0.304   |
| Symptoms, yes, n (%)             | 665 (12)  | 476 (11)              | 189 (15)           | 0.164   |
| Cardiovascular medication, yes, n (%) | 669 (44)  | 477 (33)              | 192 (70)           | <0.001* |
| Arterial hypertension, yes, n (%) | 642 (33)  | 466 (32)              | 182 (33)           | 0.888   |
| Left ventricular function (EF>50%), yes, n (%) | 596 (96)  | 429 (97)              | 167 (92)           | 0.004*  |
| Left ventricular hypertrophy, none, n (%) | 534 (82) | 392 (86)              | 142 (72)           | <0.001* |
| NYHA class <II, n (%)            | 566 (93)  | 408 (93)              | 158 (91)           | 0.356   |
| Physical activity, no regular exercise, n (%) | 627 (33) | 450 (32)              | 177 (38)           | 0.347   |
| Smoking, nonsmoker/previous smoker/smoker, n (%) | 633 (81/10/9) | 455 (81/9/10) | 178 (81/13/6) | 0.100   |

Continuous variables are presented either as mean±SD or median with interquartile range within square brackets. BMI indicates body mass index; CE, composite event (intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract, or ascending aorta); EF, ejection fraction; EQ-SD VAS, EuroQol 5-dimension visual analog scale; and NYHA, New York Heart Association.

*P values denote statistical significance.
†Arterial hypertension is defined as blood pressure ≥140/90 at the clinic visit.
‡Blood pressure gradient denotes the systolic arm-leg blood pressure gradient as a continuous variable with negative values defined as 0.

### Table 2. CE in the Order Performed, Starting With the Primary Coarctation Repair

| Type of CE                          | 1     | 2     | 3     | 4     | 5     | 6     |
|-------------------------------------|-------|-------|-------|-------|-------|-------|
| Intervention at the coarctation site| 683   | 110   | 36    | 10    | 3     | 1     |
| Intervention at the aortic valve    |       | 65    | 31    | 14    | 3     | 0     |
| Intervention at the LVOT            |       | 14    | 7     | 3     | 0     | 0     |
| Intervention on the ascending aorta |       | 7     | 0     | 1     | 1     | 0     |
| Total                               | 683   | 196   | 74    | 28    | 7     | 1     |

CE indicates composite event (intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract, or ascending aorta); and LVOT, left ventricular outflow tract.

Freedom from CE was 95% at 1 year, 91% at 5 years, 88% at 10 years, 77% at 30 years, and 60% at 50 years after the primary coarctation repair (Figure 4A). In the first year, 76% of these interventions were directed toward the coarctation site. No difference in risk of CE was seen if the primary coarctation repair had been performed before 1985 (hazard ratio [HR], 1.2 [95% CI, 0.9–1.7]; P=0.184). Freedom from Reint-CoA was 96% at 1 year, 92% at 10 years, 84% at 30 years, and 75%
at 50 years (Figure 4B). Freedom from AVR was 99% at 1 year, 97% at 10 years, 92% at 30 years, and 78% at 50 years (Figure 4C).

The risk of a CE after the primary coarctation repair was increased in men (HR, 1.6 [95% CI, 1.2–2.2]; P=0.003). Freedom from CE differed between men and women (log-rank test, P=0.002) (Figure 5A). A similar pattern was seen upon separate analysis of early and late era (primary coarctation repair performed before or after 1985; data not shown). However, there was no difference in freedom from Reint-CoA between men and women (log-rank test, P=0.157) (Figure 5B). Although the curves diverged 15 years after the primary coarctation repair with less estimated Reint-CoA among women as compared with men, the curves realigned again ≈45 years after the primary coarctation repair. Freedom from AVR after the primary coarctation repair differed between men and women (log-rank test, P=0.001) (Figure 5C). Men had more than twice the risk of AVR (HR, 2.3 [95% CI, 1.4–3.9]; P=0.001).

Figure 3. Types and proportions of primary coarctation repair and age at repair by decade.
Left y axis: proportions of different primary coarctation repairs by decade in colored bars. Right y axis: age at primary coarctation repair with the median as a black dot and distribution as a white violin plot.

Figure 4. Freedom from CE (A), Reint-CoA (B) and AVR (C) after primary coarctation repair.
AVR indicates intervention only at the aortic valve after primary coarctation repair; CE, composite event (intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract or ascending aorta) and Reint-CoA, intervention only at the coarctation site after primary coarctation repair. Ninety-five percent confidence interval demarcated by shaded area.
The risk of CE was increased in neonates, while the risk of Reint-CoA was increased in infants and neonates (Table 3). No difference in the risk of AVR was found in the different age groups. There was no difference in risk for any of the 3 outcomes based on different techniques of primary coarctation repair.

At data extraction, patients who met a CE more commonly had impaired left ventricular systolic function and left ventricular hypertrophy. These patients also more frequently had cardiovascular medication, whereas the arm-leg blood pressure gradient and the prevalence of arterial hypertension were similar compared with patients with no CE (Table 1). Arterial hypertension was present in 35% of the men and 23% of the women.

Of the 683 patients, 18 (3%) died during follow-up. The median age at death was 58.1 years [44.3–68.3 years] (mean age, 57.7±15.7 years) and 61% of the deceased were men. No difference in mortality after the primary coarctation repair was detected between men and women (log-rank test, $P = 0.849$). The age- and sex-matched mortality ratio was 2.9 (95% CI, 1.7–4.3).

**DISCUSSION**

In the present study, we show that interventions are common in adults with previously repaired coarctation of the aorta. Men are at higher risk of and have an earlier need for CE after the primary coarctation repair. Repair during the first year of life, especially during the neonatal period, infers a higher risk for Reint-CoA. Patients who met a CE were more often men, more often had cardiovascular medication, and had poorer left ventricular function. Having met a CE did not infer a higher prevalence of arterial hypertension or a higher

**Table 3. Risk of CE, Reint-CoA and AVR, Respectively, by Age at the Primary Coarctation Repair**

| Age group      | n (%) | Risk of CE, HR (95%CI) | Risk of Reint-CoA, HR (95%CI) | Risk of AVR, HR (95%CI) |
|----------------|-------|------------------------|-------------------------------|-------------------------|
| Neonate        | 142 (21) | 2.3 (1.5–3.4) $P<0.001^*$ | 3.6 (2.2–5.9) $P<0.001^*$ | 2.1 (0.8–5.5) $P=0.133$ |
| Infant         | 122 (18) | 1.5 (1.0–2.3) $P=0.071$ | 2.9 (1.7–5.0) $P<0.001^*$ | Reference               |
| Younger children | 175 (26) | 1.1 (0.7–1.6) $P=0.696$ | 1.1 (0.6–2.0) $P=0.663$ | 1.8 (0.7–4.6) $P=0.193$ |
| Older children | 194 (28) | Reference               | Reference                    | 2.1 (0.9–4.9) $P=0.101$ |
| Adults         | 50 (7)  | 1.4 (0.9–2.4) $P=0.862$ | 1.2 (0.5–2.6) $P=0.677$ | 2.7 (0.99–7.4) $P=0.054$ |

Univariate Cox proportional hazard analysis with age groups (age at primary coarctation repair) as independent variable and need of CE, Reint-CoA, and AVR as dependent variables, respectively. Neonate: 0–30 days, infant: 31–364 days, younger children: 1–5 years, older children: 6–17 years, adults ≥18 years. The overall $P$ value was $<0.001$ for CE and Reint-CoA whereas the test for AVR was not significant ($0.353$). AVR indicates intervention only at the aortic valve after primary coarctation repair; CE, composite event (intervention after primary coarctation repair at the coarctation site, aortic valve, left ventricular outflow tract or ascending aorta); HR, hazard ratio; and Reint-CoA, intervention only at the coarctation site after primary coarctation repair.

*Denotes significance.
arm-leg blood pressure gradient. The age- and sex-matched mortality ratio was 2.9. Our data provide information that is useful in risk stratification and for planning periodic outpatient follow-up in adults with a previous repair of coarctation of the aorta.

Number and Types of Interventions
Upon analysis of all interventions performed in the population (Figure 2), the first intervention was almost exclusively performed at the coarctation site. Interventions at the coarctation site also constituted the majority of the second and third interventions; this highlights the importance of vigilance for recoarctation. Intervention at the aortic valve was also common and was previously reported to be related to the high prevalence of bicuspid aortic valves.\(^{12-14}\) Closure of ventricular septal defects/pulmonary artery banding was also fairly common and was performed early after the primary coarctation repair. This reflects the association of these defects with coarctation of the aorta and the practice to sometimes handle shunt lesions after the primary coarctation repair.\(^{32,33}\)

Three of 10 patients in our study met a CE, and 40% were estimated to within 50 years of the primary coarctation repair. A single-center study previously showed that Reint-CoA was especially common around 50 years of age.\(^{34}\) In our multicenter study in which we included different levels of care, we cannot confirm these findings. We can, however, show an increase in the need for AVR 40 years after the primary coarctation repair. Since nearly half of the patients were estimated to meet a CE within 50 years after their primary coarctation repair, our data support previous suggestions on the importance of structured periodic follow-up.\(^{19,34}\)

Techniques for Primary Coarctation Repair
Throughout all decades in the observation period, end-to-end anastomosis comprised the majority of primary coarctation repairs. We showed that subclavian flap aortoplasty was common in the 1980s and early 1990s, whereas almost no such repairs were performed in the last 5 years of the 1990s. As shown by Ungerleider et al,\(^{11}\) this trend seems to have continued after the turn of the millennium. In our study, catheter-based techniques were sparsely seen as primary coarctation repairs. However, they did constitute the majority of all Reint-CoAs, even though the first catheter-based repair in our material was performed in 1986. This is likely because of the preference to use a catheter-based technique in older patients and recoarctations.\(^{6-8}\) It is of note that our study included Reint-CoA until October 6, 2017, whereas only primary coarctation repairs performed before October 6, 1999.

Trends of Interventions After Primary Coarctation Repair
In the first year after the primary coarctation repair, there was a high rate of CE that was similar in both sexes. This was mostly attributable to early Reint-CoA and is in line with previous findings.\(^{34}\) There was a difference in freedom from CE between men and women that was especially pronounced between 10 and 50 years after primary coarctation repair. To the best of our knowledge, this finding has not been previously described. The reason for this difference is unclear, but data from our material do highlight some potential explanations. Although not statistically significant, the survival curves for Reint-CoA in men and women followed a similar pattern as those previously described for CE. The catch-up for CE thus seemed attributable to a relative increase in Reint-CoA in women starting ≈45 years after the primary coarctation repair. The initial divergence of the curves, however, seemed mostly to be driven by an increase of AVR in men. Based on our register data, the prevalence of bicuspid aortic valves was previously shown not to differ between men and women with coarctation of the aorta.\(^{35}\) However, the prevalence of hypertension was shown to be higher among men.\(^{21}\) This may account for some of the difference in the rate of interventions after primary coarctation repair, especially at the aortic valve where hypertension seems to associate with increased risk in younger patients.\(^{36}\) However, other yet unknown factors may also be of importance, which makes further risk stratification difficult. Our results thus emphasize the importance of vigilance of recoarctation and aortic valve pathology, especially in women ≈40 years after the primary coarctation repair. Also, further study is needed regarding sex differences in regard to the need for Reint-CoA.

Previous reports show 71%\(^{34}\) to 89%\(^{19}\) freedom from Reint-CoA 30 years after the primary coarctation repair, which is in line with our finding of 84%. Furthermore, our results show similar freedom from AVR across ages compared with a previous finding.\(^{34}\) However, this previous study presents freedom from AVR since birth, whereas our study presents freedom from AVR since the primary coarctation repair. Notably, none of the previous studies report any sex differences in regard to the prevalence of interventions.

Significance of Age
When diagnosed in infancy, early or immediate coarctation repair might be needed because of concomitant ventricular dysfunction and hypertension.\(^{37}\) The ideal age for elective repair is still controversial, although there is a trend toward early correction, primarily to reduce the incidence of late hypertension.\(^{38,39}\) More recent studies confirm that in the current era, the
majority of primary coarctation repairs (68%–82%) are indeed performed within the first year of life.\(^9\) In our study, only 39% of the patients were repaired during their first year of life, which reflects the long observation period and different eras included. We could, however, present a clear trend over the half-century investigated of the primary coarctation repairs being performed at a successively younger age (Figure 3). An earlier single-center study with a similar observation period and cohort size to ours found that patients repaired before the age of 5 years had a higher risk of redo.\(^9\) As mentioned, however, this does not reflect current management strategies that involve primary coarctation repair more commonly during the first year of life.\(^9\) Our multicenter study showed no increase in risk of Reint-CoA unless the primary repair was performed during the first year of life. In this context, it must be remembered that early repair in the early surgical era that was included in our material probably also reflected a more severe disease.

**Patient Characteristics**

Patients who met a CE after the primary coarctation repair were more often men, more frequently had cardiovascular medication, and had affected left ventricles. The prevalence of arterial hypertension and the arm-leg blood pressure gradient at the clinic visit did not differ between the groups. The decision for Reint-CoA is often based on the blood pressure gradient.\(^1\) Since the majority of CEs were constituted by Reint-CoA, the lack of difference in gradient is thus reassuring because it implies that these interventions had been effective in that sense. The similar prevalence of arterial hypertension at the last clinic visit between the groups may mirror the same phenomenon. Notably, it should be kept in mind that hypertension is common in coarctation of the aorta irrespective of the blood pressure gradient.\(^1\)

Potentially more problematic is the higher proportion of left ventricular dysfunction (8% versus 2%) and left ventricular hypertrophy (28% versus 14%) in patients with a CE. This may be attributable to the higher age and a higher incidence of aortic valve disease in patients with a CE. It should be noted that left ventricular dysfunction is not included in the indications for Reint-CoA.\(^5,4\) One could speculate that the interventions had been performed too late to fully protect the left ventricle from the deleterious effects of coarctation complex–related pressure overload. As such, one could also suggest that left ventricular systolic function and mass could be considered in discussions regarding interventions after coarctation repair. Further prospective studies are needed to establish the status of these variables in the context of indications for Reint-CoA.

**Mortality**

A recent large single-center cohort study found a mortality ratio in patients with coarctation of the aorta >3 times that of an age- and sex-matched population.\(^3\) Another study presented the ratio to be approximately doubled.\(^4\) We present an age- and sex-matched mortality ratio of 2.9, which is in line with these previous findings.

**Limitations**

The present study is a register study and is therefore limited to the patients included in the register. However, the SWEDCON register is nationwide, has been validated with high reliability,\(^4\) and has a multicenter nature representing different regions and levels of care. Furthermore, SWEDCON has access to the majority of adults with congenital heart disease in Sweden and is hence one of the largest comparable materials, where the large numbers may compensate for the limitations of the register design.

There is a selection bias related to the age of the patients. Coarctation of the aorta has been operated on since the 1940s—many years before the register was established. Patients repaired in the earlier decades are thus “survivors,” which reflects some immortal time bias. The majority of the patients in our material were repaired in the later decades, and no difference in the risk of CE was seen if the repair was performed in the earlier era. Thus, the effect of this bias to our results is likely relatively small.

**CONCLUSIONS**

In patients with previously repaired coarctation of the aorta, the estimated freedom from CE is 60%, from Reint-CoA 75%, and from AVR 78% 50 years after the primary coarctation repair. Men are at higher risk of and have an earlier need for CE and AVR compared with women, whereas women express a catch-up phase for CE and Reint-CoA between 40 and 50 years after the primary coarctation repair. Furthermore, primary coarctation repair during the first year of life was shown to be associated with a higher subsequent risk of Reint-CoA. Patients with a CE had more ventricular dysfunction, which may suggest suboptimal timing of the intervention. Compared with an age- and sex-matched population, the mortality in patients with repaired coarctation of the aorta was increased. Our results highlight the importance of lifelong and stringent follow-up of these patients and present data that may aid in improved risk stratification for future need of reintervention at follow-up.
ARTICLE INFORMATION
Received October 1, 2021; accepted April 18, 2022.

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Acknowledgments
The authors are grateful to Simon Västerbo, Filip Pettersson Blylod, and
associate professor Milos Kesek for assistance with graphical designs.

Sources of Funding
The research is part of the program STREAM – Strategy for Research Milieu
in Örnsköldsvik, funded by Västernorrland County Council, the Municipality
of Örnsköldsvik, and the Kempe Foundation. It was also supported by the
Swedish Heart and Lung Foundation, the Heart Foundation of Northern
Sweden, Umeå University, and the County Council of Västerbotten.

Disclosures
None.

REFERENCES
1. Morgagni GB. De Sedibus et Causis Morborum per anatomen ingreditur libri quinque. Venice: Remondiniana; 1761.
2. Campbell M. Natural history of coarctation of the aorta. Br Heart J. 1970;32:633–640. doi: 10.1136/hrt.32.5.633
3. Crafoord C. Congenital coarctation of the aorta and its surgical treatment. J Thorac Surg. 1945;14:347–361. doi: 10.1097/00005588-19450301-00008
4. Kvitting JP, Olin CL. Clarence Crafoord: a giant in cardiothoracic surgery, 2013;145:150–158. doi: 10.1016/j.jtcvs.2012.09.053
5. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Price JD, LaPar DJ. The challenges of redo aortic coarctation repair in
adults. J Am Heart Assoc. 2018;7:80:840–845. doi: 10.1161/10.1016/j.aha.2017.07.012
6. Price JD, LaPar DJ. The challenges of redo aortic coarctation repair in adults. J Am Heart Assoc. 2018;7:80:840–845. doi: 10.1161/10.1016/j.aha.2017.07.012
7. Beckmann E, Jassar AS. Coarctation repair—redo challenges in the
middle-aged and older patients with congenital heart disease—a nationwide
study. Eur Heart J. 2020;41:1075–1075. doi: 10.1161/JCIRCULATIONAHA.194.2169
8. Cohen M, Fuster V, Steele PM, Driscoll D, McGoon DC. Coarctation
of the aorta. Long-term follow-up and prediction of outcome after surgical
correction. Circulation. 1989;80:840–845. doi: 10.1161/10.1016/j.aha.2017.07.012
9. Rinnström D, Dellborg M, Thilén U, Sörensson P, Nielsen NE, Christersson C, Johansson B. Hypertension in adults with repaired
coa rctation of the aorta. Ann H eart J. 2010;16:10–15. doi: 10.1161/10.1016/j.aha.2017.07.012
10. Christersson C, Johansson B. Late outcomes in adults with coarctation
of the aorta. J Cardiovasc Surg (Torino). 2015;6:1311–1320. doi: 10.1007/s00398-015-0905-9
11. Hardikar AA, Marwick TH. Surgical thresholds for bicuspid aortic valve
associated aortopathy. JACC Cardiovasc Imaging. 2013;6:1311–1320. doi: 10.1016/j.jcmg.2013.10.005
12. Rinnström D, Dellborg M, Thilén U, Sörensson P, Nielsen NE, Christersson C, Johansson B. High prevalence of ascending aortic
dilation in adults with repaired coarctation of the aorta. Cardiol Young. 2021;31:992–997. doi: 10.1017/S0269880X21000111
13. Choudhary P, Canniffe C, Jackson DJ, Tanous D, Walsh K, C elermajer D, Lat e outcomes in adults with coarctation of the aorta. Heart.
2015;101:1190–1195. doi: 10.1136/heartjnl-2014-307035
14. Lacour-Gayet F, Bruniaux J, Serraf A, Chambran P, Blaysat G, Losay J,
Petit J, Kachaner J, Vanhees L. Hypertrophic obstructive cardiomyopathy in adults with repaired coarctation of the aorta. Eur J Cardiothorac Surg. 2019;100:808–816. doi: 10.1016/j.ejcts.2019.06.011
15. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, et al. 2018
ESC/ESH guidelines for the management of arterial hypertension. The task force for the management of arterial hypertension of the
European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). G Ital Cardiol (Rome). 2018;19:3S–73S. doi:
10.17140/3026.307035
32. Neches WH, Park SC, Lenox CC, Zuberbuhler JR, Siewers RD, Hardesty RL. Coarctation of the aorta with ventricular septal defect. Circulation. 1977;55:189–194. doi: 10.1161/01.CIR.55.1.189

33. Park JK, Dell RB, Ellis K, Gersony WM. Surgical management of the infant with coarctation of the aorta and ventricular septal defect. J Am Coll Cardiol. 1992;20:176–180. doi: 10.1016/0735-1097(92)90156-H

34. Lee MOY, Babu-Narayan SV, Kempny A, Uebing A, Montanaro C, Shore DF, d’Udekem Y, Gatzoulis MA. Long-term mortality and cardiovascular burden for adult survivors of coarctation of the aorta. Heart. 2019;105:1190–1196. doi: 10.1136/heartjnl-2018-314257

35. Rinnström D, Engström KG, Johansson B. Subtypes of bicuspid aortic valves in coarctation of the aorta. Heart Vessels. 2014;29:354–363. doi: 10.1007/s00380-013-0370-x

36. Ljungberg J, Johansson B, Engström KG, Norberg M, Bergdahl IA, Söderberg S. Arterial hypertension and diastolic blood pressure associate with aortic stenosis. Scand Cardiovasc J. 2019;53:91–97. doi: 10.1080/14017431.2019.1605094

37. Saxena A, Relan J, Agarwal R, Awasthy N, Azad S, Chakrabarty M, Dagar KS, Devagourou V, Dharan BS, Gupta SK, et al. Indian guidelines for indications and timing of intervention for common congenital heart diseases: revised and updated consensus statement of the working group on management of congenital heart diseases. Ann Pediatr Cardiol. 2019;12:254–286. doi: 10.4103/apc.APC_32_19

38. Seirafi PA, Warner KG, Geggel RL, Payne DD, Cleveland RJ. Repair of coarctation of the aorta during infancy minimizes the risk of late hypertension. Ann Thorac Surg. 1998;66:1378–1382. doi: 10.1016/S0003-4975(98)00595-5

39. Nakamura K, Stefanescu SA. Treatment of hypertension in coarctation of the aorta. Curr Treat Options Cardiovasc Med. 2016;18:40. doi: 10.1007/s11936-016-0462-x

40. Rao PS. Management of congenital heart disease: state of the art; part I-ACyanotic heart defects. Children (Basel). 2019;6:42. doi: 10.3390/children6030042

41. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, Lung B, Klun J, Lang IM, Meijboom F, et al. 2020 ESC guidelines for the management of adult congenital heart disease. Eur Heart J. 2020;41:4153–4154. doi: 10.1093/eurheartj/ehaa701

42. Diller GP, Kempny A, Alonso-Gonzalez R, Swan L, Uebing A, Li W, Babu-Narayan S, Wort SJ, Dimopoulos K, Gatzoulis MA. Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary Centre. Circulation. 2015;132:2118–2125. doi: 10.1161/CIRCULATIONAHA.115.017202

43. Bodell A, Björkhem G, Thilén U, Naumburg E. National quality register of congenital heart diseases – Can we trust the data? J Congenital Cardiol. 2017;1:1–8. doi: 10.1186/s40949-017-0013-7