Clinical Research

Exercise electrocardiogram for risk-based screening of severe residual coronary lesion in children after coronary surgery

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HIGHLIGHTS

- Severe coronary lesion may occur gradually in children after coronary surgery.
- Maximal stress electrocardiogram offers excellent sensitivity for SCL detection.
- Risk markers of SCL are stress chest pain, intramural pathway and C-type pattern.
- Post-test positive probability of SCL in high-risk group exceeded 50%.

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Abstract

Background: Residual severe coronary artery (CA) lesion (SCL) in children after cardiac surgery involving the CA is a major concern.

Aim: To evaluate the value of exercise electrocardiogram (eECG) for risk-based screening of SCL.

Methods: We analysed 135 maximal eECG from 115 children (mean age 13.6 ± 3.7 years) who underwent concomitant CA imaging. SCL was defined as a stenosis exceeding 50%.

Results: Underlying congenital heart diseases were transposition of the great arteries (TGA) (n = 116), CA pathway anomaly (n = 13) and left CA from the pulmonary artery (n = 6). Eleven SCLs were identified in 10 patients, of which 3 had a known untreated non-severe lesion and 4 had no lesions on previous imaging. In multivariable analysis, risk markers for SCL were effort chest pain (OR: 4.72, 95% CI: 1.23–18.17; P=0.024), intramural pathway (OR: 4.37, 95% CI: 1.14–16.81; P=0.032). Yacoubs C-type CA was added as a risk marker for patients with TGA (P=0.0009). All patients with SCL had a positive eECG (sensitivity: 100%, 95% CI: 72–100). Specificity was 81% (95% CI: 73–87). In the low-risk group (0 risk markers), 3/95 patients had SCL (3%), and the post-test probability of SCL with positive eECG (PPr+) was 15% (95% CI: 8–21). In the high-risk group (>1 risk marker) comprising 8/40 SCLs (20%), PPr+ was 53% (95% CI: 35–67).

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1. Abbreviations

ASO arterial switch operation
eECG exercise electrocardiogram
CA coronary artery
CI confidence interval
MRI magnetic resonance imaging
SCL severe coronary lesion
TGA transposition of the great arteries

2. Introduction

Neonatal or paediatric cardiac surgeries involving the coronary arteries (CA) are primarily arterial switch operations (ASO) for the repair of transposition of the great arteries (TGA), but also include ostial coronary angioplasty and coronary reconnection for the repair of congenital anomalies of origin or pathway. A major concern during follow-up is the presence of a residual CA lesion. Their prevalence after ASO has been reported to be around 3–8% [1–3], and depends mainly on the initial coronary pattern and the presence of an intramural coronary pathway [3–5]. Most CA lesions are discovered at the time of a coronary event (e.g. myocardial infarction, rhythm disorder), often occurring in the months after surgery; other lesions are detected by systematic CA imaging or an ischaemic test performed when age permits [3,6,7]. The often-reported low sensitivity and specificity of non-invasive investigations for the detection of CA lesions after ASO, including resting electrocardiogram, echocardiography, exercise electrocardiogram (eECG) and myocardial scintigraphy in heterogeneously aged populations, have encouraged routine CA imaging when the patient is aged around 5 years [3,8,9]. Conversely, a recent meta-analysis suggested that routine CA imaging after an ASO is no longer justified due to the low incidence of coronary events such as sudden cardiac death [10]. In this context, a routine, non-invasive, non-radiating test such as eECG could be useful, although this examination requires complex and individual adaptation of the stress test in children [11]. Its value in detecting a postsurgical coronary lesion has been little studied in the school-age population. We sought to evaluate the value of eECC for risk-based screening of severe long-term severe coronary lesions (SCL) in children after CA surgery. First, we identified risk markers for SCL in children who underwent cardiac surgery involving the coronary arteries at our centre. Then we evaluated the a posteriori probability versus the a priori risk of SCL.

3. Methods

3.1. Study population

We retrospectively reviewed the eECCs of all children with previous CA surgery performed between October 2014 and October 2019 at the Necker-Enfants Malades Hospital. The standard approach at our centre is to perform a systematic eECC when the patient’s age is compatible, not always coupled with coronary imaging. An additional eECC may be performed in the event of symptoms. Patients who underwent concomitant (or within 1 year previously) CA imaging were included in the study. Patients who underwent CA imaging more than 1 year previously and who showed an untreated severe coronary lesion (SCL) were also included and considered to have an SCL at the time of the eECC. Patients who had normal results on CA imaging long after the stress test were included and considered to be without SCL at the time of the eECC, provided they had not undergone any revascularization procedure in the meantime. Patients were excluded from the study if the quality of the imaging was insufficient to accurately analyse the coronary arteries. Patients who did not perform a test considered as maximal (as defined below) were excluded. The results from two eECCs in the same patient, each coupled with coronary imaging, could be included in the analysis. The following information was collected: anthropomorphic data (sex, age at eECC, weight and height), indication for the test (routine examination or the presence of symptoms such as chest pain during exercise) and the underlying congenital heart disease, the coronary pattern according to the Yacoub classification [12] in patients with TGA, the presence of intramural course, and additional CA procedures (surgical coronary angioplasty, aorto-coronary bypass and percutaneous angioplasty procedure). We classified patients into two groups based on the presence of risk markers for SCL. Those with at least one risk marker for SCL were classified as high risk and those without were classified as low risk.

The local research ethics committee approved this study, and the parents received a complete information document with a non-opposition consent. Children whose parents or primary care giver refused to participate in the study were excluded.

3.2. Exercise electrocardiogram

All eECCs were performed by one experienced physician and a dedicated nurse, in a room with the equipment necessary for resuscitation in the case of cardiac arrest. The steep ramp test protocol was simple and was adapted for children. It required only a stationary bike (ergometer) or a treadmill (for children under 120 cm in height) with an electrocardiogram recording and a non-invasive blood pressure monitor. In addition to the saddle, the size of the crankset was adapted to the height of the patient and the straps adjusted to the foot to promote the best effort. The steep ramp test was divided into three phases: phase 1 involved workload increments of 5, 10, or 20 W every minute for the stationary bike, or a manual increase every 30 seconds from 2 to 8 km/h and from 0% to 8% of positive incline on a treadmill. High pedalling frequencies were encouraged on the ergometer, but <100/min, and low load increments, allowing more prolonged effort. Phase 2 was a 1-min resting active phase, consisting of walking on the treadmill with no inclination, at 2 km/h, or continuing to pedal on the ergometer without any workload. Phase 3 involved stopping all effort for 2–4 minutes. The test was stopped if the child became exhausted, if chest pain was reported associated with ischaemic signs on the electrocardiogram or if a complication occurred (e.g. malaise, ventricular arrhythmia). The test was considered maximal when the peak heart rate was > 85% of the theoretical maximum value (equal to 220 beats per min minus age) and the effort intensity score (on the modified Borg scale graded from 0–10) was > 8 [13]. In cases where the patient (most often < 10 years of age) showed signs of muscular fatigue that prevented them from continuing while the maximum heart rate was < 85% of the theoretical maximum value,
2 or 3 phases of split effort, alternating recovery with a low load and a more intense load with an increase in pedalling speed, were performed in the stride to increase the maximum heart rate. We defined a positive eECG if the horizontal/decreased ST-segment depression was >1 mm, beyond 60 ms after point “J” during the effort (compared with the ST segment at rest). Further details are described in the Discussion. All eEEG recordings were analysed by a second external physician to limit bias of interpretation. In cases where a positive test result was unclear, it was classified as negative.

3.3. Coronary artery imaging

Three types of coronary artery imaging were selected for the comparison with the eEEG test: coronary computed tomography (CT) scan, 3-dimensional whole-heart anatomical magnetic resonance imaging (3D-MRI) and coronary angiography. A significant (or severe) coronary lesion was defined as >50% luminal narrowing by visual assessment for the coronary angiography and as >50% extraluminal narrowing for coronary CT scan and for 3D-MRI [14]. In the case of suspected stenosis on 3D-MRI, a CT scan or coronary angiography was performed to confirm and quantify the lesion. In the event of doubt on the CT scan, angiography was available. Cases in which coronary imaging was not usable could be excluded.

3.4. Statistical analysis

Demographic characteristics are summarized using descriptive statistics. Continuous variables are expressed as means ± standard deviations. We checked the normality of the distribution of continuous variables (i.e. age, weight and height) and used the t-test for normally distributed data and a non-parametric test in the case of failure if comparisons between SCL negative and positive groups were performed. Categorical variables are expressed as counts and percentages. The χ² test with Yates correction or Fisher’s exact test (when numbers were <5) was used to compare differences between groups. Risk markers for SCL were established using a multiple logistic regression and selecting the model (from 1 to 2 variables) with the best likelihood ratio. Selected variables before the analysis were significantly associated with SCL when P was <0.1. Any independent parameters significantly associated with SCL specific to the “TGA” and “previous coronary imaging” subgroups were considered as additional risk markers for these subgroups. The sensitivity (Se) and specificity (Sp) of the eEEG test with 95% confidence intervals (CI) were calculated. The prevalence (or pre-test probability) of SCL was determined in the high- and low-risk groups, and then the a posteriori probability (post-test probability) of having SCL when having either a positive or a negative test in each group. This probability (Pr) was calculated according to Bayes’ theorem:

- in the case of positive test:
  - Pr post-test = Pr pre-test × Se / (Pr pre-test × Se + (1 - Pr pre-test) × (1 - Sp))
- in the case of negative test:
  - Pr post-test = Pr pre-test × (1 - Se) / (Pr pre-test × (1 - Se) + (1 - Pr pre-test) × Sp)

All statistical analyses were performed with XLSTAT (V.2020.3.1.1002; Addinsoft).

4. Results

4.1. Population

We retrospectively analysed 231 consecutive eEEGs from children who underwent CA surgery between October 2014 and October 2019. A total of 136 eEEGs were coupled with CA imaging. One examination was excluded because the criteria for a maximal test were not achieved. A total of 135 eEEGs (in 115 patients) were included in the study (Fig. 1). Mean age of the study population was 13.6 ± 3.7 years; the youngest participant was aged 5.7 years. Mean weight was 49.8 ± 17.0 kg and mean height was 156.1 ± 18.2 cm.

Among the 135 eEEGs included in the study, previous CA imaging (>1 year before the test) had been done for 107 (79%) and showed no CA lesion (89 eEEGs), non-severe untreated CA lesion (14 eEEGs) and SCL (4 eEEGs) (Fig. 1). The results from the previous CA imaging were not taken into account as they were performed >1 year before the test. Sixteen children (11.8%) had been treated with low doses of beta-blockers at the time of the eEEG and all reached heart rates >85% of the theoretical value or had a positive test. The characteristics of patients before the eEEG are summarized in Table 1, according to the presence or absence of SCL. Eleven SCLs were identified in 10 patients (8.1%) and are detailed in Table 2. One patient had two successive SCLs, the second SCL after an additional coronary stenting procedure. Four patients had a late diagnosis of SCL despite the absence of SCL on previous CA imaging (Fig. 1). Of these 4 patients, 3 developed SCL after a second CA procedure (2 CA angioplasty and 1 CA bypass). Three further patients had a known non-severe and untreated lesion, including 1 with an intra-stent lesion. Nine of patients with SCL were on beta-blocker therapy during the eEEG.

4.2. Risk markers for SCL

In univariate analysis, C-type coronary pattern (in the TGA subgroup), intramural course, chest pain on effort and an additional percutaneous coronary procedure were significantly associated with SCL (Table 1). Type A coronary pattern (in the TGA subgroup) was significantly associated with the absence of SCL.

In multivariable analysis (for the whole population), the model including an initial intramural course and chest pain on effort before the test had the best likelihood ratio (Table 3) and good discrimination, with an area under the curve of 0.826. The C-type pattern was added to these two risk markers as an independent risk marker for the TGA subgroup. Thus, we defined two groups of patients according to the presence of risk markers for SCL: the low-risk group (n = 95) had no risk markers and the high-risk group (n = 40) had at least one risk marker. The prevalence of SCL, confirmed on CA imaging, was 3% (3/95) in the low-risk group and 20% (8/40) in the high-risk group.

4.3. Value of eEEG

All the patients with SCL had a positive eEEG (sensitivity: 100%, 95% CI: 72–100). Twenty-four patients (18%) had a positive eEEG but negative CA imaging result, and were defined as false positives. The specificity of the test was 81% (95% CI: 73–87). One patient with CA stenosis measuring 50%, and considered as moderate, had a negative eEEG result. The positive likelihood ratio was approximately 5 in both groups. In the low-risk group, a positive eEEG increased the probability of SCL from 3% to a post-test probability of 15% (95% CI: 8–21). In the high-risk group, the probability of SCL increased from 20% to a post-test probability of 53% (95% CI: 35–67) (Fig. 2).
Table 1
Characteristics of patients according to presence of SCL.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCL absent (n = 124)</th>
<th>SCL present (n = 11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>50 ± 17</td>
<td>46 ± 14</td>
<td>0.32</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157 ± 18</td>
<td>153 ± 17</td>
<td>0.57</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.6 ± 3.7</td>
<td>13.7 ± 4.9</td>
<td>0.32</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGA</td>
<td>107</td>
<td>9</td>
<td>0.65</td>
</tr>
<tr>
<td>ALCAPA</td>
<td>6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Coronary pathway anomalies</td>
<td>11</td>
<td>2</td>
<td>0.28</td>
</tr>
<tr>
<td>Initial coronary anatomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramural coronary pathway</td>
<td>8</td>
<td>4</td>
<td>0.021</td>
</tr>
<tr>
<td>Previous additional CA procedure</td>
<td>24</td>
<td>4</td>
<td>0.24</td>
</tr>
<tr>
<td>Additional CA procedures</td>
<td>13</td>
<td>0</td>
<td>0.60</td>
</tr>
<tr>
<td>Additional surgical plasty</td>
<td>7</td>
<td>1</td>
<td>0.50</td>
</tr>
<tr>
<td>Additional percutaneous CA procedure</td>
<td>5</td>
<td>3</td>
<td>0.018</td>
</tr>
<tr>
<td>Reasons of test: systemic/chest pain at effort</td>
<td>16</td>
<td>5</td>
<td>0.015</td>
</tr>
<tr>
<td>Patients (n = 116) with TGA repair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intramural coronary pathway</td>
<td>6</td>
<td>3</td>
<td>0.06</td>
</tr>
<tr>
<td>A-type coronary pattern</td>
<td>70</td>
<td>2</td>
<td>0.026</td>
</tr>
<tr>
<td>B-type coronary pattern</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>C-type coronary pattern</td>
<td>9</td>
<td>4</td>
<td>0.009</td>
</tr>
<tr>
<td>D-type coronary pattern</td>
<td>16</td>
<td>2</td>
<td>0.63</td>
</tr>
<tr>
<td>E-type coronary pattern</td>
<td>8</td>
<td>1</td>
<td>0.53</td>
</tr>
<tr>
<td>Previous coronary imaging (n = 103, excluding previous SCL)</td>
<td>11</td>
<td>3</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Data presented as number or mean ± standard deviation. ALCAPA: anomalous left coronary artery from pulmonary artery; CA: coronary artery(ies); SCL: severe coronary lesion; TGA: transposition of the great arteries.

5. Discussion

Whereas the long-term screening strategy for SCL is still debated in patients who underwent coronary translocation during ASO, the aim of our study was to evaluate the value of an eECG test to detect SCL in children who underwent cardiac surgery involving the coronary arteries, especially according to the pretest risk of having SCL. In our series, we identified 11 SCL in 10 patients (1 patient presented 2 different and progressive SCLs). We showed that an intramural coronary pathway or a complaint of typical chest pain during effort at anamnesis allowed us to define a group at risk of SCL in multivariable analysis. In patients with TGA, the C-type pattern (to a greater extent than the intramural course) was associated with the presence of SCL. The literature on residual coronary lesions after coronary surgery mainly concerns patients with ASO. The association between the intramural pathway (often
<table>
<thead>
<tr>
<th>No.</th>
<th>CHD</th>
<th>Age (years)</th>
<th>Initial CA anatomy</th>
<th>History</th>
<th>Previous CA imaging, results</th>
<th>Chest pain at effort</th>
<th>Type of concomitant CA imaging</th>
<th>Type of SCL</th>
<th>Treatment of SCL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TGA</td>
<td>9.5</td>
<td>C pattern Intramural course</td>
<td>LMCA stenosis known since birth Early postoperative stenting of the RCA</td>
<td>Yes, SCL</td>
<td>No</td>
<td>Angiography</td>
<td>LMCA stenosis</td>
<td>Balloon dilatation</td>
</tr>
<tr>
<td>2</td>
<td>CPA</td>
<td>8.9</td>
<td>Intramural course</td>
<td>Yes, no lesion Early postoperative stenting of the RCA</td>
<td>Yes</td>
<td>Yes</td>
<td>Angiography</td>
<td>RCA stenosis (intrastent proliferation) Intrastent restenosis</td>
<td>Stenting</td>
</tr>
<tr>
<td></td>
<td>CPA</td>
<td>10.7</td>
<td>Intramural course</td>
<td>Early postoperative stenting of the right CA and re-stenting 1 year earlier</td>
<td>Yes, moderate lesion</td>
<td>Yes</td>
<td>Angiography</td>
<td>Inntestrestenosis</td>
<td>Stenting</td>
</tr>
<tr>
<td>3</td>
<td>TGA</td>
<td>12.8</td>
<td>A pattern</td>
<td>RCA occlusion detected at age 6 years known LCA stenosis dilated at age 4 years known LCA stenosis detected at age 5 years Early postoperative coronary artery bypass</td>
<td>Yes, SCL</td>
<td>Yes</td>
<td>Angiography</td>
<td>RCA occlusion</td>
<td>CAB</td>
</tr>
<tr>
<td>4</td>
<td>TGA</td>
<td>12.8</td>
<td>C pattern Intramural course</td>
<td>Yes, no lesion Known LCA stenosis</td>
<td>Yes</td>
<td>Yes</td>
<td>Angiography</td>
<td>LCA stenosis</td>
<td>CAB</td>
</tr>
<tr>
<td>5</td>
<td>TGA</td>
<td>13.5</td>
<td>D pattern</td>
<td>LCA stenosis detected at age 5 years Early postoperative coronary artery bypass</td>
<td>Yes, SCL</td>
<td>No</td>
<td>Angiography</td>
<td>LCA stenosis</td>
<td>Surgical angioplasty</td>
</tr>
<tr>
<td>6</td>
<td>TGA</td>
<td>15.4</td>
<td>C pattern Intramural course</td>
<td>Yes, no lesion Early postoperative coronary artery bypass</td>
<td>Yes, SCL</td>
<td>No</td>
<td>CT scan</td>
<td>Cx occlusion</td>
<td>Medical</td>
</tr>
<tr>
<td>7</td>
<td>TGA</td>
<td>15.5</td>
<td>A pattern</td>
<td>No Known moderate LCA stenosis Known moderate LCA stenosis with interarterial course</td>
<td>Yes, no lesion</td>
<td>No</td>
<td>CT scan MRI</td>
<td>RCA stenosis</td>
<td>Stenting</td>
</tr>
<tr>
<td>8</td>
<td>TGA</td>
<td>21.3</td>
<td>D pattern</td>
<td>Known moderate LCA stenosis Early postoperative coronary artery bypass</td>
<td>Yes, moderate lesion</td>
<td>Yes</td>
<td>Angiography</td>
<td>Severe LCA stenosis</td>
<td>Stenting</td>
</tr>
<tr>
<td>9</td>
<td>TGA</td>
<td>23.1</td>
<td>E pattern</td>
<td>Known Cx occlusion Early postoperative coronary artery bypass</td>
<td>Yes, SCL</td>
<td>No</td>
<td>Angiography</td>
<td>Cx occlusion</td>
<td>Medical</td>
</tr>
<tr>
<td>10</td>
<td>TGA</td>
<td>7.5</td>
<td>C pattern</td>
<td>Known moderate LCA stenosis with interarterial course</td>
<td>Yes, moderate lesion</td>
<td>No</td>
<td>CT scan</td>
<td>LCA stenosis</td>
<td>Surgical angioplasty</td>
</tr>
</tbody>
</table>

* Low-risk patient. CAB: Coronary artery bypass; CHD: coronary heart disease; CPA: coronary pathway anomalies; Cx: circumflex artery; LMCA: left main coronary artery; LCA: left coronary artery; RCA: right coronary artery; SCL: severe coronary lesion.
Table 3
Risk markers of SCL for the entire population.

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>P</th>
<th>Multivariable analysis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td></td>
<td>OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Intramural CA</td>
<td>5.23 (1.44–19.10)</td>
<td>0.012</td>
<td>4.37 (1.14–16.81)</td>
<td>0.032</td>
</tr>
<tr>
<td>Chest pain on effort</td>
<td>5.63 (1.54–20.59)</td>
<td>0.009</td>
<td>4.72 (1.23–18.17)</td>
<td>0.024</td>
</tr>
<tr>
<td>Additional percutaneous CA procedure</td>
<td>8.93 (1.18–44.22)</td>
<td>0.007</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

CA: coronary artery; CI: confidence interval; OR: odds ratio.

-associated with the C-type pattern) and coronary events or lesions after ASO has been observed in most centres, even in the current era [3–5,15], albeit some teams have not confirmed this observation [16]. Although exertional symptoms are frequently reported by children and are very rarely associated with a coronary cause, having exertional chest pain was a risk marker for SCL in our population even though we cannot state that all exertional chest pain was true exercise angina [17]. Most studies have observed that the majority of patients with SCL after ASO have no symptoms [1,3,7,8,18]. Although more than half of our SCL patients were also asymptomatic, it still appears important to pay special attention to stress symptoms in children after coronary surgery. In our series, most patients underwent two successive imaging studies during follow-up. We were thus able to show that some SCLs could appear secondarily, a few years after normal CA imaging (in 4 patients, including 1 without any additional CA procedure). Furthermore, 2 patients known to have a non-severe and untreated CA lesion (including 2 intrastent lesions) developed 3 SCL. The notion of progression of CA lesions is rarely described and the mechanisms are poorly understood [7]. Childhood growth, stenting/dilatation of the CA, but also the interarterial pathway of the CA (found in patient 10) could be contributing markers in our study. This observation, added to the signs of early development of atherosclerosis observed in reimplanted coronaries [19], encourage continued monitoring of these patients throughout their lives. Conversely to percutaneous angioplasty, none of the 13 patients with additional surgical CA revascularization developed SCL, in agreement with the findings from a previous study [20].

All 11 SCLs were detected by eECG in both the high-risk and low-risk groups. We believe that some particularities of our method of performing this test may have favoured good sensitivity, as detailed in the methods. The eECGs were mainly performed on an ergometer because they were safer and generated fewer artifacts on the 12 lead-eECGs. Before adolescence or in children who are not used to performing sporting activities, it is often difficult to obtain a maximal test that could trigger ischaemia. We preferred to perform the tests without the presence of the child’s parents, because it can in some cases generate negative distractions, and we spent time before the test to build patient enthusiasm and cooperation. In the case of younger children, it seemed useful to make them perceive the ergometer as a fun activity. The good sensitivity of this test in our series made us consider this test as effective in excluding an SCL, but with the small number of subjects and the corresponding large confidence intervals for the sensitivity value (72–100%) we must temper this conclusion. To our knowledge only two series, including 50 eECGs, evidenced positive eECGs in all patients with SCL after ASO [21,22]. Most other studies evidenced poor sensitivity of the eECG to detect severe SCL, ranging from 21% to 60% on populations involving between 35 and 175 patients [2,3,9]. The presence of a network of collaterals sufficiently developed in the periphery to supply the myocardium affected by SCL is the hypothesis put forward to explain the absence of ischaemia. However, these studies have some limitations: one was a treadmill study, the maximal heart rate had to be at least 80% of the theoretical maximal value for the test to be retained in the study, and it involved very young children (2 patients with SCL and negative eECGs were less than 5.5 years old) [2]. The second study was multicentre but did not specify the type of protocol or the age of the patients at the time of the eECG [3]. In the most recent study, the criterion for positivity was ST depression > 2 mm, whereas we used a threshold of 1 mm [9]. In addition, we included patients with SCL after additional coronary procedures, which may not have had the same pathophysiology as lesions occurring after an ASO alone.

The eECG specificity in our study (81%) is close to that reported in adults with coronary atherosclerosis [23,24]. The 18% false-positive rate (24 eECGs) raises the challenge of “how to deal” with patients with a positive eECG according to the pretest probability of SCL. In our opinion, regarding the probability of SCL in high-risk patients, a positive eECG may justify invasive angiography of the coronary arteries, because this examination remains the gold standard. In low-risk patients, a positive eECG confers a rather low probability of SCL, and should be confirmed by other myocardial perfusion imaging or stress echocardiography. One issue is the interpretation of patients defined as false-positive, namely those with a positive eECG but without SCL on CA imaging, regardless of their risk markers. Some authors demonstrated that after ASO, a number of patients presented an impairment of the myocardial blood flow and the coronary flow reserve without CA lesion in angiography [25,26]. Coronary denervation during translocation is a possible mechanism [27]. The prognostic significance is not well established, but medical treatment with beta-blockers decreased symptoms and signs of ischaemia in our patients.
Routine coronary imaging (angiography or CT scan) at 5 years of age has been proposed because of the difficulty of diagnosing coronary lesions in non-invasive examinations. This approach has not been followed in some centres because of the very low incidence of events related to SCL in the very long term [10,28]. However, even if coronary events are rarely reported, they do exist: Uter et al. reported 2 patients older than 10 years with ventricular fibrillation, 1 of whom died. Both patients had perioperative myocardial infarction and left coronary obstruction [29]. Effort angina may also occur, as possibly in 4 of our patients and as reported previously [30]. The physiology of coronary lesions post ASO may be similar to that of congenital anomalies of the coronary pathway and origin, known to cause sudden death on exercise, even in the absence of proven ischaemia, probably due to the existence of a collateral network from foetal life [31,32]. The collateral network that develops later in acquired coronary lesions might be less effective and explain the ischaemia detected by eECC in our series. The good sensitivity of eECC that we have demonstrated argues for dispensing with invasive or radiating routine coronary imaging. However, eECC can only be performed routinely under good conditions from the age of 6–7 years (despite occasional successes in younger patients in our series). Therefore, there is a period until eECC is performed during which SCL will not be detected, whereas early diagnosis may lead to closer monitoring and avoidance of high-intensity physical activities. During this period, if a functional test is necessary, adenosine myocardial scintigraphy is preferred to stress echography for some reasons of age limitation [33]. In addition, some potentially dangerous anatomical configurations such as inter aortic-pulmonary tracts, initial acute angle tracts, split ostium or anteriorly reimplanated left coronary artery should also be screened [34,35]. Thus, routine early screening with a low-dose coronary CT scan, which is now feasible, seems to retain a role in children who have undergone coronary surgery. Later, eECC appears to be useful for detecting the onset or progression of stenosis, probably avoiding the need for a second routine CA imaging.

5.1. Study limitations

Our study has some limitations. The small number of patients precludes us from stating that the eECC offers perfect sensitivity. Second, as this was a retrospective study we cannot exclude the possibility that selection bias may have affected the determination of risk markers, even though most patients underwent 1 or 2 routine coronary imaging studies. The excluded patients without concomitant CA imaging showed some slight differences with the final study population in terms of age, weight, height, clinical presentation and congenital heart disease (Table A1), which could lead to differences in the incidence of coronary lesions but not in terms of risk factors or screening value of the stress test. Another limitation is that the diagnosis of SCL was made by several different examinations, including MRI. Although 3D-MRI has a excellent negative predictive value, it is less accurate than CT scanning and coronary angiography for coronary stenosis [36–38]. However, in our study, all cases of suspected stenosis on MRI were confirmed by CT scan or coronary angiography.

6. Conclusions

In this study, in which many patients underwent 2 successive CA imaging procedures in their lifetime, we show that coronary lesions after surgery involving the coronary arteries can occur and develop several years after surgery, even in the absence of additional percutaneous procedures. The initial intramural CA pathway favoured the occurrence of these lesions. Although often asymptomatic, the presence of chest pain during effort was a marker of SCL. In contrast to what has been published, these lesions appeared to be well detected by eECC independently of the presence of a risk marker, provided that the effort reaches a sufficient level. In the case of a positive eECC, invasive angiography may be proposed immediately in a high-risk population, but rather a complementary ischaemia test or non-invasive imaging in a low-risk population. However, it seems difficult to dispense with earlier routine coronary imaging in very young patients because it may lead to changes in follow-up before the eligible age for eECC. Further studies are needed to confirm these results and determine the prognosis of these lesions in the very long term.

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Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.acvd.2022.10.001.

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