Archives of Cardiovascular Disease xxx (xxxx) xxx–xxx

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Clinical Research

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

Johanne Auriau [a], Zahra Belhadjer [a], Elena Panaioli [b], Neil Derridj [a], Jean-Philippe Jais [c], Regis Gaudin [a], Francesca Raimondi [d], Damien Bonnet [d], Antoine Legendre [a,*]

[a] *M3C-Necker-Enfants malades, AP–HP Paris, 75015 Paris, France*
[b] *M3C-Necker-Enfants malades, Radiology Department, hôpital universitaire Necker enfants malades, AP–HP, 75015 Paris, France*
[c] *Biostatistics Unit, hôpital universitaire Necker-Enfants malades, AP–HP, Inserm U1163, Institut Imagine, Laboratory of Human Genetics of Infectious Diseases, Necker Branch, University of Paris, 75015 Paris, France*
[d] *M3C-Necker-Enfants malades, AP–HP, University of Paris, 75015 Paris, France*

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%.

GRAPHICAL ABSTRACT

Initial intramural CA pathway, presence of chest pain during effort and C-type pattern are risk markers of a severe coronary lesion. A negative exercise ECG appears sufficient to exclude severe coronary lesion. In the high-risk group, the post-test probability of severe coronary lesion with positive exercise ECG exceeded 50%. ALCAPA: anomalous left coronary artery from pulmonary artery.

ARTICLE INFO

Article history:
Received 3 April 2022
Received in revised form
22 September 2022
Accepted 3 October 2022
Available online xxx

Keywords:
Paediatric
Coronary artery angioplasty
Exercise electrocardiogram
Risk stratification
Arterial switch

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, risks 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).

* Corresponding author. M3C-Necker-Enfants malades, AP–HP Paris, 149, rue de Sèvres, 75743 Paris cedex 15, France.
E-mail address: antoine.legendre@aphp.fr (A. Legendre).

https://doi.org/10.1016/j.acvd.2022.10.001

Please cite this article as: J. Auriau, Z. Belhadjer, E. Panaioli et al., Exercise electrocardiogram for risk-based screening of severe residual coronary lesion in children after coronary surgery, Arch Cardiovasc Dis, https://doi.org/10.1016/j.acvd.2022.10.001

Conclusions: Most SCL tended to develop gradually, years after surgery. Provided it is near maximal, a negative eECG appears sufficient to exclude SCL. In the high-risk group, PPr+ exceeded 50%.

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 eECG 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 eECGs 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 eECG when the patient's age is compatible, not always coupled with coronary imaging. An additional eECG 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 eECG. 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 eECG, 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 eECGs 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 eECG, 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 eECGs 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 eECG 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 eECG 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 χ^2 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 significatively 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 eECG 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 eECGs from children who underwent CA surgery between October 2014 and October 2019. A total of 136 eECGs were coupled with CA imaging. One examination was excluded because the criteria for a maximal test were not achieved. A total of 135 eECGs (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 eECGs included in the study, previous CA imaging (> 1 year before the test) had been done for 107 (79%) and showed no CA lesion (89 eECGs), non-severe untreated CA lesion (14 eECGs) and SCL (4 eECGs) (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 eECG and all reached heart rates > 85% of the theoretical value or had a positive test. The characteristics of patients before the eECG 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 eECG.

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 eECG

All the patients with SCL had a positive eECG (sensitivity: 100%, 95% CI: 72–100). Twenty-four patients (18%) had a positive eECG 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 eECG results. The positive likelihood ratio was approximately 5 in both groups. In the low-risk group, a positive eECG 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).

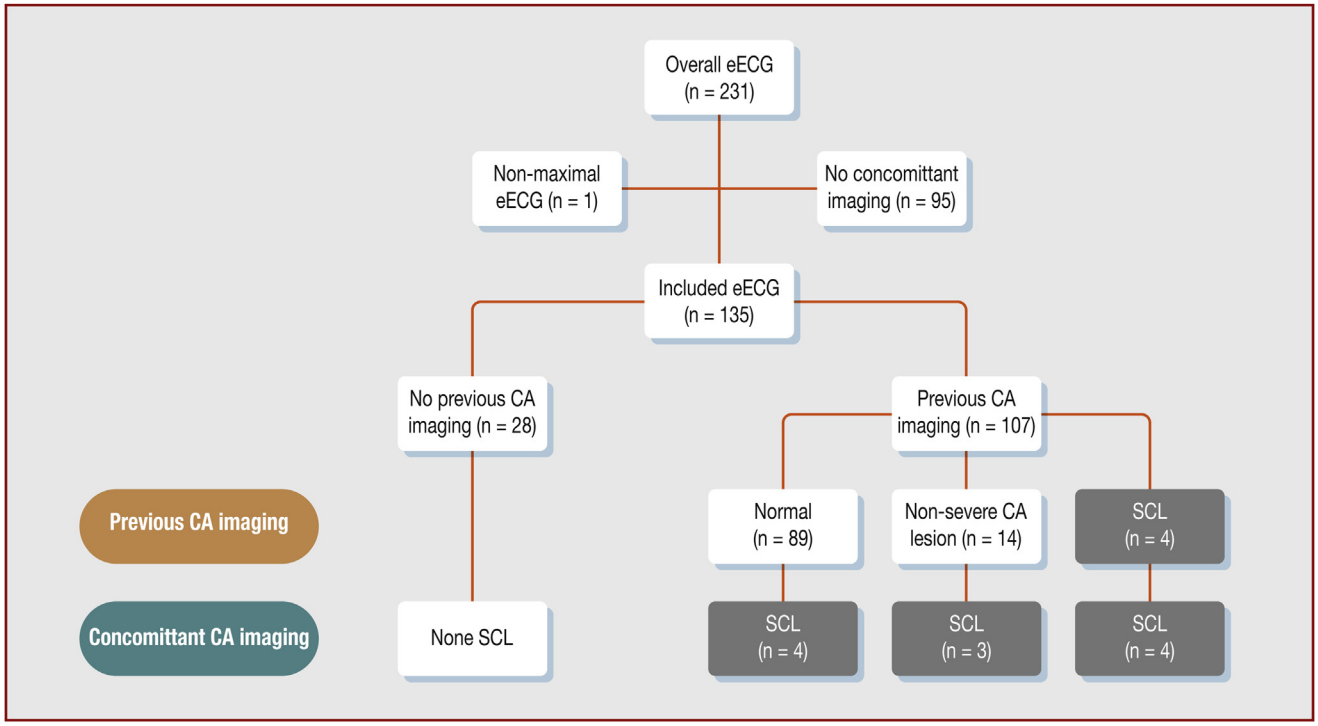

Fig. 1. Flow chart of eECG inclusion and overview of SCL. CA: coronary artery; eECG: exercise electrocardiogram, SCL: severe coronary lesion.

Table 1
Characteristics of patients according to presence of SCL.

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

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 2
Characteristics of the 10 patients with 11 SCL.

No.	CHD	Age (years)	Initial CA anatomy	History	Previous CA imaging, results	Chest pain at effort	Type of concomitant CA imaging	Type of SCL	Treatment of SCL
1	TGA	9.5	C pattern Intramural course	LMCA stenosis known since birth	Yes, SCL	No	Angiography	LMCA stenosis	Balloon dilatation
2	CPA	8.9	Intramural course	Early postoperative stenting of the RCA	Yes, no lesion	Yes	Angiography	RCA stenosis (intrastent proliferation)	Stenting
	CPA	10.7	Intramural course	Early postoperative stenting of the right CA and re-stenting 1 year earlier	Yes, moderate lesion	Yes	Angiography	Intrastent restenosis	Stenting
3	TGA	12.8	A pattern	RCA occlusion detected at age 6 years	Yes, SCL	Yes	Angiography	RCA occlusion	CAB
4	TGA	12.8	C pattern Intramural course	known LCA stenosis dilated at age 4 years	Yes, no lesion	Yes	Angiography	LCA stenosis	CAB
5[a]	TGA	13.5	D pattern	LCA stenosis detected at age 5 years	Yes, SCL	No	Angiography	LCA stenosis	Surgical angioplasty
6	TGA	15.4	C pattern Intramural course	Early postoperative coronary artery bypass	Yes, no lesion	No	CT scan	Cx occlusion	Medical
7[a]	TGA	15.5	A pattern	No	Yes, no lesion	No	CT scan MRI Angiography	RCA stenosis	Stenting
8	TGA	21.3	D pattern	Known moderate LCA stenosis	Yes, moderate lesion	Yes	CT scan MRI Angiography	Severe LCA stenosis	Stenting
9[a]	TGA	23.1	E pattern	Known Cx occlusion	Yes, SCL	No	CT scan	Cx occlusion	Medical
10	TGA	7.5	C pattern	Known moderate LCA stenosis with interarterial course	Yes, moderate lesion	No	CT scan	LCA stenosis	Surgical angioplasty

[a] 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.

	Univariate analysis OR (95% CI)	*P*	Multivariable analysis OR (95% CI)	*P*
Intramural CA	5.25 (1.44–19.10)	0.012	4.37 (1.14–16.81)	0.032
Chest pain on effort	5.63 (1.54–20.59)	0.009	4.72 (1.23–18.17)	0.024
Additional percutaneous CA procedure	8.93 (1.18–44.22)	0.007	–	–

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

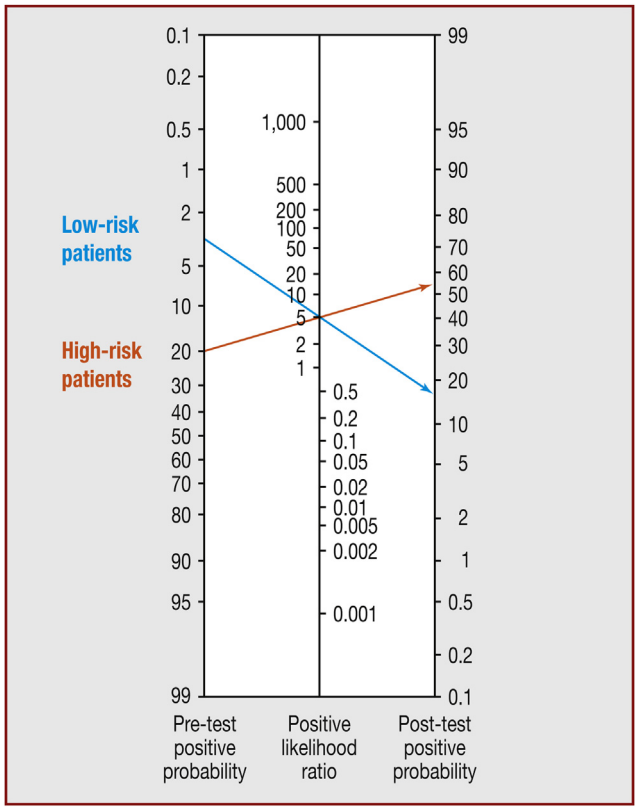

Fig. 2. Pre- and post-test positive probabilities of severe coronary lesion.

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-ECGs. 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: Utter 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 eECG in our series. The good sensitivity of eECG that we have demonstrated argues for dispensing with invasive or radiating routine coronary imaging. However, eECG 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 eECG 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 same 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 reimplanted 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, eECG 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 eECG 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 A.1), 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 eECG independently of the presence of a risk marker, provided that the effort reaches a sufficient level. In the case of a positive eECG, 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 eECG. Further studies are needed to confirm these results and determine the prognosis of these lesions in the very long term.

Sources of funding

None.

Acknowledgements

We thank Mélanie Girault, nurse in the paediatric cardiology department.

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.

References

[1] Tanel RE, Wernovsky G, Landzberg MJ, Perry SB, Burke RP. Coronary artery abnormalities detected at cardiac catheterization following the arterial switch operation for transposition of the great arteries. Am J Cardiol 1995;76:153–7, https://linkinghub.elsevier.com/retrieve/pii/S0002914999800484.
[2] Bonnet D, Bonhoeffer P, Piéchaud JF, Aggoun Y, Sidi D, Planché C, et al. Long-term fate of the coronary arteries after the arterial switch operation in newborns with transposition of the great arteries. Heart Br Card Soc 1996;76:274–9.
[3] Legendre A, Losay J, Touchot-Koné A, Serraf A, Belli E, Piot JD, et al. Coronary events after arterial switch operation for transposition of the great arteries. Circulation 2003;108:II186–90.
[4] Pasquali SK, Hasselblad V, Li JS, Kong DF, Sanders SP. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries: a meta-analysis. Circulation 2002;106:2575–80, https://www.ahajournals.org/doi/10.1161/01.CIR.0000036745.19310.BB.
[5] Koubský K, Gebauer R, Tláskal T, Matějka T, Poruban R, Jičínská D, et al. Long-term survival and freedom from coronary artery reintervention after arterial switch operation for transposition of the great arteries: A population-based nationwide study. J Am Heart Assoc 2021:10, https://www.ahajournals.org/doi/10.1161/JAHA.120.020479.
[6] Tsuda T, Baffa JM, Octavio J, Robinson BW, Radtke W, Mody T, et al. Identifying subclinical coronary abnormalities and silent myocardial ischemia after arterial switch operation. Pediatr Cardiol 2019;40:901–8.
[7] Angeli E, Raisky O, Bonnet D, Sidi D, Vouhé PR. Late reoperations after neonatal arterial switch operation for transposition of the great arteries. Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg 2008;34:32–6.
[8] Szymczyk K, Moll M, Sobczak-Budlewska K, Moll JA, Stefańczyk L, Grzelak P, et al. Usefulness of Routine Coronary CT Angiography in Patients with Transposition of the Great Arteries After an Arterial Switch Operation. Pediatr Cardiol 2018; 39:335-46. http://link.springer.com/10.1007/s00246-017-1761-z.
[9] Tsuda T, Bhat AM, Robinson BW, Baffa JM, Radtke W. Coronary artery problems late after arterial switch operation for transposition of the great arteries. Circ J 2015;79:2372–9, https://www.jstage.jst.go.jp/article/circj/79/11/79_CJ-15-0485/_article.
[10] van Wijk SWH, van der Stelt F, ter Heide H, Schoof PH, Doevendans PAFM, Meijboom FJ, et al. Sudden death due to coronary artery lesions long-term after the arterial switch operation: a systematic review. Can J Cardiol 2017;33:1180–7, https://linkinghub.elsevier.com/retrieve/pii/S0828282X17301770.
[11] Massin MM. The role of exercise testing in pediatric cardiology. Arch Cardiovasc Dis 2014;107:319–27, https://linkinghub.elsevier.com/retrieve/pii/S1875213614000801.
[12] Yacoub MH, Radley-Smith R. Anatomy of the coronary arteries in transposition of the great arteries and methods for their transfer in anatomical correction. Thorax 1978;33:418–24, https://thorax.bmj.com/lookup/doi/10.1136/thx.33.4.418.

[13] Wilson RC, Jones PW. A comparison of the visual analogue scale and modified Borg scale for the measurement of dyspnoea during exercise. Clin Sci 1989;76:277–82, https://portlandpress.com/clinsci/article/76/3/277/74502/A-comparison-of-the-visual-analogue-scale-and.
[14] Saraste A, Knuuti J. ESC 2019 guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging. Herz 2020;45:409–20, https://link.springer.com/10.1007/s00059-020-04935-x.
[15] Metton O, Calvaruso D, Gaudin R, Mussa S, Raisky O, Bonnet D, et al. Intramural coronary arteries and outcome of neonatal arterial switch operation. Eur J Cardiothorac Surg 2010;37:1246–53, https://academic.oup.com/ejcts/article-lookup/doi/10.1016/j.ejcts.2009.12.042.
[16] Fricke TA, Bell D, Daley M, d'Udekem Y, Brizard CP, Alphonso N, et al. The influence of coronary artery anatomy on mortality after the arterial switch operation. J Thorac Cardiovasc Surg 2020;160:191–9, https://linkinghub.elsevier.com/retrieve/pii/S0022522320305043.
[17] Sert A, Aypar E, Odabas D, Gokcen C. Clinical characteristics and causes of chest pain in 380 children referred to a paediatric cardiology unit. Cardiol Young 2013;23:361–7, https://www.cambridge.org/core/product/identifier/S1047951112000881/type/journal_article.
[18] Bonhoeffer P, Bonnet D, Piéchaud JF, Stümper O, Aggoun Y, Villain E, et al. Coronary artery obstruction after the arterial switch operation for transposition of the great arteries in newborns. J Am Coll Cardiol 1997;29:202–6.
[19] Pedra SRFF, Pedra CAC, Abizaid AA, Braga SLN, Staico R, Arrieta R, et al. Intracoronary ultrasound assessment late after the arterial switch operation for transposition of the great arteries. J Am Coll Cardiol 2005;45:2061–8, https://linkinghub.elsevier.com/retrieve/pii/S0735109705006820.
[20] Bergoënd E, Raisky O, Degandt A, Tamisier D, Sidi D, Vouhé P. Myocardial revascularization in infants and children by means of coronary artery proximal patch arterioplasty or bypass grafting: A single-institution experience. J Thorac Cardiovasc Surg 2008;136:298–306, https://linkinghub.elsevier.com/retrieve/pii/S002252230800651X.
[21] Massin M, Hövels-Gürich H, Däbritz S, Messmer B, von Bernuth G. Results of the Bruce treadmill test in children after arterial switch operation for simple transposition of the great arteries. Am J Cardiol 1998;81:56–60.
[22] Hövels-Gürich HH, Kunz D, Seghaye MC, Miskova M, Messmer BJ, von Bernuth G. Results of exercise testing at a mean age of 10 years after neonatal arterial switch operation. Acta Paediatr Oslo Nor 1992 2003;92:190–6.
[23] Sekhri N, Feder GS, Junghans C, Eldridge S, Umaipalan A, Madhu R, et al. Incremental prognostic value of the exercise electrocardiogram in the initial assessment of patients with suspected angina: cohort study. BMJ 2008;337:a2240, https://www.bmj.com/lookup/doi/10.1136/bmj.a2240.
[24] Barraclough K. Sensitivity and specificity of exercise ECG in heart disease. BMJ 2008;337, a3098-a3098. https://www.bmj.com/lookup/doi/10.1136/bmj.a3098.
[25] Hauser M, Bengel FM, Kühn A, Sauer U, Zylla S, Braun SL, et al. Myocardial blood flow and flow reserve after coronary reimplantation in patients after arterial switch and ross operation. Circulation 2001;103:1875–80, https://www.ahajournals.org/doi/10.1161/01.CIR.103.14.1875.
[26] Gagliardi MG, Adorisio R, Crea F, Versacci P, Di Donato R, Sanders SP. Abnormal vasomotor function of the epicardial coronary arteries in children five to eight years after arterial switch operation. J Am Coll Cardiol 2005;46:1565–72, https://linkinghub.elsevier.com/retrieve/pii/S0735109705017109.
[27] Kondo C, Nakazawa M, Momma K, Kusakabe K. Sympathetic denervation and reinnervation after arterial switch operation for complete transposition. Circulation 1998;97:2414–9, https://www.ahajournals.org/doi/10.1161/01.CIR.97.24.2414.
[28] Khairy P, Clair M, Fernandes SM, Blume ED, Powell AJ, Newburger JW, et al. Cardiovascular outcomes after the arterial switch operation for d-transposition of the great arteries. Circulation 2013;127:331–9, https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.112.135046.
[29] Hutter PA, Kreb DL, Mantel SF, Hitchcock JF, Meijboom EJ, Bennink GBWE. Twenty-five years' experience with the arterial switch operation. J Thorac Cardiovasc Surg 2002;124:790–7, https://linkinghub.elsevier.com/retrieve/pii/S0022522302001526.
[30] Michalak KW, Szymczyk K, Moll JA, Moll JJ. Severe two-vessel ostial stenosis of the main coronary arteries in a patient with transposition of the great arteries after an arterial switch operation. Ann Thorac Surg 2016;102:e567–8, https://linkinghub.elsevier.com/retrieve/pii/S0003497516305355.
[31] Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol 2000;35:1493–501, https://linkinghub.elsevier.com/retrieve/pii/S0735109700005660.
[32] Frescura C, Basso C, Thiene G, Corrado D, Pennelli T, Angelini A, et al. Anomalous origin of coronary arteries and risk of sudden death: A study based on an autopsy population of congenital heart disease. Hum Pathol 1998;29:689–95, https://linkinghub.elsevier.com/retrieve/pii/S0046817798902775.
[33] Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, et al. Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease: from the american society of echocardiography. J Am Soc Echocardiogr 2020;33:1–41, https://linkinghub.elsevier.com/retrieve/pii/S0894731719308259.
[34] Michalak KW, Sobczak-Budlewska K, Moll JJ, Szymczyk K, Moll JA, Niwald M, et al. Can we predict potentially dangerous coronary patterns in patients with transposition of the great arteries after an arterial switch operation? Cardiol Young 2019;29:1350–5, https://www.cambridge.org/core/product/identifier/S104795111900204X/type/journal_article.
[35] Raimondi F, Aquaro GD, De Marchi D, Sandrini C, Khraiche D, Festa P, et al. Cardiac magnetic resonance myocardial perfusion after arterial switch for transposition of great arteries. JACC Cardiovasc Imaging 2018;11:778–9, https://linkinghub.elsevier.com/retrieve/pii/S1936878X17307878.
[36] Cruz G, Atkinson D, Henningsson M, Botnar RM, Prieto C. Highly efficient nonrigid motion-corrected 3D whole-heart coronary vessel wall imaging. Magn Reson Med 2017;77:1894–908, https://onlinelibrary.wiley.com/doi/10.1002/mrm.26274.
[37] Henningsson M, Shome J, Bratis K, Vieira MS, Nagel E, Botnar RM. Diagnostic performance of image navigated coronary CMR angiography in patients with coronary artery disease. J Cardiovasc Magn Reson 2017;19:68, http://jcmr-online.biomedcentral.com/articles/10.1186/s12968-017-0381-3.
[38] Kato S, Kitagawa K, Ishida N, Ishida M, Nagata M, Ichikawa Y, et al. Assessment of coronary artery disease using magnetic resonance coronary angiography. J Am Coll Cardiol 2010;56:983–91, https://linkinghub.elsevier.com/retrieve/pii/S0735109710024691.