

Interobserver variability in the classification of congenital coronary abnormalities: A substudy of the anomalous connections of the coronary arteries registry

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Abstract

Objective: The diagnosis of anomalous connections of the coronary arteries (ANOCOR) requires an appropriate identification for the management of the patients involved. We studied the observer variability in the description and classification of ANOCOR between a nonexpert group of physicians and a group of expert physicians, using the ANOCOR cohort.

Patients and design: Consecutive patients identified by 71 referring cardiologists were included in the ANOCOR cohort. Anomalous connection was diagnosed by invasive and/or computed tomography coronary angiography. Angiographic images were reviewed by an angiographic committee with experience in this field. Both investigators and angiographic committee filled out a questionnaire to classify each anomaly with the type of coronary artery involved, the site of anomalous connection, and the initial course. Observer variability between investigators and angiographic committee was assessed by κ statistics. Anomalous connection with a preaortic course was defined as at-risk.

Results: Among 472 patients of the ANOCOR cohort, 496 abnormalities were identified with a preaortic course present in 31%. The agreement for the type of artery was excellent ($\kappa = 0.92$, 95% CI = 0.86-0.98, $P < .05$), while the agreement for the site of anomalous connection was moderate ($\kappa = 0.50$, 95% CI = 0.42-0.58, $P < .05$), and the agreement for the initial course was only fair ($\kappa = 0.32$, 95% CI = 0.28-0.37, $P < .05$). Observer agreement for the identification of at-risk forms was moderate ($\kappa = 0.497$, 95% CI = 0.40-0.59, $P < .05$).

Conclusions: Observer variability in the assessment of anomalous connection of the coronary arteries between nonexperienced and experienced physicians can be significant. We found that expert physicians provide a more robust classification in comparison with nonexpert physicians. Therefore, referral to physicians with a relevant experience should be considered, especially if an anomaly at-risk is suspected.

Abbreviations: ANOCOR, anomalous connections of coronary arteries; CI, confidence interval; CT, computed tomography; CTCA, computed tomography coronary angiography; Cx, circumflex; ICA, invasive coronary angiography; LAD, left anterior descending; LM, left main; RC, right coronary; SD, standard deviation.

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KEYWORDS

anomalous connection, computed tomography, congenital anomaly, coronary angiography, coronary artery

1 | INTRODUCTION

Proximal ANOMalous connections of the CORonary arteries (ANOCOR) are a diverse entity with an angiographic prevalence averaging 1%.¹ Whereas most of the ANOCOR are considered as benign abnormalities, a small number of ANOCOR can be associated with a risk of sudden cardiac death.²⁻⁵ Invasive coronary angiography (ICA) mostly enables to recognize the coronary anomaly, but sometimes cannot accurately identify the site of the connection or the ectopic initial course. Computed tomography coronary angiography (CTCA) has shown its great accuracy to improve ANOCOR characterization.⁶⁻⁸ An appropriate classification is of great value to identify ANOCOR at risk.⁹⁻¹¹ Whereas the recognition of the benign forms is equally important to reassure the patients. As the prevalence of ANOCOR is low in the general population, most cardiologists and radiologists have only limited experience in this field. To date, the accuracy of the ANOCOR classification has not been reported in a large population. The ANOCOR registry is an observational multicenter cohort study conducted to develop a database comprised of demographic, clinical, imaging, and stress testing characteristics in young patients and adults with ANOCOR. We assessed the observer variability of angiographic description and classification using the ANOCOR cohort between the ANOCOR investigators (nonexpert group) and a group of experts.

2 | METHODS

2.1 | Population

A total of 472 patients have been included in the ANOCOR cohort. The inclusion criteria were the presence of at least 1 anomalous proximal connection of a coronary artery diagnosed by ICA and/or CTCA in patients older than 14 years and without any structural congenital disease implicating the great vessels. This cohort has been previously described.¹² Seventy-one French cardiologists participated to the study by registering newly diagnosed ANOCOR between January 2010 and January 2013. All patients gave an informed consent for the use of their imaging data for research purpose.

2.2 | Image analysis

At the time of inclusion, each investigator was asked to fill out a questionnaire of medical information in order to collect all necessary data. After the initial diagnosis of ANOCOR, another imaging modality was left at the discretion of the investigator. Analysis was made utilizing CTCA if performed. The ANOCOR was then classified by the investigator following a 3-step approach:

1. Define the artery presenting the proximal anomalous connection: left main (LM) artery, left anterior descending (LAD) artery, circumflex (Cx) artery, right coronary (RC) artery, or other.
2. Specify the site of the anomalous connection: contralateral artery, contralateral sinus, noncoronary sinus, appropriate sinus, ascending aorta, pulmonary artery, single coronary artery, or other.
3. Locate the initial course of the ANOCOR in relation to the great vessels: prepulmonary course, retropulmonary course, preaortic course, retroaortic course, normal course, or other.

We chose in this study to define each initial course according to the first closest adjacent cardiac structure.¹ Nomenclature using the so-called interarterial course may be ambiguous to identify a preaortic or a retropulmonary course, and was not used for the classification. We identified 4 main ectopic courses: prepulmonary course, retropulmonary course, preaortic course, and retroaortic course. The retropulmonary course is often named intraseptal course and the preaortic course is often named course between aorta and pulmonary artery (interarterial course) in the literature. In the lack of endovascular imaging, it is difficult to assert the existence of an intramural pathway. So this latter was not included in the classification used. The principal ANOCOR (Figure 1) were classified as follow:

1. Anomalous connection of the LM artery or LAD artery, usually with the right sinus or RC artery, with all types of initial course being possible.
2. Anomalous connection of the Cx artery, usually with the right sinus or RC artery, with an initial course that was almost always retroaortic.
3. Anomalous connection of the RC artery usually with the left sinus, with a preaortic course being the most frequent.
4. Anomalous connection from the appropriate sinus with an abnormal ostium shape or an ostium more eccentric than usually.
5. Anomalous connection from the noncoronary sinus, with a retroaortic course being the most frequent.
6. Anomalous connection from the ascending aorta, defined as a connection ≥ 10 mm from the sinotubular junction, with a preaortic initial course being the most frequent.
7. Single coronary artery, an entity to be distinguished from a common ostium with an ectopic artery associated with an abnormal course to meet its named myocardial territory. Inversely, a single coronary artery follows its usual proximal course and supplies the entire coronary circulation with a retrograde filling of the artery not connected with the aorta.¹³ With our definition, a single coronary artery is never associated with an abnormal initial course.
8. Anomalous connection from the pulmonary artery, concerning the LM artery from the left posterior pulmonary sinus or the RC artery from the right posterior pulmonary sinus.

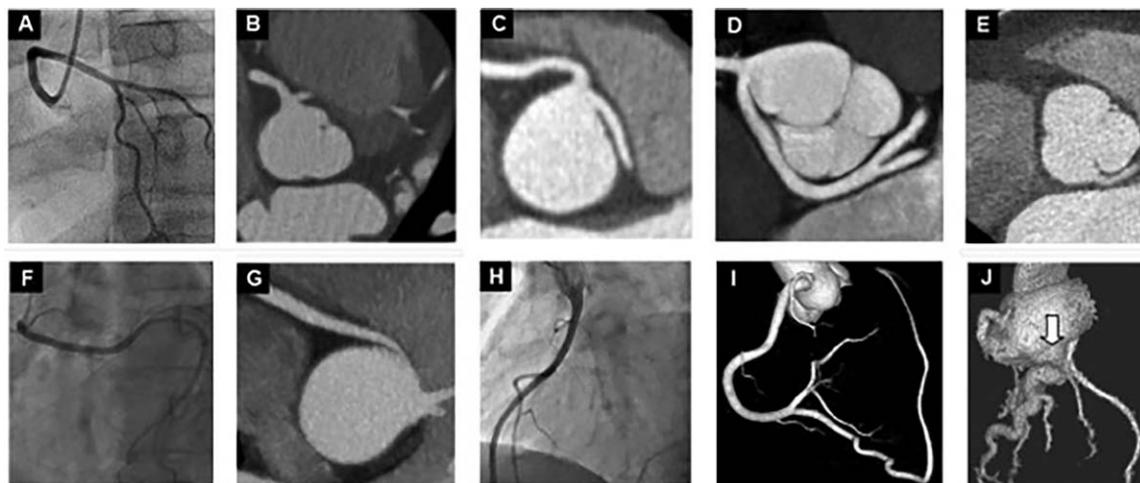


FIGURE 1 Examples of anomalous connections of the coronary arteries. Anomalous connection of the LM artery with the right aortic sinus and prepulmonary course (A), anomalous connection of the LM artery with the RC artery and retro-pulmonary course (B), anomalous connection of the LM artery with the right aortic sinus and pre-aortic course (C), anomalous connection of the LM artery with the right aortic sinus and retro-aortic course (D), anomalous of the LM artery with the non-coronary aortic sinus and retro-aortic course (E), anomalous connection of the Cx artery with the right aortic sinus and retro-aortic course (F), anomalous of the RC artery with the left aortic sinus and pre-aortic course (G), high take off of the RC artery (H), single coronary artery (*I), and anomalous connection of the LAD artery (arrow) with the left pulmonary sinus (J). Abbreviations: Cx, circumflex; LAD, left anterior descending; LM, left main; RC, right coronary

Angiographic images (ICA and/or CTCA) of each patient included in the registry were reviewed by an expert angiographic committee composed of 2 interventional cardiologists with experience in the ANOCOR field and 2 radiologists specialized in cardiovascular imaging. The angiographic committee validated and classified each ANOCOR based on the criteria mentioned above. A validation questionnaire similar to the investigator questionnaire was filled out by the angiographic committee. Additionally, anomalous aortic connections with a pre-aortic course (so-called course between aorta and pulmonary artery) with or without intramural pathway were defined as at-risk forms.¹⁴ Rare anomalous connections with the pulmonary artery, associated with a specific proximal course, were excluded for the analysis of the initial course. Other anomalous connections were defined as benign forms. Images were assessed by observers blinded to the results of other assessments. The answers given by the investigators and the angiographic committee were compared. The objective of this study was to assess the observer variability in the angiographic characterization and classification of each ANOCOR. Type of coronary artery, site of connection, and initial course were analyzed. In case that no specific answer was given or multiple answers were chosen as appropriate by the investigator for each of the above questions, data was characterized as nonanswered and excluded from the analysis.

2.3 | Statistical analysis

Interobserver variabilities were assessed by κ statistics. Regarding the initial ectopic course, the identification of a pre-aortic course is crucial. Therefore, 2 different κ values were calculated, one concerning all the possible initial courses and one concerning only the classification of the

initial course as pre-aortic or not. For the interpretation, we used a common cited scale with a value of κ less than 0.21 indicating slight agreement, 0.21–0.40 a fair agreement, 0.41–0.60 a moderate agreement, 0.61–0.80 good agreement, and more than 0.80 an excellent agreement.¹⁵ Quantitative variables are presented with mean and 95% CI. Categorical variables are expressed as frequencies and percentages. A statistically significant difference was defined as a *P* value less than 0.05. Statistical analysis was performed with Microsoft Excel software.

3 | RESULTS

A total of 472 patients (76.2% male with a mean age 63 years, one <18 year old) were included in the ANOCOR registry and 496 ANOCOR were identified (Table 1). Four hundred sixty-one patients (95.5%) presented 1 ANOCOR and 21 patients (4.5%) presented 2 or 3 ANOCOR. First imaging modality was ICA in 421 patients (89.2%) and CTCA in 51 patients (10.8%).

3.1 | Type of artery

Among 496 ANOCOR, 235 (47.4%) involved the Cx artery, 165 (33.3%) the RC artery, 60 (12.1%) the LM artery, and 27 (5.4%) the LAD artery, according to the analysis of the angiographic committee (Table 1). Among the 496 ANOCOR, 18 (3.6%) as nonanswered by the investigator were excluded from the analysis, and the type of artery was undetermined only in 6 cases (1.2%). Therefore, 472 ANOCOR (95%) were finally analyzed. The overall agreement was excellent ($\kappa = 0.92$, 95% CI, 0.86–0.98; *P* < .05) between the investigators and the angiographic committee (Table 2).

TABLE 1 Demographic and angiographic characteristics of the ANOCOR cohort

Parameters	
Number of subjects, n	472
Mean age, y (SD)	63 (13)
Gender male, %	76.2
Invasive CA alone, n (%)	297 (62.9)
Computed tomography CA alone, n (%)	20 (4.3)
Invasive + computed tomography CA, n (%)	155 (32.8)
Total number of anomalous connections	
496	
Type of artery	
Left main, n (%)	60 (12.1)
Left anterior descending, n (%)	27 (5.4)
Circumflex, n (%)	235 (47.4)
Right, n (%)	165 (33.3)
Other, n (%)	9 (1.8)
Site of connection	
Opposite sinus or contralateral artery, n (%)	451 (90.8)
Appropriate sinus	4 (0.8)
Noncoronary sinus	2 (0.4)
High take off ascending aorta	29 (6.0)
Single coronary artery	6 (1.2)
Pulmonary artery	4 (0.8)
Initial course	
Prepulmonary, n (%)	30 (6.0)
Retropulmonary, n (%)	46 (9.3)
Preaortic, n (%)	154 (31.1)
Retroaortic, n (%)	242 (48.8)
Other, n (%)	7 (1.4)
Normal, n (%)	14 (2.8)
Undetermined, n (%)	3 (0.6)

Abbreviations: CA, coronary angiography; SD, standard deviation.

3.2 | Site of connection

According to the analysis of the angiographic committee, connection with opposite sinus or contralateral artery was noticed in 451 cases (90.8%) (Table 1). A high take off from the ascending aorta was observed in 29 cases (6%). Fifty-three ANOCOR (10.7%) were excluded from the analysis as nonanswered by the investigators. The latter were unable to determine the site of connection in 50 cases

TABLE 2 Interobserver variability for the assessment of the ectopic artery ($\kappa = 0.92$, 95% CI, 0.86–0.98, $P < .05$)

Investigators	Ectopic artery	Angiographic committee					Total
		LM	LAD	Cx	RC	Other	
	LM	51	2	3	0	3	59
	LAD	2	20	1	0	2	25
	Cx	3	0	219	1	3	226
	RC	3	0	1	157	0	161
	Other	0	0	0	0	1	1
	Total	59	22	224	158	9	472

Abbreviations: Cx, circumflex artery; LAD, left anterior descending artery; LM, left main artery; RC, right coronary artery.

TABLE 3 Interobserver variability for the assessment of the connection ($\kappa = 0.50$, 95% CI, 0.42–0.58; $P < .05$)

Investigators	Connection	Angiographic committee							Total
		CA	CS	PS	AS	AA	SC	PA	
	CA	118	38	0	0	0	2	0	158
	CS	40	147	2	2	12	0	0	203
	PS	1	1	0	0	0	0	0	2
	AS	0	3	0	1	4	0	0	8
	AA	0	2	0	0	8	0	0	10
	SC	5	0	0	0	0	4	1	10
	PA	0	0	0	0	0	0	2	2
	Total	164	191	2	3	24	6	3	393

Abbreviations: AA, ascending aorta; AS, appropriate sinus; CA, contralateral artery; CS, contralateral sinus; PA, pulmonary artery; PS, posterior sinus; SC, single coronary artery.

(10%). As well, 393 ANOCOR (79%) were analyzed. There was moderate interobserver variability ($\kappa = 0.50$, 95% CI = 0.42–0.58, $P < .05$) (Table 3).

3.3 | All initial course

Concerning the type of initial course, the most frequent courses were the retroaortic course and preaortic course identified in 242 cases (48.3%) and 154 cases (31.1%), respectively, according to the analysis of the angiographic committee (Table 1). Four hundred forty-three ANOCOR (89.3%) were included in this analysis. Fifty-three cases (10.7%) were excluded from the analysis as nonanswered by the investigators. Angiographic committee and investigators failed to characterize the initial course in 2 cases (0.4%) and 132 cases (26.6%), respectively. Among the latter, 34 preaortic courses were noticed. The overall agreement between the investigators and angiographic committee was fair ($\kappa = 0.32$, 95% CI = 0.28–0.37, $P < .05$) (Table 4).

3.4 | Initial preaortic course

Analysis of the 443 ANOCOR was repeated by regrouping the abnormalities in 2 distinct groups: those ($n = 141$) with an initial preaortic course (31.8%) and those ($n = 302$) with the other initial courses (68.2%) including an undetermined course. The interobserver

TABLE 4 Interobserver variability for the assessment of the initial course ($\kappa = 0.326$, 95% CI, 0.28–0.37; $P < .05$)

Investigators	Initial course	Angiographic committee							Total
		PP	RP	PA	RA	N	Other	UN	
	PP	17	5	12	23	1	1	0	59
	RP	1	6	3	1	0	0	0	11
	PA	0	14	78	10	2	1	0	105
	RA	1	3	8	100	0	1	0	113
	N	0	0	0	0	4	0	0	4
	Other	1	0	7	8	2	1	0	19
	UN	6	14	33	75	2	0	2	132
	Total	26	42	141	217	11	4	2	443

Abbreviations: N, normal course; PA, preaortic course; PP, prepulmonary course; RA, retroaortic course; RP, retropulmonary course; UN, undetermined course.

TABLE 5 Interobserver variability for the assessment of a preaortic course ($\kappa = 0.497$, 95% CI, 0.40–0.59; $P < .05$)

Investigators		Angiographic committee		Total
		Preaortic course	Other courses*	
	Preaortic course	78	27	105
	Other courses ^a	63	275	338
	Total	141	302	443

^aIncluding undetermined course.

agreement for the classification between at-risk and benign forms was moderate ($\kappa = 0.497$, 95% CI = 0.40–0.59, $P < .05$) (Table 5).

4 | DISCUSSION

This study shows the excellent observer agreement for the assessment of the type of artery involved by ICA and/or CTCA in a large cohort of ANOCOR with almost 500 abnormalities. However, only moderate agreement for the identification of the site of connection was present between the 2 groups of observers, with on one hand the ANOCOR investigators (nonexpert physicians), and on other hand the angiographic committee of the ANOCOR registry (expert physicians). The most interesting finding of our study is that only fair agreement was found in the characterization of the initial course and only moderate agreement for the classification between at-risk and benign forms. In

this study, nearly one third ($n = 154$) of the ANOCOR were associated with a preaortic course and identified as at-risk forms. Among the latter, 63 (40.9%) were misclassified with another type of initial course or unclassified by the investigators. Interpretation of the initial course by ANOCOR investigators showed a nonrare confusion between preaortic and retroplmonary courses, especially with the LM artery and LAD artery (Figure 2). A misdiagnosis could have serious repercussions for the management to come. These results from a large multicenter registry suggest that the classification of a newly diagnosed ANOCOR constitute a real challenge in everyday practice. Despite the frequent contribution of noninvasive imaging, erroneous interpretations are still observed. The accurate diagnosis of ANOCOR remains difficult in the general cardiologist's community, even with the help of a CTCA. To our knowledge, observer variability between nonexperienced and experienced physicians has not been reported in the field of ANOCOR. Only few studies are reported in the literature, often with small populations, which compared the performance of ICA and CTCA for the diagnosis of ANOCOR.^{16,17} These studies demonstrated that CTCA improves dramatically the quality of the evaluation of ANOCOR, but did not validate that the classification between at-risk and benign forms was correct. The large number of ANOCOR included in this study allowed us to demonstrate significant differences in observer variability for the identification and classification of congenital coronary abnormalities, mainly involving the site of connection and the type of initial course. The appropriate detection of a preaortic course is a critical step in the evaluation of each ANOCOR. Patients at risk of major cardiac

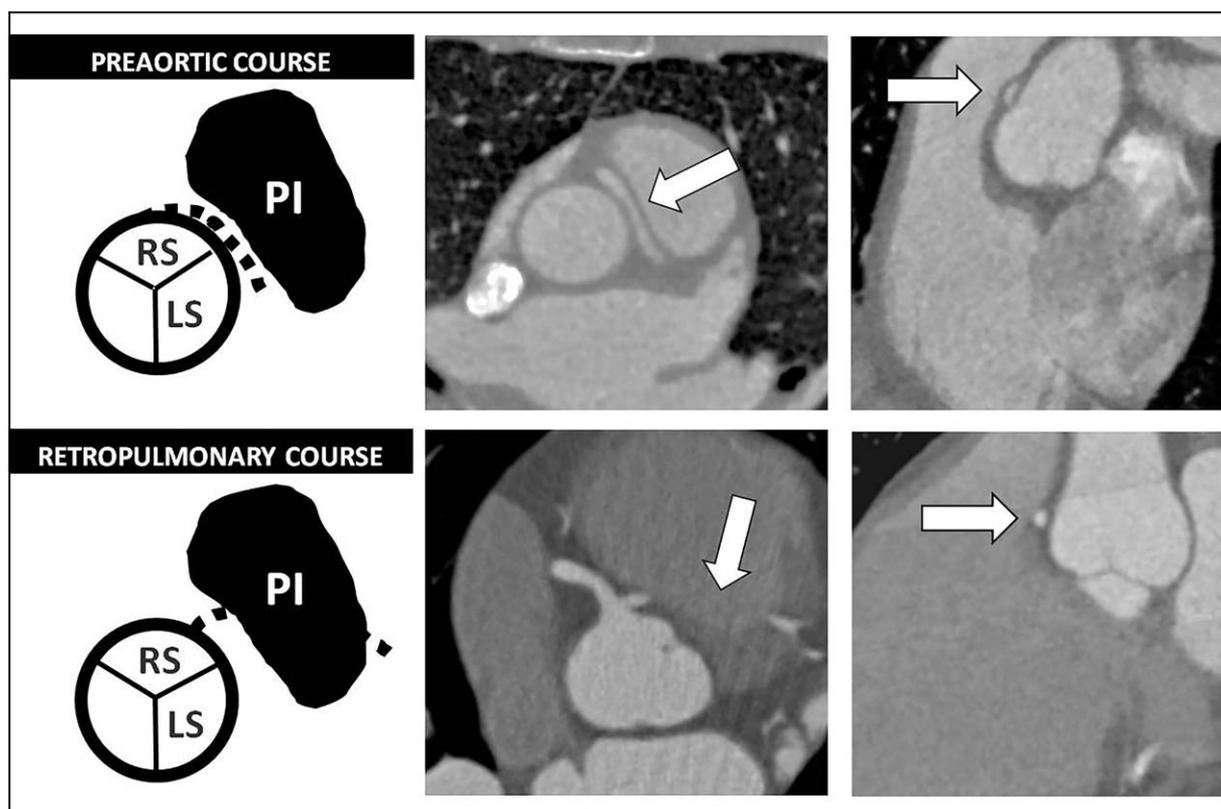


FIGURE 2 Schematic representation and computed tomography images showing anomalous connection of a left main (white arrow) with a preaortic course (top panel) or retroplmonary course (bottom panel). The latter is wrongly sometimes interpreted as a preaortic course

events require specific management.¹⁸ Conversely, numerous abnormalities are benign and should not be further explored or treated. The results of our study show that an angiographic reevaluation by an experienced group can ameliorate the classification outcomes of ANOCOR and therefore might facilitate the choice of an appropriate management. Our study is subject to some limitations. The group of ANOCOR investigators was not a homogenous group with 71 interventional cardiologists, each one classifying separately the ANOCOR diagnosed. The number of inclusions by investigator was variable in the range 1 to 45. CTCA was not performed systematically after a diagnosis of ANOCOR by ICA. This could make difficult the analysis of some cases. A high number of initial courses was undecided by ANOCOR investigators. This is obviously a major cause of the wide disparity between the 2 groups. Imaging modalities were carried out in different centers and interpreted by specialists with variable levels of experience in cardiovascular imaging. Nevertheless, these elements are representative of the current way used for the diagnosis and the classification of ANOCOR in the centers implicated in the ANOCOR registry recruitment. The main reason of the disagreements observed in our study is probably an individual variability of knowledge about rare coronary abnormalities. The classification between at-risk and benign forms was based on anatomic characteristics in this study. However, the individual risk of sudden death in patients with at-risk ANOCOR remains unknown in the lack of a stratification risk model.¹⁹ The members of the angiographic committee were selected based on their experience in the field of congenital coronary abnormalities. The final classification presented in this study was made after discussion and agreement between the members of the committee. Therefore, the intraobserver and interobserver variability was not assessed in the angiographic committee. Nevertheless, the aim of a validation committee is to share the knowledge of each member in order to improve the performance of a classification.

4.1 | Conclusion

Appropriate description is an important step for the management of patients with ANOCOR. This study showed an excellent observer agreement in defining the type of coronary artery involved between nonexperienced and experienced physicians. However, we observed a moderate observer agreement for the site of the anomalous connection, and more troublesome, a fair observer agreement for the assessment of the initial course. This last point is critical to discriminate between at-risk and benign abnormalities and thus the management of patients with ANOCOR. Therefore, when an ANOCOR is detected, especially if a form at risk is suspected, referral angiographic review by physicians with a relevant experience should be considered. Most recent recommendations move in this direction.²⁰

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CONFLICT OF INTEREST

There are no conflicts of interest in relation with the manuscript.

AUTHOR CONTRIBUTIONS

All authors have agreed to submit this manuscript to *Congenital Heart Disease* in its present form.

Pierre Aubry, Xavier Halna du Fretay, and Fabien Hyafil designed the study and revised the manuscript.

Pierre Aubry and Athanasios Koutsoukis analyzed and interpreted data.

Patrick Dupouy, Phalla Ou, Jean-Pierre Laissy, and Jean-Michel Juliard participated to the angiographic committee and revised the manuscript.

Pierre Aubry and Athanasios Koutsoukis wrote the first draft.

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