What is the best angiographic view for detection of coronary artery abnormality in Tetralogy of Fallot? A retrospective study

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Abstract

Background The definite treatment of tetralogy of Fallot (TOF) as the most common cyanotic congenital heart disease is open heart surgery and the operation technique depends on the coronary artery anatomy. We aimed to evaluate the sensitivity and specificity of various root Aortogram views to detect abnormal coronary artery configuration and course in these patients.

Methods In this retrospective study, the reports of coronary anatomy in angiography and operation notes of TOF patients since 2005 to 2017 were evaluated. The sensitivity and specificity of the two common root Aortogram views including the left anterior oblique/cranial (LAO/CRA) and left anterior oblique/caudal (LAO/CAU) were determined.

Results 451 patients with the median age of 28 months (3-432 months) were included. All patients had LAO/CRA views and 199 patients had both LAO/CRA and LAO/CAU views. The rate of coronary abnormalities reported by surgery was 8%, and abnormal origin of the left anterior descending artery from the right coronary artery was the most common reported anomaly (4.4%). The sensitivity of the LAO/CAU view was 100%, but LAO/CRA view was about 75% in detecting abnormal coronary configuration. Both of them had excellent specificity (~100%). No significant sex difference was seen between different coronary anatomy abnormalities.

Conclusion The Caudal root angiogram is an essential view to evaluate coronary artery anatomy in TOF patients and it seems that there is no need for other views like lateral view, but relying on LAO/CRA view alone may lead to significant misdiagnosis of the coronary arteries, crossing the right ventricular outflow tract (RVOT).

Background

TOF is the most common cyanotic congenital heart disease, occurring in 7% to 10% of all congenital cardiac malformations.

It can be more complicated if it coincides with the coronary tree abnormalities, like a single coronary ostium, left anterior descending coronary artery (LAD) arising from the right coronary artery (RCA), origin of a circumflex artery from the RCA, origin of the RCA from the LAD and a large conus artery or large anterior ventricular branch crossing the RVOT, double LAD. (1)

The definite treatment of these patients is open heart surgery with or without trans-annular patch dilation of the right ventricular outflow tract, which might be complicated by crossing of a coronary artery across the RVOT. Diagnosis of abnormal coronary course can lead to total surgical correction by homograft technique. Therefore determination of coronary artery anatomy is a crucial issue before any surgical correction in these patients.

In a normal coronary anatomy which is the most common type in TOF, no significant coronary branches cross the RVOT. The common coronary artery variations in TOF are LAD arising from the RCA or a single coronary artery coming from either the right or left sinus. In these two variations, the LAD or the other major branches might pass across the RVOT and complicate the surgical correction of TOF. (1-4).

The best method for detection of coronary artery anatomies, anomalies and particularly courses in preoperational evaluation of TOF is still a challenging issue and has evolved during the last years, and
coronary angiography, CT angiography or echocardiography are performed by congenital cardiology centers as mandatory workups to assess the coronary artery anomalies and courses before total surgical correction. (2, 5-7). Most surgeons and cardiologists prefer angiography and catheterization for intracardiac and extracardiac evaluations and coronary anatomy assessment, pressure determination, and possible need of intervention. (6)

On the other hand, cardiac angiography and catheterization produce hazardous X-ray radiation, and decreasing the radiation dose in angiography requires knowledge of the best and least views for detection of coronary anomaly to avoid unnecessary cineangiography and fluoroscopies. (8) The present study was conducted on a large number of patients to explore the most accurate angiography view for diagnosis of the coronary artery anatomy and courses to prevent unnecessary radiation.

**Methods**

This retrospective study investigated the patients older than 3 months of age with TOF who underwent cardiac catheterization and then total surgical correction at our tertiary heart center affiliated to Shiraz University of Medical Sciences, from March 2005 to July 2018. The patients with complex TOF physiology together with other disorders, including pulmonary atresia, complete atrioventricular canal defect, double-outlet right ventricle, absent pulmonary valve syndrome, or aortopulmonary window were excluded from the study.

Baseline characteristics including age, gender, weight at the time of surgery and past medical history of cardiac interventions were recorded. All our patients had preoperative angiography evaluation. The findings of angiography including coronary artery anomalies, and the angiographic views of all patients were extracted from our angiography database. According to our policy, non-selective coronary angiography was done in the aortic root to diagnose coronary abnormalities;

The patients were stratified into two groups: group one from 2005 to 2015 whose aortic root angiography were done in LAO/CRA view (35-40° / 20-25°), and group two, since 2015 onward, who underwent aortic root angiography in both LAO/CRA and LAO/CAU (10-15°/ 40-45°) views (9, 10). Thus, all the patients had LAO/CRA view, but LAO/CAU view was only performed in group 2 in addition to LAO/CRA view.

Both LAO/CRA and LAO/CAU were separately reviewed and reported, and then we analyzed the rate of abnormality detection in each view. Operation notes of the patients were reviewed for any coronary anatomy variation at the time of surgery, and the result recorded. The data of surgical reports were considered as a gold standard to evaluate the accuracy of the angiography reports.

Experience of a cardiologist might interfere with the interpretation of angiography records, and we tried to decrease this effect to accurately determine eligibility of these two views for detection of coronary artery anomalies and courses. Thus, the cineangiograms of the 8 patients who had abnormal coronary artery at the surgery time were reviewed blindly by an expert pediatric cardiologist with more than 10 years of congenital cardiac catheterization experience.
3-3 Statistical analysis

All the statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Values are expressed as mean±standard deviation for the quantitative variables and percentages for the categorical variables. Data were compared using the paired t-test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. To report the sensitivity and specificity, we used MedCalc, version 14.8.1. This study was conducted with the power of 80% and p-values of 0.05 or less were considered statistically significant.

Results

451 patients with TOF who underwent surgery for total correction were included in this study. The patient's age was from 3 months to 432 months with a median of 28 months. Among them, 254 patients were male and 197 female (M/F ratio: 1.2). All patients had LAO/CRA view and 199 patients had both LAO/CAU and LAO/CRA views (group 2). The percentage of the coronary abnormality in the operation notes was 8% (36 cases).

9 patients had coronary artery anomalies in the operation note that were not reported in angiography, and considered false negative of the angiography, while all were amongst the group one view.

The angiographic data in 2 patients indicated coronary abnormalities that were not confirmed during the operation, considering false positive of the angiography. Both of these cases were amongst the group one patients with LAO view.

Data for sensitivity and specificity of these two groups for diagnosis of abnormal course of coronary arteries are presented in Table 3. It clearly showed rising of the sensitivity and specificity to 100% when we included the caudal view.

According to the surgery reports, the LAD from RCA was the most common abnormality (4.4%), and both large conus branch and LAD passing across the RVOT were seen in 2 patients. Table 4 shows different coronary artery abnormalities and their sex distribution based on surgery reports. There was no significant difference between male and female patients regarding the anomalies (Table-4) (Figure 1-3).

As we mentioned in the method section, the cineangiogram of the 8 patients with abnormal coronary artery in operation were reviewed blindly by an experienced pediatric cardiologist to compare the sensitivity of the two angiographic views. As Table 5 shows, the accuracy of caudal view was significantly more than the LAO view and all cases detected in caudal views. The LAO view might misdiagnose many cases.

Discussion

Detection of coronary artery anomalies before surgery is necessary to determine the surgical technique and to provide homografts or other tube grafts for total correction of these patients (3, 8, 11-13). At the present time, either preoperational coronary angiography or coronary CT angiography can be used, although the
angiography is more common (2, 3, 9, 14). However, the accuracy of cardiac angiography and the best view of root aortogram to detect coronary anomaly is an open issue. We tried to investigate these subjects in our study by retrospective comparison of angiographic and surgical reports in large number of TOF patients.

According to the results of present study, 36 of 451 patients (8%) had coronary artery anomalies that was in concordance with results of other studies, although previous studies have wide ranges of reports from 2% to more than 30 percent (1, 4, 15). Fellow and colleagues in a retrospective study reported 8% coronary arteries anomalies (21). In another study, Shrivastava et al. reviewed coronary angiograms of 296 cases with TOF, and reported 11.8% coronary artery anomalies (16). Similar Iranian population study also report 5.9% coronary artery anomalies among 135 patients (17). The incidence of coronary anomalies in TOF varied widely regarding the method of detection.

Postmortem studies demonstrate a higher incidence of 5-9 percent, which is probably due to greater possibility of careful examination of the coronary arteries (18), and the overestimation bias can be occur due to increased surgical mortality rate related with coronary artery anomalies. Some older studies surprisingly reported a very higher rate of anomaly and even high rate of coronary fistula in TOF patients that are poorly consistent with other researcher (1, 2, 4, 15).

In agreement with the dominant reports, our study confirmed that the most common coronary anomaly was the origin of LAD from RCA which was seen in 20 cases (4.4%), and single origin coronary artery was the second most common anomaly. RCA origin from LAD or left main coronary artery had the lowest frequency in our population that were in agreement with other studies (4, 15, 17).

Sensitivity of an angiography report depends on the experience of operators, quality of images, and the most important factor image views. In our study, the specificity of angiographies to detect coronary anomaly was high (99%), but the sensitivity was dependent on the angiographic views, which ranged from 75% for LAO/CRA view to 100% for LAO/CAU view. In this study, most abnormal coronary anatomy and courses were detected in the LAO/CAU view, and LAO/CRA view missed a significant portion of the coronary anomalies. Extreme caudal view (45°) had excellent sensitivity and specificity for detection of the anomalies in angiographic evaluation.

A few studies have compared coronary anomalies in the angiography with surgical reports and we could not find a sensitivity report for angiography in similar studies (19). Li et al. studied a limited number of TOF patients and reported coronary artery anomaly in 14% of the cases, while two of them were misdiagnosed in the pre-operational caudal angiography view (8). One of their cases died due to transection of an undiagnosed coronary anomaly during repair. Compared to that study, we had more mis-diagnosis in group 1 that can be related to the lesser usage of caudal view among this group, while we had not any misdiagnosed case among group 2. Carvalho et al. also emphasized on caudal view and labeled it as an excellent view to detect coronary arteries that passing the RVOT (10), and they claimed that the lateral view was also needed to differentiate the anterior or posterior position of the crossing artery in the laid-back view; it was indicated that this view may decrease some false positive cases in the caudal view. However, we have no any misunderstanding in the caudal view, and lateral view might not be necessary, so elimination of this view can reduce the X-ray radiation.
It seems that the key view in interpreting TOF coronary anatomy is caudal view. The Caudal view illustrated in Figures 1 and 2 from our patients clearly showed an abnormal course of coronary arteries crossing RVOT, while both of them had no significant finding in the LAO/CRA view.

Cineangiograms of the 8 proven abnormal coronaries that were reviewed by an expert pediatric cardiologist also showed the weakness of LAO/CRA view to detect coronary artery anomaly with only 25% definite detection of abnormal coronary course passing across the RVOT. In the LAO/CRA view, interpretation of the anterior-posterior relationship of RVOT and LVOT is difficult and may lead to high rate of misdiagnosis of clinically significant abnormal coronary courses.

Compared to CT scan, our data showed excellent sensitivity for angiographic detection of coronary anomaly crossing RVOT if the caudal view is used, but clearly the LAO/CRA view had lesser sensitivity. New dual source CT scan can accurately explore coronary anatomy with no need to the heart rate modification even in infants, with no usual cardiac catheterization risk. In multiple studies, more than 95% sensitivity and specificity were reported to detect coronary artery anomalies that is excellent result with lesser radiation in comparison to angiography\(^{(2, 4, 15)}\). This modality may replace cardiac catheterization in future.

**Abbreviations**

TOF: tetralogy of Fallot

LAO/CRA: left anterior oblique/cranial

LAO/CAU: left anterior oblique/caudal

RVOT: right ventricular outflow tract

LAD: left anterior descending coronary artery

RCA: right coronary artery

**Declarations**

**Ethics approval and consent to participate:** All procedures performed in this study were in accordance with the ethical standards of the “Research Ethics Committee of Shiraz University of Medical Sciences” and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was submitted to and approved by the “Research Ethics Committee of Shiraz University of Medical Sciences” with code number IR.sums.med.rec.1397.272.

**Consent for publication:** This manuscript does not contain any personal data, and the consent for publication is applicable.
Ethical approval and consent to participate: The study was explained for the patients or guardians and informed consent forms were signed by them.

Availability of Data and Materials: We state that the data used and/or analyzed during the current study are available from the corresponding author on reasonable request. Data sharing is applicable to this article and datasets were generated and analyzed during the current study and data sharing is allowed.

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M.R.E: design and analysis and manuscript preparation
RD: data collection and Drafting
NM: critical revision and manuscript preparation
HM: analysis, statistics and manuscript preparation
HA: drafting
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MB: critical revision
KK: sample collection and data preparation
PM: sample collection
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Competing interest:

The authors declare that they have no competing interests.
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### Tables

#### Table 1: The rate of the coronary abnormalities in angiography reports and surgery in all patients

| Surgery (gold standard) | Normal coronary artery (%) | Coronary artery anomaly (%) | Total (%) |
|-------------------------|-----------------------------|-----------------------------|-----------|
| Angiography             |                             |                             |           |
| Normal coronary arteries (%) | 413 (91.6%)     | 9 (2%)                     | 422 (93.6%) |
| Coronary artery anomaly (%)   | 2 (0.4%)           | 27 (6%)                    | 29 (6.4%)   |
| Total (%)                | 415 (92%)          | 36 (8%)                    | 451 (100%)  |

Pearson chi-square = **305.73** P = **0.001**

#### Table 2: The rate of coronary abnormalities in angiography and surgery amongst group 2 patients with both LAO and Caudal root Aortogram

| Surgery (gold standard) | Normal coronary arteries (%) | Coronary artery anomaly (%) | Total (%) |
|-------------------------|-----------------------------|-----------------------------|-----------|
| Angiography             |                             |                             |           |
| Normal coronary arteries (%) | 189 (100%)     | 0 (0%)                     | 189 (94%)  |
| Coronary artery anomaly (%)   | 0(0%)           | 10(5%)                     | 10 (6%)    |
| Total (%)                | 189(95%)          | 10 (5%)                    | 199 (100%) |

Pearson chi-square = **312.4** P = **0.003**
Table 3: Sensitivity and specificity of the angiographies for detection of coronary abnormalities with respect to the two angiographic groups

|                                | In All cases (group1 include 451 patients) | CAU view (in 199 patients) |
|--------------------------------|--------------------------------------------|----------------------------|
| Sensitivity                   | 75.00%                                     | 100%                       |
| Specificity                   | 99.52%                                     | 100%                       |
| Positive Predictive Value     | 93.10%                                     | 100%                       |
| Negative Predictive Value     | 97.87%                                     | 100%                       |
| **Area under the curve**      | 0.87                                       | 0.98                       |

Table 4: Sex distribution between patients with and without coronary artery abnormality in surgical report

| Gender (% among gender) | Normal | LAD from RCA | P value | RCA from LAD passing the RVOT | P value | Branch of LAD Passing the RVOT | P value | Conus branch passing the RVOT | P value | Total | P value |
|-------------------------|--------|--------------|---------|-------------------------------|---------|--------------------------------|---------|--------------------------------|---------|-------|--------|
| Male                    | 232    | 13           | 0.6     | 2                             | 0.65    | 4                              | 1       | 3                              | 0.7     | 254   | (56.2%)|
| (56.2%)                 |     (65%) |             |         | (66.7%)                       |         | (50%)                          |         | (42.9%)                        |         |       |        |
| Female                  | 181    | 7            | 1       | 4                             | 4       | 4                              | 4       | 4                              | 0.7     | 197   | (43.8%)|
| (43.8%)                 |     (35%) |             |         | (33.3%)                       |         | (50%)                          |         | (57.1%)                        |         |       |        |
| Total                   | 413    | 20           | 3       | 8                             | 7       | 7                              | 7       | 451                            | 451     |       | (100%) |
| (% among total cases)   |        |             |         |                               |         |                                |         |                                |         |       |        |

LAD: Left anterior descending; RCA: Right coronary artery; RVOT: Right ventricle outflow tract; LCA: Left coronary artery;
Table 5: Comparison of LAO/CRA and LAO/CAU views in 8 patients with abnormal coronary artery course

| Diagnosis in LAO/CRA view | 2 |
|---------------------------|---|
| Diagnosis in CAU view     | 8 |
| Diagnose in both LAO/CRA and LAO/CAU views | 2 |

LAO/CRA: left anterior oblique/cranial. LAO/CAU: left anterior oblique/caudal

**Figures**

Figure 1

A 12 month old infant with TOF and previous RVOT stenting. A: In LAO/CRA view interpreting of the RCA course is very difficult in this single origin coronary artery case. B, C: Caudal view clearly showed RCA from LAD that passed anterior to the RVOT stent. The surgeons need to approach from anterior of the RVOT stent which is in the superior part of the snapshot image to release the RVOT stenosis. LAD: Left anterior descending; RCA: Right coronary artery; RVOT: Right ventricle outflow tract; LCA: Left coronary artery;
Figure 2

18 month old infant with large LAD branch passing the RVOT. A: LAO/CRA view resembles a normal configuration. B: Caudal view showed LCX from RCA and a large branch of LAD passing anteriorly to the RVOT.

Figure 3

A 1 years old infant with TOF. A: LAO/CRA view showed normal coronary arteries. B, C: caudal view and annotated picture showed normal position of the coronaries regarding the RVOT. In this case no coronary artery passed anterior to the RVOT.