Original Article

Diagnostic Value of Mitral Z-Value in Mortality of Patients with Tetralogy of Fallot: A Seven-Year Experiment

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Abstract

Background: Tetralogy of Fallot (TF) in some Iranian patients is different in that the mitral z-value is significantly lower than normal. The present study was conducted to investigate the effect of the mitral Z-value on post-surgery mortality.

Materials and Methods: The present retrospective analytical study was conducted on surgery candidate patients diagnosed with TF who had attended Shahid Modarres Hospital in Tehran between late March 2012 and late March 2019. Once the type of treatment and the need for surgery were decided and the mitral size and Z-value were determined, the patients underwent surgery, and then divided into two groups based on the outcome (death or discharge).

Results: A total of 160 patients entered the study over seven years, of whom, 110 were discharged (group 1) and 50 died (group 2). There were no significant differences between the two groups in terms of gender. The patients' mean age was 8.96±8.09 years in the group 1 and 3.16±2.7 years in the group 2 (P<0.000). Mean mitral Z-value was -2.26±2.11 in the group 1 (ranging from -7.1 to +1.3) and -3.48±1.71 in the group 2 (ranging from -6 to -1.1), and Independent Sample Test showed no significant difference between the two groups (P=0.271).

Conclusion: The mitral Z-value was significantly lower than normal in participating patients with TF, which could indicate hypo-plasticity of the left ventricle in Iranian patients with TF. No significant difference was found between the two groups in terms of surgical complications. In other words, the mitral Z-value had no effect on mortality of patients with TF.

Keywords: Congenital heart disease, Mitral valve, Tetralogy of Fallot, Mortality, Z-value, Z-score

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Introduction

It is generally accepted that the changes imposed on the heart in tetralogy of Fallot (TF) are associated with the right side of the heart (1-3), while the left ventricle is overlooked, and most studies are concerned with the right ventricle, changes in its size, and its effect on the restoration outcomes (3). However, with recent advances in diagnostic and treatment methods, more attention is paid to the left ventricle and its effect on the short- and long-term

outcomes (4, 5). A study conducted on Iranian patients with TF in 2012 showed significantly lower mitral Z-values than normal, suggesting hypo-plasticity of the left ventricle in these patients (the standard is 0±2 SD, which is -3.09±2.11 in Iranian patients with TF, ranging from +1.3 SD to -7.1 SD) (6). No study has yet investigated the mitral Z-value in patients with TF or its outcome.

The present study aims to determine if there is a relationship between mitral Z-value and postsurgical mortality of patients with TF, and whether it can be used as a predictor of mortality?.

Methods

The study protocol was assessed and approved by Institutional Ethics Board, coded IR.SBMU.RETECH.REC.1399.675, Deputy of Research, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

This was a retrospective analytical study, conducted on surgery patients diagnosed with Tetralogy of Fallot (TF) whether with initial or previous diagnosis for surgery, Modarres Hospital, Tehran, between March 2012 to March 2019. The same pediatric cardiologist measured all echocardiographic criteria, and the same surgeon conducted the surgery. According to the study inclusion criteria, any patient with TF and candidate for surgery was included.

The pediatric cardiologist jointly made decision and a cardiac surgeon about treatment of hospitalized patients diagnosed with TF. Then, the same pediatric cardiologist carried out echocardiography; mitral Z-value determined was made available to the researcher. To avoid errors, mitral Z-value was measured in several cardiac cycles and in 4- chamber and 2-chamber views; the mean was used as Z-value. Once the mitral size and body surface area (BSA) were determined, Z-value was defined as standard Z-value graphs.

Since the mitral Z-value currently has minimal effect on the surgeon's decision about the surgical method, it was not given to the surgeon until the end of surgery. The diagnosis of TF was confirmed in the course of surgery. Other data and the outcome were included in the questionnaire.

In the present study, we evaluated the following variables: Age, gender, height, weight, BSA, mitral valve size, Z-value (Z score or Z-value was determined after finding the mitral size by echocardiography and BAS, based on the available standard graph), and other concomitant anomalies, frequency of surgery, type of previous surgeries, type of current surgery, and final outcome. Considering the study was conducted over a short period and completed before discharge, we did not have withdrawal and loss of patients. After completion of each patient's special form, the related data were inserted into a code sheet.

The present study was conducted in accordance with the Helsinki Declaration principles and the checklist of ethics in research. For each patient, the informed consent form was completed and included in their record. The patients received the best available treatment, and hence, no change was made in their current treatment regimen, and no extra cost, pain, or procedure was imposed on them.

In the present study, all data were collected by the same person (cardiac surgery subspecialist), and analyzed in SPSS-18 (IBM, SPSS, Armonk, NY, USA).

Results

A total of 160 patients entered the study over seven years, who were divided into two groups based on whether they survived after surgery (group 1) or died (group 2).

In terms of gender, group 1 (Alive) included 46 males and 64 females, and group 2 included (Dead) 12 males and 38 females), with no significant difference between the two groups (based on Chi-square test, P=0.124).

Their mean age was 8.96±8.09 years in group 1 (Alive) ranging from 1 to 34 years, and 3.16±2.7 years in group 2 (Dead) ranging from 1 to 10 years (P<0.000 according to Independent Sample test).

Furthermore, the two groups were compared in terms of height, weight, and BSA (Table 1).

In the course of surgery, duration of Cardiopulmonary Bypass and Aortic clamp was determined, and CPB was found 91.84±39.04 minutes in group 1 and 130±30.02 minutes in group 2, with a significant difference between the two groups (P<0.028), while they were not significantly different in terms of aortic clamp time (P=0.062; Table 1).

Table 1: The groups' demographic distribution, data during surgery, in patients with tetralogy of Fallot attending Shahid Modarres Hospital between late march 2012 and late march 2019.

	Groups	Mean	Minimum	Maximum	P*
Age (years)	Group 1 (Alive)	8.96±8.09	1	34	P<0.000
	Group 2 (Death)	3.16±2.71	1	10	
Height (cm)	Group 1 (Alive)	126.63±33.56	75	182	P<0.000
	Group 2 (Death)	87.88±16.31	70	122	
Weight (Kg)	Group 1 (Alive)	27.76±20.68	8	79	P<0.000
	Group 2 (Death)	10.58±3.69	6	19	
BSA (m^2)	Group 1 (Alive)	0.931±0.488	0.42	2	P<0.000
	Group 2 (Death)	0.512±0.127	0.35	0.8	
CPB (Minutes)	Group 1 (Alive)	91.84±39.04	23	141	P<0.028
	Group 2 (Death)	130±30.02	116	198	
XC (Minutes)	Group 1 (Alive)	61.10±34.49	15	112	P=0.062
	Group 2 (Death)	90.57±32.53	68	160	
Hospital stay days after surgery	Group 1 (Alive)	10.98±5.06	5	27	P<0.000
	Group 2 (Death)	1	1	1	

*Using Independent Sample test; CPB: Cardio Pulmonary Bypass; XC: Aortic Cross Clamp

Table 2: Frequency distribution of mitral size and mitral Z-value in groups of patients with tetralogy of Fallot in Shahid Modarres Hospital; March 2012 to March 2019.

	Groups	Mean	Minimum	Maximum	P*
Mitral size (mm)	Group 1 (Alive)	17.69±6.42	10	27	P<0.000
	Group 2 (Death)	12.92±2.98	10	19	
Mitral Z-value	Group 1 (Alive)	-2.91±2.25	-7.1	+1.3	P=0.271
	Group 2 (Death)	-3.48±1.71	-6	-1.1	

The patients' mitral size was measured using echocardiography, which was 17.69±6.42mm in the group 1 (Alive) and 12.92±9.98mm in the group 2 (Dead), with a significant difference between them (P<0.000) (Table 2). However, no significant difference was observed between the two groups when the mitral size was measured based on BSA to determine Z-score (P=0.127), and the following data were obtained:

The mitral Z-score was -2.91±6.26 ranging from -7.1 to +1.3 in the group 1 (Alive), and -3.48±1.71 ranging from -6 to -1.1 in group 2 (Dead) (Table 2). Of 160 patients, 116 (72.5%) only had TF, and 44 (27.5%) also had other anomalies (30 patients from group 1 and 14 from group 2), with no significant difference between two groups (P=0.946); Table 3.

Of the 110 patients in group 1, only 58 were undergoing surgery for the first time. Thirty of them for the second time and 22 for the third time. Of the 50 patients in the group 2, 32 were undergoing surgery for the first time, 14 for the second time, 2 for the third time, and 2 for the fourth time. However, there was no significant difference between the two groups (Chi-square test, P=0.137).

Shunt surgery was most frequent among the 70 patients who had previously undergone surgery with 30 cases (42.9%), followed by Total Correction of Tetralogy of Fallot (TCTF) with 24 cases (34.3%) (Table 4). Out of the 160 patients, 118 (73.8%) underwent TCTF, 34 (21.3%) underwent surgery, and 8 (5%) had Shunt surgery, as shown by groups in Table 5. All patients in the group 2 (Dead) underwent TCTF, and no mortality was observed in other surgeries.

Duration of hospital stay (from surgery to discharge or death) was 7.86±6.26 days, which was 10.98±5.06 days in the group 1 (Alive), but all group 2 (Dead) patients died in the first 24 hours in surgery room or ICU (Table 1). Of the 50 patients who died in the first 24 hours, 36 (72%) were in the surgery room and 14 (28%) in ICU.

Table 3: The groups' demographic distribution, data during surgery, in patients with tetralogy of Fallot in Shahid Modarres Hospital; March 2012 to March 2019.

Results / Type of anomaly	Group 1 (Alive)	Group 2 (Death)	Total*
Tetralogy of Fallot	80	36	(72.5%) 116
TF + DTCA + DORV + PS	0	6	(3.8%) 6
TF + DORV + PDA	0	4	(2.5%) 4
Right Aortic Arch	0	4	(2.5%) 4
TF + Pulmonary Atresia + L-TGA + ASD	12	0	(7.5%) 12
TF + PDA + Cleft Lip	6	0	(3.8%) 6
TF + Cleft Lip	6	0	(3.8%) 6
Down Syndrome	6	0	(3.8%) 6
*Total	110	50	160

- P value for Chi Square test=0.946

TF: Tetralogy of Fallot, DTGA: D- Transposition of the Great Arteries, DORV: Double Outlet Right Ventricle, PS: pulmonary stenosis PDA: Patent Ductus Arteriosus, ASD: Atrial Septal Defect, L-TGA: L- Transposition of the Great Arteries

Table 4: Frequency distribution of type of previous surgery in patients with TF in Shahid Modarres Hospital; March 2012 to March 2019.

Groups / Type of previous surgery	Group 1 (Alive)	Group 2 (Death)	Total *
Shunt	18	12	(42.9%) 30
TCTF	24	0	(34.3%) 24
RVOT Repair	0	6	(8.6%) 6
Shunt + Rastelli operation With Homograft	6	0	(8.6%) 6
Shunt + TCTF	4	0	(5.7%) 4
Total	52	18	70

- P value for Chi Square test=0.03

TCTF: total correction of: Tetralogy of Fallot. RVOT: Right Ventricle out flow tract

Table 5. Frequency distribution of type of surgery in patients with TF in Shahid Modarres Hospital; March 2012 to March 2019

Groups / Type of surgery	Group 1 (Alive)	Group 2 (Death)	Total*
TCTF	68	50	(73.8%) 118
PVR	34	0	(21.3%) 34
Shunt	8	0	(5%) 8
Total	110	50	160

- P value for Chi Square test=0.02

TCTF: Total correction of Tetralogy of Fallot.
PVR: Pulmonary valve replacement or repair

Discussion

A total of 160 patients underwent surgery for TF in Shahid Modarres Hospital over seven years, who were divided into two groups, 110 in group 1 (Alive) and 50 in group 2 (Dead).

In terms of gender, 58 (36.3%) of patients were male, and 102 (63.8%) female, with no significant difference between the two groups (P=0.124), which concurs with other studies on TF. The gender proportion also matched other studies (3, 6, 7).

In terms of distribution of age, the patients'

mean age was similar to that in other studies (6, 8). However, mean age by groups was 8.96±8.09 in-group 1, and 3.16±2.7 in-group 2, suggesting that mean age was lower in group 2 patients (leading to death) and that they were in a critical state.

In a study by Amorim et al. (2005) on 66 patients with TF (7), mean age was 4±5 years in palliative surgery group and 10±8 years in TCTF group.

Mean age was 3.16±2.7 years in the group 2 patients, who had all undergone TCTF surgery. Although TCTF has been performed for four decades (3, 7) and improvement in surgical techniques in recent years has enabled most centers to perform TCTF in infant patients with TF (3), for the present study center and similar centers, palliative treatment appears to be a better initial option at lower ages, and TCTF should be performed when the child is older. As in recent studies (7), mean age at diagnosis and initial surgical treatment of TF was 6.6±7.6 years.

Due to the older age of group 1 patients, there were significant differences between the two groups in terms of height and weight. Also, due to older age and size of group 1 patients, their BSA and mitral size were higher, and the mitral Z-value was used to neutralize these effects.

Although it has been accepted that in TF, the left ventricle wall thickness is normal and its volume is normal or below normal (4-13), and the left ventricle size and mitral valves are rarely hypo-plastic, in the present study, the mitral valve Z-value was less than normal (which should normally be SD 0±2) (3). This finding suggests that contrary to existing data on TOF, the mitral Z-value and consequently the left ventricle size in the present study patients with TF are less than globally reported values (3, 10, 11, 14, 15). This difference is perhaps due to a different type of TF in Iran with smaller left ventricle size and Z-value (10).Line in some diseases such as TF, VSD site is different in Asian types (3).

Although the mitral Z-value in patients with TF was lower than normal, Z-value in-group 1 (Alive) was not significantly different group 2 (Dead) (P=0.271) and was insignificant.

CPB>120 minutes and aortic cross clamp time>90 minutes are variables that indicate a higher mortality rate in patients with TF (9), and these results were confirmed in the present study, in which CPB was 130+30.02 minutes and aortic cross clamp time was 90.5+32.53 minutes in group 2 (Dead).

In the present study, 44 patients (27.5%) had concomitant anomalies. Various studies have reported different statistics of concomitant anomalies from 30% to 60% depending on which cases are considered as an anomaly (6, 8, 9).

A review of 50 studies conducted over 40 years showed higher surgery-induced mortality in patients with TF with Complete Atrioventricular Septal Defect (16).

Down syndrome was another risk factor for early mortality (17). In the present study, six patients (3.8%) (All in-group 1) had Down syndrome. Moreover, although Multiple Ventricular Septal Defect is seen in 1% to 3% of patients with TF with pulmonary stenosis, its presence is considered to be a strong predictor of mortality (17).

In the present study, 90 patients (53%) in total were undergoing surgery for the first time, and the rest for the second, third and fourth time. However, the reoperation figure is different in domestic and foreign studies. While 40% of patients underwent surgery again in domestic studies (9), only 9% (3) in foreign studies were reoperated, where TCTF at early ages tends to have low mortality (18).

The studies conducted to determine risk factors for mortality showed that one previous operation for classic shunt is not considered a risk factor, but more than one palliative operation is (19).

Although in the present study, no significant difference was observed between the two groups in terms of number of previous operations (P=0.137), the difference between them was significant in terms of type of previous operation (P<0.03).

Given the present study limitations and difficulties, the following cases are recommended for future studies:

1. Through a complete study, normal level and standard deviation of the heart anatomical sizes should first be determined for Iranians, and sizes and standard deviations should be assessed against them (normal Z-value for Iranians).
2. The same study should be repeated by a specific echocardiologist and different cardiac surgeon to see if the mitral Z-value and size are lower in patients with TF from other centers or not.

Given that the risk of death increases three to six months after TF surgery, and then the risk flattens for the same 30-day hospital mortality, the risk of mortality of patients with TF is estimated less than the actual rate. Thus, it is recommended to conduct a study with six-month follow-up periods.

Conclusion

In patients with TF undergoing surgery at Modarres Hospital, mean mitral Z-value was significantly lower than the expected and accepted value. However, no significant difference observed between two groups of patients (Alive and Dead). Perhaps there is a different type of TF in Iran that has smaller Z-value and ventricle size (this may be one of the reasons for higher rates of early mortality in Iranian patients with TF undergoing surgery). In the present study, no significant difference was observed between the two groups in terms of mitral Z-value. However, it can be seen from the tables that patients with higher mitral Z-values were in a better state than those with lower Z-values.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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