Does Younger Age at Operation in Tetralogy of Fallot Have Influence on Early Morbidity and Mortality?

Fallot Tetralojisinde Erken Ameliyat Yaşı Erken Mortalite ve Morbiditeyi Etkiler mi?

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ABSTRACT Objective: In this study, patients who were operated for Tetralogy of Fallot were evaluated in terms of the influence of age at operation on early morbidity and mortality. **Material and Methods:** 94 patients who had undergone total correction for Tetralogy of Fallot between 2007 and 2010 were evaluated retrospectively. The patients were divided into two groups. Group I (n=40) consisted of patients younger than 12 months, Group II (n=54) consisted of patients older than 12 months. The mean age in Group I and II were 8.4±2.8 months and 19±3.9 months, respectively. **Results:** The mean length of stay in intensive care unit were 5.3±9 days, in Group I and 3.4±3 days in Group II ($p<0.05$). The mean aortic cross clamp and total cardiopulmonary bypass times were 67±16 and 98±34 minutes in Group I, whereas they were 76±27 and 105±40 minutes in Group II, respectively. There was no statistical difference between two groups. Coronary arterial abnormalities were present in 9 (10.4 %) patients. Among those, total correction operation was performed without conduits in 3 (33%) and conduits were used in the remaining 6 (66 %) patients. The early hospital mortalities were 5% (n=2) in Group I and 3,7% (n=2) in Group II, respectively. The difference between two groups was statistically insignificant. **Conclusion:** No difference in morbidity and mortality rates except length of intensive care unit stay were detected between two groups. In order to prevent the deleterious effects of hypoxia and provide normal organ development, the operation should be performed as possible as early. Because early operative age does not increase the mortality.

Key Words: Tetralogy of fallot; mortality rate

ÖZET Amaç: Bu çalışmada, Fallot Tetralojisi nedeni ile opere edilen hastalarda operasyon yaşının erken mortalite ve morbidite üzerine etkilerini belirlemek amaçlanmıştır. **Gereç ve Yöntemler:** Fallot tetralojisi tanısı ile 2007-2010 tarihleri arasında total düzeltme yoluyla opere edilen 94 hasta retrospektif olarak değerlendirildi. Hastalar 2 gruba ayrıldı. Grup I (n=40) 12 aylıktan küçük hastalar, Grup II (n=54) ise 12 aylıktan büyük hastalar tarafından oluşturuldu. Ortalama yaş Grup I'de 8,4±2,8 ay, Grup II'de 19±3,9 ay idi. **Bulgular:** Ortalama yoğun bakımda kalış süresi Grup I'de 5,3±9 gün Grup II'de ise 3,4±3 gün idi ($p<0,05$). Ortalama kardiyopulmoner baypas süresi ve aortik klemp süreleri Grup I'de sırası ile 98±34 dakika ve 67±16 dakika, Grup II'de ise 105±40 dakika ve 76±27 dakika idi. İki grup arasında istatistiksel bir fark yoktu. Dokuz hastada (%10,4) koroner arter anomalisi vardı. Tam düzeltme ameliyatı 3 hastada (%33) konduit kullanılmadan, kalan 6 (%66) hastada ise konduit kullanılarak yapıldı. Erken hastane mortalitesi Grup I'de %5 (n=2), Grup II'de ise %3,7 (n=2) idi. İki grup arasında istatistiksel bir fark yoktu. **Sonuç:** İki grup arasında yoğun bakımda kalış süreleri dışında mortalite ve morbidite bakımından farklılık tespit edilmemiştir. Organ gelişiminin normal olması için ve hipoksinin zararlı etkilerinden korunmak için operasyon mümkün olduğunca erken yapılmalıdır. Çünkü erken ameliyat yaşı mortaliteyi arttırmamaktadır.

Anahtar Kelimeler: Fallot tetralojisi; ölüm oranı

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Total correction operation in tetralogy of Fallot (TOF) has been performed since 1950. Satisfactory morbidity and mortality results have been obtained.[1,2] There has been debate on the postoperative effects of performing the operation in younger patients. Many studies have shown that early operations reduce the adverse effects of hypoxemia on myocardium and organ development and prevent right ventricular hypertrophy.[3-8] In this study, we aimed to investigate the significance of age at operation on postoperative early morbidity and mortality.

MATERIAL AND METHODS

All patients with TOF who had been operated between May 2007 and December 2010 were retrospectively investigated. The patients with additional anomalies like complete atrioventricular septal defect and pulmonary valve atresia were excluded from the study. 94 patients who were enrolled in the study were divided into two groups. Group I (n=40) consisted of patients younger than 12 months old, whereas Group II (n=54) consisted of patients older than 12 months old. All patients were preoperatively evaluated with echocardiography (ECHO) and angiography. Stenotic areas in the main and branch pulmonary arteries, additional ventricular septal defects (VSD), patent foramen ovale (PFO) or atrial septal defect (ASD), aorta-pulmonary collaterals and coronary arterial abnormalities were noted. The anatomic variations were right aortic arch (n=3), aberrant right subclavian artery (n=1), persistent left superior vena cava (n=4) and coronary arterial abnormality (left anterior descending artery from right coronary artery in 7 patients and right coronary artery from left anterior descending artery and crossing the right ventricular outflow tract in 2 patients). We detected DiGeorge syndrome in one patient.

OPERATIVE TECHNIQUES

All operations were performed under cardiopulmonary bypass. Cardiac arrest was maintained with antegrade intermittent normothermic blood cardioplegia. After right atriotomy was performed, VSD was closed with continuous stitches through tricuspid valve. Right ventriculotomy incision was made as short as possible and the muscle bands narrowing the outflow tract were resected. The decision to use transannular patch was given according to the presence of coronary anomaly and/or to the size of the main pulmonary artery and pulmonary annulus. In patients who did not need branch pulmonary artery reconstruction, right ventricular outflow reconstruction was performed after the cross clamp was removed. Modified arterio-arterial ultrafiltration was applied for 10-15 minutes when the patient was weaned off the cardiopulmonary bypass. In patients with coronary artery anomaly which crosses the right ventricular outflow, following myocardial arrest, the right atrium was opened. Right ventriculotomy was performed 3-4 mm underneath the coronary artery which crossed the right ventricular outflow. Through this right ventriculotomy, muscle bands were resected. Interventricular connection was closed with a dacron patch. Two parallel incisions on the anterior wall of the main pulmonary artery were performed. Using these incisions, a rectangular flap was cut out without interfering with the left and the right pulmonary artery orifices. Pulmonary valvotomy was performed. The distal end of the flap was sewn to the right ventriculotomy on the pulmonary artery side. The continuity between the apical end of the ventriculotomy and the pulmonary artery was maintained with autogenous pericardium. Right ventricular outflowtract (RVOT) reconstruction was performed by sewing the pericardial patch to the right ventriculotomy, pulmonary artery flap and the pulmonary artery.

The median time on mechanical ventilation, length of stay in intensive care unit (ICU), use of inotropic agents, arrhythmias and infection rates were recorded. In the first postoperative day, heart rate, blood pressure, central venous pressure and blood gas measurements were done hourly in the first four hours and every fourth hour later on. Dopamine infusion was initiated to all patients in ICU. Positive inotropic support was defined as requirement for an additional agent such as dobutamine or adrenaline.

STATISTICAL ANALYSIS

The statistical analyses were performed using the SPSS for Windows (Version 11.0, SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation and percentage as appropriate. The mean values between groups were compared with Mann Whitney U test. Significance was achieved at a p value of less than 0.05.

RESULTS

The mean age and weight of the patients in group I were 8.4±2.8 months and 7.5±1.9 kg; and in Group II they were 19±3.9 months and 13±2.0 kg, respectively. The difference was statistically significant ($p<0.05$). History of at least one cyanotic spell was present in 34 (36%) patients, and 44 (46%) patients were on prophylactic propranolol treatment preoperatively. Although it was statistically insignificant, the number of patients with history of cyanotic spell in Group I was more than that of Group II ($p>0.05$). In 8 (9.3 %) patients (6 patients from Group II), palliative Blalock Tausig (BT) shunt operations were performed before total correction. There was no statistical difference between two groups in terms of the frequency of palliative BT shunt operation ($p<0.05$). Two groups were similar in terms of preoperative RVOT tract gradients, Nakata and Mc-Goon indexes as well. Although statistically insignificant, oxygen saturation was lower in Group I (Table 1).

In all patients, VSD's were closed with Dacron patch through right atriotomy. In three patients, additional muscular VSD's were closed primarily. In Group I, RVOT reconstruction was performed with a transannular patch (89%) or an infundibular patch (7.5%) if there was no coronary artery anomaly. In Group II, transannular patch was used in 71% of the patients. There was no statistical significance between two groups in terms of use of transannular patch (Table 2).

There was coronary arterial abnormality in 9 (9.5%) patients and 6 of them were in Group I. In 7 patients (77%), left anterior descending (LAD) artery and in 2 patients (22%) right coronary artery (RCA) was crossing the RVOT. In Group I, total correction with 'double outflow technique' was used in all patients with coronary artery anomaly, whereas conduits were used in Group II.

TABLE 1: Preoperative echocardiographic and angiographic findings of patients.

	Group I	Group II	p*
RVOT Gradient (mmHg)	84±20	85±14	>0.05
Nakata (mm^2/m^2)	222±66	244±62	>0.05
Mc-Goon	1.8±0.3	1.9±0.2	>0.05
Oxygen saturation (%)	75	79	>0.05
Coronary anomaly (n)	3	6	>0.05

RVOT: Right ventricle outflow tract.

TABLE 2: Operative findings.

	Group I	Group II	p*
Transannular patch (%)	89	71	>0.05
RPA plasty (n)	2	1	>0.05
LPA plasty (n)	4	3	>0.05
BPA plasty (n)	3	1	>0.05
Conduit (n)	0	6	<0.05
DOT (n)	3	0	<0.05
RV/LV	0.69	0.61	>0.05
Gradient RVOT(mm-Hg)	18	13	>0.05
CVP (mm-Hg)	13	10	>0.05
AoCC (minutes)	67±16	76 ± 27	>0.05
CPB (minutes)	98±34	105±40	>0.05

AoCC: Aortic clamp time; BPA: Bilateral pulmonary artery; CPB: Cardio-pulmonary Bypass; CVP: Central venous pressure; DOT: Double outflow technique; LPA: Left pulmonary artery; RPA: Right pulmonary artery; RVOT: Right ventricle outflow tract; RV/LV: Right ventricle pressure /left ventricle pressure.

In the hemodynamic evaluations following cardiopulmonary bypass, the right ventricle to left ventricle pressure ratio, the pressure gradient between right ventricle and pulmonary artery and the central venous pressure were determined. There measurements were slightly higher in Group I, although this was statistically insignificant. There was also no difference in mean aortic cross clamp and cardiopulmonary bypass times.

The mean time on mechanical ventilation and length of stay in ICU were 72±23 hours and 5.3±9 days in Group I; and 39±52 hours and 3.4±3 days in Group II, respectively. The difference was statistically significant ($p<0.05$). Pneumonia was detected

in 7 (8%) patients, 5 of them were in Group I ($p<0.05$). Twenty one (24.4%) patients needed inotropic support other than dopamine during ICU stay and 18 (85%) of them were in Group I. Three (3.4%) patients needed temporary ventricular pacing for complete heart block. None of them required a permanent pacemaker later on. The most frequent arrhythmia was junctional ectopic tachycardia and there was no difference in terms of frequency of arrhythmias between the groups (Table 3). External body cooling was effective in some cases, in others with hemodynamic compromise, amiodarone was initiated. Multi organ failure (MOF) characterized by low urine output, elevated liver enzymes, prolonged prothrombin time, fever or hypothermia were detected in 4 (4.6%) patients. Peritoneal dialysis was initiated in 3 (3.4%) patients of Group I. There was no statistical difference between two groups in terms of need for peritoneal dialysis.

The early hospital mortality was 4.2% (n=4); there were 2 deaths in each group. Despite full supportive treatment, the two patients in Group I were lost because of MOF after 10th postoperative day. One patient in Group II was lost because of MOF and the other one was lost because of mediastinitis. Nine patients were lost to follow. The remaining 90% patients were followed for 19±11 months. There was no late mortality. On echocardiography, 4 (10%) patients in Group I, and 3 (5.5%) patients in Group II were found to have advanced pulmonary insufficiency. However none of the patients had postoperative right ventricular dysfunction either echocardiographically or electrocardiographically. None of these patients needed reoperation yet.

TABLE 3: Postoperative findings.

	Group I	Group II	p*
Mechanical ventilation (hours)	72±23	39±52	<0.05
Length of ICU stay (day)	5.3±9	3.4±3	<0.05
Length of hospital stay (day)	11±3.2	7±2.1	<0.05
Pneumonia (n)	5	2	<0.05
Inotropic support (n)	18	3	<0.05
Arrythmia (n)	4	5	>0.05
Peritoneal dialysis (n)	3	1	<0.05

ICU: Intensive care unit.

DISCUSSION

After the improvements in operation techniques, myocardial protection and postoperative ICU care, TOF operations are performed with low mortality rates.[9] Since the idea of performing TOF operations in infancy was first introduced by Castaneda and colleagues, the long term outcome of the operation has been debated. In Bacha et al. study 20 year-survival-rate was reported as 86% in 24 years of follow-up.[3] On the other hand, in the same study, the frequency of transannular patch use was higher in patients in whom total correction operations had been performed in the early weeks of life. Various studies reported use of transannular patch as the sole risk factor for secondary operations.[10,11] We detected higher rate of transannular patch use in patients younger than 1 year. This might be related to small pulmonary annulus seen in most of our patients. Although our follow up period is not as long as Bacha et al., none of our patients had undergone pulmonary valve replacement operation for pulmonary insufficiency.

The traditional surgical approach for TOF is the palliative treatment in early ages followed by total correction operation.[6] However, presence of RVOT stenosis until total correction operation leads to right ventricular hypertrophy and obviates more muscle resection in total correction operation. In this condition, operation time and aortic cross-clamp time have been prolonged by excessive resection of the muscle. As a matter of fact in older age group, aortic cross-clamp time were detected longer than other group.

Although, hypoxia is partially corrected with shunt operation, the adverse effect of hypoxia on organ development still continues. Furthermore, the decrease in diastolic blood pressure hampers coronary perfusion and deteriorates the hypertrophic right ventricular functions. On the other hand, shunt related pulmonary artery distortion that occurs in time prolongs the procedural time of total correction operation.[12-14] At the initial experi-

ence about repair of TOF, even though, palliative operations were performed constructed B-T shunt, relying on the facts listed above and depending on our experience in surgical management and postoperative care of TOF patients, we advocate performing total correction operations as early as possible.

In our study, the early mortality rate was similar in both groups, but the mean time on mechanical ventilation, length of stay in ICU and hospital were significantly longer in Group I. This may be related to the increased use inotropic agents in this group. We detected fluctuations in blood pressure values in the first 36 hours in the ICU stay. Although there was no statistical difference between two groups, the preoperative oxygen saturation in Group I was lower than that of Group II. The lower oxygen saturation may lead to worsening of the right ventricular functions postoperatively, which have already been deteriorated. This may explain the alterations in blood pressure in group I. In addition to this, the increased preoperative right ventricle to left ventricle pressure ratios in Group I might have contributed to the hemodynamic instability. Since the right ventricular hypertrophy was less in this group, these patients needed less muscle resection. In younger patients, the length of right ventriculotomy is longer with respect to the right ventricle mass, therefore the postoperative right ventricle adaptation might have taken longer.

Another factor that hinders surgeons to perform total correction operations at early ages is the presence of abnormal coronary arteries that cross the RVOT. We detected coronary arterial abnormality in 9 patients. In 2-9% of these patients, there is also a coronary artery anomaly which crosses the right ventricular outflow and hampers the use of a transannular patch.[15,16] In some of the symptomatic patients, systemic to pulmonary shunts are performed in the early phase of the treatment and in the late term, the right ventricle-pulmonary artery continuity is achieved through a conduit. However, conduit use in childhood gives rise to reoperation in the late term due to the relative stenosis and the degenerations in the conduit that occur as the child grows.[14] Therefore, in most of the cases, operations are delayed until the children grow up. This leads to a hypoxic state and hence impedes organ development. In the previous years, we tended to use conduits; therefore 6 patients had undergone palliative operations initially; as we changed our surgical approach towards early total correction, they have undergone total correction operation with 'double outflow' technique.[7,17] With this technique we protected the patients from the negative effects of hypoxia and decreased the possibility of reoperation since we had used native surgical material that had the potential to grow.

STUDY LIMITATIONS

The study has the limitations of a retrospective study. We tended to do total corrections in older TOF patients, but recently we changed our approach towards operating them earlier. This may explain the difference in early and late outcomes of our clinic. Our follow up duration is not long enough. However, the result of early operation can be best evaluated with long term results. Our study involves patients aged between 3 to 25 months old; this patient population does not provide adequate information about patients younger than 6 months old which is the real debated group.

CONCLUSION

There is no statistically significant difference in mortality between patients operated before and after 1 year old in our study. Although early operation prolongs length of stay in ICU, it is advantageous in preventing the patient from the adverse effects of hypoxia. In TOF patients with coronary arterial abnormalities, 'double outflow' technique may enable surgeons to operate younger patients. Longer follow up duration is needed to evaluate the advantages of early operation.

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