RESEARCH LETTER

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Outcomes of complete surgical repair versus palliative intervention in neonates with Tetralogy of Fallot

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The ideal surgical approach when managing neonates with Tetralogy of Fallot (TOF) is still controversial.[1] In 1945, subclavian artery to pulmonary artery anastomosis was created as palliation for patients with TOF.[2] A decade later, Lillehei et al.[3] performed the first intracardiac repair for TOF with ventricular septal defect closure and right ventricular outflow obstruction relief. The surgical and perfusion techniques, as well as the postoperative care, have advanced and evolved since that time. Despite that evolution, the two concepts of surgical interventions had remained the same. There is still much debate on what is the ideal surgical approach to infants with TOF, an early primary surgical repair (EPSR) versus a two-staged surgical approach with either an initial temporary shunt for pulmonary blood flow or transcatheter cardiac palliation. The aim of this study was to determine if one strategy had lower mortality than the other and to assess the hospital length of stay and cost of charge in the study groups.

The data were obtained from the National (Nationwide) Inpatient Sample, part of the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality. This is the largest publicly available all-payer inpatient care database in the United States, containing data from more than seven million hospital stays each year.[4] The National Inpatient Sample database randomly samples 20% of the discharges from participating hospitals in 47 US states and the District of Columbia. The sampling method provides a geographically distributed sample that represents all inpatient admissions in the nation.

The study population was identified using the International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9&10-CM). Data were queried from the years 2010–2018. Neonates (age < 30 days) with the diagnosis of TOF were included in the study. These patients were further stratified into the following groups: no intervention, complete EPSR, or palliative intervention (PI) group. The PI group was further divided into (systemic-to-pulmonary artery shunt [SPS], or transcatheter palliation [TCP] intervention on the pulmonary valve or ductus arteriosus stent). The primary outcome is the in-hospital mortality between the patients who underwent

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TABLE 1 Characteristics and outcomes of Tetralogy of Fallot in neonates

Variables	Early primary surgical repair ($n = 1726$)	Systemic-to-pulmonary artery shunt ($n = 2661$)	Transcatheter palliation ($n = 1702$)	*P*
Sex (male)	986 (57.3)	1461 (54.9)	940 (55.2)	ns
Chromosomal anomalies	135 (7.8)	359 (13.5)	218 (12.0)	<0.001[†,‡]
Non-cardiac anomalies	379 (21.9)	505 (18.9)	332 (19.5)	0.016[‡]
Prematurity (<37 weeks)	180 (10.4)	394 (14.8)	265 (15.6)	<0.001[†,‡]
Low birth weight (<2500 g)	178 (10.3)	399 (15.0)	274 (16.1)	<0.001[†,‡]
Necrotizing enterocolitis	54 (3.1)	108 (4.1)	44 (2.6)	0.010[§]
Death	138 (8.0)	205 (7.7)	117 (6.9)	ns
Length of stay (days)	25 (15–49)	21 (14–46)	16 (8–32)	<0.001[†,‡,§]
Cost of charge (dollars)	312 405 (162 403–558 467)	248 362 (105 719–478 382)	162 927 (82 456–238 922)	<0.001[†,‡,§]
Mechanical ventilation	870 (50.4)	1272 (47.8)	789 (46.4)	0.018[†]
ECMO	79 (4.6)	122 (4.5)	31 (1.8)	<0.001[†,§]

Data are shown as *n* (%) or median (IQR). [†]Early primary surgical repair *vs*. transcatheter palliation. [‡]Early primary surgical repair *vs*. systemic-to-pulmonary artery shunt. [§]Transcatheter palliation *vs*. systemic-to-pulmonary artery shunt. ns, not significant; ECMO, extracorporeal membrane oxygenation.

repair in the neonatal period versus those who underwent PI in the neonatal period. The secondary outcomes include the length of hospital stay and the hospital cost of charge.

Continuous variables were described using the median and interquartile range. Categorical variables were described using frequencies and percentages. Demographics, clinical characteristics, and outcomes were compared using the Mann-Whitney *U* test for continuous variables and Chi-square or Fisher's exact tests for categorical variables. Statistical significance was set at $P < 0.05$. The analysis was performed by SPSS software, version 25.0 (SPSS Inc., Chicago, IL) was used for statistical analysis.

We identified 29 292 neonates with TOF, neonates who needed intervention during the first 30 days of life were found to be 6089 (20.8%). Of those, 1726 (28.4%) had EPSR and 4363 (71.7%) had PI. The PI group included 2661 neonates with SPS and 1702 who had TCP. The basic characteristics and outcomes of groups are shown in Table 1. The majority of these patients were males, TCP (55.2%), SPS (54.9%), and EPSR (57.3%). Neonates with PI had higher frequency of diagnoses chromosomal abnormalities (TCP 12.0%, SPS 13.5%, *vs.* EPSR 7.8%, $P < 0.001$). Other non-cardiac anomalies were present at higher frequency in EPSR group (EPSR 21.9% *vs.* SPS 18.9%, $P = 0.016$). Patients who had PI had higher rate of prematurity (< 37 weeks gestation: TCP 15.6 %, SPS 14.8 %, *vs.* EPSR 10.4%, $P < 0.001$) and higher frequency of low birth weight (birth weight < 2500 g: TCP 16.1%, SPS 15.0% *vs.* EPSR 10.3%, $P < 0.001$). Hospital mortality was similar in both groups (TCP 6.9%, SPS 7.7%, *vs.* EPSR 8.0%, $P = 0.210$). Mechanical ventilation was used more frequently in the patients with EPSR (EPSR 50.4% *vs.* TCP 46.4%, $P = 0.018$). The length of hospital stay was the shortest in the TCP versus the other two groups (EPSR 25 d, SPS 21 d *vs.* TCP 16 d, $P < 0.001$). The cost of charge was significantly lower in the TCP than in the other two groups (EPSR $ 312 405, SPS $ 248 362 *vs.* TCP $ 162 927, $P < 0.001$). Extracorporeal membrane oxygenation utilization was lowest in the TCP (TCP 1.8% *vs.* EPSR 4.6% and SPS 4.5%, $P < 0.001$).

There is still much debate about the management of symptomatic neonates with TOF, a two-staged repair (the initial stage of securing a source of pulmonary blood flow followed by a later stage of a full repair) versus an early (neonatal) primary surgical repair. This study's goal was to compare the outcomes of these two approaches, we evaluated 6089 neonates with TOF who either had an EPSR (1726, 28.4%) versus 4363 neonates (71.7%) who had a PI (aortopulmonary shunt, or cardiac catheter intervention on pulmonary valve or ductus arteriosus stenting). In this study, in-hospital mortality is similar between the groups (EPSR *vs.* TCP, SPS) but the EPSR approach comes with higher resource utilization (prolonged hospital stay, higher frequency of mechanical ventilation, and higher cost of charge). It is important to mention that the resource utilization includes only the index hospitalization, however, a two-staged approach requires another hospitalization for full repair, therefore the cumulative morbidity and mortality of PI could be higher. There are advantages and disadvantages to each approach, an EPSR would restore normal cardiovascular anatomy and

physiology, resolve chronic cyanosis and promote neurodevelopment during the critical period of brain growth in early infancy. EPSR would also relieve the right ventricular afterload and allow for early myocardial remodeling. Early repair may also restore the normal development of pulmonary vasculature and alveologenesis in patients with diminished pulmonary perfusion.[5] The advantages of a two-staged repair are mainly avoiding potential organ damage with neonatal open-heart surgery and allowing for time to attain somatic growth and organ maturity prior to the utilization of cardiopulmonary bypass in the second stage. The risks associated with SPS are well described and they include shunt thrombosis, pulmonary artery distortion, excess volume load on the pulmonary vasculature and the left ventricle with potential pulmonary vasculature disease and congestive heart failure.[6–9] In this study we are comparing approaches in symptomatic neonates with TOF who needed an intervention during the 30 days of life, we are not comparing EPSR versus late surgical repair, previous studies had shown that primary surgical repair at a later age in infancy in asymptomatic TOF patients carries less morbidity and mortality than neonatal surgical repair.[10,11]

We used data from a large multicenter national database that randomly samples 20% of the discharges from hospitals across the United States with both a large number of patients and a wide range of practice variations, this allowed us to evaluate the surgical management in neonates with TOF. An important finding on the current surgical practice of TOF is that only 28.4% of neonates had an early complete surgical repair, which eludes that the majority of centers prefer PI rather than early surgical repair in neonates with TOF. We also noted a patient selection bias in this retrospective study, we find that hospitals in the United States are inclined to use a PI in patients with significant comorbidities such as low birth weight, prematurity, and chromosomal anomalies. The only comorbidity that was present at a higher frequency in the EPSR was the presence of other non-cardiac anomalies. We also found that patients with TCP had overall superior outcomes compared to SPS although having similar comorbidities. A recent study from the UK examined infants with TOF, the study showed that those who have intervention at an age less than 60 days outcomes had more favorable outcomes if they had a right ventricular outflow tract catheter intervention than SPS and EPSR.[12]

There are several limitations to this study, we were not able to assess long-term outcomes, specifically, which group will have a better neurological outcome and which group will have a better right ventricular function. We used an administrative database, and the study relied on the ICD-9 and ICD-10 diagnosis and procedure codes for identifying the study population and the associated comorbidities. Some limitations are inherent to all retrospective studies using administrative databases. Incorrect or missing data may exist and the lack of validation of the data collected by chart review is a source of potential bias for errors. However, in a large study such as ours, the patients' volume likely offset these inaccuracies.

In conclusion, the EPSR of neonates with TOF had similar in-hospital mortality to neonates with TOF who received PI. The resource utilization was much higher in the EPSR but this included only the index hospitalization, however, a two-staged approach requires another hospitalization for full repair, therefore the cumulative morbidity and mortality of PI could be higher. A future prospective randomized study with long-term follow-up is needed to further answer if early neonatal surgical repair is the ideal approach for symptomatic neonates with TOF who are not amenable to transcatheter cardiac PI.

ETHICAL APPROVAL

The use of data from approved public datasets is not considered human subject research; the study was granted exempt status from the Cleveland Clinic Institutional Review Board (Study ID 19-581).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

1. Kanter KR, Kogon BE, Kirshbom PM, Carlock PR. Symptomatic neonatal Tetralogy of Fallot: repair or shunt. *Ann Thorac Surg.* 2010;89:858-863. DOI: 10.1016/j.athoracsur.2009.12.060
2. Blalock A, Taussig HB. The surgical treatment of malformations of the heart in which there is pulmonary stenosis pulmonary atresia. *JAMA.* 1945;128:189-202.
3. Lillehei CW, Varco RL, Cohen M, Warden HE, Gott VL, DeWall RA, et al. The first open heart corrections of Tetralogy of Fallot. A 26-31 year follow-up of 106 patients. *Ann Surg.* 1986;204:490-502. DOI: 10.1097/00000658-198610000-00017
4. Agency for Healthcare Research and Quality. Overview of the National (Nationwide) Inpatient Sample (NIS). Accessed September 23, 2020. https://www.hcupus.ahrq.gov/nisoverview.jsp
5. Johnson RJ, Haworth SG. Pulmonary vascular and alveolar development in Tetralogy of Fallot: a recommendation for early correction. *Thorax.* 1982;37:893-901. DOI: 10.1136/thx.37.12.893
6. Stanley PH, Chartrand C, Davignon A, Fouron JC, Guerin R, Favreau-Ethier M, et al. Palliative surgery in Tetralogy of Fallot. *Can J Surg.* 1981;24:475-479.
7. Yuan SM, Shinfeld A, Raanani E. The Blalock-Taussig shunt. *J Card Surg.* 2009;24:101-108. DOI: 10.1111/j.1540-8191.2008.00758.x

8. Fermanis GG, Ekangaki AK, Salmon AP, Keeton BR, Shore DF, Lamb RK, et al. Twelve year experience with the modified Blalock-Taussig shunt in neonates. *Eur J Cardiothorac Surg.* 1992;6:586-589. DOI: 10.1016/1010-7940(92)90131-g
9. Gladman G, McCrindle BW, Williams WG, Freedom RM, Benson LN. The modified Blalock-Taussig shunt: clinical impact and morbidity in Fallot's tetralogy in the current era. *J Thorac Cardiovasc Surg.* 1997;114:25-30. DOI: 10.1016/S0022-5223(97)70113-2
10. Loomba RS, Buelow MW, Woods RK. Complete repair of Tetralogy of Fallot in the neonatal versus non-neonatal period: a meta-analysis. *Pediatr Cardiol.* 2017;38:893-901. DOI: 10.1007/s00246-017-1579-8
11. Ghimire LV, Chou FS, Devoe C, Moon-Grady A. Comparison of in-hospital outcomes when repair of Tetralogy of Fallot is in the neonatal period versus in the post-neonatal period. *Am J Cardiol.* 2020;125:140-145. DOI: 10.1016/j.amjcard.2019.09.025
12. Dorobantu DM, Mahani AS, Sharabiani M, Pandey R, Angelini GD, Parry AJ, et al. Primary repair versus surgical and transcatheter palliation in infants with Tetralogy of Fallot. *Heart.* 2018;104:1864-1870. DOI: 10.1136/heartjnl-2018-312958

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