Conal Septal Morphometrics Can Identify Higher Risk Neonates with Tetralogy of Fallot

Santosh C. Uppu, MD, Umesh Dyamenahalli, MD, Ritu Sachdeva, MD, Michiaki Imamura, MD, PhD, W. Robert Morrow, MD, Jeffrey M. Gossett, MS, Christopher J. Swearingen, PhD, and Himesh V. Vyas, MD, *Little Rock, Arkansas*

Background: Some neonates with tetralogy of Fallot (TOF) have rapid progression of right ventricular outflow tract obstruction, requiring early repair irrespective of Doppler gradient as measured in the neonatal period. The aim of this study was to test the hypothesis that infundibular morphology in neonates with TOF is associated with the occurrence of hypercyanotic spells and need for neonatal surgery.

Methods: Fifty patients with TOF undergoing surgical repair from 2003 to 2009 were studied. Neonatal echocardiograms were retrospectively analyzed to measure conal septal angle (the angle between the conal septum and the horizontal plane passing through the center of the aortic valve in the parasternal short-axis view, with a larger angle denoting more anterocephalad deviation of conal septum), conal septal thickness and length, the degree of aortic dextroposition, and sizes and *Z* scores of the pulmonary annulus and the main and branch pulmonary arteries. Outcomes included the occurrence of hypercyanotic spells and the need for neonatal surgery.

Results: The median age at first echocardiogram was 2 days (range, 0–12 days). The median age at surgery was 94 days (range, 5–282 days); hypercyanotic spells occurred in 17 patients (34%), and nine (18%) underwent neonatal repair. The presence of a wider conal septal angle was significantly associated with the occurrence of hypercyanotic spells (59 $\pm$ 21° vs 48 $\pm$ 13°, $P = .023$) and the need for neonatal surgery (67 $\pm$ 13° vs 48 $\pm$ 16°, $P = .004$). The positive and negative predictive values of hypercyanotic spells for conal septal angles $\geq$60° were 64% and 78%, respectively. Importantly, Doppler right ventricular outflow tract gradient at initial echocardiography, degree of aortic dextroposition, and pulmonary or aortic valve size were not associated with these outcomes.

Conclusions: A wider conal septal angle is associated with the occurrence of hypercyanotic spells and the need for neonatal surgery. (J Am Soc Echocardiogr 2013;26:200-7.)

Keywords: Tetralogy of Fallot, Echocardiography, Hypercyanotic spells, Neonatal cardiac surgery

Tetralogy of Fallot (TOF) is one of the most common cyanotic congenital heart diseases, with an incidence of about 0.2 per 1,000 live births.[1,2] Abnormal neural crest migration is thought to result in an anterocephalad displacement of the infundibular septum in relation to the rest of the ventricular septum.[3] This infundibular septal deviation results in a large, malaligned ventricular septal defect, aortic override, and right ventricular outflow tract (RVOT) obstruction.[4,5]

Symptoms of untreated patients depend on the degree of the RVOT obstruction. Patients with minimal RVOT obstruction may have symptoms of a large ventricular septal defect, may be fully saturated, and may in fact have "congestive heart failure" from pulmonary overcirculation; at the other extreme, patients with critically severe RVOT obstruction will be profoundly cyanotic and may be dependent on patency of the ductus arteriosus for pulmonary perfusion. The natural history in TOF is for RVOT obstruction to progress with time,[1,2,6] but the rate at which this happens is greatly variable in individual patients, and the ability to clinically predict how an individual patient will progress is currently limited. It is well recognized that in the early neonatal period, the peak Doppler gradient may underestimate the severity of RVOT obstruction because of elevated pulmonary vascular resistance.[7] Some patients thought to have "mild" RVOT obstruction on the basis of low Doppler gradient in the early neonatal period become significantly cyanotic soon thereafter and may present with hypercyanotic spells that may be life threatening or at the very least result in unplanned admission and/or urgent need for surgical intervention. Although some centers have recommended early neonatal surgery to circumvent this unpredictability,[8-10] data clearly suggest an increased incidence of junctional ectopic tachycardia, longer intensive care unit and hospital stays, more complicated recovery, and increased need for valve-sacrificing transannular patch repairs in patients who undergo surgery in the neonatal period.[11-17] If clinicians had a simple and reliable

From the Department of Pediatrics, Division of Cardiology (S.C.U., U.D., R.S., W.R.M., H.V.V.), the Division of Biostatistics (J.M.G., C.J.S.), and the Division of Pediatric Cardiothoracic Surgery (M.I.), Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, Arkansas.

Reprint requests: Santosh C. Uppu, MD, One Gustave L. Levy Place, Box 1201, New York, NY 10029 (E-mail: *uppusantosh@gmail.com*).

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Abbreviations
TOF = Tetralogy of Fallot
ROC = Receiver operating characteristic
RVOT = Right ventricular outflow tract

echocardiographic tool to identify patients at higher risk for rapid progression of RVOT obstruction, it might allow safer surveillance of these patients before surgery.

We hypothesized in neonates with TOF, echocardiographic morphometrics of the RVOT may predict those who are at risk for hypercyanotic spells and those who require neonatal surgery.

METHODS

Study Design

We retrospectively reviewed the medical records of patients with TOF who met our inclusion criteria and who underwent either TOF repair or shunt placement at our institution between 2003 and 2009. The study was approved by the institutional review board of the University of Arkansas Medical Center, Arkansas Children's Hospital.

Study Population

Sixty-one subjects with TOF, pulmonary stenosis underwent surgical repair between 2003 and 2009 at our institution. We excluded subjects who were diagnosed with TOF after the neonatal period and those with pulmonary valve atresia. We also excluded patients with other associated cardiac lesions, such as double-outlet right ventricle, atrioventricular septal defect, or absent pulmonary valve syndrome. No patient had a larger than small patent ductus arteriosus at the time of initial echocardiography. Fifty patients were included for the final data analysis. We excluded 11 patients from the final analysis because of diagnosis in the postneonatal period ($n = 4$), inadequate images ($n = 5$), and missing data ($n = 2$).

The following echocardiographic parameters were measured in these patients: (1) Conal septal angle: the conal septum in normal subjects divides the proximal aorta from the pulmonary artery, whereas in patients with TOF, the conal septum is displaced anteriorly and cranially in relation to the rest of the interventricular septum. The conal septal angle is the angle between the conal septum and the horizontal plane passing through the center of the aortic valve in the parasternal short-axis plane (Figure 1). (2) Conal septal length: the greatest measurement of the conal septum was measured in the parasternal short-axis plane. (3) Degree of aortic dextroposition: rightward deviation of the aorta was measured in the parasternal short-axis plane, as described by Isaaz *et al.*[18] The line passing through the atrial septum was extrapolated to intersect the aorta, as shown in Figure 2. The proportion of the aorta lying to the right of this line was measured, and the ratio of this dimension to the aortic diameter was recorded as a measure of aortic dextroposition. (4) Anterior malalignment of the conal septum: anterior deviation of the conal septum was measured in the parasternal short-axis view. A line, a, was drawn from the center of the aorta to the tip of the conal septum; another line, b, was drawn from the center of aorta to the endocardial lining of the RVOT. Anterior malalignment was expressed as the ratio of these two lines, as shown in Figure 3. (5) Sizes and *Z* scores[19] of the aortic valve, pulmonary valve annulus, and main and branch pulmonary arteries at their origin. (6) The peak pressure gradients across the RVOT on initial and follow-up echocardiography up to initial surgery were recorded.

Medical records were reviewed for demographic information, serial pulse oximetry saturation until surgery, the presence of hypercyanotic spells, and the type and date of initial surgery. The initial echocardiogram and all follow-up echocardiograms until initial surgery were reviewed.

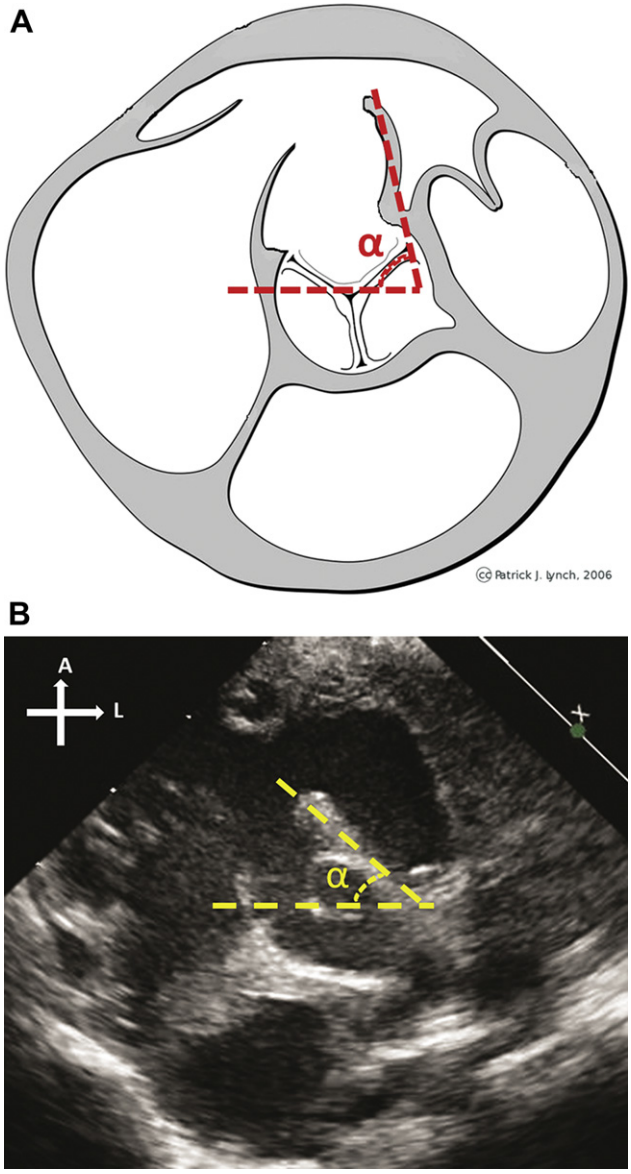

Figure 1 **(A)** Diagram and **(B)** echocardiographic image depicting measurement of the conal septal angle (the angle between the conal septum and the horizontal plane passing through the center of the aortic valve).

Echocardiographic measurements in all 50 subjects were made by a single observer (S.C.U.); the conal septal angle was analyzed for interobserver reliability by two observers (S.C.U. and H.V.V.) for all patients.

The outcomes analyzed included the occurrence of hypercyanotic spells and the need for surgery in the first month of life. For study purposes, a hypercyanotic spell was defined as an episodic decline in oxygen saturation of >10% from baseline lasting >20 sec without obvious respiratory etiology, the episodic occurrence of increased central cyanosis as perceived by parents or other nonmedical caregivers, or documentation in the medical record by the attending physician or pediatric cardiologist of the occurrence of a hypercyanotic spell if the pulse oximetry reading was not recorded in the chart.