EDITORIAL COMMENT

Fallot’s Tetralogy and Pregnancy
Prognostication and Prophesy*

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The odyssey of a blue baby from cyanotic infant to acyanotic adult is a fascinating one. The pioneering work of Dr. John H. Gibbon, Jr., in developing cardiopulmonary bypass technology was a springboard to the repair of complex congenital cardiovascular malformations (1). Over 50 years of cardiovascular surgery has resulted in one of the most impressive rehabilitative events in history (2). The approximate incidence of tetralogy of Fallot (TOF) of about 400 per million live births marks it as the most common complex or cyanotic defect (3). Corrective surgery for TOF now permits over 85% of such children to survive into adulthood (4,5). Approximately 50% of patients with TOF are women, and it was one of the first disorders to be rendered peroperative in women (6). Approximately 50% of patients with TOF are women, and it was one of the first disorders to be surgically palliated or repaired; as such, “repaired” tetralogy is one of the most frequently encountered conditions in pregnant women (6,7).

See page 174

In the U.S., there is a preponderance of pregnant women with heart disease who are now found to have some form of congenital cardiovascular malformation, whether repaired, corrected, palliated, or untreated (7,10–13). The circulatory and respiratory physiology in the normal gravid state are well known (7–9). These hemodynamic alterations are compounded in women with heart disease, at times with severe consequences. Pregnancy in cyanotic congenital heart defects (even with Eisenmenger syndrome excluded) carries a high incidence of miscarriage, premature birth, and low birth weights, the frequency of which increases with the degree of maternal cyanosis, maternal complications, and need for anticoagulation (7,10–13). The potential predictors of maternal morbidity include: functional class, ventricular dysfunction, significant arrhythmias, cyanosis, outflow tract obstruction, pulmonary hypertension, and need for anticoagulants (e.g., prosthetic valves) (8,11,12,14–17).

In the modern era, systematic data on the outcomes of pregnancy in women with TOF, both those who underwent surgery and those who did not, are few and far between. Therefore, it is fitting that a careful report of a large number of such patients, as appears in this issue of the Journal (18), should now come from an institution with a long history of excellent congenital cardiac surgery and with a program devoted to the care of adult survivors with congenital heart disease. At the time of this study from the Mayo Clinic, they had in their database 147 adult women (≥18 years old) with TOF, of which 17 had died (not related to pregnancy), 21 were lost to follow-up, and 2 were institutionalized for developmental delay. Of the remaining 107 invited to participate, 72 responded to requests for follow-up information. Of these 72, 43 had 112 pregnancies; 82 of these 112 pregnancies (73%) were successful.

Of the 43 women, 8 were unrepaired at the time of their 20 successful pregnancies; 5 of the 8 were cyanotic at the time of 12 pregnancies. In 20 (of the 43) patients (47%), TOF was initially palliated by some form of aortopulmonary shunt. Ultimately, all patients had repair with ventricular septal defect closure and right ventricular (RV) outflow tract repair. Among the 43 patients, 56% had patch reconstruction of the RV outflow tract, of which 40% were trans-anular, a pertinent precursor for future significant pulmonary regurgitation. Among the 43 TOF patients with 112 pregnancies, 16 patients had 30 miscarriages (27% rate), and there was 1 stillbirth at term (18). Low infant birth weight was related to the maternal state of women who had not undergone reparative surgery or to morphologic pulmonary artery abnormalities. Of the seven infants who were small for gestational age, five (71%) were born to women with unrepaired TOF. Of the 30 pregnancy losses (in 16 women), 3 occurred in 2 women with unrepaired TOF.

The recurrence rate of congenital defects has historically been difficult to determine with precision. A review of 6,640 consecutive pregnancies evaluated by detailed fetal echocardiography reported it is at least 2.9% in maternal and 2.2% in paternal congenital heart disease, greater in the case of outflow tract defects (such as TOF) (7,19). Other studies provide estimates of incidence in live births to a parent with congenital heart disease ranging from 4.9% to 14% (10,20). These figures contrast with a spontaneous incidence rate estimated at median of 7 per 1,000 live births (3). In the report by Veldtman et al. (18), five of the live infants (6%) had congenital abnormalities, none with TOF (one with muscular ventricular septal defect; one with mitral prolapse; one with hypoplastic left heart syndrome; one with pyloric stenosis; and one with cleft lip/palate, strabismus, and clubbed feet). One mother incidentally had a documented 22q11 deletion syndrome, but this chromosomal abnormality was not systematically evaluated in this study.

Maternal cardiovascular complications were noted in six (~14%) of the pregnant women: supraventricular tachycardia in two, heart failure in two, pulmonary embolism in one (with pre-existing pulmonary hypertension), and progressive RV dilation in one (with pre-existing severe pulmonary regurgitation) (18). Note that in one of the women with
heart failure, it appeared to be “peri-partum” cardiomyopathy rather than related to her intrinsic TOF.

The mere relief of cyanosis, although a step forward for the mother and fetus, does not guarantee that there may not be serious issues to face in the pregnant woman with TOF after long-term follow-up of the postoperative milieu. Cures in congenital heart surgery are few and far between. The challenges encountered by adults with repaired congenital heart disease include major or minor residua (abnormalities left behind) or sequelae (abnormalities caused by surgery but not technically considered complications), which includes electrophysiologic issues, anatomic or functional ventricular or valvular abnormalities, and/or prosthetic materials such as patches, conduits, and valves (4,6,21,22).

Left ventricular dysfunction may be related to chronic volume overload as a result of previous long-standing large aortopulmonary shunts, to inadequate intraoperative myocardial preservation, to significant aortic or mitral regurgitation, or even to acquired diseases (e.g., systemic arterial hypertension). Right heart dysfunction may relate to the size of RV outflow incisions and/or a patch or incisional aneurysm, residual or recurrent pulmonary stenosis or regurgitation, a large residual or recurrent ventricular septal defect shunt, or pulmonary hypertension.

Prognostication suggests a knowledgeable look at the status of a disease and prediction of outcome. The report by Veldtman et al. (18) is reassuring in that women with well-repaired TOF with no major residua or sequelae appear at an overall low risk of morbidity from pregnancy. It bears adding that even if there are no significant anatomic or hemodynamic issues at hand, the frequent presence of aortic regurgitation or prosthetic valves and conduits warrants prophylaxis against infective endocarditis at parturition (23,24). Furthermore, many have a dilated aortic root, in part the result of an intrinsic or acquired tissue defect, which may be aggravated with the hemodynamic load of pregnancy (25–27).

Prophesy implies a future that is set but can be foretold or divined from the signs at hand. Because women with surgically corrected TOF are now able to more successfully conceive and bear children, and because an incidence of transmission from the affected mother well exceeds the sporadic event in the general population, the number of TOF patients will steadily increase with each coming year. There is a strong need for carefully coordinated multidisciplinary efforts to maintain long-term follow-up of such individuals, and the recent 32nd Bethesda Conference addressed the issues in detail (13,28–30).

REFERENCES


