

Original Article

## Expected Pregnancy and its Outcome in Women after Repair of Tetralogy of Fallot: Particular emphasis on evaluation of late serious ventricular arrhythmias

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**Abstract:** Twenty-seven pregnancies in 20 patients with surgically corrected tetralogy of Fallot between 1965 and 1972 were reviewed. Most of the patients were well and asymptomatic 10-17 years after surgery, excluding three patients who were in New York Heart Association Functional Class II. Seventeen patients had a total of twenty-four successful pregnancies and deliveries. There were five abortions (13.8%) and three small-for-date babies (12.5%). None of the 24 infants had any cardiac or extracardiac anomalies. The pregnancies were relatively well tolerated and there were no life-threatening cardiac complications, however, serious ventricular arrhythmias (Lown grade 3-4A) occurred at delivery in some patients. For a patient with some residual abnormalities after surgical correction of tetralogy of Fallot, especially those with a large cardiothoracic ratio, it is important to reassess the cardiac state before pregnancy and, if once pregnant, to anticipate the possible occurrence of serious ventricular arrhythmias during labor.

**Key words:** Fallot's tetralogy, Pregnancy and delivery, Ventricular arrhythmia, Sudden death, Holter ECG

### INTRODUCTION

Intracardiac repair of tetralogy of Fallot has been performed for thirty years since the first successful report in 1956 by Dr. Sumio Manabe in Japan. Despite early criticism, this corrective approach has proven to be sound and successful, and survivors of surgery usually show an expected improvement in effort tolerance. The patients who underwent correction in the early pioneering years have now entered their third or fourth decades of life, and the very late results after surgical repair is a

growing concern because late problems can occasionally mandate reoperation for residual abnormalities or cause sudden death with or without manifest symptoms and signs of cardiac disorder<sup>1-6)</sup>.

Recently, pregnancy in patients with surgically corrected tetralogy of Fallot is increasing, but few detailed studies of such pregnancies have been reported<sup>7,8)</sup>. This study, therefore, analyzed the results of pregnancy and delivery in 20 patients with tetralogy of Fallot who had undergone intracardiac correction in an attempt to identify patients at risk for late sudden death, especially during pregnancy, delivery and the postpartum period.

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## PATIENTS AND METHODS

All 20 women who had had a total correction of tetralogy of Fallot at Niigata University Hospital during the period 1965-72 and who had had one or more pregnancies were considered for the study. Age at operation was on the average 14 years old (range 7-24). Their long-term physiological states were evaluated fully 10-17 years (average 15 years) later after surgery in a non-pregnant period by chest x-ray, electrocardiogram at rest and treadmill exercise, 24 hours Holter ECG monitoring, echocardiogram and cardiac catheterization.

The success of the operation was assessed in relation to the residual right ventricular outflow tract (RVOT) obstruction, which was shown by right ventricular/systemic (RV/S) peak systolic pressure ratio, to

cardiothoracic ratio (CTR). Also in each group, several postoperative characteristics of residual abnormalities, including persistent ventricular septal defect, pulmonary regurgitation, pulmonary hypertension, tricuspid regurgitation, ventricular dysfunction and conduction disturbance, were inspected for possible influence on exercise tolerance, late ventricular arrhythmias and sudden death.

Full obstetric details of each pregnancy were requested from the obstetric department that supervised each pregnancy.

The 17 patients were subdivided into nine subgroups (Aa-Cc) and were roughly divided into three large groups (I-III), excluding three patients who had had pregnancies which were mislabeled to spontaneous abortion (Table 1).

Operative procedure. Prior intracardiac repair, initial Blalock-Taussig shunt was

Table 1. Classification of 17 patients according to the relation of RV/S pressure ratio to CTR

P-RV/S	CTR	CTR			
		a <55%	b 56-60	c >61%	
A	>0.55	4 (8)	2 (2)	4 (6)	II
B	.56-.65	1 (2)	1 (1)	2 (2)	
C	0.66<	2 (2)		1 (1)	3 (3)
		5 (10)	5 (5)	7 (9)	17 (24)

Legend: ( ), Numbers of deliveries

P-RV/S, Right ventricular/systemic peak systolic pressure ratio.

CTR, Cardio-thoracic ratio.

Table 2. Preoperative states of initial repair in 17 patients

	Numbers of patients		
	group I 7	group II 7	group III 3
Age at operation	14.9 ± 3.5	16.1 ± 6.0	10.3 ± 1.7
MPA/Ao ratio	65 ± 25	63 ± 25	50 ± 10
Red cell counts	538 ± 73	604 ± 74	577 ± 60
Hemoglobin g/dl	16.6 ± 2.7	18.5 ± 3.7	19.0 ± 3.5
CTR %	50 ± 5	54 ± 4	46 ± 1

Legend: MPA/Ao ratio, Main pulmonary/Aortic diameter ratio.

Table 3. Procedures of right ventricular outflow tract (RVOT) reconstruction

RVOT patch	Numbers of patients			Total
	group I	group II	group III	
None	4	4	2	10 (58.8%)
RV only	1	1		2 (16.7 %)
Transannular	2	1	1	4 (23.5 %)
PVR		1		1

Legend: PVR, Pulmonary valve replacement.

done in one of the group I patients, two of the group II and one of the group III patients, as a whole, in 23.5% of the patients. Table 2 shows the preoperative physiologic data of each group.

Non-pulsatile cardiopulmonary bypass with a disc or sheet bubble oxygenator was used in all of the patients. Under moderate general hypothermia, intermittent anoxic cardiac arrest was routinely used at that time, that is, usual myocardial protection was not provided yet before 1974 in our hospital. Correlating with the pathological anatomy of RVOT obstruction, several RVOT reconstructive procedures were performed. As detailed in Table 3, ten patients (58.8%) underwent RVOT reconstruction without any patch to avoid excessive pulmonary insufficiency at the time of initial repair. In one of the group II patients, initial pulmonary valve replacement with Ionescu-Shiley bovine pericardial valve was indicated.

## RESULTS

The twenty patients had twenty-nine pregnancies. A total of five miscarriages (four spontaneous, one artificial) had occurred in five patients, but two of them had at least one successful pregnancy. There were a total of 24 successful pregnancies and deliveries in 17 patients.

### Obstetric details of the 17 patients and 24 infants.

The age at initial labor ranged from 19

to 33 years old (average 25). The interval between operation and initial labor ranged from 4 to 16 years (average 10). There were no serious cardiac complications in the 24 pregnancies. No patient developed overt cardiac failure, but three patients had received digitalis prophylactically during the late pregnant period. Little information on arrhythmias was obtained during the pregnancies. All five patients who had had continuous exact ECG monitoring during labor had transient ventricular arrhythmias (Lown grade 3 in two of patients and 4A in three). In one of the group II patients a suspected trifascicular block and transient atrioventricular dissociation developed during caesarean section. However, antiarrhythmic drugs were not required. Such arrhythmias happened in 3 patients in the first stage of delivery, in one in the third, and in one in the fourth stage.

As shown in Tables 4 and 5, labor was induced in four patients. Of the 24 deliveries, 9 were spontaneous vaginal and 2 were forceps deliveries. Three patients required caesarean section; two of the group II patients, one for cephalopelvic disproportion and her disease of moderate cardiomegaly of 68% of CTR at initial labor at 33-year-old of age and the other for obstetric problems, and in one of the group III patients it was indicated for severe residual RVOT obstruction.

Oral antibiotic prophylaxis against endocarditis was given several days during the postpartum period in all patients. No

Table 4. Methods of 24 deliveries in 17 patients

	Numbers of patients		
	group I 7	group II 7	group III 3
Age at initial labor	25.3±1.2	25.6±4.0	25.7±2.1
Interval of operation to labor (years)	10.4±3.7	9.6±3.1	15.3±0.5
Induced delivery	1/12	1/9	1/3
Spontaneous delivery	6 (CP 1)	3 (CP 1)	
Vacuum	4	4	2
Forceps	2		
Caesarean section		2 (CP 1)	1

Legend: CP, Cephalo-pelvic disproportion

Table 5. Details of 24 deliveries and newborn infants in 17 patients

group	case	labor age (year)	delivery and its time	gestation (week)	placenta weight	newborn			
						weight	sex	Apgar	
I	H. Y.	26	spont	10 h. 34 m.	41	480 g	3208 g	M	9
		28	spont	5 h. 46 m.	40	525	3570	F	10
	Y. M.	27	spont	6 h. 00 m.	36	600	1320 (SFD)	F	9
		30	spont	6 h. 00 m. (induced)	39	500	3020	M	10
	Y. K.	24	vacuum	16 h. 04 m.	40	660	3610	M	10
		28	spont (CP)	7 h. 45 m.	39	750	3480	F	10
	A. N.	22	vacuum	—	41	—	3210	M	9
		26	vacuum	—	40	480	3112	M	9
	K. T.	26	vacuum	16 h. 11 m. (induced)	41	580	2710	F	8
	T. S.	24	forcep	7 h. 50 m.	40	495	3320	F	9
S. K.	24	forcep	4 h. 10 m.	38	440	2370 (SFD)	F	10	
	27	spont	2 h. 07 m.	38	520	3030	M	9	
					548±88	2977±608			
	T. Y.	19	spont (CP)	5 h. 25 m.	40	470	3060	F	4
		21	vacuum	5 h. 46 m.	39	430	3044	M	9
	W. Y.	22	spont	4 h. 50 m.	39	550	2780	F	10
		24	spont	13 h. 50 m. (induced)	40	650	3640	M	10
II	M. J.	28	vacuum	6 h. 05 m.	40	690	3250	M	9
	Y. H.	33	caesar (CP)	—	39	455	3100	M	9
	N. T.	25	vacuum	12 h. 21 m.	38	600	2790	M	9
	I. M.	24	caesar	—	38	560	2682	F	9
	S. K.	26	vacuum	4 h. 25 m.	40	445	3080	M	9
						539±89	3047±272		
	S. S.	23	vacuum	7 h. 18 m. (induced)	39	390	2450 (SFD)	F	8
III	I. S.	26	caesar	—	39	440	3052	F	9
	O. H.	28	vacuum	17 h. 48 m.	40	670	3520	M	9
						500±122	3007±438		

Legend: CP, Cephalopelvic disproportion. spont, spontaneous. caesar, caesarean. SFD, Small-For-Date

Table 6. Late postoperative cardiac states in 17 patients

	group I	group II	group III
Age at evaluation	29.3± 3.0	30.3± 4.5	26.3± 1.0
Follow-up time (years)	14.4± 2.6	14.2± 3.5	15.7± 0.4
RV systolic pressure (mmHg)	44 ±16	54 ±13	96 ±31
PA systolic pressure (mmHg)	29 ± 7	35 ± 9	23 ± 3
PA diastolic pressure (mmHg)	13 ± 6	10 ± 5	7 ± 4
mean RA pressure (mmHg)	7.6± 3.0	7.7± 2.8	8.0± 1.4
CTR (%)	53 ± 2	63 ± 4	60 ± 2

Legend: RV, Right ventricle. PA, Pulmonary artery. RA, Right atrium.

Table 7. Onset of ventricular arrhythmias according to Lown grade in 11 patients

group	case	age		ECG			conduction disturbance
		operation	evaluation	at rest	treadmill	Holter	
I	H. Y.	11	28	0	0	0	CRBBB, RAD
	T. S.	12	25	0	1A	1A	CRBBB, RAD
	K. T.	12	29	1B	2	3	CRBBB, RAD
II	T. Y.	7	23	0	1A	1A	CRBBB, RAD
	W. Y.	12	27	1A	1A	3	RAD
	Y. H.	24	29	0	3	4A	CRBBB, RAD
	N. T.	22	24	0	0	3	CRBBB, RAD
	I. M.	12	25	1A	0	4A	CRBBB, LAD prolong-PR
III	S. S.	8	25	0	0	1A	CRBBB, RAD
	O. H.	12	28	0	—	5	CRBBB, RAD
	I. S.	11	28	3	2	4A	CRBBB, RAD

Legend: CRBBB, Complete right bundle branch block. RAD, Right axis deviation. LAD, Left axis deviation.

puerperal problems were encountered.

Most of the patients had full-term deliveries, and the birth weight of babies averaged 2,977 grams in group I patients, 3,047 grams in group II and 3,007 grams in group III. Three (27.3%) of the girls were small-for-date babies. All of the 24 infants (13 boys, 11 girls) examined in this study were essentially normal. No cardiac or extracardiac anomaly was diagnosed (Table 5).

#### Late postoperative physiological states in 17 patients.

The long-term physiological states were evaluated 10–17 years (average 15 years) after repair in a non-pregnant period.

Fourteen patients (82.4%) had the New

York Heart Association Functional Class I, and two of the group II patients and one of the group III patients were judged to be in Functional Class II.

All 17 patients were recatheterized. Table 6 shows their late hemodynamic data. Group II patients had residual mild pulmonary hypertension and, at the same time, 4 patients had residual ventricular septal defect (Qp/Qs 1.2–1.5). Moderate cardiomegaly was obvious in group II and III patients, but no tricuspid regurgitation was detected. One of the group III patients has received the reoperation accompanied by additional pulmonary valve replacement for severe residual RVOT obstruction, recently.

Echocardiographic study was done in eight patients. They all had enlargement of the right ventricle. That is, right/left ventricular endo-diastolic dimension ratio was calculated  $0.66 \pm 0.11$  in group I,  $0.70 \pm 0.17$  in group II and  $0.97 \pm 0.17$  in group III. Left ventricular dysfunction at rest was not observed in any patients.

In eleven patients, electrocardiographic analysis showed the frequent onset of ventricular arrhythmia, especially in Holter ECG (Table 7). Such ventricular ectopic beats (Lown grade 3-5) almost always occurred during exercise, but in two patients also during sleep. This tendency was not always related to the operative radicality of the disease. In one of the group III patients, asymptomatic paroxysmal supraventricular tachyarrhythmias was recorded.

#### DISCUSSION

Surgical repair of tetralogy of Fallot has a low perioperative mortality and survivors are usually much improved symptomatically. In our experience, the actuarial survival estimate for 133 discharged patients undergoing repair between 1965 and 1972 was 94% 15 years later. Seven of the patients died within the 7th postoperative year and their deaths were caused by heart failure resulting from residual abnormalities. We had no experience of late sudden death, which was probably caused by conduction disturbance or ventricular tachyarrhythmias<sup>9)</sup>.

On the other hand, pregnancy in patients with surgically corrected tetralogy of Fallot is increasing, but few detailed studies of such pregnancies have been reported<sup>7,8)</sup>. It is becoming increasingly important to analyze the truly long-term results to detect and treat new problems (how to mandate reoperation and how to prevent sudden

death) and to reassess the effectiveness of various surgical procedures, especially for tetralogy of Fallot. It might be argued that women having successful pregnancies represent those with the best results from surgery.

Specific cardiovascular changes accompanying pregnancy include an increase of total blood volume, an increase of cardiac output which is due to both increased heart rate and stroke volume, a marked reduction in systemic vascular resistance, and a diminution of venous return from supine hypotension. Besides, cardiac output increases around 20% in the first stage of labor with each contraction of the uterus and by 40% when compared to the situation before labor. The time around delivery is characterized by many kinds of strains on the heart and the central circulation<sup>10,11)</sup>.

Consequently, the changes that influence the circulation and that take place during the short time interval surrounding delivery have been thought to be of special importance for the patients with heart disease, that is, patients of tetralogy of Fallot with residual cardiac abnormalities postoperatively. Thus, most of the serious complications occur in this short time span. About two-thirds of all deaths recorded in patients with heart disease occur around delivery<sup>11)</sup>.

In our series, we fortunately had no life-threatening serious complications and pregnancies were successful, as Singh also did. These results suggest that survivors of surgery of tetralogy of Fallot are able to cope adequately with the demands of pregnancy. However, we encountered in many patients a high incidence of multiple ventricular arrhythmias during labor, especially in the first stage, and these arrhythmias could have been detected during treadmill

exercise and Holter ECG examinations in the non-pregnant period, retrospectively.

The obstetric details suggest that the incidence of miscarriage and small-for-date baby was higher than one might expect in the general population<sup>7,8)</sup>. In our series, the incidence of miscarriage was 13.8% as compared to 3.4% and that of small-for-date baby 12.5% as compared to 5.0% in the general Japanese population. On this point, our results were similar to Singh's. Although we could not explain the cause of these obstetric differences, a compensatory mechanism is a large placenta in comparison with the infant's size. The birth weight divided by the weight of the placenta is significantly lower at delivery in women at a high altitude or who has a cyanotic heart disease<sup>11)</sup>. Its normal ratio is 6.0 and in our patients it was ranged from 5.7 to 6.2, which was almost normal. We thought that their late cardiac performance were relatively well tolerated during pregnancy and at delivery, even in group II and III patients.

We have experienced no abnormal infants, but Whittemore and his associates reported in his large series that the high incidence of miscarriage and infant-birth with several congenital heart diseases was characterized at pregnancies in mothers complicated with congenital heart lesions with or without surgical correction<sup>7)</sup>.

In conclusion, although in many instances an adequate pregnancy and labor can now be expected after repair of tetralogy of Fallot, we strongly emphasize the necessity to observe the various ventricular arrhythmias during labor<sup>12)</sup> and, if possible,

to examine the late postoperative cardiac status before pregnancy.

Recently, correlating with factors to late sudden death, Stanford's group reported that older age at operation is one of the important factors including residual abnormalities<sup>13)</sup>. Patients in our series had been corrected at an older age (average 14 year-old). Therefore, a safer and sufficient pregnancy can be expected in the near future, in female patients with tetralogy of Fallot corrected by several surgical improvements.

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ファロー四徴症根治術後における妊娠出産  
—遠隔期重症心室性不整脈評価の重要性—

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抄録 Fallot 四徴症根治術後(10~17年)において妊娠出産を経験した17症例—24出産の遠隔期心機能評価による術後の妊娠出産適応上の問題点について検討した。

妊娠分娩経過を通し妊産婦、胎児および新生児死亡を含む重篤な合併症はみられなかったが、周産期医学的には心奇形児出産はみなかったものの、一般にくらべ低体重児出産(12.5%)、自然流産(13.8%)は高率であった。対象例の術後遠隔期における安静時左心機能はほぼ正常域にあったが、トレッドミル負荷時の運動能の低下など潜在的な心室機能低下が考えられ、24時間ホルター心電図において心室性不整脈の多発が問題となった。これらは分娩、とくに陣痛時に増悪する傾向にあり分娩時における連続的心電図モニターの重要性が指摘できた。

本症根治術後の妊娠出産の適応については、高度遺残狭窄を含む心拡大の著しい右室量負荷病態を示す症例では、禁忌を含めとくに慎重に対処することが重要である。

キーワード ファロー四徴症, 妊娠出産, 心室性不整脈, 突然死, ホルター心電図