Outcome of treatment for neonates referred to a supraregional cardiac centre 1976–78

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SUMMARY The clinical course and outcome of treatment for 322 consecutive neonates referred to a supraregional paediatric cardiac unit are reviewed. Two hundred and forty-eight (77%) had structural congenital cardiac defects. The remaining 74 (23%) presented with arrhythmia, non-structural cardiorespiratory problems, or problems unrelated to the cardiovascular or respiratory system. Transposition of the great arteries and coarctation of the aorta were associated with a good prognosis. Infants with cyanotic cardiac defects associated with a low pulmonary blood flow who required early palliation were found to have a poorer outlook.

The mortality rate among infants with congenital heart disease presenting within the first month of life has fallen during the last two decades partly as a result of early referral to specialised units¹ and partly owing to improved surgical management in which primary repair is replacing conventional palliative procedures.^{2,3} We review the results of treatment for all neonates referred to a supraregional paediatric cardiothoracic unit during a recent 3-year period.

Patients and methods

Between January 1976 and December 1978, 1757 new patients were seen in the cardiac unit of the Royal Liverpool Children's Hospital. Three hundred and twenty-two (18.3%) patients were younger than 1 month at the time of their first attendance. All were referred because of the presence, or suspicion, of congenital heart disease or arrhythmia. Their case records were reviewed to determine the diagnosis, clinical course, and current condition.

Patients were grouped according to the diagnosis established by necropsy, cardiac catheterisation or surgery, or clinical assessment (Table 1). Any patient with nonstructural cardiorespiratory problems or primary pulmonary disease was generally discharged to his referring unit after treatment. The duration of follow-up of these patients ranged from one week to 50 months (mean 10 months). Surviving patients with structural cardiac defects were followed up in this unit and only 2 have been lost to follow-up. The duration of follow-up ranged from 8 to 58 (mean 32) months.

Table 1 *Diagnostic groups and type of diagnosis in 322 neonates*

	Clinical		Catheter or surgery		Necropsy		Total
	No	(%)	No	(%)	No	(%)	
Structural cardiac defect	28	(11)	154	(62)	66	(27)	248
Nonstructural cardiorespiratory problem	34	(68)	10	(20)	6	(12)	50
Arrhythmia	10	(91)	1	(9)	0		11
Noncardio-respiratory problem	9	(69)	3	(23)	1	(8)	13

Results

Age at first attendance. Sixty-two (19%) infants presented on the first day of life, with cyanosis as the most common reason for referral (43 patients). Transposition of the great arteries (19 patients) and pulmonary atresia (6 patients) were the most common structural cardiac defects seen at this age. Twenty-three (37%) infants presenting on the first day of life had structurally normal hearts. The reasons for referral are shown in Table 2.

Investigation. Two hundred and eighty-eight patients were admitted during the first month of life and 34 were reviewed as outpatients. Inpatients were investigated using chest x-ray films, electrocardiography, blood gas analysis including hyperoxic test, and M-mode echocardiography. Two hundred and thirty-one have been investigated by cardiac catheterisation, with 199 (86%) having their initial

Table 2 *Diagnosis in 23 infants with no evidence of structural congenital heart disease who presented within 24 hours of birth*

Diagnosis	
Predominant cyanosis	8
Arrhythmia	4
Predominant tachypnoea	3
Septicaemia	3
Predominant congestive heart failure with ST change	2
Myopathy	1
Ascites	1
Trisomy E	1

catheter study during the first month of life (Table 3). Eighty-four (42%) of the infants catheterised at this age were investigated on the day of admission and a further 63 (32%) were investigated the next day.

Thirteen infants died within 24 hours of cardiac catheterisation (Table 3). All were younger than 3 weeks and each was critically ill at the start of the study. Eleven had major inoperable defects and active resuscitation was not attempted. One infant with simple transposition died of coliform septicaemia and one infant with persistent fetal circulation secondary to birth asphyxia died despite treatment. Although cardiac catheterisation undoubtedly hastened the death of some, no infant died directly as a result of complications occurring during the investigation.

Structural cardiac defect. Table 4 summarises the final diagnosis for the 248 patients with structural congenital heart disease; their clinical course is shown in Fig. 1.

Fifty-six (23%) patients are alive without operation. Thirty-two have minor anomalies and 23 have defects for which operation later in child-

hood may be necessary. One child with Down's syndrome and an atrioventricular canal defect has pulmonary vascular disease and is inoperable.

One hundred and forty-three (57%) patients have had operations (including one of the 2 patients lost to follow-up) and 94 (66%) were alive at the time of review. The age at the time of the first operation is shown in Table 5. Sixty-six (46%) had their initial operation as neonates. Forty-four operations were performed within 60 hours of admission to this hospital. Twenty-seven patients had more than one

Table 3 *Age at initial cardiac catheterisation*

	< 1 day	2 to 7 days	8 days to 1 month	> 1 month	No catheter study
Structural cardiac defect	19	84 (7)	82 (5)	32	31
Other	3	4 (1)	7	0	60

Figures in parentheses indicate the number of patients who died within 24 hours of the catheter study.

Table 4 *Diagnostic categories in 248 infants with structural congenital heart disease*

Transposition of great arteries	47
Ventricular septal defect	44
Coarctation of aorta	33
Tetralogy of Fallot*	20
Hypoplastic right heart syndrome†	16
Hypoplastic left heart syndrome	13
Pulmonary stenosis	12
Visceral heterotaxia	10
Aortic arch interruption	9
Patent ductus arteriosus	6
Miscellaneous	38

*Includes 5 patients with pulmonary atresia with a ventricular septal defect.

†Includes 7 patients with tricuspid atresia, and 9 patients with pulmonary atresia and intact ventricular septum.

*Includes 4 deaths from causes unrelated to the operation

Fig. 1 *Clinical course of 248 neonates with structural cardiac defects. Division into groups is made solely on the basis of anatomical and haemodynamic criteria. Figures in brackets, excluding percentages, show number of deaths after operation.*

Table 5 Age at initial operative procedure in 143 patients who underwent surgical treatment

	<1 week		8 days-1 month		1 month-1 year		>1 year		Total
	No	(%)	No	(%)	No	(%)	No	(%)	
Bypass operation	4	(8)	5	(10)	23	(44)	20	(38)	52
Non-bypass operation	15	(17)	42	(46)	30	(33)	4	(4)	91

operation each, and the total number of operations performed to the present time is 172.

Forty-eight (19%) patients died without operation. Twenty-nine were considered unsuitable for surgery, including 12 patients with hypoplastic left heart syndrome, 4 with coarctation, hypoplasia of the aortic arch, and complex intracardiac malformations, 6 with asplenia syndrome, and 2 with aortic arch interruption.

Twelve patients died for reasons unrelated to the cardiac malformation but only 2 had minor defects. The remaining 10 would have required operation had they survived. The principal causes of death were septicaemia (4 cases) and cerebral damage secondary to perinatal asphyxia (3 cases). Six patients died suddenly at home having been well when last seen. All had potentially operable defects. Permission for surgery was refused for one infant with pulmonary atresia and intact ventricular septum.

Transposition of the great arteries (47 cases) was the most common defect. Twenty-four patients had 'simple' transposition and 23 had transposition with additional defects. The actuarial survival at age 3 years for all cases of transposition was 80%. Mortality was concentrated in the first month of life often from non-cardiac causes including 2 who died from septicaemia and one who died of an intracranial haemorrhage after perinatal asphyxia. Thirty-four children have undergone Mustard's operation (with 2 deaths), one child has had a successful arterial switch, and 6 children with complex transposition have had palliative procedures (with 3 deaths). Two children with complex transposition are alive without operation but will require elective surgery later.

Forty-four infants had a ventricular septal defect (VSD) as the main cardiac defect. Thirty presented with congestive cardiac failure and 14 were referred because of the presence of a murmur. In 2 cases the presenting symptoms were the result of transient myocardial dysfunction rather than the VSD which was small. Twenty-six are regarded as having small isolated VSDs, and in 11 spontaneous closure has taken place. Ten patients have undergone closure of the defect, as a primary procedure in 8 cases and after banding of the pulmonary artery in two. Four

patients will need surgery in the future, one whose pulmonary artery was banded in infancy, and 3 who also have significant pulmonary stenosis. There were 2 deaths in infancy for reasons unrelated to the cardiac defect and one sudden death at age 5 months in a patient with a large VSD. One infant, known to have a moderately large VSD and pulmonary hypertension, has moved from the Liverpool area and his current condition is unknown.

Of the 33 patients with coarctation of the aorta, 13 had isolated lesions and 20 had additional intracardiac malformations. Two patients with simple coarctation died, one from necrotising enterocolitis before operation and one of acute appendicitis 2 days after repair of the coarctation. Six patients with complex coarctation died after the initial operation, and surgical treatment was not offered to 4 infants with coarctation, hypoplasia of the aortic arch, and complex intracardiac defects. The actuarial probability of survival for all patients with coarctation of the aorta at age 3 years is 64%. There have been no late deaths in this group but one patient has been lost to follow-up.

Fifteen patients have tetralogy of Fallot but only 10 presented with cyanosis, the remaining 5 presenting because of the presence of a murmur. Eleven are alive: 3 after repair, 5 after palliation, and 3 who have not yet required any operation. All 5 patients with pulmonary atresia and VSDs died, although one death, of meningitis at age 10 days, was unrelated to the presence of the cardiac defect. Pulmonary atresia with intact ventricular septum was present in 9 patients. An infusion of prostaglandin E_1 was used to maintain patency of the ductus arteriosus and 8 underwent aorticopulmonary anastomosis in the neonatal period. Only 3 remain alive, one after a second shunt and 2 after right ventricular outflow reconstruction.

Twenty patients with cyanotic congenital cardiac lesions associated with reduced pulmonary blood flow underwent palliative aorticopulmonary anastomosis within the first month of life. Sixteen had either tetralogy of Fallot, pulmonary atresia with VSD, or hypoplastic right heart syndrome. Four had more complex defects. Ten (50%) have died and an actuarial survival curve is shown (Fig. 2).

Nonstructural cardiorespiratory problems. The 50 patients with nonstructural cardiorespiratory problems were grouped according to the main problem at the time of first attendance. Twenty-six patients were referred because of the presence of cyanosis, and 4 died. In 18 cyanotic congenital heart disease was excluded by clinical examination and non-invasive investigation. Eight underwent cardiac catheterisation to exclude structural cardiac defects because

Fig. 2 Actuarial analysis of survival for 20 neonates undergoing aorticopulmonary anastomosis. Complication refers only to specific complications which would increase substantially the technical difficulty of further surgery. Figures in brackets indicate the number of patients alive at 12, 24, and 36 months of age.

of cyanosis persisting despite the administration of high oxygen concentrations. Thirteen patients each had a history of perinatal asphyxia, 5 were preterm, and 3 were delivered by caesarean section.

Fourteen were referred because of persistent tachpnoea. One was shown to have congenital lobar emphysema and a second had a mediastinal cyst compressing the right bronchus. Cardiac catheterisation was performed in one neonate with primary pulmonary hypertension. This infant died 2 months later. Four of the remaining 11 neonates were delivered by caesarean section, 2 had a history of perinatal asphyxia, and one was preterm. Two of these patients died.

Ten neonates presented with congestive cardiac failure and ST- and T-wave changes on the electrocardiogram. Eight had features consistent with a diagnosis of transient myocardial ischaemia.⁴ All recovered after treatment. The 2 remaining patients, both of whom underwent cardiac catheterisation, have primary myocardial disease.

Arrhythmia. Four of the 11 patients referred because of the presence of an arrhythmia had only isolated ectopic beats. Seven presented in congestive cardiac failure with a supraventricular tachycardia. All needed treatment, including one who required the insertion of a temporary transvenous pacemaker wire for overdrive ventricular pacing. At their most recent review, all were symptom free.

Noncardiorespiratory problem. Thirteen (4%) neonates had problems unrelated to the cardiovascular or respiratory system. Three seen on the first day of life were found to have septicaemia and died despite treatment. All presented with circulatory failure, hypotension, and cyanosis, and 2 had a history of prolonged rupture of membranes before delivery. One neonate with ascites died within 24

hours of admission and despite examination at necropsy no clear diagnosis was established. A cerebral arteriovenous malformation was demonstrated by cardiac catheterisation in one patient, and the remaining patients had innocent systolic murmurs.

Discussion

Neonates presenting with congenital heart disease are more likely to have a severe and perhaps untreatable malformation than patients presenting later in childhood, and the mortality is correspondingly high. Many will have other congenital anomalies or perinatal problems which influence survival. Nevertheless, during the last 10 to 15 years the mortality has fallen considerably.⁵ This change may be attributed to the earlier recognition and referral of these patients and to specific improvements in surgical technique.¹ However, a number of important problems remain. Twenty-nine (12%) of our patients were not regarded as suitable for surgical treatment. Most had either the hypoplastic left heart syndrome or visceral heterotaxia (asplenia syndrome), and complex cardiac anomalies. Although attempts have been made to palliate these infants we do not believe that the results of palliation or the long-term prospects for correction justify surgical intervention in the neonatal period. A few patients (Fig. 1) were offered palliative surgery in infancy even though the prospects for eventual repair seemed remote.

The majority of patients underwent repair as a primary procedure (or are awaiting primary repair electively later in childhood), but a significant proportion (Fig. 1) had a preliminary palliative procedure. Most had defects for which definitive surgery in infancy is not yet possible, but in particular circumstances some patients who might have undergone primary repair were submitted to initial palliation. Three infants, each with a VSD and weighing less than 3.5 kg, underwent banding of the pulmonary artery, and 5 patients with tetralogy of Fallot had an aorticopulmonary anastomosis. Recent surgical practice with regard to symptomatic infants with tetralogy of Fallot has varied considerably.^{6,7} We have followed a selective policy,⁸ reserving primary correction for cases with favourable anatomy but preferring palliative aorticopulmonary anastomosis to promote growth of hypoplastic pulmonary arteries. Conventional aorticopulmonary anastomosis in neonates is technically difficult and is associated with significant problems.⁹ The survival curve for our patients who underwent aorticopulmonary anastomosis at this age (Fig. 2) shows a cumulative mortality associated with failure of the

shunt to provide adequate palliation. Two survivors have complications that will increase the hazards of further surgery. In view of this experience, other procedures have been adopted and are currently under assessment. For patients with tetralogy of Fallot, open infundibulectomy with transannular patching¹⁰ offers some advantage in avoiding distortion of the pulmonary artery branches. In the case of patients in whom the pulmonary blood flow is dependent on patency of the ductus arteriosus, treatment with oral prostaglandin may be used to maintain an adequate pulmonary blood flow for a period of weeks or even months.¹¹ Surgical treatment, whether conventional palliation or primary repair, can then be performed in a larger patient with a greater chance of success.

For some defects, notably transposition of the great arteries and coarctation of the aorta, the prospects for survival among patients presenting as neonates are now good, in marked contrast to the results achieved before 1970.¹² Rowe and Vlad¹² showed an improvement in prognosis for patients with transposition dating from the late 1960s after the development of balloon atrial septostomy and Mustard's operation. For infants with coarctation of the aorta, they¹² were unable to record any significant improvement in outlook among patients seen between 1948 and 1968. Similarly the report of the New England Regional Infant Cardiac Program¹ concluded that little progress in the management of this lesion had been made between 1969 and 1974. It is not possible to compare our results with the New England data because the age range was different and the fact that we included patients with additional complex intracardiac anomalies within the coarctation group. The probability of survival at age 3 years for all our patients with coarctation is 64%. If the patients with complex additional problems are excluded (but retaining patients with ventricular septal defect and aortic or mitral valve lesions) the probability of survival to 3 years of age becomes 81%. This may be compared with a crude first year mortality of 47% calculated from the New England data¹ for a group of patients with comparable defects seen during the period 1969 to 1974. Some of this improvement may be related to the effective relief of the coarctation obtained by using the left subclavian flap aortoplasty.¹³ However, 18% of the patients in the New England study died before surgery. Only one of our patients who was considered operable died without operation, and it is probable that the early referral of infants for investigation and treatment has contributed appreciably to the results achieved.

Our present results show a similar trend for infants with tetralogy of Fallot, hypoplastic right

heart syndrome, and some defects within the miscellaneous category of Table 4. Although there are only 4 infants with total anomalous pulmonary venous return, all survived and the improvement in outlook for this defect which has taken place during the last 10 years has been particularly gratifying in view of the excellent long-term prognosis after successful surgery.¹⁴

Only 6 patients with an isolated patent ductus arteriosus were seen. This contrasts with the experience in Toronto reported by Izukawa and colleagues.⁵ Since 1978 the number of preterm infants with a patent ductus arteriosus referred to the Royal Liverpool Children's Hospital has increased but still does not approach the frequency with which these cases are seen in Toronto. This difference probably is related to the close relationship between the cardiac unit and the tertiary care perinatal unit in Toronto. In such circumstances a large number of low birthweight infants with signs of a patent ductus arteriosus will be seen for assessment and possible treatment whereas in Liverpool only those infants likely to require operation appear to have been referred. Several infants with unequivocal evidence of a patent ductus were grouped as non-structural cardiorespiratory problems, since the presence of the ductus was an incidental finding during the course of the illness and specific treatment was unnecessary.

Several authors have stressed the importance of early referral of infants with congenital heart disease if salvage of all potentially treatable cases is to be achieved. However, a number of newborn infants develop signs and symptoms which mimic the presence of major congenital cardiac defects^{4 15 16} and the referral of some of these infants to specialised centres appears to be inevitable since differentiation from structural congenital heart disease may be difficult. These infants now make a significant contribution to the work load of many centres.¹⁷ Many infants in this group have suffered perinatal asphyxia or have been delivered by caesarean section. A history of this kind should alert the physician to the possibility of a transient problem but it is not sufficient in itself to exclude the presence of a major cardiac defect. In several neonates who presented with cyanosis we were able to exclude cyanotic congenital heart disease by the response of the baby to breathing a high ambient oxygen concentration and we would stress the value of this simple test¹⁸ in differentiating cyanotic congenital heart disease from other causes of cyanosis. During the period covered by this report 13 (17%) patients with nonstructural cardiorespiratory problems underwent cardiac catheterisation to exclude a structural defect. Two-dimensional echocardiography offers a safe, non-invasive, and reliable means of determining cardiac

anatomy in the newborn period¹⁹ and it is thought that very few of these neonates would now be subjected to cardiac catheterisation solely to exclude a structural defect.

With early referral and prompt and accurate diagnosis and treatment, a high proportion of neonates with congenital cardiac defects will survive. This is particularly true of patients with transposition, coarctation, total anomalous pulmonary venous return and, to a lesser extent, Fallot's tetralogy. Although we have not, in this paper, attempted to assess morbidity among survivors, we are aware of some who have a significant handicap. There is evidence to show that open heart surgery can be performed safely in infancy and that residual handicaps are often related to events occurring before operation.²⁰ For maximal salvage of infants with congenital heart disease to be achieved with minimal morbidity, close co-operation between paediatrician and paediatric cardiologist is essential. A considerable part of the work load of a supraregional paediatric cardiac centre is concerned with the care of critically ill neonates, many of whom will have major problems outside the cardiovascular system. In view of these facts it is clear that a supraregional paediatric cardiac unit should have the expertise to deal not only with the cardiac defects but also with the wide range of neonatal problems which such patients may develop. The support of specialist anaesthetic and ancillary services is essential and unless such skills are available at all times optimal results will not be obtained.

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