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# Developmental Outcome in Children Undergoing Surgery with Profound Hypothermia

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The use of profound hypothermia with circulatory arrest is a recognized technique for the correction of cardiac defects in infants. Previously, we described its rationale and technique and concluded from our studies of developmental outcome that profound hypothermia can be used safely.[1] This view has been shared by some researchers,[2,3] while others[4] reported adverse effects of this technique on the subsequent psychomotor development in their patients. Animal studies[5–7] have not provided unanimous conclusions.

The present study attempts to resolve this controversy by comparing the preoperative developmental status of a series of patients with the postoperative developmental outcome.

## METHODS

Over a 3-yr period, one of us (M.J.A.B.) reviewed the waiting list of patients coming for cardiac surgery and wrote to the parents of all patients under 2 yr of age to obtain informed consent for their participation. All patients were included in the study if their parents consented, cardiopulmonary bypass was used with or without hypothermia and circulatory arrest, and the child survived the operation and returned for the postoperative assessment. Only 36 (24 male and 12 female) met all these conditions. Another 35 children were assessed preoperatively but did not survive, did not undergo a procedure involving cardiopulmonary bypass, or did not return for postoperative assessment. Some other children had been excluded from the preoperative assessment because they lived so far away that they were unlikely to return to our hospital for follow-up.

Our anesthetic technique has not changed in any major aspect since it was described in our previous study.[1] Our criterion for use of circulatory arrest under profound hypothermia is patient's weight <10 kg. Because the patient's weight was not available to us at the time the family was contacted, 26 patients subsequently had surgery under profound hypothermia with circulatory arrest, and the remaining ten patients (weight >10 kg) had surgery under continuous cardiopulmonary bypass with various degrees of hypothermia but without circulatory arrest. The latter group was studied for comparison, although the primary focus of the analyses and conclusions was on the 26 patients who experienced profound hypothermia and circulatory arrest.

Developmental examinations were performed by one of us (K.H.-I.), a pediatrician specializing in developmental pediatrics, who was unaware of the type of cardiopathy, 24–48 h before surgery. The examination was scheduled in the early morning at a time when the patient was not fatigued and had not had any prior procedures (such as cardiac catheterization). During the examination at least one parent was present. The assessment included unstructured observations of the child's behavior and developmental examination on the *Revised Yale Developmental Schedules*. This test assesses motor, adaptive, language, personal, and social development. Results are expressed as the developmental quotient (DQ), which is the ratio of developmental age to chronologic age. DQs between 90–110 are considered average, the lower end of the normal distribution being 75. The examiner then completed a physical and neurologic assessment of the child. An open-ended interview with the parent(s) provided information about the child's behavior at home and the family environment.

All children were reassessed by the same examiner between 4–29 months after their surgery. DQ changes ≤10 in either direction were considered clinically insignificant. Indeed, while the DQ of a normative population remains constant throughout childhood, fluctuations of that magnitude are expected.[8]

No child was excluded from the study because of preexisting associated physical or neurologic handicaps. Patient 21 had trisomy 21; patient 30 was the dysmorphic and retarded child of an adolescent single mother of limited intelligence; and patient 32 was retarded and microcephalic, and presented with left hemiparesis.

Socioeconomic status is believed to affect development, as children belonging to higher socioeconomic groups

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TABLE 1. Data of Patients Undergoing Profound Hypothermia

| Patient | Sex | Diagnosis | Social Class | Age at Examination (month) | | Developmental Quotient | | Difference in Developmental Quotient | Arrest Time (min) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Preoperative | Postoperative | Preoperative | Postoperative | | |
| 1 | F | VSD | IV | 21 | 28 | 95 | 95 | 0 | 56 |
| 2 | M | TGV | IV | 11 | 15 | 102 | 110 | +8 | 47 |
| 3 | M | TGV | IV | 11 | 23 | 86 | 87 | +1 | 43 |
| 4 | M | PS, ASD | IV | 6 | 13 | 110 | 105 | −5 | 10 |
| 5 | F | TGV | IV | 8 | 25 | 98 | 94 | −4 | 58 |
| 6 | M | TGV | IV | 16 | 45 | 95 | 98 | +3 | 50 |
| 7 | M | TGV | IV | 8 | 26 | 94 | 86 | −8 | 66 |
| 8 | F | AV canal | IV | 21 | 31 | 108 | 95 | −13 | 74 |
| 9 | M | TGV | III | 10 | 21 | 92 | 108 | +16 | 56 |
| 10 | M | TGV | IV | 11 | 25 | 92 | 95 | +3 | 43 |
| 11 | M | TGV | II | 13 | 33 | 80 | 88 | +8 | 45 |
| 12 | M | TGV | IV | 13 | 30 | 92 | 92 | 0 | 51 |
| 13 | F | VSD | III | 18 | 35 | 62 | 85 | +23 | 39 |
| 14 | M | TGV | IV | 12 | 18 | 75 | 80 | +5 | 62 |
| 15 | M | TGV | III | 9 | 13 | 85 | 92 | +7 | 47 |
| 16 | F | TGV | IV | 19 | 25 | 83 | 95 | +12 | 59 |
| 17 | M | TGV | IV | 18 | 36 | 90 | 98 | +8 | 55 |
| 18 | F | VSD | IV | 10 | 17 | 95 | 105 | +10 | 39 |
| 19 | M | TGV | IV | 9 | 30 | 90 | 94 | +4 | 24 |
| 20 | M | TGV | IV | 14 | 24 | 82 | 88 | +6 | 61 |
| 21 | F | VSD | III | 19 | 30 | 57 | 58 | +1 | 51 |
| 22 | F | TGV | IV | 15 | 24 | 112 | 96 | −16 | 55 |
| 23 | M | TGV | III | 10 | 15 | 97 | 90 | −7 | 63 |
| 24 | M | VSD | III | 17 | 23 | 88 | 88 | 0 | 57 |
| 25 | F | TGV | IV | 15 | 29 | 89 | 94 | +5 | 46 |
| 26 | M | VSD | III | 11 | 28 | 90 | 92 | +2 | 50 |

See text for abbreviations.

generally fare better on several developmental parameters, particularly language and cognitive skills. Therefore, we assessed the families' social status, using the Hollingshead and Redlich classification.[9] This classification is based on measures of parental education, profession, income, and place of residence, the highest class being I.

Student's $t$ test for paired samples was used to determine whether the mean change in DQ differed significantly from zero. Sample size calculations were done to determine the power of the significance test, given the number of observations and the variance of the outcome values. Student's $t$ test for independent samples was used to test differences of mean values between patient subgroups. Pearson product–moment correlation coefficients were computed to assess the potential relationship of DQ and DQ change with age, arrest time, and time between preoperative and postoperative assessment.

## RESULTS

*Profound Hypothermia and DQ (table 1).* The mean age of the 26 patients who satisfied the weight criterion for profound hypothermia and circulatory arrest was 13.3 months (range, 6–21 months). Their mean age at postoperative follow-up was 25.5 months (range, 13–45 months). Their DQs ranged from 57–112 (mean 90.0) preoperatively and 58–110 (mean 92.6) postoperatively. The difference (mean ± SD = 2.6 ± 8.5) was not significantly different from zero.

Four patients (patients 9, 13, 16, and 18) had higher DQs (16, 23, 12, and 10 points, respectively) postoperatively, while 20 remained at the same DQ or moved by less than ten points in either direction, a difference that is within expectations between two examinations.[8] Only two patients (patients 8 and 22) had significantly lower DQs postoperatively (13 and 16 points, respectively).

The change in DQ at the postoperative examination did not correlate significantly with the duration of circulatory arrest or the age of the patient. There was also no correlation with the preoperative DQ or the length of time between assessments.

The 19 cyanotic patients (18 with transposition of the great vessels [TGV], one with atrioventricular [AV] canal) had a mean DQ of 91.6 (range, 75–112) preoperatively and 93.7 (range, 80–110) postoperatively. For the 18 patients with TGV, mean DQ was 90.7 (range, 75–112) and 93.6 (range, 80–110) before and after surgery, respectively. The seven acyanotic children (six with ventricular septal defect [VSD], one with pulmonary stenosis [PS] and atrial septal defect [ASD]) had a mean DQ of 85.3 (range, 57–110) preoperatively and 89.7 (range, 58–105) postoperatively. (The mean DQ preoperatively and postoperatively is lower in the acyanotic group because of the inclusion of two severely developmentally handicapped

TABLE 2. Data of Patients Undergoing Cardiopulmonary Bypass

| Patient | Sex | Diagnosis | Social Class | Age at Examination (month) | | Developmental Quotient | | Difference in Developmental Quotient |
|---|---|---|---|---|---|---|---|---|
| | | | | Preoperative | Postoperative | Preop | Postop | |
| 27 | F | PS | IV | 18 | 25 | 88 | 90 | +2 |
| 28 | M | VSD | III | 23 | 41 | 91 | 100 | +9 |
| 29 | F | ASD | IV | 10 | 15 | 118 | 115 | −3 |
| 30 | M | VSD | V | 33 | 47 | 62 | 65 | +3 |
| 31 | F | T of F | III | 40 | 59 | 108 | 112 | +4 |
| 32 | M | TGV | III | 19 | 24 | 56 | 55 | −1 |
| 33 | M | T of F | II | 37 | 54 | 112 | 115 | +3 |
| 34 | M | ASD | II | 24 | 43 | 115 | 114 | −1 |
| 35 | M | ASD | IV | 21 | 25 | 95 | 95 | 0 |
| 36 | M | VSD | III | 31 | 40 | 88 | 92 | +4 |

See text for abbreviations.

children but the change in DQ of this group compared with the change in DQ of the cyanotic group is not statistically significant.) Thus, no evidence suggested that patients with cyanosis had lower DQs or any change in postoperative DQ.

*Cardiopulmonary Bypass and DQ (table 2).* The mean age of our ten patients who met all of our criteria and underwent continuous cardiopulmonary bypass with hypothermia but no circulatory arrest (because their weight was >10 kg) was 25.6 months (range, 10–40 months). Their mean age at postoperative follow-up was 37.3 months (range, 15–59 months). Their mean preoperative and postoperative DQs were 93.3 (range, 56–118) and 95.3 (range, 55–115), respectively. These patients were significantly older than the main study group ($P < 0.01$) but there was no significant difference in the other variables: preoperative DQ, postoperative change in DQ, and length of time between assessments.

*Neurologic Findings.* Microcephaly (head circumference <2nd percentile) was noted preoperatively in five subjects (patients 7, 16, 18, 20, and 32; age range 8–19 months). Of those, four remained microcephalic postoperatively and the fifth (patient 20) moved to the 25th percentile. Patient 32 was mildly retarded, three others (patients 7, 16, and 20) had a low-normal DQ, and patient 18 had an average DQ. One patient (patient 6) had a head circumference >98th percentile. Generally, however, there was a tendency to small head circumference, with 27 (75%) of the subjects below the 50th percentile preoperatively and postoperatively. In 17 patients (47.2%), head circumference was at a slightly higher percentile postoperatively, while in two it was slightly lower, but within normal limits.

One subject (patient 11) had significant preoperative hypotonia of central origin, and five subjects (patients 9, 13, 14, 19, and 32) showed evidence of mild hemiparesis postoperatively, but in all except one (patient 9), the hemiparesis was noted preoperatively.

*Social Class and DQ.* The three patients in social class II had a preoperative mean DQ of 102.3 and a postoperative mean of 105.7.

The 11 patients in social class III had a mean DQ of 83.1 preoperatively and 88.3 postoperatively. Inclusion of the two developmentally handicapped children (patients 21 and 32) in this group accounted for the low mean DQ in comparison with the 21 patients in social class IV, who had 94.7 preoperatively and 95.6 postoperatively. There was only one patient in class V.

*Summary of Findings.* Standard sample size calculations showed that, using a paired $t$ test and a significance level of 0.05, a sample of 22 patients would provide a 95% probability of detecting a mean postoperative change in DQ ≥7. The sample size in this study was 26, the mean change in DQ was an increase of 2.6, and the study group results were very similar to those in the ten patients who did not experience profound hypothermia with circulatory arrest.

The hypothesis that the use of circulatory arrest and hypothermia has no effect on DQ appears to be well supported by the study data.

## DISCUSSION

This study is the first to use patients as their own controls in assessing the effects of profound hypothermia with circulatory arrest on psychomotor development. Because most cardiac patients are compromised by hypoxia, cerebrovascular accidents, debilitating illness, repeated and/or prolonged hospitalizations, and various other factors, it is not relevant to compare their developmental progress with the development of their normal siblings or the intellectual status of their parents. Other advantages of the present study were that all neurodevelopmental assessments were performed by the same examiner using the same comprehensive methods of evaluation.

Our results seem to indicate that there are no harmful effects on DQ from circulatory arrest during profound hypothermia in early infancy up to 2 yr. We found no statistical significance in differences between preoperative and postoperative developmental status, regardless of the factors considered. The age of our patients at both preoperative and postoperative examinations was considerably younger than reported by other authors.[2-4] Analysis of our developmental data indicated that the most common deficits were in language and gross motor areas. Perhaps this particular developmental profile reflected the young age of our subject group, whereas other areas of deficit, such as perception, cognition, and attention, could become more prominent if the group is examined at a more advanced age.

Neither the period of the total circulatory arrest nor the age at the time of surgery seemed to be adversely related to the developmental outcome. Recent data indicate that delaying repair in cyanotic heart disease is associated with progressive delay in mental development.[10] Our data indicate that repair of complex lesions in early infancy under circulatory arrest with deep hypothermia does not appear to be associated with developmental delay in the first 2 yr of life. Therefore, postponing surgery for correction of complex lesions offers no advantage to the infant.

The inclusion of developmentally handicapped children accounted for the relatively low mean DQ in the social class III and in the acyanotic patients. Because the aim of the study was to assess the effects of circulatory arrest during profound hypothermia on subsequent development in comparison with the preoperative state, we think that such children should not be excluded from our sample on the basis of their preoperative developmental status.

Clinical neurologic findings were not indicative of deleterious central nervous system effects following total circulatory arrest except in patient 9, who had hemiparesis postoperatively. The microcephaly found preoperatively in five patients might have been due to some degree of chronic hypoxic cerebral atrophy. In the future it would be interesting to conduct neuroradiology imaging studies to clarify this point and follow its evolution postoperatively.

The results of our study continue to encourage us that the use of circulatory arrest during profound hypothermia with cardiac surgery does not have major deleterious effects on the development of infants and small children.

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