Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 50, No. 13, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.05.040

Causes of Late Deaths After Pediatric Cardiac Surgery

A Population-Based Study

Heta P. Nieminen, MD,* Eero V. Jokinen, MD,† Heikki I. Sairanen, MD*

Helsinki, Finland

Objectives We examined the causes and modes of late death after pediatric cardiac surgery.

Background The late mortality of patients operated on for congenital heart defect (CHD) is comprehensively unexamined. In this study, the causes of death were examined to obtain further knowledge of the morbidity of the patients.

Methods We studied all late deaths of patients operated on for CHD in Finland during the years 1953 to 1989. We calculated the survival of patients, identified the causes of deaths from death certificates, and examined the modes of CHD-related deaths. We compared the survival and the causes of non–CHD-related deaths to those of the general population.

Results Of the 6,024 patients who survived their first operation, 592 (9%) died during the 45-year follow-up period. The progress of treatment was seen in the survival of the patients operated on in different decades. The cause of death was confirmed with postmortem examination in 474 (81%) cases. The majority of patients (397, 67%) died owing to the CHD. Furthermore, non–CHD-related mortality was twice as high (risk ratio 1.9, 95% confidence interval 1.5 to 2.4) as expected. The main mode for CHD-related death was heart failure (40%). Other modes included perioperative (26%), sudden (22%), and cardiovascular (12%) deaths. The number of deaths caused by neurological and respiratory diseases was higher and the number of accidental deaths was lower than expected.

Conclusions The survival of patients was lower than that of the general population (relative 45-year survival 89%). Most patients died owing to CHDs, but non–CHD-related mortality was also high. (J Am Coll Cardiol 2007;50:1263–71)

This present study is the first population-based evaluation of the causes of late death after pediatric cardiac surgery. The comprehensive coverage and reliability of the Finnish population register and the Finnish research register of pediatric cardiac surgery enabled us to complete this unique study. Our study includes all children operated on for congenital heart defects (CHDs) in Finland during the years 1953 to 1989, and we were able to confirm the late outcome of 96% of them.

For the first time, the causes of death of CHD patients could be compared with those of the general population. Previously, the causes of late deaths were reported incompletely only as part of follow-up investigations (1–5).

The results of pediatric cardiac surgery are good, but mortality still remains higher than in the general population (6,7). Most of the patients die owing to their cardiac defect. With active and well-timed interventions, however, the lifespan of these patients can be prolonged. Therefore, an understanding of the causes and the mechanisms of death play an important role in improving late prognosis.

The gender difference in the late mortality of CHD patients has not yet been studied. Gender could be a factor in the prognosis of such patients, because significant differences have been found in the mechanisms of arrhythmias between genders (8), and sudden death due to coronary heart disease is more common among male patients (9).

Methods

According to the Finnish Research Registry of Pediatric Cardiac Surgery, a total of 7,240 cardiac operations were performed on 6,460 children in Finland during the years 1953 to 1989.

The current state of patients on the closing day of this study (October 28, 1998) and the dates of death and emigration were obtained from the Finnish Population Registry Centre. The causes of late death were identified from death certificates obtained from Statistics Finland. If something unclear ap-

From the Departments of *Surgery and †Cardiology, Hospital for Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland. This work was supported by the Finnish Slot Machine Association, Finnish Association for Heart Children and Adults, Finnish Foundation for Cardiovascular Research, Finnish Foundation for Pediatric Research, and the Finnish Medical Foundation.

Manuscript received December 12, 2006; revised manuscript received April 27, 2007, accepted May 22, 2007.

Abbreviations and Acronyms

ASD = atrial septal defect
CHD = congenital heart defect
CI = confidence interval
CoA = coarctation of aorta
PDA = patent ductus arteriosus
PS = pulmonary stenosis
RR = relative risk
SMR = standardized mortality ratio
TGA = transposition of the great arteries
TOF = tetralogy of Fallot
UVH = univentricular heart
VSD = ventricular septal defect

peared in the death certificate, we examined the patient's medical records.

The patients were divided into different heart defect groups according to a previously published hierarchy based on their primary diagnosis (6). We investigated separately the mortality of patients with patent ductus arteriosus (PDA), coarctation of aorta (CoA), atrial septal defect (ASD), ventricular septal defect (VSD), tetralogy of Fallot (TOF), transposition of the great arteries (TGA), and univentricular heart (UVH) who had survived their first operation (i.e., were alive >30 days after).

The deaths were first divided by their main cause into CHD-related and non–CHD-related deaths; CHD-related causes included deaths caused by diseases with ICD-10 (International Classification of Diseases) diagnosis numbers Q20 to Q28 (in old cases ICD-9 numbers 745 to 747). All other causes were classified as non–CHD-related.

An existing classification of the cardiac cause of deaths (10) served to divide the CHD-related deaths into 4 groups: heart failure, sudden, perioperative, and cardiovascular death. Sudden death was defined as death due to cardiovascular causes within 1 h of onset (or significant worsening) of symptoms or unwitnessed death during sleep (11). The perioperative deaths included all early postoperative (within 30 days) deaths due to patient's second, third or fourth operation. The cardiovascular group included all CHD-related deaths that could not be classified into the other 3 groups.

This study was conducted with the permission of the Finnish Ministry of Social Affairs and Health.

Statistical methods. Time-related mortality was assessed with survival analysis. Survival was calculated for all patients and separately for gender and diagnostic groups. The survival rate of patients operated on in different decades (1950s to 1980s) was also calculated separately to evaluate the progress of treatment. We compared the survival rates of different gender and decade groups and analyzed survival with and without non–CHD-related causes of death. The survival statistics were calculated with SURV3, the latest version of the survival analysis package developed at the Finnish Cancer Registry (12).

We compared each patient's individual survival with that of the age-, gender-, and time-matched general population. For every patient and for every year of follow-up, we obtained the mortality of the general population. The expected probability of surviving 1 year was obtained for all individuals who, regardless of their survival status, were not censored before the beginning of the interval. We used the Hakulinen method (13) for combining the individual information with an estimate for the expected survival of the group.

The relative risk (RR) (with 95% confidence intervals [CIs]) analysis was used in evaluating the differences between observed versus expected numbers of deaths and between genders. If the CI of RR did not include 1.0, the difference was considered significant. Furthermore, the narrower the range of interval, the more significant was the difference.

The non–CHD-related causes of death of the patients were compared with the cause-specific mortality of the general population. The results appear as numbers of deaths observed and expected and as standardized mortality ratios (SMRs). The SMR expresses the ratio of observed causes of death to that expected on the basis of overall mortality rates in the general Finnish population. The expected numbers of deaths were standardized for age, gender, and time. The Poisson distribution was used to calculate the 95% CI. The significance of SMR was calculated with the approximation of Byar for the exact Poisson test (14).

Results

On the closing day of the study, the condition of all 6,460 operated patients was confirmed from the population registry: 5,193 (80%) patients were known to be alive and living in Finland. Altogether, 1,028 (16%) patients had died; 436 (7%) died early (≤30 days), and 592 (9%) died late (>30 days) after the first operation. The outcome of 239 (4%) surviving patients remained unknown, because they were either unidentifiable from the population registry or had emigrated. However, 134 emigrated patients were included in the survival analysis, because their emigration date was known and served as the censoring date. Thus, the survival analysis included altogether 5,919 patients (98% of the 6,024 patients), all who were alive, had emigrated, or died late after surgery.

Of these 5,919 patients, 2,732 were male and 3,187 (54%) female. The CHDs were distributed unequally between genders. The vast majority (71%, 1,377 of 1,932) of the PDA patients and 60% (461 of 767) of ASD patients were female. Male patients more often exhibited CoA (66%, 583 of 880), TOF (60%, 246 of 413), and TGA (66%, 172 of 259). The proportion of male and female patients with VSD and UVH were equal.

A total of 592 patients died late after surgery. The mortality was highest shortly after the first operation. One hundred sixty-four (28%) deaths occurred during the first year, and almost one-half of them (n = 79, 48%) occurred during the first 3 months after surgery. The patients that died were significantly younger at the time of their first operation than the patients that survived, 3.9 (median 1.3, range 0 to 15) years versus 5.4 (median 5.1, range 0 to 15) years ($p < 0.001$), respectively. The mean age of late death