

## Original Article

# Morbidity after paediatric cardiac surgery assessed with usage of medicines: a population-based registry study

Heta P. Nieminen,<sup>1</sup> Heikki I. Sairanen,<sup>1</sup> Eero V. Jokinen<sup>2</sup>

<sup>1</sup>Department of Surgery; <sup>2</sup>Department of Cardiology, Hospital for Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland

**Abstract Objective:** To examine the overall morbidity of patients who underwent surgery for congenital cardiac defect during childhood. **Background:** A congenital cardiac defect treated with surgery is seldom totally cured. The incidence of residua, sequelae, and comorbidity is quite high. The morbidity has not been thoroughly examined. **Methods and patients:** Medication was used as an indicator of morbidity. Data from the Finnish Research Registry of Paediatric Cardiac Surgery were linked to data from the medication registry of Finland's Social Insurance Institution. This study includes 5116 patients with a mean age of 33.5 (ranged from 14.7 to 64.8) years, who had undergone surgery for congenital cardiac defect between 1953 and 1989. The use of medicines among patients in 2004 was compared with 10232 age- and sex-matched control subjects. **Results:** The overall use of medicines was frequent; 62% of patients and 53% of controls had purchased at least one prescribed medicine (risk ratio: 1.2, 95% confidence interval: 1.1–1.2). The number of patients using cardiovascular medicines (17%) and anti-thrombotic agents (5%) was higher than that of control subjects (risk ratio: 2.2 and 8.4). In addition, the patients needed medicinal care for epilepsy (3%), asthma (7%), and psychiatric diseases (10%) more often than did controls (risk ratio: 2.2, 1.5, and 1.3, respectively). **Conclusion:** Patients operated on for congenital cardiac defect had more chronic diseases and used more medicines than did controls.

Keywords: Congenital cardiac defects; cardiovascular medication; comorbidity; asthma; epilepsy; psychiatric diseases

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**A** CONGENITAL CARDIAC DEFECT TREATED WITH surgery is seldom totally cured. The incidence of residua, sequelae, and comorbidity is quite high. Re-operations are often needed, and patients even more often require medical treatment to maintain their physical competence.

Patients with cardiac defects often suffer from additional diseases. In addition, various genetic syndromes and other congenital malformations are common. There is also strong evidence of a relationship between cardiac defects and neurological sequelae.

The aim of this population-based follow-up study was to assess the actual prevalence of health problems requiring medicinal treatment after paediatric cardiac surgery.

## Methods

This is a retrospective follow-up study of the patients operated on for congenital cardiac disease. The usage of medicines and prevalence of chronic diseases during the year 2004 served as the outcome measure.

According to the Finnish Research Registry of Paediatric Cardiac Surgery, a total of 7240 cardiac operations were performed on 6460 children in Finland during the years 1953–1989. According to the Finnish Population Registry, on the closing day of the study, that is, on 23 August, 2004, 5116 (79%) of them were alive and living in Finland. Overall mortality was 18% (1142/6460). The outcome of 203 (3%) patients was unknown.

Data on the patients' medication were obtained from the medication registry of the Finnish Social Insurance Institution. The registry contains information on the

Correspondence to: H. P. Nieminen, Piippukalliontie 33, FIN - 36270 Kangasala, Finland. Tel: +358 40 8649774; Fax: +358 3 3769420; E-mail: heta.nieminen@elisanet.fi

details and costs of purchases of prescribed medicines. The records are based on on-line computerised information provided to the Social Insurance Institution by all Finnish pharmacies. In the registry, medications are categorised according to the Anatomical Therapeutic Chemical classification.<sup>1</sup> Use of a medication was defined as at least one purchase during the year 2004.

The medication registry did not include knowledge of the indication of the medicine. The knowledge of chronic diseases of the population was obtained from the registry of the entitlements to special reimbursement also maintained by the Social Insurance Institution. In Finland, individuals with certain specific chronic diseases (nearly 80 diseases) are entitled to special reimbursement for the drug treatment costs of that disease. Patients apply to the Social Insurance Institution for entitlement to special reimbursement. The application requires a certificate from a physician giving the details of diagnosis and treatment for the disease.

Purchases and entitlements to special reimbursements are linked to the social security numbers of individuals. Identification numbers also enable the information from the Social Insurance Institution to be linked to the Research Registry of Paediatric Cardiac Surgery.

We studied differences in the usage of medications between patients with various diagnoses. Patients were divided into groups according to their main diagnosis based on a previously published hierarchy.<sup>2</sup> The groups studied separately were patent ductus arteriosus, coarctation of the aorta, atrial septal defect, ventricular septal defect, tetralogy of Fallot, transposition of the great arteries, and univentricular heart.

For each patient in our study population, two matched control subjects were chosen from the population registry. The matching criteria were sex, age (plus or minus 2 years) and the hospital district in which the patient lived.

The Finnish Research Register of Paediatric Cardiac Surgery was established with the permission of the Finnish Ministry of Social Affairs and Health. The Social Insurance Institution approved the use of the data from the medication registry.

### *Statistical methods*

In this follow-up study, the prevalence of chronic diseases and the use of medications of patients were compared to that of the control subjects. Differences were calculated as risk ratios with 95% confidence intervals and were considered significant if the confidence limit did not include the value of 1.00. Student's *t*-test served in counting the difference between the mean ages of patients and controls.

## **Results**

This study included a total of 5116 patients who underwent surgery during 1953–1989. Their mean age at the first operation was 5.4 years with a median of 5.0 (ranged from 0 to 15) years. On the closing day of the study, the patients were on average of 33.4 years with a median of 32.7 (ranged from 14.7 to 64.8) years old, and their mean follow-up time was 28.1 with a median of 27 (ranged from 16.6 to 51.3) years. Altogether, 198 (3.8%) patients were mentally retarded. Most patients with mental disabilities had a genetic syndrome: 119 (2.3%) patients had Down's syndrome.

The patients studied had more entitlements to special reimbursements for medicines than did the controls, 30% (1550/5116) and 12% (1194/10,232), respectively (risk ratio: 2.60, 95% confidence interval: 2.43–2.78). The five most common chronic diseases among patients were cardiac failure (14%), hypertension (5%), asthma (5%), arrhythmias (3%), and epilepsy (3%). The controls most often had asthma (3%) and hypertension (3%). In all other diseases, the proportion of controls with a disease was less than 2% (Table 1).

Only 6 of the 20 most common diseases had the same prevalence within the patient population and control subjects. The patients' risk for diabetes, rheumatoid arthritis, inflammatory bowel diseases, coronary cardiac disease, severe dermatitis, and breast cancer was similar to that of controls (Table 1).

The patients' actual usage of medicines was somewhat higher than that of the control subjects. A total of 62% (3185/5116) of the patients had bought at least one prescribed medicine, whereas 53% (5462/10,232) of controls had purchased any medication (risk ratio: 1.16, 95% confidence interval 1.13–1.20) in 2004. Only patients with atrial septal defect used equal amount of medicines as controls (Table 2).

### *Cardiovascular medicines*

A total of 17% (855/5116) of the patients and 8% (791/10,232) of the control subjects used medications for cardiac diseases (risk ratio: 2.16, 95% confidence interval: 1.97–2.37; Table 3). Patients using cardiac medicines were younger than controls – their mean age at follow-up was 38.2 plus or minus 0.4 versus 44.9 plus or minus 0.4 years ( $p < 0.001$ ).

Patients using medication for cardiovascular diseases were older and had undergone surgery at an older age than the other patients; the mean age was 38.9 plus or minus 0.4 versus 32.3 plus or minus 0.2 years ( $p < 0.001$ ) and the mean age at the first operation was 6.4 plus or minus 0.2 versus 5.1 plus or minus 0.1 years ( $p < 0.001$ ), respectively.

Table 1. Prevalence of chronic diseases according to special medication reimbursement records.

Diseases	Patients (n = 5116)		Controls (n = 10,232)	
	n (%)	n (%)	n (%)	RR (95% CI)
Cardiac failure	692 (13.5)	12 (0.1)		115.3 (65.2–203.9)
Hypertension	273 (5.3)	257 (2.5)		2.12 (1.80–2.51)
Asthma	248 (4.8)	283 (2.8)		1.75 (1.48–2.07)
Arrhythmias	134 (2.6)	17 (0.2)		15.76 (9.53–26.1)
Epilepsy	133 (2.6)	110 (1.1)		2.42 (1.88–3.11)
Psychosis	97 (1.9)	115 (1.1)		1.69 (1.29–2.21)
Hypothyroidism	78 (1.5)	116 (1.1)		1.34 (1.01–1.79)
Diabetes	57 (1.1)	140 (1.4)		0.81 (0.60–1.11)
Rheumatoid arthritis	56 (1.1)	102 (1.0)		1.10 (0.79–1.52)
Hypogonadism	43 (0.8)	19 (0.2)		4.53 (2.64–7.76)
Anxiety disorders associated with mental retardation	29 (0.6)	17 (0.2)		3.41 (1.88–6.20)
Inflammatory bowel diseases	26 (0.5)	60 (0.6)		0.87 (0.55–1.37)
Coronary cardiac disease	26 (0.5)	34 (0.3)		1.53 (0.92–2.55)
Glaucoma	23 (0.4)	12 (0.1)		3.83 (1.91–7.70)
Status post-transplantation	16 (0.3)	5 (0.0)		6.40 (2.35–17.5)
Severe dermatitis	11 (0.2)	18 (0.2)		1.22 (0.58–2.59)
Hypopituitarism	11 (0.2)	1 (0.0)		22.00 (2.84–170.4)
Breast cancer	8 (0.2)	24 (0.2)		0.67 (0.30–1.48)
Gout	8 (0.2)	4 (0.0)		4.00 (1.21–13.3)
Hypoparathyroidism	7 (0.1)	0 (0.0)		–

95% CI = 95% confidence interval; RR = risk ratio

Table 2. Use of all medicines.

	Patients		Control subjects		RR (95% CI)
	All	n (%)	All	n (%)	
PDA	1759	1108 (63)	3518	2070 (59)	1.07 (1.02–1.12)
COA	797	491 (62)	1594	785 (49)	1.25 (1.16–1.35)
ASD	730	412 (56)	1460	804 (55)	1.02 (0.95–1.11)
VSD	617	379 (61)	1234	602 (49)	1.26 (1.16–1.37)
TOF	317	202 (64)	634	321 (51)	1.26 (1.12–1.41)
TGA	179	118 (66)	358	162 (45)	1.46 (1.25–1.70)
UVH	45	44 (98)	90	36 (40)	2.44 (1.89–3.16)
Misc	672	431 (64)	1344	677 (50)	1.27 (1.18–1.38)
All	5116	3185 (62)	10 232	5457 (53)	1.17 (1.14–1.20)

ASD = atrial septal defect; COA = coarctation of aorta; Misc = miscellaneous diagnosis; PDA = patent ductus arteriosus; RR = risk ratio; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; VSD = ventricular septal defect; 95% CI = 95% confidence interval

The proportion of patients using cardiovascular medicines was high in all diagnosis groups, varying from 11% to 82% (Table 4). The proportion was highest among patients with univentricular heart. Most patients with transposition of the great arteries (151/179, 84%) had undergone an atrial switch operation; 38% of them used cardiac medicines.

The actual usage of different medications is presented in Table 5. The group of serum lipid-reducing agents was the only group of cardiac medicines in which the proportion of users among patients and controls

was similar (risk ratio: 1.12, 95% confidence interval: 0.90–1.39).

The number of patients with entitlements to special reimbursement for cardiovascular disease medication was high in every cardiac defect group (Table 6). Hypertension was most common among patients with coarctation of the aorta (15%). The proportion of arrhythmias was greatest among patients with univentricular heart, transposition of the great arteries, and tetralogy of Fallot (27%, 9%, and 6%, respectively). Coronary cardiac disease was common among the patient and control population risk ratio 1.53, 95% confidence interval 0.92–2.55). Of the 26 patients with coronary disease, 4 (15%) had a cardiac transplantation. Surprisingly, none of the 16 patients who underwent arterial switch operation for transposition of the great arteries had coronary cardiac disease.

### Comorbidity

The health problems clustered. Altogether, 26% (397/1550) of patients and 19% (228/1194) of controls had entitlements to special reimbursement for at least two diseases. Even after omitting cardiac diseases, there were 110 patients with more than one chronic disease; 20% of all 540 patients had no entitlements to special reimbursement for cardiovascular medicines.

*Asthma.* The patients' risk ratio for asthma was 1.75 and 95% confidence interval was 1.48–2.07 (Table 1). Of the patients with asthma, 10% (26/248)

Table 3. Use of medicines.

Medicines used	Patients (n = 5116)	Controls (n = 10,232)	RR (95% CI)
	n (%)	n (%)	
Anti-infectives for systemic use	1555 (30.4)	2661 (26.0)	1.17 (1.11–1.23)
Musculo-skeletal system	905 (17.7)	1692 (16.5)	1.07 (0.99–1.15)
Non-steroidal anti-inflammatory agents	825 (16.1)	1559 (15.2)	1.06 (0.98–1.14)
Anti-gout preparations	22 (0.4)	14 (0.1)	3.14 (1.61–6.14)
Respiratory system	863 (16.9)	1568 (15.3)	1.10 (1.02–1.19)
Medicines for obstructive airway diseases	353 (6.9)	471 (4.6)	1.50 (1.31–1.71)
Cardiovascular system	855 (16.7)	791 (7.7)	2.16 (1.97–2.37)
Cardiac glycosides	112 (2.2)	2 (0.0)	112.00 (27.68–453.21)
Diuretics	176 (3.4)	84 (0.8)	4.19 (3.24–5.42)
Beta-blocking agents	475 (9.3)	384 (3.8)	2.4 (2.17–2.82)
Calcium-channel blockers	111 (2.2)	119 (1.2)	1.87 (1.44–2.41)
Agents acting on the rennin-angiotensin system	376 (7.3)	308 (3.0)	2.44 (2.11–2.83)
Serum lipid-reducing agents	125 (2.4)	224 (2.2)	1.12 (0.90–1.39)
Nervous system	766 (15.0)	1130 (11.0)	1.36 (1.24–1.48)
Anti-epileptics	153 (3.0)	142 (1.4)	2.15 (1.72–2.70)
Psycholeptics (anti-psychotics, etc.)	345 (6.7)	443 (4.3)	1.56 (1.36–1.79)
Psychoanaleptics (anti-depressants, etc.)	391 (7.6)	635 (6.2)	1.23 (1.09–1.39)
Genito-urinary system and sex hormones	454 (8.9)	833 (8.1)	1.09 (0.98–1.22)
Alimentary tract and metabolism	449 (8.6)	817 (8.0)	1.10 (0.98–1.23)
Medicines for acid-related disorders	255 (5.0)	484 (4.7)	1.05 (0.91–1.22)
Insulins and analogues	42 (0.8)	107 (1.0)	0.79 (0.55–1.12)
Oral blood glucose-lowering medicines	35 (0.7)	63 (0.6)	1.11 (0.74–1.68)
Dermatologicals	431 (8.4)	814 (8.0)	1.06 (0.95–1.18)
Blood and blood-forming organs	252 (4.9)	106 (1.0)	4.75 (3.80–5.95)
Anti-thrombotic agents	228 (4.5)	54 (0.5)	8.44 (6.29–11.34)
Systemic hormonal preparations, excluding sex hormones and insulins	233 (4.6)	353 (3.4)	1.32 (1.12–1.55)
Corticosteroids for systemic use	105 (2.1)	178 (1.7)	1.18 (0.93–1.50)
Thyroid therapy	120 (2.3)	163 (1.6)	1.47 (1.17–1.86)
Sensory organs	148 (2.9)	264 (2.6)	1.12 (0.92–1.37)
Anti-glaucoma preparations and miotics	21 (0.4)	13 (0.1)	3.23 (1.62–6.45)
Anti-neoplastic and immunomodulating agents	53 (1.0)	90 (0.9)	1.18 (0.84–1.65)
Anti-parasitic products, insecticides and repellents	36 (0.7)	94 (0.9)	0.77 (0.52–1.12)

95% CI = 95% confidence interval; RR = risk ratio

underwent surgery before the age of 1 month (risk ratio: 1.61, 95% confidence interval: 1.08–2.37), when compared to patients who underwent surgery later on. Among patients who underwent operation neonatally, the risk for asthma was highest among those with patent arterial duct (16/139, 12%) when compared to those with other cardiac defects (10/212, 5%; risk ratio: 2.46, 95% confidence interval 1.15–5.27). However, even after excluding all patients who underwent surgery neonatally, the risk ratio of asthma was 1.65 (95% confidence interval: 1.38–1.96) times higher than that among the controls. Cardiopulmonary bypass surgery had no impact on the patients' risk for asthma.

**Epilepsy.** Patients were at a 2.42 (confidence interval: 1.88–3.11) times higher risk for epilepsy than were the controls (Table 1). Altogether, 133 (2.6%) patients had epilepsy, of whom 23 (17%) had undergone cardiac surgery as neonates – risk ratio for other patients was 2.87 and 95% confidence interval was 1.85–4.43. There was no difference in the prevalence of epilepsy between the

patients with patent arterial duct and other neonatal patients. After excluding patients who underwent surgery neonatally, the risk of epilepsy remained 2.12 (95% confidence interval: 1.62–2.76) times higher than that among the controls. Open-heart surgery did not increase the risk for epilepsy.

Over one-fifth (23%, 31/133) of the patients with epilepsy were mentally retarded, most of whom had chromosomal abnormalities. However, even after exclusion of retarded patients, the number of patients with epilepsy was significantly higher than that of controls.

**Psychiatric disorders.** Altogether, 506 (9.9%) patients and 769 (7.5%) controls used medicines for psychiatric disorders (risk ratio: 1.32, 95% confidence interval: 1.18–1.46).

Depression was the biggest and most common mental health problem among both patients and controls. A total of 391 (7.6%) patients and 635 (6.2%) controls used anti-depressants (risk ratio: 1.23, 95% confidence interval: 1.09–1.39; Table 3).

A chronic disease increased the risk of depression among patients and controls. If a patient had an entitlement to special reimbursement for medication

Table 4. Use of all medicines for cardiovascular system in diagnosis groups.

	Patients			Control subjects			RR (95% CI)
	All	User	%	All	User	%	
PDA	1759	229	13	3518	392	11	1.17 (1.00–1.36)
COA	797	198	25	1594	111	7	3.57 (2.87–4.43)
ASD	730	78	11	1460	105	7	1.49 (1.12–1.96)
VSD	617	66	11	1234	51	4	2.59 (1.82–3.68)
TOF	317	62	20	634	41	6	3.02 (2.09–4.38)
TGA	179	66	37	358	6	2	22.00 (9.73–49.76)
UVH	45	37	82	90	4	4	18.50 (7.03–48.68)
Misc	672	119	18	1344	81	6	2.94 (2.25–3.84)
All	5116	855	17	10,232	791	8	2.16 (1.97–2.37)

ASD = atrial septal defect; COA = coarctation of aorta; Misc = miscellaneous diagnosis; PDA = patent ductus arteriosus; RR = risk ratio; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; VSD = ventricular septal defect; 95% CI = 95% confidence interval

of some chronic disease, the risk for using anti-depressants was 1.65 (95% confidence interval: 1.36–1.99) when compared to patients without chronic diseases (Table 7). The risk was even greater among the control population (risk ratio: 2.84, 95% confidence interval: 2.41–3.34). Symptomatic cardiac disease increased the risk for depression similarly among patients and controls: 15% of those persons with entitlement to special reimbursement for cardiovascular medicines also used anti-depressants (124/855 patients and 120/791 controls).

The patients' risk for psychosis was 1.69 (95% confidence interval 1.29–2.21) times higher than that of controls; 1.9% (97) of patients and 1.1% (115) of controls had an entitlement to special reimbursement for anti-psychotics (Table 1). The prevalence of psychosis was similar in cardiac defect groups.

*Other diseases.* Patients had hormone deficiencies more often than did controls (Table 1). Most of the patients with hormonal diseases had genetic syndromes. For instance, the difference in the prevalence of hypothyroidism disappeared when the patients with Down's

Table 5. Use of cardiac medicines in diagnosis groups.

Diagnosis	n	Mean age	Cardiac glycosides (%)	Diuretics (%)	Beta-blocking agents (%)	Calcium channel blockers (%)	Agents acting on renin-angiotensin system (%)	Serum lipid-reducing agents (%)
PDA	1759	37.2	4 (0)	50 (3)	123 (7)	33 (2)	92 (5)	51 (3)
COA	797	32.9	11 (1)	26 (3)	115 (14)	42 (5)	110 (14)	25 (3)
ASD	730	34.7	4 (1)	12 (2)	47 (6)	6 (1)	28 (4)	17 (2)
VSD	617	28.8	11 (2)	12 (2)	39 (6)	9 (1)	26 (4)	5 (1)
TOF	317	32.1	11 (3)	17 (5)	36 (11)	1 (0)	17 (5)	6 (2)
TGA	179	23.9	30 (17)	15 (8)	28 (16)	2 (1)	46 (26)	1 (1)
UVH	45	24.8	15 (33)	17 (38)	22 (49)	2 (4)	11 (24)	5 (11)
Misc	672	31.0	26 (4)	27 (4)	65 (10)	16 (2)	46 (7)	15 (2)
All	5116	33.4	112 (2)	176 (3)	475 (9)	111 (2)	376 (7)	125 (2)

ASD = atrial septal defect; COA = coarctation of aorta; Misc = miscellaneous diagnosis; PDA = patent ductus arteriosus; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; VSD = ventricular septal defect

Table 6. Entitlements to special reimbursement for cardiac diseases in diagnosis groups.

	n	Cardiac failure, n (%)	Arrhythmia, n (%)	Hypertension, n (%)	Coronary cardiac disease, n (%)
PDA	1759	40 (2)	11 (1)	85 (5)	9 (0.5)
COA	797	79 (10)	14 (2)	122 (15)	4 (0.5)
ASD	730	34 (5)	21 (3)	17 (2)	1 (0.1)
VSD	617	163 (26)	16 (3)	15 (2)	0 (0.0)
TOF	317	79 (25)	20 (6)	6 (2)	1 (0.3)
TGA	179	95 (53)	17 (9)	2 (1)	3 (1.7)
UVH	45	37 (82)	12 (27)	1 (2)	4 (8.9)
Misc	672	165 (25)	23 (3)	25 (4)	4 (0.6)
All	5116	692 (14)	134 (3)	273 (5)	26 (0.5)

ASD = atrial septal defect; COA = coarctation of aorta; Misc = miscellaneous diagnosis; PDA = patent ductus arteriosus; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; VSD = ventricular septal defect

Table 7. Chronic diseases and depression.

	All	Chronic disease, n (%)	Depression, n (%)	No chronic disease, n (%)	Depression, n (%)	RR (95% CI)
Patients	5116	1550 (30)	163 (11)	3566 (70)	228 (6)	1.65 (1.36–1.99)
Controls	10,232	1194 (12)	173 (14)	9038 (88)	462 (5)	2.84 (2.41–3.34)

95% CI = 95% confidence interval; RR = risk ratio

syndrome were excluded from the analysis. Of the 78 patients with hypothyroidism, 16 had Down's syndrome.

The patients' risk for gout was high (risk ratio: 4.00, 95% confidence interval: 1.21–13.3; Table 1). There were four out of eight patients with gout who had tetralogy of Fallot with extended cyanosis: two had had only palliative shunts, and the other two underwent corrective surgery at the ages of 11 and 27 years.

*Usage of antibiotics.* The medicines most used among all the study subjects were antibiotics; 30% of patients and 26% of controls (risk ratio: 1.2, 95% confidence interval: 1.11–1.23) purchased anti-infective medicine at least once during the year 2004 (Table 3). Patients had bought 2789 cures of antibiotics (0.55 per patient), and controls 4314 cures (0.42 per patient).

## Discussion

In this population-based follow-up study, we examined the comorbidity and the usage of medicines of the patients who underwent surgery for a congenital cardiac defect.

The accuracy of the research registry of paediatric cardiac surgery in Finland guaranteed the reliability and coverage of the study. Data on the usage of the medicines were also reliable because in Finland all medications are sold only in pharmacies and the medicine registries got knowledge of purchases on line.

Patients exhibited many chronic diseases, in addition to cardiac disease, and they used more medications than did the control subjects. Yet, the usage of medicines in this study gives too little prevalence of diseases among patients with operated congenital cardiac disease, as most of the patients who died during the follow-up time suffered from the diseases measured in 2004. In our previous study, it was shown that patients died most often due to cardiac disease, but other diseases also caused high mortality.<sup>3</sup>

Patients with chronic diseases in general often bear a big burden of medicines.<sup>4,5</sup> Part of this may result from frequent visits to the doctor, when the minor discomforts can be easily brought out, examined, and treated.

The patients in our study underwent surgery before the 1990s. The results of patients who recently underwent surgery will probably differ from this early material, as patients who undergo surgery nowadays have more severe defects and more often have chromosomal diseases. However, the leading comorbidities in our study were quite similar to those in a Belgian paediatric population published in a recent study.<sup>6</sup>

### Cardiovascular medicines

Astonishingly, 83% of the patients needed no cardiac medication. Even 62% of patients who underwent atrial switch operation for transposition of the great arteries used no medication for cardiac symptoms. However, the patients on average used more cardiovascular medicines than did the controls.

Patients who need cardiac medication were operated on at an older age than other patients. Thus, the older the patient at the time of the surgery, the more often some cardiac sequelae will appear. Patients should undergo surgery as early as possible, but neonates should undergo surgery only in urgent situations, as we discovered that the risk for neurological and pulmonary damages among them were very common.

Arrhythmias occurred most frequently among patients with univentricular heart, transposition of the great arteries, and tetralogy of Fallot; all are known to have high prevalence of both arrhythmias and sudden deaths.<sup>7–9</sup>

The risk for hypertension was equal among patients and controls with the exception of patients with coarctation of the aorta. The 15% prevalence of hypertension among patients who underwent coarctation repair as children was approximately the same as in the previously published data.<sup>10,11</sup>

Coronary cardiac disease was as common among patients as among controls. Earlier studies have claimed that the prevalence of coronary disease among patients with operated coarctation of the aorta is high.<sup>10,11</sup> Our results disagreed with those studies, and were in line with our previous study, in which we discovered that patients with aortic coarctation seldom died due to coronary cardiac disease.<sup>3</sup> That the patients were under 15 years of age at the time of the surgery may have protected them from hypertension, and through that, from coronary disease.

The emergence of coronary disease in patients with a cardiac transplant resulted from allograft vasculopathy. It was slightly surprising that none of the survivors of the arterial switch operation in our material required medication for coronary problems, though such problems have often been related to the old era of switch surgery.<sup>12</sup>

### *Comorbidity*

The health problems clustered within the patient and control populations. The vast majority of patients and controls had no entitlement to special reimbursement for medication for any disease, whereas 25% of the patients and 19% of the controls had more than one chronic disease requiring regular medication. In addition, the use of antidepressants was most common among persons with chronic diseases. This connection has been described recently in the World Health Surveys,<sup>13</sup> and should be kept in mind in day-to-day clinical work.

Heart patients often suffered from asthma. Most asthma patients were with patent arterial duct that was closed as neonates. The cause of asthma among them was most probably prematurity.<sup>14</sup> However, the difference in the prevalence of asthma between patients and controls was high even after excluding all neonatally operated patients. Thus, mature lungs may have incurred damage either because of the cardiac surgery or due to the cardiac defect itself. Open-heart surgery did not increase the risk for asthma within the patient population, which supports studies in which post-surgery lung injuries have been connected to blood transfusion and ventilation more often than to the cardiopulmonary bypass perfusion.<sup>15,16</sup>

Patients were at high risk for epilepsy. Numerous studies have been published concerning the effect of open-heart surgery on the neurodevelopment of children.<sup>17–19</sup> Our study showed that the risk for epilepsy was high regardless of the type of surgery. Of the patients with epilepsy, one-fifth underwent surgery as neonates, and one-fifth were mentally retarded. There is a strong relationship between intellectual disability and epilepsy.<sup>20</sup> In our subjects, most retarded patients had chromosomal defects, but some of the mental disability also resulted from the cardiac defect or surgery. Nowadays, the number of patients with surgery-induced brain damage would probably be much lower as the monitoring and protection of cerebral circulation has improved immensely.<sup>21</sup>

The number of patients using medicines for psychiatric diseases was significantly higher than that of controls, though the number of controls using anti-depressants was also high. In previous studies, patients have expressed some anxiety and

depression,<sup>22–24</sup> but no signs of such common phenomena have been reported. In spite of our subjects including patients with mental retardation whose condition is often complicated by psychiatric diseases,<sup>20</sup> the number of patients using psychiatric medication was high. In particular, the high prevalence of psychosis demands further investigation.

The number of patients with gout was high, which supports a previous study in which cyanotic patients had high urate levels and a high prevalence of gout.<sup>25</sup>

Patients used antibiotics more often than did controls, which could be due to their lower resistance to infections, and antibiotic prophylaxis was used before various procedures. Patients may also consult a general physician more easily when they have an infection, and perhaps doctors prescribe medicine more easily for them.

### *Limitations*

The biggest limitation of this method in studying morbidity was that no knowledge was found of diseases requiring no medicinal treatment. In addition, the medicines sold over-the-counter and used in hospitals were excluded from this study, as the medicine records provided no such information.

The rather high number of mentally retarded patients could have an increasing effect on comorbidity. Most patients with mental retardation had genetic syndromes that often cause comorbidity, as was seen in the hormone deficiencies. Unfortunately, we had no knowledge of the number of retarded persons among the control population. The expected number of control subjects with low intelligence quotient (IQ), assessed on the basis of Finnish epidemiological study,<sup>20</sup> was less than 60 patients (<0.6%).

### *Conclusion*

Patients who underwent surgery for a congenital cardiac defect as children needed a considerable number of medications for chronic diseases. The health problems clustered among both patients and controls. The hearts of most patients recovered well after surgery as 83% of patients required no cardiac medication. The neonatal brain and lungs proved quite vulnerable as patients who underwent surgery during the first month of life were at high risk for asthma and epilepsy.

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