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Sex differences in congenital heart disease in Down syndrome: study data from medical records and questionnaires in a region of Japan

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ABSTRACT

Reports indicate lower Down syndrome (DS) survival among females than among males in Australia, contrasting with female longevity in the general population. Using data on 1310 people with DS (626 females and 684 males) in Japan from five hospitals' medical records and questionnaires completed by parents of people with DS, we investigated sex differences in congenital heart disease (CHD), which may be related to mortality. The CHD rate was significantly higher for females (354, 57%) than for males (338, 49%; p=0.010). Significantly more females (199, 32%) than males (175, 26%) underwent surgery for CHD (p=0.018).

INTRODUCTION

Life expectancy for people with Down syndrome (DS) has increased in Australia,[1] Japan[2] and other advanced countries. In Japan, improvements in early survival have been attributed to surgical intervention for congenital heart disease (CHD).[3] In Australia, in contrast to female longevity in the general population, males with DS were found to have significantly longer life expectancies, compared with their female counterparts.[4] The shorter life expectancy of these females may be attributed to their higher prevalence of CHD. This study aimed to clarify sex differences in the prevalence and severity of CHD among Japanese people with DS.

METHODS

We used data from medical records from five hospitals in Tokyo and two questionnaires completed by parents of people with DS in Tokyo and Shizuoka prefectures (online supplementary file 1). People with DS were not directly involved in the design of this study. Small (diameter<6 mm) fossa ovalis defects were excluded from the diagnosis of atrial septal defect (ASD). Arterial ducts closed before 1 month of age were excluded from the diagnosis of patent ductus arteriosus (PDA). Questionnaires were mailed to parents of people with DS; completing and returning the questionnaire was considered to indicate consent to participate. Statistical analyses were performed using SPSS V.21.

RESULTS

In total, there were 1310 subjects with DS (626 females and 684 males; sex ratio=1.09). The prevalence of CHD was significantly higher among females (354, 57%) than among males (338, 49%; χ^2 test: p=0.010). Moreover, significantly more females (199, 32%) than males (175, 26%) underwent cardiac surgery (χ^2 test: p=0.018; table 1). The main CHD lesions (in order of prevalence) were ventricular septal defect (VSD), ASD, atrio-VSD (AVSD), PDA and tetralogy of Fallot (TOF; table 2). The prevalence of CHD with PDA was significantly higher in females (115, 18%) than in males (87, 13%; p=0.005), whereas the prevalence of CHD without PDA was almost equal in females (239, 38%) and males (251, 37%.)

Table 1 Congenital heart disease (CHD) and operations among people with Down syndrome by sex

Sex	CHD (+) Operation (+)	CHD (+) Operation (–)	CHD (–)	Total
Female	199	155	272	626
	32%	25%	43%	100%
Male	175	163	346	684
	26%	24%	51%	100%
Total	374	318	618	1310
	29%	24%	47%	100%

χ^2=8.05, df=2, p=0.018.
Odds: female versus male with CHD (95% CI) 1.33 (1.07 to 1.66).
Odds: female versus male with CHD operation (95% CI) 1.36 (1.07 to 1.72).

Table 2 Main congenital heart disease (CHD) lesion among people with Down syndrome by sex

Main lesion of CHD	Sex					
	Female		Male		Total	
	Number	Per cent	Number	Per cent	Number	Per cent
VSD	142	40.1	131	38.8	273	39.5
ASD	75	21.2	70	20.7	145	21.0
AVSD	55	15.5	47	13.9	102	14.7
PDA	48	13.6	40	11.8	88	12.7
TOF	23	6.5	30	8.9	53	7.7
PS	1	0.3	5	1.5	6	0.9
DORV		0.0	3	0.9	3	0.4
Ebstein	1	0.3	1	0.3	2	0.3
AR	1	0.3		0.0	1	0.1
CoA		0.0	1	0.3	1	0.1
MR	1	0.3		0.0	1	0.1
TA		0.0	1	0.3	1	0.1
TR		0.0	1	0.3	1	0.1
Unknown	7	2.0	8	2.4	15	2.1
Total	354	100.0	338	100.0	692	100.0

AR, aortic regurgitation; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CoA, coarctation of aorta; DORV, double outlet right ventricle; Ebstein, Ebstein's anomaly; MR, mitral regurgitation; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TA, tricuspid atresia; TOF, tetralogy of Fallot; TR, tricuspid regurgitation; VSD, ventricular septal defect.

Among subjects born before 1979 (female: 34, 43.6%; male: 10, 18.5%), in the 1980s (female: 63, 51.2%; male: 46, 37.7%) or in the 1990s (female: 74, 59.7%; male: 85, 47.5%), more females than males had CHD, but we found no significant sex difference in CHD prevalence for subjects born in 2000 or later (female: 183, 60.8%; male: 196, 59.8%).

DISCUSSION

In our study, females with DS had a significantly higher prevalence of CHD than did males with DS, as has previously been reported in the USA[5] and Europe.[6] Higher prevalence and greater severity of CHD in females may contribute to poor prognoses. We found that the most common cardiac anomalies (main lesions) were VSD, ASD, AVSD, PDA and TOF, which together accounted for 95.5% of all CHD cases. Likewise, a European network of population-based registers for the epidemiological surveillance of congenital anomalies study[6] found that these five anomalies accounted for more than 99% of cardiac anomaly cases in people with DS. Among people with DS born before 1979, in the1980s or 1990s, we found that significantly more female than male subjects had CHD, but we found no significant sex difference for subjects born in 2000 or later. Many factors seem to have contributed to this change, including the improvement of diagnostic techniques, such as echocardiographic examination, and improvements in heart surgery. This shift may be attributed to a great increase in the diagnosis of less severe CHD for both sexes.

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Competing interests None declared.

Patient consent for publication Not Required

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