Effect of Atrial Septal Defect in Adults on Work Participation (from a Nation Wide Register-Based Follow-Up Study Regarding Work Participation and Use of Permanent Social Security Benefits)

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Low work participation is well known in patients with chronic disease but has not been described in patients with atrial septal defect (ASD). In this nation-wide cohort study, we report the first long-term follow-up of use of permanent social security benefits and work participation in adults with ASD. All Danes born before 1994 and diagnosed with ASD from 1959 to 2013 (n = 2,277) were identified from the Danish medical registries. We used Cox proportional hazards regression to compare the risk of receiving permanent social security benefits in the ASD patients compared with an age- and gender-matched general population cohort. Using the DREAM database, we calculated work participation score and proportion of patients working or not working at the age of 30 years. Median follow-up from ASD diagnosis was 23.4 years (range 0.2 to 59.3). ASD patients had a higher risk of receiving permanent social security benefits (hazard ratio 2.3 [95% confidence interval 2.1 to 2.6]) compared with the comparison cohort with 24% of the ASD patients receiving permanent social security benefits at the end of follow-up compared with 12% of the comparison cohort. At the age of 30 years, the proportion not working was 28% in the ASD cohort and 18% in the comparison cohort. In patients with ASD, 23% of those without a job had a psychiatric diagnosis. In conclusion, the risk of receiving permanent social security benefits was twice as high in patients with ASD and the work participation score was reduced compared with the background population. **(Am J Cardiol 2019;124:1775−1779)**

Outcome in patients with atrial septal defect (ASD) is the topic of a whole array of studies.[1−3] We have found that patients with ASD have increased mortality rate[4] and increased risk of co-morbidity such as atrial fibrillation, stroke,[5,6] and pneumonia[7] compared with the background population, and our results indicate that even patients with small and hemodynamically insignificant ASDs are much more affected by their disease than first assumed.[8,9] Studies on employment status and use of social benefits in patients with congenital heart disease are rare, and to our knowledge nonexistent in patients with ASD. In adults with mixed congenital heart disease diagnoses, the overall unemployment rate has been reported from 24% to 33%.[10−12] We investigated the rate of permanent social security benefits use and the proportion of weeks working, during follow-up in adults with ASD. Furthermore, we investigated the work participation score at the age of 30 years compared with a gender- and age-matched comparison cohort from the general population.

Methods

The data in this study were based on the Danish national registries providing information on health care, employment, education, and use of social security benefits. The study population has been used previously in studies investigating mortality[4] and migraine,[13] and ongoing research on psychiatric morbidity. Since 1968, every Danish citizen has at birth or immigration received a unique personal identification number, registered in the Danish Civil Registration System,[14] where information on date of birth, migration, and death is registered. The healthcare system is publically funded and free of charge for all. Data from all hospital admittances and outpatient clinics are gathered in public registries by linking the personal identification number. Reporting to the registries is mandatory by law in Denmark. Patients were included by 2 sources. The first was based on the Danish National Patient Registry (DNPR), where all Danish patients diagnosed with ASD from 1977 to 2013 and born before 1994 where identified. In the

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DNPR, information on dates of admission and discharge, procedures, and discharge diagnoses in Danish hospitals are registered. Discharge diagnoses are coded according to the International Classification of Disease (ICD)[15] where the eighth edition was used until 1993 in Denmark after which the tenth version was used. After identification of the patients, all eligible hospital records were reviewed and validated by 2 physicians. Patients with persistent foramen ovale or concomitant congenital heart disease were excluded as well as patients with no ASD mentioned in the hospital records. During review of the medical hospital records, a few patients had an ASD diagnosis or closure performed before the initiation of the DNRP. These dates were corrected in the registry and thus diagnosis date for included patients range from 1959 and up to January 1, 2013 even though the registry was only initiated in 1977. Second, an additional population of patients was added from a cohort of patients diagnosed with an ASD before the age of 15 years from 1963 to 1974. From 1970 to 1974, an experienced physician reviewed all inpatient and outpatient hospital records in all Danish medical and pediatric departments and identified all patients with a congenital heart disease.[16] The patients who were alive in 1968 had a personal identification number created and their diagnoses were translated to ICD-10 codes. A few (n = 5) patients did not survive or migrated before receiving a personal identification number and were therefore excluded. A comparison cohort was created, using the Danish Civil Registration System, matching every verified ASD patient with 10 persons from the general population on gender and birth year. We used the date of the ASD diagnosis for the ASD patients as the date of matching between the 2 groups. ASD patients with a diagnosed syndrome and their matched controls were excluded as was subjects in the comparison cohort with a diagnosed syndrome (see Appendix for used diagnoses). Social security benefits and services are tax funded and available to all Danish citizens in need, regardless of affiliation to the labor market. The system is administered electronically and by social security workers. Short-term sickness is paid by the employer in case the citizen is employed. The municipality pays long-term sickness, and in unemployed citizens, also short-term sickness. During the study period, the definition of short-term sickness increased from 14 to 30 days. Long-term sick leave is covered for both employees and self-employed citizens.

The DREAM database contains information on all paid social security benefits registered on a weekly basis from 1991 to 2018.[17] The database covers benefits paid to citizens, but does not cover short-term sick leave, paid by the employer for employed citizens. We used the DREAM database to categorize the weeks into the following groups: (1) Work (including maternity leave and education), (2) Unemployed (all citizens including both those with and without private insurance), (3) Long-term sick leave (paid by the municipality), and (4) Permanent social security benefit, including disability pension and flexi-job (a job created for persons with limited and permanently reduced working capacity).[17] Information on co-morbidity before the ASD diagnosis date or matching date for the comparison cohort was identified in the DNPR. The Charlson Comorbidity Index (CCI) was calculated at the age of 30 years. Psychiatric diagnoses in patients, comparison cohort subjects and both groups' parents were identified in the Central Psychiatry Registry, with data since 1969. A marker for psychiatric disease before the age of 30 years was created, if any psychiatric diagnosis was registered. Highest level of completed education since 1981 was found in the Danish National Education Registry and estimated for both ASD patients and the comparison cohort. Patients and subjects in the comparison cohort with a syndrome were identified in the DNPR. ICD-8 and ICD-10 codes for all diagnoses used are shown in Appendix 1.

The total number of weeks from either the age of 18 or initiation of the database and until end of follow-up, death or retirement (not disability retirement) was generated for each patient and comparison cohort subject. The proportion of weeks in either of the 4 categories—work, unemployment, long-term sick leave, and permanent social security benefit—was calculated. The calculated work proportion was defined as the work participation score. The year the patients and the comparison cohort members turned 30 years, a marker for either work or no work was created; if more than half the year was registered as work, the subject was identified as working this year. The proportion of subjects working and not working at the age of 30 years was computed, and the proportion of subjects with a psychiatric diagnosis and a CCI >0 was calculated. Direct comparisons between groups were computed using either an unpaired Student's t test or Fischer's exact test. The date and age at initiation of permanent social security benefits were calculated. Using Cox proportional regression analysis, we computed hazard ratios for first date of permanent social security benefit for ASD patients, beginning at age 18 years, comparing them with the comparison cohort, using age as the underlying time scale. Stratification by birth year and gender did not change the results. We stratified the analyses by diagnosis before the age of 18 and closure. As closure in some patients occurred later that the eighteenth year, this exposure entered the model as a time-varying covariate. To handle competing risk from death, the cumulative incidences of permanent social security benefit in ASD patients and the comparison cohort were calculated by Fine & Grays competing risk regression. The assumption of proportional hazards was graphically verified with log-minus-log plots. Statistical tests were 2-tailed and p values under 0.05 considered significant. All analyses were performed using Stata 15/StataCorp LP, TX. The study was approved by The Central Denmark Region Research Committee (1-16-02-570-18) and the National Board of Health (j.nr. 7-604-04-2/193/KWH).

Results

We identified 4,445 patients who were born before 1994 and diagnosed with an ASD before 2013 in the DNPR. We excluded those with concomitant congenital heart disease (n = 609), 651 had a missing hospital record, thus leaving 3,286 patients eligible for validation. After exclusion, a total of 2,277 ASD patients and a matched comparison cohort of 22,756 were included in the study. Patients and the comparison cohort were followed with a median of 23.4 years after the ASD diagnosis (range 0.2 to 59.3 years). Baseline characteristics are shown in Table 1.

ASD patients, who were not working, had a very high prevalence of psychiatric morbidity (Table 2) and the ASD patients were in general younger when receiving first time permanent social security benefits (mean 42.5 years [41.0 to 44.0])

Table 1
Baseline characteristics

Variable	ASD total (n = 2,277)	Control group (n = 22,756)	p value
Diagnosed <18 years	1,115 (49%)		
Age at diagnosis, mean ± sd	22.6 ± 24.9		
Diagnosed after 1994	1,070 (47%)		
Operative ASD closure	1,067 (47%)		
Percutaneous ASD closure	481 (21%)		
Age (years) at closure, mean ± sd	29.3 ± 21.9		
Female	1,384 (61%)	13,834 (61%)	
Any diagnosed syndrome	65 (3%)	5 (0.02%)	<0.0001
Chronic lung disease	181 (8%)	1,024 (5%)	<0.0001
Diabetes Mellitus	116 (5%)	790 (3%)	<0.0001
Pulmonary heart disease	123 (5%)	52 (0.2%)	<0.0001
Hypertension	262 (12%)	1,661 (7%)	<0.0001
Ischemic Heart Disease	325 (14%)	1,212 (5%)	<0.0001
Cerebrovascular events	180 (8%)	613 (3%)	<0.0001
Arrhythmia	514 (23%)	715 (3%)	<0.0001
Marriage*	708 (37%)	8,041 (40%)	0.002
Highest education*	2,073 (92%)	21,030 (92%)	
- Basic	755 (33%)	5,775 (25%)	<0.0001
- Youth	170 (7%)	2,452 (11%)	<0.0001
- Vocational	652 (29%)	6,998 (31%)	0.065
- Higher	496 (22%)	5,811 (26%)	0.0002
-Short cycle	69 (3%)	833 (4%)	0.14
-Medium cycle	274 (12%)	3,254 (14%)	0.005
-Long cycle	153 (7%)	1,724 (8%)	0.17
- Data missing	204 (9%)	1,726 (8%)	0.3
Maternal psychiatric disorder	193 (12%)	1,730 (11%)	0.23
Paternal psychiatric disorder	132 (8%)	1,274 (8%)	0.68

ASD = atrial septal defect; Sd = standard deviation.
* Proportion calculated from patients alive at the age of 18 years and not diagnosed with any syndromes (ASD patients n = 2,253, Controls n = 22,707).

Table 2
Proportion working and not working at the age of 30 years

Variable	ASD (n = 879)	Comparison cohort (n = 8,925)	p value
Working at age 30 years	629 (72%)	7,348 (82%)	<0.0001
Psychiatric diagnosis*	41 (6.5%)	115 (1.5%)	<0.0001
Charlson Comorbidity Index >0	10 (1.5%)	24 (0.3%)	<0.0001
Not working at age 30 years	250 (28%)	1,577 (18%)	<0.0001
Psychiatric diagnosis*	57 (23%)	107 (6.8%)	<0.0001
Charlson Comorbidity Index >0	8 (3.2%)	18 (1.1%)	<0.0001

ASD = atrial septal defect.
* Any psychiatric diagnosis given before the age of 30. The proportion is calculated from number of patients either working or not working.

compared with the comparison cohort (mean 50.1 years [49.1 to 50.7]). The overall work participation score was lower for the ASD patients during follow-up compared with the comparison cohort (Table 3) and permanent social security benefits were significantly more common in the ASD patients than in the comparison cohort (Table 4) with cumulative incidence more than twice increased at any time and with a sub hazard of 2.2 (95% confidence interval 2.0 to 2.5; Figure 1). There was no difference in the proportion receiving permanent social security benefits between those with closure of their ASD and no closure of their ASD performed, but in those with an early ASD diagnosis, the patients with closure seemed to receive the benefits at an older age than those without closure. No difference was found between those with operative ASD closure and percutaneous ASD closure of their defect (hazard ratios 1.2 (95% confidence interval (0.9 to 1.6), p = 0.3).

Table 3
Proportion of time working, unemployed, on long-term sick leave or permanent social benefits

Variable	ASD (n = 1,963)	Comparison cohort (n = 20,021)	p value
Permanent social benefits	16.2%	7.7%	<0.0001
Long-term sick leave	2.9%	2.2%	<0.0001
Unemployment	10.8%	8.5%	<0.0001
Working	70.0%	81.5%	<0.0001

ASD = atrial septal defect.

Discussion

The proportion of ASD patients unemployed in our cohort was lower than in similar studies, however, the total number of patients not participating in the work force was comparable.[10,11] This could be explained by the thorough and extensive social security network in Denmark, giving social security services to patients who would be unemployed or working very low-income jobs in other countries. Stroke is known to increase the risk of disability pension and this could be one partial cause for the high risk of permanent social security benefits in the ASD patients.[18] There is a known association between being unemployed and developing mood affective disorders such as depression.[19] The high prevalence of psychiatric disease could thus be caused by unemployment rather than the psychiatric morbidity causing the unemployment, however, the large difference between psychiatric morbidity in those without a job in the ASD cohort, and in the comparison cohort, suggests that this is not the case in this study. On the contrary, we suspect that the very high prevalence of psychiatric morbidity in the ASD patients is a major contributor to the increased prevalence of permanent social security benefit and lower employment rate.

The difference between long-term sick leave between the ASD patients and the comparison cohort was not as large as might be expected. We do not have information on short-term sick leave financed by the employer, and there is a possibility that the ASD patients have increased short-term sick leave that we cannot identify. Generally the total sick leave is therefore somewhat underestimated and possibly more so in the ASD patients. The risk of receiving permanent social security benefits in the ASD population is similar to the risk seen in Danish patients diagnosed with epilepsy[20] in both childhood and adulthood, and in patients with multiple sclerosis[21] and survivors after cerebral tumors diagnosed in childhood.[22] Patients in those categories often have severe symptoms, and the similarity to patients with ASD, in regard of permanent social security benefits, is surprising. Even closure of the defect in childhood does not seem to protect against decreased work affiliation in adulthood. In these

Table 4
Proportions and risk of receiving permanent social security benefits

	N	Permanent social security benefit	p value	Hazard Ratio (95% CI)	p value
Controls	20,021	2,417 (12%)		1	
ASD total	1,963	477 (24%)	<0.0001	2.3 (2.1-2.6)	<0.0001
Diagnosis < 18 years					
Controls	6,724	457 (7%)		1	
ASD closure	670	121 (18%)	<0.0001	2.8 (2.3-3.5)	<0.0001
Controls	4,053	255 (6%)		1	
ASD no closure	388	73 (19%)	<0.0001	3.1 (2.4-4.0)	<0.0001
Diagnosis > 18 years					
Controls	7,276	1,352 (19%)		1	
ASD closure	725	222 (31%)	<0.0001	2.0 (1.7-2.3)	<0.0001
Controls	1,975	353(18%)		1	
ASD no closure	180	61 (34%)	<0.0001	2.2 (1.6-2.9)	<0.0001
ASD closed	1,395	343 (25%)		1	
ASD not closed	568	134 (24%)	0.6	0.9 (0.7-1.1)	0.3

CI = confidence interval.

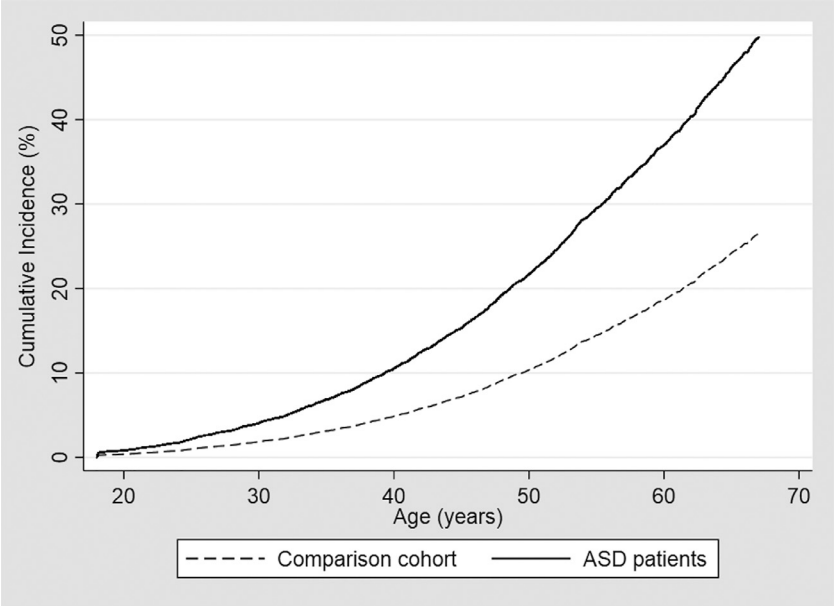

Figure 1. Competing risks of use of permanent social security benefits after the age of 18 years and until death, emigration, retirement, or end of follow-up. ASD = atrial septal defect.

studies, only disability pension is included, whereas we also included part time permanent benefit. This may explain the slightly larger proportion of patients with ASD on permanents social security benefit. We did not find an overall difference between those who underwent closure of their defect and those without closure. This suggests, that in the long term, the procedures performed and possibly even the size of the defect, plays a very little role compared with receiving and living with the ASD diagnosis itself.

Poor mental health in parents is a known risk factor for psychiatric morbidity in the offspring.[23] We did not find any difference in prevalence of psychiatric diagnoses in parents in either group. The diagnoses are, however, only the tip of the iceberg, since unreported poor mental health and diseases treated at the general practitioner are not included in the registries. The ASD patients could have home environments disposing them to both psychiatric disease and permanent social security benefits.

When using the Danish registries, certain limitations must be kept in mind. First, we do not have hemodynamic information on all the ASDs. Our data suggest that the size of the ASD and procedures performed does not influence work affiliation and use of permanent social security benefits, and these measurements seem less important in this regard. A number of patients never entered the DREAM database, because they died or migrated before entering. We do not know if these patients would use social services differently, or have an alternative association with the work force than those who entered the system. Patients who died could be expected to have more symptoms and be more affected from their ASD and we believe the potential use of social security benefits would be at least the same as those alive on entering, thus resulting in an even stronger association. Some patients may be diagnosed with their ASD when admitted to the hospital for other

diseases, and the ASD diagnosis may therefore be over-represented in patients with other morbidity. We used the CCI to minimize this bias, well knowing that it only includes severe disease. These could attribute to the lower work rate and thus overestimate our results.

In conclusion, we found that adults with ASD have a lower work participation score and a significantly higher use of permanent social security benefits that matches the unemployment proportion in patients with severe disease as multiple sclerosis. Closure of the defect does not seem to prevent the use of permanent social security benefits even when performed in childhood. The poor affiliation to the work force, as well as the lower education rate and high prevalence of psychiatric morbidity demands further investigation of patients with ASD, as well as an increased psychosocial support and vigilance by physicians caring for these patients.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.08.041.

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