Original Contribution

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Long-Term Risk of Hemorrhagic Stroke in Young Patients With Congenital Heart Disease

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Background and Purpose—The risk of ischemic stroke is increased in patients with congenital heart disease (CHD); however, data on the risk of hemorrhagic stroke, including intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), are lacking.

Methods—The Swedish Patient Register was used to identify all patients who were born with a diagnosis of CHD between 1970 and 1993. Each patient was compared with 10 randomly selected controls from the general population, matched for age, sex, and county. Follow-up data were collected until December 2011 for both cases and controls.

Results—Of 21 982 patients with CHD, 70 developed ICH and 57 developed SAH up to the age of 42 years. CHD patients had more than an 8× higher risk (incidence rate ratio, 8.23; 95% confidence interval, 6–11.2) of developing ICH and almost an 8× higher risk of developing SAH (incidence rate ratio, 7.64; 95% confidence interval, 5.41–10.7) compared with controls. The absolute risk of ICH and SAH was low, with incidence rates of 1.18 and 0.96 cases per 10 000 person-years, respectively. Patients with severe nonconotruncal defects (incidence rate ratio, 16.5; 95% confidence interval, 5.63–51.2) or coarctation of the aorta (incidence rate ratio, 17.3; 95% confidence interval, 6.63–51.8) had the highest relative risk of developing hemorrhagic stroke, with incidence rates of 3.22 and 2.79 cases per 10 000 person-years, respectively.

Conclusions—The relative risk of hemorrhagic stroke among children and young adults with CHD was almost 8× higher than that of matched controls from the general population, although the absolute risk was low. The highest risk of ICH and SAH occurred in patients with severe nonconotruncal defects and coarctation of the aorta. **(*Stroke*. 2018;49:00-00. DOI: 10.1161/STROKEAHA.117.020032.)**

Key Words: cerebral hemorrhage ■ epidemiology ■ heart defects, congenital ■ stroke ■ subarachnoid hemorrhage

Stroke is one of the leading causes of death and disability in developed countries.[1] Recent studies report that stroke incidence has decreased among the elderly population, but not the younger population, with an overall decline in stroke mortality at all ages.[2]

Congenital heart disease (CHD) is the most common congenital malformation among live births.[3] Advances in surgical procedures and treatments over time have significantly increased survival among CHD patients over the last decades[4]; the number of people with CHD reaching adulthood is therefore expected to increase.[5] Patients with CHD may have an increased risk of intracerebral hemorrhage (ICH) because of anatomic abnormalities, such as coarctation of the aorta (CoA) or persisting shunts, or because of multiple surgical and medical interventions including the use of anticoagulants, which have previously been shown to increase the risk of hemorrhagic stroke.[6] Studies have shown that the absolute risk of ischemic stroke in these patients is low, but relatively high when compared with the general population.[7] Today, most studies on CHD are based on comparatively few cases because of the complexity and diversity of the disease; there is thus a need for large studies to more precisely estimate the risk of stroke. In addition, few studies have considered the risk of death after a first-time hemorrhagic stroke among CHD patients.

The objective of our study is to investigate the risk of ICH and subarachnoid hemorrhage (SAH) separately among patients with CHD and to subsequently determine the risk of death after being hospitalized with ICH or SAH.

Methods

The computations for this study are based on individual data from the Swedish registers held by the National Board of Health and Welfare which are not publicly available. All personal data are

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subjected to secrecy in accordance with the Swedish Public Access to Information and Secrecy Act (OSL, 2009:400). The data set can be made available to researchers on request pending approval by the appropriate ethics committee. Formal requests of the data should be made to http://www.socialstyrelsen.se/statistics which can also provide information about the register and persons to contact for queries. All relevant aggregated data on number of cases and controls are already contained within the article, supporting information files and its supporting information.

A universal healthcare system is provided at a low cost to all Swedish citizens. Hospitals have been required to report principal and contributory diagnoses to the Inpatient Register since 1987, whereas data from the Outpatient Register are available from 2000. From 1961, all deaths have been reported in the Cause of Death Register, and the 6 cardiothoracic surgery clinics in Sweden have registered all procedures and hospitalizations since 1970. For this study, all data were obtained from the Inpatient, Outpatient, and Cause-of-Death Registers and linked through the unique Swedish 10-digit personal identifier. All discharge diagnoses were coded according to the *International Classification of Disease* (*ICD*) system. The *ICD* Eighth Revision (*ICD*-8) was used from 1968 to 1986, *ICD*-9 from 1987 to 1996, and *ICD*-10 from 1996 onwards.

Study Population

A more detailed description of the study population has previously been published.[4,8] In brief, all men and women born between January 1970 and December 1993 who had a diagnosis of CHD and were registered in the Inpatient, Outpatient, or Cause-of-Death Register were included. Follow-up data and comorbidities were collected until December 2011. For each case of CHD, 10 controls were matched by age, sex, and county from the Swedish Total Population Register. However, a total of 14 patients could only be matched by 9 controls each. Characterization of CHD was performed according to a hierarchical classification system.[9]

Definitions

CHD was identified as at least 1 outpatient visit, discharge diagnosis from hospital, or death certificate with an *ICD* code as shown in Table I in the online-only Data Supplement. ICH was defined as discharges or deaths with codes 431, 432X (*ICD*-8 and -9) or I61, I62.9 (*ICD*-10). SAH was defined by codes 430 (*ICD*-8 and -9) or I60 (*ICD*-10). Hypertension was defined by codes 401 to 405 (*ICD*-8 and -9) or I10 to I15 (*ICD*-10); heart failure by codes 427.00 (*ICD*-8), 428 (*ICD*-9), or I50 (*ICD*-10); atrial fibrillation by codes 427.92 (*ICD*-8), 427D (*ICD*-9), or I48 (*ICD*-10); and diabetes mellitus by codes 250 (*ICD*-8 and -9) or E10-14 (*ICD*-10). The Swedish Classification of Operations, version 6, was used to classify surgery on the cardiovascular system as codes 30 to 32, or F codes for Classification of Surgical Procedures, version 1.9.

Statistics

Statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Inc, Cary, NC), and R software, version 3.1 (R Foundation for Statistical Computing, Vienna, Austria). All patients and controls included in our analysis started their follow-up at birth, regardless of the year of diagnosis. Point estimates with 95% confidence intervals (CIs) for the incidence rate of first event and for the mortality rate were calculated for patients and controls, respectively. Incidence and mortality rates are reported per 10 000 person-years. To estimate the risk of hemorrhagic stroke and the subsequent risk of death among patients with CHD compared with controls, the Mantel–Haenszel method was used to calculate the incidence rate ratio (IRR) with corresponding 95% CI.[10] A cumulative incidence function, with death as the competing event, was used to estimate the probability of hemorrhagic stroke over time among patients and controls, respectively.[11] A Gray Test was used to estimate significance for the cumulative incidence function; a P value of <0.05 was considered as statistically significant.

Ethics

This study complies with the Declaration of Helsinki and was approved by the Regional Ethical Review Board of Gothenburg University (Gbg 540-11, T974-12). For anonymity, all personal identifiers were removed and replaced with a code in the final data set.

Results

Among 21 982 patients with CHD and 219 816 controls born between 1970 and 1993, there were 127 cases (0.58%) of hemorrhagic stroke among CHD patients and 169 cases (0.08%) among controls, totaling 296 cases altogether and with a total follow-up time of 592 577 and 6 271 786 person-years, respectively. Of these, 70 CHD patients (0.32%) and 90 controls (0.04%) had an ICH event, and 57 patients (0.26%) and 79 controls (0.04%) an SAH. The mean age for diagnosis of hemorrhagic stroke was 27 years, with a maximum follow-up time of 42 years (Table 1). Table II in the online-only Data Supplement shows comorbidities before or coinciding with hemorrhagic stroke among CHD patients and controls. Although absolute numbers were small, patients with CHD had more arrhythmia and heart failure when compared with controls, where hypertension was the dominant risk factor.

Incidence of ICH, SAH, and Mortality During Follow-Up

Table 2 shows the incidence rate and IRR by disease states and lesion groups. The overall risk of ICH in patients with CHD was 8× higher (IRR, 8.23; 95% CI, 6.0–11.2) than in matched controls, with an incidence rate of 1.18 cases per 100 000 person-years. The corresponding IRR for SAH was 7.64 (95% CI, 5.41–10.7) compared with controls, with an incidence rate of 0.96 per 10 000 person-years. The overall mortality rate after ICH and SAH was 312 and 205 deaths per 10 000 person-years, respectively, although the relative risk of

Table 1. Baseline Characteristics of the Study Population

	CHD Patients (n=21 982)	Controls (n=219 816)
Women, n (%)	10 639 (48.4)	106 390 (48.4)
Mean follow-up time, y	27.0	28.5
Born in Sweden, n (%)	20 135 (92.0)	202 230 (91.6)
Birth cohorts		
1970–1984, n (%)	11 508 (52.3)	115 079 (52.3)
1985–1993, n (%)	10 474 (47.6)	104 737 (47.6)
Lesion groups, n (%) cases/n (%) controls		
Conotruncal defects	2022 (9.2)	20 230 (9.2)
Severe nonconotruncal defects	1087 (4.9)	10 870 (4.9)
CoA	1306 (5.9)	13 060 (5.9)
VSD	4369 (19.9)	43 689 (19.8)
ASD	2405 (10.9)	24 049 (10.9)
Other heart and circulatory system anomalies	10 793 (49.1)	107 918 (49.1)

ASD indicates atrial septal defect; CHD, congenital heart disease; CoA, coarctation of the aortae; and VSD, ventricular septal defect.

Table 2. Risk of ICH and SAH in Patients With CHD Compared With Matched Controls, Grouped by Different Lesions

Lesion Groups	No. of ICH Events (Case/Control)	Incidence Rate of ICH (Case/Control)*	IRR (95% CI) for ICH	No. of Deaths After ICH (Case/Control)	Fatality Rate After ICH (Case/Control)*	IRR (95% CI) for Fatality After ICH
ICH						
Conotruncal defects	1/5	0.21/0.09	2.76 (0.10–17.9)	1/2	4240/414	10.9 (0.35–134.8)
Severe nonconotruncal defects	8/6	3.22/0.19	16.5 (5.63–51.2)	3/0	336/0	…
CoA	6/5	1.67/0.13	12.5 (3.67–44.8)	1/2	98.8/653	0.16 (0.00–1.99)
VSD	8/17	0.69/0.14	4.97 (2–11.3)	3/2	353/156	2.21 (0.37–19)
ASD	1/10	0.15/0.15	1.16 (0.05–6.12)	0/1	0/105	…
Other heart and circulatory system anomalies	46/47	1.52/0.15	10.1 (6.68–15.1)	14/8	329/227	1.43 (0.61–3.64)
All CHD	70/90	0.18/1.14	8.23 (6–11.2)	22/15	312/205	1.52 (0.79–3)
	No. of SAH events (Case/Control)	Incidence rate of SAH (Case/Control)*	IRR (95% CI) for SAH	No. of deaths after SAH (Case/Control)	Fatality rate after SAH (Case/Control)*	IRR (95% CI) for fatality after SAH
SAH						
Conotruncal defects	2/7	0.43/0.12	3.73 (0.51–15.9)	0/0	0/0	…
Severe nonconotruncal defects	0/2	0/0.06	…	0/0	0/0	…
CoA	10/6	2.79/0.16	17.3 (6.33–51.8)	4/2	381/360	1.02 (0.19–8.25)
VSD	3/13	0.26/0.11	2.51 (0.55–7.88)	0/5	0/1529	…
ASD	2/7	0.3/0.10	3.09 (0.42–13.2)	1/0	1729/0	…
Other heart and circulatory system anomalies	40/44	1.32/0.14	9.34 (6.06–14.4)	10/8	229/168	1.36 (0.53–3.6)
All CHD	57/79	0.96/0.13	7.64 (5.41–10.7)	15/15	256/186	1.38 (0.67–2.86)

ASD indicates atrial septal defect; CHD, congenital heart disease; CI, confidence interval; CoA, coarctation of the aortae; ICH, intracerebral hemorrhage; IRR, incidence rate ratio; SAH, subarachnoid hemorrhage; and VSD, ventricular septal defect.

*Incidence and mortality rate per 10 000 person-years.

death among controls and CHD patients was not significantly different (Table 2).

The highest relative risk of ICH among CHD patients when compared with matched controls was observed among patients with severe nonconotruncal defects (such as single ventricle defects, hypoplastic left heart syndrome, and endocardial cushion defects), with an IRR of 16.5 (95% CI, 5.63–51.2) and a high absolute incidence rate of 3.22 cases per 10 000 person-years. For SAH, patients with CoA had the highest relative risk, with an IRR of 17.3 (95% CI, 6.33–51.8) and an incidence rate of 2.78 cases per 10 000 person-years. The mortality rate after ICH and SAH among patients with severe nonconotruncal defects was 336 per 10 000 person-years and 381 cases per 10 000 person-years among patients with CoA. The relative risk of death after hemorrhagic stroke among patients with CHD and matched controls was not significantly different.

Table 3 shows the risk of ICH and SAH by birth cohorts. For the different birth cohorts, the risk for ICH and SAH among patients with CHD born in 1970 to 1984 was about 8× that of controls, with IRR of 8.53 (95% CI, 5.88–12.3) and 7.42 (95% CI, 5.04-10.8), respectively. In the youngest birth cohort, born in 1985 to 1993, the risk for ICH and SAH was similar, with IRR of 7.60 (95% CI, 4.13-13.7) and 8.90 (95% CI, 4.02-19.4), respectively, compared with controls. The mortality rate after ICH was 311 and 315 cases per 10 000 person-years, respectively, in subjects born in 1970 to 1984 and 1985 to 1993. The corresponding result for SAH was 288 and 148 cases per 10 000 person-years, respectively. Regardless of birth period, the mortality risk after ICH and SAH among CHD patients did not differ from controls.

Cumulative Probability of Hemorrhagic Stroke

Figure 1 shows the cumulative probability of hemorrhagic stroke in the study population. From birth until the age of 42 years, the probability of ICH and SAH among patients with CHD was 0.66% and 0.48%, respectively, compared with 0.09% and 0.10% among controls.

The cumulative probability of ICH and SAH by birth cohorts among patients with CHD is shown in Figure 2. For CHD patients born in 1984 to 1993, the probability of ICH was higher during the first years, with a cumulative probability of 0.13% at 10 years old compared with 0.09% in CHD patients born in 1970 to 1984. At 18 years old, however, the probability was similar among birth cohorts, at 0.17%. The probability for SAH was similar among birth cohorts during the study period.

Table 3. Risk of ICH and SAH in Patients With Congenital Heart Disease Compared With Matched Controls, Grouped by Different Birth Cohorts

Lesion Groups	No. of ICH Events (Case/Control)	Incidence Rate of ICH (Case/Control)*	IRR for CHD to Hemorrhagic Stroke (95% CI)	No. of Deaths After ICH (Case/Control)	Fatality Rate After ICH (Case/Control)*	IRR for Fatality After ICH (95% CI)
ICH						
1970–1984	51/64	1.38/1.16	8.53 (5.88–12.3)	15/12	311/219	1.41 (0.66–3.11)
1985–1993	19/26	0.85/0.11	7.60 (4.13–13.7)	7/3	315/162	1.89 (0.51–9.27)
	No. of SAH events (Case/Control)	Incidence rate of SAH*	IRR for CHD to SAH (95% CI)	No. of deaths after SAH (Case/Control)	Fatality rate after SAH*	IRR for fatality after SAH (95% CI)
SAH						
1970–1984	45/65	1.22/0.16	7.42 (5.04–10.8)	13/11	288/152	1.89 (0.84–4.34)
1985–1993	12/14	0.54/0.06	8.90 (4.02–19.4)	2/4	148/463	0.33 (0.04–1.79)

CHD indicates congenital heart disease; CI, confidence interval; ICH, intracerebral hemorrhage stroke; IRR, incidence rate ratio; and SAH, subarachnoid hemorrhage.
*Incidence and mortality rate per 10 000 person-years.

Figure 3 shows the cumulative probability of ICH and SAH stratified by lesion groups from birth up to 42 years of age. The highest probability for ICH was observed among patients with severe nonconotruncal defects, at 1.3%. The corresponding result for SAH was observed among patients with CoA, at 1.0%.

Discussion

Our study shows that the overall risk of hemorrhagic stroke among patients with CHD in Sweden was nearly 8× higher than in matched controls. The risk of ICH was highest among patients with severe nonconotruncal defects, whereas patients with CoA had the highest risk for SAH. Regardless of lesion

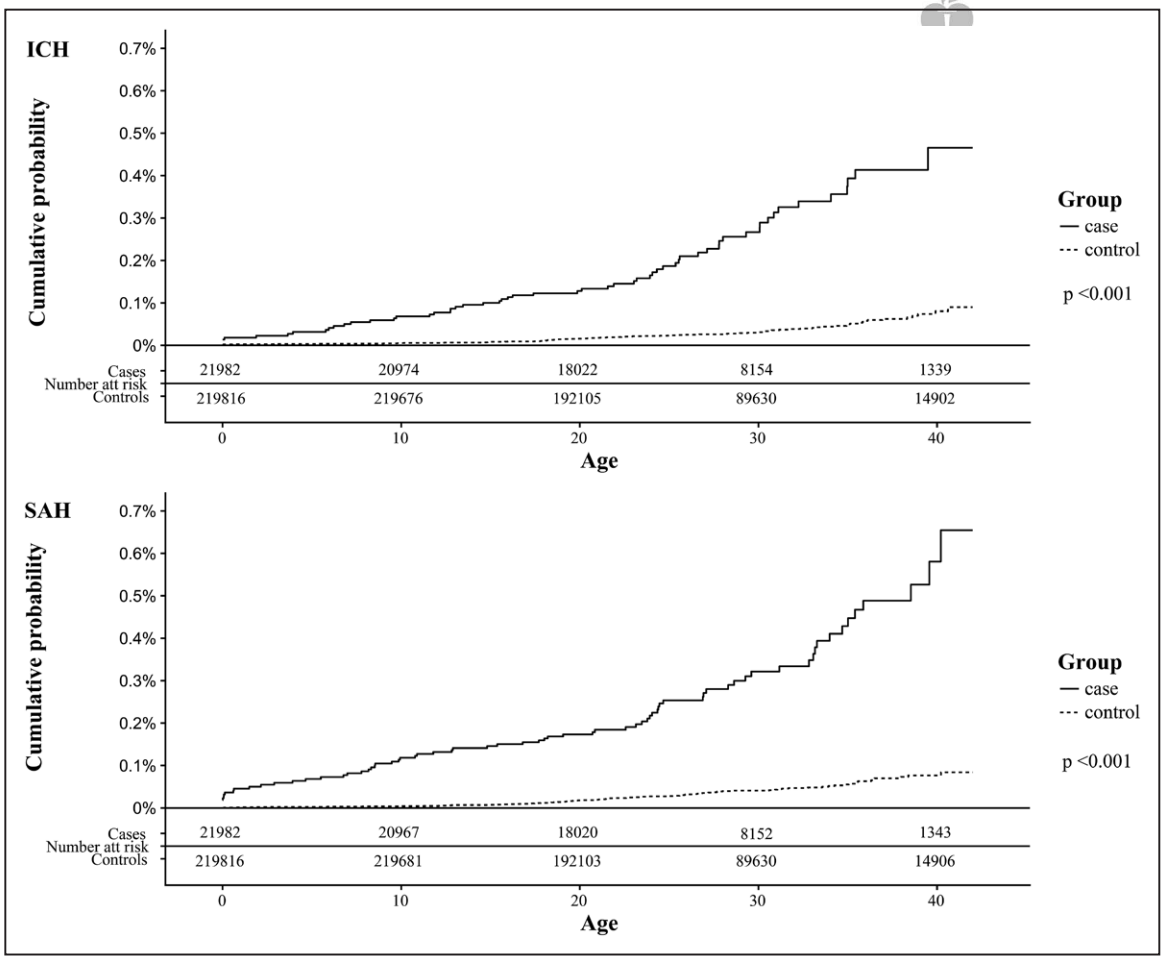

Figure 1. Cumulative probability of intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) among controls and patients with congenital heart disease.

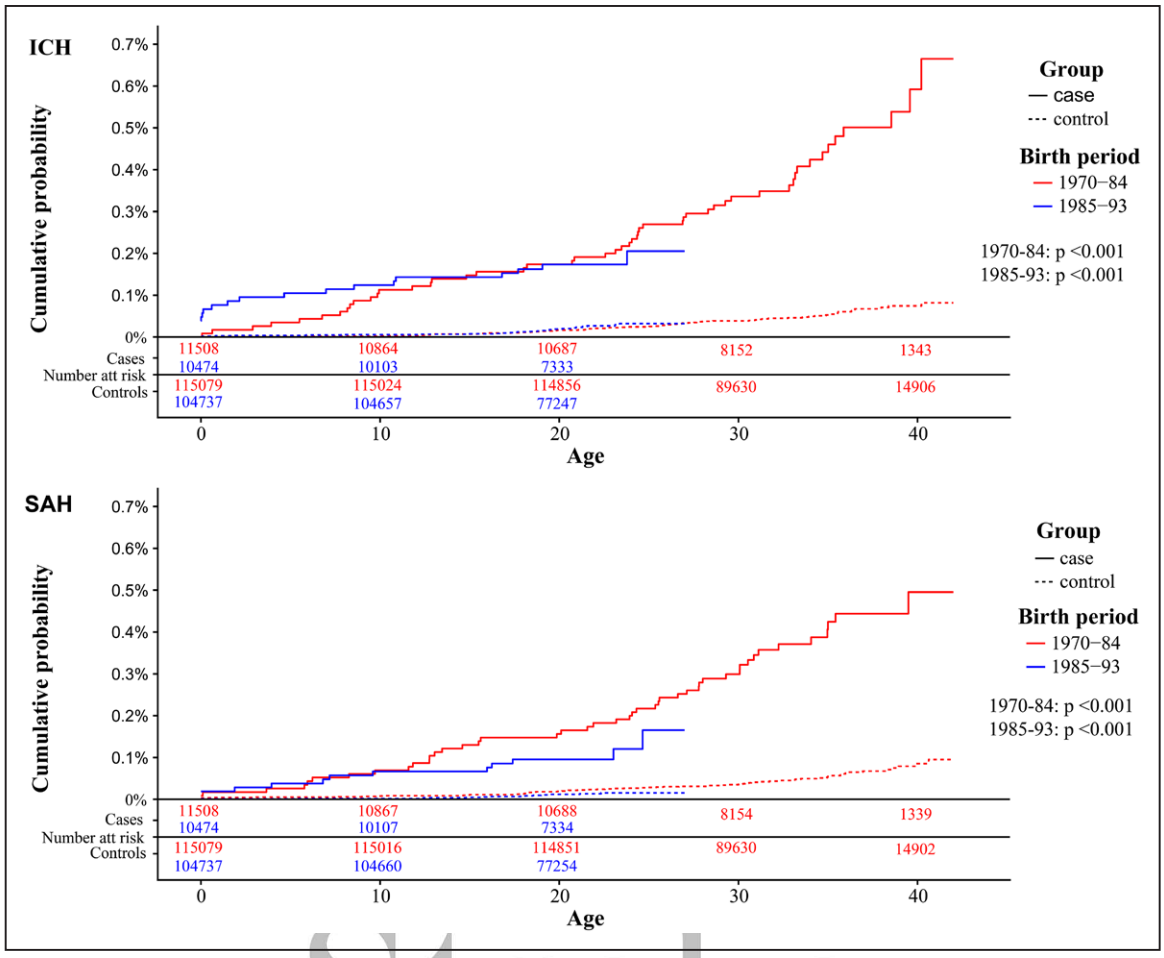

Figure 2. Cumulative probability of intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) by birth cohorts among controls and patients with congenital heart disease.

groups, the absolute risk was low, with an incidence rate among patients with CHD ranging from 0.21 to 3.22 per 10 000 person-years for ICH and from 0 to 2.79 per 10 000 person-years for SAH. The mortality risk after hemorrhagic stroke in patients with CHD was not significantly different from that of matched controls, regardless of lesions and birth cohorts.

Previous studies on the risk of hemorrhagic stroke among patients with CHD are very few and often limited in size. In a Canadian study, the overall incidence rate of hemorrhagic stroke was estimated as 14 per 100 000 person-years, which is similar to our results.[12] However, they did not investigate the risk of SAH separately. We found that the risk of ICH and SAH was increased, with risk estimates similar between the 2 hemorrhage subtypes. The relative risk of ICH and SAH in patients compared with matched controls was high. Risk factors for hemorrhagic stroke, such as hypertension and intracranial aneurysm, have previously been shown to be more prevalent among patients with CHD,[13] which may at least partially explain our results. Among different birth cohorts, the absolute risk of hemorrhagic stroke decreased over time, but the risk was still relatively high compared with controls. Improvements in perinatal and pediatric care, for both patients with CHD as well as controls, may explain the decline in the rate of ICH/SAH observed in both groups. Furthermore, centralization of surgical procedures, earlier diagnosis, and better medication may contribute to the diminished risk observed among patients with CHD, counteracting a potentially increased risk of ICH/SAH associated with more complex surgery in patients with higher initial risk performed at progressively earlier age.[4,14,15]

A challenge when studying CHD is the variability and complexity of the disease. To investigate the risk of hemorrhagic stroke by different lesion groups, we used a previously described hierarchy classification system.[9] Recent studies have shown that patients with more complex malformations have an increased risk of cardiovascular diseases such as ischemic stroke, heart failure, and myocardial infarction.[7,8] The elevated risk may be because of an associated increased risk of vascular malformations in the brain. For hemorrhagic stroke, we found different levels of risk in different lesion groups, where patients with severe nonconotruncal defects had the highest absolute and relative risks of ICH compared with matched controls. The reason for this is not clear and is difficult to deduct from the present data. However, patients with severe nonconotruncal defects often undergo multiple surgical reconstructions, which may increase the risk because of cerebral trauma and intensive anticoagulation in association with cardiopulmonary bypass. The relatively high risk among patients in lesion group 6 (other heart and circulatory system anomalies), which includes a majority of patients with valvular disease, may reflect more

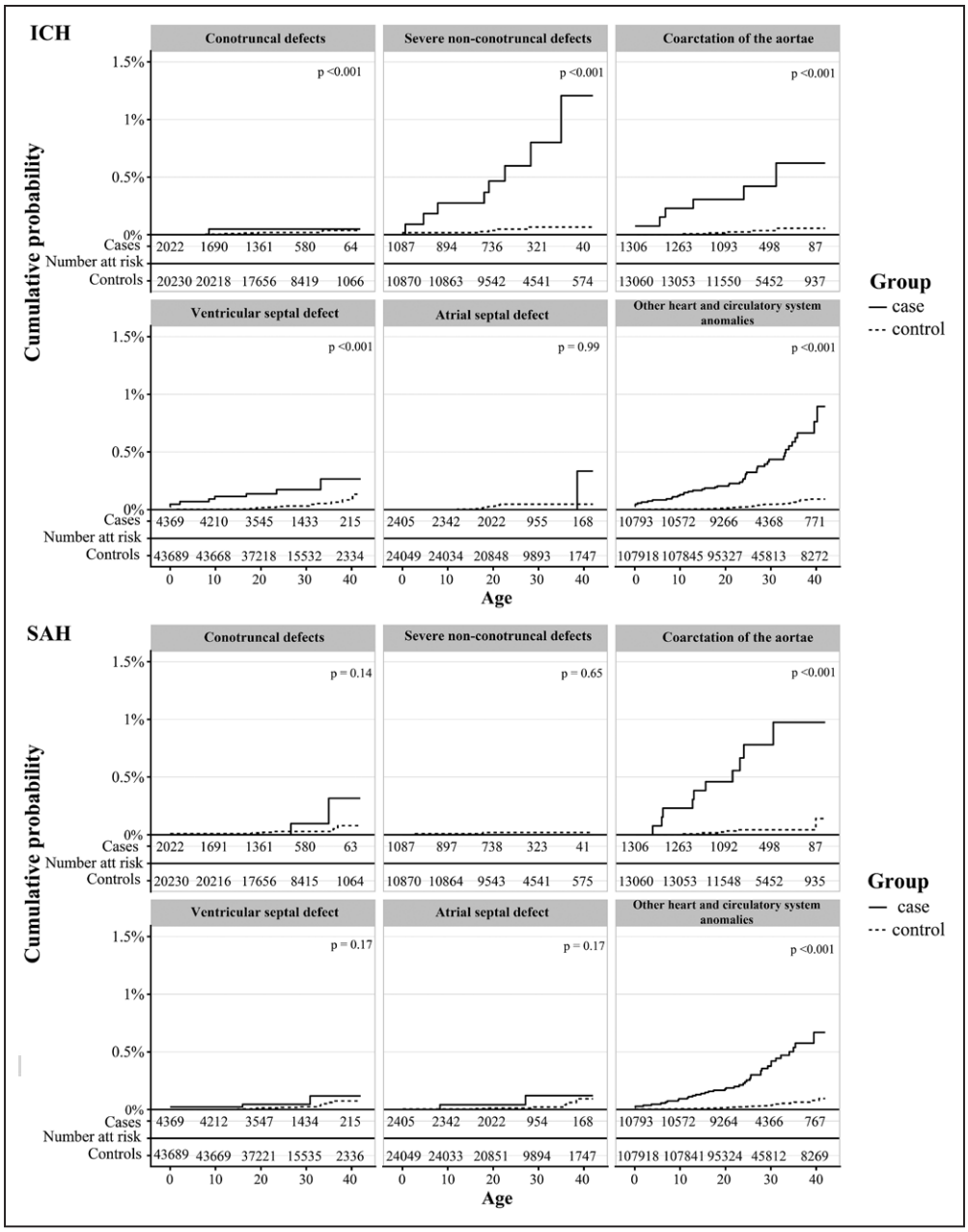

Figure 3. Cumulative probability of intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) by lesion groups among controls and patients with congenital heart disease.

frequent use of anticoagulation, although this remains speculative in the absence of detailed information on prescriptions. In addition, we observed that the probability of ICH during the first years of life was highest among patients born in 1985 to 1993. This could be because of an overall decrease in mortality rate over time among patients with CHD, with more patients surviving until adulthood.[4] Regardless, the overall probability of ICH and SAH was higher in patients with CHD compared with controls.

The risk of SAH was most marked in patients with CoA. This may be related to the association with intracranial aneurysms, as well as to the development of hypertension at an early age, among patients with CoA when compared with other lesion groups.[16]

In a previous study, ≈10% of patients with CoA had intracranial aneurysms detected.[13] However, the occurrence of intracranial aneurysms in patients with CoA has recently been questioned, as no cases of intracranial aneurysm were found in 80 children treated for coarctation.[17] Our data would seem to contradict this and lend support to previous observations of a high prevalence of intracranial aneurysms, and the potential for such aneurysms to rupture and cause SAH, in patients with CoA.[18]

The risk of death in survivors of hemorrhagic stroke has been shown to be increased when compared with the general population.[19] We found that the overall risk of death after hemorrhagic stroke was high among patients with CHD, but not significantly different from that of controls, regardless of birth cohorts and lesions. Improvements in treatment

after stroke, and the introduction of specialized stroke units for adults, have most likely contributed to better survival after stroke.[20,21] In addition, recent advances in surgical procedures, treatments, and pediatric care for patients with CHD over time may have affected overall survival.[4] The underlying pathophysiological mechanisms may also be similar among CHD patients and controls (ie, hypertension, anticoagulation, and intracranial aneurysm), although these conditions are relatively more common among children and young adults with CHD compared with controls.

Our results highlight the complexity and heterogeneity of CHD. Despite using nationwide registers that include all CHD patients for an entire nation, the number of hemorrhagic stroke events was limited. Further studies are required to investigate mechanisms and prevention strategies for hemorrhagic stroke among CHD patients.

Limitations

There are limitations and strengths in our study. A major strength is the use of the Swedish Inpatient and Cause-of-Death Registers, which have near-complete coverage of all hospitalizations for CHD for an entire nation, with a control population matched by age, sex, and county. A limitation is the validity of CHD, ICH, and SAH diagnoses in the registry data because we did not have access to medical records. However, children and adults with CHD are generally administrated and treated by specialized units. For stroke diagnosis, computed tomography has been in routine use in Sweden since the 1980s, and virtually all children and adults in this cohort will have undergone imaging studies to distinguish between ischemic and hemorrhagic stroke. In addition, previous studies on the Inpatient and Cause-of-Death Registers have shown a high validity of major diagnoses, with a positive predictive value of 85% to 95%.[22] However, data from the Outpatient Register are only available from 2000 onwards in Sweden, and so patients who were exclusively managed in outpatient clinics before 2000 could not be identified. Another limitation is the use of 3 different versions of *ICD* codes, which may have affected the comparability of the different periods; however, we do not think that this occurred to the extent that it affected our results. Finally, the Inpatient Register does not contain information on medication, blood pressure levels, or other clinical variables that may contribute to our understanding of the individual, patient-related risk.

Conclusions

In this nationwide, large cohort study, we found that the overall risk of hemorrhagic stroke among children and young adults with CHD was nearly 8× higher among patients with CHD than in matched controls from the general population; however, the absolute risk was low. The relative risk differed among lesion groups; the highest risk of ICH and SAH was found among patients with severe nonconotruncal defects and CoA, respectively. In addition, the mortality risk after a first hemorrhagic stroke was similar in patients with CHD and controls.

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Disclosures

None.

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ONLINE SUPPLEMENT

Long-term risk of hemorrhagic stroke in young patient's with congenital heart disease

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Supplementary Table I. International Classification of Disease codes (ICD) for lesion groups of congenital heart disease.

Lesion groups	Description	ICD-8	ICD-9	ICD-10
1. Conotruncal defects	Common truncus, Aortopulmonary septum defect, Transposition of great vessels, Tetralogy of Fallot.	746.0, 746.1, 746.2	745A, 745B, 745C	Q200, Q214, Q201-203, Q213
2. Severe non-conotruncal defects	Endocardial cushion defects, Common ventricle, Hypoplastic left heart syndrome	746.47, 746.37, 746.74	745G, 745D, 746H	Q212, Q204, Q234
3. CoA	Coarctation of the aortae	747.19	747B	Q251
4. VSD	Ventricular septal defect, other congenital malformations of cardiac septa	746.39, 746.89	745E, 745W	Q210, Q218
5. ASD	Atrial septal defect	746.42, 746.43, 746.46	745F	Q211
6. Other heart and circulatory system anomalies	Defined as diagnoses not classified into the 5 groups above			

CoA = coarctation of the aortae, VSD = ventricular septal defect, ASD = atrial septal defect.

Supplementary table II. Cardiovascular comorbidities in patients with CHD and control, prior to or in coinciding with index intracerebral and subarachnoid hemorrhage stroke.

	CHD n (%)	**Controls n (%)**
ICH		
Diabetes mellitus	1 (0.01)	-
Hypertension	1 (0.01)	5 (0.05)
Heart failure	7 (0.1)	-
Atrial fibrillation	3 (0.04)	-
SAH		-
Diabetes	3 (0.05)	1 (0.01)
Hypertension	5 (0.09)	3 (0.04)
Heart failure	3 (0.05)	-
Atrial fibrillation	1 (0.02)	-

CHD = congenital heart disease, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage