Cardiology in the Young

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Association between CHD and cerebral abscess: insights from a national database

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Tweet: No association between congenital heart disease and cerebral abscess in a contemporary cohort of patients in the United States #PedsCards #PedsID @mattcoghill.

Abstract

CHD has been historically associated with the development of cerebral abscess. This retrospective cohort study examines the association of CHD with the occurrence of cerebral abscess in an inpatient paediatric population. We analysed data from the Pediatric Health Information System database, an administrative database that captures data from participating children's hospitals in the United States. We included all patients admitted to participating paediatric ICUs between 2016 and 2021 for a total of 426,029 admissions. Including all admissions, 1,387 (0.3%) patients experienced a cerebral abscess, and of 80,927 (19%) patients with CHD, only 88 (0.1%) experienced a cerebral abscess (odds ratio 0.29, 0.23–0.36). Patients with seizures, cerebral oedema, stroke, shock, surgical intervention, and older age were associated with increased risk of development of a cerebral abscess. Interestingly, the development of a cerebral abscess was not associated with an increased risk of mortality ($p = 0.937$). When compared to patients without CHD admitted to the paediatric ICU, those with CHD appear less likely to develop a cerebral abscess. This study reiterates that cerebral abscess is a rare occurrence and does not demonstrate any significant association with CHD in a contemporary, inpatient population in the United States.

Introduction

Cerebral abscess is a rare but serious infection associated with significant morbidity and mortality in the paediatric population.[1] Historically, it has been observed that patients with CHD are predisposed to the development of cerebral abscesses.[2–5] This increased risk is attributed to a variety of proposed mechanisms including the presence of right-to-left shunting of blood flow bypassing pulmonary filtration, increased risk of endocarditis associated with CHD, increased blood viscosity, and cardiopulmonary bypass utilization.[4]

The detection and treatment of CHD have improved over time. The primary aim of this paper is to identify the prevalence of cerebral abscess in all paediatric ICU admissions and compare this to the prevalence of cerebral abscesses in a subset of admissions with CHD. The secondary aim was to investigate factors associated with cerebral abscesses. We provide a model to predict those at highest risk of developing a cerebral abscess.

Materials and methods

Aims

The primary aim of this study was to characterize the prevalence of cerebral abscess in paediatric ICU admissions with and without CHD. Secondary aims were to identify congenital malformations of the heart and comorbidities associated with cerebral abscess in children with CHD and to develop a risk score for cerebral abscess in those with CHD.

Ethical considerations

This study is in accordance with the Helsinki declaration. Although all data are publicly available and deidentified, institutional review board approval was received for this at Texas Children's Hospital, as this was the institution where the data were retrieved.

PHIS database

Data for this study were obtained from the Pediatric Health Information System (PHIS) database. PHIS is an administrative and billing database that contains inpatient, emergency

department, ambulatory surgery, and observation data from not-for-profit, tertiary care paediatric hospitals in the United States. Data for this study were available from 46 hospitals that contribute data to PHIS and are affiliated with the Children's Hospital Association (Lenexa, KS), a business alliance of children's hospitals. Data quality and reliability are assured through a joint effort between Children's Hospital Association and participating hospitals. For the purposes of external benchmarking, participating hospitals provide discharge/encounter data including demographics, diagnoses, procedures, and charges. Data are deidentified at the time of data submission, and data are subjected to reliability and validity checks before inclusion in the database.

Data selection and extraction

Data from the PHIS database from 2016 to 2021 were utilized, including these years. This represents the most recent data that are available that utilize ICD-10 codes. ICU admissions were identified utilizing the ICU flag. CHD was identified utilizing ICD-10 codes for various congenital malformations of the heart. Inclusion criteria for admissions utilized in the final analyses were (1) paediatric admissions under 18 years of age and (2) admission to an ICU.

The presence of cerebral abscess was determined by querying the data for ICD-10 codes for cerebral abscess. Specific congenital malformations of the heart were identified using ICD-10 codes.[6,7] The presence of specific comorbidities, including but not limited to acute kidney injury, chronic kidney disease, acute hepatic insufficiency, respiratory distress syndrome, endocarditis, and stroke, was similarly identified. Some comorbidities had a secondary effect of serving as severity of illness measures such as individual organ dysfunction, acidosis, need for mechanical ventilation, need for extracorporeal membrane oxygen, and cardiac arrest. Heart failure was a composite variable consisting of systolic and/or diastolic dysfunction of the left and/or right ventricle. Genetic anomaly was a composite variable consisting of any identified syndrome or genetic aberration that was coded. The timing of when specific morbidities occurred in the admission relative to one another was not available.

Statistical analyses

The admissions found to meet the inclusion criteria were divided into two groups: those with and without cerebral abscess. Univariate comparisons were conducted with Mann–Whitney *U* tests to compare continuous variables between groups and Fisher's exact tests to compare descriptive variables between groups. Next, a logistic regression was conducted to model cerebral abscess. This was a backward likelihood ratio logistic regression with patient age, various congenital malformations of the heart, comorbidities, and clinical interventions included as independent variables.

These analyses were conducted twice. The first was with all paediatric ICU patients and thus allowed for determining if CHD had an independent association with cerebral abscess. The second set of analyses was for only those with CHD, which allowed for determining if specific congenital malformations of the heart had an independent association with cerebral abscess.

Next, a scoring system was developed to help quantify the risk of cerebral abscess in all paediatric ICU patients. This was done using the regression results to model cerebral abscess in all patients. Independent variables that were found to be statistically significantly associated with cerebral abscess were included, and the beta-coefficient from the regression for each was utilized as the coefficient in the scoring system. A receiver operating characteristic curve was used to evaluate the scoring system and determine an optimal cutoff point.

Next, a regression was done in only patients with CHD to help determine if there was an independent association between cerebral abscess and inpatient mortality.

Results

Analyses for all ICU admissions

A total of 426,029 paediatric ICU admissions were analysed (Table 1). Of these admissions, 80,927 (19%) had CHD, and 1,387 (0.3%) experienced a cerebral abscess. On univariate analysis, the following factors were associated with an increased risk of cerebral abscess: seizures (odds ratio 5.48, 95% confidence interval 4.70–6.38), cerebral oedema (19.8, 17.55–22.45), stroke (8.07, 6.58–9.90), shock (1.47, 1.24–1.74), endocarditis (4.62, 3.05–7.00), and surgical intervention (9.17, 7.90–10.64). On univariate analysis, the following factors were associated with a decreased risk of cerebral abscess: CHD (0.29, 0.23–0.36), genetic anomaly (0.15, 0.091–0.26), acute respiratory distress syndrome (0.34, 0.13–0.92), chronic kidney disease (0.22, 0.11–0.46), heart failure (0.11, 0.046–0.26), extracorporeal membrane oxygenation (0.17, 0.051–0.51), and cardiac arrest (0.37, 0.19–0.72) (Table 1). Cerebral abscess was associated with higher adjusted billed charges (214,890 vs 226,960 $p < 0.01$), longer length of stay (5 vs 15 days; $p < 0.01$), and older age (48 months vs 113 months; $p < 0.01$). Of note, cerebral abscess was not associated with a mortality difference ($p = 0.937$).

ICU admissions with CHD

A total of 80,927 paediatric ICU admissions with CHD were analysed (Table 2). Of these admissions, 88 (0.1%) developed a cerebral abscess. On univariate analysis, the following factors were associated with an increased risk of cerebral abscess: seizures (7.7, 3.97–14.87), cerebral oedema (110, 71.65–170.64), shock (2.14, 1.16–3.93), endocarditis (8.15, 3.55–18.74), surgical intervention (2.19, 1.29–3.72), and brain death (11.3, 1.56–82.24). On univariate analysis, the following factors were associated with a decreased risk of cerebral abscess: genetic anomaly (0.37, 0.16–0.83) and heart failure (0.19, 0.048–0.79). Cerebral abscess was associated with longer length of stay (8 vs 20 days; $p < 0.01$) and older age (8 months vs 22 months; $p < 0.01$). Of note, cerebral abscess was not associated with a mortality difference ($p = 0.173$).

Cerebral abscess risk score

A model to determine those at highest risk of developing a cerebral abscess in the paediatric ICU patients was developed: (CHD × −0.361) - (Acute Kidney Injury × 0.250) - (Respiratory Failure × 0.956) - (Heart Failure × 0.422) - (Arrhythmia × 0.287) + (Infection × 1.554) + (Mechanically Ventilated × 0.259) - (ECMO × 0.618) + (Seizures × 1.272) + (Stroke × 1.599) + (Endocarditis × 0.540). This resulted in an area under the receiver operating characteristic of 0.873 (0.867–0.879) with $p < 0.001$, an optimal cutoff point of 1.19. A score of less than -1 was associated with a near-zero probability of cerebral abscess, a score between -1 and 1 was associated with 0.1% probability of cerebral abscess, a score between 1 and 3 was associated with a 1.1% probability of cerebral abscess, and a score above 3 was associated with a 5.5% probability of cerebral abscess.

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Table 1. Univariate analysis of cerebral abscess risk for all paediatric ICU patients. Values reported as frequency with percentages or medians and ranges where appropriate

Heart failure	13,555 (3.2)	5 (0.4)	0.11 (0.046–0.26)	<0.01
Myocarditis	353 (0.1)	2 (0.1)	0.71 (0.43–6.97)	0.437
Chylothorax	1,745 (0.4)	0 (0)	–	–
Infection	219,500 (51.7)	1,387 (100)	***	***
Surgical intervention	164,558 (38.8)	1,183 (85.3)	9.17 (7.90–10.64)	<0.01
Mechanical ventilation	153,141 (36.1)	509 (36.7)	1.03 (0.92–1.15)	0.623
Extracorporeal membrane oxygenation	5,519 (1.3)	3 (0.2)	0.17 (0.051–0.51)	<0.01
Cardiac arrest	7,306 (1.7)	9 (0.6)	0.37 (0.19–0.72)	<0.01
Brain death	1,668 (0.4)	5 (0.4)	0.92 (0.38–2.21)	0.848
Mortality	11,791 (2.8)	39 (2.8)	1.01 (0.74–1.39)	0.937
Adjusted billed charges	214,890	226,960	–	<0.01
Length of stay	5 (1–2,448)	15 (1–46.7)	–	<0.01
Age (months)	48 (0–1,413)	113 (0–576)	–	<0.01

Table 2. Univariate analysis of cerebral abscess risk for patients with CHD. Values reported as frequency with percentages or medians and ranges where appropriate

	No cerebral abscess (n = 80,839)	Cerebral abscess (n = 88)	Odds ratio	p-value
Female gender	36,544 (54.7)	28 (31.8)	–	–
Genetic anomaly	13,219 (16.4)	6 (6.8)	0.37 (0.16–0.83)	0.020
Acute respiratory distress syndrome	436 (0.5)	1 (1.1)	2.1 (0.30–15.25)	0.456
Acute kidney injury	7,683 (9.5)	8 (9.1)	0.95 (0.46–1.97)	0.895
Chronic kidney injury	1,261 (1.6)	0 (0)	–	–
Acute hepatic failure	562 (0.7)	1 (1.1)	1.64 (0.23–11.80)	0.622
Chronic hepatic failure	83 (0.1)	0 (0)	–	–
Seizures	1,327 (1.6)	10 (11.4)	7.7 (3.97–14.87)	<0.01
Cerebral oedema	503 (0.6)	36 (40.9)	110 (71.65–170.64)	<0.01
Stroke	***	***	***	***
Shock	5,564 (6.9)	12 (13.6)	2.14 (1.16–3.93)	0.015
Malignancy	1,341 (1.7)	3 (3.4)	2.09 (0.66–6.63)	0.209
Heart failure	8,646 (10.7)	2 (2.3)	0.19 (0.048–0.79)	0.22
Myocarditis	49 (0.1)	0 (0)	–	–
Chylothorax	1,276 (1.6)	0 (0)	–	–
Infection	35,400 (43.8)	88 (100)	–	–
Surgical intervention	52,997 (65.6)	71 (80.7)	2.19 (1.29–3.72)	<0.01
Mechanical ventilation	48,819 (60.4)	47 (53.4)	0.75 (0.49–1.14)	0.182
Extracorporeal membrane oxygenation	3,366 (4.2)	2 (2.3)	0.54 (0.13–2.18)	0.382
Cardiac arrest	1,805 (2.2)	1 (1.1)	0.50 (0.070–3.62)	0.495
Brain death	82 (0.1)	1 (1.1)	11.3 (1.56–82.24)	0.016
Mortality	3,191 (3.9)	6 (6.8)	1.78 (0.77–4.08)	0.173
Adjusted billed charges	428,191	587,486	–	0.079
Length of stay	8 (1–1020)	20 (1–435)	–	<0.01
Age (months)	8 (0–882)	22 (0–572)	–	<0.01

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Regression analysis for association of cerebral abscess with mortality

On multivariable regression analysis for cerebral abscess in patients with CHD, cerebral abscess was not found to be independently associated with mortality (beta-coefficient -0.245, $p = 0.165$). The following independent variables were found to be independently associated with mortality in admissions with CHD: seizures, malignancy, arrhythmia, shock, acute respiratory distress syndrome, stroke, and acute kidney injury.

Discussion

To our knowledge, this is the largest multi-institutional study to date documenting the prevalence of cerebral abscess for paediatric ICU patients in the United States, as well as the prevalence of co-incident cerebral abscess and CHD in the paediatric ICU. In this retrospective study of the PHIS database, the prevalence of cerebral abscess for all paediatric ICU admissions was 0.3% (1,387 patients), and for patients with CHD, the prevalence of cerebral abscess was 0.1% (88 patients). Previous studies include single-centre approaches in the United States as well as a population-based study in Denmark.[2,5,8–12]

In contrast to historical observations, patients with CHD in the modern era were found to be less likely to develop a cerebral abscess than those without. Additionally, of the 1,387 patients with cerebral abscess, the prevalence of CHD was only 6.3% (88 patients). This is a change when compared to smaller studies from earlier time periods and from other countries, which have reported a prevalence of CHD in those with cerebral abscesses to be anywhere from 9.3 to 67%.[2,11,12] This difference in prevalence could potentially be explained by the early elimination of cyanotic CHD through improved diagnostic modalities (such as nationwide screening programmes for cyanotic heart disease), improved surgical technique and earlier surgical timing, and different epidemiological risk factors faced by the study population.

Patients with cerebral abscess were older than those without; however, among patients with cerebral abscess, those with CHD were younger than those with cerebral abscess but no associated CHD. It is reasonable to surmise that this might be related to the age distribution of persistent right-to-left shunts in the study population, as well as the preferential exposure to cardiopulmonary bypass, given the timing of surgical repairs in the modern era.

Additional risk factors were found, on univariate analysis, to be associated with increased risk of cerebral abscess in the CHD population. Endocarditis was a risk factor for the development of a cerebral abscess in those with and without CHD. Historically, endocarditis is associated with CHD.[13] Other risk factors such as cerebral oedema and surgical intervention are associated with cerebral abscess on univariate analysis.

Interestingly, our data did not show a mortality decrement with brain abscess development in patients regardless of CHD status. There have been significant improvements in the diagnosis and treatment of cerebral abscess compared with previous eras.[1] This study does not examine other important prognostic factors for cerebral abscess such as size of various cerebral abscess, initial Glasgow coma score, or intraventricular rupture of the abscess. Our analysis cannot directly assess morbidity associated with cerebral abscess.

Despite the large number of patients included in this study, the heterogeneity of CHD and small numbers of patients with cerebral abscess limit our analysis specific to various subsets of CHD. The administrative nature of the database is limited by the inputted data from participating centres and may contain variances and outright inaccuracies in disease classification. We are only able to make associations and not causal inferences. The nature of the data also does not allow an analysis of other likely important factors such as unrepaired versus repaired lesions, baseline hypoxia, and baseline haemoglobin. The classification of disease, such as the type of CHD and complicating diagnosis, in this dataset cannot be validated.

Paediatric patients with CHD admitted to the paediatric ICU appear less likely to develop a cerebral abscess when compared to similar patients without CHD. This change from the historical association potentially reflects the earlier diagnosis and interventions for cyanotic disease. Cerebral abscess, based on historical reports, likely remains a concerning complication in certain subtypes of CHD, but its consequence is minimized in the current era among an inpatient population in the United States.

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Competing interests. The author(s) declare none.

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