

RISK OF VERTEBROBASILAR STROKE AND CHIROPRACTIC CARE

Results of a Population-Based Case-Control and Case-Crossover Study

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ABSTRACT

Study Design: Population-based, case-control and case-crossover study.

Objective: To investigate associations between chiropractic visits and vertebrobasilar artery (VBA) stroke and to contrast this with primary care physician (PCP) visits and VBA stroke.

Summary of Background Data: Chiropractic care is popular for neck pain and headache, but may increase the risk for VBA dissection and stroke. Neck pain and headache are common symptoms of VBA dissection, which commonly precedes VBA stroke.

Methods: Cases included eligible incident VBA strokes admitted to Ontario hospitals from April 1, 1993 to March 31, 2002. Four controls were age and gender matched to each case. Case and control exposures to chiropractors and PCPs were determined from health billing records in the year before the stroke date. In the case-crossover analysis, cases acted as their own controls.

Results: There were 818 VBA strokes hospitalized in a population of more than 100 million person-years. In those aged <45 years, cases were about three times more likely to see a chiropractor or a PCP before their stroke than controls. Results were similar in the case control and case crossover analyses. There was no increased association between chiropractic visits and VBA stroke in those older than 45 years. Positive associations were found between PCP visits and VBA stroke in all age groups. Practitioner visits billed for headache and neck complaints were highly associated with subsequent VBA stroke.

Conclusion: VBA stroke is a very rare event in the population. The increased risks of VBA stroke associated with chiropractic and PCP visits is likely due to patients with headache and neck pain from VBA dissection seeking care before their stroke. We found no evidence of excess risk of VBA stroke associated chiropractic care compared to primary care. (J Manipulative Physiol Ther 2009;32:S201-S208)

Key words: *vertebrobasilar stroke; case control studies; case crossover studies; chiropractic; primary care; complications; neck pain*

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Neck pain is a common problem associated with considerable comorbidity, disability, and cost to society.¹⁻⁵ In North America, the clinical management of back pain is provided mainly by medical physicians, physical therapists and chiropractors.⁶ Approximately 12% of American and Canadian adults seek chiropractic care annually and 80% of these visits result in spinal manipulation.^{7,8} When compared to those seeking medical care for back pain, Canadian chiropractic patients tend to be younger and have higher socioeconomic status and fewer health problems.^{6,8} In Ontario, the average number of chiropractic visits per episode of care was 10 (median 6) in 1985 through 1991.⁷ Several systematic reviews and our best evidence synthesis suggest that manual therapy can benefit neck pain, but the trials are too small to evaluate the risk of rare complications.⁹⁻¹³

Two deaths in Canada from vertebral artery dissection and stroke following chiropractic care in the 1990s attracted much media attention and a call by some neurologists to avoid neck manipulation for acute neck pain.¹⁴ There have been many published case reports linking neck manipulation to vertebral artery dissection and stroke.¹⁵ The prevailing theory is that extension and/or rotation of the neck can damage the vertebral artery, particularly within the foramen transversarium at the C1-C2 level. Activities leading to sudden or sustained rotation and extension of the neck have been implicated, included motor vehicle collision, shoulder checking while driving, sports, lifting, working overhead, falls, sneezing, and coughing.¹⁶ However, most cases of extracranial vertebral arterial dissection are thought to occur spontaneously, and other factors such as connective tissue disorders, migraine, hypertension, infection, levels of plasma homocysteine, vessel abnormalities, atherosclerosis, central venous catheterization, cervical spine surgery, cervical percutaneous nerve blocks, radiation therapy and diagnostic cerebral angiography have been identified as possible risk factors.¹⁷⁻²¹

The true incidence of vertebrobasilar dissection is unknown, since many cases are probably asymptomatic, or the dissection produces mild symptoms.²² Confirming the diagnosis requires a high index of suspicion and good vascular imaging. The cases that are most likely to be diagnosed are those that result in stroke.^{19,22} Ischemic stroke occurs when a thrombus develops intraluminally and embolizes to more distal arteries, or less commonly, when the dissection extends distally into the intracranial vertebral artery, obliterating branching vessels.²² The best incidence estimate comes from Olmstead county, where vertebral artery dissection causing stroke affected 0.97 residents per 100,000 population between 1987 and 2003.²³

To date there have been two case-control studies of stroke following neck manipulation. Rothwell et al used Ontario health data to compare 582 cases of VBA stroke to 2328 age and sex-matched controls.²⁴ For those aged <45 years, cases were five times more likely than controls to have visited a

chiropractor within 1 week of VBA stroke. Smith et al studied 51 patients with cervical artery dissection and ischemic stroke or transient ischemic attack (TIA) and compared them to 100 control patients suffering from other strokes not caused by dissections.²⁵ Cases and controls came from two academic stroke centers in the United States and were matched on age and sex. They found no significant association between neck manipulation and ischemic stroke or TIA. However, a subgroup analysis showed that the 25 cases with vertebral artery dissection were six times more likely to have consulted a chiropractor within 30 days before their stroke than the controls.

Finally, because patients with vertebrobasilar artery dissection commonly present with headache and neck pain,²³ it is possible that patients seek chiropractic care for these symptoms and that the subsequent VBA stroke occurs spontaneously, implying that the association between chiropractic care and VBA stroke is not causal.^{23,26} Since patients also seek medical care for headache and neck pain, any association between primary care physician (PCP) visits and VBA stroke could be attributed to seeking care for the symptoms of vertebral artery dissection.

The purpose of this study is to investigate the association between chiropractic care and VBA stroke and compare it to the association between recent PCP care and VBA stroke using two epidemiological designs. Evidence that chiropractic care increases the risk of VBA stroke would be present if the measured association between chiropractic visits and VBA stroke exceeds the association between PCP visits and VBA strokes.

METHODS

Study Design

We undertook population-based case-control and case-crossover studies. Both designs use the same cases. In the case-control design, we sampled independent control subjects from the same source population as the cases. In the case-crossover design, cases served as their own controls, by sampling control periods before the study exposures.²⁷ This design is most appropriate when a brief exposure (e.g., chiropractic care) causes a transient change in risk (i.e., hazard period) of a rare-onset disease (e.g., VBA stroke). It is well suited to our research questions, since within person comparisons control for unmeasured risk factors by design, rather than by statistical modeling.²⁸⁻³⁰ Thus the advantage over the case control design is better control of confounding.

Source Population

The source population included all residents of Ontario (109,020,875 person-years of observation over 9 years) covered by the publicly funded Ontario Health Insurance Plan (OHIP). Available utilization data included hospitaliza-

tions with diagnostic coding, and practitioner (physician and chiropractic) utilization as documented by fee-for-service billings accompanied by diagnostic coding. We used two data sources: (1) the Discharge Abstract Database (DAD) from the Canadian Institute for Health Information, which captures hospital separations and ICD codes, and (2) the OHIP Databases for services provided by physicians and chiropractors. These databases can be linked from April 1992 onward.

Cases

We included all incident vertebrobasilar occlusion and stenosis strokes (ICD-9433.0 and 433.2) resulting in an acute care hospital admission from April 1, 1993 to March 31, 2002. Codes were chosen in consultation with stroke experts and an epidemiologist who participated in a similar past study (SB).²⁴ Cases that had an acute care hospital admission for any type of stroke (ICD-9433.0, 433.2, 434, 436, 433.1, 433.3, 433.8, 433.9, 430, 431, 432, and 437.1), transient cerebral ischemia (ICD-9435) or late effects of cerebrovascular diseases (ICD-9438) before their VBA stroke admission or since April 1, 1991 were excluded. Cases residing in long-term care facilities were also excluded. The index date was defined as the hospital admission date for the VBA stroke.

Controls

For the case-control study, four age and sex-matched controls were randomly selected from the Registered Persons Database, which contains a listing of all health card numbers for Ontario. Controls were excluded if they previously had a stroke or were residing in a long-term care facility.

For the case-crossover study, four control periods were randomly chosen from the year before the VBA stroke date, using a time-stratified approach.³¹ The year was divided into disjoint strata with 2 week periods between the strata. For the 1 month hazard period, the disjoint strata were separated by 1 month periods and the five remaining control periods were used in the analyses. We randomly sampled disjoint strata because chiropractic care is often delivered in episodes, and this strategy eliminates overlap bias and bias associated with time trends in the exposure.³²

Exposures

All reimbursed ambulatory encounters with chiropractors and PCPs were extracted for the one-year period before the index date from the OHIP database. Neck-related chiropractic visits were identified using diagnostic codes: C01–C06, cervical and cervicothoracic subluxation; C13–C15, multiple site subluxation; C30, cervical sprain/strain; C40, cervical neuritis/neuralgia; C44, arm neuritis/neuralgia; C50, brachial radiculitis; C51, cervical radiculitis; and C60, headache. For PCP visits, we included community

Table 1. Age, Sex, and Comorbid^a Condition of Cases and Controls

Variable	Cases (n = 818)	Controls (n = 3164)
Age: mean, median (SD) ^b	63.1, 66 (15.5)	62.6, 65 (15.4)
Males: n (%)	518 (63.3)	2022 (63.9)
Hypertension ^a : n (%)	276 (33.7)	738 (23.3)
Heart Disease ^a : n (%)	275 (33.6)	506 (16.0)
Diabetes ^a : n (%)	155 (19.0)	247 (7.8)
High Cholesterol ^a : n (%)	62 (7.6)	200 (6.3)
At least one comorbid condition ^c : n (%)	515 (63.0)	1294 (40.9)

^a Comorbid conditions determined by ambulatory diagnostic codes from the Ontario Health Insurance Plan (OHIP) during year prior to index date.

^b SD is standard deviation.

medicine physicians if they submitted ambulatory fee codes to OHIP. Fee codes for group therapy and signing forms were excluded. Headache or neck pain-related PCP visits were identified using the diagnostic codes: ICD-9307, tension headaches; 346, migraine headaches; 722, intervertebral disc disorders; 780, headache, except tension headache and migraine; 729, fibrositis, myositis and muscular rheumatism; and 847, whiplash, sprain/strain and other traumas associated with neck (These codes include other diagnoses, and we list only those relevant to neck pain or headache). There is no limit on the number of reimbursed PCP visits per year. However, there are limits chiropractors, but less than 15% of patients surpass them.²⁴

Statistical Analysis

Conditional logistic regression was used to estimate the association between VBA stroke after chiropractor and PCP visits. Separate models were built using different a priori specified hazard periods, stratified by age (<45 years and ≥45 years) and by visits with or without head and neck pain related diagnostic codes. For the chiropractic analysis, the index date was included in the hazard period, since chiropractic treatment might cause immediate stroke and patients would not normally consult a chiropractor after having a stroke. However, the index day was excluded from the PCP analysis, since patients might consult these physicians after experiencing a stroke. We tested different hazard periods, including 1 day, 3 days, 1 week, 2 weeks, and 1 month before the index date. Exposure occurred if any chiropractic or PCP visits were recorded during the designated hazard periods.

We also measured the effect of cumulative numbers of chiropractic and PCP visits in the month before the index date by computing the odds ratio for each incremental visit. These estimates were similarly stratified by age and by diagnostic codes related to headache and/or neck pain. Finally, we conducted analyses to determine if our results were sensitive to chiropractic and PCP visits related to neck

Table 2. No. (n) and Percentage (%) of Chiropractic (DC) and Primary Care Physician (PCP) Visits Before the Index Date

Exposures	Entire Cohort		Age <45 yr		Age ≥45 yr	
	Cases (n = 818)	Controls (n = 3164)	Cases (n = 102)	Controls (n = 408)	Cases (n = 716)	Controls (n = 2756)
Most recent DC visit						
0–1 day: n (%)	6 (0.7)	22 (0.7)	^a	^a	^a	21 (0.8)
0–3 days: n (%)	9 (1.1)	40 (1.3)	^a	6 (1.5)	^a	34 (1.2)
0–7 days: n (%)	14 (1.7)	56 (1.8)	8 (7.8)	14 (3.4)	6 (0.8)	42 (1.5)
0–14 days: n (%)	27 (3.3)	88 (2.8)	12 (11.8)	17 (4.2)	15 (2.1)	71 (2.6)
0–30 days: n (%)	36 (4.4)	125 (4.0)	13 (12.7)	18 (4.4)	23 (3.2)	107 (3.9)
Most recent PCP visit						
1–1 day: n (%)	63 (7.7)	41 (1.3)	12 (11.8)	6 (1.5)	51 (7.1)	35 (1.3)
1–3 days: n (%)	111 (13.6)	130 (4.1)	18 (17.6)	10 (2.5)	93 (13.0)	120 (4.4)
1–7 days: n (%)	205 (25.1)	290 (9.2)	25 (24.5)	27 (6.6)	180 (25.1)	263 (9.5)
1–14 days: n (%)	311 (38.0)	517 (16.3)	38 (37.3)	46 (11.3)	273 (38.1)	471 (17.1)
1–30 days: n (%)	437 (53.4)	945 (29.9)	46 (45.1)	83 (20.3)	391 (54.6)	862 (31.3)
No. of DC visits						
None in past month	782 (95.6)	3039 (96.0)	89 (87.3)	390 (95.6)	693 (96.8)	2649 (96.1)
1 or 2 in past month	21 (2.6)	96 (3.0)	^a	13 (3.2)	16 (2.2)	83 (3.0)
3 or more in past month	15 (1.8)	29 (0.9)	8 (7.8)	^a	7 (1.0)	24 (0.9)
Mean (SD) ^b in past month	0.13 (0.82)	0.08 (0.52)	0.50 (1.65)	0.09 (0.49)	0.08 (0.60)	0.08 (0.53)
No. of PCP visits						
None in past month	381 (46.6)	2219 (70.1)	56 (54.9)	325 (79.7)	325 (45.4)	1894 (68.7)
1 or 2 in past month	384 (46.9)	875 (27.7)	40 (39.2)	79 (19.4)	344 (48.0)	796 (28.9)
3 or more in past month	53 (6.5)	70 (2.2)	6 (5.9)	^a	47 (6.6)	66 (2.4)
Mean (SD) in past month	0.85 (1.09)	0.41 (0.73)	0.74 (1.01)	0.27 (0.61)	0.87 (1.10)	0.43 (0.74)

^a Cell size <6 and cannot be reported.

^b SD is standard deviation.

Table 3. Odds Ratios and 95% Confidence Intervals (CI) and Accelerated and Bias Corrected Bootstrap 95% CI for Case-Control Estimates of the Association Between Chiropractic (DC) Visits and Vertebrobasilar Stroke

Exposures	Case-Control		Age <45 yr		Age ≥45 yr	
	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI
Any DC visit						
0–1 day	1.06 (0.43–2.62)	0.36–2.61	12.00 (1.25–115.36)	^a	0.55 (0.16–1.85)	0.14–1.93
0–3 days	0.87 (0.42–1.81)	0.40–1.78	3.33 (1.02–10.92)	0.80–14.00	0.44 (0.16–1.26)	0.12–1.25
0–7 days	0.98 (0.54–1.77)	0.51–1.79	2.41 (0.98–5.95)	0.80–6.29	0.55 (0.23–1.30)	0.21–1.23
0–14 days	1.22 (0.78–1.90)	0.77–1.92	3.07 (1.41–6.70)	1.25–7.31	0.82 (0.47–1.45)	0.45–1.47
0–30 days	1.14 (0.78–1.67)	0.75–1.62	3.13 (1.48–6.63)	1.34–7.21	0.83 (0.52–1.32)	0.51–1.30
Headache or cervical DC visit						
0–1 day	1.59 (0.56–4.54)	0.44–4.67	^a	^a	0.63 (0.14–2.81)	0.00–3.37
0–3 days	1.22 (0.51–2.88)	0.48–3.01	5.00 (1.34–18.62)	^a	0.41 (0.09–1.77)	0.00–1.72
0–7 days	1.42 (0.71–2.86)	0.66–3.00	3.11 (1.16–8.35)	1.07–9.60	0.71 (0.24–2.10)	0.17–2.18
0–14 days	1.36 (0.79–2.33)	0.78–2.34	3.27 (1.36–7.90)	1.23–8.67	0.84 (0.41–1.75)	0.35–1.68
0–30 days	0.98 (0.60–1.61)	0.56–1.57	3.00 (1.26–7.12)	1.18–8.00	0.63 (0.33–1.19)	0.30–1.13

^a Unable to compute due to small numbers.

complaints and headaches. We report our results as odds ratios (OR) and 95% confidence intervals. Confidence intervals were estimated by accelerated bias corrected bootstraps with 2000 replications using the variance-covariance method.³³ All statistical analyses were performed using STATA/SE version 9.2.³⁴

RESULTS

A total of 818 VBA strokes met our inclusion/exclusion criteria over the 9 year inception period. Of the 3272 matched control subjects, 31 were excluded because of prior stroke, one had died before the index date and 76 were

Table 4. Odds Ratios and 95% Confidence Intervals (CI) and Accelerated and Bias Corrected Bootstrap 95% CI for Case-Control Estimates of the Association Between Primary Care Physician (PCP) Visits and Vertebrobasilar Stroke

Exposure	Case Control		Age <45 yr		Age ≥45 yr	
	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI
Any PCP visit						
1–1 day	7.22 (4.70–11.08)	4.62–11.23	11.21 (3.59–35.03)	2.67–52.00	6.65 (4.18–10.58)	4.16–10.73
1–3 days	3.61 (2.76–4.73)	2.73–4.75	9.53 (3.96–22.97)	3.52–28.00	3.21 (2.41–4.27)	2.38–4.32
1–7 days	3.27 (2.67–4.00)	2.73–4.00	4.81 (2.57–9.02)	2.40–8.72	3.12 (2.52–3.87)	2.52–3.87
1–14 days	3.11 (2.61–3.69)	2.62–3.65	4.66 (2.78–7.84)	2.71–7.85	2.95 (2.46–3.54)	2.47–3.54
1–30 days	2.76 (2.35–3.24)	2.35–3.26	3.57 (2.17–5.86)	2.08–6.16	2.67 (2.25–3.17)	2.26–3.17
Headache or cervical PCP visit						
1–1 day	32.00 (7.36–139.17)	^a	12.00 (1.25–115.36)	^a	52.00 (6.80–397.50)	^a
1–3 days	25.19 (8.78–72.24)	8.69–104.00	25.64 (3.13–209.78)	^a	25.04 (7.41–84.62)	^a
1–7 days	16.72 (8.39–33.29)	8.52–35.63	37.60 (4.80–294.70)	^a	14.39 (6.88–30.08)	6.88–35.31
1–14 days	10.89 (6.53–18.16)	6.59–18.76	37.60 (4.80–294.70)	^a	9.48 (5.56–16.19)	5.56–16.61
1–30 days	6.96 (4.66–10.41)	4.68–10.42	11.45 (3.68–35.62)	3.50–53.57	6.42 (4.17–9.89)	4.20–10.18

^a Unable to compute due to small numbers.

Table 5. Odds Ratios and 95% Confidence Intervals (CI) and Accelerated and Bias Corrected Bootstrap 95% CI for Case-Crossover Estimates of the Association Between Chiropractic (DC) Visits and Vertebrobasilar Stroke

Exposure	Case Crossover		Age <45 yr		Age ≥45 yr	
	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI
Any DC visit						
0–1 day	1.77 (0.66–4.79)	0.49–5.60	5.04 (0.82–30.99)	^a	1.09 (0.30–4.02)	0.00–4.84
0–3 days	1.14 (0.52–2.51)	0.50–2.76	3.44 (0.96–12.28)	^a	0.61 (0.20–1.84)	0.18–2.11
0–7 days	0.80 (0.41–1.56)	0.35–1.85	12.19 (2.52–58.98)	^a	0.30 (0.12–0.77)	^a
0–14 days	1.50 (0.89–2.52)	0.84–2.74	4.49 (1.60–12.63)	^a	0.98 (0.51–1.87)	0.47–2.01
0–30 days	1.25 (0.76–2.06)	0.74–2.13	3.60 (1.39–9.35)	1.46–10.84	0.86 (0.47–1.56)	0.45–1.57
Headache or cervical DC visit						
0–1 day	6.67 (1.59–27.90)	^a	^a	^a	2.67 (0.45–15.96)	^a
0–3 days	2.42 (0.88–6.66)	0.70–8.00	17.70 (2.04–153.32)	^a	0.70 (0.14–3.40)	0.00–6.00
0–7 days	1.77 (0.80–3.94)	0.68–4.68	^a	^a	5.18 (0.16–1.66)	^a
0–14 days	3.16 (1.57–6.36)	1.43–7.35	33.61 (4.24–266.38)	^a	1.40 (0.58–3.34)	0.45–3.41
0–30 days	2.17 (1.09–4.31)	0.97–4.68	29.47 (3.60–241.54)	^a	1.03 (0.45–2.39)	0.37–2.42

^a Unable to compute due to small numbers.

receiving long-term care. Thus, 3164 control subjects were matched to the cases. The mean age of cases and controls was 63 years at the index date and 63% were male. Cases had a higher proportion of comorbid conditions (Table 1). Of the 818 stroke cases, 337 (41.2%) were coded as basilar occlusion and stenosis, 443 (54.2%) as vertebral occlusion and stenosis and 38 (4.7%) had both codes.

Overall, 4% of cases and controls had visited a chiropractor within 30 days of the index date, while 53% of cases and 30% of controls had visited a PCP within that time (Table 2). For those under 45 years of age, 8 cases (7.8%) had consulted a chiropractor within 7 days of the index date, compared to 14 (3.4%) of controls. For PCPs, 25 cases (24.5%) under 45 years of age had a consultation within 7 days of the index date, compared to 27 (6.6%) of controls. With respect to the number of visits within 1 month of the index date, 7.8% of cases under the age of

45 years had three or more chiropractic visits, whereas 5.9% had three or more PCP visits (Table 2).

The case control and case crossover analyses gave similar results. (Tables 3–7) Age modified the effect of chiropractic visits on the risk of VBA stroke. For those under 45 years of age, there was an increased association between chiropractic visits and VBA stroke regardless of the hazard period. For those 45 years of age and older, there was no association. Each chiropractic visit in the month before the index date was associated with an increased risk of VBA stroke in those under 45 years of age (OR 1.37; 95% CI 1.04–1.91 from the case crossover analysis) (Table 7). We were not able to estimate bootstrap confidence intervals in some cases because of sparse data.

Similarly, we found that visiting a PCP in the month before the index date was associated with an increased risk of VBA stroke regardless of the hazard period, or the age of

Table 6. Odds Ratios and 95% Confidence Intervals (CI) and Accelerated and Bias Corrected Bootstrap 95% CI for Case-Crossover Estimates of the Association Between Primary Care Physician (PCP) Visits and Vertebrobasilar Stroke

Exposure	Case Crossover		Age <45 yr		Age ≥45 yr	
	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI
Any PCP visit						
1–1 day	4.36 (3.02–6.28)	3.09–6.54	15.24 (4.29–54.20)	3.70–68.00	3.72 (2.52–5.50)	2.53–5.64
1–3 days	2.91 (2.25–3.77)	2.24–3.71	5.62 (2.56–12.36)	2.10–14.60	2.68 (2.03–3.53)	2.02–3.55
1–7 days	2.36 (1.93–2.89)	1.92–2.95	2.90 (1.64–5.13)	1.56–5.09	2.30 (1.85–2.85)	1.85–2.93
1–14 days	2.38 (1.99–2.86)	1.96–2.87	3.53 (2.09–5.97)	1.96–6.49	2.26 (1.86–2.74)	1.85–2.80
1–30 days	2.42 (2.01–2.91)	2.01–2.96	2.99 (1.81–4.96)	1.69–5.09	2.34 (1.92–2.85)	1.91–2.96
Headache or cervical PCP visit						
1–1 day	16.00 (5.35–47.86)	5.20–72.00	^a	^a	13.00 (4.24–39.87)	4.00–56.00
1–3 days	13.00 (5.89–28.71)	6.00–31.00	28.00 (3.44–227.58)	^a	10.86 (4.56–25.83)	4.57–32.00
1–7 days	8.28 (4.86–14.10)	4.87–14.82	20.00 (4.38–91.28)	^a	6.99 (3.93–12.44)	3.85–12.85
1–14 days	7.28 (4.60–11.52)	4.58–11.36	9.46 (2.95–30.31)	2.86–44.00	6.92 (4.20–11.40)	4.19–11.85
1–30 days	5.65 (3.88–8.22)	3.80–8.30	12.42 (3.95–38.99)	3.59–54.74	5.04 (3.37–7.54)	3.32–7.53

^a Unable to compute due to small numbers.**Table 7.** Odds Ratios and 95% Confidence Intervals (CI) and Accelerated and Bias Corrected Bootstrap 95% CI for Case-Control and Case Crossover Estimates of the Association Between the Total Number of Chiropractic (DC) and Primary Care Physician (PCP) Visits in the Month Prior to the Index Date

Exposures	All Cases		Age <45 yr		Age ≥45 yr	
	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI	Odds Ratio (95% CI)	Bootstrap 95% CI
Case control estimates						
Any DC visit	1.14 (1.02–1.27)	1.00–1.27	1.58 (1.19–2.10)	1.19–2.19	1.01 (0.86–1.17)	0.83–1.18
Any PCP visit	1.77 (1.61–1.93)	1.61–1.94	2.12 (1.58–2.84)	1.53–3.01	1.73 (1.57–1.90)	1.58–1.91
Headache or cervical DC visit	1.13 (0.98–1.30)	0.96–1.31	1.57 (1.17–2.11)	1.08–2.18	0.95 (0.77–1.18)	0.67–1.20
Headache or cervical PCP visit	6.33 (4.27–9.37)	4.38–9.18	10.00 (3.26–30.63)	^a	5.87 (3.85–8.95)	4.04–9.04
Case crossover estimates						
Any DC visit	1.10 (0.99–1.22)	0.97–1.24	1.37 (1.10–1.70)	1.04–1.91	0.98 (0.84–1.14)	0.80–1.15
Any PCP visit	1.49 (1.36–1.63)	1.34–1.66	1.34 (1.05–1.70)	0.94–1.87	1.52 (1.38–1.67)	1.36–1.68
Headache or cervical DC visit	1.18 (1.02–1.37)	0.99–1.45	2.80 (1.43–5.48)	^a	1.01 (0.83–1.22)	0.74–1.29
Headache or cervical PCP visit	3.99 (2.88–5.53)	2.74–5.80	10.64 (3.45–32.78)	3.53–43.56	3.53 (2.51–4.98)	2.35–5.25

^a Unable to compute due to small numbers.

the subject. Each PCP visit in the month before the stroke was associated with an increased risk of VBA stroke both in those under 45 years of age (OR 1.34; 95% CI 0.94–1.87 from the case crossover analysis) and 45 years and older (OR 1.52; 95% CI 1.36–1.67 from the case crossover analysis) (Table 7).

Our results were sensitive to chiropractic and PCP visits related to neck complaints and headaches, and we observed sharp increases in the associations when restricting the analyses to these visits (Tables 3–7). Overall, these associations were more pronounced in the PCP analyses. However, the data are sparse, and we were unable to compute bootstrap confidence intervals in many cases.

DISCUSSION

Our study advances knowledge about the association between chiropractic care and VBA stroke in two respects.

First, our case control results agree with past case control studies that found an association between chiropractic care and vertebral artery dissection and VBA stroke.^{24,25} Second, our case crossover results confirm these findings using a stronger research design with better control of confounding variables. The case-crossover design controls for time independent confounding factors, both known and unknown, which could affect the risk of VBA stroke. This is important since smoking, obesity, undiagnosed hypertension, some connective tissue disorders and other important risk factors for dissection and VBA stroke are unlikely to be recorded in administrative databases.

We also found strong associations between PCP visits and subsequent VBA stroke. A plausible explanation for this is that patients with head and neck pain due to vertebral artery dissection seek care for these symptoms, which precede more than 80% of VBA strokes.²³ Since it is unlikely that PCPs cause stroke while caring for these

patients, we can assume that the observed association between recent PCP care and VBA stroke represents the background risk associated with patients seeking care for dissection-related symptoms leading to VBA stroke. Because the association between chiropractic visits and VBA stroke is not greater than the association between PCP visits and VBA stroke, there is no excess risk of VBA stroke from chiropractic care.

Our study has several strengths and limitations. The study base includes an entire population over a 9-year period representing 109,020,875 person-years of observation. Despite this, we found only 818 VBA strokes, which limited our ability to compute some estimates and bootstrap confidence intervals. In particular, our age stratified analyses are based on small numbers of exposed cases and controls (Table 2). Further stratification by diagnostic codes for headache and neck pain related visits imposed even greater difficulty with these estimates. However, there are few databases that can link incident VBA strokes with chiropractic and PCP visits in a large enough population to undertake a study of such a rare event.

A major limitation of using health administrative data are misclassification bias, and the possibility of bias in assignment of VBA-related diagnoses, which has previously been raised in this context.²⁴ Liu *et al* have shown that ICD-9 hospital discharge codes for stroke have a poor positive predictive value when compared to chart review.³⁵ Furthermore, not all VBA strokes are secondary to vertebral artery dissection and administrative databases do not provide the clinical detail to determine the specific cause. To investigate this bias, we did a sensitivity analysis using different positive predictive values for stroke diagnosis (ranging from 0.2 to 0.8). Assuming nondifferential misclassification of chiropractic and PCP cases, our analysis showed attenuation of the estimates towards the null with lower positive predictive values, but the conclusions did not change (*i.e.*, associations remained positive and significant—data not shown). The reliability and validity of the codes to classify headache and cervical visits to chiropractors and PCPs is not known.

It is also possible that patients presenting to hospital with neurologic symptoms who have recently seen a chiropractor might be subjected to a more vigorous diagnostic workup focused on VBA stroke (*i.e.*, differential misclassification).³⁶ In this case, the predictive values of the stroke codes would be greater for cases that had seen a chiropractor and our results would underestimate the association between PCP care and VBA stroke.

A major strength of our study is that exposures were measured independently of case definition and handled identically across cases and controls. However, there was some overlap between chiropractic care and PCP care. In the month before their stroke, only 16 (2.0%) of our cases had seen only a chiropractor, while 20 (2.4%) had seen both a chiropractor and PCP, and 417 (51.0%) had just seen only a

PCP. We were not able to run a subgroup analysis on the small number of cases that just saw a chiropractor. However, subgroup analysis on the PCP cases ($n = 782$) that did not visit a chiropractors during the 1 month before their stroke did not change the conclusions (data not shown).

Our results should be interpreted cautiously and placed into clinical perspective. We have not ruled out neck manipulation as a potential cause of some VBA strokes. On the other hand, it is unlikely to be a major cause of these rare events. Our results suggest that the association between chiropractic care and VBA stroke found in previous studies is likely explained by presenting symptoms attributable to vertebral artery dissection. It might also be possible that chiropractic manipulation, or even simple range of motion examination by any practitioner, could result in a thromboembolic event in a patient with a pre-existing vertebral dissection. Unfortunately, there is no acceptable screening procedure to identify patients with neck pain at risk of VBA stroke.³⁷ These events are so rare and difficult to diagnose that future studies would need to be multicentered and have unbiased ascertainment of all potential exposures. Given our current state of knowledge, the decision of how to treat patients with neck pain and/or headache should be driven by effectiveness and patient preference.³⁸

CONCLUSION

Our population-based case-control and case-crossover study shows an association between chiropractic visits and VBA strokes. However, we found a similar association between primary care physician visits and VBA stroke. This suggests that patients with undiagnosed vertebral artery dissection are seeking clinical care for headache and neck pain before having a VBA stroke.

Key Points

- Vertebrobasilar artery stroke is a rare event in the population.
- There is an association between vertebrobasilar artery stroke and chiropractic visits in those under 45 years of age.
- There is also an association between vertebrobasilar artery stroke and use of primary care physician visits in all age groups.
- We found no evidence of excess risk of VBA stroke associated chiropractic care.
- The increased risks of vertebrobasilar artery stroke associated with chiropractic and physician visits is likely explained by patients with vertebrobasilar dissection-related neck pain and headache consulting both chiropractors and primary care physicians before their VBA stroke.

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