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A Population-Based Study of 30-day Incidence of Ischemic Stroke Following Surgical Neck Dissection

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Abstract: The objective of this study was to determine the 30-day incidence of ischemic stroke following neck dissection compared to matched patients undergoing non-head and neck surgeries.

A surgical dissection of the neck is a common procedure performed for many types of cancer. Whether such dissections increase the risk of ischemic stroke is uncertain.

A retrospective cohort study using data from linked administrative and registry databases (1995–2012) in the province of Ontario, Canada was performed. Patients were matched 1-to-1 on age, sex, date of surgery, and comorbidities to patients undergoing non-head and neck surgeries. The primary outcome was ischemic stroke assessed in hospitalized patients using validated database codes.

A total of 14,837 patients underwent surgical neck dissection. The 30-day incidence of ischemic stroke following the dissection was 0.7%. This incidence decreased in recent years (1.1% in 1995 to 2000; 0.8% in 2001 to 2006; 0.3% in 2007 to 2012; P for trend <0.0001). The 30-day incidence of ischemic stroke in patients undergoing neck dissection is similar to matched patients undergoing thoracic surgery (0.5%, $P = 0.26$) and colectomy (0.5%, $P = 0.1$). Factors independently associated with a higher risk of stroke in 30 days following neck dissection surgery were of age ≥75 years (odds ratio (OR) 1.63, 95% confidence interval (CI) 1.05–2.53), and a history of diabetes (OR 1.60, 95% CI 1.02–2.49), hypertension (OR 2.64, 95% CI 1.64–4.25), or prior stroke (OR 4.06, 95% CI 2.29–7.18).

Less than 1% of patients undergoing surgical neck dissection will experience an ischemic stroke in the following 30 days. This incidence of stroke is similar to thoracic surgery and colectomy.

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Abbreviations: CABG = coronary artery bypass grafting, CCI = Canadian classification of health interventions, CCP = Canadian classification of diagnostic, therapeutic, and surgical procedures, CHF = congestive heart failure database, CI = confidence interval, CIHI-DAD = Canadian Institute for Health Information's Discharge Abstract Database, COPD = chronic obstructive pulmonary disease, HYPER = hypertension database, ICD = International classification of diseases, ICES = Institute for Clinical and Evaluative Sciences, IQR = interquartile range, NACRS = National Ambulatory Care Reporting System, ODD = Ontario diabetes database, OHIP = Ontario health insurance plan, OMID = Ontario myocardial infarction database, OR = odds ratio, RPDB = registered persons database, RR = relative risk, SD = standard deviation, TIA = transient ischemic attack.

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INTRODUCTION

A surgical dissection of the neck is a common procedure performed for many types of head and neck cancer. Some patients experience an ischemic stroke in the 30 days following the procedure, which is a devastating outcome increasing the risk of perioperative mortality by 8 fold.[1–4] When such a stroke occurs, this usually raises the question, to which degree was the stroke attributed to the neck dissection? A neck dissection involves hemodynamic changes, manipulation of the carotid artery, and neck extension, all of which could lead to an ipsilateral stroke. Patients, however, undergoing a neck dissection often have comorbidities, including regional radiotherapy, systemic chemotherapy, tumor-related disorders, coagulation disturbances, and susceptibility to infection, which predispose to a higher risk of perioperative stroke even if a neck dissection was not undertaken.[5–10] Previous studies on this topic are limited by small sample sizes and single institution or regional experiences.[3,11]

Data from population-based studies provide a high level of evidence for the effectiveness and complications associated with a medical intervention.[12] Population-based studies provide the most generalizable study design and if the appropriate mechanisms for outcome ascertainment are included, population studies may capture outcomes that are missed in other retrospective studies. The goal of this study was to determine, at the population level, the 30-day incidence of ischemic stroke following neck dissection, to assess trends during time, and to evaluate the impact of manipulation of the neck by assessing the incidence in similar patients undergoing non-head and neck surgeries.

METHODS

Design and Setting

Residents of Ontario, Canada (2012 population estimate: 13,505,900) have universal access to hospital care and physician services. These encounters are recorded in large population-based linked health care databases that are held at the Institute for Clinical and Evaluative Sciences (ICES). We conducted a population-based retrospective cohort study of all patients who underwent a neck dissection between January 1, 1995 and December 31, 2012. The reporting of this study followed guidelines for observational studies.[13] The study was approved by the Sunnybrook Health Science Centre Research Ethics Board in Toronto, Ontario.

Data Sources

We linked multiple administrative data holdings from Ontario, Canada. The Canadian Institute for Health Information's discharge abstract database (CIHI-DAD) records all admissions to hospitals and includes information on diagnoses and procedures performed. The Ontario Health Insurance Plan database (OHIP) contains information on all fee-for-service physician claims for inpatient and outpatient services. The Registered Persons Database (RPDB) contains vital statistics on all permanent residents of Ontario. The National Ambulatory Care Reporting System (NACRS) database collects data on ambulatory care visits, including day surgery, outpatients' clinics, cancer clinics, and emergency department visits. In addition, we used 4 databases derived from validated case definitions: the Ontario Diabetes Database (ODD),[14] the Congestive Heart Failure (CHF) Database, the Hypertension Database (HYPER),[15] and the Ontario Myocardial Infarction Database (OMID).

We used OHIP to identify patients who had a neck dissection and a combination of CIHI-DAD, OHIP, ODD, CHF, HYPER, OMID, NACRS, and RPDB to define patient characteristics, baseline comorbidities, and report patient outcomes. Diagnoses and procedures were defined using the *International Classification of Diseases, ninth revision (ICD-9*; pre-2002), *10th revision* (*ICD-10*; post-2002), *Canadian Classification of Health Interventions (CCI*; post-2002), and *Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP*; pre-2002) codes. Whenever possible, we applied database codes that have been validated with chart review.[14,16–20]

Patients

We included patients 18 years of age and older with a billing code of a comprehensive neck dissection or radical neck dissection between the years 1995 to 2012. We restricted our cohort to patients who were residents of Ontario and who had no prior history of carotid occlusion, aneurysm repair, or carotid body resection (Supplemental Table 1, http://links.lww.com/MD/A323). We also excluded patients who had a limited neck dissection (OHIP code R910) as some of these patients would have had a central compartment (level 6) neck dissection with no exposure of the carotid arteries. We further excluded patients who were not hospitalized for the neck dissection. The date of the procedure code for neck dissection served as the start time for follow-up (also referred to as the index date).

We obtained information on the patient diagnoses and other baseline characteristics (age, sex, socioeconomic status, and residency status) on the surgery date. We assessed the comorbidity status of our cohort using health care records in 3 years preceding the surgery date, including the Charlson comorbidity index.[21,22]

To compare the incidence of ischemic stroke in patients undergoing neck dissection to patients undergoing non-head and neck surgery, we performed a 1-to-1 match between our cohort with patients who received surgery for thoracic surgery (pneumonectomy and lobectomy), colectomy, coronary artery bypass grafting (CABG), and hip replacement. These 4 non-head and neck surgeries (thoracic surgery, colectomy, CABG, and hip replacement) are performed on a similar patient demography and they are distant from the carotid artery. Matching criteria included exact age (±1-year difference), sex, year of surgery, Charlson comorbidity index group (0, 1–2, 3 or more), history of congestive heart failure, history of atrial fibrillation, history of diabetes, history of hypertension, and history of previous stroke. Ontario health insurance plan surgical procedure codes for matched surgeries are listed in Supplemental Table 2, http://links.lww.com/MD/A323.

Outcomes

We assessed the primary outcome of ischemic stroke in 30 days following surgery using ICD-9 and ICD-10 codes (see Supplemental Table 3, http://links.lww.com/MD/A323). This set of ICD codes for ischemic stroke has been well validated for administrative hospital discharge databases.[18,23-26]

Statistical Analysis

We calculated the 30-day incidence of stroke after neck dissection surgery. We performed a Cochrane-Armitage trend test to determine whether the risk of ischemic stroke following neck dissection has changed during 3 time periods (1995–2000, 2001–2006, and 2007–2012). We used multivariable logistic regression to assess the association between baseline characteristics and the occurrence of stroke amongst the neck dissection cohort. These included age, sex, the type of tumor requiring neck dissection (mucosal head and neck malignancy, thyroid malignancy, malignant melanoma, skin, salivary gland, other diagnosis), previous radiation, year of surgery (1995–2000; 2001–2006; 2007–2012), emergency surgery, and history of congestive heart failure, diabetes, hypertension, atrial fibrillation, or prior stroke. We applied a log-binomial model with clustering on matched pairs to compare the incidence of ischemic stroke between the neck dissection cohort and matched patients undergoing non-head and neck surgeries, adjusting for patients who had emergency surgery. Using this log-binomial model, we included a time interaction term for neck dissection compared with thoracic surgery, abdominal surgery, hip replacement, and coronary artery bypass graft adjusting for emergency surgery to determine if there was a time interaction.

We conducted all analyses with SAS software (version 9.3, SAS Institute Inc., Cary, North Carolina). We interpreted *P* values <0.05 as statistically significant.

RESULTS

Baseline Characteristics

From January 1, 1995 to December 31, 2012, 16,646 patients had a neck dissection in Ontario, and 14,837 patients met study inclusion criteria (Figure 1). Neck dissections for 14,837 patients in our study cohort were performed at 115

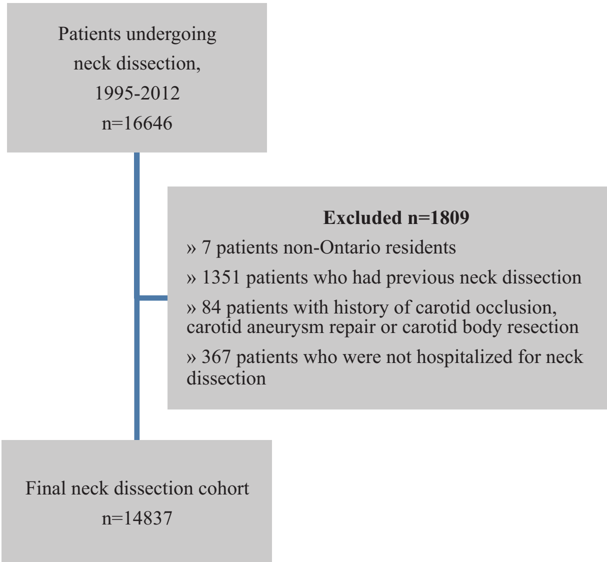


FIGURE 1. Study cohort.

unique Ontario institutions during the study period. Twenty-two percent (N = 3321) of patients had a bilateral neck dissection. Demographic characteristics of the patients are listed in Table 1 and Supplemental Tables 5 and 6, http://links.lww.com/MD/A323. The majority of the patients were men 66% (N = 9788) and the median age was 61 years (interquartile range 50–71). Fifty-one percent (N = 7533) of patients were diagnosed with mucosal head and neck cancer, followed by thyroid cancer (15.3%, N = 2264). The most common comorbidities were hypertension (N = 6583, 44.4%) and diabetes (N = 2455, 16.5%).

Primary Results

The rate of perioperative ischemic stroke within 30 days of neck dissection was 0.7% (N = 101). For patients who were diagnosed with mucosal head and neck malignancy, the rate of ischemic stroke was 0.8% (N = 62) and for patients who were diagnosed with thyroid malignancy, the rate was (0.2%) (N $\leq$ 5). The rate of ischemic stroke decreased during the study period from 1.1% (N = 40) in the era 1995 to 2000 to 0.3% (N = 21) in the era 2007 to 2012 ($P < 0.0001$) (Table 2). The rate of ischemic stroke in patients undergoing bilateral neck dissection was 1.0% (33 patients of 3288 undergoing bilateral neck dissection). The rate of stroke in patients undergoing unilateral neck dissection was (0.6%) (68 patients of 11,516). The difference in stroke rate between patients undergoing unilateral and bilateral neck dissection was statistically significant ($P = 0.01$).

When matching 1-to-1 between neck dissection patients and non-head and neck surgeries, we achieved complete match for 10,026 (67.6%) patients for thoracic surgery, 13,365 (90.1%) patients for colectomy, 12,421 (83.7%) patients for hip replacement, and 12,608 (85.0%) for patients undergoing CABG. A comparison of the baseline characteristics of patients undergoing neck dissection compared with non-head and neck surgery is summarized in Supplemental Table 4, http://links.lww.com/MD/A323. Compared with the incidence observed in neck dissection (ranging from 0.6% to 0.7% for retained patients in each cohort), matched patients undergoing thoracic surgery had a rate of ischemic stroke of 0.5% ($P = 0.26$), colectomy 0.5% ($P = 0.1$), CABG 1.2% ($P < 0.001$), and hip replacement 0.2% ($P < 0.001$) (Table 3). The incidence of ischemic stroke in patients undergoing thoracic surgery (P for trend 0.41), colectomy (P for trend 0.74), and hip replacement (P for trend 0.19) was not decreasing during time (Figure 2). The incidence of ischemic stroke in patients undergoing neck dissection (P for trend <0.0001) and CABG (P for trend <0.0001) was decreasing during time (Figure 2). Using an interaction term (type of surgery and time) in the log-binomial model, we found that there was no statistical evidence that the rate of ischemic stroke was declining more for neck dissection compared with other surgeries.

Predictors of Ischemic Stroke

When the outcome ischemic stroke was modeled, age $\geq$75 years (OR 1.63 95% CI 1.05–2.53), history of diabetes (OR 1.59 95% CI 1.02–2.49), history of hypertension (OR 2.64 95% CI 1.64–4.25), and previous stroke (OR 4.06 95% CI 2.29–7.18) were predictive of increased risk of ischemic stroke (Table 4). Year of neck dissection surgery in 2007 to 2012 predicted a lower risk of stroke compared with the eras 2001 to 2006 and 1995 to 2000 (OR 0.26 95% CI 0.15–0.46).

DISCUSSION

It has been suggested that there may be an increased risk of stroke in patients undergoing neck dissection owing to manipulation of the carotid artery, neck extension, and hemodynamic disturbances. In a population-based cohort of patients undergoing neck dissection, we found that the incidence of perioperative ischemic stroke was 0.7% and this incidence has declined in more recent years with a rate of 3 per 1000 patients in most recent years. The rate of ischemic stroke in patients undergoing neck dissection was similar to the rate of ischemic stroke in age, sex, year of surgery, and comorbidity matched patients undergoing thoracic surgery and colectomy of similar duration, suggesting that manipulation of the neck or its contents does not play a role in postoperative stroke risk. We established preoperative predictors of ischemic stroke risk in patients undergoing neck dissection that can be used to help guide clinical practice.

To our knowledge, this is the first population-based study to report the rate of ischemic stroke in patients undergoing neck dissection. Nosan et al[3] described a case series of 105 head and neck cancer patients, 4.8% of which had a postoperative stroke after undergoing head and neck surgery. Their study was limited by small sample size and low event rate (N = 5). Thompson et al studied patients undergoing neck dissection for head and neck cancer at 3 centers between 1994 and 2002. One patient in their cohort (0.2%) was confirmed to have had a perioperative stroke amongst 499 patients studied.[11] The at-risk population used for the denominator by Thompson et al[11] was the total number of neck dissections instead of the total number of patients and may account for the lower incidence rate of ischemic stroke compared with our result. Amongst patients undergoing surgery for head and neck tumor (20,057 patients), Mashour et al[1] found that the incidence of perioperative stroke was <0.1% (7 patients). It is unclear, which surgical procedures were included in this group and the diagnostic criteria used for the stroke outcome. Compared with previous studies, we included a large number of patients with a well-defined procedure code and validated outcome of ischemic stroke. In addition, the

TABLE 1. Baseline Characteristics of Patients Undergoing Neck Dissection in Ontario and Canada from 1995 to 2012

Years of New Diagnosis	1995–2000 N (%)	2001–2006 N (%)	2007–2012 N (%)	1995–2012 N (%)	P Value
Number of patients undergoing neck dissection	3762	4894	6181	14837	
Number of patients undergoing bilateral neck dissection	793 (21.1)	1163 (23.8)	1365 (22.1)	3321 (22.4)	0.009
Demographic Characteristics					
Age mean (SD)	58.36 (17.1)	58.79 (16.3)	60.04 (16.3)	59.20 (16.5)	<0.001
Median (IQR)	61 (49–71)	60 (49–71)	61 (50–72)	61 (50–71)	
<50	954 (25.4)	1291 (26.4)	1458 (23.6)	3703 (25.0)	
50–59	769 (20.4)	1076 (22.0)	1358 (22.0)	3203 (21.6)	
60–69	974 (25.9)	1135 (23.2)	1498 (24.2)	3607 (24.3)	
70–79	814 (21.6)	980 (20.0)	1175 (19.0)	2969 (20.0)	
80–89	232 (6.2)	390 (8.0)	633 (10.2)	1255 (8.5)	
≥90	19 (0.5)	22 (0.4)	59 (0.9)	100 (0.7)	
Men	2550 (67.8)	3212 (65.6)	4026 (65.1)	9788 (66.0)	0.022
Rural residence	585 (15.5)	636 (13.0)	870 (14.1)	2091 (14.1)	<0.001
Socioeconomic status					0.037
Quintile 1 and 2 (lowest)	1643 (43.7)	2058 (42.0)	2522 (40.8)	6223 (41.94)	
Quintile 3	675 (17.9)	954 (19.5)	1217 (19.7)	2846 (19.18)	
Quintile 4 and 5 (highest)	1426 (37.9)	1870 (38.2)	2429 (39.3)	5725 (38.60)	
Diagnosis					
Mucosal head and neck malignancy	2121 (56.4)	2470 (50.5)	2942 (47.6)	7533 (50.8)	
Thyroid malignancy	439 (11.7)	689 (14.1)	1136 (18.4)	2264 (15.3)	
Malignant melanoma, skin, salivary gland, other	740 (19.7)	1099 (22.4)	1400 (22.7)	3239 (21.8)	
Comorbidity History					
Charlson comorbidity index					<0.001
No hospitalizations	809 (21.5)	1262 (25.8)	1790 (29.0)	3861 (26.0)	
0	1745 (46.4)	2127 (43.5)	2508 (40.6)	6380 (43.0)	
1	281 (7.5)	275 (5.6)	368 (5.9)	924 (6.2)	
2	354 (9.4)	521 (10.6)	604 (9.8)	1479 (10.0)	
3	106 (2.8)	107 (2.2)	182 (2.9)	395 (2.7)	
4	24 (0.6)	45 (0.9)	68 (1.1)	137 (0.9)	
≥5	443 (11.8)	557 (11.4)	661 (10.7)	1661 (11.2)	
Previous radiation for head and neck cancer	2452 (65.2)	2856 (58.4)	3428 (55.5)	8736 (58.9)	<0.001
Previous Comorbid Conditions					
Ischemic stroke or TIA	110 (2.9)	139 (2.8)	142 (2.3)	391 (2.6)	0.092
Myocardial infarction	63 (1.7)	161 (3.3)	259 (4.2)	483 (3.3)	<0.001
Deep vein thrombosis	7 (0.2)	13 (0.3)	16 (0.3)	36 (0.2)	0.715
Pulmonary embolism	6 (0.2)	10 (0.2)	18 (0.3)	34 (0.2)	0.373
Hypertension	1297 (34.5)	2145 (43.8)	3141 (50.8)	6583 (44.4)	<0.001
Diabetes mellitus	442 (11.7)	752 (15.4)	1261 (20.4)	2455 (16.5)	<0.001
Atrial fibrillation/flutter	86 (2.3)	96 (2.0)	168 (2.7)	350 (2.4)	0.032
Congestive heart failure	238 (6.3)	309 (6.3)	426 (6.9)	973 (6.6)	0.381
History of Cardiovascular Procedure/Investigation					
Cardiac valve replacement	11 (0.3)	10 (0.2)	10 (0.2)	31 (0.2)	0.383
Carotid endarterectomy	<5 (0.1)*	6 (0.1)	10 (0.2)	≤21 (0.1)*	0.536
Carotid doppler	218 (5.8)	304 (6.2)	469 (7.6)	991 (6.7)	<0.001
Coronary revascularization	41 (1.1)	75 (1.5)	117 (1.9)	233 (1.6)	0.007
Holter monitoring	159 (4.2)	289 (5.9)	528 (8.5)	976 (6.6)	<0.001
Coronary artery bypass graft	41 (1.1)	75 (1.5)	117 (1.9)	233 (1.6)	0.007
Length of hospital stay mean days (SD)	12.4 (16.1)	10.3 (14.6)	9.7 (15.5)	10.6 (15.4)	<0.001
Emergency surgery	245 (6.5)	13 (0.3)	0 (0.0)	258 (1.7)	<0.001

IQR = interquartile range; SD = standard Deviation; TIA = transient ischemic attack.
* In accordance with privacy regulations imposed by the Ontario Ministry of Health, event rates, odds ratios, and 95% confidence intervals for absolute numbers ≤5 cannot be reported.

TABLE 2. Incidence Rate of Ischemic Stroke among Patients Undergoing Neck Dissection in Ontario and Canada from 1995 to 2012

Years of Neck Dissection	1995–2000 (N = 3762)	2001–2006 (N = 4894)	2007–2012 (N = 6181)	1995–2012 (N = 14837)	*P* value
Ischemic stroke	40 (1.1)	40 (0.8)	21 (0.3)	101 (0.7)	<0.0001

discrepancy between our overall rate of ischemic stroke and that reported by other studies may be explained by our observation of decreasing incidence of ischemic stroke during time. That is, earlier studies[3] reporting higher incidence of stroke and later studies reporting lower incidence of stroke[1] are consistent with our findings of decreasing incidence during time.

The results of this study support the findings of previous studies that have examined predictors of stroke risk. We found that known risk factors for ischemic stroke were also predictive of increased risk of perioperative stroke. Patients over 75 years of age and those with a history of diabetes, hypertension, and previous stroke were at increased risk of perioperative stroke. Predictors of perioperative stroke in the noncardiac, nonneurologic surgical population identified in other studies were of age ≥62 years, myocardial infarction within 6 months of surgery, renal disease or dialysis, history of stroke or transient ischemic attack, hypertension, chronic obstructive pulmonary disease, congestive heart failure (or ejection faction <40%), atrial fibrillation, deep vein thrombosis, diabetes, urgent or emergent surgery, peripheral vascular disease, and patients who were current smokers.[1,27,28] Differences between the predictors of ischemic stroke in our study compared with other studies have several possible explanations. Our databases may lack the sensitivity to detect all preoperative conditions such as congestive heart failure or atrial fibrillation (6.3% of patients in our study had a diagnosis of congestive heart failure and 2.3% had a diagnosis of atrial fibrillation). There are differences in the definition of preoperative comorbidities between our study and other studies.[1,28] For example, the prediction models described by Charlesworth and Mashour for ischemic stroke are based on clinical databases, not administrative databases.[1,28] The prediction models by Selim and Charlesworth include congestive heart failure; however, these models are developed from CABG, which is longer in duration and has more significant hemodynamic changes than neck dissection.[1,28,29] Furthermore, the prediction model developed by Likosky[30], which includes atrial fibrillation is based on intra- and postoperative diagnoses and not preoperative comorbidities, which our study was based on. Our data together with published stroke prediction models can be used to counsel patients before neck dissection and ensure that medical comorbidities are optimized preoperatively.

The incidence of ischemic stroke in patients undergoing neck dissection is decreasing during time (1.1%–0.3%, *P* value <0.0001 trend test). Overall, the incidence of ischemic stroke is stable in all non-head and neck surgeries, including thoracic surgery, colectomy, and hip replacement but decreasing for CABG (Figure 2). Statistically, this magnitude of decline in stroke rate for neck dissection was not significant compared with non-head and neck surgeries. The reasons for a declining stroke rate are unknown; however, there are several possible explanations. This may be because of an improvement in the intraoperative management of hemodynamic status, better perioperative care of surgical patients, improved selection of patients for surgery, or preoperative optimization of risk factors for ischemic stroke. Specifically, for the procedure of neck dissection, the use of radical neck dissection has decreased during time coinciding with an increased use of selective neck dissection in patients with node positive disease.[31]

Given the similar rate of ischemic stroke in patients undergoing thoracic and abdominal surgery that was demonstrated in

TABLE 3. Matched Comparison of Rate of Ischemic Stroke in Patients Undergoing Neck Dissection Compared With Thoracic Surgery, Colectomy, Hip Replacement, and Coronary Artery Bypass Graft

Matching Cohort	RR (95% CI)	*P* Value	
Neck dissection	Thoracic surgery		
N = 10026			
65 (0.6)	53 (0.5)	1.23 (0.86–1.75)	0.26
Neck dissection	Colectomy		
N = 13365			
83 (0.6)	65 (0.5)	1.31 (0.95–1.80)	0.1
Neck dissection	Hip replacement		
N = 12421			
82 (0.7)	23 (0.2)	3.54 (2.23–5.61)	<0.0001
Neck dissection	CABG		
N = 12608			
87 (0.7)	149 (1.2)	0.59 (0.45–0.77)	<0.0001

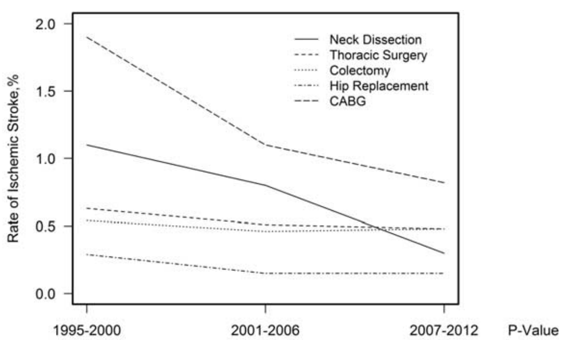
CABG = coronary artery bypass graft; CI = confidence interval; RR = relative risk. RR adjusted for emergency surgery. Matching criteria included age (±1 year), same sex, same year of surgery, same Charlson group (0, 1–2, and 3 or more), history of congestive heart failure, history of diabetes mellitus, history of atrial fibrillation, history of stroke. Thoracic surgery included pneumonectomy and lobectomy.

TABLE 4. Stratified Incidence and Risk of Ischemic Stroke Within 30 Days of Neck Dissection Surgery

Variable	Incidence of Ischemic Stroke N (%)	Odds Ratio (95% Confidence Interval)	*P* Value
Diagnosis	101 (0.7)		
Thyroid malignancy	≤5 (0.2)*	1.0 (reference)	
Mucosal head and neck malignancy	62 (0.8)	2.37 (0.82–6.85)	0.110
Malignant melanoma, skin, salivary, other	≥ 34 (1.0)	1.54 (0.53–4.46)	0.429
Age, years			
<75	66 (0.5)	1.0 (reference)	
≥75	35 (1.3)	1.63 (1.05–2.53)	0.031
Sex			
Men	71 (0.7)	1.0 (reference)	
Women	30 (0.6)	0.92 (0.60–1.43)	0.724
Previous Radiation			
No	28 (0.5)	1.0 (reference)	
Yes	73 (0.8)	1.23 (0.78–1.96)	0.375
Comorbidities			
Congestive heart failure	16 (1.6)	1.38 (0.77–2.46)	0.277
Diabetes mellitus	30 (1.2)	1.59 (1.02–2.49)	0.042
Hypertension	74 (1.1)	2.64 (1.64–4.25)	<0.001
Atrial fibrillation	≤5 (1.4)*	0.99 (0.37–2.60)	0.978
Previous stroke	16 (4.1)	4.06 (2.29–7.18)	<0.001
Year of New Diagnosis			
1995–2000	40 (1.1)	1.0 (reference)	
2001–2006	40 (0.8)	0.70 (0.45–1.11)	0.130
2007–2012	21 (0.3)	0.26 (0.15–0.46)	<0.001
Emergency surgery	≤5 (1.9)*	1.09 (0.33–3.59)	0.890
Length of hospital stay	N/A†	1.02 (1.01–1.02)‡	<0.0001

* In accordance with privacy regulations imposed by the Ontario Ministry of Health, event rates, ORs, and 95% CIs for absolute numbers ≤5 cannot be reported.
† Length of hospital stay was reported as a continuous variable and therefore the incidence of ischemic stroke in the category could not be reported.
‡ Length of hospital stay was not included in the final adjusted model.

our study, manipulation of the carotid artery and neck extension is less likely a cause of ischemic stroke. The low rate of ischemic stroke after hip arthroplasty may point to hemodynamic instability during general anesthetic as a plausible explanation. This is supported by two observational studies of patients undergoing hip arthroplasty in which general anesthesia was an independent predictor of postoperative stroke.[32,33] In patients undergoing noncardiac surgery, the POISE trial suggested that significant intraoperative bleeding may be a risk factor for stroke.[34] Intraoperative hypotension has also been shown to increase the risk of perioperative stroke; however, the association is poorly defined.[35] We were unable to determine how many patients in our study had a regional anesthetic or significant intraoperative hemodynamic changes given the limitations of our databases. As expected, we found that the rate of stroke was highest for patients who had a CABG. This stroke rate, which was derived from a cohort matched on age, sex, and comorbidity is slightly lower than the reported rates from the literature.[29] Intraoperative and postoperative factors, such as cardiopulmonary bypass and aortic cross-clamp time, arrhythmias, hypotension, and heart failure are plausible causes for the higher rate of stroke for CABG.[29] Further research is needed to clarify the intraoperative risk factors for perioperative stroke in patients undergoing noncardiac and nonneurologic surgery.



	1995-2000	2001-2006	2007-2012	P-Value
Neck Dissection	1.06	0.82	0.34	<.0001
Thoracic Surgery	0.63	0.51	0.48	0.4085
Colectomy	0.54	0.46	0.48	0.7361
Hip Replacement	0.29	0.15	0.15	0.1897
CABG	1.90	1.10	0.82	<.0001

FIGURE 2. Incidence rate of ischemic stroke for neck dissection surgery and non-neck dissection surgery: 1995 to 2012.

Strengths and Limitations

The conclusions of this study should be considered in the context of its strengths and limitations. Because this is a retrospective cohort drawing on hospital discharge, many of the potential limitations are inherent to large administrative databases. We cannot exclude the possibility that data-entry errors may have occurred and not all variables of interest, including some potential confounders, are available, including previous use of chemotherapy, radiotherapy doses and planning type, laterality of stroke, and smoking status. In our dataset, the code for neck dissection does not differentiate between radical, modified radical, or selective neck dissections. The sensitivity of the code for ischemic stroke is well validated in Ontario's administrative databases but it has not been validated specifically in the postoperative setting. The outcomes measured herein, however, are derived from a very large sample size with extended follow-up to 30-days postoperative and used a population-based design from a cohort of patients with comprehensive, universal health insurance, thereby minimizing selection bias. Although the rates of stroke we describe are estimates at the 30-day time-point, in distinction to longer-term actuarial estimates, the likelihood of stroke being attributed to an operation would likely diminish during time.

CONCLUSIONS

Our study suggests that the incidence of perioperative stroke in patients undergoing a neck dissection is 0.7% and has decreased during time. We report the first population-based study to determine the incidence of this common procedure performed for head and neck cancer patients. This information may help to counsel patients preoperatively on their risk of perioperative stroke. Most importantly, our results indicate that exposure of the carotid artery during neck dissection does not increase the risk of perioperative ischemic stroke. Future research should focus on determining reversible factors to mitigate stroke risk as well as the development of a stroke prediction score for neck dissection surgery.

REFERENCES

1. Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, nonneurologic surgery. *Anesthesiology.* 2011;114:1289–1296.
2. Rechtweg J, Wax MK, Shah R, et al. Neck dissection with simultaneous carotid endarterectomy. *Laryngoscope.* 1998;108: 1150–1153.
3. Nosan DK, Gomez CR, Maves MD. Perioperative stroke in patients undergoing head and neck surgery. *Ann Otol Rhinol Laryngol.* 1993;102:717–723.
4. Thompson SK, McKinnon JG, Ghali WA. Perioperative stroke occurring in patients who undergo neck dissection for head and neck cancer: unanswered questions. *Can J Surg.* 2003;46:332–334.
5. Lindvig K, Moller H, Mosbech J, et al. The pattern of cancer in a large cohort of stroke patients. *Int J Epidemiol.* 1990;19:498–504.
6. Rogers LR. Cerebrovascular complications in cancer patients. *Neurol Clin.* 2003;21:167–192.
7. Cestari DM, Weine DM, Panageas KS, et al. Stroke in patients with cancer: incidence and etiology. *Neurology.* 2004;62:2025–2030.
8. Nguyen T, DeAngelis LM. Stroke in cancer patients. *Curr Neurol Neurosci Rep.* 2006;6:187–192.
9. Zhang YY, Chan DK, Cordato D, et al. Stroke risk factor, pattern and outcome in patients with cancer. *Acta Neurol Scand.* 2006;114:378–383.
10. Grisold W, Oberndorfer S, Struhal W. Stroke and cancer: a review. *Acta Neurol Scand.* 2009;119:1–16.
11. Thompson SK, Southern DA, McKinnon JG, et al. Incidence of perioperative stroke after neck dissection for head and neck cancer: a regional outcome analysis. *Ann Surg.* 2004;239:428–431.
12. Institute NC. Levels of Evidence for Adult and Pediatric Cancer Treatment Studies (PDQ). 2015. Accessed July 2, 2015. http://www.cancer.gov/publications/pdq/levels-evidence/treatment#section/all
13. von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344–349.
14. Hux JE, Ivis F, Flintoft V, et al. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care.* 2002;25:512–516.
15. Tu K, Campbell NR, Chen ZL, et al. Accuracy of administrative databases in identifying patients with hypertension. *Open Med.* 2007;1:e18–e26.
16. Fleet JL, Dixon SN, Shariff SZ, et al. Detecting chronic kidney disease in population-based administrative databases using an algorithm of hospital encounter and physician claim codes. *BMC Nephrol.* 2013;14:81.
17. Schultz SE, Rothwell DM, Chen Z, et al. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can.* 2013;33:160–166.
18. Austin PC, Daly PA, Tu JV. A multicenter study of the coding accuracy of hospital discharge administrative data for patients admitted to cardiac care units in Ontario. *Am Heart J.* 2002;144:290–296.
19. Liu L, Reeder B, Shuaib A, et al. Validity of stroke diagnosis on hospital discharge records in Saskatchewan, Canada: implications for stroke surveillance. *Cerebrovasc Dis.* 1999;9:224–230.
20. Raiford DS, Perez Gutthann S, Garcia Rodriguez LA. Positive predictive value of ICD-9 codes in the identification of cases of complicated peptic ulcer disease in the Saskatchewan hospital automated database. *Epidemiology.* 1996;7:101–104.
21. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373–383.
22. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005;43:1130–1139.
23. Tirschwell DL, Longstreth WT Jr. Validating administrative data in stroke research. *Stroke.* 2002;33:2465–2470.
24. Spolaore P, Brocco S, Fedeli U, et al. Measuring accuracy of discharge diagnoses for a region-wide surveillance of hospitalized strokes. *Stroke.* 2005;36:1031–1034.
25. Heliovaara M, Reunanen A, Aromaa A, et al. Validity of hospital discharge data in a prospective epidemiological study on stroke and myocardial infarction. *Acta Med Scand.* 1984;216:309–315.
26. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA.* 2001;285:2864–2870.
27. Bateman BT, Schumacher HC, Wang S, et al. Perioperative acute ischemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. *Anesthesiology.* 2009;110:231–238.
28. Charlesworth DC, Likosky DS, Marrin CA, et al. Development and validation of a prediction model for strokes after coronary artery bypass grafting. *Ann Thorac Surg.* 2003;76:436–443.
29. Selim M. Perioperative stroke. *N Engl J Med.* 2007;356:706–713.
30. Likosky DS, Leavitt BJ, Marrin CA, et al. Intra- and postoperative predictors of stroke after coronary artery bypass grafting. *Ann Thorac Surg.* 2003;76:428–434discussion 435.
31. Ferlito A, Rinaldo A, Silver CE, et al. Neck dissection: then and now. *Auris Nasus Larynx.* 2006;33:365–374.

32. Mortazavi SM, Kakli H, Bican O, et al. Perioperative stroke after total joint arthroplasty: prevalence, predictors, and outcome. *J Bone Joint Surg Am.* 2010;92:2095–2101.
33. Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology.* 2013;118:1046–1058.
34. Group PS, Devereaux PJ, Yang H, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet.* 2008;371:1839–1847.
35. Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study. *Anesthesiology.* 2012;116:658–664.