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RESEARCH

The association between preoperative clinical risk factors and in-hospital strokes and death following carotid endarterectomy in South African patients

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Background: Current surgical management of carotid artery disease includes carotid endarterectomy (CEA). In-hospital strokes and death following CEA might be associated with preinduction blood pressure (BP) measurements and other clinical risk factors.
Method: The aim of our study was to determine whether or not there is an association between preinduction BP, other clinical risk factors, and in-hospital strokes or death following CEA in a cohort of South African patients. We collected data from medical records relating to clinical risk factors in patients, preinduction BP measurements, and in-hospital strokes and death, following CEA. The association between preinduction BP and clinical risk factors, and postoperative neurological morbidity and mortality, was analysed using univariate statistical methods.
Results: Our cohort consisted of 76 patients who underwent CEA. Eight of these patients had in-hospital strokes or death following their surgery. An association between a history of hypertension or other clinical risk factors and an in-hospital stroke and death was not identified in these 76 CEA patients following univariate analysis. However, patients with preinduction BP within the lowest or highest quartile for preinduction BP were at a significantly increased risk of an in-hospital stroke and death following their surgery (p-value = 0.003). A subanalysis of patients who were hypertensive also showed this univariate association (p-value = 0.003).
Conclusion: It is possible that extremes of preinduction BP might be associated with in-hospital strokes and death in CEA patients following their surgery, although further research is required to confirm this.

Keywords: carotid endarterectomy, carotid stenosis, mortality, strokes, surgery

Introduction

Carotid artery disease is associated with neurological morbidity and mortality. Stroke is among the leading causes of death worldwide. Carotid artery stenosis accounts for approximately 20% of strokes in adult populations.[1] Atheromatous plaques reduce the luminal diameter of carotid arteries, decreasing blood flow and promoting thrombus formation. Thromboembolism and neurological injury may result from plaque rupture.[1] Carotid endarterectomy (CEA) is commonly recommended in the treatment of carotid artery disease.[2,3]

However, even within the group of patients with accepted indications for CEA, a subgroup of patients remains who are at increased risk of an early postoperative stroke or death. A number of models have been developed to identify patients at increased risk of early postoperative neurological complications or death.[4,5] Several preoperative clinical risk factors, including hypertension, have been associated with major morbidity within 30 days of CEA. However, these risk factors have not been evaluated in South African vascular surgery patients, who are characterised by a higher burden of cardiovascular co-morbidities and significantly less adoption of established medical therapies than similar patients from developed-world studies.[6] This may be partly because of the epidemiological transition of cardiovascular disease in South Africa,[7] and inadequate access to effective primary health care. Therefore, it is important to determine what risk factors are associated with an increased risk of postoperative stroke and death in South African vascular surgery patients, e.g. patients undergoing CEA.

The aim of this study was to determine if an association exists between preinduction blood pressure (BP), other clinical risk factors and in-hospital strokes or death following CEA in a cohort of South African patients.

Method

Ethical approval for this study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal. This study was conducted at the Inkosi Albert Luthuli Central Hospital, located in Durban. The hospital provides tertiary and quaternary service to patients residing in the province of KwaZulu-Natal. We defined a stroke as rapidly developing signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours, or leading to death with no apparent cause other than that of vascular origin.[8] Our observational cohort study consisted of 76 vascular surgery patients ≥ 45 years old, who had CEA at Inkosi Albert Luthuli Central Hospital between 2008 and 2012. The selection of patients for CEA, as opposed to carotid stenting, was made at the sole discretion of the attending vascular surgeon. The decision to proceed to CEA is made on an individualised basis within our surgical unit. In addition, there are no standard exclusion criteria for CEA in our unit. Surgeries were carried out by five experienced vascular surgeons over the four-year study period. We obtained information on preinduction BP measurements from pre-existing patient anaesthetic records. The preoperative co-morbidities (a history of ischaemic heart disease, diabetes mellitus requiring insulin therapy, a history of cerebrovascular accident, a history of congestive heart failure and a serum creatinine > 177 μmol/l) of the 76 CEA patients were prospectively collected using the definitions specified by Lee et al in their derivation of the Revised Cardiac Risk Index, a widely utilised perioperative cardiovascular risk stratification index.[9] We classified patients as having a history of hypertension if they were diagnosed with hypertension by a physician prior to their surgery, or if they were taking antihypertensive medication. We identified in-hospital strokes and death following CEA from procedure notes, progress notes, and patient hospital discharge summaries. We were blinded to the clinical risk factors and preinduction BP when we evaluated the perioperative neurological outcomes. We also ensured that perioperative neuropraxia associated with the regional anaesthetic techniques was not incorrectly classified as a postoperative, in-hospital stroke.

We conducted univariate statistical analyses of our data, using the chi-square or Fisher's exact test for categorical data, and independent-sample Student's *t*-test for normally distributed continuous data. We were unable to analyse our data using multivariate statistical methods owing to the low number of outcomes per variable in our cohort.[10] Statistical analyses were performed using the Statistical Package for the Social Sciences® version 21.

Results

Over the four-year study period, 76 patients underwent CEA. Eight patients (10.5%) suffered in-hospital strokes or death following their surgery. The characteristics of our study cohort are shown in Table 1.

A large proportion of our patients presented with a history of hypertension (67/76 patients, 88%). More than 86% of patients presenting for surgery had symptomatic carotid artery disease, with a prior history of stroke.

Patients who presented with preinduction systolic BP within the lowest or highest quartile (extremes of BP) were associated with in-hospital stroke or death following CEA (*p*-value = .003, Table 1). Owing to poor BP control in our patients, the lowest quartile had a preinduction systolic BP (SBP) of < 145 mmHg, and the highest quartile had an SBP of >187 mmHg. A subanalysis of the 67 CEA patients with a preoperative history of hypertension identified an association between the quartile extremes of preinduction SBP (< 145 mmHg or > 195 mmHg) and poor clinical outcomes in these patients following CEA (*p*-value = 0.003, Table 2). We did not find a statistically significant association between any of the other clinical variables and in-hospital strokes or death following CEA in patients with a preoperative history of hypertension.

Discussion

Perioperative stroke is an important cause of morbidity and mortality, following intervention for carotid artery disease. Although the incidence of postoperative, in-hospital strokes and death in our cohort was concerning (10.5%), our results are in agreement with projected results based on the predictive model of Tu and colleagues.[4] Based on three of the five risk factors from the Tu model which we evaluated, our cohort had a projected risk of between 6.1% and 9.5% for a stroke or death following CEA. As we could not evaluate two of the five risk factors, this was obviously a very conservative risk estimate. In contrast to the findings of Tu and colleagues,[4] we did not find a statistically significant association between a prior history of a stroke, congestive heart failure or diabetes, and an in-hospital stroke or death, following CEA, in our study. It is likely that our findings of no statistically significant association between these clinical variables and poor postoperative clinical outcomes could be attributed to our modest sample size. However, the clinical significance of these variables (congestive heart failure, diabetes or a prior history of a stroke), should not be disregarded in patients undergoing CEA.

Hypertension is a common co-morbidity in patients with carotid artery disease. Some researchers have estimated a prevalence of approximately 66% in this group,[11] although 88% of our patients presented with a history of hypertension. Severe hypertension is associated with labile intraoperative arterial BP.[12] This haemodynamic instability may result in periods of intraoperative cerebral hypo- and hyperperfusion. A meta-analysis by Rothwell et al summarised the results of four studies on hypertension and CEA.[13] In a pooled sample of 4 814 patients (cases and controls) there was a statistically significant relationship between hypertension and stroke incidence post CEA (*p*-value < 0.0001). Wong, Findlay and Suarez-Almazor found a similar relationship between postoperative hypertension and stroke in a cohort of 291 consecutive patients undergoing CEA.[14] The rate was 5.2% for perioperative stroke or death. Postoperative hypertension was a significant risk factor (*p*-value = 0.04). Furthermore, the authors also found preoperative hypertension to be an independent predictor of postoperative hypertension. In a study by Asiddao et al on 166 patients undergoing CEA, the incidence of postoperative neurological deficit was three times higher in the presence of postoperative hypertension versus normotension.[11]

Overall, our study did not find any statistically significant association between a history of hypertension and in-hospital strokes or death following CEA. However, our subanalysis of hypertensive CEA patients demonstrated an association between extremes of preinduction systolic BP and poor postoperative clinical outcomes in these hypertensive patients. The prevalence of poor preoperative systolic BP control is a

Table 1: Baseline clinical characteristics of carotid endarterectomy patients, expressed as a frequency (percentage) or mean (standard deviation)

Patient characteristics	Total cohort $n = 76$	Patients with in-hospital strokes or death, $n = 8$	Patients without in-hospital strokes or death, $n = 68$	*p*-value
Female	29 (38.2)	3 (37.5)	26 (38.2)	1.000
Age	64.1 (7.8)	66 (6.6)	63.9 (8)	0.475
History of hypertension	67 (88.2)	7 (87.5)	60 (88.2)	1.000
History of ischaemic heart disease	39 (51.3)	6 (75)	33 (48.5)	0.263
Diabetes	41 (53.9)	6 (75)	35 (51.5)	0.275
History of congestive heart failure	4 (5.3)	1 (12.5)	3 (4.4)	0.365
Prior history of a stroke	66 (86.8)	6 (75)	60 (88.2)	0.282
Creatinine > 177 µmol/l ($n = 72$)	3 (3.9)	1 (12.5)	2 (2.9)	0.301
General anaesthesia	32 (42.1)	3 (37.5)	29 (42.6)	1.000
Preinduction mean (SBP, mmHg)	166.8 (30.4)	172.4 (41.8)	166.1 (29.1)	0.584
Preinduction mean (DBP, mmHg)	78.3 (12.6)	74.8 (15.7)	78.8 (12.2)	0.397
Preinduction SBP within the lowest or highest quartile for SBP	38 (50)	8 (100)	30 (44.1)	0.003

DBP: diastolic blood pressure, SBP: systolic blood pressure

Table 2: Baseline clinical characteristics of hypertensive carotid endarterectomy patients, expressed as a frequency (percentage) or mean (standard deviation)

Patient characteristics	Total cohort $n = 67$	Patients with in-hospital strokes or death, $n = 7$	Patients without in-hospital strokes or death, $n = 60$	p-value
Female	28 (41.8)	3 (42.9)	25 (41.7)	1.000
Age	64.9 (7.3)	66.1 (7.1)	64.8 (7.4)	0.650
History of ischaemic heart disease	35 (52.2)	5 (71.4)	30 (50)	0.431
Diabetes	38 (56.7)	6 (85.7)	32 (53.3)	0.129
History of congestive heart failure	4 (6)	1 (14.3)	3 (5)	0.364
Prior history of a stroke	58 (86.6)	5 (71.4)	53 (88.3)	0.235
Creatinine > 177 µmol/l ($n = 63$)	3 (4.8)	1 (14.3)	2 (3.6)	0.302
General anaesthesia	29 (43.3)	3 (42.9)	26 (43.3)	1.000
Preinduction mean (SBP, mmHg)	167.4 (30.7)	167.3 (42.4)	167.5 (29.4)	0.989
Preinduction mean (DBP, mmHg)	78.2 (13.3)	73.4 (16.5)	78.8 (13)	0.319
Preinduction SBP < 145 mmHg or > 195 mmHg	31 (46.3)	7 (10.4)	24 (35.8)	0.003

DBP: diastolic blood pressure, SBP: systolic blood pressure

concern. In our cohort, 54% of patients had a preoperative SBP > 160 mmHg, while in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) surgical cohort, the prevalence of preoperative patient SBP > 160 mmHg was 20%.[3] Certainly, based on the work of Rothwell et al,[13] this may have accounted for some of the morbidity observed in our patients.

In the NASCET study,[3] and the study by Tu and colleagues,[4] the prevalence of hypertension was approximately 60%, while it was nearly 90% in our patients. Therefore, it is possible that the degree of hypertension control in South African patients is a more important determinant of major morbidity and mortality following CEA than a history of hypertension itself. However, this hypothesis requires further research.

Limitations

A major limitation to our study was our small sample size. As a result, we could not conduct multivariate statistical analysis, and therefore we limited our results to univariate data analyses only. Furthermore, preinduction BP was taken as a single measurement. A single preinduction BP measurement may have been confounded by other factors, such as missed antihypertensive medication on the day of surgery or patient stress. We were also unable to present data stratified according to the severity of hypertension in hypertensive patients as these data were not routinely collected during the study period.

However, globally, the question of which preoperative clinical risk factors are associated with in-hospital strokes and death following CEA will no doubt be answered by the subanalysis of data from the Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) study, a multicentre observational study on 40 000 noncardiac surgery patients, in which patient recruitment was completed in late 2013. Our study highlights the possible importance of including preoperative BP control in these analyses.

Conclusion

The rate of in-hospital stroke and death following CEA in South African patients is high, and it is possible that the preoperative control of SBP could be an important determinant of adverse outcomes. Further research involving larger surgical cohorts is required to confirm our observations. We suggest that a South African collaborative research group attempt to verify the findings of this paper.

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Conflict of interest — The authors declare no conflict of interest.

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