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The importance of early carotid endarterectomy in symptomatic patients

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ABSTRACT

INTRODUCTION Early carotid endarterectomy (CEA) in symptomatic patients may prevent repeat cerebral events. This study investigates the relationship between waiting time for CEA and the incidence of repeat cerebral events prior to surgery in symptomatic patients.

PATIENTS AND METHODS A prospective database of consecutive patients undergoing CEA between January 2002 and December 2006 was reviewed. Repeat event rates prior to surgery were calculated using Kaplan–Meier analysis and predictive factors identified using Cox regression analysis.

RESULTS A total of 118 patients underwent CEA for non-disabling stroke, TIA and amaurosis fugax. Repeat cerebral events occurred in 34 of 118 (29%) patients at a median 51 days (range, 2–360 days) after the first event. The estimated risk of repeat events was 2% at 7 days and 9% at 1 month after first event (Kaplan–Meier survival analysis). Age (HR 1.059; 95% CI 1.014–1.106; $P = 0.009$] was identified as a predictor of repeat events. Patients underwent surgery at median 97 days (range, 7–621 days) after the first event. Eleven of 60 (18%) patients waiting ≤ 97 days for surgery and 23 of 58 (40%) patients waiting > 97 days had repeat events. ($P = 0.011$, chi-squared test).

CONCLUSIONS Delays in surgery should be reduced in order to minimise repeat cerebral events in patients with symptomatic carotid stenosis, particularly in the elderly population.

KEYWORDS

Carotid endarterectomy – Transient ischaemic attacks – Non-disabling stroke – Amaurosis fugax – Repeat cerebral events

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Stroke is one of the leading causes of death in industrialised countries.[1] Rapid assessment stroke clinics have been shown to be an effective way of selecting patients for early carotid intervention[2] with delays reduced by the early identification of symptoms and efficient direction towards appropriate care.

Carotid endarterectomy (CEA) has been shown to be helpful in prevention of further strokes following a non-disabling cerebral ischaemic event.[3,4] The early period after a transient ischaemic attack (TIA) or non-disabling stroke is associated with a high incidence of further cerebral events. Recent data from population-based studies suggest that the risk of sustaining a repeat event following a TIA is 8% at 7 days, 11.5% at 1 month and 17.3% at 3 months and the risk increases slightly following a minor stroke.[5] The Oxford Community Stroke Project (OCSP) reported a stroke risk of 8.6% at 7 days and 12% at 1 month after first-ever TIA and 2.4% in the first week after referral rising to 4.9% at 1 month.[6] As a result, timing of carotid endarterectomy following cerebral ischaemic event has been a topic of considerable interest.[7–11]

Carotid endarterectomy is beneficial in reducing risk of stroke in the presence of > 70% carotid stenosis,[3,4] with greater absolute risk reduction seen if surgery is carried out within 1–2 weeks of the ischaemic event.[11–14] Despite one observational study which suggested an increased risk of peri-operative stroke in those patients operated on within 1 month of the preceding event,[15] most clinicians advocate prompt surgical intervention in patients with symptomatic high-grade stenosis. The aim of this study was to investigate the relationship between waiting time for CEA and the incidence of repeat cerebral events prior to surgery.

Patients and Methods

Setting and patients

Consecutive patients from a single vascular unit who had CEA for symptomatic carotid stenosis between January 2002 and December 2006 were identified from a prospectively maintained vascular database and their case notes reviewed retrospectively. All patients underwent bilateral carotid duplex scans carried out by experienced vascular technologists and dates of key events including onset of symptoms, initial presentation, specialist referral and review, carotid duplex and surgery were recorded. Indications for surgery were classified as hemispheric transient ischaemic attacks (TIA), amaurosis fugax and non-disabling stroke (defined as focal neurological deficit persisting for more than 24 h and leading to a slight disability but able to look after own affairs without assistance; equivalent to modified Rankin scale[16] of 1 and 2). Any specific reasons for delayed assessment of patients were noted. Requirements for further carotid imaging including computed tomography (CT) scan and magnetic resonance imaging (MRI) in difficult cases, echocardiography and need for a further specialist referral were also noted. Details of repeat cerebral events were obtained from the case notes.

Statistical analysis

All analyses were performed in consultation with a medical statistician using Statistical Package for Social Sciences (SPSS for Windows, v.13.0; Chicago, IL, USA). Repeat events after initial presentation were analysed using Kaplan–Meier survival analysis. Predictive factors for repeat cerebral events were identified using Cox regression analysis; repeat cerebral events and waiting time for surgery were compared with chi-squared test and a *P*-value less than 0.05 was considered statistically significant.

Results

Initial presentation

A total of 118 patients underwent carotid endarterectomy during the study period. The median age was 73.5 years (range, 45–88 years) and 72% patients were male (M:F ratio, 85:33). Of these, 78 (66%) patients presented initially to their general practitioner following first symptoms whilst the remaining patients presented to a physician, ophthalmologist, vascular surgeon or cardiologist (Fig. 1A). Median time from the first symptom to initial presentation was 3 days (range, 0–609 days); however, 25% of patients waited over 1 month before seeking medical attention. Of the 118 patients, 69 (58.4%) presented initially within a week of the first symptom and a further 19 patients (16.1%) presented within a month. Initial symptoms were non-disabling stroke

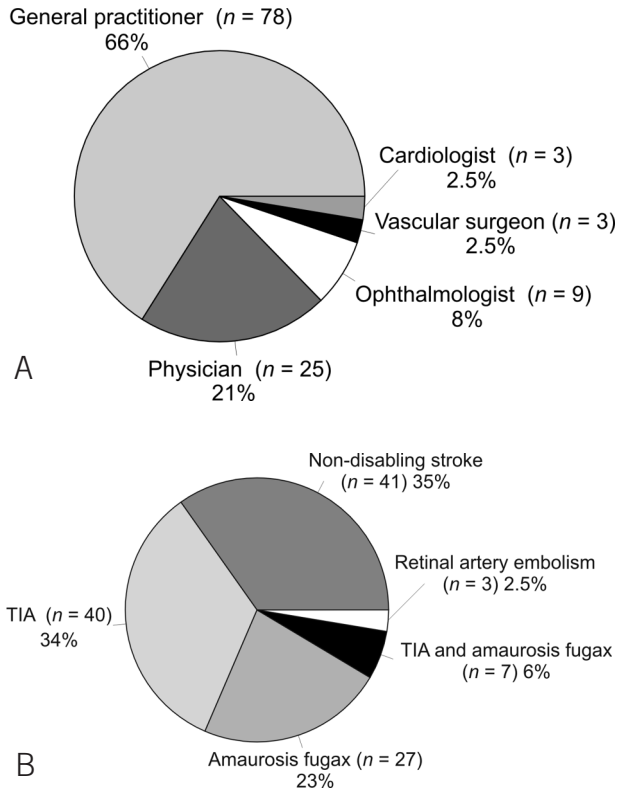

Figure 1 (A) Initial presentation; (B) initial symptoms.

Table 1 Key events from first symptom

Key events	Median (days)	Range (days)
Initial event to initial presentation	3	0–609
Initial event to carotid duplex	41	1–615
Initial event to visiting vascular specialist	58	1–609
Initial event to surgery	97	7–621
Initial event to repeat cerebral events	51	2–360

(35%), TIA (34%), amaurosis fugax (23%) and TIA and amaurosis fugax (6%). Three patients were found to have retinal artery embolism on routine diabetic screening (Fig. 1B). Times to key events after first symptoms are shown in Table 1. Patients waited for a median 97 days (range, 7–621 days) from initial event to CEA and 21 days (range, 1–156 days) from vascular consultation to CEA. All patients had > 70% internal carotid artery stenosis. In 14 patients, carotid duplex was not conclusive and so the diagnosis was confirmed by carotid CT or MRI.

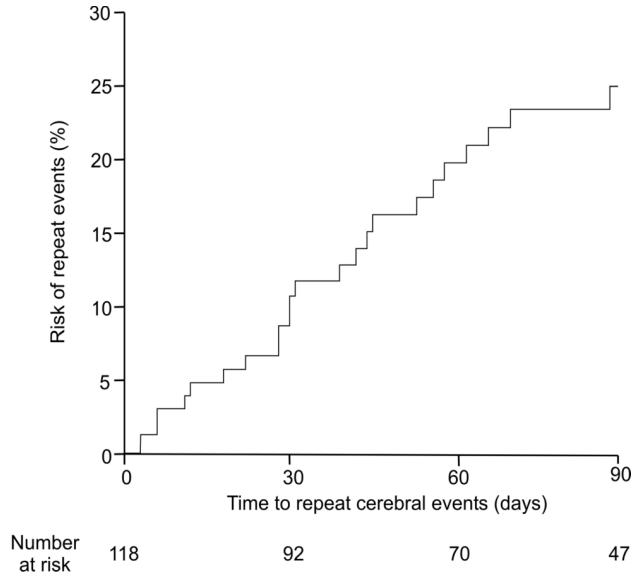

Figure 2 Time to repeat cerebral events curve prior to surgery.

Repeat cerebral events

Of the 118 patients, 34 (29%) suffered repeat cerebral events before undergoing CEA; of these, 16 had transient limb weakness, 13 had amaurosis fugax and 5 had transient speech-related symptoms. None of these 34 patients had a disabling stroke. Repeat cerebral events occurred at a median 51 days (range, 2–360 days) after first event. The estimated risk of repeat events prior to surgery was 1.7% at 7 days, 8.9% at 1 month and 25% at 3 months (Kaplan–Meier survival analysis; Fig. 2). Using a Cox regression analysis, patient age (HR 1.059; 95% CI 1.014–1.106; $P = 0.009$) was identified as a predictor of repeat events (Table 2). Other factors including gender, limb symptoms (motor or sensory), TIA alone, amaurosis fugax and non-disabling stroke were not found to be predictors of repeat events. Of the 60 patients who waited for surgery for ≤ 97 days, 11 (18%) had repeat cerebral events and of the remaining 58 patients who waited for surgery for >97 days, 23 (40%) had repeat cerebral events ($P = 0.011$, chi-squared test; Table 3).

Table 2 Cox regression analysis of risk factors for repeat cerebral events

Risk factor	Hazard ratio (95% CI)	*P*-value
Age	1.059 (1.014–1.106)	0.009
Gender	0.548 (0.264–1.137)	0.106
Limb symptoms	1.625 (0.789–3.344)	0.188
TIA alone	1.274 (0.557–2.913)	0.566
TIA and amaurosis fugax	1.848 (0.575–5.934)	0.302
Amaurosis fugax alone	1.004 (0.384–2.620)	0.994
Non-disabling stroke	1.227 (0.591–2.549)	0.583

Table 3 Repeat cerebral events

Repeat events	Waiting time to surgery in days (%)		*P*-value*
	≤ 97 ($n = 60$)	> 97 ($n = 58$)	
Yes	11 (18%)	23 (40%)	0.011
No	49 (82%)	35 (60%)	

*Chi-squared test.

Discussion

This study demonstrates that a prolonged delay between initial presentation and carotid endarterectomy increases the risk of repeat cerebral events. This highlights the importance of prompt referral, efficient investigation and early surgery. It also supports the findings from a pooled data analysis of patients from the European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) that showed the benefit of performing surgery within the first 2 weeks of last ischaemic cerebral event.[12]

The estimated risk of repeat cerebral events observed in this study was slightly higher than the risk of recurrent stroke observed in previous studies.[5,6] Furthermore, the risk factor analysis in the current study showed that elderly patients waiting longer for surgery are more likely to suffer from repeat cerebral events. This supports the view that repeat events are likely to have different predictive factors and early recognition of these may be useful in preventing any delays in carotid intervention. In contrast to a previous study, initial symptoms such as TIA, amaurosis fugax and limb symptoms including sensory and motor symptoms were not predictive of repeat events in this study which may be a chance finding.[17]

In this study, carotid endarterectomy was delayed for various reasons which included delayed presentation, referral and waiting times for investigation and surgery. Pre-hospital delays can be reduced by primary care physician education regarding the importance of promptly and fully evaluating patients with TIA. There may be a case for seeing all TIA patients in rapid-access clinics as recommended in the past.[18,19] Pre-operative delays may arise for various reasons including delay in initial duplex scan, the

need for additional imaging, or further specialist opinion. Attempts to reduce these delays by speeding up definitive investigations after initial presentation, possibly by introducing local treatment pathways and better organisation of referral services, may avoid delays in patients undergoing surgery.

Many patients following an ischaemic cerebral event delay seeking medical attention, as reported previously.[20] In our study, 25% of patients waited for more than a month before seeking medical attention which suggests that an effective public education plan needs to be implemented to increase patient knowledge and attitude following TIA or stroke.

It is likely that the risk of repeat cerebral events is much higher than previously thought. The current study focused exclusively on patients who underwent carotid surgery and was not designed to identify patients who were not considered for surgical intervention as a result of fatal or severe cerebrovascular events following initial ischaemic event. It may, therefore, underestimate the risk of repeat stroke whilst awaiting surgery.

Whilst the results are interesting, this study does not give a clear view on an optimum time interval for carotid endarterectomy following a cerebrovascular event. Nonetheless, the risk of repeat cerebral event increased linearly with time from initial event to surgery suggesting that there may be no 'safe' period of delay for carotid endarterectomy following TIA, minor stroke or amaurosis fugax. These patients, in many ways, are analogous to those presenting with unstable angina and, accordingly, must be urgently assessed or indeed admitted as an emergency and those with a carotid stenosis of > 70% should be offered surgery as soon as possible. This is in keeping with the UK Department of Health national stroke strategy which recommends that carotid intervention for recently symptomatic severe carotid stenosis should be regarded as an emergency procedure and should ideally be performed within 48 hours of a TIA or minor stroke.[21]

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