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Delayed Carotid Surgery: What Are the Causes in the North West of England?

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WHAT THIS PAPER ADDS

- Up until recently, carotid endarterectomy in UK was not done sufficiently early following symptoms of cerebral ischaemia. This study suggests that the early management of patients with symptoms of cerebral ischaemia at a one-stop stroke prevention or TIA clinic with Duplex imaging could promote rapid surgery. It also supports the current initiative to focus stroke services in the UK within specialist centres.

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ABSTRACT

Introduction: Carotid endarterectomy (CEA) should be performed within two weeks of symptoms for patients with carotid stenosis >50%. Whether these standards are being achieved and causes of delay between symptoms and CEA were investigated.

Design: An analysis of prospectively collected multi-centre data.

Materials: Consecutive data for patients undergoing CEA between January-2006 and September-2010 were collected. Asymptomatic patients and those with no details on the timing of cerebral symptoms were excluded.

Methods: 'Delay' from symptom to CEA was defined as more than two weeks and 'prolonged-delay' more than eight weeks. Univariable and multivariable analyses were used to identify factors associated with these delays.

Results: Of 2147 patients with symptoms of cerebral ischaemia, 1522(70.9%) experienced 'delay' and 920(42.9%) experienced 'prolonged delay'. Patients with ischaemic heart disease were more likely to experience 'delay' (OR = 1.56; 95% CI 1.11–2.19, $p = 0.011$), whereas patients with stroke (OR = 0.77; 95% CI 0.63–0.94, $p = 0.011$) and those treated at hospitals with a stroke-prevention clinic (OR = 0.57; 95% CI 0.46–0.71, $p < 0.001$) were less likely to experience 'delay'. Patients treated after the publication of National Institute for Health and Clinical Excellence (NICE) guidelines were less likely to experience 'prolonged delay' (OR = 0.77; 95% CI 0.65–0.91, $p = 0.003$) but not 'delay'.

Conclusion: Few patients achieved CEA within two weeks of symptoms. Introducing stroke-prevention clinics with one-stop carotid imaging appears important.

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Introduction

Carotid endarterectomy (CEA) reduces the risk of stroke in patients with recently symptomatic severe carotid artery stenosis and, to a lesser extent, patients with asymptomatic carotid stenosis.^{1–4} The main benefit of surgery, the reduction in stroke risk, is greatest if surgery is performed early following symptoms

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of cerebral ischaemia with a meta-analysis of the North American Symptomatic Carotid Endarterectomy (NASCET) and European Carotid Surgery (ECST) trials demonstrating that surgery delayed beyond 12 weeks from the onset of symptoms had equivalent efficacy to that for asymptomatic disease.⁵

The National Institute for Health and Clinical Excellence (NICE) issued guidelines in July 2008⁶ which recommended that stable patients following acute non-disabling stroke or transient ischaemic attack (TIA) who have symptomatic carotid stenosis of 50–99% (NASCET), or 70–99% (ECST) criteria, should:

- i. be assessed and referred for CEA within one week of onset of symptoms.
- ii. undergo surgery within two weeks of symptoms.

Although the NICE guidelines and others⁷ have raised awareness of the importance of offering early CEA to symptomatic patients, unacceptable delays to surgery have still been demonstrated in the UK.⁸ The aim of this study was to investigate the causes of delay in carotid surgery in the North West of England.

Materials and Methods

This was a prospective multi-centre study conducted on behalf of the Vascular Governance North West (VGNW) programme. VGNW is a peer-led clinical governance programme that currently audits the results of 55 vascular surgeons who perform CEA at 21 hospitals in the North West of England and Wales. Data were collected prospectively using a purpose-designed data-entry form on consecutive CEAs performed between January 2006 and October 2010. Data were mainly supplied by the operating surgeons with missing data completed where possible from patient medical records. Data collected included patient demographics, date of symptom onset, referral details, the indication for surgery, medical history, pre-operative medications and pre-operative investigations.

All data was entered into a central Microsoft Access database held at the University Hospital of South Manchester (UHSM). To test the completeness of data, the numbers of operations carried out at participating hospitals were validated against Hospital Episode Statistics (HES) and cross checked with discharge summaries. Follow-up data was obtained by contacting the clinical team responsible for each patient following discharge.

The primary outcome measure for the study was delay from symptoms to CEA of over two weeks. Secondary outcome measures were delay from symptoms to CEA of over eight weeks (prolonged delay) and post-operative stroke or mortality. Mortality was defined as death within 30-days following CEA regardless of cause and stroke was as defined by the contributing surgeon. All variables missing for more than 15 percent of patients were excluded from the analysis. Categorical variables were coded as 1 if they were present; otherwise they were coded as 0, meaning that if a condition or finding was not recorded or mentioned in the patient's record, or the test had not been performed, the condition was assumed to be absent. For continuous variables the sample median was substituted for missing values.

Statistical Analysis

The χ^2 test or univariable logistic regression was used for statistical analysis of categorical or ordinal variables which are shown as percentages. Standard statistical tests were used to calculate odds ratios and 95% confidence intervals (CI). A multivariable logistic regression analysis was undertaken using the forward stepwise technique, to identify risk factors for delay and

prolonged delay from symptoms to CEA. All analysis was performed using SPSS 16.0 (SPSS Inc., Chicago IL).

Results

Over the study period, a total of 2976 CEAs were performed. CEA was performed for symptomatic carotid artery stenosis in 2573 (86.5%) patients. Information on the interval between symptoms and the surgery was available for 2147 (83.4%) of the symptomatic patients with this group representing the final cohort for all subsequent analyses.

Patient characteristics

The median age of the patients was 72 years (range 39–100) and 1465 (68.4%) were men. TIA, stroke and amaurosis fugax were the presenting symptoms for 1065 (49.6%), 632 (29.4%) and 450 (21.0%) patients respectively. Ipsilateral carotid stenosis was 70–99% for the majority (1804, 84.0%) of patients and 50–69% in a further 625 (13.7%). The ipsilateral stenosis was <50% for 34 (1.6%) patients with 15 (0.7%) patients having complete ipsilateral occlusion. Carotid imaging was by Duplex ultrasound initially in 2028 (94.5%) patients with confirmatory imaging, usually by magnetic resonance angiography (MRA) or CT angiography performed in 412 (19.2%) patients. Most patients were referred by a hospital physician (1883, 87.7%).

Symptom to carotid surgery delay

The majority of patients (1522, 70.9%) waited longer than two weeks between initial symptoms and CEA with the median delay being 5–7 weeks. A total of 920 (42.9%) patients underwent CEA more than eight weeks from the symptoms that precipitated referral. The percentage of patients who underwent CEA more than two weeks or more than eight weeks after symptoms for each year of the study is shown in Fig. 1. The publication of NICE guidelines has been associated with a reduction in the number of patients waiting for longer than two weeks (68.4% vs. 73.7%, OR 0.77 95%CI 0.64–0.93, $p = 0.007$), and the number of patients waiting longer than eight weeks (39.5% vs. 46.6%, OR 0.75 95%CI 0.63–0.89, $p = 0.001$).

Univariable analysis for causes of delay from symptoms to CEA

Factors associated with a delay from symptoms to CEA of more than two weeks are shown in Table 1. Patients with a history of

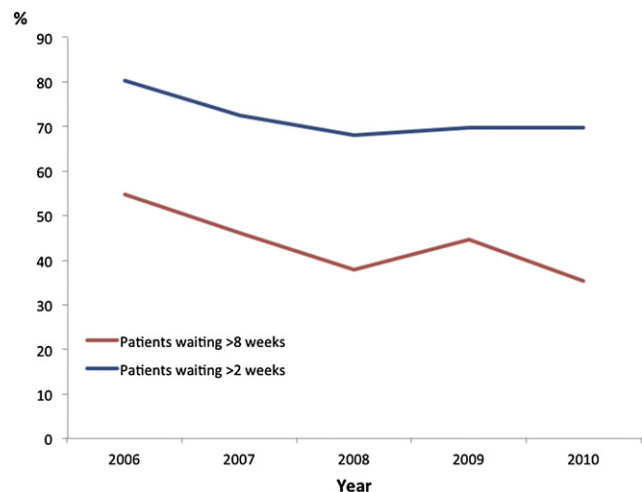


Figure 1. Percentage of patients waiting longer than two or eight weeks from symptoms to CEA in the North West of England by year of procedure.

Table 1Association between cohort characteristics and delay from symptoms to CEA of >2 weeks or >8 weeks; univariable analysis ($n = 2147$).

		% of patients	% >2 week CEA delay	Odds ratio (95% CI)	<i>p</i> value	% >8 week CEA delay	Odds ratio (95% CI)	<i>p</i> value
Age (years)	<65	23.9	69.3	Ref.		43.0	Ref.	
	65–74	39.6	72.4	1.16(0.92–1.48)	0.217	44.2	1.05(0.84–1.31)	0.668
	≥75	36.4	70.3	1.05(0.83–1.34)	0.681	41.3	0.93(0.75–1.17)	0.546
Gender	Male	68.4	70.3	Ref.		42.8	Ref.	
	Female	31.6	72.2	1.10(0.90–1.34)	0.376	42.9	1.00(0.83–1.20)	0.997
Diabetes	No	83.7	70.8	Ref.		42.9	Ref.	
	Yes	16.3	71.5	1.04(0.81–1.34)	0.780	42.5	0.98(0.78–1.24)	0.868
Ischaemic heart disease	No	90.0	70.1	Ref.		41.9	Ref.	
	Yes	10.0	78.1	1.53(1.09–2.14)	0.014	51.2	1.45(1.09–1.92)	0.010
Indication for surgery	Other	70.6	72.7	Ref.		44.7	Ref.	
	Stroke	29.4	66.6	0.75(0.61–0.92)	0.005	38.4	0.77(0.64–0.94)	0.008
Ipsilateral stenosis	<70%	15.3	69.5	Ref.		41.8	Ref.	
	≥70%	84.7	70.9	1.08(0.84–1.40)	0.551	42.9	1.05(0.83–1.34)	0.667
Contralateral stenosis	<70%	76.6	70.1	Ref.		41.9	Ref.	
	≥70%	23.4	73.4	1.17(0.94–1.47)	0.164	45.9	1.18(0.96–1.44)	0.112
Referral source	GP	12.3	76.5	Ref.		50.0	Ref.	
	Physician	87.7	70.1	0.72(0.53–0.97)	0.032	41.8	0.72(0.56–0.93)	0.012
Hospital stroke-prevention clinic	No	76.3	73.8	Ref.		45.5	Ref.	
	Yes	23.7	61.6	0.57(0.46–0.70)	<0.001	34.4	0.63(0.51–0.78)	<0.001
Initial imaging modality	MRA/CT	5.5	63.0	Ref.		43.3	Ref.	
	Duplex ultrasound	94.5	71.4	0.68(0.47–1.01)	0.053	35.3	0.71(0.49–1.05)	0.088
NICE guidelines	Pre	47.6	73.7	Ref.		46.6	Ref.	
	Post	52.4	68.4	0.77(0.64–0.93)	0.007	39.5	0.75(0.63–0.89)	0.001

Other = TIA or amaurosis fugax; MRA = magnetic resonance angiography; CT = CT angiography, *p* values calculated using univariable logistic regression; ref = reference group; GP = general practitioner; CEA = carotid endarterectomy; NICE = National Institute for Health and Clinical Excellence. Bold = significant at $p < 0.05$.

ischaemic heart disease were more likely to have a delay of more than two weeks from initial symptoms to CEA. Patients that were referred for surgery by a hospital physician, presented with a stroke, or were treated at a hospital with a dedicated stroke-prevention clinic were less likely to have CEA more than two weeks from initial symptoms. Factors associated with a delay from symptoms to CEA of more than eight weeks were the same as for a delay of more than two weeks and are also shown in Table 1.

Multivariable analysis

Factors associated with a delay from initial symptoms to CEA of more than two weeks on multivariable analysis are shown in Table 2. Patients with a history of ischaemic heart disease were found to be more likely to have a delay from symptoms to CEA of more than two weeks. Patients who presented with a stroke or who underwent CEA at a hospital with a dedicated stroke-prevention clinic were less likely to undergo CEA more than two weeks after the symptoms that caused referral.

Factors found to be associated with a less than eight week delay from symptoms to CEA on multivariable analysis are shown in Table 3 and included; presentation with stroke, referral by a hospital physician and CEA performed at a hospital with a dedicated stroke-prevention clinic. CEA after the introduction of NICE guidelines was also found to be a factor associated with a delay from initial symptoms to CEA of less than eight weeks.

Table 2Risk factors for delay from symptoms to CEA of >2 weeks; logistic regression analysis ($n = 2147$).

	Odds ratio (95% CI)	<i>p</i> value
Stroke as indication for surgery	0.77(0.63–0.94)	0.011
Ischaemic heart disease	1.56(1.11–2.19)	0.011
Hospital with stroke-prevention clinic	0.57(0.46–0.71)	<0.001

CEA = carotid endarterectomy.

Outcomes following CEA

Post-operative stroke occurred in 32 (1.5%) patients with 21 of these strokes within 24 hours and 11 over the next 30 days. The overall 30-day mortality rate in the cohort was 0.6% (12 deaths) giving a combined stroke and death rate of 2.0%. Patients who underwent CEA within two weeks of symptoms had a stroke rate of 2.2% compared to 1.2% (OR 1.92 95%CI 0.95–3.87, $p = 0.066$) for patients who were delayed for more than two weeks. The stroke rates in patients who underwent CEA within eight weeks of symptoms or more than eight weeks from symptoms were 1.4% and 1.6% respectively (OR 0.85 95%CI 0.42–1.71, $p = 0.643$). There was also a non-significant reduction in stroke rate since the publication of the NICE guidelines from 1.8% to 1.2% (OR 0.70 95%CI 0.35–1.42, $p = 0.324$).

Discussion

Despite the introduction of NICE guidelines⁶ recommending that patients with symptoms of symptomatic carotid stenosis should have CEA within two weeks; this was not achieved for most patients in the North West of England. These findings are consistent with the first National UKCEA audit.⁸ However, since the publication of the NICE guidelines, the proportion of patients waiting for more than two weeks or eight weeks from symptoms to CEA has reduced. This improvement was significant for two week delay on

Table 3Risk factors for delay from symptoms to CEA of >8 weeks; logistic regression analysis ($n = 2147$).

	Odds ratio (95% CI)	<i>p</i> value
Stroke as indication for surgery	0.82(0.68–0.99)	0.043
Post NICE guidelines	0.77(0.65–0.91)	0.003
Referral by hospital physician	0.77 (0.59–1.00)	0.047
Hospital with stroke-prevention clinic	0.64(0.52–0.79)	<0.001

CEA = carotid endarterectomy; NICE = National Institute for Health and Clinical Excellence.

univariable analysis and for eight week delay on multivariable analysis. The fact that the improvement demonstrated is not more significant is unsurprising given that the NICE guidelines, although published in 2008, were only widely implemented in the UK during 2010–2011. Other drivers for change have however been implemented during the period of this study and a reduction in CEA waiting times was demonstrated in round two of the UKCEA audit.⁹

The data used for this study was collected prospectively and validated locally. It has not been externally validated which is a limitation of this study. Contribution to VGNW is voluntary and it is likely that not all CEAs performed during the study period have been included. As with any registry study, data quality and completeness were a limitation although any data fields with more than 15% missing data were excluded from the analysis. We have conducted an appropriate statistical analysis of our available data but as with any observational study it is impossible to eliminate other confounding factors that may have contributed to the conclusions.

The post-operative 30-day stroke rate, 30-day death rate and combined stroke and death rate in this study is similar to the recent UKCEA study⁹ but lower than the major randomised clinical trials and other earlier registries, perhaps reflecting continued improvements in care.^{1,2,10–16} However, the patients in this study were followed up by the teams who undertook the surgery, and it is recognised that higher post-operative stroke rates are often reported when follow-up is by a stroke physician. The stroke rate in this study was non-significantly higher for patients operated on within two weeks of symptoms. This has previously been demonstrated in a systematic review¹⁷ and could possibly be explained in this study by the observation that stroke was a more common indication for surgery in the group operated on within two weeks of symptoms. The stroke rate was also found to have fallen non-significantly in this study following the publication of the NICE guidelines.

Reducing waiting times from symptoms to surgery is imperative if CEA is to be effective.⁵ Delays are common in the literature with studies from the late 1990s onwards in England,^{11,18} Sweden,¹² Canada,¹³ and Scotland,¹⁴ reporting median delays between symptoms of cerebral ischaemia and CEA ranging from two to five months. In the ECST, the median delay from randomization to CEA in the 29 UK centres (1086 patients) in the 1980s and early 1990s was more than two months, meaning a delay from symptom to surgery of much more than this.¹ The median randomisation to surgery delay in ECST was also more than a month in Denmark, Finland, Italy, Norway, Portugal, and Sweden, and no country achieved a median delay of less than two weeks. In the NASCET only 45% of patients underwent CEA within one month of randomisation, with nearly 20% operated on after more than four months.¹⁹ A recent study from a Swedish tertiary referral centre found only 11% of patients underwent CEA within two weeks of symptoms.²⁰ The majority of patients in the literature have therefore undergone CEA after the critical time interval when the benefits of surgery most clearly outweigh best medical treatment.⁵ In addition to reduced clinical effectiveness; the cost effectiveness of such delayed surgery is clearly poor.

This study has identified a number of risk factors for delayed CEA, addressing these would be important if CEA services are to continue to improve. Patients with a history of ischaemic heart disease were significantly more likely to wait longer than two weeks from symptoms to CEA. As it is likely that these patients will undergo additional pre-operative investigations or may require coronary interventions for their ischaemic heart disease prior to CEA, this may be difficult to address. In this study, patients who presented with a stroke were more likely to undergo CEA within two weeks. Reducing delays from symptom to CEA for patients with TIA or amaurosis fugax is important and potentially achievable.

One of the key findings in this study is that hospitals having stroke-prevention clinics were more likely to achieve CEA within two weeks of symptoms and were less likely to have patients waiting more than eight weeks. This suggests that rapid access to stroke prevention clinics with one-stop carotid imaging is essential for reducing delay from symptoms to CEA in the future. It is also a powerful argument supporting the current initiative to focus stroke services in the UK within specialist centres. However as suggested by the UKCEA study,⁹ stroke services are probably underutilised and strategies should also focus on utilising stroke services to capacity as well as making it easier for smaller hospitals to access them. It has also been suggested that the urgent assessment of patients with symptoms of cerebral ischaemia in a specialised clinic can reduce stroke risk and healthcare costs.^{21,22}

Patients who were referred for CEA directly by their GP were more likely to wait longer than both two and eight weeks for CEA although this was only significant on multivariable analysis for eight week delay. This finding of lower delay for patients referred by hospital physicians was also demonstrated in the UKCEA study.⁹ This could potentially be addressed by direct access stroke prevention or TIA clinics. Alternatively fast track carotid imaging by Duplex, such as that introduced in Gloucester halving symptom to CEA intervals to a median of under seven weeks, may be an approach suitable for other geographical areas.²³

As patients treated at hospitals with stroke-prevention clinics and patients who were referred by hospital physicians were less likely to be delayed, it is likely that a regional protocol defining the early management of patients with symptoms of cerebral ischaemia, and greater use of stroke prevention clinics, would improve access to rapid CEA.²¹ This protocol would involve suitable patients being seen urgently in open access stroke prevention or TIA clinics with “one stop” Duplex imaging available immediately. Patients who are then considered fit for surgery with >50% carotid stenosis should be referred directly to vascular surgeons who have pre-booked operating capacity for urgent CEAs. Implementing such protocols will involve significant efforts from clinicians, managers and commissioners but will be of important clinical benefit.

Appendix. VGNW participants

Arrowe Park Hospital: M Greaney, S Blair, R Chandrasekar, C Chan, A Chaudhuri, L Williams, V Kappadath. *Blackburn Royal Infirmary:* S Hardy, R Salaman. *Blackpool Victoria Hospital :* V Perricone, H Osman. *Burnley General Hospital:* H Al-Khaffaf, A Rahi. *Countess of Chester:* L de Cossart, P Edwards, S Dimitri. M Hamish. *Glan Clwyd Hospital:* O Klimach, Y Rouhani. *Leigh Infirmary:* J Mosley. *Leighton Hospital:* M Hanafy. *Manchester Royal Infirmary:* JV Smyth, F Serracino-Inglott. *North Manchester District General Hospital:* G Williams, M Madan, W Tait. *Royal Bolton Hospital:* G Ferguson, M Onwudike. *Royal Lancaster Infirmary:* J Abraham, P Wilson, M Bukhari, J Calvey, M Tomlinson. *Royal Liverpool University Hospital :* J Brennan, V Rao, R Fisher. *Royal Oldham Hospital:* T Oshodi, M Hadfield. *Royal Preston Hospital:* G Thomson, A Egun. *University Hospital of South Manchester:* C McCollum, M Baguneid, M Welch. *Southport District General Hospital:* D Jones. *Tameside District General Hospital:* A Woodyer, C Pratap, L Wolowczyk. *University Hospital Aintree:* J Joseph, F Torella. *Warrington District General Hospital:* P Moody, T Nicholas, P Wake, D Olojugba. *Wrexham Maelor Hospital:* U Kirkpatrick, A da Silva.

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Conflict of Interest

All authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the North West Research Ethics Committee (09/H1010/1).

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