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Dual Antiplatelet Therapy Prior to Expedited Carotid Surgery Reduces Recurrent Events Prior to Surgery without Significantly Increasing Peri-operative Bleeding Complications

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WHAT THIS PAPER ADDS

A reconfiguration of TIA services reduced the median delay from symptom to CEA to 9 days. However, an audit revealed that during the median 3-day period between transfer from the TIA clinic to undergoing CEA, 13% of patients suffered recurrent events, despite having been previously started on aspirin. In the current audit, a change to early implementation of dual antiplatelet therapy (in the TIA clinic after CT/MR exclusion of parenchymal haemorrhage) was associated with a fivefold reduction in recurrent neurological events prior to expedited CEA and a fourfold reduction in spontaneous embolization, compared with data observed in the preceding audit. This was achieved without a significant increase in major peri-operative bleeding complications.

Objective: A daily Rapid-Access TIA Clinic was introduced in 2008, where symptomatic patients were started on 75 mg aspirin + 40 mg simvastatin by the referring doctor, before attending the clinic. Following clinic assessment, patients with 50–99% stenoses were transferred to the vascular unit for carotid endarterectomy (CEA). In two audits ($n = 212$ patients), the median delay from transfer to the vascular unit to undergoing CEA was 3 days, during which time 28 patients (13%) suffered recurrent neurological events. It was hypothesized that early introduction of dual antiplatelet therapy (by adding clopidogrel 75 mg once parenchymal haemorrhage was excluded in the TIA clinic) might significantly reduce recurrent events between transfer to the surgical unit and undergoing CEA.

Methods: Prospective audit in 100 consecutive, recently symptomatic patients receiving dual antiplatelet therapy. Endpoints were: prevalence of recurrent events between transfer from the TIA clinic and undergoing CEA; rates of spontaneous embolization prior to undergoing CEA; and prevalence of haemorrhagic complications

Results: The median delay from symptom to CEA was 8 days (IQR 5–15). The median delay between transfer from the TIA clinic to CEA was 3 days (IQR 2–5), during which time three patients (3%) suffered recurrent TIAs. This represents a fivefold reduction compared with previous audit data (OR 4.9, 95% CI 1.5–16.6, $p = .01$) and was matched by a fourfold reduction in the prevalence of spontaneous embolization from 39/189 (21%) previously to 5/83 (5%) in the current audit (OR 4.1, 95% CI 1.5–10.7, $p = .0047$). The 30-day death/stroke rate was 1%. There were three haemorrhagic complications: stroke caused by haemorrhagic transformation of an infarct; exploration for neck haematoma; and debridement and skin grafting for spontaneous shin haematoma.

Conclusion: Early introduction of dual antiplatelet therapy was associated with a significant reduction in recurrent neurological events and spontaneous embolization prior to CEA, without incurring a significant increase in major peri-operative bleeding complications.

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INTRODUCTION

There has been an international move towards performing carotid endarterectomy (CEA) as soon as possible after onset of symptoms, driven by increasing awareness that the highest risk period for recurrent stroke is the first few days after suffering a transient ischaemic attack (TIA) or minor stroke.[1–7]

To deliver expedited CEA, a daily Rapid Access TIA service was established in Leicester in October 2008.[8] The referring

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family doctor/emergency room doctor started anyone with a suspected TIA/minor stroke on 300 mg aspirin and 40 mg simvastatin at the time of seeing the patient. A consultant physician (who specialized in stroke medicine) then saw each referral in the daily TIA clinic and was responsible for optimizing risk factors and ensuring the patient was still taking aspirin and a statin. Anyone with an ipsilateral 50—99% ICA stenosis was transferred from the TIA clinic to the vascular unit for urgent CEA.[8]

This protocol was associated with a reduction in the delay from symptom to CEA to a median of 9 days (95% CI 7—10).[9] Following transfer from the TIA clinic, patients underwent CEA within a median of 3 days. However, two sequential audits showed that during this 3-day time period (between transfer from the TIA clinic and undergoing CEA), 11% and 15% of patients (respectively) suffered recurrent TIAs or strokes,[9,10] emphasizing just how unstable underlying carotid plaques were during this early time period.

Following a review of practice, and with the aim of trying to prevent recurrent symptoms between referral and surgery, the stroke physicians and vascular surgeons proposed adding 75 mg clopidogrel (i.e. implementing early dual antiplatelet therapy) as soon as intracranial haemorrhage (ICH) or parenchymal haemorrhage was excluded on CT/MRI in the TIA clinic.

The principle aims of the current audit were to establish whether earlier introduction of dual antiplatelet therapy reduced the prevalence of recurrent events between transfer from the TIA clinic and undergoing CEA, without increasing the risk or peri-operative haemorrhagic complications.

MATERIALS AND METHODS

Between August 17, 2013 and July 27, 2014, 100 consecutive, recently symptomatic patients undergoing CEA were recruited. Asymptomatic patients undergoing CEA during this time period were excluded. All patients had been transferred to the vascular unit at the Leicester Royal Infirmary via the Rapid Access TIA clinic, or acute stroke unit. The Leicestershire, Northamptonshire and Rutland Research ethics committee advised that this study did not fall under the remit of the NHS research ethics committee, as it was audit/service evaluation. This prospective audit was registered with the University Hospitals of Leicester Clinical Audit and Quality Improvement Project (ref 6625).

Rapid Access TIA clinic

October 2008—August 2013. The Rapid Access TIA clinic started in October 2008 and operates every day of the year.[8] The referring family doctor/emergency department doctor starts 300 mg aspirin and 40 mg simvastatin in anyone suspected of having suffered a TIA/minor stroke. Electronic referrals were triaged based on the patient's $ABCD^2$ score.[11] Patients with an $ABCD^2$ score of 0—3 (7-day predicted stroke risk = 1%) were seen within 7 days of referral. Patients with an $ABCD^2$ score of 4—7 (7—10% predicted stroke risk within 7 days) were seen either the same day or the following morning.

At the TIA clinic, baseline bloods were taken (haematology/biochemistry) and patients underwent CT/MRI plus carotid Duplex ultrasound assessment. A consultant stroke physician then saw each patient and assumed responsibility for optimizing risk factors and ensuring the patient was taking aspirin and a statin. Any patient who had an ipsilateral 50—99% carotid stenosis was transferred to the vascular unit for urgent CEA. Following transfer, the aspirin dose was reduced from 300 mg to 75 mg daily and this was continued throughout the peri-operative period. Between October 1, 2008 and August 16, 2013, it was unit policy for all CEA patients to receive a single 75 mg dose of clopidogrel the night before surgery (in addition to regular aspirin therapy) to prevent early post-operative thromboembolic stroke.[12] However, no other doses of clopidogrel were administered between admission and surgery during this time period.

August 2013—July 2014: the current audit. The main protocol change related to the start date for dual antiplatelet therapy. All other aspects of referral, investigation, and treatment remained the same. Patients with an ipsilateral 50—99% stenosis and who had no evidence of ICH or parenchymal haemorrhage on CT/MRI were started on 75 mg clopidogrel (in addition to their regular aspirin). Dual antiplatelet therapy (75 mg aspirin, 75 mg clopidogrel) was then continued throughout the peri-operative period. Immediately prior to hospital discharge, aspirin was stopped, but clopidogrel was continued as per NICE guidelines.[13] No patients in the current audit were taking warfarin at the time of TIA clinic attendance.

Expedited CEA

The protocol for performing CEA did not change during the 6-year period from 2008 to 2014. Following admission, each patient underwent work-up for theatre, the goal being to perform CEA safely and as soon as possible. Poorly controlled hypertension was relatively common and treatment was started prior to surgery and then 'finetuned' following the procedure. Where necessary, referrals were made to other medical disciplines for advice regarding the treatment of comorbid conditions that might otherwise delay surgery. Two half-day theatre lists were 'ring-fenced' for CEAs on Tuesdays and Fridays. If these lists were filled, alternative arrangements were made (emergency theatre, ad hoc space on elective lists, deferral to next unfilled CEA list). During the current audit, CEA was performed only once on a Saturday/Sunday.

CEA was performed in the same standardized manner between 2008 and 2014, using general anaesthesia with routine shunting/patching, intra-operative transcranial Doppler (TCD) monitoring and completion angioscopy.[12] The policy regarding the type of patch closure did, however, change. Between October 1, 2008 and December 31, 2011, ultrathin collagen-coated polyester patches were used to close the arteriotomy (Hemagard Ultrathin, Atrium