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Risk Factors For Stroke, Myocardial Infarction, or Death Following Carotid Endarterectomy: Results From the International Carotid Stenting Study

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WHAT THIS PAPER ADDS

The International Carotid Stenting Study (ICSS) compared carotid artery stenting with CEA for patients with recently symptomatic carotid stenosis. The aim of the present study was to determine whether there were subgroups of surgical patients in ICSS at higher risk of stroke, myocardial infarction, or death, and whether specific surgical factors are associated with higher risk. It was found that increasing diastolic blood pressure was the only independent risk factor. Cautious attention to blood pressure control following symptoms attributable to carotid stenosis could reduce the risks associated with subsequent CEA.

Objectives: Carotid endarterectomy (CEA) is standard treatment for symptomatic carotid artery stenosis but carries a risk of stroke, myocardial infarction (MI), or death. This study investigated risk factors for these procedural complications occurring within 30 days of endarterectomy in the International Carotid Stenting Study (ICSS).
Methods: Patients with recently symptomatic carotid stenosis >50% were randomly allocated to endarterectomy or stenting. Analysis is reported of patients in ICSS assigned to endarterectomy and limited to those in whom CEA was initiated. The occurrence of stroke, MI, or death within 30 days of the procedure was reported by investigators and adjudicated. Demographic and technical risk factors for these complications were analysed sequentially in a binomial regression analysis and subsequently in a multivariable model.
Results: Eight-hundred and twenty-one patients were included in the analysis. The risk of stroke, MI, or death within 30 days of CEA was 4.0%. The risk was higher in female patients (risk ratio [RR] 1.98, 95% CI 1.02–3.87, $p = .05$) and with increasing baseline diastolic blood pressure (dBP) (RR 1.30 per +10 mmHg, 95% CI 1.02–1.66, $p = .04$). Mean baseline dBP, obtained at the time of randomization in the trial, was 78 mmHg (SD 13 mmHg). In a multivariable model, only dBP remained a significant predictor. The risk was not related to the type of surgical reconstruction, anaesthetic technique, or perioperative medication regimen. Patients undergoing CEA stayed a median of 4 days before discharge, and 21.2% of events occurred on or after the day of discharge.
Conclusions: Increasing diastolic blood pressure was the only independent risk factor for stroke, MI, or death following CEA. Cautious attention to blood pressure control following symptoms attributable to carotid stenosis could reduce the risks associated with subsequent CEA.

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INTRODUCTION

Three major trials of carotid surgery versus best medical therapy for symptomatic carotid stenosis (the North American Symptomatic Carotid Study, NASCET,[1] the European Carotid Surgery Trial, ECST,[2] and the smaller Veteran's Affairs Trial)[3] demonstrated the benefit of carotid endarterectomy (CEA) in reducing the long-term rate of recurrent stroke.[4] Since these trials published their results, CEA has become

[i] For a list of ICSS investigators see Lancet 2010;375:985–97.

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the standard of care for patients with >50% symptomatic carotid stenosis. However, despite developments in secondary prevention medical therapy, anaesthetic technique, surgical technique, and processes of care, there remains a significant risk of major complications associated with CEA.[5] Trials have focussed on the endpoints of stroke, myocardial infarction (MI), and death. Stroke and MI have a significant adverse impact on the patient's long-term survival — in-hospital stroke in particular has been shown in one study to confer a two-fold lower survival in the first year after surgery.[6]

There is variability in surgical technique for CEA[7,8] and debate remains over optimal processes of care, including perioperative antiplatelet therapy, type of arterial reconstruction (standard, patch, or eversion CEA) and mode of anaesthesia (general, local, or combined local-general anaesthesia).

The International Carotid Stenting Study (ICSS) was an international multicentre randomized controlled open clinical trial that compared the newer technique of carotid artery stenting (CAS) with CEA for patients with recently symptomatic carotid stenosis. This study aimed to determine whether there were subgroups of surgical patients in ICSS at higher risk of stroke, MI, or death, and whether specific surgical factors are associated with higher risk.

METHOD

Patient selection and protocol design

The trial protocol for ICSS is published elsewhere.[9] In summary, patients aged >40 years were eligible for randomization in ICSS if they experienced symptoms within the 12 months before randomization attributable to a >50% diameter-reducing stenosis in the region of the common carotid artery bifurcation caused by atheromatous disease. They were required to be able to undergo either CAS or CEA. Patients were excluded if they would not be suitable for surgery because of a surgically inaccessible distal stenosis or hostile neck, had a major stroke with poor recovery of function, if they were clinically unstable (e.g. had progressive symptoms), if their vascular anatomy rendered CAS or CEA unsuitable, if cardiac bypass was planned within 1 month of the revascularization procedure, or if there had been previous revascularization of the symptomatic artery. The study was approved by ethics committees at local sites and the Northwest Multicentre research ethics committee in the UK.

Carotid endarterectomy in ICSS was performed according to the surgeon's usual practice: local, general, or combined anaesthesia was allowed for the procedure. The type of arterial reconstruction to be carried out was not specified in the protocol, nor was a specific peri-procedural medication regimen. The use of shunts or patches was optional. However, all patients were required to receive "best medical therapy," including antiplatelet agents or anticoagulation where appropriate, and control of vascular risk factors. In addition to collecting the above technical information, centres supplied demographic information about the patient at the time of enrolment into the trial, and specified whether their general policy was to send patients to a specialized post-procedure ward following CEA, such as an intensive care unit, or a general surgical or medical ward.

Only patients assigned to CEA in ICSS in whom CEA was initiated were included. Initiation of CEA was defined as the administration of either local or general anaesthesia prior to commencement of surgery. Patients in whom CEA was abandoned after administration of anaesthesia were included in the analysis. Patients who crossed over without CEA or who received CEA after an attempt at stenting were excluded.

Outcome events

Patients underwent face-to-face follow-up by a trial investigator — a neurologist or physician interested in stroke — at 30 days after surgery. Stroke, MI, or death occurring within 30 days of the procedure was reported to the central trial office by investigators. Stroke was defined as "an acute disturbance of focal neurological function lasting more than 24 hours resulting from intracranial vascular disturbance." A diagnosis of MI required two of the following: cardiac enzymes more than twice the upper limit of normal, a history of chest discomfort lasting at least 30 minutes, or the development of specific ECG abnormalities.

Outcome events were reported in detail to the central office by the local neurologist or stroke physician, along with confirmatory evidence (e.g. CT/MRI, blood test results, or death certificate) where available. Major outcome events were submitted to an independent external adjudicator, who was masked to treatment allocation and who determined the cause, severity, and duration of the event. If this assessment differed from the initial assessment, a second external adjudicator reviewed the event and any differences were resolved by consensus.

Role of the funding source

The trial funders had no role in the design of ICSS or this analysis, data collection, drafting of the manuscript, or the decision to publish.

Statistical analysis

Risk factors for the combined outcome of stroke, MI, or death were examined sequentially in univariable binomial regression analysis using maximum likelihood estimation. Subsequent events within 30 days of the procedure were not included in the analysis. Patients with missing data were excluded from each relevant analysis. The risk ratio for each factor was estimated with a 95% confidence interval. Wald tests were used for continuous and binary predictors, with an overall likelihood ratio test for categorical predictors of more than two levels. A multivariable model was developed using a forward stepwise approach. Analyses were performed using Stata (Stata Statistical Software: Release 12, StataCorp 2011, College Station, TX).

Clinical trial registration

ICSS is a registered clinical trial: ISRCTN 25337470 (http://www.controlled-trials.com/ISRCTN25337470).