Synchronous Carotid Endarterectomy and Off-pump Coronary Bypass: An Updated, Systematic Review of Early Outcomes

K.R. Fareed, P.M. Rothwell, Z. Mehta, A.R. Naylor

The Department of Vascular Surgery, Clinical Sciences Building, P.O. Box 65, Leicester Royal Infirmary, Leicester, UK
The Stroke Prevention Unit, University Department of Clinical Neurology, The John Radcliffe Hospital, Oxford, UK

Submitted 7 October 2008; accepted 16 December 2008
Available online 10 February 2009

KEYWORDS
Carotid endarterectomy; Coronary bypass; Off-pump bypass; Stroke

Abstract
Objectives: To update our previous systematic review of outcomes following synchronous carotid endarterectomy (CEA) and off-pump coronary artery bypass grafting (OFF-CABG).
Design: A systematic review of operative risks reported in published studies of synchronous CEA plus OFF-CABG procedures.
Results: We identified 12 eligible studies, including data on 324 synchronous CEA plus OFF-CABG procedures. Operative mortality was 1.5% (95% confidence interval (CI): 0.3–2.8), the risk of death or ipsilateral stroke was 1.6% (0.4–2.8%), risk of death or any stroke was 2.2% (95% CI: 0.7–3.7) and the risk of death, stroke or myocardial infarction was 3.6% (95% CI: 1.6–5.5).
Conclusions: Limited published data on 324 patients suggest that early outcomes after synchronous CEA plus OFF-CABG are better than those following staged or synchronous CEA plus CABG where the cardiac procedure was performed on-pump. This may, however, be attributed to publication bias, case selection or the fact that the aorta was not manipulated or cannulated, rather than CEA being primarily responsible for the lower stroke risk. Colleagues with unpublished experience of CEA plus OFF-CABG are encouraged to submit their data to further inform the debate.

Stroke complicates approximately 2% of coronary artery bypass grafting (CABG) procedures,\(^1\) and its aetiology is multifactorial. Although many believe that macroembolisation of atherothrombotic debris from the aortic arch remains the most important cause of post-CABG stroke,\(^2\) considerable controversy still exists regarding the role of prophylactic carotid endarterectomy (CEA) in CABG patients with coexistent carotid artery disease. In many
centres around the world, the detection of a carotid stenosis greater than 70% (irrespective of neurological symptom status) will prompt either synchronous or staged CEA plus CABG.

A 2003 systematic review of 8972 patients undergoing synchronous or staged CEA and CABG identified three studies (99 patients) wherein CEA was performed immediately prior to off-pump coronary bypass (OFF-CAB) with a reported 30-day death/stroke rate of 1.0%. This was considerably less than comparable reported risks for patients undergoing synchronous CEA plus CABG (30-day death/stroke 8.7% (95% confidence interval (CI): 7.7–9.8)), staged CEA—CABG (30-day death/stroke 6.1% (95% CI: 2.9–9.3)) and reverse-staged CABG—CEA (30-day death/stroke rate 7.3% (95% CI: 1.7–12.9)).

The extremely low procedural risk observed following synchronous CEA plus OFFCAB may simply reflect small numbers and selective reporting. However, given the emergence of staged carotid artery stenting (CAS) plus CAbG16 as a further therapeutic strategy, it seemed appropriate to determine whether publications on CEA plus OFFCAB in the 5 years since the 2003 review showed whether this lower apparent risk was maintained.

Materials and Methods


The studies were included if they were published between January 1972 and June 2008 inclusively. Patients undergoing cardiac valvular reconstructions or carotid reconstructions other than endarterectomy (e.g., aorto-carotid bypass) were excluded. Since some studies report all events occurring less than 30 days after surgery, and others often report only ‘in-hospital’ events, the two outcomes have been combined as perioperative events for the purpose of pooled analyses. It is accepted that this may under-represent the true risk, but this currently cannot be avoided.

A statistician (ZM) performed all analyses. Risks were combined across studies, allowing for extra-binomial variation to account for heterogeneity of risk between studies. Overall risks with 95% CIs were calculated; CIs for zero observed risks were estimated with Hanley’s simple formula, ‘the rule of three’. Heterogeneity between studies was calculated as the sum of the weighted squared deviations of each study risk from the weighted average risk, weighted by the inverse of the variance and compared to χ² distribution.

Results

A total of 13 series were eligible for potential inclusion. One was later excluded as it had been superseded by a more recent update.

Patient demographics

Overall, the quality of patient demographic data reported in the 12 published series was inconsistent and generally poor. The mean age of patients undergoing CEA plus OFF-CABG was 65 years. Five series (10,13,14,17,18) (247 patients) reported that the majority of their patients (62%) were neurologically asymptomatic prior to CEA plus OFF-CABG, while six reports (9,13–15,17,20) (121 patients) indicated that all of their patients had unilateral internal carotid artery (ICA) stenoses. Accordingly, most patients included in this systematic review were neurologically asymptomatic with unilateral carotid disease.

Eight series published no data regarding left ventricular ejection fraction (EF), while four documented the proportion of their patients who had an EF less than 30% (13%13, 18%17, 19%18 and 43%20). In the largest published series (n = 166), only 34% of patients had an EF greater than 50%. Similarly, there was no consistent reporting regarding the severity of the underlying cardiac disease. Four studies (236 patients) documented the proportion of patients with multi-vessel cardiac disease (55%,17 96%18 and 100%10,20), but only four studies (220 patients) detailed whether there was severe left main-stem disease. The latter proportion varied from 7% in the largest published study of 166 patients18 to 58%,13 62%10 and 66%14 in other studies. The urgency for performing CEA plus OFFCAB was also not consistently reported. In Mishra’s series (166 patients), 20% of procedures were undertaken as emergencies18 while nine out of the 13 operations in Youssuf’s study10 were deemed ‘urgent’. Finally, six studies (277 patients) reported the mean number of coronary grafts performed during OFF-CABG. The lowest mean number of bypass grafts was 1.2 (±0.4) in Eren’s study of 27 patients. Five other studies (250 patients) reported a mean of between three and four grafts performed per patient.10,13,14,18,20

The 30-day outcomes

Table 1 details the pooled outcomes for mortality, death/ipsilateral stroke, death/any stroke and death/stroke/myocardial infarction (MI) in the 12 constituent studies in this updated systematic review. The majority of these patients were neurologically asymptomatic with unilateral carotid stenoses. For comparative purposes, the principal data from the 2003 systematic reviews on outcomes following synchronous CEA plus CABG (stratified for whether CEA was performed pre-bypass or on bypass), staged CEA—CABG and reverse-staged CABG—CEA are also provided.3,4

The overall number of patients in this updated review still remains relatively small (n = 324). However, this value now represents more patients than were included in the reverse-staged (CEA—CABG) cohort in the 2003 systematic review (n = 302). Synchronous CEA plus OFF-CABG still appears to be associated with the lowest operative mortality (1.5%; 95% CI: 0.3–2.8) compared with all other management strategies (Table 1), the lowest rate of death/ipsilateral stroke (1.6%; 95% CI: 0.4–2.8), the lowest rate of death/any stroke (2.2%; 95% CI: 0.7–3.7) and the lowest risk of death/stroke and MI (3.6%; 95% CI: 1.6–5.5). Note
that there was no significant heterogeneity, indicating that
each of the constituent studies was tending to report
similar outcomes.

Discussion

There are a number of controversies regarding the
management of CABG patients with coexistent carotid
disease. Increasing evidence suggests that the most
common single cause of post-CABG stroke is embolisation of
atherothrombotic debris from the aortic arch.\textsuperscript{2} As a conse-
quence, a number of surgical strategies have evolved to
reduce the risk of macroembolisation during aortic dissec-
tion, cannulation, cross-clamping and completion of anas-
tomoses. Many of these high-risk phases of the procedure
are lessened by performing the CABG procedure off-pump,
but these potential benefits have to be offset against an
underlying worry that technical difficulties associated with
OFF-CABG might predispose to an inferior, less complete re-
vascularisation.\textsuperscript{22} Observational studies have reported
considerable reductions in the risk of post-CABG stroke
using OFF-CABG, although this has not been substantiated
in meta-analyses of randomised trials.\textsuperscript{23} One of the main
problems with meta-analyses of randomised trials
comparing off-pump with on-pump CABG, however, is that
they rarely include stratification for 'high-risk' patients.\textsuperscript{24}

One important 'high-risk' subgroup to be considered is
the CABG patient who also presents with carotid disease, as
studies suggest that the presence of a carotid stenosis of
greater than 70% is also an important predictor of severe
aortic arch disease.\textsuperscript{25} Accordingly, one possible interpre-
tation of the data from this updated review may be that the
lower stroke risk in patients undergoing CEA plus OFF-CABG
may be more likely to be attributable to the simple fact
that, during OFF-CABG, there is minimal manipulation and
no cannulation of the aorta (i.e., less potential for aortic
embolisation), rather than that via prophylactic CEA.

How should these results be interpreted? First, the
cohort of patients undergoing CEA plus OFF-CABG in this
updated review remains relatively small ($n = 324$), and it is
likely that they represent a highly selected subgroup of
patients. It is important to remember that none of these
patients underwent valvular surgery (associated with
a higher risk of procedural stroke), and most were neuro-
logically asymptomatic with unilateral carotid disease.
However, the reduced risk of death/stroke associated with
this strategy is of importance to document. There may be
centres with comparable experience that have, so far,
decided to publish, possibly because less favourable
outcomes have been encountered. Similarly, and given the
general success of the constituent studies to date, many of
the authors of the smaller published series in this

| Table 1 Perioperative outcomes for synchronous CEA + CABG, staged CEA + CABG, reverse-staged CABG + CEA and synchronous CEA + off-pump CABG |
|---------------------------------|---------------------|----------------------|---------------------|
| Operative mortality            | Death +/− ipsilat CVA | Death +/− any CVA | Death +/− any CVA+/−MI |
| (1) Synchronous CEA + CABG     |                     |                      |                      |
| CEA pre-bypass observed risk   | 245/5386            | 307/4189             | 442/5386            | 395/3426             |
| risk%                          | 4.5%                | 7.3%                 | 8.2%                | 11.5%                |
| 95% CI                         | 3.9−5.2             | 6.4−8.2              | 7.1−9.3             | 10.1−13.1            |
| heterogeneity ($p = $)         | 0.1469              | 0.0423               | 0.0000              | 0.0000               |
| CEA performed on bypass        |                     |                      |                      |
| observed risk                  | 40/844              | 52/807               | 68/844              | 26/273               |
| risk%                          | 4.7%                | 6.4%                 | 8.1%                | 9.5%                 |
| 95% CI                         | 3.1−6.4             | 4.7−8.2              | 5.8−10.3            | 5.9−13.1             |
| heterogeneity ($p = $)         | 0.1802              | 0.3732               | 0.0770              | 0.3399               |
| (2) Synchronous CEA + off-pump CABG                                      |                     |                      |                      |
| observed risk                  | 5/324               | 5/318                | 7/318               | 11/309               |
| pooled risk (%)                | 1.5%                | 1.6%                 | 2.2%                | 3.6%                 |
| 95% CI                         | 0.3−2.8             | 0.4−2.8              | 0.7−3.7             | 1.6−5.5              |
| heterogeneity ($p = $)         | 1.00                | 1.00                 | 1.00                | 0.99                 |
| (3) Staged CEA—CABG           |                     |                      |                      |
| observed risk                  | 36/917              | 39/809               | 56/917              | 72/709               |
| risk%                          | 3.9%                | 4.8%                 | 6.1%                | 10.2%                |
| 95% CI                         | 1.1−6.7             | 2.8−6.8              | 2.9−9.3             | 7.4−13.1             |
| heterogeneity ($p = $)         | <0.0001             | <0.0001              | <0.0001             | <0.0001              |
| (4) Reverse-staged CABG—CEA    |                     |                      |                      |
| observed risk                  | 6/302               | 3/87                 | 22/302              | 11/221               |
| risk%                          | 2.0%                | 3.4%                 | 7.3%                | 5.0%                 |
| 95% CI                         | 0.0−6.1             | 0.0−9.8              | 1.7−12.9            | 0.0−10.6             |
| heterogeneity                  | <0.0001             | 0.0060               | <0.0001             | 0.0102               |
systematic review must surely have increased their overall experience by now. The authors, therefore, urge cardiology and vascular surgery colleagues to publish their data on CEA plus OFF-CABG (irrespective of outcomes achieved to date) in order that future updated reviews may be more likely to reflect practice in the ‘real world’. This is especially important with the emergence of staged CAS plus CABG as a further therapeutic strategy. The authors also recommend that future publications should provide clear information regarding the status of the carotid arteries (symptomatic/asymptomatic, unilateral/bilateral disease and stenosis thresholds for intervention) and important aspects regarding the coronary intervention (EURO-score, age, EF, elective/emergency reconstruction, proportion with stable/unstable angina, single-/multi-vessel disease, New York Heart Association (NYHA) classification, left main-stem disease, the exact method of performing OFF-CABG, status of the aortic arch regarding severity of atherosclerosis, whether there was any/no handling of the aorta or tangential aortic cross-clamping and the number of bypass grafts).

In the interim, the results published to date suggest that one solution might be to consider more careful scrutiny of the thoracic aorta (preferably using epi-aortic ultrasound) in CABG patients who are found to have significant carotid disease on preoperative screening. Even if prophylactic CEA is not undertaken thereafter, OFF-CABG may reduce the risk of procedural stroke due to aortic thrombo-embolism.

References