REVIEW

A Systematic Review of Outcomes Following Staged and Synchronous Carotid Endarterectomy and Coronary Artery Bypass

A. R. Naylor, R. L. Cuffe, P. M. Rothwell and P. R. F. Bell

1Department of Vascular Surgery at Leicester Royal Infirmary and 2University, Department of Clinical Neurology, The Radcliffe Infirmary, Oxford

Objectives: to determine the overall cardiovascular risk for patients with combined cardiac and carotid artery disease undergoing synchronous coronary artery bypass (CABG) and carotid endarterectomy (CEA), staged CEA then CAGB and reverse staged CABG then CEA.

Design: systematic review of 97 published studies following 8972 staged or synchronous operations.

Results: mortality was highest in patients undergoing synchronous CEA + CABG (4.6%, 95% CI 4.1–5.2). Reverse staged procedures (CABG – CEA) were associated with the highest risk of ipsilateral stroke (5.8%, 95% CI 0.0–14.3) and any stroke (6.3%, 95% CI 1.0–11.7). Peri-operative myocardial infarction (MI) was lowest following the reverse staged procedure (0.9%, 95% CI 0.5–1.4) and highest in patients undergoing staged CEA – CABG (6.5%, 95% CI 3.2–9.7).

The risk of death + any stroke was highest in patients undergoing synchronous CEA + CABG (8.7%, 95% CI 7.7–9.8) and lowest following staged CEA – CABG (6.1%, 95% CI 2.9–9.3). The risk of death/stroke or MI was 11.5% (95% CI 10.1–12.9) following synchronous procedures versus 10.2% (95% CI 7.4–13.1) after staged CEA then CABG.

Conclusions: 10–12% of patients undergoing staged or synchronous procedures suffered death or major cardiovascular morbidity (stroke, MI) within 30 days of surgery. Overall, there was no significant difference in outcomes for staged and synchronous procedures and no comparable data for patients with combined cardiac and carotid disease not undergoing staged or synchronous surgery.

Key Words: Carotid endarterectomy; Coronary bypass; Stroke.

Introduction

A recent systematic review observed that the risk of stroke after coronary artery bypass grafting (CABG) was <2% in patients with no significant carotid disease (bilateral 0–49% stenoses), 3% in predominantly asymptomatic patients with unilateral 50–99% stenoses, increasing to 5% in those with bilateral 50–99% stenoses and 7–11% in patients with carotid occlusion. However, it was not possible to determine whether the risk of death + stroke + MI (i.e. the overall cardiovascular risk) was significantly increased in patients with combined carotid and cardiac disease undergoing isolated CABG, especially in those with more severe degrees of stenosis (80–99%). This information was rarely (if ever) systematically reported. More importantly, none of these data are available for patients with 70–99 or 80–99% stenoses. If, however, the cardiovascular risk were shown to be very high, it would support the stance adopted by surgeons advocating a more proactive surgical approach regarding staged or synchronous interventions.

The current study is a systematic review of outcomes following staged or synchronous procedures in 97 studies (8972 procedures) between 1972 and 2002. Only one contained any element of randomisation. The impetus for undertaking the study was the publication of a one-year community based prospective audit following 236 synchronous CEA + CABGs from 10 states in the United States of America between 1995 and 1996 that reported a 17.4% risk of death/stroke at 30 days. If this does reflect current practice around the world, then the overall cardiovascular risk in patients with cardiac and carotid disease undergoing...
CABG alone would have to be extremely high to justify any staged or synchronous interventions at all.

**Materials and Methods**

A systematic literature review was undertaken to determine outcomes following (i) staged (CEA - CABG), (ii) reverse staged (CABG - CEA) and (iii) combined/synchronous (CEA + CABG). Studies were identified by manual journal reviews (European Journal of Vascular and Endovascular Surgery, Journal of Vascular Surgery, Annals of Vascular Surgery, Stroke, Annals of Thoracic Surgery, Journal of Thoracic and Cardiothoracic Surgery), cross-referencing and an electronic PUBMED search using the advanced search option. A number of combinations of search terms were used that included one of “carotid endarterectomy”, “carotid surgery”, “coronary surgery”, or “bypass surgery” in combination with one of “stroke”, carotid or “cardiac” as appropriate.

Studies were included if published in English language journals between January 1972 and June 2002 inclusive. Patients undergoing cardiac valvular reconstructions or carotid reconstructions other than endarterectomy (e.g. aorto-carotid bypass) were excluded. One hundred and twelve series were identified for inclusion.\(^2\) Fifteen were subsequently excluded.\(^99\) Reasons for exclusion included; inability to secure a copy of the manuscript,\(^99\) nine studies were updated from the same centre at a later date,\(^100\) while in four it was not possible to differentiate outcomes for staged and synchronous procedures.\(^109\) The remaining study\(^113\) was excluded because it included fewer patients than a similar series from the same centre published one year earlier.\(^62\)

Ninety-seven studies\(^2\) reporting the outcome following 8972 staged or synchronous procedures were included in the systematic review. Each was scrutinised to provide demographic and outcome data. Demographic data included; (i) pre-operative neurological status (asymptomatic or symptomatic carotid disease (irrespective of timing to the staged or synchronous procedure), (ii) the presence of unilateral or bilateral carotid disease, (iii) whether the CABG was performed “urgently” e.g. for unstable angina, (iv) the prevalence of left mainstem coronary artery disease and (v) the proportion of patients deemed to be NYHA class III or IV for cardiac disease.

Peri-operative events included any specified end-point occurring <30 days of synchronous CEA + CABG or within 30 days of the latter of any staged procedure. Endpoints included; (i) death, (ii) any stroke, (iii) ipsilateral stroke appropriate to the side of the CEA and (iv), myocardial infarction. It should be noted, however, that there was no systematic means of diagnosing peri-operative myocardial infarction over the 30-year period of this review (serial ECG and/or enzyme changes) and many studies did not document this outcome. Most were probably diagnosed following acute clinical deterioration. Accordingly, the true incidence of peri-operative myocardial infarction will be much higher. Most studies documented events occurring <30 days of surgery. Others only recorded “in-hospital” events. For the purpose of this review, the two have been combined as peri-operative events. It is accepted that this may under-represent the true risk, but this currently cannot be avoided.

Previous publications and systematic reviews have tended to document the prevalence of mortality, stroke and myocardial infarction (MI) as discrete endpoints.\(^114\) However, this does not necessarily reflect the fact that patients undergoing staged or synchronous procedures may suffer more than one cardiovascular event during the peri-operative period. Accordingly, it has been difficult to gauge the overall cardiovascular risk (operative death ± stroke ± MI).

Data have therefore been presented in an alternative format so that the following end-points are clearly documented where possible; (1) mortality, (2) any stroke, (3) ipsilateral stroke, (4) myocardial infarction, (5) death ± ipsilateral stroke, (6) death ± any stroke and (7) death ± any stroke ± MI. Not all papers reported this information and hence the denominator may not be the same as the total number of patients in the meta-analysis. In order to aid data interpretation, the actual numbers of patients at risk for each of the subgroups has been documented in the tables.

A statistician (RC) performed all analyses. Outcomes have been analysed in two ways. In the first, specific outcomes following each of the three procedures were estimated by combining all the studies that reported data on that particular outcome. Heterogeneity and 95% confidence intervals were determined (see below), but no direct statistical comparisons were made.

In order to compare the risk of any given outcome between staged and synchronous procedures directly, the second method of analysis identified publications reporting results for both staged and synchronous procedures in a manner similar to Borger.\(^115\) Mantel-Haenzal estimates of the Odds Ratio\(^116\) were then determined along with measurements of heterogeneity and 95% confidence intervals. In the latter analysis, confidence intervals for the odds ratio were determined using Miettinen’s test based formula.\(^117\)
In those analyses where there was significant heterogeneity, 95% confidence limits were expanded to account for extra-binomial variation arising from the differences in risk between studies. The heterogeneity of the actual risk and/or the odds ratio was assessed by calculating the weighted sum of squared deviations from the estimate. This statistic was then compared to a chi-squared distribution to produce the p-values listed in the tables and results. Measurement of heterogeneity enables the reader to gauge whether the pooled/calculated risks were measuring the same thing. Statistically significant heterogeneity (p < 0.05) in estimates between studies indicates that the overall variation in the reported risk is greater than would be expected by chance. This could be due to differences in case-mix, operative technique or other factors.

Results

Overview of all published series

Table 1 summarises the available demographic data for 7863 patients undergoing synchronous CEA + CABG (94 studies) and 917 patients undergoing staged CEA – CABG (24 studies). Although 302 patients underwent reverse staged CABG – CEA (11 studies), there was often insufficient data to meaningfully interpret patient demographics. Overall, about 60% of patients undergoing staged/synchronous procedures were neurologically asymptomatic, while 30–37% had bilateral 50–99% stenoses or contralateral occlusion. The majority of synchronous cases (72%) were NYHA grade 3 or 4 (cardiac disease resulting in marked limitation of physical activity (grade 3) or cardiac disease resulting in inability to carry out physical activity without discomfort (grade 4)), 39% of synchronous cases were classed as “urgent” and left mainstem disease was present in about 25% of patients.

Table 2 details the principal outcomes following each procedure. Operative mortality was highest in patients undergoing synchronous CEA + CABG (4.6%, 95% CI 4.1–5.2). Reverse staged procedures (CABG – CEA) were associated with the highest risk of both ipsilateral stroke (5.8%, 95% CI 0.0–14.3) and any stroke (6.3%, 95% CI 1.0–11.7). The risk of “any operative stroke” was lowest following staged CEA – CABG (2.7%, 95% CI 1.6–3.9). The risk of myocardial infarction was lowest following reverse staged procedures (0.9%, 95% CI 0.5–1.4) and highest in patients undergoing staged CEA – CABG (6.5%, 95% CI 2.9–10). Note, however, that for each surgical strategy, the 95% confidence intervals for all endpoints overlapped and that there was significant heterogeneity in virtually every endpoint.

Table 2 also details the cumulative cardiovascular risk following the three types of intervention. Death ± any stroke was highest in patients undergoing synchronous CEA + CABG (8.7%, 95% CI 7.7–9.8) and lowest following staged CEA – CABG (6.1%, 95% CI 2.4–9.2), although the confidence intervals overlapped. However, the apparent benefit conferred by staging the operation was reduced when the risk of myocardial infarction was subsequently included in the analysis (synchronous = 11.5% (95% CI 10.1–12.9), staged CEA – CABG = 10.2% (95% CI 7.4–13.1). Note, however, that the p-value indicative of heterogeneity was <0.05 for almost every parameter.

Table 1. Demography on patients undergoing staged or synchronous CEA + CABG.

<table>
<thead>
<tr>
<th></th>
<th>Synchronous CEA + CABG</th>
<th>Staged CEA – CABG</th>
<th>Staged CABG – CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>94</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>7863</td>
<td>917</td>
<td>302</td>
</tr>
<tr>
<td>Symptomatic carotid stenosis *</td>
<td>2830/6827</td>
<td>266/611</td>
<td>33/71</td>
</tr>
<tr>
<td></td>
<td>41.1% (95% CI 37.4–44.9)</td>
<td>43.5% (95% CI 31.1–56.0)</td>
<td>46.5% (13.9–79.1)</td>
</tr>
<tr>
<td>Asymptomatic carotid stenosis *</td>
<td>4048/6878</td>
<td>351/611</td>
<td>38/62</td>
</tr>
<tr>
<td></td>
<td>59.3% (95% CI 55.6–63.0)</td>
<td>57.4% (95% CI 44.4–70.5)</td>
<td>61.3% (29.0–99.6)</td>
</tr>
<tr>
<td>Unilateral 50–99% stenosis *</td>
<td>3826/6137</td>
<td>396/570</td>
<td>Insufficient data</td>
</tr>
<tr>
<td></td>
<td>62.3% (95% CI 58.6–66.1)</td>
<td>69.5% (95% CI 59.6–79.4)</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>Bilateral 50–99% stenosis/occlusion *</td>
<td>2261/6137</td>
<td>186/570</td>
<td>Insufficient data</td>
</tr>
<tr>
<td></td>
<td>36.8% (95% CI 32.9–40.8)</td>
<td>30.5% (95% CI 22.2–43.1)</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>“Urgent” CABG *</td>
<td>1675/4287</td>
<td>1675/4287</td>
<td>1675/4287</td>
</tr>
<tr>
<td></td>
<td>39.1% (95% CI 33.9–44.2)</td>
<td>39.1% (95% CI 33.9–44.2)</td>
<td>39.1% (95% CI 33.9–44.2)</td>
</tr>
<tr>
<td>Left mainstem disease</td>
<td>1240/5017</td>
<td>1240/5017</td>
<td>1240/5017</td>
</tr>
<tr>
<td></td>
<td>24.7% (95% CI 21.5–27.9)</td>
<td>28.9% (95% CI 9.4–48.4)</td>
<td>28.9% (95% CI 9.4–48.4)</td>
</tr>
<tr>
<td>NYHA grade 3 or 4 *</td>
<td>885/1251</td>
<td>137/499</td>
<td>137/499</td>
</tr>
<tr>
<td></td>
<td>71.9% (95% CI 65.1–78.7)</td>
<td>27.5% (95% CI 9.9–45.0)</td>
<td>27.5% (95% CI 9.9–45.0)</td>
</tr>
</tbody>
</table>

* Some papers did not provide all of this information and hence the denominator will not be the same as the total number of patients in the meta-analysis.

Eur J Vasc Endovasc Surg Vol 25, May 2003
under analysis. This indicates that there was no systematic similarity in the reporting of events between studies.

The available evidence therefore suggests that 10–12% of patients undergoing staged or synchronous procedures suffer death or a major non-fatal cardiovascular event in the peri-operative period. However, the extent of risk varied across studies (0–30%) with seven out of 32 series documenting outcome in 450 patients reporting a 415% risk of death/stroke/MI.

Only five studies (containing 50 patients) have reported the overall cardiovascular risk following staged CEA + CABG and they also reported a similar spread of risk to that observed with synchronous procedures. The risk of death + any stroke + MI in the five studies was 5.8,76 8.2,63 10.7,62 13.0,96 and 16.9%.8 Only one study with 50 patients10 documented the overall cardiovascular risk following staged CABG then CEA (4.8%).

Comparison with previous meta-analyses

Table 3 summarises the principal findings from the 1992 meta-analysis by Brener,114 which was based on observations from 35 studies (2928 patients). When compared with the same data from the 2002 systematic review (Table 3), several important trends have emerged.

Firstly, all discrete risks (mortality, stroke, MI) have decreased. Outcomes following synchronous procedures have improved by 1–2% across all end-points. Operative mortality following staged CEA – CABG has fallen from 9.4 to 3.9%, largely because the mortality following 630 staged CEA – CABG procedures published in 10 series between 1992 and 2002 was only 3.3%,49,52,55,62,63,69,72,76,82,98 The same studies documented a 2.4% operative stroke rate that undoubtedly contributed towards the fall in overall stroke rate from 5.3 (1972–1992) to 2.7% (1972–2002). A similar trend was observed for declining risks of myocardial infarction.

There have been only 11 published studies (302 patients) documenting outcome following staged CABG then CEA over the last 30 years. Since the 1992 overview, only three "new" studies have been published36,62,71 adding 71 patients to the available literature. These three studies, however, documented a zero percent mortality, a 1.4% stroke rate and a 1.4% risk of MI. Overall, the cardiovascular risk (death/stroke/MI) in these three studies was 2.8%. The latter results have contributed significantly to the improvement in outcomes following staged CABG – CEA when compared to the 1992 meta-analysis (Table 3).
**Studies publishing outcomes on both staged and combined procedures**

An alternative method of presenting comparative data (allowing for some element of statistical comparison) is to specifically analyse only those studies reporting results for both staged (either CABG/CEA or CEA/CABG) and synchronous procedures. In 1999, Borger et al. performed this type of analysis based upon 16 studies (1764 patients) published between 1972 and 1998. Outcomes for staged CEA – CABG were combined with those for staged CABG – CEA and then compared with synchronous procedures (Table 4). Although, synchronous procedures were associated with a systematically worse outcome than staged operations, none of the differences reached statistical significance.

The current review undertook a similar analysis having identified a total of 24 studies (2284 patients) from the literature. Table 5 summarises the absolute risks, 95% CIs, heterogeneity and Odds Ratios. Note that the absolute risks will inevitably be slightly different to those presented in Table 2.

Staged procedures were associated with a lower absolute risk than synchronous operations for all endpoints with the exception of myocardial infarction. The confidence intervals overlapped and only death + ipsilateral stroke was associated with an Odds Ratio and 95% CIs > 1 (1.57 (95% CI 1.05–2.35)). However, it is important to note that the p values for heterogeneity were consistently > 0.05. The lack of significant heterogeneity in estimates between studies indicates that the overall variation in the reported odds ratios is compatible with that expected by chance alone. This consistency suggests that the estimates are likely to be both reliable and generalisable.

### Discussion

There has been much controversy regarding the optimum management of patients with combined cardiac and coronary artery disease. To-date, no level I evidence exists to guide practice. In reality, however, most carotid patients will have varying degrees of ischaemic heart disease (and vice versa), but the vast majority can safely undergo surgery (CEA or CABG) with the choice reflecting the clinical priority. In practice, therefore, only a relatively small minority of patients require the clinician to even consider a staged or synchronous reconstruction.

In this era of evidence-based medicine, it seems ironic that a multi-centre randomised trial could easily address this issue. In practice, however, the planning and implementation of such a trial has been beset with many practical, theoretical and logistical problems.

#### Table 4. Summary of Borger’s meta-analysis of 16 studies (1764 patients) reporting outcomes where both staged and synchronous procedures were reported.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Patients</th>
<th>Stroke</th>
<th>Death</th>
<th>Stroke/death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synchronous procedure</td>
<td>844</td>
<td>6.0%</td>
<td>4.7%</td>
<td>9.5%</td>
</tr>
<tr>
<td>Any staged procedure</td>
<td>920</td>
<td>3.2%</td>
<td>2.9%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Odds ratio (95% CI) for synchronous versus staged procedures</td>
<td>(0.97–2.32)</td>
<td>(0.94–2.53)</td>
<td>(1.03–2.15)</td>
<td></td>
</tr>
</tbody>
</table>

*Outcomes for staged CEA – CABG added to those with staged CABG – CEA and compared with synchronous outcomes from same paper.

† Adapted from Borger et al.

‡ Odds Ratio of hazard occurring as a function of synchronous versus staged procedures. If the OR is > 1.0 this indicates that the risk is more commonly associated with synchronous procedures (and vice versa). For the Odds Ratio to be statistically significant, both 95% CIs must be either > 1.0 or < 1.0.

#### Table 5. Risk/hazard ratio of suffering an adverse event during staged or synchronous operations: both procedures reported in the same paper.

<table>
<thead>
<tr>
<th>30 day parameter</th>
<th>Observed risk</th>
<th>% risk (95% CIs)</th>
<th>95% CIs</th>
<th>p-value</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Synchronous</td>
<td>Staged</td>
<td>Synchronous</td>
<td>Staged</td>
<td></td>
</tr>
<tr>
<td>Operative death</td>
<td>57/1171</td>
<td>40/1113</td>
<td>4.9 (3.7–6.1)</td>
<td>3.7 (1.7–5.7)</td>
<td>1.28 (0.80–2.05)</td>
</tr>
<tr>
<td>Any stroke</td>
<td>62/1171</td>
<td>40/1113</td>
<td>5.4 (3.4–7.2)</td>
<td>3.7 (1.8–5.5)</td>
<td>1.28 (0.82–2.00)</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>37/941</td>
<td>20/766</td>
<td>3.9 (2.4–5.4)</td>
<td>2.7 (0.8–4.7)</td>
<td>1.33 (0.71–2.48)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>42/971</td>
<td>50/958</td>
<td>4.3 (2.9–5.8)</td>
<td>5.3 (3.4–7.2)</td>
<td>0.68 (0.42–1.10)</td>
</tr>
<tr>
<td>Death/ipsilateral stroke</td>
<td>78/941</td>
<td>36/766</td>
<td>8.3 (6.2–10.5)</td>
<td>4.8 (2.5–7.3)</td>
<td>1.57 (1.03–2.39)</td>
</tr>
<tr>
<td>Death/any stroke</td>
<td>111/1171</td>
<td>73/1113</td>
<td>9.5 (7.2–11.8)</td>
<td>6.6 (4.4–8.8)</td>
<td>1.34 (0.96–1.87)</td>
</tr>
<tr>
<td>Death/stroke/MI</td>
<td>105/920</td>
<td>81/869</td>
<td>11.5 (8.9–14.0)</td>
<td>9.4 (6.4–12.4)</td>
<td>1.09 (0.75–1.59)</td>
</tr>
</tbody>
</table>

*Outcomes for staged CEA – CABG were added to staged CABG – CEA and reported as “staged” and then compared with synchronous outcomes from the same paper.

† Odds Ratio of hazard occurring as a function of synchronous versus staged procedures. If the OR is > 1.0 this indicates that the risk is more commonly associated with synchronous procedures (and vice versa). For the Odds Ratio to be statistically significant, both 95% CIs must be either > 1.0 or < 1.0.
including; (i) is the principle reason for considering staged/synchronous surgery the prevention of operative stroke, long term stroke or both, (ii) relatively little emphasis is placed on preventing peri-operative myocardial infarction, (iii) there are a number of different patient populations under consideration and management strategies will inevitably be influenced by the dominant pathology. The symptomatic carotid patient with unstable angina is a completely different problem to the elective CABG patient with a unilateral asymptomatic carotid stenosis, who is in turn, a better prospect than urgent CABG in a patient with a recently symptomatic carotid stenosis, (iv) what is actually neurologically asymptomatic) had no significant disease undergoing CABG, (iv) whether staged or synchronous surgery can reduce this risk and (v) evidence that either staged or synchronous procedures are preferable?

It is difficult to ascertain the true risk of stroke in patients undergoing CABG with carotid disease. This is primarily because most centres performing pre-operative duplex screening tend to advocate staged CEA – CABG or synchronous CEA + CABG in patients with severe carotid disease. In a recent systematic review (1), three studies documented the risk of carotid disease and the ensuing stroke risk in 4674 patients undergoing CABG. Approximately, 91% of screened patients (who would have been predominantly neurologically asymptomatic) had no significant carotid disease (<50% stenoses bilaterally) and incurred an operative stroke risk of 1.8% (95% CI 1.4–2.1) (1). Unilateral 50–99% stenoses were detected in 5.5% of patients (stroke risk 3.2%, 95% CI 0.0–6.5), bilateral 50–99% stenoses affected 2.2% (5.2% stroke risk, 95% CI 0.0–10.8), while only 1.5% of CABG patients had unilateral or bilateral carotid occlusions (incurred the highest operative stroke risk of 7–12%, 95% CI 0.0–20). There were insufficient data to perform a similar meta-analysis for patients with >80% carotid stenoses (few trials, even fewer patients not subjected to prophylactic CEA, stroke data seldom subgrouped for unilateral, bilateral stenoses or occlusion). This is unfortunate as patients with more severe carotid disease (e.g. 80–99% stenoses, bilateral stenoses/occlusions) may be at particular risk during CABG and could obtain the greatest benefit from staged or synchronous interventions. Accordingly, the evidence for planning management strategies currently has to be based on data derived from patients with 50–99% stenoses, despite the fact that few surgeons would actually advocate staged or synchronous CEA in patients with 50–70% stenoses.

The second issue relates to whether carotid disease is the predominant cause of post-CABG stroke. The systematic review (1) observed that significant “carotid” predictors included; (i) carotid bruit (Odds Ratio 3.6 (95% CI 2.8–4.6), (ii) prior stroke/TIA (Odds Ratio 3.6 (95% CI 2.7–4.9) and (iii) a severe carotid stenosis or occlusion (Odds Ratio 4.3 (95% CI 3.2–5.7). However, a number of observations suggested that the majority of post-CABG strokes could not, simply, be attributed to carotid disease alone (1). These included; (i) 62% of operative strokes occurred after >24 h had elapsed, i.e., they could not simply be attributed to intra-operative haemodynamic failure (ii) 50% of stroke sufferers in the overview did not have significant ipsilateral carotid artery disease (>50% stenosis or occlusion) and (iii) up to 60% of territorial infarctions on CT/autopsy were not ipsilateral to significant carotid disease (>50% stenosis or occlusion) (1). Thus, although the available evidence suggests that carotid disease is an important aetiological factor in post-CABG stroke, it is probably only responsible for about 50% of post-CABG strokes. There is now a prevailing view that aortic arch atheroembolism is the single most important cause of post-CABG stroke. Interestingly, carotid bruit is the only clinical predictor for significant aortic arch disease and the combination of aortic arch disease and carotid stenosis in CABG patients has been associated with a 14% operative stroke risk.

The third issue relates to cumulative cardiovascular risk. To-date, most publications have concentrated on reporting discrete variables (death, stroke or MI) in patients undergoing isolated, staged or synchronous CABG. Surprisingly, little is known about whether the cardiovascular risk (death/stroke or death/stroke/MI) is significantly increased in patients with carotid and cardiac disease. Most clinicians, intuitively, view the presence of asymptomatic, severe carotid disease in CABG patients as being a marker of generalised atherosclerotic disease and of increased cardiovascular risk. Interestingly, the converse does not appear to hold true. This is a key issue to resolve as the concept of planning isolated, staged or synchronous operations is ultimately based on the premise that all major risks should be reduced rather than discrete reductions in individual end-points. In short, the rationale underlying staged CEA – CABG or
synchronous CEA + CABG is not simply to reduce operative stroke. It should be to minimise the risk of death, stroke and MI.

In one of the few studies of its kind, Das observed that the risk of death and/or stroke in patients with severe carotid stenoses undergoing CABG alone could be as high as 11.5%. This therefore suggests that combined carotid and cardiac disease does confer excess cardiovascular risk. However, no systematic review, to-date, has documented the overall cardiovascular risk (death/stroke/MI) in CABG patients with carotid disease undergoing isolated CABG. If one assumes that Das’ data are correct, the overall cardiovascular risk might be as high as 12–15%.

The current systematic review has addressed the two remaining issues relating to the role of staged and synchronous procedures in patients with combined carotid and cardiac disease. Tables 2 and 5 indicate that staged and synchronous interventions were associated with a 7–10% risk of death and/or stroke and a 10–12% risk of death/stroke or MI. Although not a randomised comparison, the available data suggests that staged/synchronous operations might be able to reduce the death ± stroke rate from the 11.5% risk observed in isolated CABG procedures. It remains uncertain, however, as to whether either strategy could ever confer a clinically significant reduction. Clearly, more information is required regarding age, unilateral/bilateral nature of carotid artery disease, increasing disease severity and whether the patient was neurologically symptomatic or not. Moreover, the risks of operative MI must also be considered. In the current overview, staged procedures were associated with a 9.4% risk of death/stroke/MI as compared with synchronous operations (11.5%). We still do not know how this compares with the risk observed in patients undergoing isolated CABG in the presence of significant carotid artery disease.

Finally, if one assumes that staged or synchronous surgery might confer some benefit, is there any evidence that either strategy is preferable? The data from Tables 2 and 5 suggest that although staged procedures were generally associated with a lower overall complication rate than synchronous ones, none of the comparisons reached statistical significance. The lack of heterogeneity suggests that this was a consistent finding across most of the constituent studies.

Accordingly, there is no systematic evidence that, when faced with the same type of patient, one strategy is preferable to the other. It remains debatable as to whether the patient groups included in the overall and paired analyses were really comparable, as most surgeons will inevitably exercise some form of preference and prioritisation depending upon the urgency of presentation. In particular, one should be aware of the potential for introducing bias when interpreting the results of staged procedures. One of the largest series reporting both synchronous (n = 255) and staged (n = 257) procedures (data included in Table 5) observed that unstable and/or urgent cases tended to undergo synchronous operations, while staged interventions were reserved for less severe cases. This is to be expected, but must be taken into account when interpreting the findings in Table 5. Secondly, there is the potential for “non-reporting” of major adverse events (death, stroke, MI) following the primary procedure that were sufficiently severe to abandon plans for the second staged procedure. An indeterminate number of studies (largely retrospective) did not specify whether adverse events occurring after the first operation (thereby precluding performance of the second) were always included in the overall results on an “intention to treat basis” or were they censored and the patient excluded on the basis that they did not undergo a staged double procedure. Finally, the definition of “staging” must be clarified. At present it seems to include any combination of CEA or CABG within a six-month period of each other.

In conclusion, this systematic review has observed that staged and synchronous procedures were associated with a 7–9% risk of death/stroke and a 10–12% risk of death/stroke or MI in the peri-operative period. Until parallel data are available for similar patients undergoing isolated CABG, it remains unclear whether staged or synchronous procedures confer any overall benefit. In the absence of randomised trial data, future publications must clearly discriminate between patient subgroups, e.g., the highly symptomatic carotid patient with unstable cardiac disease as compared with the elective CABG patient with asymptomatic carotid disease. Second, centres with data documenting the risk of death/stroke and MI in CABG patients with 70–99 and 80–99% stenoses who do not undergo staged or synchronous CEA are urged to submit their results for publication.

References


Eur J Vasc Endovasc Surg Vol 25, May 2003
Synchronous Carotid Endarterectomy


47 Fillinger MF, Rosenberg JM, Semel L, Levy IE, Byrne J, Marvasti MA, Zaman SN. Combined carotid endarterectomy...


