Simultaneous hybrid carotid stenting and coronary bypass surgery versus concomitant open carotid and coronary bypass surgery: a pilot, feasibility study†

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Received 2 September 2013; received in revised form 14 December 2013; accepted 30 December 2013

Abstract

OBJECTIVES: Concomitant carotid and cardiac surgery carries an increased perioperative morbidity and mortality risk. Whether the hybrid procedure of carotid artery stenting (CAS) and coronary bypass surgery decreases the risk of stroke and other complications is still unknown. The aim of this study was to assess early outcomes after simultaneous hybrid CAS and coronary bypass grafting versus open concomitant carotid and coronary bypass surgery.

METHODS: We included 20 patients in this study. According to the protocol, all the patients were divided into two groups: Group 1 (10 patients) with hybrid CAS and coronary bypass surgery and Group 2 (10 patients) with concomitant carotid and coronary surgery. Different preoperative, intraoperative and postoperative variables were compared. The primary end point was combined incidence of stroke and death 30 days after surgery or during initial hospitalization. The secondary end points were myocardial infarction, atrial fibrillation, blood loss and need for blood transfusion and duration of intensive care unit and hospital stay.

RESULTS: Groups 1 and 2 were similar in preoperative characteristics including age (65.3 ± 6.8 vs 70.7 ± 7.0, P = 0.191) New York Heart Association class (2.3 ± 0.5 vs 1.8 ± 0.7, P = 0.218), EuroSCORE (2.8 ± 2.0 vs 3.6 ± 2.3, P = 0.547), the degree of carotid stenosis (79 ± 12 vs 87 ± 13%, P = 0.224) and average left ventricular ejection fraction (44.3 ± 12.4 vs 43.4 ± 13.3%, P = 0.896). Also, the groups did not differ in intraoperative variables with an exception of extracorporeal circulation time (65.7 ± 14.1 vs 90.0 ± 17.4 min, P = 0.224), the degree of carotid stenosis (79 ± 12 vs 87 ± 13%, P = 0.224) and average left ventricular ejection fraction (44.3 ± 12.4 vs 43.4 ± 13.3%, P = 0.896). Also, the groups did not differ in intraoperative variables with an exception of extracorporeal circulation time (65.7 ± 14.1 vs 90.0 ± 17.4 min, P = 0.023), which was significantly shorter in Group 1. Although rare, and without significant difference, primary end point occurred only in Group 2 (1 stroke and 1 death, 20%). There was no difference in the duration of mechanical ventilation, need for transfusion and duration of intensive care unit and hospital stay between the two groups.

CONCLUSIONS: Although limited by a small sample size, our results show that the hybrid procedure of carotid stenting and coronary surgery might be a good therapeutic option but further extended studies are needed to assess its real value.

Keywords: Hybrid procedure • Carotid stenting • Coronary bypass • Stroke

INTRODUCTION

The prevalence of severe carotid artery disease among patients undergoing coronary artery bypass grafting (CABG) is estimated to be 6–12% [1]. These patients have 3-fold higher risk of neurological complications even if the carotid artery disease is asymptomatic [2]. Several trials have shown that, in patients with asymptomatic carotid artery disease, incidence of stroke after CABG ranges between 3 and 11% [3].

†Presented at the 27th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Vienna, Austria, 5–9 October 2013.

Despite the acknowledgment of its significance, treatment options for the significant carotid artery disease in patients undergoing CABG remain controversial [4]. Overall, two protocols are widely used: staged procedure, with carotid artery stenting (CAS) or carotid evasion endarterectomy (CEA) followed by CABG (2–4 weeks later), and simultaneous CAS/CEA with CABG [5–7]. However, either of these proved not to be superior [8]. Moreover, there have been no randomized trials aiming to assess properly which strategy is more appropriate. In the staged surgical approach that addresses the carotid artery lesion with CEA or CAS first, the risk of acute myocardial infarction (MI) prior to CABG is rather high when performing CEA while the risk of stroke is increased in patients undergoing CAS [6, 7]. On the other hand,
the combined surgical approach is associated with an increased risk of mortality and morbidity [9]. With combined CEA/CABG, despite eliminating interstage risk, outcomes have been similar to those of staged CEA/CABG [5, 10] and in many studies inferior to those of staged CAS/CABG, mainly due to higher operative stroke risk [11].

Recently, more data are available for the fourth option—the simultaneous, combined approach of CAS and CABG [12–15]. All series were non-randomized, most were retrospective and all with limited number of patients and different peri- and postprocedural protocols [12–15]. Also, data comparing this procedure with traditional simultaneous CEA/CABG are scarce. For these reasons, we performed a prospective, randomized, feasibility, pilot study with the aim of comparing the early post-procedural results of simultaneous hybrid CAS and coronary bypass surgery versus concomitant CEA and CABG.

MATERIALS AND METHODS

This was a prospective, randomized, pilot, single-centre study done between April 2011 and June 2012. The study was approved by the local Ethics Committee. Before enrollment, all patients provided written informed consent. A medical team consisting of a cardiologist, a cardiac surgeon, a vascular surgeon, an interventional radiologist and a neurologist performed initial evaluation and determined whether the patient was eligible for the trial. Randomization was done in a 1:1 fashion into two groups: Group 1, hybrid CAS and CABG and Group 2, concomitant CEA and coronary bypass surgery.

Patient selection

Patients were included in the study if they had severe triple vessel coronary artery disease or significant left main stenosis unsuitable for percutaneous treatment and significant carotid artery disease (defined as carotid artery stenosis >50% in the symptomatic disease or >80% in asymptomatic disease, as determined by the North American Symptomatic Carotid Endarterectomy Trial criteria [16], manageable both by surgery or percutaneous intervention. The exclusion criteria were need for urgent carotid/coronary treatment, severe heart failure, left ventricular ejection fraction ≤20% or New York Heart Association (NYHA) class IV, valvular disease requiring surgery and preoperative atrial fibrillation. Also patients were not included in the trial if they had intolerance to aspirin or clopidogrel, ischaemic stroke within the previous 6 weeks, presence of intraluminal thrombus, vascular disease precluding use of catheter-based techniques and large intracranial aneurysm and anatomy of aortic arch unsuitable for percutaneous intervention (Type 3 aortic arch). Carotid artery disease was determined during routine preoperative assessment using Doppler sonography of the aortic arch and neurological examination. If significant stenosis was found, multidetector row computed tomography (MDCT) of the aortic arch was performed to assess feasibility for CAS, as well as the nature of plaque and other lesion characteristics (degree of calcification).

Procedures

In order to avoid the influence of diversity of techniques and learning curve to our results, carotid stenting was performed only by experienced radiologists (performing more than 30 CAS procedures/year) and CABG by senior surgeons (performing more than 100 cases/year).

The CAS procedure was performed under local anaesthesia using a percutaneous transfemoral access, with the use of stents and protection devices approved by the local Medical Agency. XACT stents (Abbott Vascular, IL, USA) and Angioguard RX (Cordis Endovascular, FL, USA) distal filter protection devices were used in all patients. All patients received 100 mg of aspirin starting at least 2 days before CAS. After sheath introduction, heparin was given in a dose of 10 mg/kg. Suitability of the carotid lesions for CAS was once again assessed by angiography immediately before the beginning of the procedure. Predisatiation of the stenosis was done before placement and final stent expansion. Results of the CAS were considered successful if residual stenosis was ≤20% and if complications such as stroke or transitory ischaemic attack (TIA) did not occur. Within 3 h of completion of the procedure, patients were transferred to the operating theatre for coronary artery bypass surgery.

CEA was done just before myocardial revascularization during the same deep general anaesthesia. In the case of bilateral disease, intervention was done on the carotid artery with a more important lesion. All patients underwent eversion endarterectomy without the shunt. Antiplatelet therapy was not given preoperatively and heparin bolus (5000 IU) was given immediately before the procedure. Wound closure was done by the end of the cardiac intervention.

CABG was performed under general anaesthesia using cardio-pulmonary bypass according to standard practice. Left internal mammary artery (LIMA) was used as a first choice conduit for the left anterior descending artery. Saphenous veins and radial arteries were used as second choice conduits for other targets. The surgery was done under general heparinization (aiming for the activated clotting time [ACT] of > 480 s) using extracorporeal circulation in mild hypothermia and using crystalloid or blood cardioplegic solution. After completion of the intervention and coming off from the cardiopulmonary bypass, complete reversal of heparin was done by infusion of full dose protamine and antifibrinolytic agent (tranexamic acid).

Periprocedural pharmacological protocol

Preprocedural antiplatelet regimen, as described above, differed among treatment groups. Aspirin (100 mg) was started 2 days before intervention only in patients randomized for CAS, while the patients from the CEA group did not have any kind of preoperative antiplatelet regimen (department protocol). Immediately after CAS and in order to avoid acute stent thrombosis, heparin infusion was continued until CABG. ACT was checked every 60 min and was constantly maintained at ≥200 s until the beginning of the CABG operation.

Aspirin was restarted during the first 24 h after CABG in all patients. A 300-mg loading dose of clopidogrel was given exclusively to CAS patients in the ICU through a nasogastric tube, 6 h after arrival to the ICU, provided that bleeding from the thoracic drains was acceptable, or when it was <50 ml/h for three consecutive hours from the sixth hour. Dual antiplatelet treatment was continued in CAS/CABG patients for 6 months.

Since all patients were on antiplatelet regime early after the procedures, great caution was taken regarding additional usage of antifibrinolytic agent and platelets. Desmopressin in a single dose
of 0.3 μg/kg was given only if drainage was ≥100 ml/h for three consecutive hours or >500 ml in 6 h providing that the thromboelastogram indicated decreased platelet function. Platelet infusion was given in the case of excessive drainage defined as >500 ml in 3 h or >800 ml/6 h if the result of the thromboelastogram showed low platelet count and decreased function. Early reintervention was endorsed if the blood loss was >300 ml/h for three consecutive hours, despite replacement of necessary blood products, indicated by the results of the thromboelastogram.

**Follow-up and end points**

All patients were followed during initial hospitalization and for 30 days after the procedure. Routine haemodynamic and clinical monitoring was available to all patients. Neurological examination was performed after the patients became fully conscious, as well as on discharge and 30 days after the procedure. If any kind of neurological deterioration was observed, patients underwent computed tomography (CT) scan of the brain, in order to determine the nature and extensity of the lesion. Determination of residual neurological defects was done using Rankin score, scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability.

Primary end point was defined as combined incidence of stroke and death 30 days after surgery or during hospitalization following surgery. Secondary predetermined end points included occurrence of postoperative MI and atrial fibrillation, postoperative blood loss and need for blood transfusion, duration of hospital stay and the time spent in the intensive care unit.

**Statistical analysis**

Analysis of immediate and 30-day outcomes was possible in all patients. Continuous variables were presented by their mean ± standard deviation. Statistical analysis was performed using the SPSS 17.0 software. When examining the differences between the two defined groups, the t-test was used for numerical parameters and the χ² test for attribute characteristics.

**RESULTS**

Overall, 20 patients (Group 1: CAS/CABG, 10 patients and Group 2: CEA/CABG, 10 patients) were included in the study. Baseline patient characteristics did not differ between groups (Table 1). The majority of patients (16 of 20) had depressed left ventricular ejection fraction (defined as EF ≤50%) and were in the low/intermediate risk groups according to EuroSCORE. Only 4 of 20 patients had EuroSCORE ≥6, with equal distribution in both groups.

CAS was successful in all cases and there were no immediate complications and the average time between the end of CAS and beginning of the CABG was 2.1 ± 0.4 h. Average clamping time for the CEA group was 21.5 ± 7.7 min. CABG using cardiopulmonary bypass was done in 19 of 20 patients, while 1 patient had off-pump surgery. In that case, severe atherosclerosis of the ascending aorta was noted on MDCT. Inability to clamp the aorta led the surgeon to use the off-pump technique, with LIMA and the left radial artery as Y-graft. LIMA was used in 19 of 20 patients. The average number of grafts used did not differ between study groups (CAS/CABG group 47.6 ± 10.8 vs CEA/CABG group 58.4 ± 9.7 min, P = 0.106). On the contrary, duration of extracorporeal circulation was significantly shorter in the CAS/CABG group (65.7 ± 14.1 vs 90.0 ± 17.4 min, P = 0.023).

During the follow-up period, two primary end point events occurred, both in the CEA/CABG group. One patient died of sepsis and multiorgan failure, 42 days after surgery. Also, 1 patient developed stroke 4 days after CEA/CABG with mild right-sided limb weakness and disorientation that almost completely resolved within 30 days of surgery (Rankin score 1). Right CEA (90% stenosis of the right internal carotid artery) was performed in this patient using the standard surgical technique (eversion technique without shunting). Cerebral ischaemic time was 14 min and no excessive and calcified atherosclerosis was noted during operation. Interestingly, the patient did not have significant stenosis of the left internal carotid artery. New ischaemic lesion in the left brain hemisphere was confirmed on the CT scan. Although no death/stroke occurred in the CAS/CABG group, there was no significant difference in primary outcomes between study groups (P = 0.631). Other postoperative characteristics are given in Table 2.

<table>
<thead>
<tr>
<th>Table 1: Baseline patient characteristics</th>
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<tbody>
<tr>
<td><strong>CAS/CABG (n = 10)</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male (%)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
</tr>
<tr>
<td>Previous myocardial infarction (%)</td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
</tr>
<tr>
<td>NYHA class</td>
</tr>
<tr>
<td>EuroSCORE</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
</tr>
<tr>
<td>Carotid stenosis (%)</td>
</tr>
<tr>
<td>Bilateral carotid disease</td>
</tr>
<tr>
<td>Previous stroke/transitory ischaemic attack</td>
</tr>
</tbody>
</table>

CAS/CABG: carotid artery stenting/coronary artery bypass grafting; CEA/CABG: carotid eversion endarterectomy/coronary artery bypass grafting.
The duration of hospital stay was 9 days (range 6–43 days) and median of extubation was 16 h (range 6–24 h). Also, there were no difference between groups in the duration of mechanical ventilation and the period spent in hospital and ICU. Our study is, to our knowledge, the first randomized, prospective trial comparing the efficacy and safety of two treatment approaches for carotid disease, percutaneous and surgical, in the setting of combined treatment with coronary artery bypass surgery. These data, although done on a limited number of patients, confirm that both approaches are safe. Only 1 death and 1 stroke occurred and both in the CEA/CABG group. Also, there was no difference in secondary end points between the study groups. The only difference observed between the study groups was in the duration of CPB time. This might be explained with technical difficulties that surgeons had in 2 patients who underwent the CEA/CABG procedure. In one case the patient had an atheromatous aorta together with severely calcified coronary arteries, and the other patient had severe diffuse distal coronary disease and decreased left ventricular ejection fraction which increased the necessary time for CPB.

CAS and CAGB procedures were performed separately in our study with a time delay of just 2.1 h. This was done intentionally, in order to assess the neurological status of the patient after CAS procedure and eventually proceed with CAGB. Another potential option was to use hybrid operating theatre. However, no data in literature were found comparing these procedures and surgical methods. Although performing CAS/CAGB in such an environment might shorten the procedure time and diminish the influence of dual antiplatelet treatment on bleeding complications, there are several important questions that led us to perform our protocol as previously described. First, evaluation of the neurological status after CAS has to be delayed for the period of general anaesthesia. Therefore, if neurological complications develop, one cannot attribute it solely to the CAS procedure. Second, performing ad hoc CEA if CAS is unsuccessful might be delayed and complicated.

Combined CAS/CABG treatment has been described in other studies and has recently emerged as a valid treatment option [12–15]. In the simultaneous hybrid revascularization by carotid artery stenting and coronary artery bypass grafting (SHARP) study, which included 101 patients, early incidence of death, stroke and MI was 4%, similar to our study [13]. However, this trial, as many others, included only high-risk cardiac patients with EuroSCORE ≥ 5. Also, it enrolled patients in need of valve surgery, which additionally increases risk of cardiac mortality and morbidity [17]. Contrary to all these studies, although our patients had severe carotid/coronary disease, our study included patients with relatively low perioperative risk (average EuroSCORE was 3.2). Results similar to those of the SHARP trial were reported in other studies. All comprised of small groups of patients, but the mortality and stoke incidence was acceptable, ranging from 2.2 to 8.1% [12–15, 18], and occurrence of other postoperative complications was negligible.

**Table 2: Clinical outcomes during the follow-up period**

<table>
<thead>
<tr>
<th></th>
<th>CAS/CABG (n = 10)</th>
<th>CEA/CABG (n = 10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Perioperative MI</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Postoperative AF</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Acute kidney failure*</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
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Perioperative MI, defined as the presence of at least two out of three criteria for MI such as: (i) ECG changes involving the presence of new Q waves, (ii) the increase of cardiac enzymes, i.e. creatine phosphokinase ≥1000 IU/l, (iii) echocardiographic confirmation of new wall motion abnormality.

*Acute kidney failure was defined as rise of creatinine for at least 20% from baseline values or need for dialysis.

**Table 3: Drainage and markers of cardiac injury**

<table>
<thead>
<tr>
<th></th>
<th>CAS/CABG (n = 10)</th>
<th>CEA/CABG (n = 10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 h drainage (ml)</td>
<td>165 ± 110</td>
<td>245 ± 116</td>
<td>0.133</td>
</tr>
<tr>
<td>24 h drainage (ml)</td>
<td>350 ± 141</td>
<td>405 ± 170</td>
<td>0.432</td>
</tr>
<tr>
<td>CK (IU/l)</td>
<td>499 ± 387</td>
<td>435 ± 237</td>
<td>0.667</td>
</tr>
<tr>
<td>CK-MB (IU/l)</td>
<td>23.3 ± 8.3</td>
<td>21.7 ± 9.2</td>
<td>0.690</td>
</tr>
<tr>
<td>Troponin T</td>
<td>1.1 ± 0.8</td>
<td>2.5 ± 2.0</td>
<td>0.107</td>
</tr>
</tbody>
</table>


Postoperative atrial fibrillation occurred frequently in both groups, but there was no difference between the treatment groups (P = 0.104). Rate of infection was low and did not differ between study groups (P = 0.748). Need for blood transfusions was similar in both study groups (P = 0.603). Also, there was no difference in the blood loss during the first 6 and 24 h after CAGB despite the usage of aggressive dual antiplatelet treatment in Group I (Table 3). Markers of cardiac injury were similar in both groups with an exception of troponin, where a trend towards lower levels was noticed in the CAS/CABG group (P = 0.107) (Table 3). Overall median time of extubation was 16 h (range 6–696 h). Also median duration of stay in ICU was 2.0 days (range 1–39 days) and median duration of hospital stay was 9 days (range 6–43 days). Finally, there were no difference between groups in the duration of mechanical ventilation and the period spent in hospital and ICU (Table 4).

**DISCUSSION**

Our study is, to our knowledge, the first randomized, prospective trial comparing the efficacy and safety of two treatment approaches for carotid disease, percutaneous and surgical, in the setting of combined treatment with coronary artery bypass surgery. These data, although done on a limited number of patients, confirm that both approaches are safe. Only 1 death and 1 stroke occurred and both in the CEA/CABG group. Also, there was no difference in secondary end points between the study groups. The only difference observed between the study groups was in the duration of CPB time. This might be explained with technical difficulties that surgeons had in 2 patients who underwent the CEA/CABG procedure. In one case the patient had an atheromatous aorta together with severely calcified coronary arteries, and the other patient had severe diffuse distal coronary disease and decreased left ventricular ejection fraction which increased the necessary time for CPB.

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Design of our study was encouraged by the experience of our centre with the treatment of this subset of patients [6] and still unresolved question of timing and type of carotid intervention proceeding CABG. Although there is a clear correlation between the presence of carotid disease in cardiac surgery patients and the stroke, there is still no consensus in the scientific community about the treatment of these patients [4]. The views differ sharply from complete ignorance of carotid artery disease, over separate operations, to the combined, simultaneous procedures. In operations separated by significant time intervals, where carotid artery intervention was done prior to coronary bypass surgery, there has been an increased incidence of MI [5]. On the contrary, if myocardial revascularization was done prior to carotid surgery, the incidence of neurological deficit during the intervention was higher [4, 5]. Moreover, it was suggested that it is very difficult to design a diagnostic and surgical protocol suitable for all clinical situations. These findings were extensively analysed in the most recent retrospective analysis of 350 patients with severe carotid and coronary artery disease in which the combined CEA/CABG and staged CAS/CABG approaches were superior to staged CEA/CABG treatment regarding short-term outcomes [10]. Staged CEA/CABG unlike staged CAS/CABG in this trial was associated with significantly higher risk of interstage MI, given the presence of concomitant severe coronary artery disease. Furthermore, additional data demonstrated a consistent pattern in favour of the staged CAS/CABG strategy in this population [7, 10, 11].

Nowadays in general, patients are older, with more diffuse coronary artery disease, have a higher SYNTAX score and are more often symptomatic. These factors endorse simultaneous carotid and coronary interventions as a choice of treatment. However, the combined procedure carries an increased risk of morbidity and mortality [10]. Levy et al. recently reported results on 80 patients performing combined carotid endarterectomy and myocardial revascularization. While operative mortality was 3.7%, combined incidence of death, perioperative cerebrovascular accident (2.5%) and MI (3.7%) reached almost 10%. Also, 6 patients (7.6%) had a stroke during the mean follow-up period of 10 years.

With the introduction of stenting, a new option became available, i.e. CAS. Several concerns exist with this treatment option: problem with adequate antiocoagulation, haemodynamic instability during and immediately after stenting as well as long-term efficacy of the procedure. On the other hand, advantages of this approach include immediate awareness of the procedural result in an awake patient, shortening of the hospital stay, less invasive procedure and even more acceptable cosmetic results [20]. The efficacy and safety of CAS and comparison with surgical procedures were extensively studied [17, 21]. A recent meta-analysis showed that overall, in the short term, CAS patients develop more strokes and less MI than those who undergo CEA, but the incidence of disabling strokes and death is similar [17]. Also, CEA might be preferable in patients with recent symptomatic carotid disease [22]. Another concern regarding CAS is the long-term outcome. Recent studies such as the CREST and SPACE trials have shown promising results [17, 23]. Moreover, a higher incidence of stroke and death with CAS was reported in the long-term outcome meta-analysis, but noticeably only in elderly population (≥68 years) [21]. Finally, everyday technology improvement in stent design and structure, especially the recent introduction of biodegradable stents might influence further results in a positive way towards CAS notably in stable patients with carotid artery disease.

Many questions and dilemmas remain regarding optimal treatment of patients with concomitant severe carotid and coronary diseases. One of the approaches might be individual and preferable by the operators. In the CARE registry CAS was performed more frequently in patients with high-risk comorbidities, such as left main coronary artery disease, significant contralateral carotid disease and recent neurological events, and CEA was done more in acutely decompensated patients [24]. These results, although opposite to the results of the meta-analysis, once again emphasize the need for large-scale randomized trials of CAS versus CEA especially in the setting of concomitant CABG.

Timing and type of antiplatelet and anticoagulation treatment present another open question with staged and concomitant carotid/coronary procedures. These patients might have increased risk of bleeding due to complexity of the surgical procedure and introduction of dual antiplatelet treatment. In the setting of CAS followed by CABG, there is always a concern that dual antiplatelet therapy might increase incidence of haemorrhage immediately after CABG. Mandatory dual antiplatelet regimen after the staged CAS/CABG procedure therefore delays cardiac intervention for 4 weeks. Also, the protocol for concomitant CAS/CABG varies. Some investigators introduced, as in our trial, aspirin 2 days before CAS, and others started aspirin only after CABG was performed [12–15, 18]. Particular concern regarding potential acute stent thrombosis before CABG led different authors to use different protocols (GP IIb/IIIa inhibitors, low molecular heparin, heparin infusion) [12–15, 18]. In our small group of patients, we did not face this problem, therefore showing safety of continuous heparin infusion (aiming ACT ≥200 s) while awaiting CABG. On the other hand, we did not notice increased early blood loss, more frequent need for transfusion after surgery or increased incidence of late tamponade, proving that introduction of dual antiplatelet treatment immediately after CAS/CABG is safe.

Regarding limitations of the study, the small patient sample was a main obstacle to drawing any strong conclusion. Fully aware that a small sample size, although done in a prospective and randomized fashion, could mask results on a larger patient population, we believe that comparison of these different strategies should be continued. Therefore, the results of this pilot study encouraged us to proceed with further randomization. We project that with around 110 patients overall included in the trial, some firm conclusions might be achieved.

Also, the short follow-up period did not allow us to monitor long-term effects, especially in the group with CAS, in which patients might experience more complications such as restenosis or stent thrombosis.

CONCLUSION

Our study has shown that the hybrid procedure of carotid stenting and coronary surgery is feasible in experienced centres and has similar early post-procedural results with standard combined carotid and cardiac surgery when performed in stable, low-risk, cardiac patients with severe carotid stenosis. However, further, multicentre, randomized trials comparing these two approaches are mandatory before assessing the real value of this procedure. Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr H. Reichenspurner (Hamburg, Germany): You rightly mentioned that this was a relatively small number of patients, of course, therefore drawing final conclusions is a little bit difficult. Let me just ask you, you said one patient had a stroke and one patient died. Was it the same patient or a different patient?

Dr Micovic: A different patient. The patient who died didn’t have any neurological deficit; we were not able to wean him from respiratory support and he had an unfortunate outcome. The other patient developed stroke, essentially a minor one, four days after the procedure. The CT brain scan showed patent carotid artery anastomosis. It was ipsilateral stroke and the patient almost recovered, with a Rankin disability score of 1, 30 days after the procedure.

Dr S. Ramathan (Coimbatore, India): I have a basic question regarding the indication of carotid endarterectomy or stenting in patients having more than 80% carotid artery stenosis. I do understand that the NASCET (North American Symptomatic Carotid Endarterectomy Trial) showed that asymptomatic patients have a higher incidence of stroke. But do you have any data to say that such a thing happens in patients undergoing coronary surgery, because based on our unpublished data, which looked at all the strokes in patients who undergo coronary artery bypass grafting, we did not find the carotid artery stenosis gradient to be an independent predictor of postoperative stroke in CABG patients. So by extrapolating the data from NASCET to coronary patients, are you not subjecting these patients to a simultaneous procedure with a higher risk?

Dr Micovic: It is well known that the risk of stroke after coronary bypass surgery is increased in the patient with a severe carotid stenosis. We had our data published in the European Journal years ago with comparison of simultaneous and staged carotid and coronary procedures. Mortality for patients having a simultaneous procedure was 6%. A lot of studies with retrospective analysis of a similar patient population showed that the combined incidence of stroke, myocardial infarction and death is around 10%.

Although we know that severe carotid stenosis carries a higher risk for stroke after CABG, we don’t know the actual aetiology. Maybe those patients have more diseased ascending aorta. This group of patients is very hard to assess. It was suggested by my colleagues years ago that maybe each department should make its own protocol.

Nowadays we are dealing more often with an elderly population with diffusely diseased coronaries. They have a higher SYNTAX score; that means that they are not suitable for any kind of percutaneous intervention. We are more keen to revascularize both territories at the same time.

Our indication for simultaneous intervention would be asymptomatic carotid stenosis of more than 80% or symptomatic higher than 50%. We are carefully examining each patient both with Doppler ultrasound and with multi-detector row computed tomography to be able to see the quality of the plaque, to see whether the plaque is complicated, ulcerous, because the presence of ulcerous plaque is a predictor of stroke after CABG.

Dr Ramanathan: If I may just add a comment, I think from what you tried to explain, I presume we all know that carotid artery stenosis per se is not the only risk factor for stroke following coronary artery bypass grafting. We know that handling of the aorta, no-touch technique, the perfusion pressures you keep during bypass, all these matter, and how you manage your sugars. So you don’t need to address significant carotid artery disease just because it is present.

Dr Micovic: No, I agree, but I need just to say one thing. A no-touch off-pump technique has not yet been proven to be superior to on-pump bypass surgery. There is a study comparing off-pump and use of partial clamping during coronary bypass surgery, and it showed that single cross-clamp grafting is superior regarding the stroke incidence.

Dr M. Jahangiri (London, UK): You said these 20 patients are part of an ongoing trial. May I please ask what number of patients you are aiming to recruit into the trial?

Dr Micovic: We are aiming to recruit 60 patients and then to perform statistical observation to see whether we reached any statistical significance.

Dr Jahangiri: If you are considering a stroke rate of 1% following coronary artery bypass graft surgery, you would need to recruit 1,700 patients in each limb.

Dr Micovic: I know. It is very difficult to design a study that is going to give us the exact answer in such a difficult patient population.