Abstract. – Background and Objective: Due to increased life expectancy, the risk profile of the patients undergoing cardiac surgery changed dramatically. This is especially important in case of concomitant coronary artery disease and carotid artery stenosis (CAS). Careful decision making and appropriate surgical strategy in these patients is critical for the success of the operation. Controversy about relationship between staged and concomitant carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG) still exists.

In the current study, we present our case load in treating patients with concomitant carotid artery stenosis and coronary artery disease.

Patients and Methods: CABG with additional CEA due to neurologic symptoms or high grade (>80%) CAS has been performed in 835 patients in the period of 1982-2010. Results of evaluation of perioperative mortality and morbidity in regard to the surgical approach have been discussed.

Results: The average patient age was 62.6 ± 8.7 years. Echocardiography revealed that 28% of the patients had poor left ventricle ejection fraction (<30%). Coronarography demonstrated that 21.4% of the operated patients had significant left main coronary artery stenosis (>60%). In terms of neurological status, majority of the patients (88.3%) were neurologically asymptomatic. The overall mortality regardless the sequence of procedures was 2.3% (19 patients). In the group of concomitantly treated patients 44.6% (50 patients) required triple coronary bypass while the mean number of coronary bypasses was 2.6. Postoperative neurologic complications were present in 102 patients (12.2%). Eighty-four patients (10.0%) have had TIA, while 18 patients (2.2%) have had permanent neurologic deficit while 4 patients (0.5%) died as a result of it.

Conclusions: It is imperative that every patient being considered for CABG should undergo ultrasonic evaluation of the carotid arteries regardless the neurological symptomatology. Concomitant surgery on patients with severe CAS and coronary disease carries a slightly higher operative risk and, therefore, should be avoided. Concomitant surgical treatment should only be considered in patients with unstable angina and significant CAS in whom we may expect higher morbidity and mortality.

Key Words: Carotid surgery, Coronary artery bypass grafting, Cerebral ischemia.

Introduction

Cardiac surgery is one of the most prominent and most performed fields of surgery today, while coronary artery bypass grafting (CABG) is one of the most frequently performed operations in the USA and Europe¹. Due to increased life expectancy, the risk profile of the patients undergoing cardiac surgery changed dramatically. Also, the expansion of the stents in myocardial revascularization have changed the profile of the coronary revascularization patients. The adequate approach has been further complicated by the advent of carotid artery stenting. Atherosclerosis, a generalized process, imposes a necessity to surgically treat patients with concomitant vascular lesions. Therefore, a careful decision making regarding which vascular lesion is to be treated first is critical. This is especially important in case of concomitant coronary artery disease (CAD) and carotid artery stenosis (CAS).

A new perioperative stroke is recognized in about 3% of coronary bypass patients in the current era². One of five patients with stroke after coronary bypass will die in the hospital. It is estimated that at least one third of perioperative
stroke is attributable to unrecognized and thus preventable carotid occlusive disease, although this is still controversial issue. A direct correlation between the risk of stroke and the patient age has been established. Perioperative stroke related to CABG is of increasing concern knowing that the average age of coronary bypass patients continues to rise and with it the risk of stroke. Carotid endarterectomy (CEA) proved its value in both symptomatic and asymptomatic high-grade CAS, but considerable controversy still exists regarding the role of prophylactic CEA in CABG patients with coexistent CAD. The results of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) have shown that the future risk of stroke is halved following CEA. It is clear now that CEA confers significant improvement in long-term stroke protection compared with best medical management. Hertzer et al. were the first to recognize that there has been no significant difference in terms of survival between the patients treated operatively with CEA or treated with medications. On the other hand, patients with a greater than 70% unilateral stenosis treated operatively yielded significantly better freedom from late stroke.

Controversy about relationship between staged and concomitant CEA and CABG still exists. By convention, staged procedure means doing CEA followed by CABG in two acts in case of unilateral CAS or three acts in the case of bilateral CAS (CABG being performed after two consecutive CEAs), while concomitant surgery imply doing these two procedures in one act (Figure 1). Since the first report of concurrent CEA and CABG by Bernhard et al. in 1972, ambiguous results have been reported, from ones stating that there has not been any significant reduction in perioperative stroke rate to ones stating that the incidence of perioperative complications actually increased. Daily et al. reported that synchronous approach might be more cost-effective than staged approach (longer hospitalization, two anesthetics). Even though the optimal surgical approach is still under debate, adequate evidence exists that significant CAS is an important incremental risk factor for the development of perioperative stroke following CABG and thus should be treated prior or concomitantly to CABG.

In the current study, we present our caseload in treating patients with concomitant CAS and CAD. Results of evaluation of perioperative mortality and morbidity in regard to the surgical approach have been discussed.

Patients and Methods

Data were collected prospectively and analyzed retrospectively. The study included 835 patients operated of occlusive coronary and carotid artery disease during the period 1st of January 1982 to 31st of December 2010. After institutional ethics approval was obtained, the records of all included patients were retrieved from database for analysis. Because of the retrospective nature of the study, requirement for informed consent was waived by the Ethics Committee.

All patients underwent standard clinical examination protocol, chest X-ray, echocardiographic examination, Doppler examination of the carotid arteries and laboratory examination. CEA was performed at the Multi-Specialty Institute of Vascular Surgery Dr. Vladimir J. Ivanovic, Belgrade, Serbia. The data were collected from all the patients undergoing CAE and CABG and included main symptoms, clinical and laboratory findings, modality of surgical treatment, intraoperative finding and course of postoperative recovery. Cerebral status of all the patients was preoperatively scored by the Vollmar modification of the Natali-Thevenet scale [Vollmar I – asymptomatic, Vollmar II – transient ischemic attack – (TIA), Vollmar III – permanent neurologic deficit – stroke]. We then performed a systematic overview of morbidity and mortality of the surgical strategies.

**Figure 1.** Different surgical approaches in patients with CAS and CAD (Coronary artery; Carotid artery).
Several operative techniques were used when performing CEA. Carotid arteries were operated using standard technique with longitudinal opening of carotids, endarterectomy and direct suture or patch closure. During the last 10 years, we have been using both approaches: classical CEA with patch plasty (cerebral protection was established with the use of Javed shunt) and eversion technique with no cerebral protection. In two cases of heavily calcified carotid arteries, proximal part of internal carotid has been replaced with tube graft of the appropriate size.

Conventional CABG was performed using cardiopulmonary bypass (CPB). During CPB, pump flow was maintained between 2.0 and 2.4 l/min/m², and mean arterial pressure between 50 and 80 mmHg (depending on level of carotid artery stenosis), under mild systemic hypothermia. First, all distal coronary anastomoses were created followed by proximal anastomoses mostly created before release of the aortic cross-clamp.

As for the operative approach, three modalities were used in our hospital. Two-stage operation – patients with unilateral CAS and CAD – CEA followed by CABG in the second act. Three-stage operation – patients with bilateral CAS and CAD – CEA followed by another CEA of the opposite carotid artery followed by CABG afterwards. Simultaneous operation – patients with unilateral CAS and CAD – CEA and CABG at the same time (Figure 1). Practically, all the patients with bilateral CAS and CAD underwent three-stage operation, i.e. no simultaneous operation (CEA and CABG at the same time) has been performed pre-/post CEA. Only 3 cases with bilateral CAS have been operated in staged simoultaneous fashion (simoultaneous – CEA and CABG, followed by CEA of the opposite side) due to hemodynamic instability (acute myocardial infarction). This group is discarded from this study because of small number of patients.

In case of concomitant CEA and CABG, our approach was to perform CEA during harvesting of conduits for the CABG prior to CPB. In case of staged approach, CABG has been performed, usually, 7-10 days after the initial CEA.

**Statistical Analysis**

Numerical variables were presented as mean value and categorized variables were summarized by absolute frequencies and percentages in parenthesis. Continuous variables were compared by Student’s t test and categorized variables were compared by the $\chi^2$ test across the groups. All analyses were conducted with SPSS software (version 16.0) (SPSS Inc., Chicago, IL, USA).

**Results**

During the observed period, CABG with additional CEA due to neurologic symptoms or high grade CAS has been performed in 835 patients. These patients constituted 3.4% of all operated patients at our Clinic. The average patient age was 62.6 ± 8.7 years. More than 90% of the patients were in the age group of 50+ years (Figure 2). There were 558 (66.8%) male patients and 277 (33.2%) female patients, thus male to female ratio was 2:1. The characteristics of the patient’s population are summarized in Table I.

Typical angina was the most prominent symptom in these groups of patients. Stable angina was present in 494 (59.2%) patients, non-stable angina in 163 (19.5%) patients, 149 patients (17.8%) had myocardial infarction and 29 (3.5%) patients were asymptomatic. Echocardiography revealed that 234 (28.0%) had poor ejection fraction (LVEF < 30%). On the other hand, coro-

**Figure 2.** Age distribution patients with CEA and CABG.

**Table 1.** Preoperative characteristics of patients with concomitant CAS and CAD.

<table>
<thead>
<tr>
<th></th>
<th>Pts.</th>
<th>%</th>
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<tbody>
<tr>
<td>Hypertension</td>
<td>532</td>
<td>63.7</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>311</td>
<td>37.3</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>149</td>
<td>17.8</td>
</tr>
<tr>
<td>Left main stenosis &gt; 60%</td>
<td>179</td>
<td>21.4</td>
</tr>
<tr>
<td>Ejection fraction &lt; 30%</td>
<td>234</td>
<td>28.0</td>
</tr>
</tbody>
</table>
narography demonstrated that 179 (21.4%) of the operated patients had significant left main coronary artery stenosis (> 60%). Doppler examination of the carotid arteries revealed that bilateral significant CAS was present in 15.7% (131) of the patients while the remaining 84.3% (704) of the patients had unilateral significant CAS.

In terms of neurological status, majority of the patients, 737 (88.3%), were neurologically asymptomatic. Previous cerebrovascular disease was present in the form of transient ischemic attack (TIA) in 83 patients (9.9%) and stroke – 15 patients (1.8%).

The overall mortality rate regardless the sequence of procedures was 2.3%. A significant difference of mortality exists between subgroups, i.e. selected modality of treatment. Two staged surgical approach has been the most commonly performed approach. There were 599 (71.7%) patients treated in this manner (Table II). Unilateral significant CAS was present in all of these patients. CEA was performed as the first act followed by CABG several days later. Mortality in this group was 1.2% (7 patients). Three-stage operation has been performed in 124 (14.9%) patients. All of them had significant bilateral CAS requiring CEA of both carotids which has been performed in two acts followed by CABG. Mortality in this group was 1.6% (2 patients). The least opted approach was simultaneous operation of the coronary and carotid artery. This type of surgery has been performed in 112 (13.4%) patients, yielding highest mortality of 8.92% (10 patients). These patients were characterized with high grade CAS with unstable plaques, hemodynamic instability, low left ventricle ejection fraction and poor coronary artery status requiring coronary endarterectomy. In 2 patients (0.2%), carotid artery has been replaced by tube graft due to severely calcified carotid artery.

In the group of concomitantly treated patients, 65 (58.0%) patients required three or more coronary bypasses (multi-vessel disease). The average number of coronary bypasses was 2.63 (Table III). Coronary endarterectomy has been performed in large number of these patients, 40 (35.7%). During the first ten years of the observed period, coronary endarterectomy has been performed more frequently with poorer results and higher mortality rate (around 11%) in concomitantly treated patients. The mortality cause was mainly due to cardiac-related complications. In the field of coronary surgery, operative tactics has changed dramatically over the time, especially during the last decade. Nowadays, coronary endarterectomy is performed in selected patients less frequently than before, yielding better postoperative results. Coronary endarterectomy has been abandoned as a routine treatment of severe coronary artery lesions 12 years ago. During the last 12 years, 50 patients have been treated concomitantly with operative mortality of 2% (1 patient) which is more than a tenfold reduction of mortality rate ($p = 0.01$). It is very important to emphasize that during the last 12 years, the majority of the patients had the left anterior descending artery revascularized by left internal mammary artery.

Postoperative neurologic complications were present in 102 patients (12.2%). No significant difference was present with respect to the operative tactics. Eighty-four patients (10.0%) have had TIA, while 18 patients (2.2%) have had permanent neurologic deficit while 4 patients (0.5%) died as a result of it.

Overall mortality rate was 2.3% regardless the operative approach. Nine patients (1.1%) died as a result of cardiac related complication (acute myocardial infarction or acute right heart insufficiency). Six patients who have died from cardiac related complication were concomitantly treated. Four patients (0.5%) died as a result of neurologic complication (fatal stroke), 2 patients (0.2%) died as a result of gastrointestinal bleeding, 2 patients (0.2%) died as a result of pulmonary embolism and 2 patients (0.2%) died as a result of respiratory failure. During the observed period, 3 patients with performed CEA died while waiting

<table>
<thead>
<tr>
<th>Operative tactics</th>
<th>Pts.</th>
<th>%</th>
<th>Mortality (pts)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-stage operation (CEA followed by CABG)</td>
<td>599</td>
<td>71.7</td>
<td>7</td>
<td>1.2</td>
</tr>
<tr>
<td>Three-stage operation (bilateral staged CEA followed by CABG)</td>
<td>124</td>
<td>14.9</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Simultaneous operation (CEA + CABG)</td>
<td>112</td>
<td>13.4</td>
<td>10</td>
<td>8.9</td>
</tr>
</tbody>
</table>
for the next step procedure – CABG. These patients were excluded from the study because they did not meet our inclusion criteria: CEA and CABG performed in any manner. However, if they were treated with different approach, i.e. simultaneously, mortality could have been avoided.

It is interesting to present the cumulative frequency of mortality and permanent morbidity in regards to different operative tactics (Table IV). It is clear that simultaneous operation carries the highest risk (11.6%). These results may be somewhat misleading but one must bear in mind that this risk is mainly due to cardiac complications, specifically – coronary endarterectomy which has been abandoned as a routine treatment.

### Discussion

Postoperative neurological complications in cardiac patients increase morbidity and mortality and also may prolong hospital stay and costs. CAD is recognized as one of the possible causes of perioperative stroke. Medical history and physical examination are neither sensitive nor specific for carotid disease. Age, stigmata of peripheral vascular disease, a smoking history, previous cerebrovascular event, left main coronary disease, female gender, diabetes, hypertension, carotid bruit all point to the need for further evaluation. The presence of symptoms of carotid disease is alarming and certainly correlates with poor outcome, but the absence of symptoms is not particularly protective. Unfortunately, the first symptom of CAS in cardiac patients may be a permanent stroke. For this reason, several imaging modalities have been proposed to screen patients with CAD before surgery including: carotid artery duplex scanning, magnetic resonance angiography (MRA), single photon emission tomography (SPECT), computerized tomography (CT), conventional coronary angiography (CCA). Screening for carotid disease implies that treatment options exist. Multiple multicenter, prospective randomized trials comparing CEA to medical treatment for moderate to high grade CAS have shown significant stroke reduction for the CEA groups.

To date, no well designed prospective randomized trial has clarified relationship between CEA and CABG in a patient with concomitant CAS and CAD. Unlike isolated CAS or CAD where treatment strategy is clearly defined, the treatment strategy of patients with combined CAS and CAD vary from simultaneous (same anesthetic) to a staged procedure, whereby CEA is performed several days prior to (staged approach) or after (reverse staged approach) coronary revascularization. The investigations presented in the literature to date on this topic do not support any treatment strategy with level 1 evidence mandating a uniform therapeutic approach. There is pro et contra for each suggested surgical approach regarding mortality and the appearance of adverse outcomes after surgery. Operating on the carotid lesion first exposes the patient to an increased risk of perioperative morbidity and mortality from myocardial infarction (MI); operating on the coronary arteries first exposes the patient to an increased risk of perioperative stroke, while conducting both operations simultaneously may result in excessive surgical stress for the patient.

### Table III. Number of revascularized coronary arteries in patients undergoing simultaneous operation.

<table>
<thead>
<tr>
<th>Number of revascularized coronary arteries</th>
<th>Pts.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>One vessel</td>
<td>14</td>
<td>12.5</td>
</tr>
<tr>
<td>Two vessels</td>
<td>33</td>
<td>29.5</td>
</tr>
<tr>
<td>Three vessels</td>
<td>50</td>
<td>44.6</td>
</tr>
<tr>
<td>Four and more vessels</td>
<td>15</td>
<td>13.4</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>100</td>
</tr>
<tr>
<td>Coronary endarterectomy</td>
<td>40</td>
<td>35.7</td>
</tr>
</tbody>
</table>

Table III. Number of revascularized coronary arteries in patients undergoing simultaneous operation.

### Table IV. Combined mortality and permanent morbidity (stroke) for different surgical approaches.

<table>
<thead>
<tr>
<th>Mortality (n)</th>
<th>Mortality (%)</th>
<th>Stroke (n)</th>
<th>Stroke (%)</th>
<th>Combined mortality and permanent morbidity (n)</th>
<th>Combined mortality and permanent morbidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two stage operation</td>
<td>7</td>
<td>1.2</td>
<td>10</td>
<td>1.7</td>
<td>24</td>
</tr>
<tr>
<td>Three stage operation</td>
<td>2</td>
<td>1.6</td>
<td>5</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Simultaneous operation</td>
<td>10</td>
<td>8.9</td>
<td>3</td>
<td>2.7</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>2.3</td>
<td>18</td>
<td>2.1</td>
<td>44</td>
</tr>
</tbody>
</table>
The prevalence of significant carotid stenosis in patients undergoing CABG ranges between 2.8% and 22%\textsuperscript{13}. On the other hand, 50-60% of the patients being evaluated for the CEA have significant CAD\textsuperscript{16}. Most of the complications that occur in these patients are cardiac related while MI is responsible for 25-50% of all perioperative deaths following CEA\textsuperscript{17}. On the other hand, the prevalence of CAS in patients undergoing myocardial revascularization is considerably lower, 6-16%\textsuperscript{18,19}. The stroke rate after CABG is approximately 3%, with only one third attributable to the high grade CAS. The perioperative stroke may be the result of embolus from left heart, thrombus, air embolus, hypoperfusion during CPB, debris from the aorta dislodged during cannulation or decannulation.

If we agree that synchronous CEA and CABG operation is more technically demanding, carries greater mortality, increases intensive care unit (ICU) time, we may ask ourselves why do we even consider it. Why not do it sequentially? The answer is because of the fear of the stroke. The prevalence of major complications occurring during CABG is reported to be between 1-6\%\textsuperscript{20}. Perioperative risk in patients with CAS of <50% is estimated to less than 2%, in patients with CAS of 50-80% to 10% and in patients with CAS of >80% to 11-19\%\textsuperscript{21}. It is clear that the risk of perioperative stroke highly correlates with the degree of CAS. The asymptomatic carotid atherosclerosis study (ACAS) supports surgical intervention for asymptomatic CAS >60\%; ACAS reported that after 2.7 years the estimated 5 year risk of perioperative stroke or death was 5.1% following CEA and 11% for patients medically treated\textsuperscript{22}. In the same time, it is not uncommon to have a hemodynamically unstable patient requiring surgical revascularization, having severe CAS: this is a prototype of the patient suitable for synchronous operation. If we consider high level of CAS with consequent increased risk of stroke on one side, and the necessity for CABG on the other side, we might find this patient suitable for this type of operation. This approach is based on the assumptions that a combined operation might provide protection to both the cardiac and cerebrovascular system.

Hertzer et al\textsuperscript{7} reported a study containing of randomized groups of patients with unstable CAD and incidental asymptomatic CAS. In their study, only 9% of the patients had CAD that was stable enough to perform CEA prior to CABG. 4.2% of these patients suffered a perioperative stroke after CEA and died from MI awaiting CABG. Mortality rate of 6.1% in the group of concomitantly treated patients was reported, while the perioperative stroke rate was 7.1%. The remaining group of the patients who underwent sequential operation had 5.3% mortality rate. This study was one of the first to advocate the advantage of concomitant approach over the staged procedures. Akins et al\textsuperscript{23} published results of concomitant operation which included 500 patients. Hospital mortality was 3.6%, MI was 2.0% and stroke occurred in 4.6%. The conclusion they have reached was that concomitant CEA and CABG have neutralized the impact of CAS as a risk factor for stroke during surgical myocardial revascularization.

Remarkable results for combined procedures were reported by Chang et al\textsuperscript{24} in Albany with only 1% stroke and 2% mortality (n=189). Seventeen of these patients had undergone bilateral CEA and CABG. Darling et al\textsuperscript{25} subsequently reported their personal experience of 470 patients with similar results, with 70% of the cases asymptomatic in terms of neurological status, operative mortality was 2.4% and stroke rate 1%.

Several meta-analyses have been conducted in order to summarize the abundance of divergent data reported in the literature. The most recent meta-analysis including 97 published studies following 8972 staged or combined operations concluded that there is no significant difference in treatment outcomes for these different surgical approaches\textsuperscript{15}. The current trend favors combined procedures, as this approach provides protection from significant CAS as well as reducing risk of intra-operative myocardial events at CEA. The highest reported risk of stroke and mortality for combined procedures is around 26% and the lowest is nil depending on the patient population, the number of emergency cases and small sample sizes which can be misleading\textsuperscript{25}. The explanation of this mortality reduction is changed method of myocardial protection and the broader use of arterial conduits. Combined procedures have been criticized for their higher mortality and morbidity. However, they have often been reserved for the sickest urgent cases with bilateral CAS or symptomatic CAS, associated with unstable angina and poor cardiac properties such as poor ejection fraction and significant left main stenosis\textsuperscript{26}. Such selection bias may influence morbidity and mortality of the strategy.
Conclusions

The age of the patients undergoing CABG increases over time as well as the risk of perioperative stroke following CABG mainly due to increased incidence of severe asymptomatic or symptomatic CAS. Therefore, it is imperative that every patient being considered for CABG should undergo ultrasonic evaluation of the carotid arteries regardless the neurological symptomatology. An aggressive, formalized system of screening should be organized at the institutional level.

Selection of the best treatment strategy for both symptomatic and asymptomatic patients is of utmost importance. Concomitant surgery in patients with severe CAS and CAD carries a slightly higher operative risk. Operative risk of concomitant surgery is increased in contrast to patients with isolated lesions of either carotid or coronary arteries. Thus, we would consider concomitant surgical treatment only in patients with unstable angina and significant CAS.

Individual assessment of every patient in terms of carotid and coronary arteries status is imperative. Until a contemporary, totally randomized study resolves the confusion surrounding the appropriate management of patients with concomitant severe coronary and carotid artery disease, the surgical approach should be individualized according to the patient benefit, with sequential or simultaneous approach concurrently used.

This study was conducted in retrospective manner and it was carried out in a single centre by a single academic surgical team. Therefore, caution should be exercised in generalizing these findings to other surgeons and centers.

References

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