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Concurrent coronary and carotid artery surgery: factors influencing perioperative outcome and long-term results†

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ABSTRACT

Aims To assess risk factors for early and late outcome after concurrent carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG).

Methods and results Records of all 311 consecutive patients having concurrent CEA and CABG from 1989 to 2002 were reviewed, and follow-up obtained (100% complete). In the group (mean age 67 years; 74% males), 62% had triple-vessel disease, 57% unstable angina, 31% left main coronary stenosis, 19% congestive heart failure, and 35% either a history of vascular procedures or existing vasculopathies. Preoperative assessment revealed transient ischaemic attack in 16%, stroke in 7%, and bilateral carotid disease in 20%. There were 7% emergent and 19% urgent operations, and ascending aorta was described as atheromatous or calcified in 21%. Hospital death occurred in 19 patients, myocardial infarction in seven, and permanent stroke in 12. Significant multivariable predictors of hospital death were aortic calcifications, coexisting vasculopathy, and emergent procedure. Significant predictors of postoperative stroke were calcified or dilated aorta, and of prolonged hospital stay were advanced age, unstable angina, and coexisting vascular disease. For hospital survivors, 10-year actuarial late event-free rates were: death, 50%; myocardial infarction, 84%; stroke, 93%; percutaneous angioplasty, 95%; redo CABG, 98%; and all morbidity and mortality, 48%. Significant multivariable predictors of late deaths were coexisting vasculopathy, age, renal insufficiency, previous cardiac surgery, tobacco abuse, calcified or atheromatous aorta, and duration of intensive care unit stay.

Conclusion Concurrent CEA and CABG can be performed with acceptable operative mortality and morbidity, and good long-term freedom from coronary and neurologic events. Atheromatous aortic disease is a harbinger of poor operative and long-term outcome.

KEYWORDS: Carotid artery stenosis; Coronary artery disease; Carotid endarterectomy; Coronary artery bypass grafting; Stroke; Concurrent procedures

INTRODUCTION

Perioperative stroke after coronary artery bypass grafting (CABG) is an issue of paramount importance, particularly as the age of patients referred for cardiac surgery increases and the risk of stroke along with it.[1,2] Evidence has demonstrated that part of this increased stroke risk is related to carotid artery stenosis,[3-5] but controversy remains concerning the best approach for patients with concomitant severe carotid and coronary artery disease. Such managements vary from ignoring carotid lesions at the time of cardiac surgery, to performing staged operations with delay of one of the procedures, to combining coronary artery grafting and carotid endarterectomy during the same anaesthesia.

Each of these methods has its benefits and disadvantages, which can essentially be measured by the global mortality and the incidence of myocardial infarction and stroke.

To analyse this issue further, we have reviewed our early and long-term results in all patients who underwent concurrent carotid endarterectomy (CEA) and CABG at our institution, between January 1989 and December 2002.

METHODS

Methods and definitions

Records of all 311 consecutive patients who underwent concomitant CEA and CABG between January 1989 and December 2002 were reviewed (retrospective study). A total of 47 preoperative, operative, and postoperative variables were recorded and tested as possible predictors for operative events and long-term survival (postoperative variables were only tested as possible predictors for long-term survival) (Appendix 1). Follow-up information was obtained from all hospital survivors through clinic visits and annual letters, and was 100% complete. Mean follow-up was 112.1 months, and cumulative follow-up was 2690 patient-years. Between January and March 2004, all known survivors were questioned to obtain information regarding subsequent coronary or neurologic events, and New York Heart Association (NYHA) functional class. If subsequent hospitalization, death, or other events had occurred, the patient's physician or appropriate hospital record department was contacted to document the events and hospitalization.

Coronary artery disease was defined as a reduction of vessel diameter by at least 50% in one view on coronary angiography. Stenosis to this degree in the left anterior descending system, circumflex system, or right coronary system was used for the criterion of single, double, or triple vessel disease. Urgent operations were defined as operative procedures performed in patients whose accelerated symptoms prompted urgent hospital admission for evaluation and who were judged to be too unstable for discharge before surgery. Emergency operations were defined as procedures performed on patients whose cardiovascular instability required operative intervention either outside of normal operative hours or displaced another patient on the surgical schedule.

Operative mortality was any death occurring within 30 days of the operation or death during the same hospital admission as the operation. Postoperative course was followed-up in terms of bleeding, cardiac and renal status, assisted ventilation duration, and neurological events. Congestive heart failure was determined by the presence of pulmonary congestion or opacities consistent with oedema on chest roentgenograms. Perioperative myocardial infarction was defined as either a new Q wave or the elevation of the myocardial fraction of creatinine kinase in association with persistent ST segment changes or a new conduction abnormality.

With the exception of emergency, all patients scheduled for CABG underwent clinical and (echo)duplex examination to search for aortic and peripheral coexisting arterial disease. Arteriopathy was defined as aorto-iliac or femoro-popliteal occlusive disease that was symptomatic or associated with an ankle-brachial index <0.9, whereas abdominal aortic aneurysm was defined as an enlargement of the infrarenal aorta >3 cm.

Non-invasive carotid testing was routinely performed for patients with recent neurologic symptoms, history of stroke, audible carotid bruits, evidence of other extensive vascular disease, or advanced age. Sixty-nine patients (22%) had their CEA performed solely on the basis of non-invasive findings without angiography. A carotid artery diameter reduction of greater than 70% was considered a surgical indication in symptomatic patients. In asymptomatic patients, a stenosis of at least 80% was required, especially since 1996 considering the results of the ACAS study.[6] CEA was always performed before cardiopulmonary bypass was installed for myocardial revascularization. An intraluminal carotid shunt was used in all patients. After completion of the endarterectomy, the neck incision was left open until heparin reversal after cardiopulmonary bypass.

Anaesthaesiological protocol was the same throughout this period, extracorporeal circulation was performed with a membrane oxygenator, and myocardial protection used cold crystalloid cardioplegia solution added to topical cooling. Preoperatively, the ascending aorta was searched for atheromasia or calcifications by palpation and, since 1996, by transoesophageal echocardiography. An ascending aorta with a diameter >3.5cm was considered dilated.

Patient population and operative data

The population consisted of 311 consecutive patients ranging in age from 35 to 84 years (mean age: 67.2 ± 7.7 years). Clinical characteristics of these patients are listed in *Table 1.* The incidence of female sex was about 6% more than the average for all coronary bypass patients performed during the same period. Among the 187 patients with a history of tobacco abuse, 108 patients were current smokers. One patient was on haemodialysis. Twenty-one patients had previous CABG, one had aortic valve replacement, and one had mitral valve replacement. Ninety-six patients (31%) had a left main coronary artery disease, and 193 (62%) had triple-vessel disease.

Table 1 : *Patient clinical characteristics*

Variable	Patients (%)
Males	230 (74)
Females	81 (26)
Age (years)	67.2 ± 7.7
Unstable angina	177(57)
Previous myocardial infarction	126(41)
Congestive heart failure	60(19)
New York Heart Association, class III	53 (17)
New York Heart Association, class IV	6(2)
Diabetes mellitus	74 (24)
Hypertension	223 (72)
Hypercholesterolemia	181 (58)
Tobacco abuse	187(60)
Chronic obstructive pulmonary disease	68 (22)
Renal insufficiency	21 (7)
Previous cardiac surgery	23(8)
Permanent cardiac pacing	4(1)
Previous percutaneous coronary intervention	27(9)
Previous vascular surgery	55(18)
Coexisting vascular disease	76 (24)
Neurologic history	
Asymptomatic	236 (76)
Transient ischaemic attacks	49 (16)
Reversible neurological deficit	3(1)
Permanent stroke	23(7)

Previous surgical vascular procedures were aorto-iliac or aorto-femoral bypass for occlusive disease in 20 patients, femoro-popliteal bypass in 14 patients, contralateral CEA in 17 patients, and abdominal aortic replacement for aneurysmal disease in four patients. Coexisting non-operated vasculopathies were femoro-popliteal lesions in 53 patients, abdominal aortic aneurysm in 13 patients, and aorto-iliac occlusive disease in 10 patients. One hundred and eight patients (35%) had either a history of vascular procedure or an existing vasculopathy. In total, 17 patients had an occlusion of the contralateral carotid artery. Among the 75 patients with preoperative neurological symptoms, 57 patients had one symptomatic episode, 10 patients had two episodes, and eight patients had three or more neurologic episodes.

Operative characteristics are listed in *Table 2.* There were 81 (26%) urgent or emergent procedures. Cardiopulmonary bypass was used in most patients, with a mean time of 85.1 ± 31.2min. Mean aortic cross-clamp time was 41.8 ± 22.0 min. Coronary surgery consisted in single CABG in 13 patients (4%), double in 105 patients (34%), triple in 139 patients (45%), quadruple in 46 patients (15%), and quintuple in eight patients (3%). Mean number of grafts per patient was 3.2 ± 0.4. Ascending aorta was considered diseased (either calcified, atheromatous, or dilated) in 66 patients (21%). No-touch aorta technique was used in 28 patients.

Statistical analysis

Distribution for all relevant variables was expressed either as percentages or as mean ± standard deviation (except for the duration of hospital or ICU stay, which was expressed as min ≤ 1st quartile ≤ median ≤ 3rd quartile ≤ max). The effects of nominal risk factors, such as presence of hypertension, on early mortality were evaluated univariately with χ^2 test or Fisher's exact test. The effects of continuous variables, such as age, were univariately evaluated with Pearson's correlation test or with Wilcoxon rank sum tests when necessary. Combinations of risk factors were multivariably evaluated with multiple logistic regression models, using the stepwise method (for which input and output *P*-values were 0.10) to determine the best predictors. Survivorship to death, for all patients and for operative survivors only, was estimated with the Kaplan-Meier method. To assess separately those risk factors related to late survival as distinct from operative deaths, we analysed only operative survivors. Nominal risk factors for survival and for prolonged hospital stay were assessed with log-rank tests. Continuous measurable risk factors, such as age, and combinations of risk factors, both nominal and continuous, were evaluated with Cox's proportional hazard models. A *P*-value <0.05 was considered statistically significant. All tests were two-sided. The proportional hazards assumptions were verified by assessing the parallelism of survival curves for nominal risk factors and by testing the independence to time for continuous variables. Moreover, the behaviour of the Schoenfeld residuals was studied. For all continuous variables, we considered the logarithm of the variable and the polynomial until the third degree, to keep the form, which improved the model at best.

Statistical analysis was performed using the software SAS (SAS Institute Inc., Cary, NC, USA).

Table 2 *: Operative characteristics*

Variable	Patients (%)
Operative priority	
Elective	230 (74)
Urgent	58(19)
Emergent	23(7)
Cardiopulmonary bypass	303 (97)
Grafts used for coronary artery bypass	
Saphenous vein	298 (96)
Left internal mammary artery	223 (72)
Right internal mammary artery	24(8)
Radial artery	17(5)
Ascending aortic disease	
Calcification	32(10)
Atheromatous disease	22(7)
Dilatation	17(4)

RESULTS

Operative mortality and complications

Early postoperative events are listed in *Table 3.* Twenty-three patients (7.5%) developed neurological complications, including 12 permanent strokes, among which eight were ipsilateral hemispheric to the carotid surgery. Of those 23 neurological events, 15 were ipsilateral hemispheric to the endarterectomy, seven were contralateral, and one was in the distribution of the vertebral-basilar arteries. Of the seven patients who suffered a contralateral neurologic event, the non-operated internal carotid artery was characterized as occluded in two patients, with a non-significant (<50%) lesion in two patients, with a moderate (50-69%) stenosis in one patient, with a severe (>70%) stenosis in one patient, and was normal in one patient.

Cardiac complications developed in 99 patients (32%), but only seven patients suffered myocardial infarction. Arrhythmias occurred in 83 patients (27%), of whom 62 (20%) had atrial fibrillation or supraventricular tachycardia, and 21 (7%) had ventricular tachycardia. Among the nine patients who developed an atrio-ventricular bloc, none required a permanent pacemaker.

Other postoperative events, such as pulmonary complications, renal insufficiency, septicaemia, and re-operation are listed in *Table 3.*

Length of hospital stay and of intensive care unit stay averaged 17.5 ± 14.2 and 4.0 ± 5.1 days, respectively. Excluding 34 patients who stayed in the hospital for more than 30 days, average hospital stay was 14.1 ± 5.5 days, and average intensive care unit stay was 2.8 ± 2.4 days. Further summary statistics for hospital and ICU stays are given in *Table 3.*

Hospital deaths occurred in 19 patients (6%), of which 16 (5%) represent 30-day mortality *(Table 3).* Of the 19 patients, 17 were men and two were women. Three patients were operated on urgently or emergently and 16 were operated on electively. Six patients were in NYHA class III, and one was in class IV. Causes of hospital death were myocardial infarction in six patients, cerebro-vascular accident in five, respiratory insufficiency in four, and multisystem organ failure in four. Overall, stroke/death rate was 8.3% (19 deaths, including five stroke deaths, and seven stroke survivors).

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During the 1989-1995 operative period, 12/147 (8%) patients died, whereas only 7/164 (4%) patients died during the 1996-2002 operative period (*P*= 0.15).

Independent variables predicting early mortality, postoperative stroke or prolonged hospital stay on multivariable logistic regression analysis are listed in *Table 4.*

***Table 3** : Operative results*

Variable	No. of patients (%)
Deaths	19(6)
Neurological complications	
Transient ischaemic attack	6(2)
Reversible neurological deficit	5(1.5)
Permanent stroke	12(4)
Cardiac complications	
Myocardial infarction	7(2)
Arrhythmia	83 (27)
Transient atrio-ventricular bloc	9(3)
Pulmonary complications	
Prolonged mechanical ventilation (>24 h)	45 (14.5)
Pneumonia	37(12)
ARDS	4(3)
Renal insufficiency	28(9)
Dialysis	5(1.5)
Septicaemia	6(2)
Reoperation	
Sternal infection	8 (2.5)
Mediastinal bleeding	6(2)
Pericardial effusion	4(1)
Cervical haematoma	1
Hospital stay (days)	
Min ≤ 1st quartile ≤ Median ≤ 3rd quartile ≤ Max	1 ≤ 13 ≤ 15 ≤ 22 ≤ 168
ICU stay (days)	
Min ≤ 1st quartile ≤ Median ≤ 3rd quartile ≤ Max	1 ≤ 2 ≤ 3 ≤ 6 ≤ 96

ARDS, acute respiratory distress syndrome; ICU, intensive care unit.

Table 4 Variables associated with operative mortality and morbidity, by multivariable analysis

Variables	*P*-value	OR (95%CI)
Predictive of operative mortality		
Aortic calcifications	0.0003	6.3 (2.3-17.0)
Coexisting vascular disease	0.003	4.9 (1.1-21.3)
Emergent procedure	0.03	4.4 (1.2-16.6)
Predictive of postoperative CVA		
Aortic calcifications	0.004	5.2 (1.8-18.1)
Aortic dilatation	0.002	6.5 (2.0-21.1)
Predictive of prolonged hospital stay[a] (>14 days)		
Age	0.006	0.9 (0.9-1.0)
Unstable angina	0.009	0.7 (0.6-0.9)
Coexisting vascular disease	0.01	0.4 (0.2-0.8)

OR, odds ratio; CI, confidence interval; CVA, cerebro-vascular accident. [a]
The model assessed the probability of leaving the hospital, and therefore a risk ratio of less than 1% is predictive of prolonged hospital stay.

Late mortality and functional activity

Two hundred and ninety-two patients were discharged from hospital. A total of 105 patients have died at follow-up. Of the 187 long-term survivors, a majority of patients were in NYHA functional class I (142/187, 76%) or class II (32/187, 17%). Eleven patients (6%) were in NYHA class III, and only two patients (1%) were in class IV.

Five- and 10-year actuarial event-free rates for follow-up coronary and neurological complications are summarized in *Table 5*.

Ten patients had developed recurrent symptomatic coronary artery disease, treated with percutaneous coronary intervention in six patients, medical therapy in three patients, and redo CABG in one patient.

Late neurologic events developed in 11 patients and consisted in transient ischaemic attack in four patients and permanent stroke in seven patients. During follow-up, 20 patients had contralateral CEA.

Long-term survival is depicted in *Figure 1*. Median survival was 107 months for the entire population, and survival at 1, 5, and 10 years was 85.5 ± 2.0% (264 patients at risk), 72.8 ± 2.6% (162 patients at risk), and 46.1 ± 3.9% (45 patients at risk), respectively.

Independent predictors of late mortality by multiple Cox-regression are listed in *Table* 6.

Table 5 *Five- and 10-year late actuarial cardiac and neurological event-free rates*

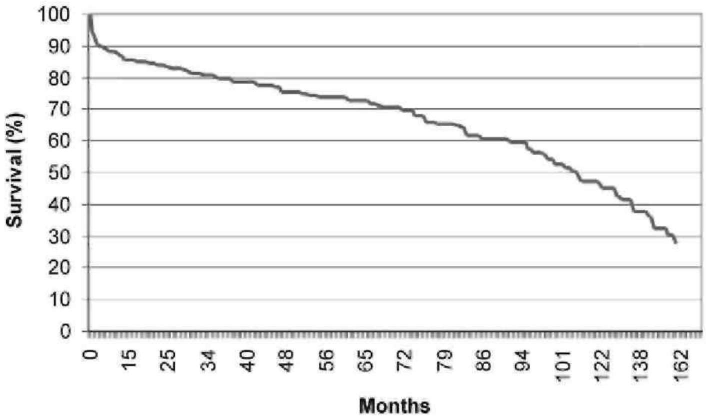
Event	Five-year freedom (%)	10-year freedom (%)
Death	79.1 ± 2.5	50.0 ± 4.2
Myocardial infarction	92.3 ± 1.8	84.5 ± 2.3
Percutaneous coronary intervention	99.4 ± 0.9	95.2 ± 2.1
Reoperative coronary grafting	99.1 ± 0.8	97.8 ± 1.4
Total stroke	98.2 ± 1.8	93.4 ± 2.4
Ipsilateral stroke	99.4 ± 0.9	95.5 ± 2.6
All events	77.8 ± 3.6	48.1 ± 5.1

Table 6 *Variables associated with long-term survival (operative survivors), by multivariable analysis*

Variables	*P*-value	HR (95%CI)
Preoperative variables		
Age	<0.0001	1.1 (1.0-1.1)
Coexisting vascular disease	0.005	2.3 (1.3-6.0)
Tobacco abuse	0.006	2.0 (1.2-3.3)
Previous cardiac surgery	0.01	2.7(1.2-6.0)
Renal insufficiency	0.04	2.7(1.0-6.9)
Operative variables		
Calcified aorta	0.002	2.3 (1.3-4.0)
Atheromatous aorta	0.004	2.2 (1.2-3.8)
Postoperative variables		
Duration of ICU stay	0.01	1.0 (1.0-1.1)

HR, hazard ratio; ICU, intensive care unit.

Figure 1 *Survival curve of all patients after concurrent coronary and carotid artery surgery.*



DISCUSSION

Concomitant carotid and coronary disease, with severe atherosclerosis damaging both arterial systems, is a current and frequent clinical problem. Indeed, prospective studies have shown that 8-14% of CABG patients have significant carotid stenosis,[7,8] whereas it has been estimated that up to 28% of patients undergoing exploration for CEA have severe correctable coronary disease.[9] Furthermore, coronary artery disease is the leading cause of both early and late mortality after CEA.[10-12]

Similarly, one of the most concerning complications after CABG is stroke. In fact, although the overall incidence of complications after CABG has decreased, the incidence of major neurological complications, such as stroke, remains relatively unchanged, being reported from 0.8 to 3.2% in retrospective studies,[13,14] and from 1.5 to 6% in prospective studies.[15,16] Postoperative stroke remains a catastrophic and costly complication of CABG, with a reported 24.8% mortality and a mean hospital stay of 28 days among survivors.[17]

Carotid vascular disease may lead to stroke during cardiopulmonary bypass via embolization from unstable plaques or by decreased cerebral blood flow distal to critical stenosis. Brener *et al*.[18] reported a 9.2% rate of stroke or transient ischaemic attacks in cardiac surgical patients with asymptomatic carotid stenosis when compared with 1.3% of patients with no carotid stenosis.

Surgical approaches for patients with coronary and carotid artery lesions

Although CEA for high-grade carotid lesions is beneficial in reducing stroke[6,19] and CABG is effective in reducing mortality from coronary artery disease,[20] the management of severe disease in both coronary and carotid arteries remains controversial.

Several therapeutic options exist for patients with concomitant carotid and coronary artery disease: CABG alone, staged CEA and CABG, reversed staged CEA and CABG, and combined procedure during the same anaesthesia.

Recently, Naylor *et al.*[21] performed a systematic review of outcomes following staged, reverse staged, and synchronous CEA and coronary artery bypass. They found that mortality was highest in patients undergoing synchronous CEA/CABG (4.6%, 95%CI 4.1-5.2), whereas reversed staged procedures (CABG followed by 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). As expected, perioperative myocardial infarction 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/stroke/myocardial infarction was 11.5% (95%CI 10.1-12.9) following synchronous procedure vs. 10.2% (95% CI 7.4-13.1) after staged CEA-CABG. Overall, these authors conclude that there was no significant difference in outcomes for staged and synchronous procedures.

It should, however, be emphasized that none of the analysed studies were completely randomized trials. Such randomized trials would have obviously been preferable to minimize patient selection bias, but, unfortunately, no such study exists in the literature. Furthermore, several studies stated that a combined approach was used in patients with severe lesions of both arterial systems, which may have resulted in greater atheromatous burden in the combined group.

Operative mortality and morbidity

We report an operative mortality rate of 6%, dropping from 8% in the first half, to 4% in the second half of the operative period examined in this study, decrease which however fails to reach statistical significance.

We sought to define risk factors that would be predictors of early mortality in this population. By univariate analysis, factors associated with operative deaths were congestive heart failure, chronic obstructive pulmonary disease, coexisting vascular disease or percutaneous coronary intervention, emergent procedure, cross-clamping and cardiopulmonary bypass times, and ascending aortic calcifications or atheromasia. However, by multivariable analysis, only proximal aortic calcifications, coexisting vasculopathy, and emergent procedure were predictors of operative mortality.

Non-elective surgery has long been known to be a risk factor for increased mortality, and the finding here is not surprising. Given the higher risk associated with urgent CABG, it could be advisable to defer CEA for asymptomatic disease to a later operation in this patient population.

On the opposite, our data indicate that neither unstable angina nor left main trunk disease were associated with increased operative mortality, and that these patients should not be denied the possible benefits of the procedure, provided they are appropriately managed. This should be emphasized because the presence of left main trunk stenosis has been shown to be significantly higher in patients with associated carotid artery disease. In their recent concomitant CABG/CEA series, Zacharias *et al.*[22] found a 27% incidence of left main disease, as opposed to 17% in their remaining CABG population. We report here an incidence of left main disease of 31%, when compared with 16% in our regular CABG population.

We report a permanent stroke rate of 4%. Proximal aortic dilatation or calcifications were associated with stroke, reflecting the risk of atheroembolization during cardiac surgery in patients with a diseased proximal aorta.

As an element of comparison, the incidence of ascending aortic lesions was 8.7% in our general CABG population operated during the same period, with a perioperative permanent stroke rate of 3.4% among those patients.

Risk factors for stroke during CABG that are frequently quoted in the literature, in addition to carotid artery stenosis, are ascending aortic atherosclerosis, previous stroke or transient ischaemic attack, age, hypertension, diabetes, smoking, peripheral vascular disease, left ventricular dysfunction, left main coronary artery disease, renal failure, and increased cardiopulmonary bypass time.[7,8,17,23-26] Among these demonstrated risk factors, ascending aortic atherosclerosis is probably the most important. In our study, proximal aortic atheromasia was associated both with operative mortality and with stroke.

John *et al.*[17] retrospectively reviewed 19 224 CABG patients undergoing surgery at 31 hospitals in New York State in 1995. Aortic calcifications were the leading risk factor for stroke, with an odds ratio of 3.0. Atherosclerosis of the ascending aorta leads to stroke via macroembolization to the cerebral vessels. Macroemboli are most likely to occur during aortic manipulation, such as canulation, cross-clamping, or construction of proximal anastomoses, but may also occur at other times because of the sandblasting effect of cardiopulmonary bypass.

We cannot rule out that a delayed procedure, postponing CEA in patients with diseased ascending aorta, at highest risk of stroke, and to stage it after CABG would have yielded better neurological results. To determine the optimal treatment for severe carotid stenosis in those patients would require the comparison of a group of patients with ascending aortic disease undergoing concurrent surgery and another group with delayed strategy, which is beyond the scope of this study.

However, we believe that prevention of non-carotid related stroke with the use of epiaortic imaging before clamping, avoidance of aortic clamping or cannulation, and the use of off-pump technique may be as important factors as concomitant CEA in limiting adverse neurological events.

Late survival and events

For hospital survivors, survival at 1, 5, and 10 years was 93.4 ± 1.5%, 79.1 ± 2.5%, and 50.0 ± 4.2%, respectively. These survival rates are good and comparable with other studies,[27,28] although long-term results are scarce.

We also sought to define risk factors that would be predictors of late mortality in our population. Significant multivariable predictors of late deaths were coexisting vasculopathy, age, renal insufficiency, previous cardiac surgery, tobacco abuse, calcified or atheromatous aorta, and duration of intensive unit stay. These findings emphasize that extensive atheromatous arterial disease, damaging not only the carotid and coronary arteries, but also the ascending aorta and the peripheral vessels, is a harbinger of poor outcome.

Our long-term results, particularly the excellent freedom from late neurological events, certainly support the combined operative approach. In 1995, Akins *et al.*[27] also reported a 10-year freedom from late ipsilateral stroke of 96.4 ± 2.2% after concomitant carotid and coronary artery surgery.

Study limitations

Because of the retrospective nature of this study, the problem of missing data should be fully addressed, although rare and always at random. When it occurred for a continuous variable, the missing data was replaced by the median value of this variable. We have also checked our results without replacing a missing data with the median value of this continuous variable, simply deleting the patient. Doing so, our results were not different, the same variables remaining statistically significant, with only very minor changes in estimates and P-values.

Such a replacement not being possible for a qualitative variable, the patient was excluded when such a data was unavailable. Certainly, by simply excluding patients with missing data, the population that is being included is different at every stage of the model building procedures. Therefore, when comparing the different models in the stepwise model building procedures, it is impossible to distinguish the effect of the added (or deleted) variable from a possible effect of a different population. However, the number of patients with missing data was always lower than 3%, for any variable. Moreover, for the multivariable model, the estimate and P-values for the significant variables were obtained by running the program again, with only the significant variables introduced in the final model, after the selection step. The method used for model validation is described in Appendix 2.

Perspectives

A new treatment option for patients with combined carotid and coronary vascular disease is CABG plus carotid angioplasty/stenting.[29,30] The theoretical advantages of carotid stenting is that it is less invasive and does not require a general anaesthesia, therefore decreasing myocardial risks. It should, however, be emphasized that carotid stenting is relatively new and that the long-term results are unknown. Therefore, in our opinion, only patients who are considered at unacceptable risk for CABG plus CEA, either by synchronous or delayed procedures, should currently be considered for carotid stenting. However, indications for carotid stenting could potentially be enlarged in the future if long-term results are good.

Finally, as our data may suggest, the clinical question of the possible benefits of combined procedures compared with staged procedures for concomitant coronary and carotid artery disease could best be addressed in trials where patients are randomized to the two treatment strategies. Indeed, one cannot disprove the possibility that the same set of patients may have had similar or superior results using a staged surgical approach.

Such a prospective study would require a multi-institutional effort, to achieve the appropriate sample size. For example, based on an expected incidence of stroke or death of 7.5%, as well as an α-level of 0.05 and a β-level of 0.20, a sample size of 1500 patients per group would be required to detect a relative risk reduction of 33%. Therefore, such a large prospective trial would be difficult to achieve, and a retrospective analysis with a rigorous and well-described inclusion criterion, comparing several approaches performed by the same surgeons, would also yield a lot of informations. However, as most surgical teams use either the combined or the staged approach, and not both, such data are also very difficult to collect.

CONCLUSIONS

Stroke is a devastating complication of coronary artery bypass surgery. Carotid stenosis is among the important causes of stroke during CABG, and several treatment alternatives exist for patients with concomitant carotid and coronary artery disease. Synchronous CEA/CABG offers the economic benefit of avoiding two separate procedures and hospitalizations, with a combined death/ stroke/myocardial infarction risk ranging from 6 to 12%, and good long-term freedom from coronary and neurologic events.

Our data also concur with other studies to demonstrate that proximal aortic atheromatous disease is a major cause of stroke during CABG, and that every effort should be made to address this problem. Potential solutions that should be considered are the use of epiaortic imaging before clamping, avoidance of aortic clamping or cannulation, the use of off-pump technique for myocardial revascularization, and carotid stenting. In addition, extensive atheromatous arterial disease remains a harbinger of poor long-term outcome, and aggressive treatment of atheromatous risk factors is of paramount importance in those patients.

Conflict of interest: none declared.

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Appendix 1

Variables tested for operative events and long-term survival

Preoperative variables
- Sex
- Age
- Stable angina
- Unstable angina
- Previous myocardial infarction
- Congestive heart failure
- NYHA functional class
- Diabetes mellitus
- Hypertension
- Hypercholesterolaemia
- Tobacco abuse
- Chronic obstructive pulmonary disease
- Renal insufficiency
- Previous cardiac surgery
- Permanent cardiac pacing
- Previous percutaneous coronary intervention
- Previous vascular surgery
- Coexisting vascular disease
- Neurologic symptoms
- Contralateral carotid artery occlusion
- Left main disease
- Number of diseased coronary arteries

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Ejection fraction
End-systolic volume
End-diastolic pressure

Operative variables
Operative priority
Cardiopulmonary bypass
Cardiopulmonary bypass time
Aortic cross-clamping time
Cardiopulmonary bypass temperature
Number of CABGs
Calcified aorta
Atheromatous aorta
Dilated aorta
No-touch aorta technique

Postoperative variables (only tested for long-term survival)
Neurological complications
Myocardial infarction
Arrhythmia
Transient atrio-ventricular bloc
Prolonged mechanical ventilation (>24 h)
Pneumonia
ARDS
Renal insufficiency
Septicaemia
Reoperation
Length of hospital stay
Length of ICU stay

Appendix 2

Model validation

First, the interpretation of the coefficient for each model can be performed, because we have no problem of co-linearity (the hazard ratios for each variable are in the same order in the multi-variable model and the univariate model). Secondly, to check if chance predictors were included in the final model, we took 100 different samples of 250 randomly selected patients out of the full population of 311 patients for the models of *Table 4,* and 230 out of 285 patients for late survival. For each sample, we did a stepwise selection. For the model studying the predictors of operative deaths, we found 70% of the models, which contained at least two of the three predictors. Further, each predictor was almost equally represented. For the model studying postoperative CVA, we had 81 % of the models with at least one of the two variables. Again each predictor was almost equally represented. For the model studying the duration of hospitalization, we had 45% of the models with at least two of the three predictors. For the model studying late survival, we had 57% of the models with at least five of the eight predictors *(Table 6)* and we reached 86% for at least four predictors.

The logistic model studying the operative death improved by 11% the prediction of death (positive predictive value was 18.5%, prevalence 7.39%, and negative predictive value 95%). The logistic model studying postoperative CVA improved by 42% the prediction of CVA (positive predictive value was 50%, prevalence 7.71%, and negative predictive value 74%).