Prognostic Impact of Asymptomatic Carotid Artery Stenosis in Patients Undergoing Coronary Artery Bypass Grafting

Short title: Asymptomatic carotid artery stenosis and CABG

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What does this study/review add to the existing literature and how will it influence future clinical practice

This study showed that, among patients with asymptomatic carotid artery stenosis undergoing isolated coronary artery bypass grafting, the risk of postoperative stroke is significant only in patients with a stenosis ≥90%, but the incidence of stroke in these patients is rather low (7.0%). Since asymptomatic, severe carotid artery stenosis has a low prevalence and when left untreated is associated with a relatively low risk of stroke, preoperative screening of asymptomatic carotid artery stenosis before coronary artery bypass grafting may not be justified.

Abstract

Objectives: The aim of this study was to evaluate the prognostic impact of asymptomatic, untreated carotid artery stenosis (CS) in patients undergoing isolated coronary artery bypass grafting (CABG).

Design: Post hoc analysis of data from a prospective multicenter observational study.

Methods: This study included patients without history of stroke or transient ischemic attack from the multicenter E-CABG registry who were screened for CS before isolated CABG.

Results: Among 2813 patients screened by duplex ultrasound and who did not undergo carotid intervention for asymptomatic CS, 11.1% had a stenosis of 50-59%, 6.0% of 60-69%, 3.1% of 70-79%, 1.4% of 80-89%, 0.5% of 90-99%, and 1.1% had carotid occlusion. In the screened population postoperative stroke occurred in 25 patients (0.9%), with an incidence of 1.5% among patients with CS ≥50% (n=649). Preoperative screening had not found a relevant CS in 15 out of 25 patients suffering stroke after CABG. Brain imaging identified cerebral ischemic injury in 20 patients, which was bilateral in five patients (25%), ipsilateral to a CS ≥50% in six (30%) and ipsilateral to a CS ≥70% in three (15%). In univariate analysis, the severity of CS was associated with a significantly increased risk of stroke (CS <50%, 0.7%; 50-59%, 1.0%; 60-69%, 0.6%; 70-79%, 1.2%; 80-89%, 5.1%; 90-99%, 7.7%; occluded, 6.7%, p<0.001). In multivariate analysis, a CS of 90-99% (OR 12.03, 95%CI 1.34-108.23) and the presence of an occluded internal carotid artery (OR 8.783, 95%CI 1.820-42.40) were independent predictors of stroke along with urgency of the procedure, severe-massive bleeding according to the E-CABG classification and the presence of a porcelain ascending aorta.

Conclusions: Among screened patients with untreated asymptomatic patients, CS ≥90% was an independent predictor of postoperative stroke. Since this condition has a low prevalence and when left untreated is associated with a relatively low rate of stroke, preoperative screening of asymptomatic CS before CABG may not be justified.

Keywords: Coronary artery bypass grafting; stroke; carotid artery stenosis.

Introduction

Stroke is the Achille's heel of coronary artery bypass grafting (CABG) (1). Carotid artery stenosis (CS) is thought to play a direct role in the occurrence of neurological complications after adult cardiac surgery (2). However, the mechanisms underlying the development of postoperative stroke are multiple and mostly of cardiac origin since embolism may occur from the left-sided cavities of the heart as a result of atrial fibrillation (3) or myocardial infarction (4). Manipulation of a diseased ascending aorta is also responsible for embolic stroke (5). Furthermore, there is some evidence on the significant role of blood transfusion on the development of stroke after cardiac surgery and interventional cardiology procedures (6). The uncertainty regarding the impact of CS on the development of postoperative stroke and the risk of medico-legal litigation in case on unscreened carotid arteries prompted several cardiac surgery centers to adopt a policy of preoperative duplex ultrasound screening and, when indicated, by invasive treatment of CS, also in patients without prior neurological symptoms. However, the efficacy of such a strategy is not demonstrated. In the present study we evaluated the prognostic impact of untreated asymptomatic CS in patients undergoing isolated CABG.

Material and Methods

Patient Population and Data Collection

This is a post hoc analysis of the prospective, multicenter European Coronary Artery Bypass Grafting (E-CABG) registry. This registry enrolled patients undergoing isolated CABG at 16 European centers of cardiac surgery (Besançon, France; Catanzaro, Italy; Genoa, Italy; Hamburg, Germany; Leicester, UK; Milan, Italy; Nuremberg, Germany; Naples, Italy; Oulu, Finland; Parma, Italy; Pedara, Italy; Rennes, France; Rome, Italy; Stockholm, Sweden; Trieste, Italy; Verona, Italy). This study is registered in Clinicaltrials.gov (Identifier: NCT02319083). The study protocol and the definition criteria of baseline-, operative and postoperative variables are described elsewhere (7). The Institutional Review Board or Ethical Committee of the participating centers approved this study. For

the purpose of this study, patients undergoing isolated CABG without history of stroke or transient ischemic attack (TIA) and not undergoing any concomitant carotid endarterectomy or stenting were included in this analysis. Patients with any prior stroke or TIA and previous or recent carotid intervention were excluded from this study.

Patients underwent duplex ultrasound of the carotid arteries upon admission for isolated CABG according to Institutional policies. The definition criteria to grade the stenosis of the carotid arteries was not collected in this prospective registry, were based on local practice and interpretation, and were not centrally adjudicated. The severity of CS was stratified as follows: CS <50%, 50-59%, 60-69%, 70-79%, 80-89%, 90-99%, and carotid occlusion.

Outcome End-points

Stroke occurring after CABG during the index hospitalization was the primary end-point of this study. A composite outcome including stroke and/or all-cause death occurred during the index hospital stay was the secondary end-point of this study. Stroke was defined as any focal or global neurological syndrome occurring during the in-hospital stay caused by ischemia not resolving within 24 hours (8). The diagnosis and nature of stroke was made on the basis of findings at computed tomography (CT) and/or magnetic resonance imaging of the brain and confirmed by a neurologist. Stroke was defined transitory when neurological signs and symptoms disappeared before discharge, otherwise it was defined as permanent.

Statistical Analysis

Statistical analyses were performed using the SPSS statistical software v. 24.0 (IBM Corporation, New York, USA) and the Stata statistical software v. 14.2 (StataCorp LLC, Texas, USA). Mann-Whitney U-test, Fisher's exact test and Chi-square test were used for univariate analysis. Ordinal regression was used to identify risk factors of CS of increasing severity. Logistic regression with the backward

method was used to identify the risk factors associated with postoperative stroke and/or death, including covariates with $p<0.05$ in univariate analysis. Non-parsimonious logistic regression was used to adjust the impact of CS on the outcomes of interest for the following covariates: age, gender, anemia, estimated glomerular filtration rate, dialysis, P2Y12 receptor antagonists pause less 5 days, poor mobility, extracardiac arteriopathy, diabetes, preoperative atrial fibrillation, pulmonary disease, left ventricular ejection fraction ≤50%, recent myocardial infarction, urgency of the procedure, critical preoperative state, off-pump surgery, porcelain aorta, bilateral internal mammary artery grafting and untouched ascending aorta. All tests were two-sided and $p<0.05$ was set for statistical significance.

Results

Out of 7352 consecutive patients who underwent isolated CABG from January 2015 to May 2017 and enrolled in the E-CABG registry, 231 patients (7.4%) had a history of stroke or TIA and were excluded from the analysis (Fig. 1). Thirty-nine patients without history of stroke or TIA underwent concomitant carotid intervention and their stroke rate was 7.7%. Five of these patients underwent percutaneous carotid intervention and none suffered postoperatively stroke.

Asymptomatic screened patients

Complete data on the status of the internal carotid arteries and the method of preoperative imaging was available in 2813 patients without history of stroke or TIA who did not undergo any carotid artery intervention concomitantly or immediately before the index CABG procedure (Fig. 1). The characteristics of these patients are summarized in Table 1. Among these patients, 311 (11.1%) had a CS of 50-59%, 170 (6.0%) of 60-69%, 86 (3.1%) of 70-79%, 39 (1.4%) of 80-89%, 13 (0.5%) of 90-99%, and 30 (1.1%) had carotid occlusion. Among the latter, four patients (13.3%) had a contralateral CS ≥70%.

Ordinal regression analysis showed that advanced age (coefficient 0.043, 95%CI 0.032-0.054), SYNTAX score (coefficient 0.016, 95%CI 0.009-0.024), decreased baseline hemoglobin (coefficient -

0.010, 95%CI -0.016 - -0.005) and increased baseline platelets count (coefficient 0.003, 95%CI 0.002-0.004) were independent predictors of increasing severity of CS.

Primary outcome: incidence of stroke after CABG

In the screened population without history of stroke and/or TIA (n=2813), postoperative stroke occurred in 25 patients (0.9%), with an incidence of 1.5% among patients with CS ≥50% (n=649) (p=0.44). Therefore, preoperative screening had not found a relevant CS in 15 out of 25 patients suffering stroke after CABG. Baseline characteristics and operative data of patients who suffered postoperative stroke are summarized in Table 1. CT of the brain was performed in all patients, except one with critical hemodynamic conditions. In four patients, CT findings were negative. Among 20 patients with signs of brain ischemic injury, the ischemic lesions were bilateral in five patients (25%) and ipsilateral to a CS ≥50% in six patients (30%). Stroke was ipsilateral to CS ≥70% in three patients (15%) (Tab. 2).

Epiaortic ultrasound was employed in only 0.8% of patients. This prevented the identification of atherosclerotic plaques in the ascending aorta, which may formally contraindicate any aortic cannulation or clamping maneuvers. Furthermore, only 10.8% of patients had their operation performed without manipulation of the ascending aorta. In 13 patients (54.2%) with porcelain aorta the aorta was not left untouched and these maneuvers might have resulted in postoperative stroke in at least two patients without ipsilateral CS (Tab. 2).

In univariate analysis, the severity of internal carotid artery stenosis was associated with a significantly increased risk of stroke (Tab. 3). In multivariate analysis, a stenosis of the internal carotid artery of 90-99% (crude rate, 1/13, 7.7%, 95%CI 1.4%-33.3%; OR 12.034, 95%CI 1.338-108.230) and the presence of an occluded internal carotid artery (crude rate, 2/30, 6.7%%, 95%CI 1.9%-21.3%; OR 8.783, 95%CI 1.819-42.398) were associated with a significantly higher risk of postoperative stroke along with urgency of the procedure, severe-massive bleeding according to the E-CABG classification and the presence of a porcelain ascending aorta (Hosmer-Lemeshow test: p=0.67; area under to ROC

curve, 0.75, 95%CI 0.63-0.86) (Tab. 4). When emergency procedures were excluded from this analysis, a stenosis of the internal carotid artery of 90-99% (OR 16.81, 95%CI 1.99-142.00) and the presence of an occluded internal carotid artery (OR 10.18, 95%CI 2.21-52.08), but not less severe CS, were still associated with a significantly higher risk of postoperative stroke.

Secondary outcome: incidence of stroke and/or hospital death after CABG

In the screened patient population (n=2813), postoperative stroke and/or hospital death occurred in 60 patients (2.1%), with an incidence of 3.2% among patients with CS ≥50% (p=0.027). Only 6 patients (24%) out of those suffering a stroke (n=25) died of consequences related to stroke. A further 35 patients died of unrelated causes. The severity of internal carotid artery stenosis was associated with a significantly increased risk of stroke and/or hospital death (Tab. 3). Furthermore, baseline hemoglobin (p=0.005), extracardiac arteriopathy (p=0.002), dialysis (p=0.043), pulmonary disease (p=0.047), recent myocardial infarction (p=0.003), urgency of the procedure (p<0.001), critical preoperative state (p=0.019), porcelain aorta (p=0.004), amount of postoperative blood loss (p=0.006), amount of transfused red blood cell units (p<0.001) and E-CABG bleeding grades 2-3 (p<0.001) were associated with stroke and/or hospital death in univariate analysis. When adjusted for these covariates, the severity of internal carotid artery stenosis was not associated with a significantly increased risk of stroke or hospital death either in the overall series (p=0.466) or after elective/urgent CABG (p=0.554).

Discussion

The main findings of this multicenter study are: 1) duplex ultrasound identified CS ≥70% in 6.0%, CS ≥80% in 2.9% and carotid occlusion in 1.1% of the screened patients; 2) the rate of stroke among screened patients without history of stroke or TIA was rather low (0.9%), but one fourth of strokes were fatal; 3) among patients with signs of brain ischemic injury at brain imaging, the lesions were bilateral in 25% of cases and ipsilateral to a CS ≥70% in 15% of patients; 4) in multivariate analysis, CS ≥90% or carotid occlusion, but not less severe CS, were associated with an increased risk of

stroke; 5) beside the limited prevalence of carotid occlusion, only 13% of patients had a contralateral CS ≥70%, which might be considered for treatment; 6) severe perioperative bleeding was predictive of stroke after CABG; 7) the status of the ascending aorta was seldom investigated by epiaortic ultrasound in these patients and diseased ascending aorta was often not left untouched becoming an independent predictor of postoperative stroke.

The present analysis showed that carotid intervention in patients with asymptomatic CS resulted in a rate of stroke (7.7%) which was similar to untreated patients with CS of 90-99% (7.7%), who are the ones at highest risk of neurological complications. The rather low risk of stroke in asymptomatic, untreated patients with CS should be viewed also in the light of a modest prevalence of severe CS. Therefore, these findings provide a strong argument against a policy of ultrasound screening of CS prior to CABG. Importantly, a number of patients had carotid occlusions, which infrequently was associated with a contralateral significant CS. These results strengthen the current evidence on an increased risk of stroke in patients undergoing CABG with concomitant carotid intervention (9-11).

Multivariate analysis and evaluation of individual data of patients who suffered postoperative stroke shed further light on the multifactorial nature of postoperative stroke after adult cardiac surgery and the limited role of CS in the occurrence of such a severe complication. Indeed, prior observational and randomized studies as well as several pooled analyses (9-11) focused on the role of carotid intervention in these patients without considering that manipulation of the ascending aorta (12) and cardioembolic events from the left cardiac cavities related to postoperative atrial fibrillation (13) could be the main determinants of postoperative neurological events in patients undergoing cardiac surgery. Indeed, in this series, only 30% of patients with ischemic brain injury at computed tomography had a stroke ipsilateral to a CS ≥50%, 25% of patients had bilateral brain ischemic lesions and not all strokes occurred in territories perfused by the internal carotid artery (Tab. 2). These findings suggest that cardioembolism may be responsible for most of these events. Previous studies evaluated the incidence of stroke in patients with CS undergoing off-pump versus on-pump CABG. Although off-pump surgery can be associated with a significant reduced risk of stroke (14), its effects are most likely

related to a limited or no manipulation at all of the ascending aorta and its benefits could be more evident when epiaortic ultrasound is used to guide the revascularization strategy (14). In this regard, the present series showed a pitfall in the treatment of these patients as epiaortic ultrasound was employed in only 0.8% of patients: this prevented the identification of atherosclerotic plaques in the ascending aorta, which may formally contraindicate any aortic cannulation or clamping maneuvers. Furthermore, only 10.8% of patients had their operation performed without manipulation of the ascending aorta. It is worth noting that in some cases even in patients with porcelain aorta detected by manual palpation, the aorta was not left untouched and, in absence of ipsilateral severe CS, these maneuvers might have resulted in postoperative stroke (Tab. 2).

Interestingly, this analysis confirmed that perioperative bleeding is an independent predictor of postoperative stroke in patients undergoing CABG (6), such a risk being most pronounced in patients with severe-massive perioperative bleeding. In this series, one fourth of patients who suffered stroke had severe-massive bleeding as defined by reoperation for bleeding and/or transfusion of ≥4 units of red blood cells. It is unclear whether stroke may be the result of a prothrombotic status induced by the use of blood products or triggered by a temporary or prolonged decrease of oxygen delivery secondary to bleeding-related hypotension and anemia. Still, severe bleeding is a preventable condition (15) and meticulous surgical technique, adequate surgical hemostasis and optimization of patient-blood management are expected to prevent neurological and other major adverse events after cardiac surgery.

This analysis has some limitations, which should be acknowledged. First, the E-CABG registry is a multicenter prospective study and ultrasound screening of CS was not performed in all centers. Second, the estimation of the severity of CS was not assessed in an ultrasound corelab and these analyses might therefore have been biased by interinstitutional and interobserver variability of duplex ultrasound measurements. Also the definition criteria of CS possibly varied between institutions, even if we believe that CS was uniformly graded by the Society of Radiologists in Ultrasound Consensus criteria (16). Third, epiaortic ultrasound was performed in a very limited number of patients and this

prevents more conclusive results on the mechanisms underlying the development of stroke in these patients. Fourth, the lack of data on the ultrasonographic characteristics of the carotid plaque prevents an analysis of the potential embolic nature of stroke originating from the carotid arteries. Fifth, the lack of data of intra- and postoperative hemodynamics prevents a more in-depth analysis of unstable hemodynamic condition as a determinant of the neurological events. Finally, this data does not clarify whether CS might have contributed to contralateral stroke in presence of diffuse cerebrovascular disease and incomplete circle of Willis.

Conclusions

Among screened patients with asymptomatic CS, the risk of hospital stroke after isolated CABG is significant only in patients with a stenosis ≥90%. Since this condition has a low prevalence and when left untreated is associated with a relatively low rate of stroke, preoperative screening of asymptomatic CS before CABG may not be justified. Instead, avoiding manipulation of diseased ascending aorta and avoidance of excessive bleeding may be more effective measures to prevent stroke after CABG.

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Table 1. Baseline characteristics, operative variables, outcomes and predictors of postoperative in univariate and multivariate analysis.

	No postop. stroke 2788 pts	Postop. stroke 25 pts	Univariate analysis p-value
Baseline variables			
Age (years)	67.4±9.4	68.7±8.2	0.565
Female	474 (17.0)	3 (12.0)	0.788
Anemia	724 (26.0)	6 (24.0)	0.823
eGFR (mL/min/1.73 m^2)	83±27	79±31	0.535
Dialysis	37 (1.3)	0	1.000
Hypertension	2445 (87.7)	22 (88.0)	1.000
Atrial fibrillation	202 (7.2)	2 (8.0)	0.855
Diabetes	997 (35.8)	9 (36.0)	0.980
Poor mobility	53 (1.9)	0	1.000
Recent myocardial infarction	975 (35.0)	12 (48.0)	0.174
Pulmonary disease	328 (11.8)	4 (16.0)	0.527
Extracardiac arteriopathy	872 (31.3)	12 (48.0)	0.073
Prior percutaneous coronary intervention	547 (19.6)	4 (16.0)	0.650
Prior cardiac surgery	17 (0.6)	1 (4.0)	0.149
LVEF≤50%	843 (30.2)	6 (24.0)	0.499
Syntax score	29±12	32±12	0.246
No. of diseased vessels	2.6±0.6	2.8±0.5	0.240
Out-of-hospital cardiac arrest	17 (0.6)	0	1.000
Urgency of the procedure			**0.001**
Urgent	1111 (39.9)	12 (48.0)	
Emergency	67 (2.4)	5 (20.0)	
Critical preoperative state	170 (6.1)	3 (12.0)	0.196
2PY12 inhibitor, pause <5 days	344 (12.3)	3 (12.0)	1.000
Oral anticoagulants	25 (0.9)	0	1.000
Severity of carotid stenosis			**<0.0001**
<50%	2149 (77.1)	15 (60.0)	
50-59%	308 (11.0)	3 (12.0)	
60-69%	169 (6.1)	1 (4.0)	
70-79%	85 (3.0)	1 (4.0)	
80-89%	37 (1.3)	2 (8.0)	
90-99%	12 (0.4)	1 (4.0)	
100%	28 (1.0)	2 (8.0)	
EuroSCORE II (%)	2.8±3.5	5.5±11.8	0.081
Operative variables			
Off-pump surgery	421 (15.1)	3 (12.0)	1.000
Epiaortic ultrasond	22 (0.8)	0	1.000
Porcelain ascending aorta	23 (0.8)	2 (8.0)	**0.001**
Aorta left untouched	302 (10.8)	1 (4.0)	0.511
Outcomes			
Postop. IABP or ECMO	146 (5.2)	4 (16.0)	**0.041**
Postop. atrial fibrillation	14 (0.7)	11 (1.4)	0.062
Nadir hemoglobin (g/L)	99±16	97±16	0.610
Nadir hematocrit (%)	29.5±4.5	28.9±4.4	0.459
RBC units transfused, intraop.	0.3±0.7	0.5±1.0	0.290
RBC units transfused, overall	1.1±2.2	3.2±5.2	**0.019**
E-CABG bleeding grades			**<0.0001**
0	1891 (67.8)	11 (44.0)	
1	736 (26.4)	8 (32.0)	
2	148 (5.3)	4 (16.0)	
3	13 (0.5)	2 (8.0)	
E-CABG bleeding grades 2-3	161 (5.8)	6 (24.0)	**0.021**

Continuous variables are reported as means and standard deviation and nominal variables as counts and percentages. Clinical variables are according to the EuroSCORE II definition criteria. eGFR: glomerular filtration estimated according to the MDRD equation; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; ECMO: extracorporeal membrance oxygenation; E-CABG: European registry of Coronary Artery Bypass Grafting**.** In bold are statistical significances.

Table 2. Characteristics of patients who suffered postoperative stroke after coronary surgery.

No.	Age (years)	Euro SCORE 2 (%)	Carotid stenosis right side (%)	Carotid stenosis left side (%)	Urgency	Off-pump surgery	Porcelain aorta	Untouched aorta	Severe-massive bleeding	Permanent stroke	Death	Neurological deficit	Site	Side of the brain affected	Stroke ipsilateral to arotid stenosis ≥50%
1	71	7.2	80	60	Emergency	Yes	No	Yes	Yes	Yes	Yes	Comatous state	Negative CT findings	NA	-
2	66	8.1	80	70	Emergency	No	No	No	No	Yes	No	Hemiparesis	Temporo-frontal areas	Right	Yes
3	71	60.8	70	70	Emergency	Yes	No	No	Yes	Yes	No	Hemiparesis, vertigo	Temporal area	Right	Yes
4	70	2.9	0	0	Emergency	No	No	No	Yes	Yes	Yes	Tetraparesis	Cerebellum, pontomesencefalic region	Left	No
5	52	2.1	0	0	Emergency	No	No	No	No	No	No	Hemiparesis	Thalamic region	Right	No
6	68	3.5	100	0	Urgent	No	No	No	No	Yes	No	Hemiparesis	Temporo-occipital areas	Right	Yes
7	57	1.9	55	40	Urgent	No	No	No	Yes	Yes	Yes	Hemiparesis	CT not performed because of unstable conditions	NA	-
8	78	3.2	0	0	Urgent	No	No	No	No	Yes	Yes	Tetraplegia	Cerebellum	Bilateral	No
9	62	1.0	55	60	Urgent	No	No	No	No	No	No	Comatous state	Thalamus area, nucleo-basal area	Left	Yes
10	68	5.2	50	55	Urgent	No	No	No	Yes	Yes	No	Hemiparesis	Cerebellum, frontal area	Left	Yes
11	75	1.9	30	30	Urgent	No	Yes	No	No	No	No	Hemiparesis	Occipital area	Left	No
12	67	2.2	30	30	Urgent	No	No	No	No	Yes	No	Hemiparesis, dysarthry	Temporo-frontal areas	Right	No
13	84	10.8	30	0	Urgent	No	No	No	Yes	Yes	No	Hemiparesis, aphasia	Anterior horn of the lateral ventricle, pons, basal ganglia	Bilateral	No
14	54	1.2	0	0	Urgent	Yes	No	No	No	No	No	Tetraplegia	Occipital area	Bilateral	No
15	68	2.2	0	0	Urgent	No	No	No	No	No	No	Aphasia	Negative CT findings	NA	-
16	61	1.0	0	0	Urgent	No	No	No	No	Yes	No	Hemiparesis, dysphasia	Temporo-frontal areas	Left	No
17	70	7.8	0	0	Urgent	No	No	No	No	Yes	No	Hemiparesis	Occipital, parietal and frontal areas	Bilateral	No
18	70	2.7	100	30	Elective	No	No	No	No	No	No	Aphasia	Negative CT finding	NA	-
19	78	4.2	90	80	Elective	No	No	No	No	No	No	Aphasia	Temporo-frontal areas	Left	Yes
20	82	4.2	50	0	Elective	No	Yes	No	No	Yes	Yes	Hemiparesis	Temporo-frontal areas	Left	No
21	72	1.1	30	30	Elective	No	No	No	No	No	No	Hemiparesis	Frontal area	Right	No
22	70	0.7	30	30	Elective	No	No	No	No	Yes	No	Hemiparesis, dysphasia	Occipital area	Bilateral	No
23	74	1.0	30	0	Elective	No	No	No	No	Yes	No	Hemiparesis, dysarthry	Negative CT findings	NA	-
24	73	0.7	0	0	Elective	No	No	No	No	Yes	Yes	Aphasia	Temporo-parietal areas	Left	No
25	56	0.7	0	0	Elective	No	No	No	No	No	No	Hemiparesis, dysarthry	Frontal area	Left	No

Table 3. Outcomes according to the severity of carotid stenosis.

Severity of carotid stenosis	No. of patients (%)	Stroke (%)	p-value	Stroke and/or hospital death (%)	p-value
<50%	2164 (76.9)	15 (0.7)	<0.001	39 (1.8)	0.029
50-59%	311 (11.1)	3 (1.0)		8 (2.6)	
60-69%	170 (6.0)	1 (0.6)		6 (3.5)	
70-79%	86 (3.1)	1 (1.2)		1 (1.2)	
80-89%	39 (1.4)	2 (5.1)		3 (7.7)	
90-99%	13 (0.5)	1 (7.7)		1 (7.7)	
100%	30 (1.1)	2 (6.7)		2 (6.7)	
<70%	2645 (94.0)	19 (0.7)	0.025	53 (2.0)	0.099
70-99%	138 (4.9)	4 (2.9)		5 (3.6)	

Table 4. Independent predictors of postoperative stroke after isolated coronary artery bypass grafting.

Covariates	Multivariate analysis OR, 95%CI
Urgency of the procedure	
Elective	Reference
Urgent	1.815, 0.723-4.554
Emergency	**10.912, 3.237-36.782**
Severity of carotid stenosis	
<50%	Reference
50-59%	1.008, 0.276-3.677
60-69%	0.706, 0.088-5.636
70-79%	1.188, 0.146-9.692
80-89%	4.925, 0.982-24.708
90-99%	**12.034, 1.338-108.230**
100%	**8.783, 1.819-42.398**
Porcelain ascending aorta	**10.912, 3.237-36.782**
E-CABG bleeding grades 2-3*	**3.251, 1.194-0.853**

In bold are statistical significances. E-CABG: European Coronary Artery Bypass Grafting registry; *: reoperation for excessive bleeding and/or transfusion of >4 units of red blood cells.

Legend to figure

Figure 1. Flow chart of the study cohort.