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Early and long-term results of carotid endarterectomy in diabetic patients

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Purpose: To evaluate results of carotid endarterectomy (CEA) in diabetic patients in a large single-center experience.

Methods: Over a 13-year period ending in December 2008, 4305 consecutive CEAs in 3573 patients were performed. All patients were prospectively enrolled in a dedicated database. Interventions were performed in diabetic patients in 883 cases (20.5%; group 1) and in nondiabetics in the remaining 3422 (79.5%; group 2). Early results in terms of 30-day stroke and death rates were analyzed and compared. Follow-up results were analyzed with Kaplan-Meier curves and compared with log-rank test.

Results: Diabetic patients were more likely to be females and to have coronary artery disease, peripheral arterial disease, hyperlipemia, and arterial hypertension than nondiabetics. There were no differences between the two groups in terms of preoperative clinical status or degree of carotid stenosis. Interventions were performed under general anesthesia with somatosensory-evoked potentials (SEPs) monitoring in 67% of the patients in both groups, while the remaining interventions were performed under clinical monitoring. Shunt insertion (14% and 11%, respectively) and patch closure rates (79% and 76%, respectively) were similar between the two groups. There were no differences between the two groups in terms of neurological outcomes, while the mortality rate was higher in group 1 than in group 2 ($P = .002$; odds ratio [OR], 3.5; 95% confidence interval [CI], 1.5-8.3); combined 30-day stroke and death rate was significantly higher in group 1 (2%) than in group 2 (0.9%; $P = .006$; 95% CI, 1.2-3.9; OR, 2.2). At univariate analysis, perioperative risk of stroke and death in diabetic patients was significantly higher in patients undergoing intervention with SEP cerebral monitoring (95% CI, 0.9-39.9; OR, 5.9; $P = .01$), and this was also confirmed by multivariate analysis (95% CI, 1.1-23.1; OR, 8.3; $P = .04$). The same analysis in nondiabetics demonstrated that again the need for general anesthesia significantly increased perioperative risk, but this was not significant at multivariate analysis. Follow-up was available in 96% of patients, with a mean duration of 40 months (range, 1-166 months). There were no differences between the two groups in terms of estimated 7-year survival (87.3% and 88.8%, respectively; 95% CI, 0.57-1.08; OR, 0.8) and stroke-free survival (86.8% and 88.1%, respectively; 95% CI, 0.59-1.07; OR, 0.8). Diabetic patients had decreased severe (>70%) restenosis-free survival rates at 7 years than nondiabetics (77.4% and 82.2%, respectively; 95% CI, 0.6-1; OR, 0.8; $P = .05$). Univariate analysis demonstrated again that the use of instrumental cerebral monitoring significantly decreased stroke-free survival in diabetics ($P = .01$; log rank, 10.1), and this was also confirmed by multivariate analysis (95% CI, 1.7-17.7; OR, 5.4; $P = .005$).

Conclusions: In our experience, the presence of diabetes mellitus increases three-fold the risk of perioperative death after CEA, while there are no differences with nondiabetics in terms of perioperative stroke. However, the rate of stroke and death at 30 days still remains below the recommended standards. During follow-up, this difference becomes negligible, and results are fairly similar to those obtained in nondiabetics. Particular attention should be paid to patients undergoing intervention under general anesthesia, who seem to represent a subgroup of diabetics at higher perioperative risk, suggesting neurologic monitoring should be used when possible. (J Vasc Surg 2010;■■■■■■■■■■.)

Carotid endarterectomy (CEA), when performed with acceptably low perioperative morbidity and mortality rates, still represents the gold standard for the treatment of extracranial carotid disease.¹ In high-volume centers, the 30-day overall rate of stroke and death is typically under the

levels recommended by published guidelines.² When perioperative complication rates exceed these recommended limits, the benefits of CEA dramatically decrease, particularly in asymptomatic patients.³

For this reason, the identification of subgroups of patients at higher surgical risk seems to be necessary to allow a proper selection of patients for surgical interventions. Diabetes mellitus (DM) has been described by several authors⁴⁻⁶ as a factor significantly affecting the results of CEA, even if other articles reported conflicting results.⁷ Moreover, there are few data in the literature concerning the analysis of risk factors influencing early and late results in diabetics.⁸

The aim of this study was to evaluate early and late results of CEA in diabetic patients in our experience, with particular attention to clinical, anatomical, and technical factors affecting early and long-term outcomes.

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MATERIALS AND METHODS

From January 1996 to December 2008, 4305 consecutive CEAs in 3573 patients were performed at the University of Florence. Five hundred eighty cases had bilateral intervention and 152 cases had reintervention performed. Data concerning these interventions were prospectively collected in a dedicated database containing 150 fields, including anatomical, clinical, diagnostic, and technical variables. This database also contains perioperative (<30 days) results in terms of mortality and neurological morbidity and all relevant clinical and diagnostic data collected during follow-up.

A post-hoc analysis of this prospective database was performed and two subgroups of patients were identified: diabetic patients (730 patients, 883 interventions; group 1) and nondiabetic patients (2843 patients, 3422 interventions; group 2).

DM was defined as the need for specific drugs to maintain metabolic control; patients with diet-controlled diabetes or impaired glucose tolerance alone were not included in the diabetic group.

The two groups of patients were compared in terms of demographic data, common risk factors for atherosclerosis, and comorbidities. Risk factors and comorbidities included arterial hypertension (defined as blood pressure greater than 130/85 mm Hg or the need for antihypertensive drugs), hyperlipemia (defined as triglycerides and cholesterol values >200 mg/dL), coronary artery disease (history of myocardial infarction [MI], angina, previous coronary revascularization), and peripheral arterial disease (ankle/brachial index <0.9). Patients were considered to be asymptomatic in the absence of neurological symptoms (transient ischemic attack or stroke) within 6 months from the intervention, and the degree of carotid stenosis was measured with North American Symptomatic Carotid Endarterectomy Trial criteria. Intraoperative data included type of anesthesia, cerebral monitoring and protection, and technique of carotid reconstruction.

The choice of anesthetic method was at the discretion of the operating surgeon and of the anesthesiologist, but patient's preference was also taken into account. Patients undergoing CEA under general anesthesia had cerebral monitoring with somatosensory-evoked potentials (SEPs) and selective shunt insertion on the basis of SEP abnormalities.⁹ With local anesthesia or our previously described Cooperative Patient General Anesthesia (CoPaGeA)¹⁰ technique, a carotid shunt was inserted on the basis of clinical neurologic monitoring during carotid clamping. To make our analysis simpler, in our results, we considered both pure local anesthesia and CoPaGeA as a unique entity.

Neurological evaluation at 30 days was independently performed in all the patients by an experienced neurologist who assessed the presence of minor and major stroke. Minor stroke was defined as any postoperative neurological event lasting more than 24 hours with recovery in the following weeks or months without or with minimal residual functional impairment. Major stroke was defined as any

postoperative neurological event lasting more than 24 hours with residual invalidity and/or inability. Clinical and anatomical indications for surgery, intraoperative technical features, and perioperative (<30 days) results of interventions were analyzed in terms of stroke and death with χ^2 test and Fisher's exact test, when necessary. Univariate analysis for 30-day stroke and death rate in the whole study group and in the two subgroups separately was performed. The analysis included the following risk factors: gender, age higher than 79 years, coronary artery disease, peripheral arterial disease, arterial hypertension, presence of contralateral carotid occlusion, preoperative symptoms, kind of anesthesia and cerebral monitoring, shunt insertion, and the type of reconstruction (patch closure or not). In diabetic patients, the role of different medical treatment of diabetes (orally treated DM or insulin-requiring DM) was also analyzed. Multivariate analysis (stepwise logistic regression analysis) for the same outcome with the inclusion of the factors resulted significant at univariate analysis was performed. Statistical significance was defined as a *P* value less than .05.

Follow-up was performed at 1, 3, 6, and 12 months, and yearly thereafter by clinical exam and duplex scan. All studies were performed using an Acuson Sequoia 512 Ultrasound System (Acuson Corporation, Mountain View, Calif). Patients who did not complete follow-up examinations had phone interviews. During the phone interview, some points were assessed: patient's survival and cause of death, if known, neurological events, and their time of appearance. Moreover, the patient was asked to report the results of his last duplex ultrasound control, where it was performed, to assess the status of operated internal carotid artery. Additional data regarding long-term survival and major cardiovascular events were obtained from the Regional Health Care database.

Follow-up data were analyzed by life-table analysis (Kaplan-Meier test) in terms of stroke, death, and significant (>70% North American Symptomatic Carotid Endarterectomy Trial criteria) restenosis, and results in the two groups were compared by means of log-rank test. In patients of group 1, both univariate analysis of the above-mentioned risk factors and multivariate analysis (Cox's regression), which included the significant factors from the univariate analysis, were performed for late ipsilateral neurological events.

Statistical analysis was performed by means of SPSS 15.0 for Windows (SPSS Inc, Chicago, Ill).

RESULTS

Demographic data, risk factors, comorbidities, and clinical and anatomical status. There were significant differences between the two groups of patients in terms of demographic data, risk factors, and comorbidities (Table I). Diabetic patients were more likely to be females and to have coronary artery disease, peripheral arterial disease, hyperlipemia, and arterial hypertension than nondiabetics. The majority of patients (652/730) had oral medication-treated DM, and 78 patients had insulin-requiring DM.

Table I. Patients' demographic data, risk factors, and comorbidities

	Group 1 (n = 730)	Group 2 (n = 2843)	P
Female gender	252 (34.5%)	862 (30%)	.03
Median age (years)	71.3	71.7	.6
Age >79 years	91 (12.5%)	455 (16%)	.02
Hypercholesterolemia	313 (43%)	1245 (44%)	.8
Hypertriglyceridemia	260 (35%)	827 (29%)	.001
Arterial hypertension	535 (73%)	1897 (66%)	.001
Coronary artery disease	186 (25%)	552 (10%)	<.001
Peripheral artery disease	289 (39%)	764 (27%)	<.001
Smoker or past smoker	455 (62%)	1966 (69%)	.01

Table II. Clinical and anatomical features

	Group 1 (CEAs = 883)	Group 2 (CEAs = 3422)	P
Presence of preoperative symptoms	286 (33%)	1183 (35%)	.6
Transient ischemic attack	163	707	
Minor stroke	39	142	
Major stroke	14	33	
Vertebrobasilar	70	301	
Asymptomatic patients	597 (67%)	2239 (65%)	.6
Degree of stenosis			
60%-80%	370 (42%)	1501 (44%)	.8
>80%	488 (55%)	1809 (53%)	.8
Near-occlusion	25 (3%)	112 (3%)	.9
Contralateral occlusion	47 (5%)	203 (6%)	.6
Redo surgery	26 (3%)	125 (3.5%)	.6

Among nondiabetics, there was a higher percentage of smokers and of patients older than 79 years. There were no differences between the two groups in terms of clinical presentation at the time of the operation, of degree of carotid stenosis, and type of intervention (primary or secondary intervention; Table II).

Intraoperative details. Local anesthesia or CoPaGeA with clinical monitoring was used in 286 interventions in group 1 (32%) and in 1132 cases in group 2 (33%; $P = ns$). In the entire study group, general anesthesia was used in 73% of symptomatic patients and in 64% of asymptomatic ones ($P < .001$), and the same difference was found among both diabetics (73% and 64.5%; $P = .007$) and nondiabetics (72.5% and 64%, respectively). Shunt insertion rate was similar between the two groups (14% in group 1 and 11% in group 2, $P = ns$). In group 1, the shunt insertion rate was 15% in patients undergoing local anesthesia or CoPaGeA and 13% in patients done with general anesthesia; the corresponding values in group 2 were 13.5% and 10%, respectively. Concerning arterial reconstruction, a wide use of patch closure was noted in both groups (79% in group 1 and 76% in group 2; $P = ns$); similar percentages of primary closure (17% and 19%, respectively), eversion technique (3% in both groups), and of carotid bypass (1% and 2%, respectively) between the two groups were recorded.

Table III. Perioperative (<30 days) results

	Group 1 (CEAs = 883)	Group 2 (CEAs = 3422)	P
Postoperative stroke			
Minor stroke	4 (0.4%)	16 (0.5%)	
Major stroke	6 (0.7%) ^a	9 (0.2%) ^b	
Cumulative stroke rate	10 (1.1%)	25 (0.7%)	.3
Death	10 (1.1%)	11 (0.3%)	.002
30-day stroke and death rate	18 (2%)	32 (0.9%)	.006

^aTwo lethal strokes.

^bFour lethal strokes.

Early results. Perioperative results are reported in Table III. There were no differences between the two groups in terms of neurological outcomes; both postoperative transient ischemic attack rates (0.8% and 0.5%, respectively) and stroke rates (1.1% and 0.7%, respectively) were similar between the two groups. Mortality rate was higher in group 1 than in group 2 ($P = .002$; odds ratio [OR], 3.5; 95% confidence interval [CI], 1.5-8.3). Consequently, the 30-day stroke and death rate was significantly higher in group 1 (2%) than in group 2 (0.9%; $P = .006$, 95% CI, 1.2-3.9; OR, 2.2).

The rates of postoperative fatal (three cases in both groups; 0.3% and 0.1%, respectively; $P = ns$) and nonfatal (three cases in group 1 [0.4%], and 10 cases in group 2 [0.3%]; $P = ns$) acute MIs were similar in the two groups.

The cause of deaths in group 1 were stroke in two cases, acute MI in three cases, intracranial haemorrhage in two cases, acute respiratory failure in two cases, and ventricular arrhythmia in the remaining one case. The cause of deaths in group 2 were stroke in four cases, acute MI in three, intracranial hemorrhage in two, massive pneumonia in one, and rupture of an iliac aneurysm in the remaining one.

Univariate analysis for the risk of stroke and death at 30 days in the entire cohort of patients demonstrated that, beyond diabetes, also the need for general anesthesia, the need for shunting, and the performance of alternative arterial reconstructions to patching significantly affected this outcome (Table IV). At multivariate analysis, significance was confirmed for all these risk factors.

Univariate analysis for the risk of stroke and death at 30 days in group 1 demonstrated that only instrumental monitoring under general anesthesia increased perioperative risk (Table V). Multivariate analysis confirmed that general anesthesia (OR, 9.1; 95% CI, 1.1-63.5; $P = .03$) was independently associated with an increased perioperative risk of stroke and death. The separate analysis for stroke and death demonstrated that the use of general anesthesia was associated with an increased perioperative death rate ($P < .001$) but not of stroke rate ($P = .2$).

The same analysis in group 2 demonstrated that again the need for general anesthesia, the need for shunting, the performance of alternative arterial reconstructions to patching, and the presence of preoperative symptoms sig-

Table IV. Univariate and multivariate (for factors resulted significant at univariate) analysis for 30-day stroke and death rate in the entire study group

Risk factor	Univariate analysis		Multivariate analysis		
	30-day stroke and death rate	P	95% CI	OR	P
- Female gender	14/1311 (1%)				
- Male gender	36/2994 (1.2%)	.7			
- Age <79 years	46/3662 (1.2%)				
- Age >79 years	4/643 (0.6%)	.1			
- Coronary artery disease	13/933 (1.4%)				
- No coronary artery disease	37/3372 (1.1%)	.4			
- Peripheral artery disease	21/1330 (1.5%)				
- No peripheral artery disease	29/2975 (1%)	.2			
- Arterial hypertension	39/2963 (1.3%)				
- No arterial hypertension	11/1342 (0.9%)	.2			
- Diabetes	18/883 (2%)		1.1-3.8	2.1	.01
- No diabetes	32/3422 (0.9%)	.006			
- Contralateral occlusion	4/249 (1.6%)				
- No contralateral occlusion	46/4056 (1.1%)	.9			
- Symptomatic	23/1470 (1.5%)				
- Asymptomatic	27/2835 (1%)	.08			
- Local or CoPaGeA anesthesia	6/1418 (0.4%)		1.3-7.8	3.2	.008
- General anesthesia	44/2887 (1.5%)	.002			
- Shunt insertion	18/493 (3.6%)		2.8-9.4	5.1	<.001
- No shunt insertion	32/3912 (1.9%)	<.001			
- Patch closure	30/3293 (0.9%)		1.2-3.1	2	.01
- No patch closure	20/1012 (1.9%)	.006			

CoPaGeA, Cooperative Patient General Anesthesia.

Table V. Univariate analysis for 30-day stroke and death rate in group 1

883 CEAs in diabetic patients	30-day stroke and death rate	P
- Female gender	7/303 (2.3%)	
- Male gender	11/580 (1.9%)	.6
- Age <79 years	17/772 (2.2%)	
- Age >79 years	1/111 (0.9%)	.3
- Coronary artery disease	6/237 (2.5%)	
- No coronary artery disease	12/646 (1.9%)	.5
- Peripheral artery disease	9/369 (2.4%)	
- No peripheral artery disease	9/514 (1.7%)	.5
- Arterial hypertension	13/654 (2%)	
- No arterial hypertension	5/229 (2.1%)	.8
- Orally treated diabetes mellitus	16/782 (2%)	
- Insulin-requiring diabetes mellitus	2/101 (2%)	.9
- Contralateral occlusion	1/47 (2.1%)	
- No contralateral occlusion	17/836 (2%)	.9
- Symptomatic	5/287 (1.7%)	
- Asymptomatic	13/596 (2.1%)	.6
Preoperative symptoms		
- Transient ischemic attack	3/163 (1.8%)	
- Stroke	1/53 (1.8%)	
- Vertebrobasilar	1/70 (1.4%)	.8
- Local or CoPaGeA anesthesia	1/286 (0.3%)	
- General anesthesia	17/597 (2.8%)	.014
- Shunt insertion	3/123 (2.4%)	
- No shunt insertion	15/760 (1.9%)	.7
- Patch closure	13/701 (1.8%)	
- No patch closure	5/182 (2.7%)	.4

CoPaGeA, Cooperative Patient General Anesthesia.

nificantly increased perioperative risk (Table VI). At multivariate analysis, the need for shunting, alternative arterial closure techniques, and the presence of preoperative symptoms maintained their significance.

Follow-up results. Follow-up was available for 4157 interventions (96% of the study group) for a mean duration of 40 months (range, 1-166 months). Less than 10% of the patients had a phone interview as their unique follow-up. During follow-up, 207 deaths, 45 ipsilateral and contralateral neurological events, and 211 moderate-to-severe (>60%) restenoses were recorded.

Overall estimated 84-month survival, stroke-free survival, and restenosis-free survival rates were 88.5% (SE, 0.009), 87.9% (SE, 0.009), and 79.3% (SE, 0.01), respectively.

There were no differences between the two groups in terms of estimated 7-year survival (87.3% and 88.8%, respectively; 95% CI, 0.57-1.08; OR, 0.8; Fig 1) and stroke-free survival (86.8% and 88.1%, respectively; 95% CI, 0.59-1.07; OR, 0.8; Fig 2). Also the 7-year rates of freedom from any ipsilateral neurological event (98.9% and 98.3%, respectively; $P = .9$, log rank = 0.7) and from any ipsilateral and contralateral neurological events (98.1% and 97.4%, respectively; $P = .9$, log rank = 0.2) were similar. Diabetic patients had slightly poorer 7-year restenosis-free survival rates than nondiabetics (77.4% and 82.2%, respectively; 95% CI, 0.6-1; OR, 0.8; $P = .05$; Fig 3).

Univariate analysis in diabetics failed to identify any factor affecting the risk of any ipsilateral neurological events during follow-up (Table VII).

Table VI. Univariate and multivariate (for factors resulted significant at univariate) analysis for 30-day stroke and death rate in group 2

Risk factor	Univariate analysis		Multivariate analysis		
	30-day stroke and death rate	P	95% CI	OR	P
- Female gender	7/1008 (0.7%)				
- Male gender	25/2414 (1%)	.3			
- Age <79 years	29/2890 (1%)				
- Age >79 years	3/532 (0.5%)	.3			
- Coronary artery disease	7/696 (1%)				
- No coronary artery disease	25/2726 (0.9%)	.8			
- Peripheral artery disease	12/962 (1.2%)				
- No peripheral artery disease	20/2460 (0.8%)	.5			
- Arterial hypertension	26/2309 (1.1%)				
- No arterial hypertension	6/1113 (0.5%)	.09			
- Contralateral occlusion	3/203 (1.4%)				
- No contralateral occlusion	29/3219 (0.9%)	.9			
- Symptomatic	18/1184 (1.5%)		1-4.2	2.1	.04
- Asymptomatic	14/2238 (0.6%)	.01			
- Local or CoPaGeA anesthesia	5/1132 (0.4%)		0.8-1.9	1.2	.1
- General anaesthesia	27/2290 (1.1%)	.03			
- Shunt insertion	15/372 (3.9%)		4.4-18.6	9.1	<.001
- No shunt insertion	17/3050 (0.5%)	<.001			
- Patch closure	17/2592 (0.6%)		1-4.5	2.4	.005
- No patch closure	15/830 (1.8%)	.003			

CoPaGeA, Cooperative Patient General Anesthesia.

DISCUSSION

DM is a major risk factor for the development of ischemic stroke. Patients with diabetes are more likely to suffer from a stroke than nondiabetics,¹¹ and their stroke is associated with worse functional outcome and higher mortality rates.¹² For these reasons, diabetic patients might be expected to derive particular benefit from CEA. However, the increased prevalence of cardiovascular disease and of cerebrovascular events among diabetics has been felt to increase the risk for postoperative complications in diabetics undergoing major vascular surgery.⁶ With respect to CEA, the role of DM as a contributor to perioperative risk is disputed. Some authors have demonstrated that patients with DM who present for CEA are not at an increased risk,^{7,8} while several others supported the role of DM as an independent risk factor.^{4,13,14} Also, in our series, perioperative results in diabetics were significantly poorer than those obtained in nondiabetics, with a 2% rate of perioperative stroke and death compared with 0.8% in nondiabetics.

As suggested by several authors,¹⁵ the increased risk in diabetics seems to be mainly due to an increased rate of perioperative mortality, since diabetes is correlated with silent myocardial ischemia and an increased risk of all forms of early and late cardiac mortality. Also in our series, diabetics had an increased risk of death but not of stroke with respect to nondiabetics, even if the risk of any perioperative neurological event was only numerically higher among diabetics (1.9% and 1.2%, respectively). It can be theorized that the higher prevalence of unstable features in carotid plaques from diabetic patients than in those from nondiabetics could explain the mild increase of perioperative neurological complications in diabetics that were reported in other studies.¹⁶

However, even in the presence of DM, our perioperative risk remains largely below the limits recommended by published guidelines, confirming the feasibility and safety of CEA also in diabetic patients. We did not find any differences between diabetics and nondiabetics in terms of postoperative MI. This may be secondary to the extremely low incidence of postoperative MI in general among our CEA population, possibly attributed to our strategy of extensive preoperative cardiac evaluation.¹⁷

In this study, we also examined specific predictors of poor early and late outcome among diabetic patients in more detail. We analyzed the role of different medical management of DM in determining the results of CEA, and we are aware of only two other published studies making such a comparison. Axelrod et al⁶ reported, in a large series of mixed vascular procedures from the Department of Veteran Affairs (VA), that, after controlling for the main cardiovascular comorbidities, neither insulin-treated nor oral medication-treated DM appeared to increase the risk of postoperative death. Diabetes did appear to be a moderate independent risk factor for nonfatal cardiovascular complications, but this increased risk was confined to patients with diabetes with insulin treatment. Similarly, Stoner et al,¹⁴ in a large series of more than 13,000 CEAs from the same VA database, reported that the presence of insulin-treated DM was found to be the strongest independent patient risk factor for an adverse outcome on the basis of an increased risk of cardiac events and death.

In our experience, we did not find any difference in terms of perioperative results between patients with insulin-requiring DM and patients with oral agent-controlled diabetes.

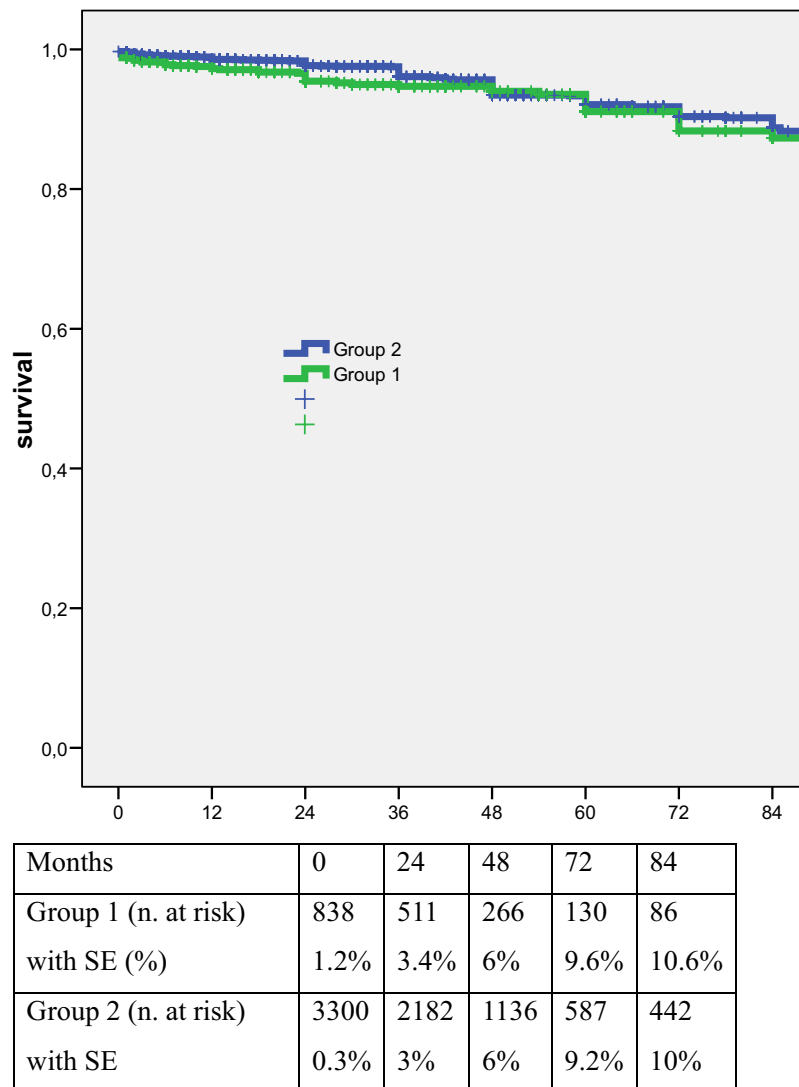


Fig. 1. Kaplan-Meier curve survival in group 1 and 2 with number of patients at risk.

Anatomical factors such as contralateral occlusion also did not increase the risk of perioperative complications in diabetics, confirming previous data from our group.¹⁸

We did not find any difference in terms of cumulative 30-day stroke and death rate between symptomatic and asymptomatic diabetic patients, and this was also true when a separate analysis for 30-day death and stroke rates was performed. Of interest is the observation that, when comparing 30-day stroke and death rate in asymptomatic diabetic and nondiabetic patients, the corresponding values were 2.1% and 0.7%, confirming that diabetes plays an important role in increasing perioperative risk of CEA also in asymptomatics, who are usually considered at lower surgical risk, as suggested by the results in the entire study group and in group 2. These results suggest the need for careful selection of asymptomatic diabetic patients.

Other patients characteristics such as older age, the presence of coronary artery disease and peripheral artery

disease, and technical issues, such as the need for shunting, and the use of primary closure did not significantly affect perioperative results in diabetics, while some of these factors (shunt use, primary closure) were found to be significantly associated with worse perioperative results in the whole study group and in group 2. One can suppose that the extremely low incidence of overall complications in group 1 is rendering it difficult to demonstrate a statistically significant difference when one in fact exists (type II statistical error).

The only factor significantly affecting perioperative results in diabetics was the use of general anesthesia. These results are similar to those reported by Rockman et al.⁸ It is likely that there is significant bias in the choice of the patients who undergo surgery with general anesthesia, as partially confirmed by the results of univariate and multivariate analysis in the entire cohort of patients: as previously described,¹⁹ many of these patients have re-

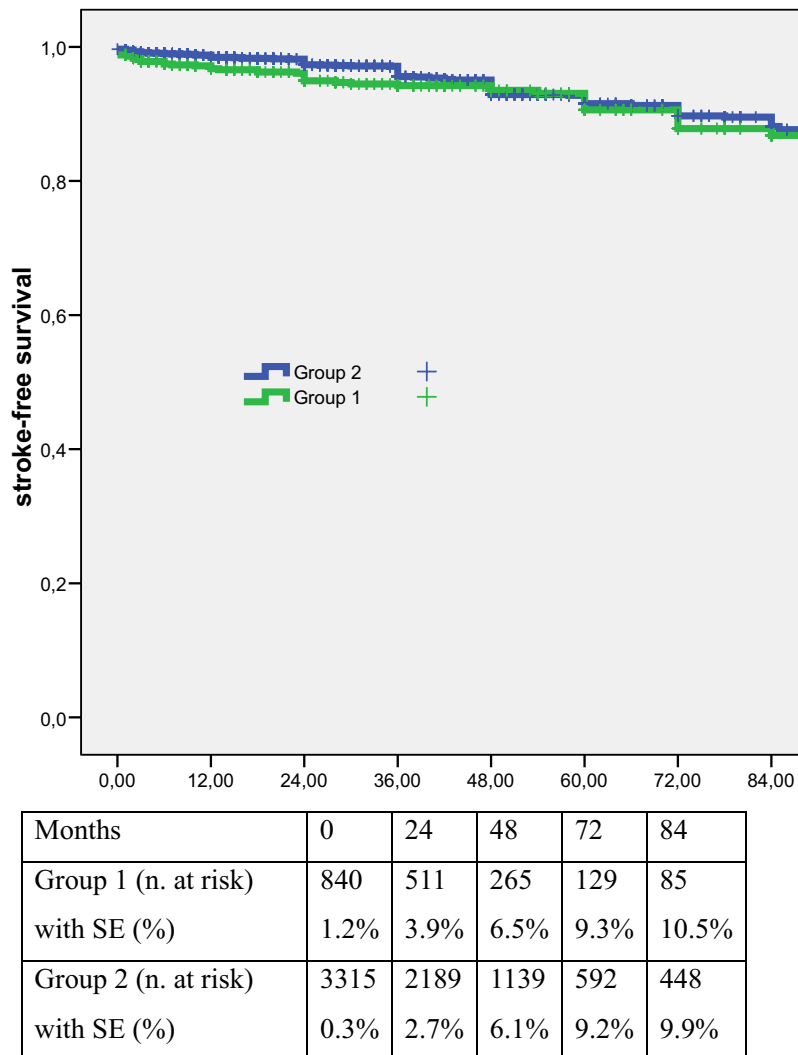


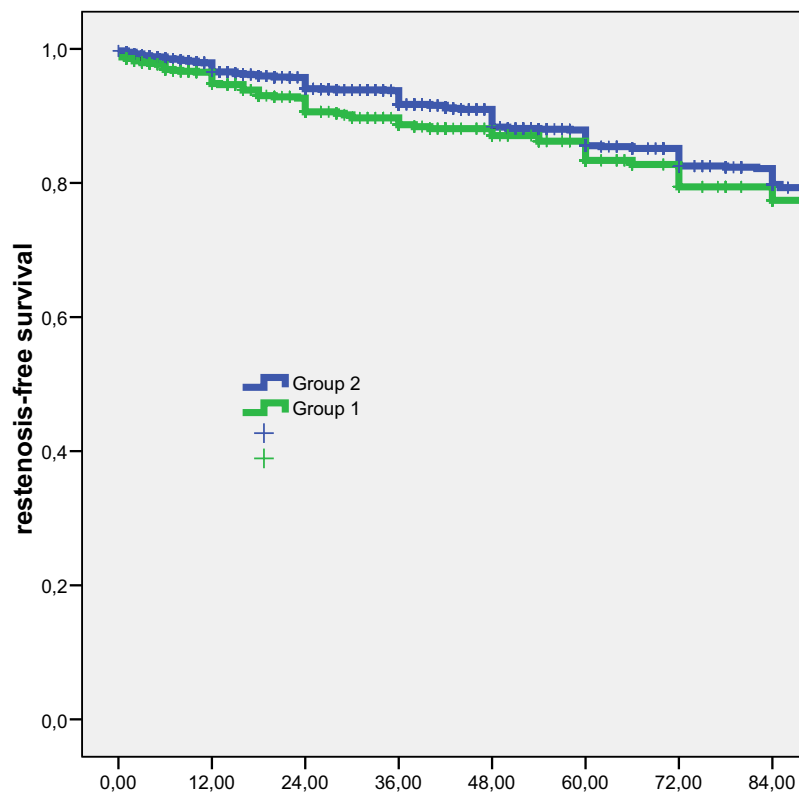
Fig. 2. Kaplan-Meier curve for stroke-free survival in group 1 and 2 with number of patients at risk.

cent neurological events or had sustained preoperative strokes. This patient group would be at increased risk for perioperative complications based on these innate factors. However, the observation that, in nondiabetics, the use of general anesthesia increased perioperative risk at univariate but not at multivariate analysis, could suggest a stronger impact of the kind of anesthesia on diabetic patients. Even if we found increased mortality but not stroke rates with general versus local/regional anesthesia in diabetics, one can suppose that these patients, having an increased burden of cerebrovascular disease involving both large and small intracranial vessels, could benefit from the precise and sensitive neurologic monitoring during CEA that occurs under regional anesthesia or CoPaGeA technique.

We did not find any difference between diabetics and nondiabetics in terms of survival, stroke-free survival, and

freedom from ipsilateral and contralateral events during follow-up. The risk of developing new neurological events during follow-up is extremely low in diabetics, confirming the assumption that CEA is able to provide a durable long-term reduction in stroke.²⁰ The presence of diabetes was associated with a higher risk of developing significant restenosis during follow-up, and this finding confirms previous studies,²¹ suggesting the presence of diabetes can both increase neointimal hyperplasia after arterial injury²² and accelerate the growth of new carotid plaques at the site of CEA.²³

Despite the intrinsic limits of a nonrandomized, retrospective study with a large number of cases but with a relatively small number of events, our analysis confirmed that the presence of DM significantly increases the risk of mortality, but not of neurological events, during CEA. In high-volume centers, perioperative risk typically remains



Months	0	24	48	72	84
Group 1 (n. at risk)	840	498	256	123	78
With SE (%)	0.4%	6%	8%	9%	11.2%
Group 2 (n. at risk)	3315	2147	1101	553	415
With SE (%)	0.3%	3.6%	8%	9%	10.5%

Fig. 3. Kaplan-Meier curve for restenosis-free survival in group 1 and 2 with number of patients at risk.

Table VII. Univariate analysis for the risk of any ipsilateral neurological event during follow-up in group 1

	Univariate analysis			
	Log-rank	P	95% CI	OR
Female gender	1.3	.2	0.5-8.8	2.2
Hyperlipemia	0.2	.7	0.3-5.5	1.3
Arterial hypertension	1.8	.2	0.6-10.1	2.5
Insulin-requiring diabetes mellitus	0.9	.4	0.1-1.7	0.4
Contralateral carotid occlusion	0.4	.6	0.6-7.8	2.1
Preoperative symptoms	1.7	.2	0.2-1.2	0.6
Clinical monitoring	0.2	.6	0.2-14.1	1.5
Kind of reconstruction	4.4	.09	0.01-1.3	0.2

below the recommended standards. Moreover, the need for insulin treatment seems not to affect early and long-term results, confirming the safety of the intervention also in this subgroup of diabetic patients.

CONCLUSIONS

In our experience, carotid endarterectomy can be performed with good results in diabetic patients, who are, however, at higher risk for perioperative mortality than nondiabetic patients. General anesthesia with instrumental monitoring when compared with regional anesthesia or CoPaGeA with neurologic monitoring is associated with increased risk in diabetics by both univariate and multivariate analyses. The need for insulin treatment does not seem to affect early and late results of the intervention.

AUTHOR CONTRIBUTIONS

Conception and design: CP, WD
 Analysis and interpretation: RP, WD, CP
 Data collection: AF, GP, AI
 Writing the article: WD, JM
 Critical revision of the article: RP, JM
 Final approval of the article: CP, AI, RP

Statistical analysis: WD
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