

Cardiac troponin I assessment and late cardiac complications after carotid stenting or endarterectomy

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Purpose: When compared with carotid endarterectomy (CEA), percutaneous carotid angioplasty with stent replacement (CAS) is a less invasive technique in the treatment of carotid stenosis. However, periprocedural hemodynamic instability still remains a challenge. This instability might lead to myocardial damage, which is now measured accurately by using cardiac troponin I (CTnI).

Methods: This study was designed to compare the periprocedural variation of CTnI in 150 consecutive patients scheduled to undergo CEA (n = 75) or CAS (n = 75). The levels of CTnI were measured until the third postoperative day in all patients. Short-term (1 month) and long-term (up to 5 years) postoperative cardiac outcome were assessed by means of chart review, regular follow-ups, and telephone calls.

Results: There was not any statistically significant difference between the 2 groups regarding the demographic characteristics and preprocedural medical status. The incidence of increase of CTnI (>0.5 ng/mL) was significantly higher in the CEA group (13%) compared with that in the CAS group (1%; $P = .001$). During the acute postprocedural period, the CAS group was significantly more prone to hypotension, requiring vasopressor therapy, whereas the CEA group had more hypertension, necessitating hypotensive medications ($P < .001$). At 5 years, the overall incidence of major cardiac complications (nonfatal myocardial infarction and death related to cardiac origin) was significantly more frequent in the CEA group (20% vs 5%, $P < .01$).

Conclusion: The results of our study suggest that CAS yielded less myocardial damage in the short and long term when compared with CEA. Larger randomized multicenter trials with long-term outcomes are necessary to confirm our findings. (J Vasc Surg 2005;41:769-74.)

Carotid angioplasty and stent placement (CAS) has been introduced as an alternative to surgical carotid endarterectomy (CEA) for the treatment of carotid artery stenosis.¹⁻⁷ Although it is a less invasive percutaneous procedure, hemodynamic instability is reported as being as frequent if not higher than in CEA.⁸⁻¹⁰ This instability might be related to the triggering of baroreflex after balloon dilatation, stent delivery in the carotid sinus region, or both.^{8,9} Cardiac troponin I (CTnI) is a reliable marker of myocardial injury in patients undergoing vascular surgery.¹¹⁻¹³ Moreover, its use in predicting short-term and midterm cardiac outcome in this population has been verified in 2 studies.^{12,14} A cutoff value of 1.5 ng/mL is sensitive and specific for myocardial infarction (MI), even in the postoperative period, whereas values of between 0.5 and 1.5 ng/mL are observed in unstable angina and are considered to be the expression of myocardial ischemia or more limited myocardial damage.² To our knowledge, no study has reported the periprocedural variation of this enzyme in a group of consecutive patients undergoing CAS. This study

was designed primarily to measure CTnI variation and other cardiac complications after this procedure and compare the results with those of a similar group of consecutive patients scheduled for CEA. The second purpose of this study was to assess prospectively the long-term cardiac outcomes (up to 5 years) in both groups of patients.

METHODS

Patients. From July 1998 through December 1999, 150 consecutive patients undergoing elective CAS or surgical CEA were prospectively included in the study, which was conducted in a single university hospital. Patients having renal dysfunction or undergoing emergency procedures were excluded.

Exposure variable: CTnI. CTnI was assessed after the procedure (1-3 hours) in the postanesthesia care unit and on days 1, 2, and 3 postoperatively. No further measurements were made if the results of these 4 analyses remained normal. This sample-taking schedule was chosen according to previous findings.¹⁵ Postoperative cardiac events were assessed by means of clinical examination and electrocardiography (ECG) until patient discharge.

The CTnI concentrations were determined by using an immunoenzymofluorometric assay on a Stratus analyzer (Dade, Massy, France). At the time of the study, the detection limit of the immunoassay was 0.1 ng/mL. A CTnI value of greater than 1.5 ng/mL associated or not

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Competition of interest: none.

0741-5214/\$30.00

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doi:10.1016/j.jvs.2005.02.017

with Q wave was considered a diagnosis of MI. CTnI values of between 0.5 and 1.5 ng/mL were considered myocardial ischemia.^{12,16}

Data collection and follow-up. Clinical data were prospectively collected and recorded during the patients' hospitalizations. Long-term follow-up was assessed by means of a systematic clinical review of patients by the surgical team from 1 month to 5 years postoperatively. For the accuracy of the clinical data assessment, all patients or the family, except those who were lost to follow-up, were interviewed by telephone. The interview was conducted by 2 independent investigators who were not aware of the initial procedure. Any significant clinical events were noted. All cardiology follow-ups were investigated and recorded. This phase of the study lasted from March through December 2003.

The clinical end points were major and minor cardiac events. In the group of patients who died during the study time frame, the cause of death was classified as cardiac or noncardiac (including all other causes). Cardiac death was defined by the occurrence at the time of death of MI, heart failure, arrhythmia, and/or sudden death that was not explained by another cause.

Late cardiac events were classified as major or minor. Major cardiac events included nonfatal MI and cardiac death. If cardiac death occurred at a different time point after a nonfatal MI, only cardiac death was counted. Other cardiac events included episodes of congestive heart failure, coronary revascularization, valvular replacements, supraventricular and ventricular arrhythmia, and the need for a pacemaker.

Anesthetic and surgical management. The choice between stenting and endarterectomy was mostly based on the anatomic evaluation of the carotid bifurcation. Angioplasty was performed in cases of healthy aortic arch, no severe angulations of the common carotid arteries, and absence of any floating thrombus or circular calcification within the carotid stenosis. In the angioplasty group patients were informed of the investigative nature of the technique and signed an informed consent form.

All procedures (CEA and CAS) were performed in an operating room equipped with a radiologic C arm by a single team of vascular surgeons and anesthesiologists. In patients who had undergone CEA, both regional and general anesthesia were used. The technique was chosen according to the vascular surgeons' and anesthesiologists' preferences. General anesthesia was performed with propofol, sufentanyl, atracurium, and isoflurane. Regional anesthesia included the combined cervical block technique described elsewhere.¹⁷

In patients who had undergone CAS, a percutaneous femoral approach was routinely used. Local anesthesia of the groin was performed with lidocaine 1%, without any additional sedation. Cardiovascular monitoring was performed with a 5 lead-ECG and continuous intra-arterial blood pressure measurements.

Hemodynamic instability was defined as a pulse rate of less than 40 beats/min or greater than 100 beats/min, a

blood pressure variation of $\pm 30\%$ of the preoperative systolic pressure, or both.

Contrary to other institutions,⁸ atropine was not injected systematically but only in cases of extreme bradycardia (pulse rate <40 beats/min). Ephedrine, neosynephrine, and norepinephrine were used in case of a decrease in blood pressure of greater than 30% compared with the preoperative value. Nicardipine or β -blockers were used when the blood pressure exceeded 30% of the preoperative value. Doses of 50 and 100 U/kg body weight of heparin were injected in patients undergoing CEA and CAS, respectively. Postoperatively, all patients were monitored in the postanesthesia care unit for at least 6 hours.

Postoperative management. All patients were followed for at least 1 night in the vascular intensive care unit by means of continuous 5-lead ECG, invasive blood pressure measurements, oxygen saturation monitoring, and neurological assessment. ECG was repeated every day for 3 postoperative days.

Patients undergoing CAS were prescribed clopidogrel (75 mg/d) and aspirin (100 mg/d) for 1 month and then one antiplatelet drug thereafter,¹⁸ and patients undergoing CEA were started on low-molecular-weight heparin for 48 hours and then aspirin (100 mg/d).

Statistical analysis. The sample size was chosen on the basis of previous rate of significant increase in CTnI in patients undergoing vascular surgery (10%-12%).¹⁴ Statistical analysis was performed with Statistica version 5 (Tulsa, Okla).

Values are presented as means \pm SD. The following tests were used when appropriate: Student *t* test, Mann-Whitney U test, χ^2 test, and Fisher exact test. Actuarial survival curves (freedom from major cardiac events, including the short-term events) were calculated with the Kaplan-Meier method and compared with the log-rank test. The status of patients lost to follow-up was considered until their last visit. Logistic regression was performed to detect a possible significant influence of the following factors, which are presumed to affect cardiac morbidity: age greater than 75 years, hemodynamic instability, β -blockade, antiplatelet therapy, and general anesthesia. The Cox regression hazard model was used to adjust the baseline value of survival with the inclusion of factors significantly affecting major cardiac events.

A *P* value of less than .05 was considered statistically significant.

RESULTS

There were not any statistically significant differences in demographic characteristics between the 2 groups (Table I).

Early postprocedural events. A significant CTnI increase (>0.5 ng/mL) was more frequent in the patients undergoing CEA (13%) when compared with the patients undergoing CAS (1%; *P* = .02). All CTnI increases occurred within the 24 first postoperative hours.

In the CEA group 4 of 10 patients had an MI, with CTnI levels of greater than 0.15 ng/mL associated with ECG changes (Q-wave MI). The patients in the CAS group

Table I. Patients characteristics

	CEA, n = 75 (%)	CAS, n = 75 (%)	P value
Age, mean ± SD (y)	72 ± 11	70 ± 10	.32
Age >75 y (n)	20	21	.6
Sex (female/male)	12/63	16/59	.27
ASA (II/III)	34/41	37/38	.66
Body mass index (kg/m ²)	25 ± 2	25 ± 2	.8
Prior cardiac risk factor			
Hypertension	58 (77)	62 (82)	.38
Diabetes	14 (18)	10 (13)	.43
History of tobacco use	40 (53)	37 (49)	.18
History of myocardial infarction	12 (16)	10 (13)	.8
Prior CABG or coronary stenting	10 (13)	9 (12)	.9
Congestive heart failure	6 (8)	7 (9.3)	.9
Cardiac rhythm abnormalities	11 (14.6)	6 (8)	.25
Preoperative cardiac medications			
β-Blockade	40 (53)	43 (57)	.6
Antiplatelets (aspirin, clopidogrel, or both)	52 (69)	65 (86)	.14
Carotid stenosis with neurologic symptoms	42 (56)	38 (51)	.57
General anesthesia	39 (52)	2 (2.6)	<.01

CEA, Carotid endarterectomy; CAS, carotid angioplasty and stent placement; ASA, American Society of Anesthesiologist classification; CABG, coronary artery bypass grafting.

Table II. Perioperative cardiac complications

	CEA, n = 75 (%)	CAS, n = 75 (%)	P value
Asystole <15 s, severe bradycardia during the procedure, or both (n)	8 (10)	35 (46)	<.001
Hypotension during procedure	21 (28)	3 (4)	<.001
Hypertension during procedure	12 (16)	2 (2.6)	<.001
Postoperative hypotension	9 (12)	21 (28)	.004
Postoperative hypertension	14 (18)	3 (4)	.002
CTnI >0.5 ng/mL	10 (13.3)	1 (1.3)	.001
CTnI >1.5 ng/mL	4 (5.3)	1 (1.3)	.2
Cardiac failure	3 (4)	1 (1.3)	.36
Supraventricular arrhythmia	6 (8)	3 (4)	.37
Ventricular arrhythmia	4 (5.3)	1 (1.3)	.2

CEA, Carotid endarterectomy; CAS, carotid angioplasty and stent placement; cTnI, cardiac troponin I.

also had a true MI associated with ECG changes. In the current series no patient presented with non-Q-wave MI.

No significant correlation was found between perioperative hemodynamic instability and increase of troponin levels.

Nonischemic cardiac complications are listed in Table II.

There were no deaths in the CAS group. One patient in the CEA group died on day 8 from an acute mesenteric infarct.

Finally, none of these patients experienced stroke or transient ischemic attack during the first 30 postoperative days.

Late postoperative events. The mean time of follow-up was 44 ± 12 months. Twelve (8%) patients were followed for an average of 36 months and then lost to follow-up. Four were in the CAS group, and 8 were in the CEA group. They were not considered for the late outcome crude calculation but were included in the Kaplan-Meier curve analysis and the log-rank test. During this period, 2 patients (1 in each group) died of stroke.

The accuracy of these events were verified in 89% (122/138) from hospital records, in 8% (12/138) from cardiologists' and/or general practitioners' letter or interviews, and 3% (4/138) from patients and family interviews alone.

Long-term cardiac events. The incidence of long-term major cardiac events (MI or death of cardiac origin) was significantly higher in the CEA group (20% vs 5%, P < .01). No significant difference was noted for minor cardiac events (Table III).

Kaplan-Meier analysis of survival (freedom from major cardiac events) is presented in the Figure. The patients undergoing CAS had a significantly lower incidence of major cardiac events and death of cardiac origin ($\chi^2 = 8.75$, P = .003, hazard ratio = 5.3 [95% confidence interval = 1.66-12.2]).

Logistic regression analysis could not detect any statistically significant association between the absence of perioperative β-blockade, the absence of antiplatelet therapy, and the presence of general anesthesia with major cardiac

Table IV. Summary of cardiac complications at 5 years in patients undergoing CEA and CAS

	CEA, n = 67 (%)	CAS, n = 71 (%)	P value
Total mortality	15 (22)	4 (5)	<.01
Major cardiac complications			
Mortality related to cardiac cause	6 (8)	1 (1.3)	.2
Nonfatal myocardial infarction	8 (10)	4 (5)	.3
	14 (20)	5 (5)	<.01
Other cardiac complications			
Episode of congestive heart failure	2 (2.6)	2 (2.6)	
Coronary revascularization	5 (6.6)	5 (6.6)	
Valvular replacement	1 (1.3)	2 (2.6)	
Supraventricular arrhythmia	2 (2.6)	1 (1.3)	
Ventricular arrhythmia	1 (1.3)	1 (1.3)	
Need for pacemaker	1 (1.3)	2 (2.6)	
	12 (16)	13 (17)	.9

CEA, Carotid endarterectomy; CAS, carotid angioplasty and stent placement.

cardiac mortality alone does not entirely account for this difference. It should also be noted that the statistical significance for major cardiac events was obtained only by pooling cardiac death and nonfatal MI.

The other limitations of this study include a group assignment on the basis of surgical and anatomic factors rather than a classic randomization procedure and a limited number of patients, which do not permit us to integrate all factors into a multivariate model. In addition, as an important factor, general anesthesia was poorly balanced between the 2 arms because only 2 patients in the CAS group had general anesthesia. However, the superiority of regional anesthesia concerning the major cardiac events, especially in carotid surgery, is not documented. Despite these shortcomings, the increase in CTnI levels is an objective measurement of ischemic injury of the heart and a reliable predictor of cardiac morbidity in the short-term and mid-term postoperative periods (6 months).¹²⁻¹⁴ Another possible factor that could explain partly the difference between the 2 procedures might be the fact that all patients in the CAS group had clopidogrel associated with aspirin in the first month, whereas this combination was not systematically administered in the CEA arm (Table IV). Nevertheless, it is unlikely that this difference could affect early outcome because almost all early cardiac complications occurred in the first postprocedural day, whereas for late outcomes, treatments were similar. Because of the periprocedural hemodynamic instability in the CEA group but also in the CAS group, routine dosage of CTnI and intensive care monitoring of high-risk patients should be discussed.³⁵⁻³⁷ Future randomized controlled studies should also evaluate the short- and long-term cardiac outcomes of these procedures (Table IV).

We thank Dr Murat Aksoy, who kindly reviewed the manuscript.

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Submitted Sept 9, 2004; accepted Feb 5, 2005.

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