

Incidence and Timing of Hypotension After Transcervical Carotid Artery Stenting: Correlation With Postoperative Complications

Objectives: To assess the incidence and timing of hypotension after carotid artery stenting (CAS) and its correlation with postoperative complications.

Background: CAS-associated postoperative hypotension has been linked to surgical morbidity and mortality, especially to stroke and cardiac complications.

Methods: Ninety-seven consecutive patients undergoing transcervical CAS were monitored for at least 12 hr after operation. Hypotension was defined as systolic blood pressure < 90 mm Hg. Patients were divided into three groups: normal blood pressure and early (<6 hr) and late (>6 hr) hypotension. Complications were recorded.

Results: Hypotension occurred in 34% of the patients (early hypotension in 63% of them). Hypotension was recorded in 21.6% of patients during surgery and in 21.6%, 15.5%, and 1.0% at 6, 12, and 24 hr postoperatively. Bradycardia occurred in 26.8% during operation and in 25.8%, 13.4%, and 10.3% at 6, 12, and 24 hr after surgery. Intraoperative bradycardia ($P = 0.01$) and hypotension ($P = 0.02$) were predictors of postoperative hypotension. The overall rate of complications was 5% without differences between the study groups. The mean length of stay was 3, 3.6, and 2.8 days in the normotensive, early hypotension, and late hypotension groups, respectively.

Conclusions: Most postoperative hypotension episodes occurred within the first 6 hr, and more than one-third between the 6 and 12 hr post-procedure. All patients with late hypotension were asymptomatic. There was no difference in complications between the study groups. In patients undergoing ambulatory CAS, hemodynamic monitoring in the postoperative period is particularly important during the first 12 hr. © 2014 Wiley Periodicals, Inc.

Key words: blood vessel prosthesis; carotid arteries/surgery; hypotension; stents

INTRODUCTION

Hypotension is a well-recognized complication of carotid artery stenting (CAS) [1–5]. Most episodes occur within the first 6 hr of the procedure [5,6] and different clinical, angiographic, and ultrasonographic factors for predicting hypotension during CAS have been reported [2,6–8]. CAS-associated hypotension has been linked to surgical morbidity and mortality, especially to cerebrovascular events and cardiac complica-

tions [1,2,9-11]. Transcervical CAS with flow reversal for cerebral protection has been shown to be effective and safe, with some advantages over the transfemoral approach with protection devices [12,13]. Exposure of common carotid artery and internal jugular vein is achieved through a small incision at the base of the neck, and together with a careful haemostasis appears to reduce the risk of bleeding complications and/or postsurgical hematomas [13]. However, the time required for postoperative hemodynamic monitoring in CAS is not well established. This single-center study was conducted to assess the incidence and timing of hypotension after CAS and its correlation with postoperative complications.

METHODS

Design and Study Population

A prospective observational study of 110 consecutive patients with severe carotid artery stenosis undergoing transcervical CAS with flow reversal at our hospital between January 2008 and December 2009 was carried out. The study was approved by the Ethics Committee and written informed consent was obtained from all patients.

The diagnosis and morphometry of the carotid lesion was determined by Doppler ultrasound of the supra-aortic trunks. All patients were prescribed acetylsalicylic acid (100 mg/day) and clopidogrel (75 mg/day) for at least 4 days before the procedure. In cases of non-compliance with this treatment, a 300-mg loading dose of clopidogrel was administered 24 hr before treatment and in the immediate postoperative period. Double antiplatelet therapy was used for the first 30 days and, thereafter, simple antiplatelet therapy was maintained.

Surgical Procedure, Hemodynamic Monitoring, and Postoperative Treatment

The technique of transcervical CAS with flow reversal protection was performed as described by Criado et al. [12] and reported in the study of Matas et al. [14]. Briefly, through a 3—4 cm vertical incision at the base of the neck, a shunt is established between the common carotid artery and the internal jugular vein using a 8-Fr introducer sheath for cannulation and connected with a 15-cm long catheter. Proximal occlusion of the common carotid artery is then carried out, achieving flow inversion in the internal carotid artery (ICA). Systemic heparin is administered to maintain the activated clotting time between 250 and 300 sec. An angiogram is obtained to assess correct functioning of the fistula. This angiogram allows localization of the carotid bifurcation and indicates the

level, length, and diameter of the carotid lesion. Under fluoroscopic guidance, a 0.014 guidewire is advanced through a 4- Fr catheter into the ICA across the lesion. Balloon pre-dilatation of the lesion is optional. In all patients, self-expanding stents were used. Types of stents used included Wallstent (Boston Scientific), Acculink and Xact (Abbott), and Precise (Cordis). Based on the vessel diameter, generally a 5-6 mm x 30 mm or 5—6 mm x 20 mm balloon is selected for stent post-dilatation. Prior to declamping of the common carotid artery, manual aspiration to remove potential debris was performed and a final arteriography was obtained.

Patients were hospitalized and the procedure was carried out in the operating room, with continuous ECG (five leads) and pulse oximetry for arterial oxygen saturation (SaO_2) monitorization. Invasive blood pressure (IBP) monitoring was performed through a 20-G catheter in the radial artery (Leader Cath, Vygon, Ecouen, France) connected to a processing module attached to a General Electric Datex Ohmeda S/5 monitor (General Electric Healthcare Division, Firefield, CT) and calibrated at midaxillary level. All patients received continuous intravenous sedation with midazolam (0.05—0.2 mg/kg) and remifentanil (0.05—0.1 mcg/kg/min) during the procedure. Cerebral hemodynamics was monitorized by transcranial Doppler ultrasound and the patients' clinical symptoms. In only 1% of patients, deterioration in the level of consciousness was observed, which in all cases improved by common carotid artery declamping.

After the procedure, patients were admitted to the PACU for hemodynamic monitoring (ECG, SaO_2 , IBP) for a minimum of 12 hr. After that time, patients were discharged to the hospital ward or transferred to the intensive care unit (ICU) if necessary. Hypotension was first treated with fluid bolus (250 mL of 0.9% saline or 6% hydroxyethyl starch) and in case of non-response, with ephedrine (5-20 mg) and/or continuous infusion of norepinephrine (0.25-3 mg/kg/min) until restoring systolic blood pressure (SBP) $> 20\%$ of baseline.

Collection of Data and Study Variables

Demographics, clinical features, preoperative variables, intraoperative findings, postoperative data, and outcome were collected.

Intraoperative and postoperative hypotension was defined as SBP < 90 mm Hg or the need of vasoactive drugs. Patients were divided into three groups as follows: normal blood pressure (BP), early hypotension (≤ 6 hr), and late hypotension (> 6 hr). Bradycardia

was defined as heart rate 55 beats per min. Treatment of bradycardia included the administration of atropine 0.5 mg intravenously in the presence of signs or symptoms of poor peripheral perfusion (altered consciousness, thoracic pain, hypotension, or other signs of shock) up to a total dose of 3 mg. If atropine was ineffective, isoproterenol 0.05 μ g/kg/min was administered and in patients without response, a temporary pacemaker was inserted.

Postoperatively, neurological and cardiovascular complications were assessed [15-17]. Complications related to the cervical approach, syncope, and postoperative mortality were also recorded. All patients were followed during in-hospital stay until discharge from the hospital and then for one month at the outpatient clinics.

Statistical Analysis

Data are expressed as frequencies and percentages for categorical variables and as mean and standard deviation (SD) for continuous variables. The relationship between categorical variables and the use of vaso-pressor drugs was analyzed with the Student's *t* test or the Mann—Whitney *U* test according to the normal or non-normal distribution of variables. The Pearson's product moment correlation coefficient was calculated to assess the relationship between quantitative variables. The McNemar's test was used to assess the relationship of categorical variables between the intraoperative and postoperative period, and the chi-square (χ^2) test for the relationship of quantitative variables at different time points after operation. Statistical significance was set at $P < 0.05$. The SPSS statistical program (version 17.0) was used for the analysis of data.

RESULTS

Thirteen of the 110 patients who underwent transcranial CAS with flow reversal protection were excluded from the analysis because of incomplete data in 8, conversion to an open procedure in 3, and indication of CAS for previous stent restenosis in 2.

The study population consisted of 97 patients (78 men, 19 women) with a mean age of 77.4 years (range 51—90). Fifty-four (55.7%) patients presented with history of neurological symptoms in the previous 6 months. The median ratio stenosis was 6.79 (velocity ratio).

Postoperative hypotension was recorded in 33 patients (34%), 21 of which had early hypotension (/6 hr) and 12 had late hypotension (>6 hr) group (Fig. 1). As shown in Table I, postoperative hypotension was unrelated to any preoperative variable. Post-operative

bradycardia occurred in 25.8% of patients within the first 6 hr, in 13.4% within the first 12 hr, and in 10.39% within the first 24 hr (Fig. 2).

Intraoperative factors, including design of the stent (open-cell vs. closed-cell) and whether or not balloon predilatation was performed during the procedure had no effect on postoperative hypotension (Table II). Intraoperative hypotension and/or intraoperative bradycardia were the only variables significantly associated with hypotension within the first 6 hr after the procedure (21.69%, $P = 0.02$ and 26.8%, $\# = 0.01$ of the patients, respectively). A total of 57.1% (12/21) of patients with early hypotension suffered from an episode of intraoperative hypotension and 52.4% (11/21) an episode of intraoperative bradycardia (Table II). All patients in the group of late hypotension required treatment with norepinephrine infusion and were admitted to the ICU to complete intensive hemodynamic monitoring and treatment. The remaining six patients treated with norepinephrine infusion presented early hypotension and also required ICU admission. Overall, 54% of patients with postoperative hypotension required continuous infusion of norepinephrine, whereas the remaining hypotensive patients received fluid therapy and/or ephedrine boluses.

The distribution of patients according to timing of hypotension and need of ICU admission or transfer to the hospital ward is shown in Fig. 3.

Complications were recorded in five patients [transient ischemic attack (TIA) in two, angina in three], with an overall rate of 5.1%. The two cases of TIA occurred in patients in the normotensive group. The three cases of angina developed in one patient in the early hypotension group and in two patients in the normotensive group. The distribution of complications among the three study groups did not show statistically significant differences ($P = 0.341$). The mean length of hospital stay was 3, 3.6, and 2.8 days in the normotensive, early hypotension and late hypotension groups, respectively. Complications related to the cervical approach (bleeding or hematoma) were not found. None of the patients required reoperation. No case of hyperperfusion syndrome occurred.

DISCUSSION

In this retrospective study of 97 patients undergoing transcervical CAS with flow reversal protection, we describe the incidence of hypotension after CAS and the relationship between the timing of appearance of post-CAS hypotension and the incidence of postoperative ischemic events. All patients were at high-risk for carotid endarterectomy

because of the presence local factors (previous carotid surgery, tracheal stoma, cervical irradiation, neurological lesion of the cranial nerves, lesions that extended below the clavicle or dis-surgical risk due to high comorbidity, such as coronary heart disease with recent myocardial infarction and/or unstable angina, heart failure or chronic obstructive pulmonary disease). The technique of transcervical CAS with carotid flow reversal avoids complications related to embolic potential from aortic arch and supra- aortic trunk instrumentation, and provides cerebral protection by reversing flow before crossing the stenosis. Transcervical CAS is the routine technique used in our service. Transfemoral CAS is used occasionally, the indications of which include a short primitive carotid artery and/or low carotid bifurcation with a distance clavicle-bifurcation of less than 5 mm (preoperative echo-Doppler measurement), atheromatous primitive carotid artery lesions, and hostile neck due to previous cervical radiation therapy.

The incidence of hypotension after CAS procedure was 34%, which is similar to data reported in other series. Most episodes of low BP occurred early after surgery (+6 hr), although in more than one-third of patients, hypotension was diagnosed after the first 6 hr of operation. These findings are consistent with the study of McKevitt et al. [5] in which hemodynamic changes were registered within 6 hr in 739a of the cases. These authors, however, showed that hemodynamic depression persisted for an average of more than 20 hr. On the other hand, Lavoie et al. [8] reported an incidence of hypotension after 6 hr of surgery of 17%, and many of the patient had also presented early hypotension. Eight percent of patients had new onset of hypotension or bradycardia later than 6 hr post-CAS, which were attributed to the short monitoring period, among other factors.

Despite the fact that about one-third of patients presented postoperative hypotension, no cases of stroke, acute myocardial infarction, or death were recorded. The incidence of cerebrovascular complications was 1% and of cardiovascular complications of 39c. Hypotension after CAS has been characterized by a benign and self-limited course. However, prolonged hypotension may be associated with an increased risk of neurological, ischemic, and cardiologic events [9-11,18]. Different predictors of postoperative hypotension after CAS have been reported, including advanced age [19,20], female sex [20], previous acute myocardial infarction [19—21], intraoperative hypotension or bradycardia [21], morphological characteristics of the atheroma plaque [22—24], relationship between the diameters of the balloon and the artery [23], and presence of contralateral carotid stenosis [23]. In the present study, patients with intraoperative

hypotension or bradycardia showed a higher incidence of postoperative hypotension, but correlation with other preoperative (age, sex, previous clinical symptoms, or contralateral stenosis) or intraoperative (affected side, balloon pre- dilatation, or type or stent) variables was not observed, probably due to the size of the study population. None of these variables were related to the presence or timing of postoperative hypotension, which is in agreement with results of Mlekusch et al. [19], which in a series of 471 patients undergoing CAS did not find differences between the groups with and without hypotension or bradycardia in relation to the frequency of neurological complications.

The present findings should be interpreted taking into account some limitations of the study, including the retrospective design and the lack of statistical power of the available data to perform multivariate models adjusting for confounders to assess the relationship among preoperative variables and postoperative hypotension, as well as intraoperative hypotension/bradycardia and other factors. Imaging studies like CT scan or MRI post-intervention were not used, and only clinical symptoms were evaluated. Although the results obtained suggest that hemodynamic monitoring during a 6-hr period would be able to identify most patients at risk for postoperative hypotension, the fact that all patients received the same type of postoperative care does not allow excluding that patients transferred to the ward after this period may have a higher risk of postoperative complications. However, none of the patients with late hypotension developed ischemic events, and hypotension was benign in 100% of cases. Moreover, in the group of normotensive patients, all cases of postoperative complications were observed within the first 6 hr after CAS. Accordingly, a change in the postoperative management of these patients may be possible, given that between 6 and 12 hr after surgery and during the remaining days of in-hospital stay, 74.29% of patients (60 normotensive patients and 12 patients with late hypotension) were asymptomatic, which a priori may be candidates to be discharged after 12 hr of the procedure and then controlled at home. This may not only reduce the time of hemodynamic monitoring in specialized units, but also and in previously selected cases, even to perform transcarotid CAS with flow reversal in ambulatory conditions.

CONCLUSION

Most postoperative hypotension episodes occurred within the first 6 hr, and more than one-third developed between the 6 and 12 first hours after the procedure. Also, all patients with late hypotension were asymptomatic. There was no difference in complications

between the study groups. In patients undergoing ambulatory CAS, hemodynamic monitoring in the postoperative period is particularly important during the first 12 hr.

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REFERENCES

1. Pappadà G, Beghi E, Marina R, Agostini E, Cesana C, Legnani F, Parolin M, Petri D, Sganzerla EP. Hemodynamic instability after extracranial carotid stenting. *Acta Neurochir (Wien)* 2006; 148:639-645.
2. Dangas G, Laird JR Jr, Satler LF, Mehran R, Mintz GS, Larrain G, Lansky AJ, Gruberg L, Parsons EM, Laureno R, Monsein LH, Leon MB. Postprocedural hypotension after carotid artery stent placement: Predictors and short- and long-term clinical outcomes. *Radiology* 2000;215:677—683.
3. Mendelsohn FO, Weissman NJ, Lederman RJ, Crowley JJ, Gray JL, Phillips HR, Alberts MJ, McCann RL, Smith TP, Stack RS. Acute hemodynamic changes during carotid artery stenting. *Am J Cardiol* 1998;82:1077-1081.
4. Gil-Peralta A, Mayol A, Gonzalez Marcos JR, Gonzalez A, Ruano J, Boza F, Duran F. Percutaneous transluminal angioplasty of the symptomatic atherosclerotic carotid arteries. Results, complications, and follow-up. *Stroke* 1996;27:2271— 2273.
5. McKevitt FM, Sivaguru A, Venables GS, Cleveland TJ, Gaines PA, Beard JD, Channers KS. Effect of treatment of carotid artery stenosis on blood pressure. A comparison of hemodynamic disturbances after carotid endarterectomy and endovascular treatment. *Stroke* 2003;34:2576—2582.
6. Hwang KW, Suh S, Seo WK, Seol HY, Kim JH, Koh SB, Lee YH, Lee NJ, Kim JH. Hemodynamic depression during carotid angioplasty with stenting: Potential risk factors determined by multidetector computed tomography angiography and related clinical factors. *J Comput Assist Tomogr* 2008;32:124—129.
7. Cayne NS, Rockman CB, Maldonado TS, Adelman MA, Lamparello PJ, Veith FJ. Hemodynamic changes associated with carotid artery interventions. *Perspect Vasc Surg Endovasc Ther* 2008;20:293-296.

8. Lavoie P, Rutledge J, Dawoud MA, Mazumdar M, Riina H, Gobin YP. Predictors and timing of hypotension and bradycardia after carotid artery stenting. *AJNR Am J Neuroradiol* 2008;29: 1942-1947.
9. Howell M, Krajcer Z, Dougherty K, Strickman N, Skolkin M, Toombs B, Panaigua D. Correlation of periprocedural systolic blood pressure changes with neurological events in high-risk carotid stent patients. *J Endovasc Ther* 2002;9:810—816.
10. Hans SS, Glover JL. The relationship of cardiac and neurological complications to blood pressure changes following carotid endarterectomy. *Am Surg* 1995;61:356—359.
11. Masaki KH, Schatz IJ, Burchfiel CM, Sharp DS, Chiu D, Foley D, Curb JD. Orthostatic hypotension predicts mortality in elderly men. The Honolulu Heart Program. *Circulation* 1998;98: 2290-2295.
12. Criado E, Doblas M, Fontcuberta J, Orgaz A, Flores A. Trans- cervical carotid artery angioplasty and stenting with carotid flow reversal: Surgical technique. *Ann Vasc Surg* 2004;18:257-261.
13. Alvarez B, Matas M, Ribo M, Maeso J, Yugueros X, Alvarez- Sabin J. Transcervical carotid stenting with flow reversal is a safe technique for high-risk patients older than 70 years. *J Vasc Surg* 2012;55:978-984.
14. Matas M, Alvarez B, Ribo M, Molina C, Maeso J, Alvarez- Sabin J. Transcervical carotid stenting with flow reversal protection: Experience in high-risk patients. *J Vasc Surg* 2007;46:49— 54.
15. Fonarow GC, Saver JL, Smith EE, Broderick JP, Kleindorfer DO, Sacco RL, Pan W, Olson DM, Hernandez AF, Peterson ED, Schwamm LH. Relationship of national institutes of health stroke scale to 30-day mortality in medicare beneficiaries with acute ischemic stroke. *J Am Heart Assoc* 2012;1:42-50.
16. Jauch EC. Power of National Institutes of Health Stroke Scale in assessing stroke systems of care. *J Am Heart Assoc* 2012;1: 6—7.
17. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined—A consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-969.

18. Qureshi AI, Luft AR, Janardhan V, Suri FK, Sharma M, Lanzino G, Wakhloo AK, Guterman LR, Hopkins LN. Identification of patients at risk for periprocedural neurological deficits associated with carotid angioplasty and stenting. *Stroke* 2000; 31:376-382.
19. Mlekusch W, Schillinger M, Sabeti S, Nachtmann T, Lang W, Ahmadi R, Minar E. Hypotension and bradycardia after elective carotid stenting: Frequency and risk factors. *J Endovasc Ther* 2003;10:851-859.
20. Trocciola SM, Chaer RA, Lin SC, Ryer EJ, De Rubertis B, Morrissey NJ, McKinsey J, Kent KC, Faries PL. Analysis of parameters associated with hypotension requiring vasopressor support after carotid angioplasty and stenting. *J Vasc Surg* 2006;43: 714—720.
21. Qureshi AI, Luft AR, Sharma M, Janardhan Y, Lopes DK, Khan J, Guterman LR, Hopkins LN. Frequency and determinants of postprocedural hemodynamic instability after carotid angioplasty and stenting. *Stroke* 1999;30:2086—2093.
22. Gupta R, Abou-Chebl A, Bajzer CT, Schumacher HC, Yadav JS. Rate, predictors, and consequences of hemodynamic depression after carotid artery stenting. *J Am Coll Cardiol* 2006;47: 1538-1543.
23. Leisch F, Kerschner K, Hofmann R, Steinwender C, Grund M, Bibl D, Leisch FA Jr, Bergmann H. Carotid sinus reactions during carotid artery stenting: predictors, incidence, and influence on clinical outcome. *Catheter Cardiovasc Interv* 2003;58:516—523.
24. Nonaka T, Oka S, Miyata K, Mikami T, Koyanagi I, Houkin K, Yoshifuji K, Imaizumi T. Prediction of prolonged postprocedural hypotension after carotid artery stenting. *Neurosurgery* 2005;57:472—477.

Fig. 1. Percentage of patients with hypotension during the procedure and along the postoperative hours.

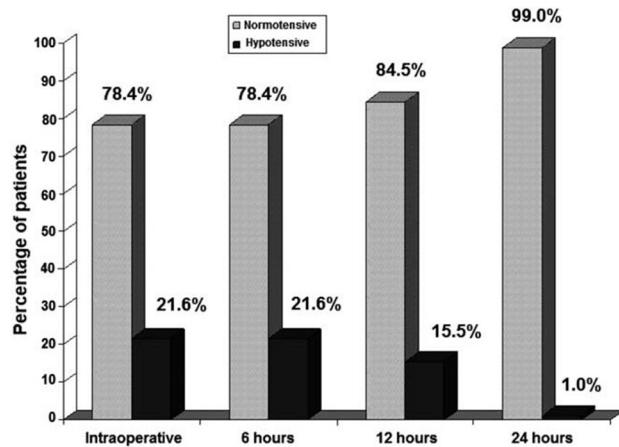


Fig. 2. Percentage of patients with bradycardia during the procedure and along the postoperative hours.

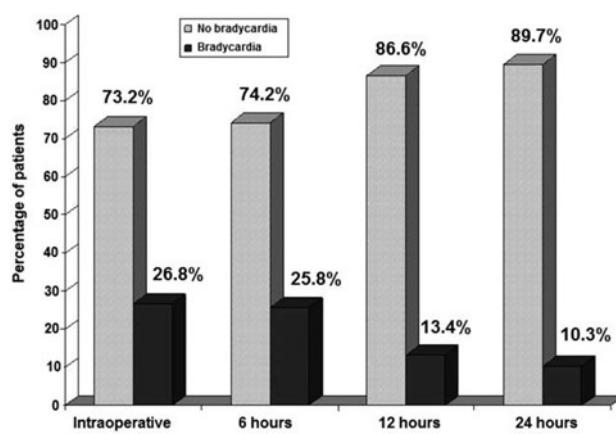


Fig. 3. Distribution of patients according to timing of hypo- tension and admission to the ICU or transfer to the hospital ward

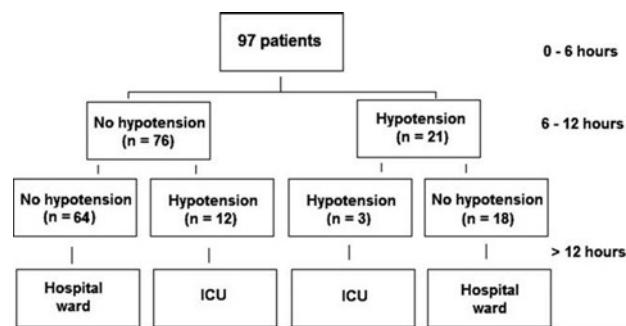


TABLE I. Demographic and Clinical Variables of the Study Population

	All patients	Postoperative hypotension			<i>P</i> value
		Early (<6 hr)	(<6 hr)	Late (>6 hr)	
Total patients, no.	97	21	12	64	
Men/women, no.	78/19	17/4	9/3	52/12	0.880
Age, years, mean (range)	77.4 (51—90)	79.1 (59—90)	77.4 (57—88)	76.9 (51.89)	0.163
History of smoking, no. (to)	65 (67.0)	11 (52.4)	7 (58.3)	47 (73.4)	0.162
Hypertension, no. ('7o)	86 (88.7)	20 (95.2)	11	55 (85.9)	0.476
			(91.7)		
Dyslipidemia, no. ('7o)	69 (74.2)	13 (61.9)	9 (75)	47 (73.4)	0.740
Diabetes mellitus, no. (to)	33 (34.0)	7 (33.3)	1 (8.3)	25 (39.1)	0.119
Ischemic heart disease, no. (to)	37 (38.1)	7 (33.3)	6 (50)	24 (37.5)	0.627
Cerebrovascular disease, no. (to)	54 (55.7)	11 (52.4)	6 (50)	37 (57.8)	0.949
Peripheral artery disease, no. (to)	29 (29.9)	4 (19.0)	7 (58.3)	18 (28.1)	0.052
Symptomatic lesion, no. (to)	54 (55.7)	11 (52.4)	6 (60)	37 (57.8)	0.949
Contralateral stenosis > 50%	48 (49.5)	11 (52.4)	6 (50)	31 (48.4)	0.935
ICA, no. ('7o)					

ICA: internal carotid artery.

P value of chi-square test refers to the homogeneity of distribution of each variable among the three groups of early and late postoperative hypotension and normotensive.

TABLE II. Relationship Between Intraoperative Variables and Postoperative Outcome

	All patients	Postoperative hypotension			Normotensive	<i>P</i> value
		Early (<6 h)	Late (>6 h)			
Total patients, no.	97	21	12	64		
Type of carotid stent (n = 94)‘					0.13	0
Open-cell, no. (to)	27 (28.7)	3 (15)	2 (16.7)	22 (35.5)		
Closed-cell, no. (to)	67 (71.3)	17 (85)	10 (83.3)	40 (64.5)		
Balloon pre-dilatation, no.13 (13.4) (to)		1 (4.8)	2 (16.7)	10 (15.6)	0.42	0
Right side, no. (to)	45 (46.4)	10 (47.6)	5 (41.7)	30 (46.9)	0.94	0
Intraoperative hypotension,21 (21.6) no. (to)		12 (57.1)	2 (16.7)	7 (10.9)	0.02	
Intraoperative bradycardia,26 (26.8) no. (to)		11 (52.4)	2 (16.7)	13 (20.3)	0.01	

‘Data of three patients were missed. Open-cell: Acculink, Precise. Closed-cell: Wallstent, Xact.

P value of chi-square test refers to the homogeneity of distribution of each variable among the three groups of early and late postoperative hypotension and normotensive.