Thrombosis Research 130 (2012) 12–15

Contents lists available at SciVerse ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Chronic oral anticoagulant therapy in carotid artery stenting: The un-necessity of perioperative bridging heparin therapy

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ARTICLE INFO

Article history:
Received 18 April 2011
Received in revised form 5 September 2011
Accepted 28 September 2011
Available online 29 October 2011

Keywords:
Carotid artery stenosis
Oral anticoagulant therapy
Bridging heparin therapy
Carotid artery stenting

ABSTRACT

Introduction: Chronic oral anticoagulant therapy (OAT) is of widespread use, and usually its management in patients undergoing carotid artery stenting (CAS) is through perioperative bridging heparin therapy. Aim of the present study is to analyze a single center experience of CAS in patients maintaining OAT without perioperative bridging heparin therapy.
Materials and methods: A retrospective evaluation of consecutive patients submitted to CAS was performed. Clinical anatomical characteristics and chronic OAT were evaluated to find a correlation with stroke, death, myocardial infarction and bleeding from the access site by Chi-square, Fisher's tests and regression analysis.
Results: 502 CAS were performed in a 5-year period. Twelve (2.4%) strokes, 1 (0.2%) death, no myocardial infarctions and 4 (0.8%) access site bleeding occurred in the perioperative period. In the overall population the presence of type 3 or bovine aortic arch was associated with stroke (5.5% vs. 1.5% $p = 0.02$), and preoperative neurological ischemic symptoms were correlated with higher incidence of the composite event of stroke/death (4.8% vs. 1.4%, $p = 0.05$). Twenty patients (4.0%) under chronic OAT were submitted to CAS without perioperative bridging heparin therapy with no complications. Overall, patients under OAT had no significantly different outcome compared with patients without OAT.
Conclusions: OAT without perioperative bridging heparin therapy is safe and effective. This data could be useful in the management of patients with chronic OAT submitted to CAS.

Introduction

Approximately 4 million patients are currently receiving oral anticoagulant therapy (OAT) to prevent thromboembolism from atrial fibrillation, mechanical heart valves or deep vein thrombosis in western countries [1]. The management of patients in OAT undergoing surgical procedures requires usually a perioperative bridging heparin therapy, with substitution of OAT by heparin infusion few days before the surgical procedure and perioperatively [2].

The management of this bridging therapy causes, patients discomfort, costs - ranging from 672 $ to 5196 $ for patient [3–5] - and risks of thrombosis/hemorrhage due to an incorrect dosage or adverse heparin reaction, even with low-molecular-weight and with unfractionated heparin [6–9]. OAT patients candidate to endovascular procedures, usually undergo to perioperative bridging heparin therapy, in order to prevent possible bleeding complications, however some authors report safe and effective results in percutaneus coronary interventions or pacemaker/defibrillator implantation without interrupting OAT thus avoiding the necessity of heparin bridging therapy [10–13].

Carotid artery revascularization by stenting (CAS) is nowadays an alternative to standard surgical therapy [14]; in this setting, OAT patients are usually managed with bridging heparin therapy, but there are no data establishing the effective value of this management compared with unstopped OAT. We have therefore reviewed a single center experience of CAS in patients with unstopped OAT, in order to assess its safety and effectiveness.

Materials and methods

Patients

All consecutive CAS performed in a five years period in a single centre were retrospectively reviewed. From 2005 to 2008 CAS were chosen as an alternative to CEA according patients' clinical and anatomical characteristics ("hostile neck" or pulmonary or cardiac diseases) or surgeon's experience in endovascular carotid artery revascularization. The first operator for all the CAS procedures were an expert surgeon (FG) with more than 500 procedures performed. From early 2009 CAS indications were

Abbreviations: CAS, carotid artery stenting; OAT, oral anticoagulant therapy; MI, myocardial infarction.

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doi:10.1016/j.thromres.2011.09.031

modified according SVS recommendations: endovascular carotid revascularization was performed in symptomatic with high surgical or anesthesiologic risk patients [14,15]. Clinical and anatomical characteristics were recorded in a database software for the statistical analysis.

Clinical characteristics considered were: hypertension (presence of systolic blood pressure >140 or/and diastolic >90 mmHg, or specific therapy), dyslipidemia (total cholesterol >200 mg/dl or low density lipoprotein >120 mg/dl or specific therapy), diabetes mellitus (prediagnosed in therapy with oral hypoglycemic drugs or with insulin), current smoking, coronary artery disease (CAD) considered as history of angina pectoris or myocardial infarction or coronary revascularization. Pre-operative ischemic neurological symptoms were considered any hemispheric events (stroke, transient ischemic attack, amaurosis fugax) ipsilateral with the carotid stenosis within 6 months of the revascularization. Anatomical characteristics considered were: aortic arch type – arches have been divided into "simple aortic arch" [i.e. type I or II] and "difficult aortic arch" [type III and "bovine"], as previously described [16] and carotid plaque echogenic structure - evaluated as ipo-echogenic, iso-echogenic and iper-echogenic/calcified according to Tromso classification (type I, II and III/IV) [17]. The events considered in perioperative (30-day) period were: stroke, clinically evaluated by an in hospital neurologist and new acute ischemic lesion identified by cerebral CT scan, myocardial infarction (with hospital cardiologist and electrocardiography and serologic evaluation) and death and bleeding at the access site requiring surgical evacuation that corresponds to the mild GUSTO [18] bleeding classification or minimal of TIMI [19] classification.

Patients under OAT were submitted to CAS without interrupting the therapy and maintaining the assigned target INR according to their pathology (atrial fibrillation, mechanical prosthesis or deep vein thrombosis); in these patients, the usual heparin administration during the CAS procedure was avoided. Single antiplatelet therapy were administered to all patients in OAT in the perioperative period.

CAS procedure

CAS procedure was conducted as follows and as described in previous papers [20]. Briefly, patients were taken to the angiographic suite after appropriate informed consent and cardiological evaluation and medicated with aspirin 100 mg and clopidogrel 75 mg for 3 days before the procedure. Clopidogrel therapy was maintained for a month. All procedures were performed under local anaesthesia, systemic unfractionated heparinisation according the ACT values and an 8 F groin introducer. Common carotid cannulation was achieved with 40° Boston Scientific® or Medtronic® HS I and II catheters over a Terumo® stiff guide wire. When cannulation was not achievable by these means, several different alternative techniques were used (i.e., buddy wire, coaxial). Brachial or carotid access was not attempted in any case. Routine cerebral protection was by Filterwire EZ (Boston Scientific®) and stenting by closed-cell (Wallstent, Boston Scientific®). 'Technical success' was defined as the ability of treating the stenosis with less than 30% residual stenosis.

Haemostasis of the point of access was achieved with vascular closure device platform (Angio-Seal™ St. Jude Medical Inc., St. Paul, Minnesota, USA.) or manual and elastic groin compression.

Neurological outcome was evaluated both at the end of the procedure and in the following 24 h by a neurologist according to the NIH stroke scale and the modified Rankin scale.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as numbers with percentage. Chi-squared and Fisher's test and logistic regression were used to compared different frequencies between groups. The value of $p<0.05$ was considered significant. Statistical tests were performed using Statistical Package for Social Sciences for Windows® (SPSS® 13.0) computer software (SPSS, Chicago, IL, USA).

Results

From 2006 to 2010, 502 CAS procedures were performed. Mean patients age was 75.7 ± 6.7 years. The overall clinical and anatomical characteristics and perioperative events are summarized in Tables 1 and 2. In the population study, 145 (29.1%) patients were symptomatic: there were 57 (11.4%) ipsilateral strokes, 69 (13.9%) TIA and 19 (3.8%) amaurosis fugax. The aortic arch was type I in 259 (51.6%) cases, type II in 121 (24.1%) cases, type III in 40 (8.0%) cases and bovine or other anomalies in 69 (13.7%) cases. In 34 procedures technical success was not achieved due to unstable common carotid access in 28 cases and severe tortuosity of the common carotid artery in 6 cases; all these patients were submitted to carotid endarterectomy afterwards. An arterial closure device (Angioseal) was used in 483 (96.2%) cases and manual and elastic compression of the femoral point of access in 19 (3.8%) cases. The latter kind of hemostasis was used in 1 OAT patients and was not correlated with any adverse events.

In the perioperative period 12 strokes (3 major and 9 minor stroke) occurred; there was one death at 30 day and 4 cases of bleeding requiring surgical intervention. In the overall population the elements associated with adverse events were the aortic arch type and the preoperative neurological ischemic symptoms, as shown in Table 3.

Twenty patients under OAT (4.0%) underwent to CAS in this series. Indication for OAT with appropriate INR is shown in Table 4. The clinical and anatomical characteristics of patients in OAT were homogeneous with the overall patients' populations (Table 1). Patients under OAT did not experience any adverse event in term of strokes, death, myocardial infarction or hemorrhage/hematoma. There were not significant differences in clinical outcome between patients in OAT and the overall population underwent to CAS.

Discussion

Our data show that no thrombotic or hemorrhagic events occurred in CAS patients under uninterrupted OAT; thus to maintain OAT unmodified could be a valid alternative to bridging heparin therapy. Currently, bridging heparin therapy for endovascular procedures in

Table 1
Clinical and anatomical characteristics of the study population. CAD: coronary artery disease.

	N (Tot: 502)	%
Age ≥ 80 years	142	28.5
Male gender	326	65.5
Clinical risk factors		
Pre-operative ischemic neurological symptoms	145	29.1
Stroke	57	11.4
Transient Ischemic Attack	69	13.9
Amaurosis Fugax	19	3.8
Hypertension	437	87.8
Dislipidemia	184	36.9
Diabetes	133	26.5
Smoke	92	18.8
CAD	185	37.1
Oral Anticoagulant Therapy	20	4.0
Anatomical characteristics		
Type III or bovine aortic arch	109	21.9
Carotid plaque at duplex scan		
Iper-echogenic/calcified	314	62.5
Ipo-echogenic	116	23.1
Iso-echogenic	72	14.3