CARLO SETACCI

Reinterventions in VASCULAR and ENDOVASCULAR surgery

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FOREWORD

The technological improvement associated with new skills in treatment of aortic and peripheral vascular diseases has led to an increase in life expectancy in vascular patients.

In their daily practice, vascular surgeons deal with patients and lesions of great complexity. New techniques are now available to manage most of the clinical conditions.

Reinterventions after both classical open surgery and endovascular procedures are more and more frequent, representing one of the most important part of the daily activity of a vascular surgery unit.

New endovascular techniques represent a safe, effective and quite simple solution in most cases of reintervention. However, in many situations open surgery still remains the only viable procedure, also considering that the presence of a pre-existent scar is a negative predicting factor for surgery.

Ethical rules compel us to take on a new challenge every day of our clinical practice, searching for the best care for every patient.

This book tries to summarize all the possible types of reintervention in all vascular fields for both acute complication or late failure after open surgery and endovascular procedures.

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CHAPTER 1

Reinterventions in vascular and endovascular carotid surgery

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Carotid endarterectomy (CEA) and carotid artery stenting (CAS) are considered the two alternative solutions to treat the carotid artery stenosis. The classical surgical approach has been performed by DeBakey in 1953 [1] and remained broadly unchanged with just a bit of technical improvement. The history of the endovascular approach is different, in fact from the first carotid angioplasty approach performed by Mathias in 1978, many technical improvements were made and the real innovation has been made by Theron who introduce new techniques more similar to the actual strategies.[2]

Nowadays the rapid expansion in the volume of carotid surgery together with the growing proportion of operations performed for asymptomatic lesions, demanded a more complete understanding of the long-term results. From the early days of carotid reconstructions, surgeons had better long-term results with carotid endarterectomy (CEA) than with other sites. Whereas endarterectomy for leg ischemia was frequently followed by restenosis or occlusion, the carotid artery seemed to be relatively free from these problems.

However, despite the technical evolutions of new available materials and the expertise of the operators, complications, although not very frequent, are possible.

The aim of this review is to assess local complications which can lead to re-interventions after CEA and CAS.

Local complications which may potentially require operative intervention after CAS

Stent-related complications

Stent thrombosis which led to acute thrombotic occlusion of the treated carotid artery

It is a potentially fatal complication which usually appears as intrastent filling defect or diffuse haziness located inside the stent or at its edge. It is a rare complication which incidence ranges from 0.04% to 2% [3] and requires rapid diagnosis and reperfusion to limit cerebral ischemia. It is mainly related with a suboptimal pre-procedural antiplatelet therapy and for this reason double antiplatelet therapy is mandatory in the periprocedural setting. In fact, acute thrombosis derives from platelet aggregation which can be triggered either by predisposing patient's factors (hypercoagulation state that may

generally cause microvascular complications and/or resistance to antiplatelet agents, inadequate antiplatelet monotherapy, early discontinuation of antiplatelet treatment) or by procedural findings (technical error during the endovascular procedure, vessels dissections during the endovascular procedure, and plaque prolapse especially in recently symptomatic patients who had a carotid lesion with echo-color-Doppler signs of "vulnerable plaque") (Figure 1). For the best of our acknowledgements, we have to cite a recent review which concluded that CAS, in recently symptomatic patients, could be proposed as a possible alternative to CEA in selected cases and if the procedure is performed in high-volume center with documented low perioperative stroke and death rates.[4]

As we know, Clark *et al.* utilizing intravascular ultrasound (IVUS), defined plaque prolapse as "the part of plaque prolapsing at least 0.5 mm through the stent struts".[5] Angiographically, a plaque tissue which prolapses through the stent cells into the artery lumen causing intra-arterial filling defect of various degree could be regarded as a sufficient definition for plaque prolapse. It could be a possible site for stent thrombosis or embolic source.

Nowadays, there is great interest in the possibility to recognize further details regarding the interaction between a carotid plaque and a stent by optical coherence tomography (OCT) imaging, considering that plaque prolapse through the cell stent has been suggested as one of the major causes of post-procedural complications following CAS and that available periprocedural imaging systems (angiography, IVUS and duplex ul-

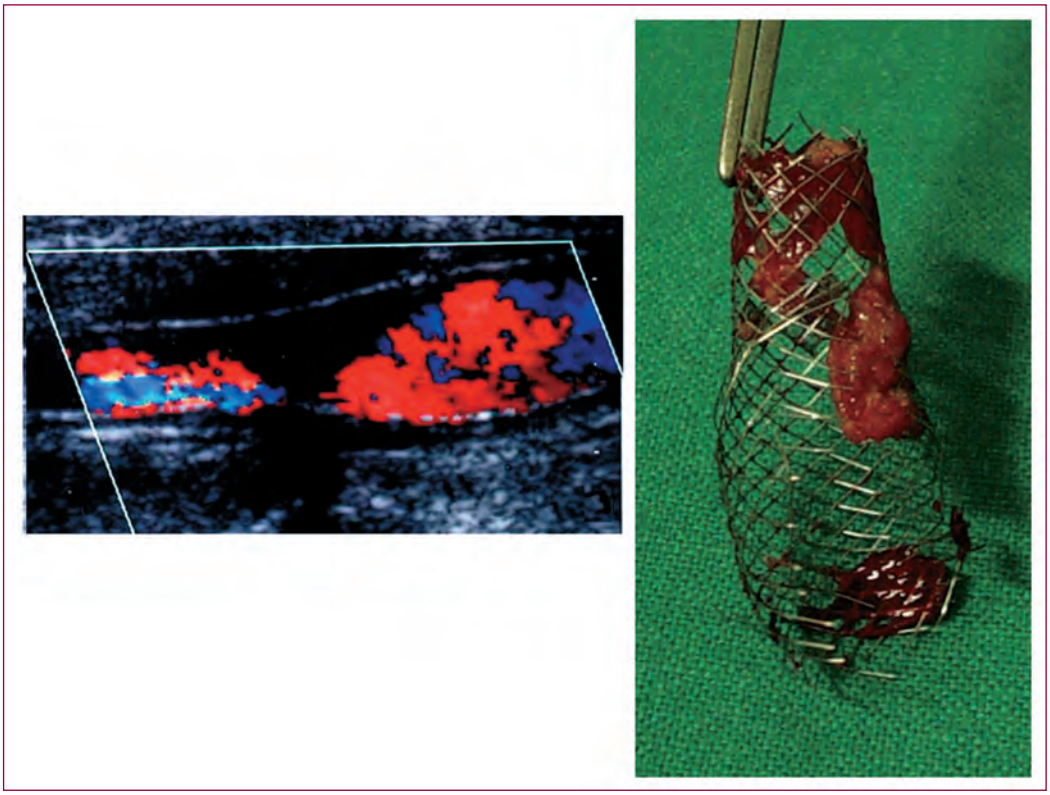

Figure 1.—Case of incomplete in-stent thrombosis diagnosed by eco-color-Doppler and its intraoperative finding in which it's evident plaque prolapse through the stent struts.

trasound) may not be able to detect such micro-defects. In this direction a recent study correlates micro-defects detected with OCT after stent deployment and the design of implanted stents: stent malapposition seems to be more frequent with closed-cell design stents, while plaque prolapse is more common with open-cell designed stents.[6]

However, the appropriate treatment of plaque prolapse is not codified and is related to the severity of the luminal encroachment: double antiplatelet therapy is mandatory while the use of low-molecular-weigh heparin may be recommended for the first weeks. If the defect fills significantly the vessel lumen, it should be treated with repeated in-stent balloon inflations and, if it persist, could be recommended an implantation of a second stent (stent over stent).

Even as regarding the optimal treatment for acute thrombosis, it is not yet established. Several authors have provided different management of this complication: both intra-arterial and intravenous administration of abciximab have been described as a treatment option.[7-9]

Some authors report successful treatment of acute carotid stent thrombosis by combination therapy using percutaneous mechanical thrombectomy and adjunctive intravenous abciximab.[10, 11]

Despite a number of cases with good results described in the literature, the endovascular approach for acute carotid thrombosis presents some concerns about the possibility of thrombus embolization during treatment. The intraluminal manipulation of guides and catheters in association with thrombolysis can cause the fragmentation of clots and subsequently increase the risk of distal intracerebral embolization. For these reasons, with a diagnosis of intracranial vessel occlusion, our group choose a prompt endovascular approach with intraluminal thrombolysis; in contrast, we have some concerns about treating an extracranial vessel occlusion with an endoluminal approach and we believe that all endovascular attempts should be avoided and that immediate surgical neck exploration is the only alternative.[12] Emergent surgical intervention can consist of stent removal and thromboendarterectomy or, in selected cases, cerebral reperfusion can be established by simple thromboembolectomy without removing stent.

Moreover we have to cite Parodi *et al.*[13] which described an endovascular treatment of a symptomatic free-floating thrombus of the internal carotid artery using flow reversal.

However, in patients suffering from acute poststenting carotid thrombosis, all efforts should be undertaken to minimize neurologic sequelae.

Stent migration or inaccurate stent placement either proximally or distally

It could be a cause of incomplete plaque covering with exposed thromboemboligen surface and high risk of early or late cerebral neurologic complications. Residual stenosis may be another consequence of incorrect stent placement: therefore a second stent placement to cover all the plaque is mandatory. Stent migration occurring far away from the planned site is a rare event: in this case the stent could be left in place if it does not cause flow disturbances due to vessel oversizing or covering at bifurcation point; on the contrary, emergent surgical removal of the stent displaced at a distant zone might be required.

Dissection of common or internal carotid artery

The incidence of common carotid artery dissection increased with vessel's tortuosity, hard aortic arch anatomies, and the number of maneuvers required to advance

the devices while engaging the common carotid artery. Dissections could led to thrombotic occlusion of the artery or thrombotic embolization arising from the area of dissection causing stroke of various degree. Linear dissections which not limit flow usually don't require treatment, instead spiral dissections must be treated, especially when anterograde flow is impaired: it is advisable to cover these dissections using self-expandible stent (which offers better conformability to the vessel anatomy and reduces the risk of further dissection expansion, compared to a balloon expandible stent that is more used to cover the ostial dissections of the common carotid artery). However, in case of severe symptomatic dissections unable to be treated with an endovascular approach, urgent surgical repair may be necessary.[14]

As regarding internal carotid artery dissection, it generally occurs when the operator try to overpass a filter protection device through a distal tortuous part of the artery. Linear dissections could be managed with a gentle and prolonged ballooning dilatation and if it is unsuccessful, positioning a stent is mandatory. Instead spiral dissections have to be treated first with stent implantation.

Stent fracture

It is a usually asymptomatic event who has been documented in the literature and in the majority of cases arises from the exposition of the stent to unfavorable stresses and biomechanical forces. In a review article, Sfyroeras *et al.*[15] noticed that carotid stent fractures are mainly reported after implanting of self-expandable nitinol stents instead no difference was observed between open and closed-cell stent design. Furthermore heavy plaque calcification of the carotid artery may be a risk factor for stent fracture since it impedes complete expansion of the stent and creates a more rigid artery and a point of fixation on the stent in situ, necessitating that the proximal and distal un-stented segments of artery accommodate in-neck movement: this creates regional friction, increasing the risk of fracture.[16]

There are several implications of carotid artery stent fracture, including artery thrombosis (and subsequent stroke), migration of fractured segments (particularly if the fractured segment is small), and even carotid false aneurysm as recently reported (Figure 2);[17] Moreover a stent fracture significantly increases the likelihood of in-stent restenosis (ISR). Principles of management of stent fracture are the same as those used for the management of ISR and its optimal treatment remain to be clarified: it could be managed with a less invasive endovascular approach, or alternatively with a surgical endarterectomy and patch repair preceded by stent removal.

Filter device- related complications

Generally are uncommon and mainly associated with the filter type distal protection devices.

The most common complication caused by filters is the spasm of the internal carotid artery that in most cases is transient and resolves itself.

Filter occlusion

Filter occlusion is generally a benign complication too and it is the consequence of a large load of embolic material captured into the filter's basket causing obstruction of its cells: in these cases, an aspiration using special catheters must be attempted before retrieving the filter and the filter should never be fully withdrawn into the

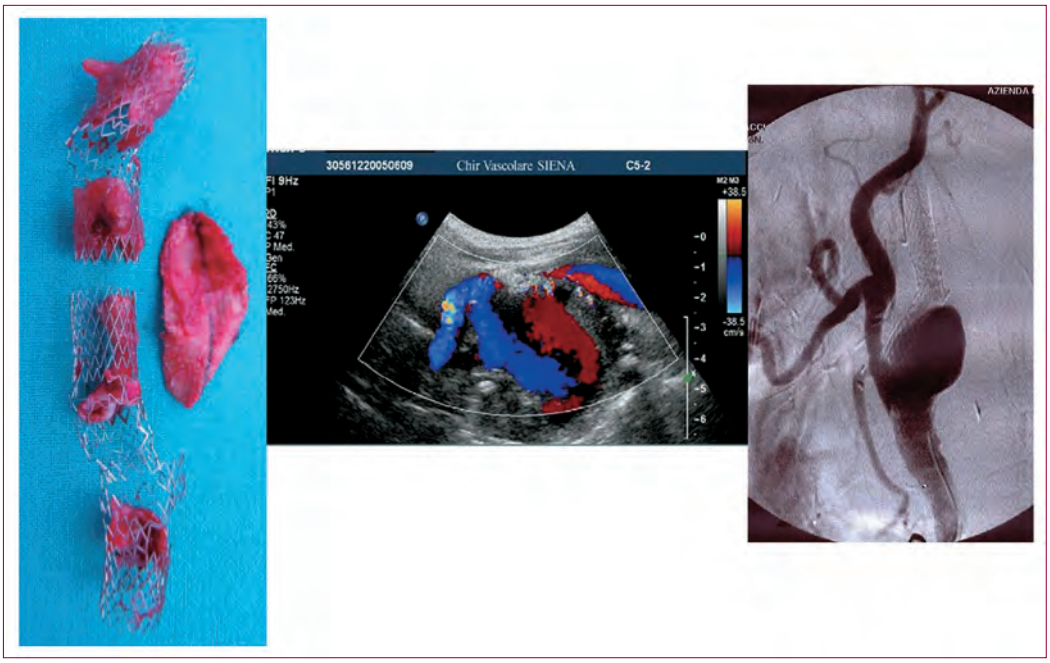

Figure 2.—Intraoperative, eco-color-Doppler and angiographic findings of carotid false aneurysm following stent fracture after CAS.

retrieval sheath to avoid material squeezing. These latter two complications, spasm and filter occlusion, generally don't require re-interventions and are mentioned to be thorough.

Dissection of the distal carotid internal artery

Dissection of the distal carotid internal artery the landing zone of the filter whose management is mentioned before.

Difficult retrieval of the filter

This could be due to the unskillful of the operator such as because the filter has been trapped into the stent struts during removal.[18, 19] Several endovascular maneuvers can be tried to overcome the complication, but occasionally it requires surgical removal.

Local complications which may potentially require operative intervention after CEA

Hemorrhage and hematoma formation

It may be benign or potentially life threatening if airway compromise ensues. It could be a consequence of surgical technical errors with a failure of the suture line and/or it could be caused by incomplete hemostasis after systemic heparinization and widespread usage of antiplatelet agents.

Surgical re-exploration and evacuation of symptomatic hematomas should always be considered. Other precautions to minimize this complication are blood pressure control, utilization of temporary drains, whereas most surgeons do not reverse systemic anticoagulation because of the risk of potentially deleterious neurologic events. However, there is no substitute for good surgical technique.

False aneurysm of the carotid arteries after CEA

It is a not frequent complication following CEA and may develop either after direct suture of the arteriotomy or patch angioplasty, using vein or prosthetic materials.[20]

Mechanical factors and infection both have a role in pathogenesis, the first are thought to be important when haemorrhage occurs early due to rupture of the vein patch or technical errors during surgery; instead infection is thought to be important when hemorrhage occurs later.[21]

Acute thrombotic occlusion of the treated carotid artery that can led to stroke and neurologic deficits. It could derive from any technical defects such as intimal flaps or irregularities associated with the anastomotic site: prevention relies on adequate surgical exposure, generous arteriotomies beyond the disease endpoint, meticulous endarterectomy and patch angioplasty to reduce technical error.

The management of acute post-CEA thrombosis is very similar to the management of acute post-CAS carotid thrombosis.

Dissection of distal internal carotid artery

Dissection of distal internal carotid artery which is mainly a complication of the shunt placement during the surgical procedure and it could be managed with the positioning of a stent to cover the dissection.

Local complications which may potentially require operative intervention after both CAS and CEA

Graft/stent infection

According to the Centers for Disease Control (CDC) National Nosocomial Infections Surveillance System,[22] vascular and endovascular interventions are clean procedures (risk index categories 1 and 2). Overall incidence of vascular site infections should range between 2% and 6%.

Actually the precise overall incidence vascular surgical site infections and prosthesis graft infection is difficult to determine because most reported series are retrospective. The reported incidence of infection involving synthetic vascular grafts is around 2%, occurring after 0.2% to 6% of interventions.[23-25] This variability can be partially explained by differences in duration of postoperative follow-up, type of graft material and method of construction, use of antibiotic prophylaxis, and virulence of the infecting pathogens.

Moreover, the actual incidence may be higher, since many graft infection do not become clinically evident until years after implantation, and the hospital that manages the complication is often different from the original one. The true incidence of graft infection may be estimated as high as 5%, if both early and late infection is included.

Several factors predispose to graft infection and first of all the infection rates after reoperative vascular procedures for hematoma or graft thrombosis reflect the frequency of arterial wall and wound colonization. Beyond surgical site healing, host defense mechanism and underlying patient's disease are involved: patients with impaired immune function due to malnutrition, malignancy, or autoimmune disease will have more difficulty fighting infection. Similarly, the administration of medications such as steroids or immunosuppressive chemotherapy will alter the patient's immunological disease. Moreover, graft infection is more likely to occur after emergent procedures: breaks in sterile surgical technique and improper sterilization of grafts or instrumentation are obvious sources of contamination.

Early infection generally arises from contamination of the graft by skin commensals at the time of surgery. *Staphylococcus Aureus* (including Methicillin-resistant Staphylococcus Aureus) is the most common pathogen to present in this way. However, as we know, vascular surgeons now realize that the potential for graft infection extends well beyond the postoperative period. Late-presenting infections can arise from a number of sources; either by hematogenous spread from another focus of infection, or from infection acquired at the time of surgery with relatively indolent bacteria such as coagulase-negative *Staphylococcus*.

Luckily, graft infection at cervical level is extremely rare (0-0.8%). A recent publication by Knight *et al.*[26] reports all known cases of synthetic patch infection following carotid endarterectomy over the last 12 years. Fourteen publications have been identified totaling 77 cases of graft infection (0.25-0.5%) of all dacron patches appear to get infected. Infection may present early or late and appears to have a bi-modal distribution depending on the presence of low- or high-grade infection. Post-operative complications especially wound hematoma is associated with the later development of infection. Most patients present with pseudoaneurysm formation (false aneurysm after CEA occurs infrequently and, however, those associated with infection are extremely rare and reports in the Literature involve solitary or small numbers of cases), pain, neurological deficit, neck swelling or a draining local sinus and are infected with either *Staphylococcus Epidermidis* or *Staphylococcus Aureus*. Presumably, if patch infection is allowed to take its natural course, it would begin with systemic sepsis and culminate in patch rupture: so its management should aim to remove all infected material and to minimize perioperative morbidity and mortality.

The very low incidence of infection is probably related to the excellent vascularization of this district. Another factor which predisposes to infection after CEA, is the use of synthetic graft to repair the vessel. Synthetic patch infection is a rare but recognized complication of CEA.[27, 28]

In fact, as we know, in Literature there are several commonly employed techniques used to repair the carotid artery following CEA in addition to direct suture: they include interposition of vein graft, vein patch (with either the long saphenous vein, facial vein or internal jugular vein), and synthetic patch with woven polyester, Polytetrafluoroethylene or bovine pericardium. Synthetic grafts are essentially equal to vein grafts in terms of recurrent restenosis and perioperative stroke rate.[29]

They are frequently used since they are readily available, avoid additional wounds, preserve saphenous vein and have a lower graft rupture rate than vein patches. A disadvantage is that they well be susceptible to suture hole haemorrhage, pseudoaneurysm formation and higher infection rates.[30]

After diagnosis of patch infection, all efforts should be undertaken to remove radically all infected material and surgical exploration and drainage of infection should

be regarded as mandatory. Most Authors advocate wide excision of the patch and of all infected material following by vascular carotid reconstruction. However, no consensus exist over the arterial reconstruction methods: in the six largest series reconstruction with vein patch or vein graft was the most popular option.[31-36]

We have to remember that El Sabrout *et al.*[36] reported a replacement of 6 infected Dacron patches with further Dacron patches after thorough excision of all apparent infected material: however this management is not recommended since carries a high re-infection rate.

In literature successful outcomes are achieved too by excision of the infected tissue and leaving the graft intact if deemed reasonable at the time of exploration. Carotid artery ligation has been proposed by Naylor *et al.*[34] with a positive outcome, with no infective recurrences or associated perioperative morbidity, likely due to a judicious pre-operative planning with duplex ultrasonography and to intra-operative transcranial Doppler to monitor cerebral perfusion. Chaudhuri *et al.*[27] proposed the balloon occlusion test of the internal carotid artery, to evaluate the collateral circulation from the contra-lateral hemisphere, as a predictor of the feasibility of its ligation.

Acute carotid thrombosis and occlusion of the treated vessels

As mentioned before, the management of acute thrombosis is very similar either it is a consequence of CAS or it follows a CEA: both require emergent evaluation and emergent definitive repair to minimize neurologic morbidity.

Restenosis

Restenosis that still remain a critical issue after vascular and endovascular surgery and a challenge for the vascular surgeon. Carotid artery stenosis after CAS or CEA should be considered a serious complication that could limit the long-term efficacy of the revascularization.[37]

Usually, even if restenosis represents a stable, asymptomatic, non embolic lesion, it can evolve resulting in cerebral ischemia.

The reported incidence of post-CEA stenosis ranges from 1% to 36% according to study.[38, 39]

Most restenosis occur within the region of a previous endarterectomy, suggesting that recurrence is the result of postoperative alterations of the healing process.

The remainder of the lesions are found above or below the extent of the arteriotomy, reflecting technical problems, including clamp injuries, endpoint problems and incomplete or inadequate extent of endarterectomy.

Intimal fibrosis, also called myointimal hyperplasia or fibroplasia, is the lesion most often found with restenosis in the first 2 years. At operation there is smooth narrowing with a white, glistening appearance and a firm or rubbery consistency.

The process may extend through the thickness of the media, so that it is not possible to establish a dissection plane for endarterectomy.

Late restenosis usually results from recurrence of atherosclerosis and have the same gross and microscopic features found in the original lesions, including lipid collections, foam cells and calcification. The luminal surface may be irregular or ulcerated. Some plaques can be easily removed by endarterectomy, whereas others have more fibrous reaction, making it difficult to create a suitable plane for dissection. The fact that some restenosis have elements of both initial fibrosis and

atherosclerotic changes leads to speculation over whether these pathologic findings represents two different entities or early and late manifestation of the same process.

The incidence of ISR among studies varies between 3.4% and 8%, with a relatively short surveillance period of 12-20 months.[40] The historic SAPPHIRE trial at 3-year follow-up reported a higher, but not statistically significant, incidence of post-CEA stenosis: 7.1% *vs.* 3%.[41] Nevertheless, many investigators recently observed that the stenosis rate after CAS is much higher than post-CEA.[42] The SPACE trial showed that stenosis occurred more frequently in the 2 years after CAS than after CEA (11.1% vs.4.6% of patients).[43]

There are several putative causes of restenosis after carotid angioplasty. First of all smoking which appears to have the greatest association with this complication, instead hyperlipidemia, diabetes, and other risk factors have failed to demonstrate a consistent association with recurrence of stenosis.[44, 45] A multivariate analysis of factors determining restenosis after CAS, showed that patient who develop restenosis after CEA are also prone to develop restenosis after CAS.[46] Moreover older age, female gender, implantation of multiple stents, residual stenosis after the first procedure, symptomatic carotid lesions and neck radiotherapy were associated with an increased risk of ISR (Figure 3).[47-49]

While restenosis following conventional balloon angioplasty represents a multifactorial entity with complex interplay between neo-intimal hyperplasia, elastic recoil and negative vascular remodeling, luminal narrowing after stent implantation is almost exclusively due to neo-intimal hyperplasia. Within minutes to hours of intimal injury, deposition of mural thrombus and inflammatory cell infiltration occur. Over the ensuing days, smooth-muscle cells (SMCs) are activated, proliferate and migrate to the site of intimal injury, with subsequent deposition of extracellular matrix (ECM) proteins, giving rise to the neo-intima. Stent-induced arterial wall injury leads to a complex interaction between platelets and local inflammatory cells, causing the release of multiple chemotactic and activating molecules that ultimately lead to the activation of medial SMCs. Activated SMCs enter a proliferative phase before their intimal migration. Proliferation of medial SMCs in evident 24 hours after intimal injury and continues for at least 2 weeks.

After intimal injury, platelets adhere to the injured site and become activated under the influence of collagen and local thrombin. Activated platelets release multiple factors involved in the restenosis process. Moreover, emerging experimental and clinical data indicate that leucocytes may be involved to a large extent in intimal growth after mechanical arterial injury. Infiltration and accumulation of monocytes and macrophages is a dominant pathophysiological response after stent-induced arterial injury.

As regarding the indication for treatment after carotid revascularization, there

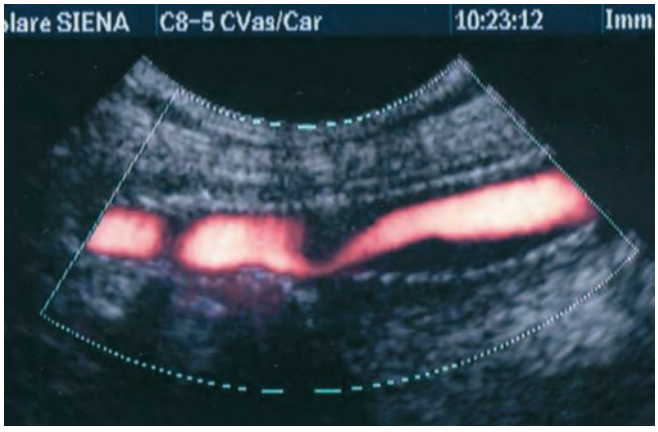

Figure 3.—Case of ISR diagnosed by eco-color-Doppler.

are concerns about the indication in asymptomatic patients, instead it is widely accepted for symptomatic patients with narrowing of the lumen >50%.

Although there are no data regarding the exact incidence of thromboembolic stroke from recurrent stenosis, the topic about treating asymptomatic lesions in order to reduce the risk of stroke is still debatable: the management of an asymptomatic restenosis in neither simple nor clear-cut, primarily because there are few data on the risk of stroke if the lesion is left untreated. Overall the generalization that appears in the current literature is that the asymptomatic restenosis is well tolerated by most, since less than one fifth of these patients became symptomatic.

Many studies have shown that the new lesion may be quite different from the original one, so that it is not appropriate to presume the same prognosis or risk of stroke. The risk is likely to be related to the pathology of the new lesions: fibrous or atherosclerotic. It is also probable that the prognosis depends on the status of the contralateral carotid artery.

Currently there is no consensus as to which is the best surgical/medical strategy to treat restenosis.

However, for stenosis after CEA is usually accepted stenting as a further procedure; instead as regarding restenosis post CAS, is generally accepted to attempt all endovascular possibilities before to perform stent removal. This concept is based on some evidences: patients who undergo CAS are at high risk of surgical intervention, particularly if that have post surgical restenosis and therefore undergo a less invasive treatment; redo open surgery after CAS is more complex either for scar tissue, for the loss of normal dissection plane and for the need to access the artery proximal and distal to the stent. Moreover special care must be taken with the identification and mobilization of the cranial nerves: the hypoglossal nerve usually presents the greatest problems, because it can be pulled down over the bifurcation by the fibrosis and could be difficult to free up as much as needed. However recent studies showed good results with open surgery and stent removal after post-CAS restenosis.[50, 51]

Techniques usually used are repeat angioplasty with a conventional balloon, cutting balloon or with drug eluting balloon, and placing of further stent if there is still a residual stenosis >30%.

In our experience we noticed that is better to avoid an additional stent because the application of another stent distally to first one, can change the anatomy of the internal carotid artery, resulting even in a sharper bend at the end of the new stent. Consequently, one edge of the stent is projecting into the vessel lumen, whereas the other edge touches the vessel wall and can stimulate a hyperplasia reaction. Other investigators confirm our hypothesis that stenting for ISR results in event higher rates of new in-stent stenosis.[52, 53]

At last, emerging and encouraging data underline the possibility of recourse to best medical therapy to treat restenosis, even using cilostazol which improves long term patency after carotid revascularization thanks to its inhibitory effects on smooth muscle cell growth.[54]

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