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Coronary artery bypass grafts in patients with coronary stents

Revascularização cirúrgica do miocárdio em pacientes com stents coronários

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Abstract

Objective: **To observe the surgical characteristics of patients operated on after percutaneous coronary interventions (PCI).**

Method: **Fifty-six patients (41 M and 15 F), at the time of coronary artery bypass grafting (CABG), had already been submitted to coronary stenting procedures. In 101 PCI, 116 stents were implanted. At the time of the first PCI, 32 patients had three or more coronaries affected by severe stenosis. Six patients were treated with PCI for severe left coronary trunk stenosis. After the implantation of the first stent, 12 patients developed severe de novo lesions of the left coronary trunk. In 6 of these, stenosis developed within 6 months of stent implantation. Diabetes was present in 35.7% of the patients. In 22 patients (39.2%), at the time of CABG, the left ventricular function was reduced (p<0.001). During surgery, 160 grafts were implanted. Surgical studies included coronary and muscle biopsies.**

Results: **Surgical observation showed more arteritis and inflammatory tissues adjacent to the stent when compared to other areas. Seventeen patients that could not have platelet antiaggregates withdrawn needed more blood transfusions. There were no hospital deaths.**

Conclusion: **In patients operated on after stent implantation, facts like loss in LV function or de novo vascular lesions complicate surgical procedures and may impair long-term results. Due to endothelial dysfunction caused by stents, grafts may obstruct earlier. In addition the efficiency of clinical therapy may not be the same.**

Descriptors: **Stents. Myocardial revascularization. Coronary atherosclerosis**

Resumo

Objetivo: **Analisar as características cirúrgicas de pacientes operados após a intervenção coronária percutânea (ICP).**

Método: **Cinqüenta e seis pacientes (41 H e 15 M), no momento da revascularização cirúrgica do miocárdio, já tinham sido manejados com o implante de stents coronarianos. Foram implantados 116 stents em 101**

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intervenções. Trinta e dois pacientes tinham três ou mais vasos com estenose significativa. Seis pacientes com lesões graves no tronco da artéria coronária esquerda (TCE) foram tratados com stents. Desde a colocação do primeiro stent, 12 pacientes desenvolveram lesões *de novo* graves no TCE. Em seis (50%), a estenose grave se desenvolveu em até seis meses da colocação do stent. Vinte (35,7%) pacientes eram diabéticos. Em 22 (39,2%) doentes, no momento da cirurgia, havia diminuição significativa da fração de ejeção do VE (p< 0,001), quando comparada à da primeira ICP. A revascularização cirúrgica constou do implante de 160 enxertos coronarianos. A análise transoperatória incluiu biópsia da parede coronária e do músculo adjacente.

Resultados: **Achados transoperatórios evidenciaram tecidos adjacentes à área do stent mais endurecidos e inflamados quando comparados a outros sítios coronarianos. Dezessete pacientes operados sem descontinuidade dos antiadesivos plaquetários necessitaram de maior reposição sangüínea. Não houve mortalidade hospitalar pós-cirúrgica.**

Conclusão: **Nos pacientes operados após a colocação de stents, questões como perda da função ventricular, arterite ou lesões *de novo* adicionam complexidade ao ato cirúrgico. Em razão da disfunção endotelial causada pelos stents, enxertos poderão ocluir mais cedo. Em adição, a eficiência do tratamento clínico associado poderá não ser a mesma.**

Descritores: **Contenedores. Revascularização miocárdica. Arteriosclerose Coronária.**

INTRODUCTION

With the growth in the use of stents to correct coronary stenosis, it is natural that coronary artery bypass grafts are also being indicated for patients previously implanted with endovascular prostheses. Although there are still few publications reporting the inherent problems of this specific group of patients [1-3], observations show that the presence of vascular and specific myocardial alterations in regions surrounding stents are causing increasing concern. There is evidence that prostheses installed in the lumen of vessels may cause systemic inflammatory response syndrome [4] and also stimulate the release of growth factors and cytosine, resulting in endothelial dysfunction [5]. The aim of this current work is to report the vascular and myocardial changes identified in these patients and to correlate the alterations with the indication of initial percutaneous coronary intervention (PCI). An additional objective is to warn about the implications of the previous use of stents in coronary arteries on the surgical result of this group.

METHOD

A group of 56 patients submitted to coronary artery bypass grafting was analysed. At the moment of the surgery, all patients had already been implanted with coronary stents. Forty-one men and fifteen women with a mean age of 60 ± 6.25 years were studied. Twenty patients were diabetics (35.7%). One hundred and sixteen stents had been implanted during 101 interventions. At the time of the first procedure, 32 patients had significant stenosis of three or more vessels (57%). Severe injuries of the left coronary trunk (LCT) in six patients were also treated with stents. Eighteen patients underwent PCI twice, ten on three occasions and two four times. The most commonly treated artery was the anterior descending (39 patients). In one patient of this group of 39, four stents were implanted over a period of eight months due to frequent restenosis and balloon angioplasties were performed in the same artery as well as in its diagonal branch. Within the same period, another stent was placed in the right coronary artery.

Since the placement of the first stent, 12 patients developed severe lesions of the LCT detected in preoperative angiographies (21.4%, p-value < 0.005). In six patients (50%) this injury occurred within six months after placement of the stent. In twenty-two patients (39.2%), at the time of the surgery, there was a significant reduction in the left ventricle ejection fraction (LVEF) when compared with the time of the first PCI (p-value < 0.001). In this subgroup of patients with significant deterioration of the LVEF (Figure 1), seven were diabetics (31%), all had lesions of three vessels and they received 44 stents (two per patient) and were operated on within a mean period of 9.5 months after the first PCI. In the general group, forty patients (72%) were operated on in the first 12 months after stent implantation. At the time of the surgery, 160 coronary grafts were performed and in five patients the grafts were exclusively venous. Following the idealized model described by Gomes et al. [1], the trans-operative analysis included biopsy of the wall of the coronary artery immediately distal to the stent and of the adjacent muscle. Additionally, in some patients, biopsies of the endoprosthesis and of muscle distant from the site of the stent were also performed in order to make a histologic comparison. Seventeen operated patients (30%) were prescribed platelet antiaggregates, which are usually suspension in surgical cases, as they were cases with unstable angina. Statistical analysis was performed employing the Fisher exact test and the Student t-test. Patients signed written consent forms after a detailed explanation of the study.

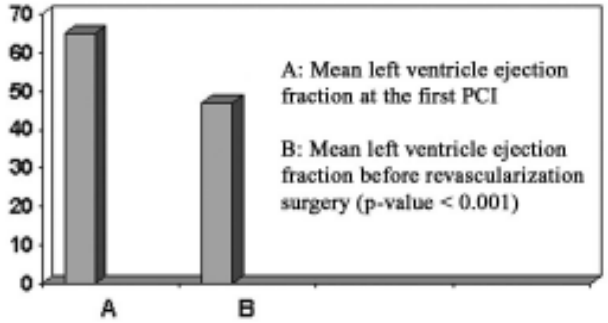

Fig. 1 - Fall in the left ventricle ejection fraction after PCI

RESULTS

Trans-operative findings showed that tissues adjacent to the stent area were harder and more inflamed in relation to the other parts of the coronary artery. In some patients, these macroscopic findings were very obvious (Figure 2a and 2b). The microscopic photograph of Figure 3 demonstrates intimal hyalinosis; Figure 4 shows a thrombus in the vascular lumen substituted by fibroblastic proliferation with recanalization; Figure 5 shows adventitial layer inflammatory infiltration. Figure 6 shows the appearance of a severe lesion to the LCT seven months after stent implantation in the marginal branch of the circumflex artery. Due to the continuous use of platelet antiaggregates in 30% of the patients in this group, postoperative bleeding was more intense, requiring more blood transfusions and the use of pleural and mediastinal drains was for a longer period (Figure 7). There were no in-hospital surgical mortalities.

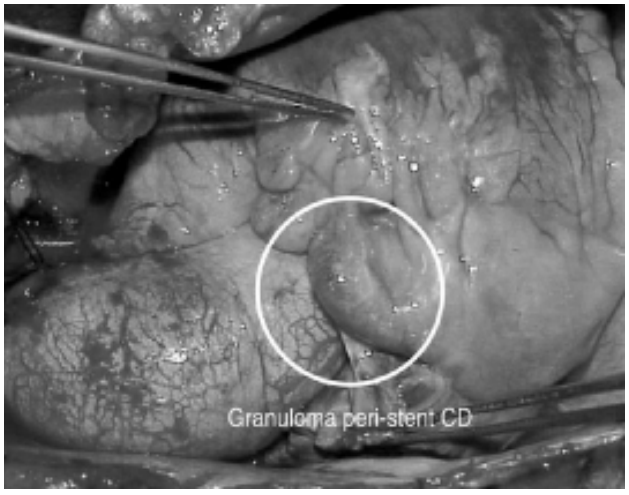

Fig. 2A - Trans-operative image in which the formation of a granuloma in the region of the stent in the left coronary artery is observed

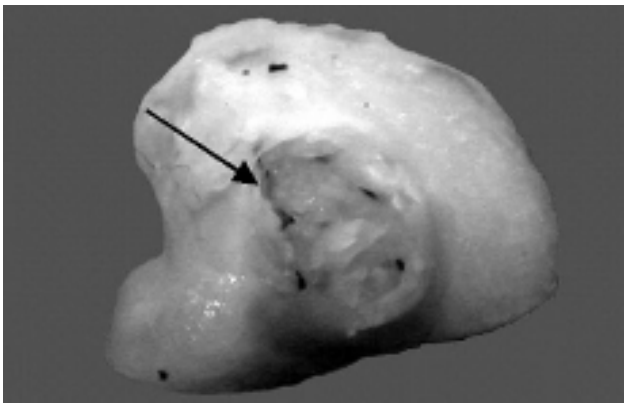

Fig. 2B - Crosswise section of the coronary artery with proliferation of inflammatory tissue and intra-stent occlusion

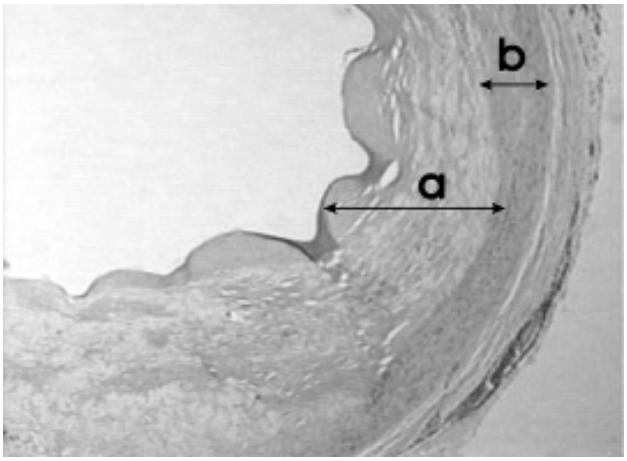

Fig. 3 - Crosswise histological section of the anterior descending coronary artery post-implantation of stent demonstrating intimal hyalinosis (a) and the muscle of the wall of the vessel (b)

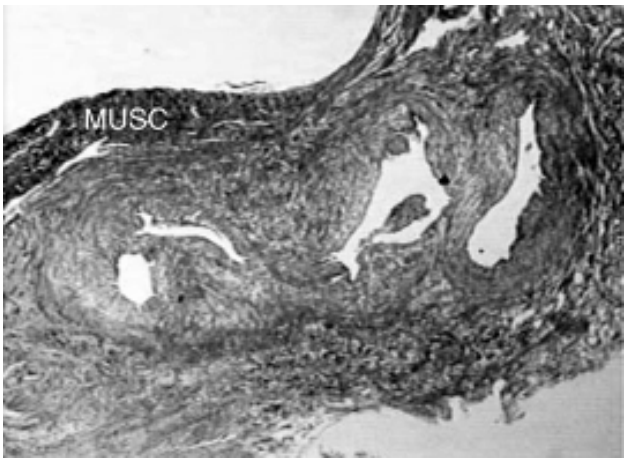

Fig. 4 - Crosswise histological section of the coronary artery with the presence of a thrombus in the vascular lumen substituted by fibroblastic proliferation with recanalization. Muscular tissue fragment of the coronary wall can also be seen (Mallory Trichrome)

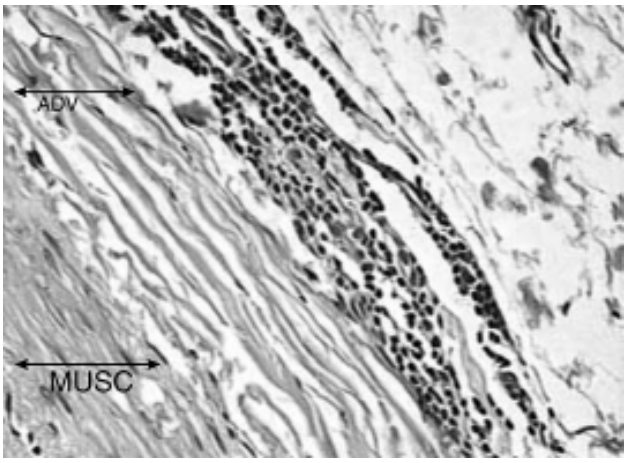

Fig. 5 - Histological section demonstrating adventitial inflammatory infiltration

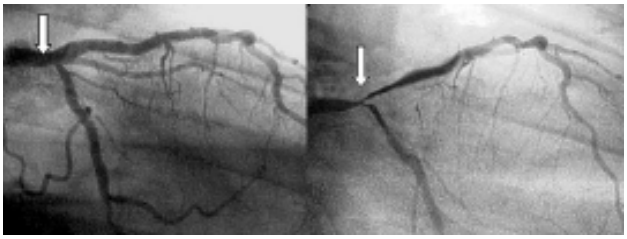

Fig. 6 - Cinecoronariography demonstrating normal LCT when a stent was implanted in the marginal branch of the circumflex artery. There was severe injury of the LCT including the circumflex and anterior descending arteries seven months after

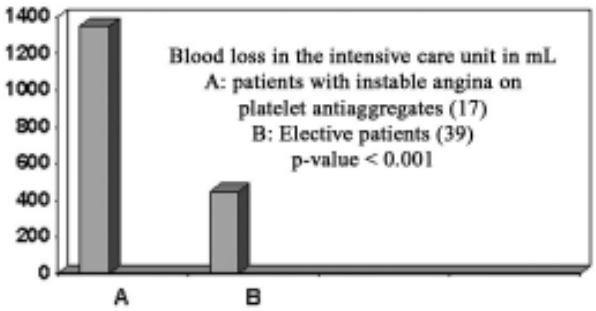

Fig. 7 - Postoperative bleeding rate in operated patients with and without elective suspension of the platelet antiaggregates

COMMENTS

Coronary stents have been widely used throughout the world to treat severe coronary injuries. A recent analysis of six North-American hospitals demonstrated the growth in the use of stents at a rate of 6.8% per year, in contrast to coronary artery bypass grafting, which is declining at a rate of 1.9% per year (6). In the group of patients treated for ischemic heart disease, 65.4% were treated with PCIs, of which 83% of cases underwent interventions involving a single vessel. Over the last three years, these numbers have not changed significantly. However, it is comprehensible that, for a growing number of cases in which surgery is indicated, the patients have already been treated using endoprostheses. Surgical group reports concerning these patients include the observation that the tissues which surround stents and even the coronary arterial wall itself present with an inflammatory-type reaction not previously identified in patients without stents. The formation of a granuloma-type reaction in the region of the stent is commonly observed. The reaction of the intracoronary foreign body may trigger a chronic inflammatory process involving many macrophages, a great number of phagocytic vacuoles and few secretor organelles [7]. Moreover, the presence of large numbers of macrophages near to the implantation may precede the emergence of another region of stenosis after stent implantation [8]. There is evidence that the inflammatory lesions caused by stents are more accentuated than those caused by balloon insufflation alone. With stents, there is an intense inflammatory reaction, composed of lymphocytes, histiocytes and eosinophils, that infiltrates the metallic structure [9,10].

The risk stratification of patients with chronic heart ischemic normally involves factors such as ventricular function (VF) and left ventricle ejection function (LVEF), accurate long-term survival predictors of patients with coronary disease. These are summed to the anatomic extension and the severity of the atherosclerotic involvement of the coronary arteries, the number of vessels involved and evidence of recent coronary plaque ruptures. Thus, it is possible to quickly predict a high risk for myocardial infarction or even death [11]. In the group of patients referred to surgery after PCI, these factors are commonly seen due to lack of success in using endoprostheses. It is not uncommon that perivascular and myocardial alterations close to the implantation of stent impede the implantation of vascular grafts in positions close to the most significant stenosis, a common practice among surgeons. The multiple use of balloons, rotating blades and stents to treat stenosis and restenosis provokes accentuated perivascular and myocardial reactions inducing a distant reduction of the lumen of the vessel and requiring the anastomoses to be performed much more distally than was initially necessary. The release of cytokines, neointimal proliferation, accumulation of lipids and consequent endothelial dysfunction, the synergism of the stent with the atherosclerotic plaque and the increase in the local inflammatory reaction [5] may be mechanisms that explain that, in this series of 12 patients, there were several severe lesions to the LCT which were not seen at the time of the first PCI. In half of these patients, this severe injury formed in less than six months. In spite of there being no deaths in

the hospital period, it is worrying that in this series, 39.2% of the operated patients had the VF and LVEF significantly lower at the time of the surgery than at the time of the first PCI, a situation that will probably affect long-term results.

In spite of ischemic heart disease still being a severe public health problem, the therapeutic options, both clinical as surgical, have significantly improved over the last decades. Grüntzig et al. [12], in 1977, with the utilization of balloon catheter, were pioneers in this therapy. Several additional forms of percutaneous treatment have been developed over the years, such as rotating blades, laser, photoablation and stents. In spite of all the benefits and developments with this treatment option which is not as invasive as surgery, many patients do not have a favorable anatomy for percutaneous treatment, so restenosis occurs in between 30 and 40% of the treated lesions within six months of the procedure [13,14]. The introduction of stents covered with drugs tries to achieve an antiproliferative effect and, thus, to reduce restenosis [15,16]. However, rapamycin (Sirolimus) has been blamed for being a platelet agonist, possibly inducing intracoronary thrombosis [17], a situation that is being investigated by the Food and Drug Administration (FDA) [18]. Virmani et al. reported a case of local hypersensitivity and late coronary thrombosis secondary to Cypher stent implantation [19]. In spite of the study by Bari [20] demonstrating that the mean reduction in the mortality of diabetic patients after 5.4 years of follow-up was greater in operated patients than patients treated by angioplasty (5.8% against 20.6%, p-value = 0.0003), 35.7% of the patients described here were diabetics. The coronary artery bypass surgery has been used for more than thirty years. But, although there have been many technical developments, including less-invasive surgeries and off-pump surgeries for selected cases, the possibility of treating complex and extensive lesions is still by open surgery a technique much more invasive than PCI. This is a reason that patients accept PCI even in unfavorable technical conditions and with a lower chance of success over the mid and long terms. Initially, one of the advantages of PCI was the lower cost compared to surgery. Today, with the more frequent multiple vessel treatment and repeated interventions because of restenosis, through the government healthcare plan, the conventional surgical procedure is, as a rule, less expensive (hospital cost of a stent for the government healthcare plan: R$ 4.843; complete coronary artery bypass grafting: R$.5.694). It is known today that there is a consensus that the objective for the treatment of ischemic heart disease will become, through necessity, preventative, directed at the development of atherosclerosis. Until this happens, methods such as PCI and surgery, which aim at treating the effects of atherosclerotic plaque, have achieved promising results by reducing the risk of coronary events, morbidity and death. In respect to stents, the current situation is worrying; even with second-generation stents in the first post-implantation year using pharmacological agents, 40% of new PCIs are not indicated for the treatment of restenosis at the site of the stent, as they are the reason of the progression of the coronary disease. In recent years, the progression of atherosclerosis has still been the main cause of adverse clinical results (four times more probable than restenosis at the site of stents) [21]. If these observations are confirmed in the near future, the benefits of the stents with drugs over the long term may be substantially minimized (effect of a foreign body, endothelial dysfunction?). The selection of patients, the best method to be employed in subgroups with diabetes, severe injuries of the LCT, multiple artery treatment with an unfavorable anatomy and the moment to choose a specific intervention are already well defined in the guidelines available in the literature [11,12]. Technical options, whether by the insistence of percutaneous methods, or whether through surgery, based on personal choice or because of available technological invocations and not based on established scientific evidence, can worsen the results of each method.

CONCLUSION

Patients of coronary artery bypass grafting, when previously treated with the implantation of stents, belong to a group with a greater initial morbidity and probably, greater long-term mortality rate. It is believed that with the indiscriminate use of stents, especially with the pronunciation that their technological improvement is solving the problems of precocious occlusion and inflammatory reaction, worsens the surgical results of patients previously submitted to PCI. Due to the endothelial dysfunction caused by these endoprosthesis, grafts may become occluded earlier and we fear that the efficiency of the associated clinical treatment may not be the same.

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