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SURGICAL MYOCARDIAL REVASCULARIZATION - CRITICAL ANALYSIS OF ITS EVOLUTION AND CURRENT STATE

REVASCULARIZAÇÃO CIRÚRGICA DO MIOCÁRDIO - ANÁLISE CRÍTICA DA EVOLUÇÃO E ESTADO ATUAL

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ABSTRACT

The development of coronary angiography by Sones, in the early 1960s, opened the way for modern myocardial revascularization surgery. In 1967, Favarolo performed the first saphenous vein coronary artery bypass grafting (CABG) surgery, and the technique expanded worldwide. Despite its exciting start, at the beginning of the 1970s, angiographic studies showed vein graft occlusion rates, in the first year, of between 10% and 15%. In 1986, Loop and colleagues showed increased 10-year patient survival when the left anastomosed internal thoracic artery was used in the left anterior descending artery. Lytle, in 1999, indicated that this benefit was improved when both internal thoracic arteries were used. Meanwhile, new techniques were also emerging, such as off-pump CABG and since 1995, the use of minimally invasive surgery. During these years, numerous studies were carried out, including: the SYNTAX Trial, with its major contribution with the development of the syntax score; and the Freedom Trial, which showed that diabetic patients still benefit most from myocardial revascularization surgery compared to percutaneous treatment. In relation to lesions of the left coronary trunk, two large studies (NOBLE and EXCEL) showed that percutaneous treatment in patients with a low syntax score is a good therapeutic option. In acute coronary syndromes without ST segment elevation in the electrocardiogram, the opinion of the Heart Team is extremely important for deciding on the best treatment, be it clinical, percutaneous, or surgical. In ACS with ST segment elevation in the electrocardiogram, catheter treatment with stent placement is the preferred choice, reserving surgical treatment only for cases of percutaneous treatment failure, or where there are mechanical complications.

Keywords: Stents; Myocardial revascularization; Treatment.

RESUMO

O desenvolvimento da cinecoronariografia por Sones, no início da década de 1960, abriu caminho para a moderna cirurgia de revascularização do miocárdio. Em 1967, Favarolo realizou as primeiras pontes de veia safena e a técnica se expandiu mundialmente. Apesar de seu começo empolgante, no início da década de 1970, estudos angiográficos mostraram taxas de oclusão dos enxertos venosos, no primeiro ano, entre 10 a 15%. Em 1986, Loop e colaboradores mostraram o aumento da sobrevida dos pacientes em 10 anos, quando utilizava-se a artéria torácica interna esquerda anastomosada na artéria descendente anterior. Lytle, em 1999, indicou que esse benefício era melhorado quando utilizava-se ambas as artérias torácicas internas. Paralelamente, novas técnicas também foram surgindo, como a cirurgia sem o uso da circulação extracorpórea e, também, a partir de 1995, a utilização de mini acesso. Durante todos esses anos, inúmeros estudos foram realizados, dentre eles podemos destacar: o estudo SYNTAX e sua grande contribuição com o desenvolvimento do syntax score; o estudo Freedom, mostrando que pacientes diabéticos apresentam maior benefício com a cirurgia de revascularização do miocárdio em comparação ao tratamento percutâneo. Em relação às lesões de tronco de coronária esquerda, dois grandes estudos (NOBLE e EXCEL) mostraram que o tratamento percutâneo, em pacientes com syntax score baixo, é uma boa opção terapêutica. Nas síndromes coronarianas agudas sem elevação do segmento ST no eletrocardiograma, a opinião do Heart Team é de extrema importância para decisão de qual tratamento realizar, seja ele clínico, percutâneo ou cirúrgico. Já nas SCA com elevação do segmento ST no eletrocardiograma, o tratamento por cateter, com a colocação de stent, é o preferencial, reservando o tratamento cirúrgico apenas para casos de falha no tratamento percutâneo ou quando há aparecimento de complicações mecânicas.

Descritores: *Stents; Revascularização miocárdia; Tratamento.*

HISTORY

The development of coronary angiography by Sones at the beginning of the 1960s enabled the "*in vivo*" identification and quantification of obstructive coronary artery lesions, paving the way for modern coronary-artery bypass grafting (CABG).

In 1967, Favaloro[1] began the implementation of saphenous vein bridges (SVBs), which was quickly spread across the world. In 1968, Green et al.[2] described the systematic use of the left internal thoracic artery (LITA) for anastomosis to the anterior descending artery with the aid of a microscope for the completion of the anastomosis. This was soon replaced with optic magnifying loupes.

The SVBs, initially implemented for the right coronary artery, were then implemented for the left anterior descending and circumflex arteries. They were implemented as isolated bridges, double, triple, or greater number of grafts, according to the needs of each patient. Sequential anastomoses were developed to facilitate the implementation of multiple grafts when grafts are sutured with two or more arterial segments.

Special care must be ensured when removing and preparing the saphenous vein, and the integrity of the graft must be maintained. The withdrawal can be performed through small incisions or via videoscopy. Recently, a technique was proposed for the removal of the saphenous vein with maintenance of the surrounding tissues, avoiding trauma on the graft.[3] The results, yet preliminary, suggest that this technique can dramatically decrease the rates of saphenous vein graft occlusion. Further studies are needed to confirm these benefits.

At the beginning of the 1970s, postoperative angiographic studies showed that the rate of venous graft occlusion within the first year was approximately 10%–15%. Saphenous vein grafts that were patent at the end of the first year had 87% chance of remaining patent even after 5 years.[4] However, other studies showed that at the end of 10 years, 45% of the bridges became stenotic or were occluded.[5] Besides the revascularization strategy used, the postoperative clinical follow-up is fundamental for the reduction of graft occlusion rates, through the strict control of risk factors and the use of dual antiplatelet therapy.

The internal thoracic artery (ITA) grafts are the most commonly used arterial grafts in myocardial revascularization surgery. The anastomosis of the LITA to the anterior descending artery is currently a consensual strategy, either owing to high rates of patency over the years or owing to the ability to adapt to the myocardial demands of blood. The work of Loop et al.[6] was critical for this recognition, showing that in patients who underwent anastomosis of the LITA to the anterior descending artery, those with a single lesion of the anterior descending artery had a survival rate of 93.4%, those with lesions in two arteries had a survival rate of 90%, and those with triple vessel lesions after 10 years of postoperative follow-up had a survival rate of 82.6%. The 20-year follow-up of these patients showed an event-free survival in 78% of those with isolated lesions of the anterior descending artery.[7]

In 1999, Lytle et al.[8] showed that the use of two internal ITAs yielded better results than the use of only one artery. A retrospective, nonrandomized study, with a 10-year follow-up, was conducted in patients who underwent elective and primary isolated CABG, who received either one graft (8,123 patients) or bilateral ITA grafts (2,001 patients), with or without additional grafts. Those patients who received two internal thoracic arteries had postoperative survival rates of 94%, 84%, and 67% at 5, 10, and 15 years, respectively. In the group with only one internal thoracic artery, the survival rates were 92%, 79% and 64% ($P<0.001$). Thus, the patients who received two ITAs had a lower risk of death, reoperation, or angioplasty.[9] This study reviewed the results of the 20-year follow-up and confirmed and extended the benefits in the second decade of follow up with the use of two internal thoracic arteries.

Other arterial grafts have been used, such as those for the radial arteries, right gastroepiploic arteries, and inferior epigastric arteries. The radial artery is susceptible to spasm when distally anastomosed to a calibrous coronary artery, with proximal lesions of small magnitude; the prolonged spasm of the vessel may cause the so-called string signal effect that explains its efficiency. However, when used in arteries with marked proximal lesions, its patency is close to that of the LITA.[10,11] Currently, in addition to the internal thoracic arteries, only the radial arteries are more often used.

Despite the strong clinical evidence in favor of the use of two internal thoracic arteries, their use is still limited. In the United States, only about 5% of the myocardial revascularizations use these two grafts. In Europe, this number, although higher, is below 10%.[12]

Myocardial revascularization without the use of extracorporeal circulation (ECC) was initially used by Goetz (1961)[13] and Kolesov (1967).[14] In Brazil, Buffolo et al.[15] resumed myocardial revascularization surgeries without the use of ECC in 1981, accumulating expressive casuistry with good results. From 1995, with the initiation of mini-access revascularization, initiated by Benetti[16] and Calafiori,[17] anastomosing the LITA to the anterior descending artery, there was improvement of devices for regional immobilization of tissues and exposure of the lateral, inferior, and posterior sides of the heart without compromising blood flow. Intracoronary shunts were also developed that allowed myocardial perfusion and maintained the the anastomosis site exsanguine. These resources enabled the accomplishment of the revascularization surgery without ECC with efficiency and safety. In August of 1995, our group initiated the CABG through mini-access, without the use of ECC. A total of 120 consecutive patients had their left internal thoracic artery anastomosed to the anterior descending artery. Only one patient died (0.8%). Among the patients who underwent postoperative coronary angiography, 98% showed anastomosis patency, with survival at 42 months of 98.3%.[18]

Myocardial revascularization surgery without ECC can be performed with *in situ* arterial grafts of the right and left internal thoracic arteries and with the radial artery as a free "Y" graft from one of the internal thoracic arteries, enabling revascularization without manipulating the aorta, preventing or minimizing the occurrence of stroke. Arrigoni et al.[19] reported the results of a consecutive series of 400 patients operated with three arterial grafts, without ECC and without

aortic manipulation. This group had lower rates of stroke compared with the *Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery* (SYNTAX) study group (1.3% versus 3.4%, P=0.032) and a similar rate when compared with the percutaneous intervention group of the same study (1.3% versus 2.0%, P=0.347). These results need to be confirmed in future prospective and randomized studies.

Currently, patients referred for surgery are elderly individuals with more complex coronary lesions who already received one or several percutaneous interventions. Patients with left coronary artery trunk lesions or with proximal triple vessel lesions, with good ventricular function and without previous interventions, are good candidates for total arterial revascularization; however, these patients are increasingly less referred for surgery. This is true especially in patients with a long life-expectancy, who would mostly benefit the greater durability of arterial grafts.

The exclusion of ECC has been controversial for a long time, mainly due to the lack of expressive, prospective, and randomized studies. Recently, the prospective, randomized CORONARY study conducted in 79 centers in 19 countries showed that after a 5-year follow-up, the rates of mortality, stroke, myocardial infarction, renal failure, and repeated revascularizations were similar among patients who underwent CABG with and without the use of ECC.[20]

The benefit of the surgery without ECC has also not been reported in clinical practice for the majority of patients, possibly due to the advances of extracorporeal perfusion that made the operations with ECC safer. For many of the patients who currently undergo myocardial revascularization surgery, the use of two internal thoracic arteries is perhaps more important than performing the surgery with or without ECC.[12]

CABG has been considered as the standard treatment for patients with more complex coronary lesions. However, only a limited number of randomized and long-term follow-up studies have been conducted.

SYNTAX STUDY

An important and innovative study was the SYNTAX trial,[21] which compared surgical treatment with percutaneous intervention using a first-generation eluting stent (TAXUS Express paclitaxel-eluting stent). A total of 1,800 patients with left coronary artery trunk and/or triple vessel lesions were randomized to receive percutaneous intervention (PCI) or CABG. Patients eligible only for one treatment option were entered into the registry. Rates of major cardiac and cerebrovascular events (MACCE) were analyzed after 5 years of follow-up. After randomization, 897 patients comprised the CABG group and 903 the PCI group. These events occurred in 26.9% of patients with CABG and 37.3% in the PCI group (P<0.001). Myocardial infarction occurred in 3.8% of patients in the CABG group versus 9.7% of patients in the PCI group (P <0.001), while repeated revascularizations occurred in 13.7% of patients in the CABG group versus 25.9% of patients in the PCI group (P<0.001). The rate of death due to any cause was 11.4% in the CABG group *versus* 13.9% in the PCI group (P=0.10), while the rate of stroke was 3.7% in the CABG group *versus* 2.4% in the PCI group (P=0.09). The rates of events were also analyzed based on the complexity score of the coronary lesions: low, intermediate, and high.

Among the patients with a low SYNTAX score, the prevalence of MACCE in the CABG group was 28.6% while that in the PCI group was 32.1% (P=0.43). However, among the patients with intermediate and high scores, MACCE rates were significantly higher in the PCI group: intermediate score: CABG 25% versus 36% PCI (P=0.008) and high score: CABG 26.8% versus 44.0% PCI (P<0.0001). The researchers concluded that myocardial revascularization surgery should remain the standard treatment for patients with complex lesions (high/intermediate SYNTAX score). For patients with less complex lesions (low SYNTAX score) or lesions of the left main coronary artery alone with a low or intermediate score, percutaneous intervention is also an acceptable alternative.

With regard to location of the lesions, considering only patients with triple vessel lesions were included in this SYNTAX study (n=1,095), the rates of cardiac events and cerebrovascular diseases were significantly higher in patients with PCI than in those with CABG (37.5% *versus* 24.2%, respectively; P<0.001). The degree of complexity of the lesions also significantly influenced these results.[22]

Considering only patients with unprotected left coronary artery trunk lesions (n=705), the composite outcomes (death, myocardial infarction, stroke, or repeated myocardial revascularization) in 5 years occurred in 31% of patients in the CABG group versus 36.9% of patients in the PCI group (P=0.12). The CABG group had a mortality rate of 14.6%, while the PCI group had a mortality rate of 12.8% (P=0.53); the incidence of cerebrovascular accident was significantly higher in the CABG group (4.3%) than in the PCI group (1.5%) (P = 0.03), and the incidence of repeated revascularizations in the CABG group was 15.5% while that in the PCI group was 26.7% (P<0.01). The major events were similar between the groups with low and intermediate SYNTAX scores, but were significantly higher in the PCI group in patients with high SYNTAX score (equal or greater than 33). In patients with unprotected left coronary artery trunk lesions, the complexity of the lesion should be taken into account when choosing the intervention modality.[23]

A subanalysis of the SYNTAX[24] study assessed the causes of death in the population who underwent percutaneous and surgical interventions. After the 5-year follow-up, a total of 97 (11.4%) patients who underwent CABG and 123 (13.9%) patients who underwent PCI died due to any cause. However, death rates from myocardial infarction were 10-fold higher in the PCI group compared with those in the CABG group (4.1% vs 0.4%, P <0.0001). This finding was particularly striking among patients with triple vessel lesions with a high SYNTAX score and in diabetic patients .[25]

Boiden and Mancini[26] emphasized that patients who received optimized medical therapy, defined as a combination of at least one antiplatelet agent, beta-blocker, statin, and the angiotensin-converting enzyme inhibitor, have lower mortality rates after surgery and percutaneous intervention. Despite the proven benefits of this association in the surgical group of the SYNTAX study, the optimized medical therapy was underused, with probable detriment to the reduction of the 5-year mortality rate.[27]

Another important observation was that incomplete revascularizations were more frequent among patients who received percutaneous interventions (43.3%) than in patients who received surgery (36.8%), and incomplete revascularization is an important risk factor for death in the 5-year follow-up.[28,29]

DIABETES MELLITUS

Several observational and randomized studies comparing the different strategies of myocardial revascularization in diabetic patients showed that CABG presents better results compared with percutaneous interventions. In recent years, there has been significant progress in the treatment of these patients. To define whether an aggressive clinical treatment and the use of stents alter the indications for intervention in diabetic patients and multivessel coronary disease, the *Future Revascularization in Patients with Diabetes Mellitus: Optimal Management of Multivessel Diseases* (FREEDOM)[30]study was proposed.

The FREEDOM study, conducted between 2005 and 2010 in 140 international centers, randomized 1,900 patients for CABG or PCI with eluting stents (sirolimus-eluting stent used in 51% of patients and paclitaxel-eluting stent in 43% of patients). The average duration of post-intervention follow-up was 3.8 years; the clinical and angiographic characteristics were well balanced in both study groups, and the mean age was 63.1±9.1 years; approximately 83% of the patients had three-vessel lesions. The SYNTAX score was 26.2 (±8.6).

The primary outcomes (death from any cause, non-fatal myocardial infarction, and non-fatal stroke) occurred more frequently in the PCI group, with rates of 26.6% after a 5-year follow-up *versus* 18.7% in the CABG group (P=0.005). The surgery resulted in lower rates of myocardial infarction (CABG 6% *versus* 13.9% PCI; P<0.01) and death from any cause (CABG 10.9% *versus* 16.3% PCI; P=0.049). However, strokes were more frequent in the surgical group (CABG 5.2% *versus* 2.4% PCI; P=0.03). The FREEDOM study confirmed that CABG is superior to CPI in diabetic patients with advanced coronary heart disease, significantly reducing the rates of death and myocardial infarction but with a higher rate of stroke.

Two contemporary studies, *Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease* (EXCELL) and NOBLE, addressed the treatment of the lesion of the left coronary artery trunk comparing angioplasty and CABG in patients with a low or intermediate complexity SYNTAX score.

The EXCEL[31] involved 1,905 patients with left coronary artery trunk lesions with low or intermediate anatomical complexity that were randomized for PCI with fluoropolymer-based cobalt-chromium everolimus-eluting stents (948 patients) or CABG (957 patients). The anatomical complexity was defined by a SYNTAX score ≤32. After a 3-year follow-up, the primary outcomes (death from any cause, stroke, or acute myocardial infarction) occurred in 15.4% of patients in the PCI group and in 14.7% of patients in the surgical group (P=0.02 for non-inferiority and P=0.98 for superiority). The same outcomes were reported when analyzed at 30 days and were called major secondary outcomes, with rates of 7.9% in the CABG group and 4.9% in the PCI group (P<0.01 for superiority).

The researchers concluded that in patients with stenosis of the left coronary artery trunk with low or intermediate complexity SYNTAX score, PCI with everolimus-eluting stents were not inferior to CABG with regard to the compound rates by death, stroke, or myocardial infarction at 3 years.

Despite the similar results in primary outcomes (death from any cause, stroke, and myocardial infarction) at 3 years, it should be noted that the percutaneous intervention group had a greater increase in primary outcomes, in the interval between 30 days and 3 years (CPI of 4.9% to 15.4% *versus* 7.9% to 14.7% in the CABG group (P=0.02). As with several other similar studies, at the end of 5–10 years, many of the differences became more evident, and we need to wait for long-term results.[32]

The controlled, randomized, non-inferiority NOBLE[33] study compared the results of surgical treatment with those of percutaneous second-generation stent (Biolimus eluting stent). Approximately 1,200 patients were randomized in the United Kingdom, Germany, Sweden, Norway, Finland, Lithuania, Estonia, Latvia, and Denmark, of which 598 were treated by IPC and 603 by CABG.

The results of the 5-year follow-up, analyzed by intention to treat, showed that the incidence of major adverse events (death due to any cause, myocardial infarction, stroke, and revascularization) in the PCI group was 29% while that in the CABG group was 19% (P=0.0066), exceeding the limits for non-inferiority. When these results were analyzed based on the treatment performed, the incidence of adverse events in the PCI group was 28% versus 19% in the CABG group (P=0.0015). The all-cause mortality in the PCI group was 12% versus 9% in the CABG group (P=0.77); The incidence of myocardial infarction in the PCI group was 7% versus 2% in the CABG group (P=0.040); the incidence of revascularization in the PCI group was 16% versus 10% in the CABG group (p = 0.032); the incidence of stroke in the PCI group 5% versus 2% in the CABG group (P=0.073).

The findings of this study suggest that myocardial revascularization surgery may be better than percutaneous intervention in the treatment of unprotected left coronary artery trunk lesions.

MYOCARDIAL REVASCULARIZATION SURGERY IN ISCHEMIC HEART FAILURE

The *Surgical Treatment for Ischemic Heart Failure* study[34] compared surgical treatment with clinical treatment in a group of 1,212 high-risk individuals with multivessel coronary lesions and severe left ventricular dysfunction (ejection fraction ≤35%). After a 10-year follow-up, results showed that patients in the surgical group had lower rates of death due to any cause (58.9% *vs* 66.1%, P=0.02), deaths from cardiovascular cause (40.5% *versus* 49.3%, P=0.006), and death from any cause or hospitalization due to cardiovascular diseases (76.6% *vs* 87.0%, P=0.001) compared with those in the clinical group. These results strongly suggest that myocardial revascularization surgery should be considered as a complement to clinical treatment of patients with ischemic heart failure and arteries viable for revascularization.[35]

ACUTE CORONARY SYNDROME (ACS)

ACS encompasses unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Unstable angina and

non-ST infarction present similar clinical manifestations; what distinguishes them is the release of myocardial injury markers in the NSTEMI. Didactically, the diagnosis and therapy of UA and NSTEMI can be discussed together.

The determination of myocardial necrosis biomarkers for the diagnosis and prognosis of UA and NSTEMI should be monitored from the onset of the crisis, as well as serial electrocardiographic study and early echocardiogram. Once the diagnosis is confirmed, clinical measures should be established to control pain and support hemodynamic conditions.

Coronary angiography should be performed early, especially when the clinical manifestations are repetitive or continuous. Patients with a history of coronary artery disease and especially those with previous percutaneous or surgery interventions should be re-examined early using computerized angiotomography of the coronary arteries or preferably coronary angiography. The findings of these tests and the use of scores such as SYNTAX II, with its anatomical and clinical variables, will play a relevant role in deciding the best form of intervention. These indications are reasonably well updated in the guidelines of the major European, American, and Brazilian Cardiology Societies and most of the time follow the same guidelines already discussed previously, in the indications for patients with stable angina.

ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

STEMI is a well-defined clinical condition through elevation of the ST segment of the electrocardiogram and laboratory confirmation of the release of myocardial necrosis biomarkers into the bloodstream. Once the diagnosis of myocardial infarction has been established, the treatment should be the reperfusion of the culprit artery in the shortest possible time, with percutaneous intervention or with fibrinolytic agents, to rescue the myocardium at risk. After salvage angioplasty, many patients persist with multivessel and complex lesions, requiring invasive treatment. The decision on the type of intervention, surgery or angioplasty, in the residual lesions should be discussed by the heart team and the patient, according to the criteria already established in previous discussions.

MECHANICAL COMPLICATIONS OF MYOCARDIAL INFARCTION

Cardiogenic shock is usually associated with extensive areas of myocardial impairment or by mechanical complications, such as rupture of the papillary muscle of the mitral valve, rupture of the interventricular septum, or rupture of the free wall of the left ventricle. If multivessel obstructive lesions are present, surgical or percutaneous revascularization should be performed, as well as pharmacological and mechanical support with the use of an intravenous balloon or venoarterial extra corporeal membrane oxygenation.

Rupture of the papillary muscle of the mitral valve, most commonly of the anterolateral papillary muscle, causes severe heart failure and must be operated quickly, and the valve is replaced when there is no possibility of repairing the muscle. Interventricular septum rupture is also a severe complication that begins with small perforations, with rapid progression to a wide rupture, provoking cardiogenic shock. Surgical treatment should be indicated early. The surgical exclusion of ruptured septal area is a well-established procedure. Usually, the coronary lesion is unique, most commonly involving the anterior descending artery. Most postoperative deaths commonly occur due to multiple organ failure, caused by prolonged shock, especially when the intervention was delayed. The rupture of the free wall of the left ventricle is usually fatal by cardiac tamponade. Since at the initial stage its detection with echocardiogram can be difficult as only a slight wall leakage is detected, the early treatment of this complication is postponed. Cardiac magnetic resonance imaging assists in the early diagnosis, enabling a timely correction.

The occurrence of these mechanical complications as well as the left ventricular aneurysm are fortunately increasingly less frequent, thanks to advances in early treatment of patients in the acute phase of myocardial infarction. However, many patients in the late follow-up can progress to refractory heart failure.

With few treatment options, patients with advanced heart failure have a poor prognosis with low quality of life. The rapid technological advances of mechanical circulatory assist devices, currently miniaturized and continuous flow, allow for survival rates of 80% and 70% at 1 and 2 years, respectively.[36] The use of these devices as destination therapy is a good treatment option, especially in patients who are not eligible for cardiac transplantation.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest in conducting this study.

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