Abstract

Objective: To compare the effectiveness of the radial artery graft with the saphenous vein graft for myocardial revascularization in association with the internal thoracic artery.

Methods: A systematic review of the literature was made, searching for articles in the MEDLINE and LILACS databases. Two independent researchers performed the selection of articles, carefully evaluating the methodology described in articles considered relevant to the subject. Only controlled trials with an adequate randomization system were included. In all situations, when the researchers did not reach an agreement, a consensus meeting was held. No restrictions were stipulated in respect to the follow-up period for the angiographic evaluation of the graft, the vessel treated or the characteristics of the patients included in the studies. The results are expressed as Relative Risks (RR), with 95% Confidence Intervals (CI) to compare the effectiveness between the radial artery and the saphenous vein.

Results: Based on these criteria, three studies were included. We did not find statistical differences between the patencies of the grafts (RR 0.53 [95% IC 0.13 – 2.18]).

Conclusion: Despite the studies having good methodologies we did not observe statistically significant differences between the grafts. The statistical power of the meta-analysis is low and therefore, more randomized controlled trials are necessary, with adequate sample sizes to detect possible differences between the different treatments.

INTRODUCTION

Coronary artery disease (CAD) is the main cause of death in practically all countries around the world in spite of the advances in clinical and surgical cardiology [1].

Coronary artery bypass grafting (CABG) is a well-established procedure used to treat advanced CAD. Although the results of this operation are excellent [2,3], long-term benefits are influenced by the type of graft used. It is well known that saphenous vein (SV) grafts, although they are widely employed, have an unsatisfactory perviability over the long-term. Around 15% of SV grafts occlude within the first postoperative year [4], and only 50 to 60% of the grafts are patent over ten years of the postoperative period [5,6].

Thus, the use of the internal thoracic artery (ITA) is, without doubt, one of the most important advances in the treatment of CAD over the last 25 years. These arteries are associated with a better long-term angiographic perviability when compared to SV grafts, promoting a significant reduction in mortality [7-10]. In view of these results, the use of the ITA became the gold standard for CABG, with the SV utilized as complementary grafts for complete revascularization.

On the other hand, the better results of arterial grafting encouraged surgeons to explore other arteries to complement the ITA aiming at substituting the SV grafts. Thus the gastroepiploic artery [11-13], the inferior epigastric artery [14] and the radial artery (RA) were investigated.

Of these, the RA is currently the most commonly used. Initially described in 1973 by Carpentier et al. [15], the use of the RA was abandoned soon after due to its susceptibility to spasms and functional occlusion [16,27]. However, with the advent of drugs that prevent spasms and the adoption of better dissection techniques, interest for the RA as an additional arterial conduit was revitalized in the 1990s [18].

Many institutions have reported that the RA can be used with acceptable mortality and morbidity rates and that the angiographical results are similar to those of the ITA [19-27]. On the other hand, some published data present limitations related to the long-term angiographical results of these grafts.

A recent observational study by Khot et al. [28] in 2004, showed a reduction in the perviability of RA grafts when compared to ITA and SV grafts. Despite of being a study with a low level of significance, with high potential of bias in the selection and follow-up, there was a stir in the credibility of surgeons who used RA grafts. Thus we decided to perform a scientific metanalytic review of publications to assess the effectiveness of the RA graft in CABG comparing its patency with SV grafts when used in association with the ITA graft.

METHOD

Inclusion criteria in the review study

Controlled and randomized or quasi-randomized clinical trials that compared the perviability of RA and SV grafts in association with ITA grafts were included. Double-blind studies are not possible in this type of intervention however, masking was assessed, but was not considered as a decisive requisite for inclusion of studies.

Type of participants

Coronary disease patients, independently of age or ethnic group who required CABG due to obstruction greater than 70% in any coronary artery were included. The necessity of better dissection techniques, interest for the RA as an additional arterial conduit was revitalized in the 1990s [18].

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of revascularization was considered from clinical, laboratorial, electrocardiographic and coronarographic signs and symptoms of the patient.

Types of interventions
The perviability of RA and SV grafts was evaluated. The number of grafts that each patient was submitted to was considered rather than the number of patients.

Measured results
Occlusion of the vessel at 1 year and 5 years after the surgical procedure.

Strategy to identify studies
The electronic databases of MEDLINE via PubMed and LILACS via the Virtual Health Library were accessed up to September 2005. The search strategy utilized was formulated using key words relative to the review theme grouped in a way to filter all the articles. The authors chose a highly sensitive filtering strategy and restrictions in respect to the publication language were not used thereby diminishing publication bias.

Research strategy for MEDLINE
(Aortocoronary Bypass OR Aortocoronary Bypasses OR Bypass, Aortocoronary OR Bypasses, Aortocoronary OR Bypass Surgery, Coronary Artery OR Coronary Artery Bypass Granting OR Coronary Artery Bypass Surgery OR Bypass, Coronary Artery OR Artery Bypass, Coronary OR Artery Bypasses, Coronary OR Bypasses, Coronary Artery OR Coronary Artery Bypasses OR CABG OR Coronal artery bypass graft surgery OR CABG surgery OR Coronary Artery Bypass, Off Pump OR Beating Heart Coronary Artery Bypass OR Coronary Artery Bypass, Beating Heart OR Off-Pump Coronary Artery Bypass OR Off Pump Coronary Artery Bypass OR Off-pump coronary artery bypass graft surgery OR Off-pump coronary artery bypass graft surgery OR Off-pump coronary artery bypass grafting OR Off pump coronary artery bypass grafting OR OPCAB OR Off-pump CABG surgery OR Off-pump CABG surgery) AND ((Arteries, Radial OR Artery, Radial OR Radial Arteries OR RA OR RA conduit* OR RA graft* OR Radial arterial conduit* OR Radial arterial graft* OR Radial aortocoronary bypass OR Radial aortocoronary bypass graft* OR Radial by pass OR Radial bypass OR Radial bypass graft* OR Radial bypass graft surgery OR Radial bypass operation OR Radial bypass surgery OR Radial conduit flap OR Radial conduits OR Radial coronary OR Radial coronary anastomoses OR Radial coronary bypass graft* OR Radial coronary bypass surgery) AND (Saphenous Veins OR Vein, Saphenous OR Veins, Saphenous OR SVG OR Saphenous allograft* OR Saphenous aortocoronary bypass OR Saphenous aortocoronary bypass graft* OR Saphenous by pass OR Saphenous bypass OR Saphenous bypass graft* OR Saphenous bypass graft surgery OR Saphenous bypass operation OR Saphenous bypass surgery OR Saphenous conduit flap OR Saphenous conduits OR Saphenous coronary OR Saphenous coronary anastomoses OR Saphenous coronary bypass graft* OR Saphenous coronary bypass surgery)) AND (randomized controlled trial[Publication Type] OR randomized controlled trial[Publication Type] OR randomized controlled trials[MeSH Terms] OR random allocation[MeSH Terms] OR double blind method[MeSH Terms] OR single blind method[MeSH Terms] OR clinical trial[Publication Type] OR clinical trials[MeSH Terms] OR clinical["Text Word"] AND trial["Text Word"] OR single["Text Word"] OR double["Text Word"] OR triple["Text Word"] OR placebo[MeSH Terms] OR placebo["Text Word"] OR random["Text Word"] OR research design[MeSH Terms] OR comparative study[MeSH Terms] OR evaluation studies[MeSH Terms] OR follow-up studies[MeSH Terms] OR prospective studies[MeSH Terms] OR control["Text Word"] OR prospective["Text Word"] OR volunteer["Text Word"]).

Research strategy for LILACS
(Aortocoronary Bypass OR Aortocoronary Bypasses OR Bypass, Aortocoronary OR Bypasses, Aortocoronary OR Bypass Surgery, Coronary Artery OR Coronary Artery Bypass Granting OR Coronary Artery Bypass Surgery OR Bypass, Coronary Artery OR Artery Bypass, Coronary OR Artery Bypasses, Coronary OR Bypasses, Coronary Artery OR Coronary Artery Bypasses OR CABG OR Coronal artery bypass graft surgery OR CABG surgery OR Coronary Artery Bypass, Off Pump OR Beating Heart Coronary Artery Bypass OR Coronary Artery Bypass, Beating Heart OR Off-Pump Coronary Artery Bypass OR Off Pump Coronary Artery Bypass OR Off-pump coronary artery bypass graft surgery OR Off-pump coronary artery bypass graft surgery OR Off-pump coronary artery bypass grafting OR Off pump coronary artery bypass grafting OR OPCAB OR Off-pump CABG surgery OR Off-pump CABG surgery) AND ((Arteries, Radial OR Artery, Radial OR Radial Arteries OR RA OR RA conduit* OR RA graft* OR Radial arterial conduit* OR Radial arterial graft* OR Radial aortocoronary bypass OR Radial aortocoronary bypass graft* OR Radial by pass OR Radial bypass OR Radial bypass graft* OR Radial bypass graft surgery OR Radial bypass operation OR Radial bypass surgery OR Radial conduit flap OR Radial conduits OR Radial coronary OR Radial coronary anastomoses OR Radial coronary bypass graft* OR Radial coronary bypass surgery) AND (Saphenous Veins OR Vein, Saphenous OR Veins, Saphenous OR SVG OR Saphenous allograft* OR Saphenous aortocoronary bypass OR Saphenous aortocoronary bypass graft* OR Saphenous by pass OR Saphenous bypass OR Saphenous bypass graft* OR Saphenous bypass graft surgery OR Saphenous bypass operation OR Saphenous bypass surgery OR Saphenous conduit flap OR Saphenous conduits OR Saphenous coronary OR Saphenous coronary anastomoses OR Saphenous coronary bypass graft* OR Saphenous coronary bypass surgery)) AND (randomized controlled trial[Publication Type] OR randomized controlled trial[Publication Type] OR randomized controlled trials[MeSH Terms] OR random allocation[MeSH Terms] OR double blind method[MeSH Terms] OR single blind method[MeSH Terms] OR clinical trial[Publication Type] OR clinical trials[MeSH Terms] OR clinical["Text Word"] AND trial["Text Word"] OR single["Text Word"] OR double["Text Word"] OR triple["Text Word"] OR placebo[MeSH Terms] OR placebo["Text Word"] OR random["Text Word"] OR research design[MeSH Terms] OR comparative study[MeSH Terms] OR evaluation studies[MeSH Terms] OR follow-up studies[MeSH Terms] OR prospective studies[MeSH Terms] OR control["Text Word"] OR prospective["Text Word"] OR volunteer["Text Word"]).

4 Surgical procedure.

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aortocoronary bypass grafts OR Saphenous by pass OR Saphenous bypass OR Saphenous bypass grafts OR Saphenous bypass graft surgery OR Saphenous bypass operation OR Saphenous bypass surgery OR Saphenous conduit flap OR Saphenous conduits OR Saphenous coronary OR Saphenous coronary anastomoses OR Saphenous coronary bypass grafts OR Saphenous coronary bypass surgery) AND (Pt randomized controlled trial) OR (Pt controlled clinical trial) OR (Mh randomized controlled trials) OR (Mh random allocation) OR (Mh double blind method) OR (Mh single blind method) AND NOT (Ct animal) AND NOT (Ct human and Ct animal) OR (Pt clinical trial) OR (Ex E05.318.760.535) OR (Tw clin$) AND (Tw trial$) OR (Tw ens$) OR (Tw estud$) OR (Tw experim$) OR (Tw investig$) OR (Tw sing$) OR (Tw simple$) OR (Tw double$) OR (Tw duplo$) OR (Tw trip$) AND (Tw sing$) OR (Tw casual$) OR (Tw random$) OR (Tw random allocation) OR (Tw placebo$) OR (Tw masks) OR (Tw mascar$) OR (Mh placebo$) OR (Tw placebo$) OR (Tw random$) OR (Tw random allocation) OR (Tw casual$) OR (Tw casual allocation) OR (Tw azar) OR (Tw aleator$) OR (Mh research design) AND NOT (Ct animal) AND NOT (Ct human and Ct animal) OR (Ct comparative study) OR (Ex E05.337) OR (Mh follow-up studies) OR (Mh prospective studies) OR (Ct control$) OR (Tw control$) AND (Tw volunt$) OR (Tw volunteer$) AND NOT ((Ct animal) AND NOT (Ct human and Ct animal))).

**Standard review method**

**Study selection**

Two independent researchers selected the trials for inclusion or exclusion after analyzing the titles and abstracts of the studies identified using the search strategies. The selected trials were compared and any discrepancy was solved by discussion and consensus. Subsequently, the trials included were independently evaluated by the two researchers to ensure that they obeyed the stipulated inclusion criteria. Finally, the articles selected for review were checked to prevent the inclusion of duplicated data.

**Quality of evaluation**

Two researchers independently evaluated the quality of the methods of the included studies. The enrolment of patients was verified stipulating a classification of studies in categories, in which category A (adequate random allocation and described in the methodology of the study), B (random allocation mentioned but not described in the methodology of the study), C (inadequate random allocation) and D (non-randomized study with allocation). Any difference of opinion was solved by discussion and consensus.

**Data Extraction**

The data of the studies were independently extracted by two researchers using a standard form. The forms were set up based on data previously defined as relative to the theme. When necessary, the authors of the primary studies were contacted to add information or data in the results of their studies.

**Methodological quality of the included studies**

All the included studies were randomized or quasi-randomized, that is, only studies classified in categories A, B and C were included. Studies from Category D were excluded from this systematic review. Two studies were classified in Category A (Dessai et al., 2004; Buxton et al., 2003) [29,30] and one study was classified as Category B (Mumeretto et al., 2004) [31].

**RESULTS**

After extracting all the data relative to the studies, evaluating their quality, they were plotted in the Review Manager – RevMan 4.2.8 program – for analysis. Comparisons of the effects between the two interventions of interest were expressed as Relative Risk (RR) with a 95% confidence interval (CI).

A total of 398 articles were selected from the MEDLINE and LILACS databases. Of these, only three corresponded to the inclusion criteria of study type, that is, they were controlled and randomized or quasi-randomized clinical trials.

The metanalysis of the studies, involved 116 grafts up to the cutoff date of this systematic review is presented as an analysis of subgroups in respect to the evaluation of the patency of the grafts at 12 months and five years. The results of the subgroup and overall metanalysis are presented in a random model (Figure 1).

There is no statistical difference between the groups in respect to patency at 12 months (RR 0.1 [95% CI 0.5 – 1.4]) or patency at five years (RR 2.75 [95% CI 0.31 – 24.52]). An estimation of the overall effect does not give statistically significant proportions of events between the two groups when expressed as a RR (RR 0.53 [95% CI 0.13 – 2.18]).

**DISCUSSION**

CABG is, without doubt, the treatment of choice for patients with severe CAD. This procedure requires vascular grafts, both arterial and venous, with an aim of optimizing blood irrigation of the myocardial tissue of the post-stenotic regions. Thus, a series of studies have been carried out to compare the efficacy of venous and arterial grafts. It has been proven that the viability of left ITA grafts is greater than grafts using the SV [7,9,10], which currently are utilized as a complement to the ITA to achieve complete revascularization. Thus, surgeons tried other arteries that may substitute SV grafts. Currently, the RA is the most commonly employed and most studied for this procedure in association with the ITA.
It is well known that the patency of the graft, independently of whether it is venous or arterial, depends both on factors inherent to the patient such as the presence of comorbidities (diabetes, dyslipidemia, arterial hypertension and renal insufficiency), and on factors related to the method of dissection, preservation and pharmacological protection of the vessel and the implantation technique used [10]. Additionally, the territory of the target coronary vessel is also related to the higher or lower patency of the graft [21].

A series of observational studies indicated that the patency of RA grafts is greater than the SV [32,33]. On the other hand, Khot et al. in 2004 concluded that the patency of the RA grafts is worse than the patency of all other vessels employed in CABG [28]. However, all of these studies were not randomized or controlled but observational, whether prospective or retrospective, and so they have little reliability and are subject to a considerable amount of bias. Thus, we performed a systematic review of publications to evaluate the patency of RA grafts compared to SV grafts.

We followed a wide ranging objective without restricting the postoperative period for the angiographic evaluation of the graft, the involved vessel and the characteristics of the patients included. This conduct was adopted to offset the extreme lack of controlled and randomized clinical trials that cover this theme. Only three randomized trials were included in this systematic review. The databases investigated include a considerable percentage of the most important periodicals of cardiovascular surgery, showing that there is insignificant bias of publication. The search strategy utilized was highly sensitive, checking all the studies related to the theme. The controlled and randomized or quasi-randomized trials were chosen for inclusion in this systematic review as they had the greatest reliability and level of evidence with the lowest Type 1 ($\alpha$) and Type 2 ($\beta$) errors. Masking was not demanded for inclusion and the number of patent grafts were evaluated and not the number of patients.

The randomized and controlled trial by Dessai et al. [29] published in 2004, compared the patency at 12 months of RA and SV grafts. Its methodology is reproducible and scientific with an adequate method of randomization, and a reasonable number of patients ($n = 440$). The angiographic evaluations were pre-determined and the results gave a higher patency for RA grafts compared to SV grafts.

Muneretto et al. [30], also in a publication from 2004, compared the patency of RA and SV grafts over 12 months. The angiographic results of 152 patients distributed into two groups were evaluated. The number of participants is relatively small, increasing the uncertainty of the results and conferring a considerable confidence interval. The methodology is reproducible, with pre-programmed angiographs, however, the form of randomization of the patients was not described. The authors concluded that the RA graft has a better patency than the SV graft.

The other randomized controlled clinical trial was performed by Buxton et al. [31] in 2003. These authors recruited 438 patients who were randomized in two groups. In the first, the 285 patients were randomized into two other groups, one with 140 patients who received RA grafts and the other of 145 patients received right ITA grafts. The second group contained 153 patients who were randomly distributed in two other groups, one with 73 patients who received RA grafts and the other with 80 patients who received SV grafts. The methodology is adequate with programming of the angiographic evaluation of 40% of the patients at five years and 60% of the patients at 10 years. The number of patients was not adequate and the results at five years did not give a significant difference between the two groups with RA and SV grafts. The data of patency at ten years are not available yet.

It is important to note that these clinical trials have a predetermined angiographic study in their methodology, even if the patient does not present with ischemic symptoms. Angiographic studies based on symptoms do not offer a satisfactory representativity of the population, as the failure rate of the grafts of these patients is expected to be high [10]. Buxton et al. [10] in 2005 published a study whose result stated that the patency of the ITA, RA and SV grafts
were higher in protocols in which the patients were evaluated independently of the symptoms than those in which the patients were submitted to angiographic examination due to symptoms.

In the results, we present a graph of the overall effect, edited in a random model. This model highlights the clinical and methodological heterogeneities present in the studies, showing them in the statistical calculations. However more reliable results were expected, that showed the possible aforementioned heterogeneities better as the included studies were not homogeneous. The method to select the patients, the diagnostic criteria, the form of angiographic evaluation and the surgical procedures were not similar among the included clinical trials. Thus, no significant difference was observed between the effects of using RA and SV grafts.

Nevertheless, although the included studies were good quality with satisfactory values in the study quality scale of Jadad et al. [34], the statistical power of this metaanalysis is low, as the number of accumulated grafts was very small (n = 1116). Nonetheless, there is a greater proportion of patency of the RA graft compared to the SV graft expressed in the results of the random model. However, a convict affirmation that the RA graft is better than the SV graft requires more expressed sample size following a standardized, uniform methodology. The authors suggest that the RA graft is better than the SV graft expressed in the overall effect, showed in the statistical calculations. However more reliable results were expected, that showed the possible heterogeneities better as the included clinical trials. Thus, no significant difference was observed between the effects of using RA and SV grafts.

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