

## Prevalence of Atherosclerotic Lesions in the Left Internal Thoracic Artery, Evidenced by Selective Angiographic Findings

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### Abstract

**Background:** By observing the high prevalence of failures in the surgical treatment of myocardial revascularization (MR), with the use of the Left Internal Thoracic Artery (LITA) as a graft, evidenced by the international literature, it was sought to demonstrate the prevalence of lesions that would not allow the use of LITA as a graft in myocardial revascularization surgery, with possible alteration in the surgical management performed by the cardiac surgeon, and reduction of the morbimortality of these patients.

**Objectives:** To evaluate the prevalence of atherosclerotic lesions of the LITA, through selective preoperative angiography, in patients submitted to coronary angiography and indicated for myocardial revascularization. We also analyzed other lesions that made the use of LITA unfeasible as a main graft in cases of myocardial revascularization surgery (MRS).

**Methods:** This was a cross-sectional, prevalence study that evaluated, through selective angiography, the LITA of 39 patients with a median age of 63 years, submitted to coronary angiography, with indication of Coronary Artery Bypass Graft (CABG). Categorical variables were compared by chi-square test and Fisher's exact test. The single continuous variable, age, was tested for normality by the Kolmogorov-Smirnov test, described in median (P25; P75) and the groups compared with the Mann-Whitney test. The level of statistical significance adopted was  $p < 0.05$ . The analyzes were performed in SPSS® software version 20.

**Results:** It was identified the presence of 7.7% of disorders in the LITA that made it unfeasible to be used. In all of the patients there was no specific symptomatology evidencing the lesion. No variable was shown as a predictor for the occurrence of the outcomes.

**Conclusion:** The prevalence of the lesions found in the study was significant, indicating that a preoperative evaluation of LITA could bring future benefits to the patients submitted to CABG. (Int J Cardiovasc Sci. 2018;31(2)97-106)

**Keywords:** Atherosclerosis; Myocardial Revascularization; Mammary Arteries; Coronary Angiography.

### Introduction

Among the principal means available for the diagnosis of atherosclerotic coronary disease, coronary angiography, an invasive imaging method, is the choice to examine the evaluation of patients with high cardiovascular risk, calculated through non-invasive scores. Coronary angiography is also indicated in patients who present angina and symptoms of

heart failure, and these recommendations are based on a high degree of evidence.<sup>1</sup>

After the diagnosis of coronary artery disease is established, and according to the characteristics perceived by analyzing the images, three main therapeutic approaches are recommended: clinical treatment, percutaneous coronary intervention, and myocardial revascularization surgery.

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Following the establishment of the criteria for surgical indication, one should proceed to choose the type of graft to be used by the surgeon. Among the arterial options, the best choice is the internal thoracic artery.<sup>2</sup>

In 1986, a study performed at the Cleveland Clinic demonstrated superiority in the use of the LITA, or left internal thoracic artery, compared to the use of the saphenous vein when anastomosed to the left anterior descending branch of the left coronary artery, with patency indices (90%) in 10 years.<sup>3</sup> This study was confirmed by Boylan MJ et al,<sup>4</sup> with a 20-year follow-up and maintenance of patency rates of around 90% of patients undergoing LITA graft surgery. Studies indicate that only 4% of LITA present atherosclerosis, and only 1% are considered major stenoses.<sup>5</sup>

The possible disadvantages are the presence of spasms, possibility of atrophy when used to revascularize an artery without significant stenosis, and in case of bilateral use (LITA and right internal thoracic artery), a possible increase in the incidence of sternal infections in obese and diabetic patients.<sup>2</sup>

On the other hand, the *PREVENT IV* study observed 1539 patients undergoing myocardial revascularization, with LITA grafting for 12-18 months after surgery, evidencing a considerable rate of graft failure in LITA of about 8.6%.<sup>6</sup> Recently, Shavadia et al.<sup>7</sup> (2015), followed 5276 patients who underwent coronary artery bypass grafting, where 281 patients had graft failure after 12 months of follow-up, demonstrating the presence of lesions that made the use of the LITA unfeasible.

This is an analytical, cross-sectional, prevalence study performed through the analysis of images by interventional cardiologists obtained through angiography, which quantified the prevalence of left internal thoracic artery stenosis in patients submitted to coronary artery bypass grafting (CABG). The images analyzed were from patients who were admitted to the hemodynamic service between January 2012 and August 2016.

## Methods

The study was carried out with patients who underwent coronary angiography at the hemodynamics department of the Centro de Diagnósticos Paraná - CEDIPAR - Hospital Paraná, in the city of Maringá, PR.

Patients were selected independently of age, sex and comorbidities, and were indicated by interventional cardiologists of the CEDIPAR hemodynamic service to surgical correction of the lesions, CABG, based on the severity of the coronary artery lesions found.

After completion of the cardiac catheterization examination by radial route, and the need for coronary artery bypass grafting was confirmed, a Simmons 1 or 2 catheter was inserted, depending on the conformation of the aortic arch of the patient, and a selective catheterization of the artery left subclavian and internal thoracic with manual injection or through injection pump, of approximately 10 mL of contrast, iodixanol.

Data were collected from all patients in the study, including comorbidities and life habits, such as smoking, sedentarism, diabetes mellitus type 1 and 2, systemic arterial hypertension, hypercholesterolemia, previous history of AMI with supra-ST-segment elevation, without ST-segment elevation, and previous ischemic and hemorrhagic stroke. The degree of stenosis of the LITA was not evaluated, considering only the presence or absence of lesion. This data was organized and tabulated using the *Microsoft Excel 2010*<sup>®</sup> program.

The primary objective of this study was to identify the presence of atherosclerotic lesions in the LITA, analyzed by means of angiography, in patients with indication for coronary artery bypass grafting, and the quantification of lesions that would not allow LITA to be used as a graft for the anterior descending branch of the left coronary artery.

The following study respected ethical standards, since it was submitted to the ethics and research committee, through the Plataforma Brasil<sup>®</sup> applying the free and informed consent form for all patients, and its approval was registered by opinion 1,651,761 (CAAE: 57529416.0.0000.5539).

## Statistical analysis

Patients were divided into groups with and without changes in the LITA. Categorical variables were described in percentages and groups compared with chi-square test and Fisher's exact test. The only continuous variable, age, was tested for normality by the Kolmogorov-Smirnov test and, because it had no normal distribution, was described in the median (P25; P75) and the groups compared with the Mann-Whitney test. The level of statistical significance was  $p < 0.05$ . The analyzes were performed in *SPSS*<sup>®</sup> software version 20.

## Results

This study analyzed the prevalence of atherosclerotic lesions and other lesions that made the use of the LITA unfeasible in 39 patients who were candidates for CABG. The median age (25th percentile, 75th percentile) of the

patients was 63 years, being 79.5% male and 20.5% female. The prevalence of 7.7% of lesions in the LITA was identified (Graph 1). A case of LITA stenosis was observed, with > 70% of obstruction, and two lesions that made the LITA unfeasible as a graft, being collateral circulation to lower limbs through the LITA and epigastric, and a total occlusion of the subclavian artery in a portion proximal. The analysis of categorical variables using the chi-square test, and Fisher's exact test of predictors for outcomes, took into account patient's age, smoking, sedentary lifestyle, type 1 and type 2 diabetes mellitus, systemic arterial hypertension, hypercholesterolemia, previous history of AMI with supra-ST segment elevation, without ST-segment elevation, and previous ischemic and hemorrhagic encephalic vascular accident, where no variable was shown as a predictor factor for the occurrence of outcomes (Table 1). All patients were asymptomatic with regard to LITA alterations.

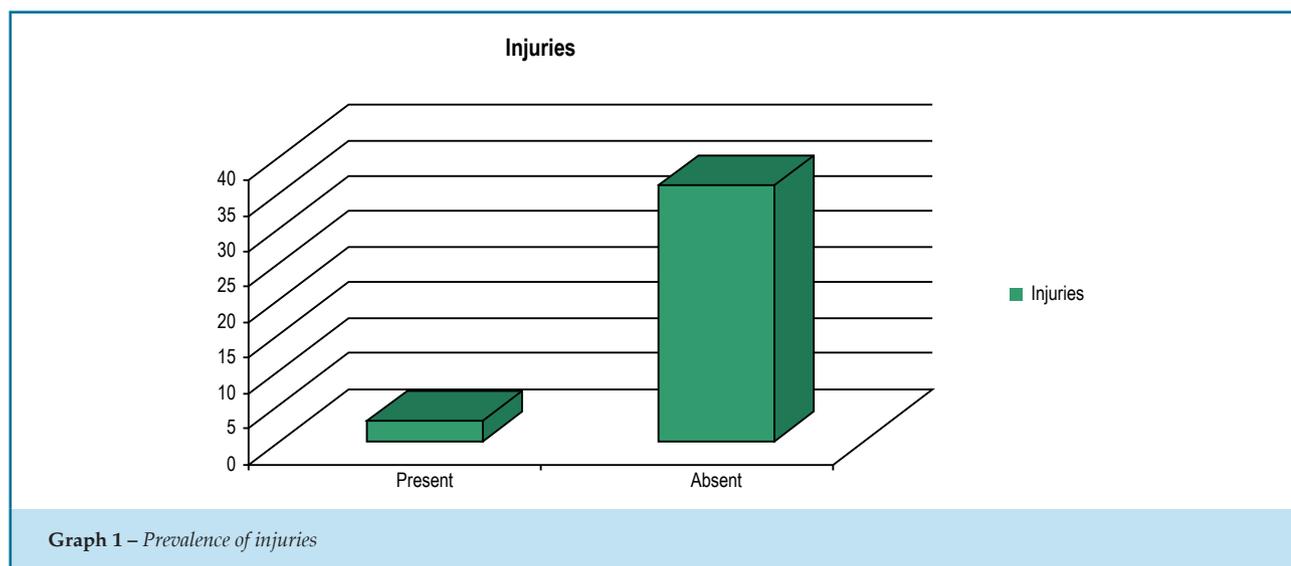
### Discussion

After the determination of the degree of coronary lesions, evidenced by the cinecoronariography examination, and based on its severity, the conduct to be taken is determined by choosing among: clinical treatment, percutaneous coronary intervention or myocardial revascularization surgery.

The criteria for indication of myocardial revascularization surgery are based on two main objectives, being them the improvement of survival and improvement of symptoms. When we think of improved survival, the main indication (Class IB) is for patients with significant stenosis (> 50% of the diameter) of the trunk of the left coronary artery.<sup>8-9</sup>

When analyzing other anatomical regions out of the trunk of the left coronary artery, there is a surgical indication for improvement of survival (Class IB) in cases of significant stenosis (> 70% of diameter) in three main coronary arteries, without involvement of the proximal region of the anterior descending artery, or if there is involvement of the proximal region of the anterior descending artery, the association with a major coronary artery.<sup>10-11</sup> Still related to the improvement of survival, the surgical procedure is indicated for patients post cardiac arrest with presumed ischemia, mediated by ventricular tachycardias due to significant stenosis (> 70% of the diameter) in coronary artery (Class IB).<sup>12</sup> Related to the improvement of symptoms, there is indication for surgery

Table 1 – Values of p	
	Values for p
Gender	0.508
Sedentarism	0.480
Family history for CHD	0.711
Smoker	0.101
Ex-smoker	0.674
High blood pressure	0.457
Type 2 diabetes mellitus	0.637
AMI without supra ST	0.597
Unstable angina	0.457
Dyslipidemia	0.444



Graph 1 – Prevalence of injuries

when one or more significant stenosis of coronary arteries may be revascularized, or cases of unacceptable angina in patients undergoing drug treatment.<sup>2</sup>

After the establishment of the criteria for surgical indication, one should proceed to choose the type of graft to be used by the surgeon. The arterial options include the internal thoracic, radial, gastroepiploic, and inferior epigastric, and among the veins, the saphenous vein is chosen. The efficacy of the procedure is directly related to graft viability. According to the American Heart Association's latest Guideline for coronary artery bypass grafting (CABG), the use of the left internal thoracic artery (LITA) is preferred to revascularize the left anterior descending artery (AD) when indicated (Class IB). In cases of non-viability of the LITA, it is recommended to use the right internal thoracic artery (Class IC).<sup>2</sup>

The internal thoracic artery, described by the Jena Nomina Anatomica in 1936, originates in the subclavian artery, appearing antero-inferiorly in the first part of the subclavian, about 2 cm above the clavicle, medially to the first rib.<sup>13</sup> In 4-30% of patients may arise from a common trunk along with other arteries that also originate in the subclavian, such as the thyrocervical trunk, suprascapular and lower thyroid arteries.<sup>14</sup> After its origin, it continues its course posterior to the brachiocephalic vein and medially to the scalene muscle anteriorly, descending vertically near the sternal border, and later crossing the six upper costal cartilages, ending at a bifurcation at the level of the sixth rib, giving rise to the superior epigastric and musculophrenic arteries.<sup>15</sup>

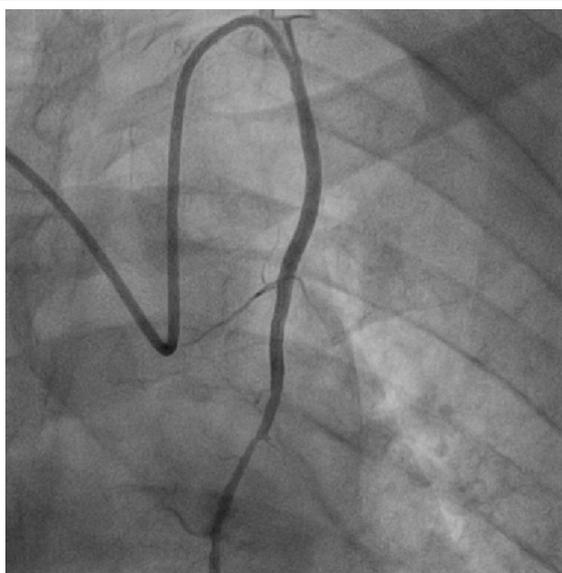
The PREVENT IV study analyzed 1539 patients through selective angiography, in order to describe the number of LITA grafts for the anterior descending (AD) graft, in a period of 12 to 18 months after being submitted to coronary artery bypass grafting. We found 132 patients with significant stenosis of LITA, being considered as significant, a stenosis greater than or equal to 75% of the vessel diameter. Among the patients under study, 61 had total occlusion of the LITA, three had a subtotal stenosis, between 95 and 99%, and a stenosis between 75-95%. The same study carried out a four-year follow-up of these patients, in order to evaluate the rate of major outcomes, such as death, AMI, and revascularization, and to compare it with the group without significant stenosis.<sup>16</sup> In cases of stenosis (32% vs. 16.5%), clearly demonstrating the negative impact of graft patency on the prognosis of patients submitted to surgical treatment. The study considers as one of the main predictors of failure, non-significant left-sided stenosis, less than 75%; however, the study did not evaluate the presence of previous lesions

through a control angiography performed prior to surgery, and it was not possible to relate the non-viability after previous atherosclerotic disease, or even its contribution to the long-term stenosis process.<sup>16</sup>

The results of our study show that in the selected population of patients who are candidates for CABG, the prevalence of atherosclerotic lesions and lesions that impair LITA is significant, and this artery is not routinely evaluated by interventional cardiology, and it is difficult to make a clinical diagnostic, since patients are usually asymptomatic, and the changes are only evidenced by selective angiography. In one patient in our study, who underwent selective angiography during catheterization, the presence of atherosclerotic lesion in LITA was evidenced, with stenosis >70% (Figure 1). In order to differentiate from a possible vasospasm, infusion of 200mcg intra-arterial nitroglycerin was performed, where the subocclusive lesion remained (Figure 2). Taking into account the small number of the sample, 39 patients underwent cardiac catheterization with indication of CABG, the result is relevant, since in this patient the graft alteration used for myocardial revascularization was chosen, excluding the use of the LITA, due to the great risk of treatment failure and increased mortality.

In 1993, Sons et al.<sup>17</sup> demonstrated the high prevalence of atherosclerotic lesions of LITA in patients with functional heart disease. The study analyzed 117 patients, all of whom had coronary artery disease (CAD), associated with valve abnormalities, or some other cardiac pathology. Atherosclerosis of the LITA was found in 11.1% of all patients investigated, indicating that risk factors such as the presence of peripheral arterial disease and hyperlipidemia deserve special attention in a patient with an indication for CABG, due to the high prevalence of the association of these factors with atherosclerosis of the main graft used for this surgery at the present time.

Chen et al.<sup>18</sup> carried out a prospective study of LITA in eighty-six patients with indication for performing CABG. The investigation was performed through selective angiography of the LITA, during cardiac catheterization, seeking to evidence the presence of significant stenosis that could render the graft unfeasible. A significant lesion in the internal thoracic artery (1.2%) was found at the right subclavian artery, along with five other lesions (5.8%) that made its use unfeasible. The author considers as the only and important risk factor, the female sex. The study concludes that selective angiography of LITA during catheterization, especially in patients with indication for CABG, is a safe and necessary procedure, and should be



**Figure 1** – LITA with stenosis.



**Figure 2** – LITA with stenosis after nitroglycerin infusion.

performed due to the high prevalence of lesions that may make it unfeasible, with possible future complications to the patient submitted to the surgical treatment.

In contrast, Perić et al.<sup>19</sup> also analyzed by means of selective angiography the characteristics of LITA and its anatomical variations, in 80 randomly selected patients, and different from that found in the studies cited previously, no patient presented atherosclerosis in LITA. However, the degree of anatomical variations was greater, about 13.25% of

the LITAs evaluated, proving that the indication of selective angiography in all patients who would use the LITA graft for myocardial revascularization may be necessary.

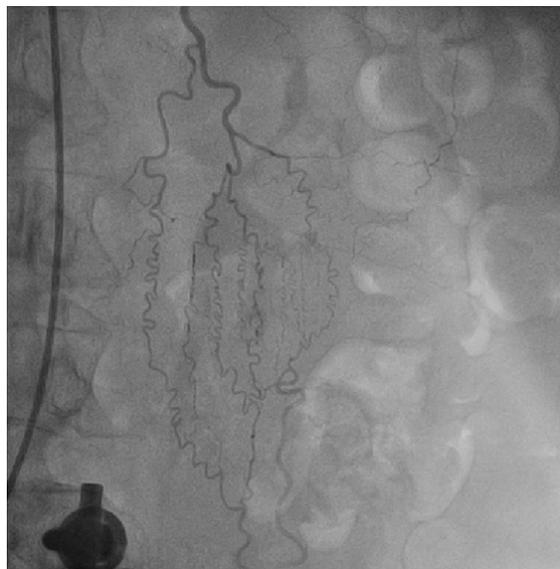
The disagreement regarding the presence of atherosclerosis between the studies, and even in our study, can be attributed to the population used as the basis for each author, since Sons et al.<sup>17</sup> and Chen et al.<sup>18</sup> evaluated patients candidates for surgical correction of myocardium, as the present study, unlike Perić et al.<sup>19</sup>, who randomly

selected patients. All the studies present a reduced number of patients evaluated, which hinders both the homogeneity of the data and the agreement between the prevalence of the lesions. What is clear is the need to evaluate preoperative LITA in patients candidates for CABG, since in addition to diagnosing lesions that will impair the effectiveness of CABG, it is also possible to identify possible changes that cause consequences for patients, such as lower limb ischemia in cases of IAC acting as collateral circulation, and subclavian steal syndrome in patients with significant subclavian occlusion or stenosis.

The presence of chronic aortoiliac occlusive disease is considered an important predictor for the development of anatomical alterations involving LITA. Usually these patients develop collateral perfusions in order to reconstruct the arterial system of the pelvis and lower limbs, avoiding the ischemia of the same. The LITA, together with the superior and inferior epigastric arteries, work as the main parietal collateral pathway in the reconstruction of the external iliac artery, and if this graft is used for myocardial revascularization, the patient may have an acute ischemia of the lower limbs in the post-surgery.<sup>20-25</sup> The presence of this collateral pathway is of such importance that the LITA becomes one of the main arteries responsible for irrigation of the lower limbs, accounting for 38% of the blood flow in the region, and doubling the volume of blood (LITA) every minute.<sup>26</sup> Studies show that the presence of LITA and epigastric as a collateral route to the lower extremities is not an uncommon finding in patients with AOD, and its

prevalence is estimated in up to 12% of cases in that AOD was greater than or equal to 75% of the vessel diameter.<sup>25</sup> In our study, one patient presented LITA and epigastric as a collateral route for irrigation to the legs (Figure 3), alteration identified by preoperative selective angiography in patients with coronary artery bypass indication, without the presence of clinical changes which give evidence of the existence of AOD.<sup>26</sup> The identification of LITA as a collateral route occurred through the progression of contrast to lower vessels, upper and lower epigastric arteries (Figure 3), and continuity to the level of the pelvic vessels (Figure 4). We did not investigate alterations that might indicate the presence of AOD in the present study. However, authors such as Kim et al.<sup>25</sup> point out that the presence of weakened femoral pulses in the affected extremity, with decreased amplitude and volume, and alterations in the ankle index doppler probe, less than 0.7, are important indicators of the presence of AOD. After identification of the presence of collateral circulation to the lower limbs by LITA and epigastric lesions, the presence of aortoiliac-atherosclerotic lesions at the site was demonstrated by selective aorto-iliac angiography (Figure 5).

Another alteration found in our study was a patient with total occlusion of the subclavian artery, characterized by complete interruption in contrast progression, at the proximal level of the subclavian, evidenced by selective angiography (Figure 6). Such alteration may compromise the results of CABG, where the presence of occlusion is one of the main causes of recurrent angina in the postoperative



**Figure 3** – LITA with presence of collateral circulation.



**Figure 4** – Collateral circulation of the LITA to the pelvic region.



**Figure 5** – Aorta with subocclusive atherosclerotic lesions.

period, leading the patient to perform a myocardial revascularization surgery without effectiveness, since the blood flow of the LITA has its inverted direction, due to subclavian occlusion.<sup>27</sup> In addition, patients may have a characteristic clinical presentation, due to vertebral artery flow also being directed to the subclavian, with symptoms such as dizziness, syncope and vertigo due to the ischemia generated by the deviation of the blood supply. The entire clinical picture generated by this pathophysiology is called

the subclavian steal syndrome, and these patients can be screened for both upper limb blood pressure difference, as well as for murmur survey at subclavian level, and pulse difference. Patients with total occlusion of the subclavian artery are at high risk of developing this syndrome before and after CABG.<sup>28-30</sup> The patient in this study was asymptomatic when submitted to angiographic evaluation.

The limitation of this study was the small population analyzed, resulting in an absence of relationship between



**Figure 6** – Total occlusion of the left subclavian artery.

the predictors and the outcome. However, we consider this prevalence value to be significant, since a CABG with arterial graft failure can lead to serious complications, increasing mortality, and decreasing the effectiveness of the procedure.

## Conclusion

In this study, the prevalence of atherosclerotic lesions and lesions that made the use of the LITA as an arterial graft unfeasible in patients candidates for CABG, evidenced by coronary angiography, were 7.7%. Thus, it is prudent to consider the preoperative assessment of the LITA in patients with indication for CABG, especially in the presence of clinical evidence of subclavian occlusion and AOD.

## Author contributions

Conception and design of the research: Balzan HFM, Battilani RVL, Mangili OC, Franchetti M, Mangili LC, Maia JP. Acquisition of data: Balzan HFM, Battilani RVL, Moura DD, Lage BFM. Analysis and interpretation of the data: Balzan HFM, Battilani RVL, Mangili OC, Franchetti M, Mangili LC, Maia JP, Moura DD, Lage BFM. Statistical analysis: Balzan HFM, Battilani RVL, Mangili OC, Mangili LC, Maia JP. Obtaining financing:

Balzan HFM, Battilani RVL, Mangili OC, Franchetti M. Writing of the manuscript: Balzan HFM, Battilani RVL, Mangili OC, Franchetti M, Moura DD, Lage BFM. Critical revision of the manuscript for intellectual content: Balzan HFM, Battilani RVL, Mangili OC, Franchetti M, Mangili LC, Maia JP, Moura DD, Lage BFM. Supervision / as the major investigator: Balzan HFM, Battilani RVL, Mangili OC, Franchetti M.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any thesis or dissertation work.

## Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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