

Ligation of the Branches of the Anastomosed Internal Thoracic Artery in the Anterior Descending Coronary Artery and the Effect on Flow Velocities and Functional Status of the Graft

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Summary

Introduction: Modification of internal thoracic artery flow occurs after its anastomosis in the left anterior descending coronary artery.

Objective: To evaluate the effect of ligation of the proximal branches of anastomosed internal thoracic artery flow on the left anterior descending in relation to velocities and coronary flow velocity reserve in patients with left ventricular ejection fraction preserved (> 50%).

Methods: Prospective study of patients with left ventricular ejection fraction > 50% and revascularized. Group I was composed of 25 patients with ligation of the major branches of the internal thoracic artery flow before its anastomosis in the left anterior descending coronary artery, and Group II was composed of 28 patients without ligation. Doppler was recorded at the proximal level of internal thoracic artery flow in the preoperative, early postoperative and 6 months later. The systolic peak velocity and diastolic, and systolic mean velocity and diastolic were measured. Coronary flow velocity reserve was obtained during dobutamine stress echocardiography in postoperative period 6 months later.

Results: In the postoperative, the systolic peak velocity and the systolic mean velocity decreased while increasing the diastolic peak velocity and the diastolic mean velocity in the groups ($p < 0.05$). From the postoperative to the postoperative period 6 months later, only the diastolic peak velocity modified, occurring its decrease in the groups ($p < 0.05$). During the dobutamine stress echocardiography, diastolic peak velocity and the diastolic mean velocity increased ($p < 0.05$) and groups did not differ, however, the systolic peak velocity and the systolic mean velocity increased only in Group II ($p < 0.05$). The coronary flow velocity reserve of the groups calculated by diastolic peak velocity (Group I = 2.17 ± 0.64 and Group II = 2.28 ± 0.63) and diastolic mean velocity (Group I = 2.27 ± 0.54 and Group II = 2.5 ± 0.79) did not differ.

Conclusion: In patients with preserved left ventricular ejection fraction, the ligation of the large branches of the anastomosed internal thoracic artery flow into the left anterior descending coronary artery does not compromise the coronary flow velocity reserve, but determines limitation in the increase of the systolic velocities. (Arq Bras Cardiol: Imagem cardiovasc. 2018;31(4):231-240)

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Introduction

The internal thoracic artery (ITA) is a conduit in which the patency after coronary artery bypass grafting (CABG) presents greater longevity than the saphenous vein.¹ However, the extent of the cardiac muscle impairment, the functional status of the coronary bed and the possibility of competition between the native and the graft flow are relevant conditions to be observed in CABG planning.²⁻⁷ However, when the conduit

selected for the CABG is the ITA, and it has an important proximal branch, the ligation of this branch can be performed or not, depending on the routine of the surgical team.⁸⁻¹⁰

The anastomosis of the ITA in the left coronary system is characterized as a hybrid system, due to the different hydrodynamic impacts of the subclavian and left coronary artery flows, in which the predominance of the systolic and diastolic component occurs, respectively. Consequently, Doppler recording in the proximal segment of its origin reveals the expressive influence of the left subclavian flow, while the most distal segment reflects the hydrodynamic effect of the underlying coronary artery, which makes it important to mention the segment in which the ITA was evaluated.^{4,9,11-14}

After the anastomosis of the anterior descending coronary artery (ADA), the ITA flow changes the systolic and diastolic components in the early postoperative (EPO) and late postoperative (LPO) period.¹⁴⁻¹⁸ In this period, the evaluation

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of the functional status of the ITA after CABG can be performed using a vasodilator drug (dipyridamole or adenosine) or a drug with a positive inotropic vasodilatory effect during Dobutamine Stress Echocardiography (DSE).

Echocardiography under pharmacological stress is a safe examination that allows to determine, through segmental contraction abnormality, if the myocardial flow is compromised, by establishing the good accuracy of the method for the diagnosis of myocardial ischemia.¹⁹⁻²¹ On the other hand, it can be difficult to measure the flow in the coronary artery and in the ITA, given the need to measure the vessel size – particularly during DSE. The diastolic flow velocity measurement is used more frequently to infer the functional status of both vessels by calculating the Coronary Flow Velocity Reserve (CFVR).²²⁻²⁷

The proximal branch determines the effect on the ITA flow, but there is no publication analyzing the changes in velocity in this context.

We aimed to determine the effect of ligation of the important proximal branches of the anastomosed ITA in the ADA, regarding the flow velocities and CFVR in patients with preserved left ventricular ejection fraction (LVEF) (> 50%).

Methods

This is a prospective study performed in a cardiology hospital, in which the patients underwent CABG with anastomosis of the ITA in situ for ADA. Inclusion criteria were: sinus rhythm, ADA proximal stenosis > 75% and clinical decision that surgical CABG was the best option for the case. The ITA was anastomosed only in the ADA, immediately after proximal stenosis. Exclusion criteria were: akinesia of the anterior left ventricular (LV) wall due to previous myocardial infarction, LVEF < 50%, presence of LV diastolic dysfunction above grade II, fine ITA, absence of major branch in the ITA of a patient assigned to the group with ligation, presence of thick coronary branch between the ADA stenosis site and the ITA anastomotic site, hemodynamic instability, contraindication

or limitation to the use of dobutamine or atropine, evidence of ischemia in the LV anterior wall or not reaching the submaximal heart rate (HR) during DSE. All patients signed an Informed Consent Form. This study was approved by the local Research Ethics Committee of Hospital de Messejana Dr. Carlos Alberto Studart Gomes.

All CABG surgeries were performed by the same surgical team. After sternotomy and hemostasis, it was determined whether there was a proximal branch with a diameter apparently comparable to that of the ITA.

The patients were allocated sequentially in a group for ligation of the proximal branch of the ITA (Group I) or for the group without ligation (Group II). If the patient assigned to Group I did not present the proximal branch during the surgical procedure, the patient was excluded from the study.

The CABG procedure followed the usual sequence adopted by the surgical team and, when indicated, coronary artery bypass grafting of the other coronary arteries was performed with saphenous vein grafts.

All tests were performed using Vivid 7 echocardiograph (GE Healthcare, Milwaukee, WI, USA) equipped with multifrequency transducers. M4S with a frequency of 2 to 4 MHz was used for the transthoracic echocardiography. The 7S pediatric transducer, with a frequency ranging from 3.5 to 6.9 MHz, was positioned in the left supraclavicular fossa for two-dimensional record and Doppler of the ITA (Figure 1). To view the ATI, the patient in the supine position kept the cervical region partially extended and slightly rotated to the opposite side of the vessel under study. The ITA was recorded as emerging from the subclavian artery and, adjusting with small angles or rotations of the transducer, the ITA was viewed in its greatest possible extent. Then, we positioned the pulsatile Doppler sample-volume with the lowest possible angle and selected the best spectral curve, analyzing its systolic and diastolic components, and recorded and measured the systolic (SVP) and diastolic (DVP) velocity peaks, and the mean systolic (MSV) and mean diastolic (MDV) velocities.²⁶

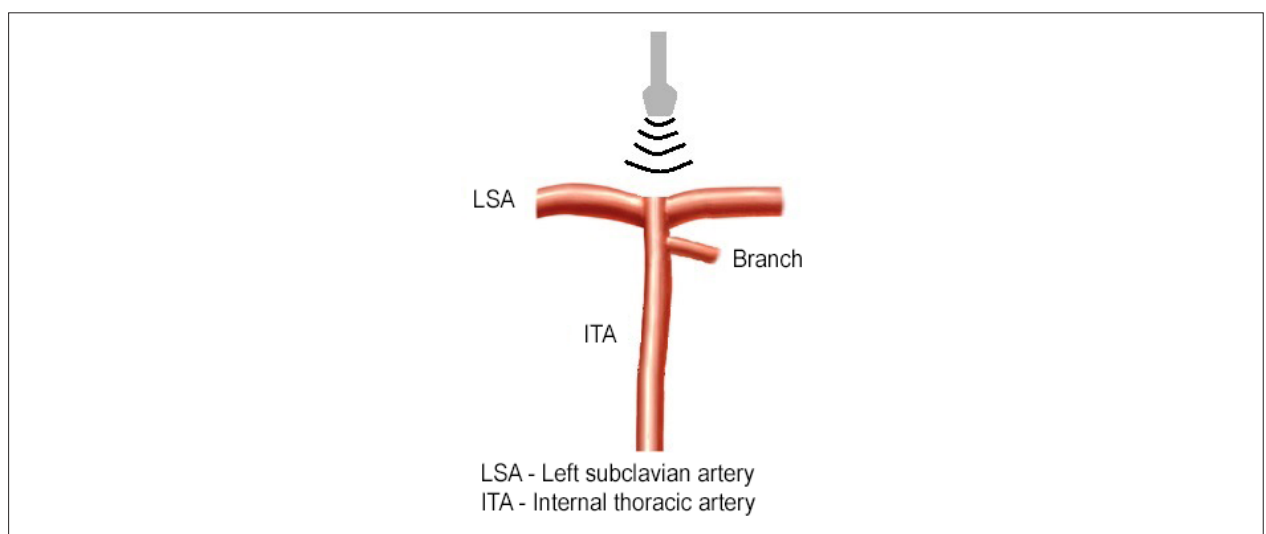


Figure 1 – Schematic drawing of the proximal register of the internal thoracic artery. LSA: left subclavian artery; ITA: internal thoracic artery.

All patients underwent complete transthoracic echocardiography and ITA Doppler with preoperative (PRE) velocity measurements. In the EPO, echocardiography was repeated to perform a new measurement of the anastomosed ITA velocities and evaluation of the ventricular dynamics. Six months after the surgery (LPO6M), the patients underwent another complete transthoracic echocardiography. Shortly thereafter, the velocities of the anastomosed ITA were measured at baseline and peak DSE. CFVR was calculated with the DVP (DVP in DSE/ DVP in baseline) and with MDV (MDV in DSE/MDV in baseline).

After recording the resting images on the quadruple screen, continuous infusion of dobutamine into the peripheral vein was initiated and administered with increasing doses in stages of 3 minutes. Atropine was associated when necessary. Submaximal HR [(220 – age) × 85%] should be reached in all cases during DSE. Ischemia was reported as typical angina, ST-segment depression greater than 3 mm, new contractile abnormality or worsening of a preexisting one (except for akinesia for dyskinesia). At the end of the DSE, an intravenous esmolol bolus (2 to 5 mg) was administered to reduce HR to approximately 100 bpm, with DSE being completed with the recovery stage.^{20,21,28,29}

The LV was divided into 16 segments and the following patterns were found in the score for the contraction of each segment: 1 score if normal; 2, hypokinetic; 3, akinetic; or 4, dyskinetic. In the calculation of the segmental contraction score index, the score was divided by 16.

Statistical analysis

The data observed in this study are repeated measurements, in a time sequence of two groups of patients.

The distributions of continuous variables were compared using Student's *t*-test when the variables were approximately normal, or Wilcoxon's test (Mann-Whitney) when the variables were not approximately normal. Proportions were compared using Fisher's exact test.

The data were analyzed using the software Stata/SE, version 12.1 (StataCorp LP, College station, Tx, USA).

The intraobserver and interobserver variability of the measurements of velocities obtained in the ITAs were determined through the intraclass correlation coefficient derived from the Analysis of Variance (ANOVA). The results were obtained from the program Statistical Package for Social Science (SPSS), version 13, using the Reliability Analysis module. The level of significance was $p < 0.05$.

Results

From the 58 patients initially included in the study, five of them (two in Group I) were excluded at a later stage. One case had persistent atrial fibrillation; another, pericardial effusion attributed to postpericardiotomy syndrome; one was lost in the follow-up; and the other two refused to remain in the study. Thus, a total of 53 patients were included in the final sample of the study, forming the group of 25 patients with ligation of the important proximal branches, called Group I, and Group II included 28 patients without ligation of branches.

The clinical and demographic characteristics of the patients are detailed in Table 1. The groups did not differ in mean age, sex, drug therapy to control cardiovascular risk factors, history of unstable angina or acute myocardial infarction. The mean hemoglobin of Groups I and II was similar (11.6 ± 1.4 g/dL vs. 11.5 ± 1 g/dL; $p = 0.673$), and all patients had serum creatinine < 1.3 mg/dL. LVEF was preserved in the groups, and there was no significant difference between them, as there was no difference in left atrial volume, indexed mass and LV diastolic function.

In an EPO assessment (4.6 ± 1.5 days after CABG), echocardiography showed preserved LV global systolic function, and no patient presented complications. The segmental contraction was normal, including in the three cases with LV anterior wall hypokinesis in the PRE.

In the LPO6M, the evaluation in baseline condition and during DSE showed no difference between the groups regarding HR, systolic blood pressure, diastolic blood pressure, double product and segmental contraction score index (Table 2). The groups were also similar regarding the cumulative doses of dobutamine and atropine administered during the DSE, with submaximal HR achieved in all cases. One patient in each group developed contractile LV abnormality compatible with ischemia, but in both cases only the inferior wall was compromised. Other abnormalities included isolated (15% of cases) ectopia (ventricular and supraventricular) and one case of supraventricular tachycardia in each group with spontaneous resolution. There was no death, myocardial infarction or any major complication in any patient.

In the reproducibility check, velocity measurements were repeated in ten patients of each group (randomly selected), with a minimum interval of 3 months between them. The intraclass correlation coefficients for DVP, SVP, MDV and MSV indicated high intraobserver and interobserver agreement (Table 3).

Figures 2 and 3 illustrate the ITA Doppler at different times of the study, revealing changes in systolic and diastolic velocities in the patients of Groups I and II.

The ITA flow velocities were measured in PRE, EPO and LPO6M in all patients. The velocity modifications during the study can be seen in Figure 4. In PRE, there was no difference between the velocities of the groups. In the LPO, there was an increase in the diastolic velocities ($p < 0.05$) and a decrease in the systolic velocities ($p < 0.05$), and the only difference between the groups was in MSV (Group II $>$ Group I; $p < 0.05$). During the 6-month postoperative period, there was no change in the systolic velocities or in the MDV. However, there was a decrease in the PDV in the groups ($p < 0.05$), but no difference between them. During the DSE, the diastolic velocities increased in the groups ($p < 0.05$), but did not differ between the two groups. However, during the DSE, systolic velocities increased only in Group II (Group II $>$ Group I; $p < 0.05$).

The functional state of the ITAs determined by CFVR (Figure 5) did not show any difference between Groups I and II, when evaluated with DVP (2.17 ± 0.64 vs. 2.28 ± 0.63 ; $p = 0.537$) or with MDV (2.27 ± 0.54 vs. 2.5 ± 0.79).

Table 1 – Clinical and echocardiographic preoperative characteristics in the groups

Variable	Group I	Group II	p value
Patients, n	25	28	
Age, years	56.48 ± 9.53	57.21 ± 9.97	ns
Men	17 (68)	18 (64)	ns
Therapy			
Hypoglycemic agent	9 (36)	15 (54)	ns
Statin	24 (96)	24 (86)	ns
ASA	21 (84)	27 (96)	ns
Beta-blocker	22 (88)	19 (68)	ns
ACEI/ARB	18 (72)	22 (79)	ns
Nitrate	11 (44)	10 (36)	ns
Diuretics	5 (20)	7 (25)	ns
Calcium antagonist	4 (16)	5 (18)	ns
Acute myocardial infarction	8 (32)	6 (21.4)	ns
Unstable angina	17 (68)	22 (78.6)	ns
LVEF, %	64.2 ± 8.2	66.4 ± 8.8	ns
LA volume, mL/m ²	24.2 ± 8.1	24.3 ± 10.4	ns
LVMI, g/m ²	142 ± 39.3	148 ± 32.5	ns
Mitral Doppler			
E wave, (m/s)	0.67 ± 0.15	0.68 ± 0.17	ns
E/A ratio	0.92 ± 0.35	0.98 ± 0.26	ns
E/e' ratio	10.4 ± 6.02	9.98 ± 5.38	ns

Results expressed as n, mean ± standard deviation and n (%). ns: non-significant; ASA: acetylsalicylic acid; ACEI: angiotensin converting enzyme inhibitor; ARA: angiotensin receptor antagonist; LVEF: left ventricular ejection fraction; LA: left atrium; LVMI: left ventricular mass index.

Table 2 – Mean hemodynamic and echocardiographic measurements after 6 months of evolution in baseline condition and under dobutamine stress

Variable	Group I	Group II	p value
Heart rate, bpm			
Rest	70 ± 12	72 ± 11	ns
DSE	155 ± 11	151 ± 7	ns
Systolic blood pressure, mmHg			
Rest	138 ± 25	132 ± 18	ns
DSE	162 ± 28	163 ± 35	ns
Diastolic blood pressure, mmHg			
Rest	85 ± 7	81 ± 6	ns
DSE	82 ± 9	85 ± 12	ns
Double product			
Rest	9.591 ± 2.249	9.620 ± 2.404	ns
DSE	24.983 ± 4.519	24.796 ± 5.726	ns
SCSI			
Rest	1.05 ± 0.09	1.06 ± 0.14	ns
DSE	1.04 ± 0.08	1.05 ± 0.14	ns

Results expressed as mean ± standard deviation. DSE: dobutamine stress echocardiography; SCSI: segmental contraction score index.

Table 3 – Intraclass correlation coefficient (ICC) of measurements taken from the internal thoracic artery by two observers

Variables	Evaluator 1 vs. evaluator 1		First vs. second evaluator	
	ICC	CI 95%	ICC	95% CI
Mean systolic velocity	0.990	(0.976-0.996)	0.993	(0.982-0.997)
Mean diastolic velocity	0.998	(0.994-0.999)	0.996	(0.990-0.998)
Peak systolic velocity	0.997	(0.992-0.999)	0.999	(0.997-1.000)
Peak diastolic velocity	0.996	(0.990-0.998)	0.999	(0.997-0.999)

95% CI: confidence interval.

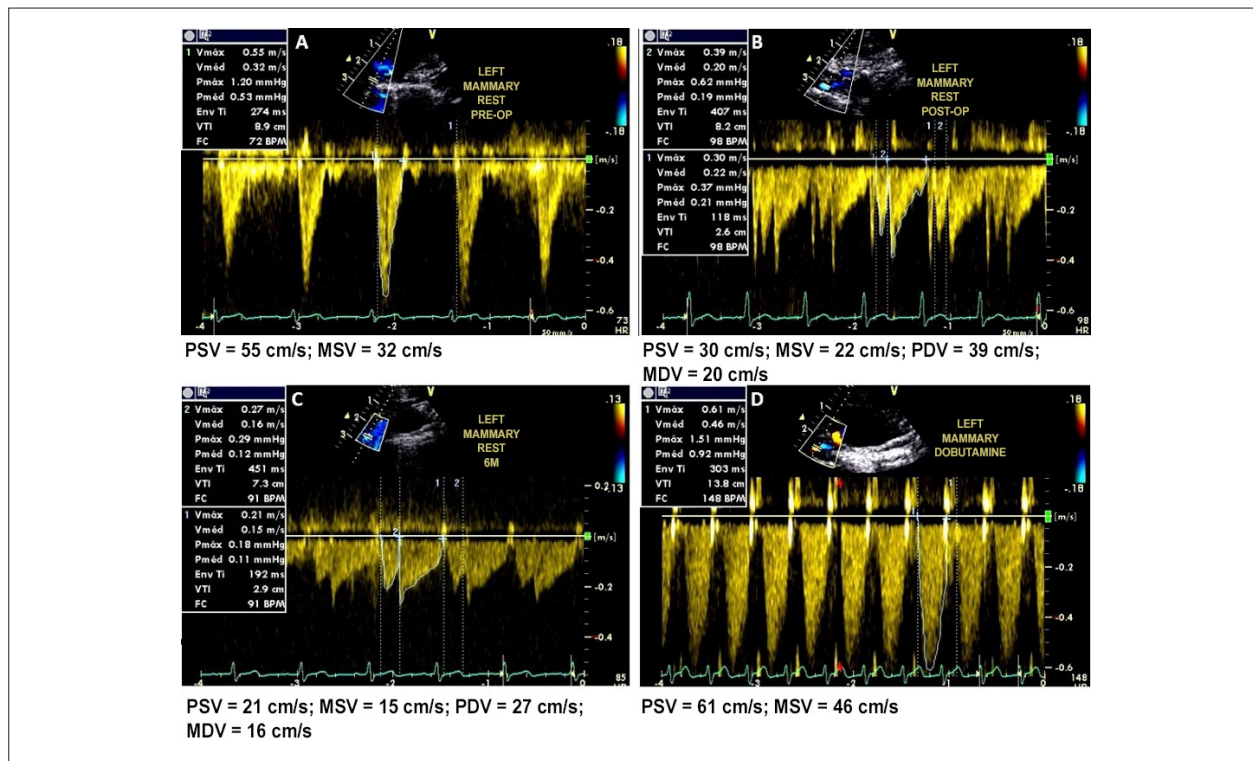


Figure 2 – Patient from Group 1 with ligation of the large branches. Internal thoracic artery Doppler shows only preoperative systolic velocities (A), higher postoperative diastolic velocities (B and C), and only diastolic velocities during dobutamine stress (D). PSV: peak systolic velocity; MSV: mean systolic velocity; PDV: peak diastolic velocity; MDV: mean diastolic velocity.

Discussion

The long-term patency and the ITA ability to adapt to the needs of the underlying coronary bed are conditions that contribute significantly to indicate it as the preferred coronary graft.¹⁻⁷

The predominance of systolic flow seen in the ITA in situ in the PRE tends to change to diastolic after its graft in the left coronary system, characterizing a hybrid pattern of its adaptability.^{4,11-14} We can see this flow dynamics in a quick and easy way through the ITA at the proximal level, denoting excellent feasibility (93% to 98%), even when the HR is high.^{12, 30-33}

Ligation of the important proximal branches of the ITA before anastomosing it in the ADA determines an additional

modification in the graft flow.¹⁸ Our study pioneered in analyzing the effects on the flow velocities of the ITA grafted after this ligation, both at baseline and during DSE.

Modifications from the preoperative period to the early postoperative period

Changes to the ITA flow velocities taking place from the PRE to the POP period in both groups were considerable and distinct, due to the hybrid graft condition, determining the exacerbation of the diastolic velocity at the same time as the reduction of systolic velocity. However, part of this modification may have been due to reactive hyperemia, which is observed in the flow after thoracotomy.³⁴ The diastolic velocities and the MSV did not differ between the groups.

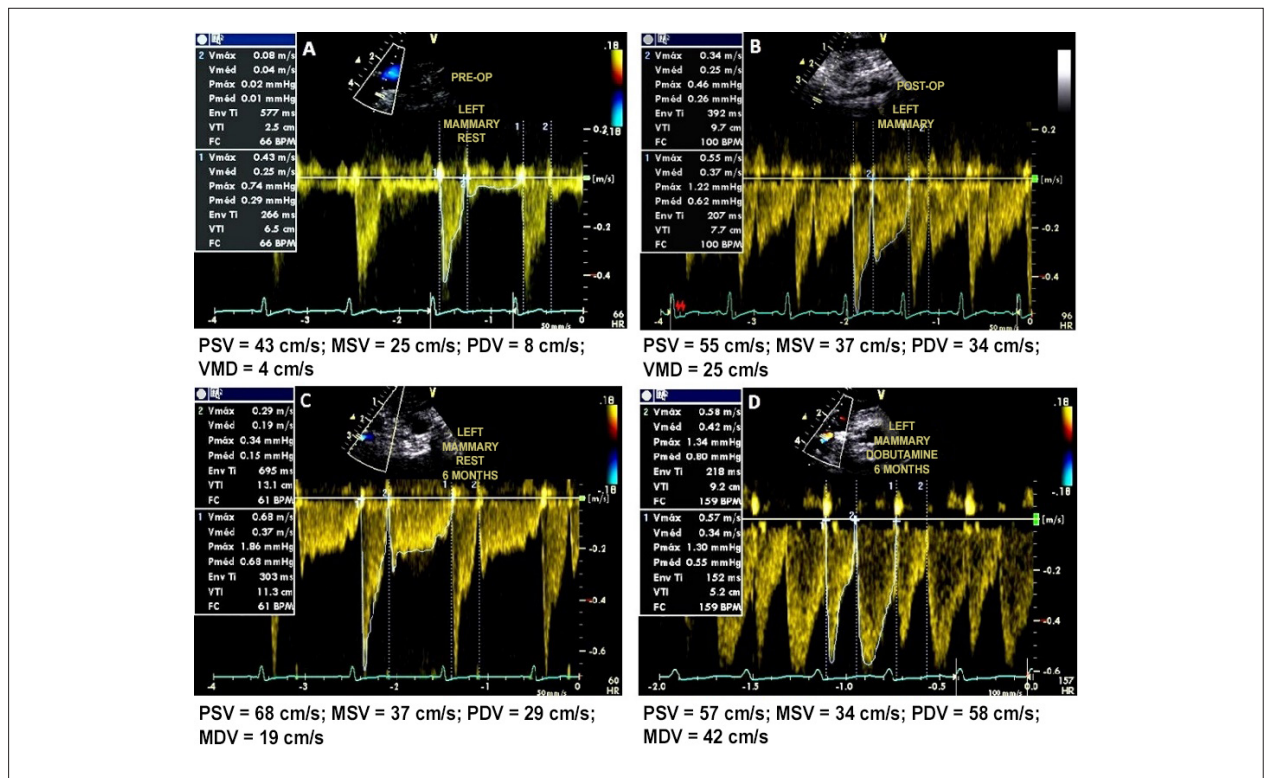


Figure 3 – Patient from Group II without ligation of the large branches. Doppler of the internal thoracic artery shows a large predominance of preoperative systolic velocities (A). In the early postoperative period (B) and after 6 months (C), there is no predominance of diastolic velocity in this case, but during the dobutamine stress, both the peak and the mean diastolic velocity are predominant (D). PSV: peak systolic velocity; MSV: mean systolic velocity; PDV: peak diastolic velocity; MDV: mean diastolic velocity.

However, they differed as to the PSV, and this was lower in the GI. This condition may be relevant in the case of a researcher using the relationship between the PSV and the PDV when studying the ITA after anastomosis in the ADA.^{32,35}

Modifications of velocities from the early postoperative period to the 6-month evaluation at baseline condition

While in the EPO the changes in the ITA flow velocities were accentuated, it was found that, from that moment until the test done 6 months after the CABG in the baseline condition, the variations in the measurements were less expressive. The only change was the reduced PDV in the groups. Because CFVR is a ratio between diastolic (stress/rest) velocities, a lower baseline PDV can lead to a higher coronary reserve value.

Modifications to the velocities taking place in the baseline condition to stress, at the 6-month evaluation after the surgery.

In LPO6M, the graft is better adapted and, therefore, a hyperemic stimulus allows to obtain, through the ITA, the CFVR that represents its functional state.^{15,16,36,37} From the baseline condition to stress, there was a similar increase in the diastolic velocities in the groups, determining that the CFVR, calculated with the PDV or MDV, was not different between the groups with or without ligation of ITA branches.

As for systolic velocities, the changes were due to a significant increase in Group II only. This finding shows that the ligation of the ITA branches is a limiting condition for the increased systolic velocity component. It was interesting to find that in five patients (four in Group I) there was total suppression of the systolic velocities during the DSE.

Closing remarks

In this study, we tried to minimize the confounding biases for assessing the ITA flow velocities, with or without branch ligation. In addition to the good ADA distal bed, the proximal stenosis of the native artery greater than 75% reduces the possibility of flow competition with the ITA,^{4,38} which avoids underestimating the calculation and accuracy of CFVR obtained from the ITA, a fact that occurred in the publication by Pizzuto et al.,⁷ in which a high number of patients with ADA proximal stenosis was found to be between 20% and 60%.

According to the established criteria, the baseline segmental contraction score index was low throughout the study, and there was no evidence of anterior wall ischemia postoperatively. The double product values were similar and expressed the great increase of metabolic demands during stress, so that all patients reached the submaximal HR, without any difference in CFVR between the groups.

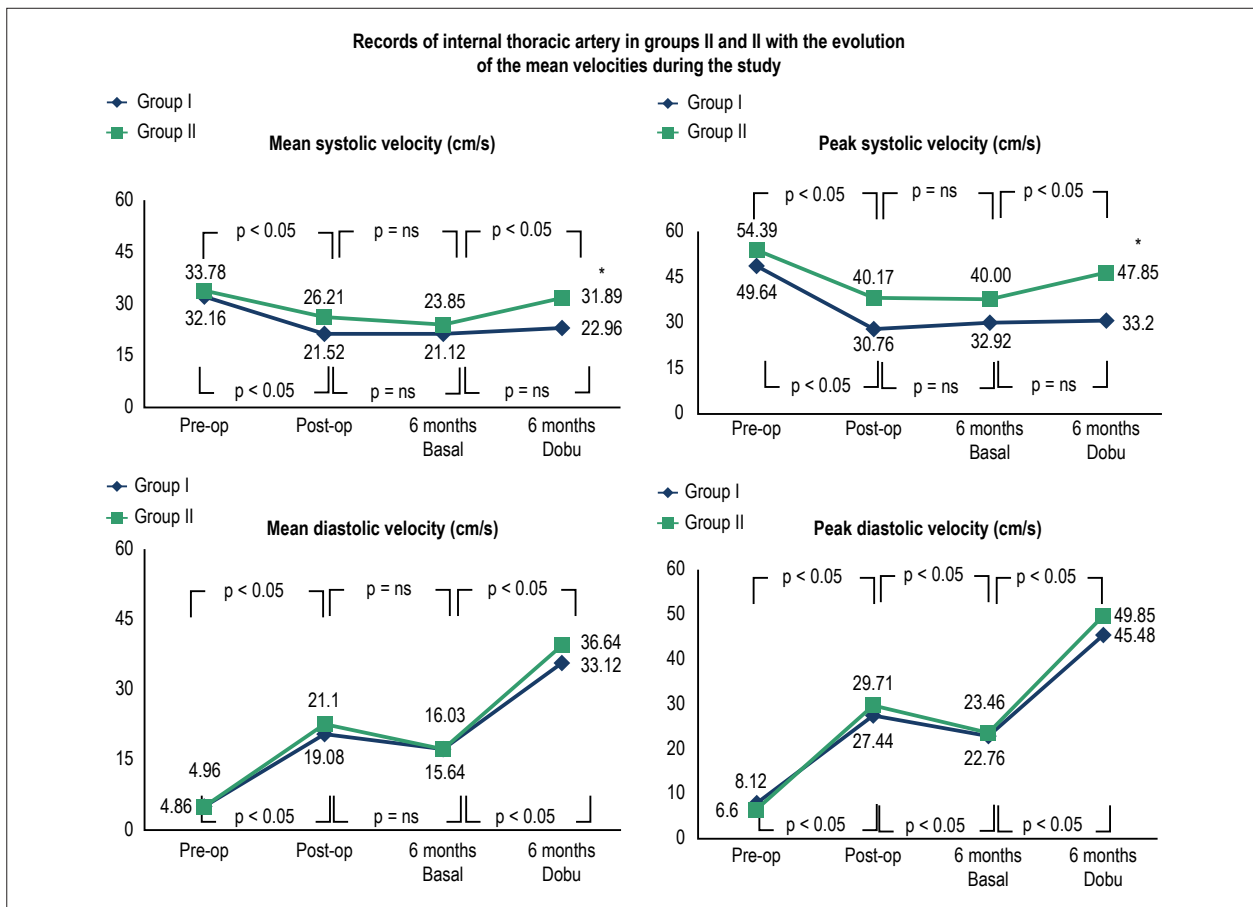


Figure 4 – Internal thoracic artery records in Groups I and II with the evolution of mean velocities during the study. In the preoperative period (pre-op), in the early postoperative period (post-op), 6 months after the surgery in the baseline test (6 months baseline) and during dobutamine stress (6 months dobu). ns: non-significant.

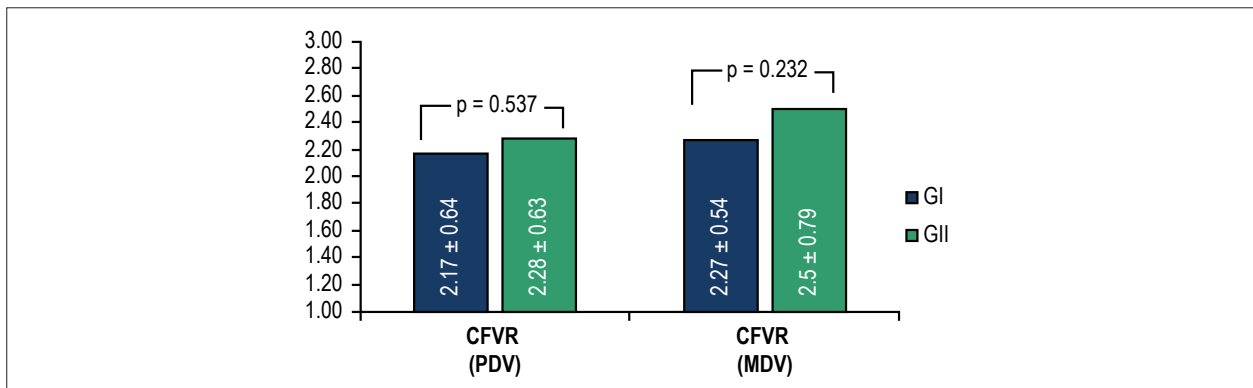


Figure 5 – Coronary flow velocity reserve (CFVR) calculated with the peak diastolic velocity (PDV) and the mean diastolic velocity (MDV).

According to Van Son et al.,³⁴ reactive hyperemia virtually does not exist 6 months after thoracotomy, so that, as in other articles,^{16,17} we consider this period adequate to evaluate the coronary reserve. The intact endothelium may modulate the vasomotor tone of the ITA. This may occur in response to the change in blood flow and longitudinal stress in the endothelium by laminar flow with high velocity, favoring vascular remodeling and release of nitric oxide. These modifications are important to determine lower basal

velocities, suggesting adaptation to lower metabolic demand and providing a greater coronary reserve.^{15,16,36,37,39}

In a study that evaluated the anastomosed ITA (without considering the branches) at the supraclavicular level during the DSE, the Receiver Operating Characteristic (ROC) curve showed that the cut-off point for CFVR ≥ 1,8 provided good accuracy in the identification of the grafts with an adequate functional status, although in 20% of the cases, the occurrence of CFVR < 1.8 – in the absence of ITA-ADA conduit lesion.²⁶

Among the 53 patients in our study, 26% of them reported CFVR < 1.8, with seven cases occurring in each group. It was found that these 14 cases had mean baseline PDV (27.1 cm/s) above the mean baseline PDV of Group I (22.76 cm/s) and Group II (23.46 cm/s), as well as lower mean PDV during stress (42.36 cm/s) than in Group I (45.48 cm/s) and in Group II (49.86 cm/s), which may explain the occurrence of lower CFVR values, but not necessarily ITA stenosis.

When hyperemia is determined with vasodilators, such as adenosine or dipyridamole, there are significant increases in both the systolic and diastolic components of the anastomosed ITA flow. However, in addition to the significant vasodilatory effect of dobutamine, it also presents a marked positive inotropic effect, which, concomitant with the additional HR increase determined by association with atropine, may lead to inhibition or even total suppression of the systolic flow component.^{11,26,40,41}

Of the 53 cases studied, five (9.4%) presented total suppression of the systolic component during the DSE, and all occurred with submaximal HR levels, four of them being in Group I. Suppression of the systolic flow component did not prevent the high myocardial metabolic demand, considering the double product obtained. This suggests that, under the circumstances of our study, the systolic flow component is dispensable for maintaining a good myocardial performance, considering the criterion of the contractile response preserved with high HR.

The intraobserver and interobserver agreements of the ITA flow velocity measurements in our study were high, as were those of other publications,^{30,35,42} making our findings highly reproducible and representative of what actually occurs in the coronary circulation after CABG in the two surgical strategies studied.

Limitations

A sample with a greater number of cases could be more informative, even though our sample was larger than that presented in other noninvasive studies to evaluate the effect of the anastomosed ITA branches.

During the ITA Doppler, we did not perform angle correction, but this loses relevance, because we used the same strategy for both groups.

We cannot rule out the possibility that some DSE has presented false-negative results for myocardial ischemia, because it did not reach the maximum HR. However, the guidelines establish that achieving submaximal HR corroborates the high accuracy of the methodology.

Conclusion

In patients with preserved left ventricular ejection fraction, ligation of the large branches of the anastomosed internal thoracic artery in the anterior descending coronary artery does not compromise the reserve of coronary flow velocity but determines limitation in the increase in systolic velocities. Complete suppression of systolic velocities of the anastomosed internal thoracic artery may occur in the absence of ischemic disorders during echocardiography under dobutamine stress.

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Authors' contributions

Research creation and design: Abreu JS; Data acquisition: Abreu JS, Pinheiro TCD, JA Feitosa; Data analysis and interpretation: Abreu JS, Farias AGLP, Carneiro MM, Falcão SNR, Manuscript writing: Abreu JS, Abreu MEB; Critical revision of the manuscript as for important intellectual content: Abreu JS, Falcão SNR.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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