Doppler echocardiographic criteria in patency assessment of composite grafts from left internal thoracic artery

Parâmetros Dopplerfluxométricos de perviedade do enxerto composto de artéria torácica interna esquerda

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Abstract

Objectives The purpose of our study was to establish, with an entirely noninvasive method, transthoracic Doppler echocardiography, criteria for patency of composite left internal thoracic artery grafts when placed on the left anterior descending artery and other branches of the left coronary system.

Methods: The control group comprised 20 patients with single graft and 20 patients with composite graft; all forty having their patency confirmed by coronary angiogram (CA). In this control group, two Doppler echocardiographic variables, diastolic mean velocity-time and integral diastolic peak velocity to systolic peak velocity ratio were recorded. For each variable, established cut-off points were established, using the ROC (Receiver Operator Characteristic) curves, to identify criteria which could differentiate the composite grafts. Only patients with composite grafts were included in the 159-patients study group. The criteria established by the cut-off points in the control group were then applied to detect patency using a diastolic fraction of ≥ 0.5 as the gold standard. The sensitivity, specificity, and positive and negative predictive values of these two criteria were determined.

Results: In the control group, cut-off points of 0.71 and 0.09m were established for the diastolic peak velocity/systolic peak velocity ratio and for diastolic mean velocity-time integral, respectively. In the study group phase, the sensitivity and negative predictive value of the diastolic peak velocity/systolic peak velocity ≥ 0.71 criterion were 36% and 11%, respectively. Diastolic mean velocity-time integral $\geq 0.09m$ criterion, were 40% and 10.48%. The specificities and positive predictive values of each criterion were 100%.

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Abbreviations, Acronyms & Symbols	
CA	Coronary angiography
CABG	Coronary artery bypass graft surgery
CPB	Cardiopulmonary bypass
DPV	Diastole peak velocity
DVTI	Diastole velocity-time integral
FN	False-negative
FP	False-positive
LAD	Left anterior descending coronary artery
LCS	Left coronary system
LITA	Left internal thoracic artery
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver Operator Characteristic
SMV	Saphenous magna vein
SPV	Systole peak velocity
SVTI	Systole velocity-time integral
TDE	Transthoracic Doppler echocardiography
TN	True-negative
TP	True-positive
VTI	Velocity/time integral

Conclusion: Values reaching the criteria established for each variable indicate high probability of composite graft patency. Lower values have a large proportion of false negatives and are not conclusive as patency criteria.

Keywords: Coronary artery bypass. Doppler echocardiography. Mammary arteries. Myocardial ischemia. Myocardial revascularization.

Resumo

Objetivo: O objetivo deste estudo é estabelecer parâmetros preditores de perviedade, avaliados por Dopplerfluxometria, do enxerto composto de artéria torácica interna esquerda, quando revasculariza a artéria interventricular anterior e outro ramo do sistema esquerdo.

Métodos: O grupo controle foi formado por 20 pacientes com enxerto simples e 20 pacientes com enxerto, composto cuja perviedade foi confirmada por cineangiocoronariografia. No grupo controle, as variáveis de fluxo relação velocidade pico diastólico/velocidade pico sistólico e integral da velocidade média/tempo na diástole foram registradas. Para cada variável, estabeleceram-se pontos de corte para identificar enxertos compostos, usando-se curvas ROC (*receiver operator characteristic*). No grupo estudo, foram avaliados 159 pacientes com enxerto composto, determinando-se os dois parâmetros de fluxo. Pontos de cortes estabelecidos no grupo controle foram usados para determinar sensibilidade, especificidade, valores preditivos positivo e negativo de cada variável relacionada à perviedade dos enxertos, tomando-se como referência a fração diastólica $\geq 0,5$.

Resultados: No grupo controle, os pontos de corte estabelecidos para as variáveis velocidade pico diastólico/velocidade pico sistólico e integral velocidade média/tempo na diástole foram, respectivamente, 0,71 e 0,09m. No grupo estudo, a sensibilidade para a velocidade pico diastólico/velocidade pico sistólico e integral da velocidade média/tempo na diástole, considerando seus pontos de corte, foi de 36,4% e 40%, respectivamente. Os respectivos valores preditivos negativos foram 11% e 10.48%, enquanto especificidade e valor preditivo positivo foram de 100% para os dois parâmetros.

Conclusão: Valores maiores ou iguais aos estabelecidos para cada variável indicam alta probabilidade de perviedade do enxerto composto. Valores inferiores apresentam grande proporção de falsos negativos, não sendo conclusivos quanto à perviedade.

Descritores: Ponte de artéria coronária. Ecocardiografia Doppler. Isquemia miocárdica. Artéria torácica interna. Revascularização miocárdica.

INTRODUCTION

Anatomic confirmation of patency and functional evaluation of the coronary grafts is crucial in the coronary artery bypass graft surgery (CABG). The most commonly used method for assessing bypass patency in CABG is coronary angiography (CA). The routine tests for myocardial ischemia are often difficult to interpret in patients who underwent CABG. Therefore, a method that directly analyzes the graft and is less invasive than CA is needed [1]. In recent years, coronary angiography by multidetector computed tomography has been used with good sensitivity and specificity [2], but these two methods are expensive, and the patients are exposed to radiation [3-5]. The transthoracic Doppler echocardiography (TDE) is a particularly interesting tool.

The first descriptions of using Doppler applications in CABG were reported by Fusejima [6], in 1987, and Takagi et al. [7], in 1993. It is a noninvasive and low cost method, and of quick completion even at bedside setting. It can identify left internal thoracic artery (LITA) graft, measure its blood flow [8], and it can be carried out in every routine echocardiogram requested in the follow up appointments. Furthermore, it can be used to provide information on a patient's physiological response to increased myocardial oxygen demand, the coronary reserve flow [9,10].

The flow of the in situ LITA has systolic predominance. When anastomosed to a coronary artery, the flow begins to show an increment of the diastolic component. This is justified because the coronary arteries inflow occurs primarily during diastole [11]. Thus, the LITA starts to assume the pattern of the coronary flow, including varying its diastolic component according to demand [12].

Several measurements can be recorded by Doppler spectral imaging such as: peak velocities during systole and dias-

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tole (SPV and DPV), mean velocities, mean velocity-time integrals during systole (SVTI) and diastole (DVTI), diastolic fraction, cross-sectional vessel area, and blood flow at rest and under stress. Using these recorded measurements, the flow reserve can also be measured by comparing flow under stress to flow at rest [13].

When LITA revascularizes the left anterior descending coronary artery (LAD), the presence of a diastolic component is a promising sign of graft patency. In a composite graft, when two coronary arteries are revascularized by LITA, determining their patency is a challenge. TDE has a high sensitivity and specificity when performed on left internal thoracic arteries (LITA) grafted to the LAD. It is known that the flow is greater in composite grafts than in single grafts since there is a naturally increased demand at rest. This observation throught 10 years of experience was the motivation for our research. This difference has not yet been quantified [14,15]. How much flow increment would it be necessary to suggest that both grafts in configuration of the composite graft were patent?

The purpose of this study is to contribute to the field of physiology and cardiology. The clinical relevance of this paper is to find out if transthoracic Doppler echocardiographic criteria could estimate the patency of the composite LITA graft when it revascularizes LAD and another branch of the left coronary system (LCS).

The overall objective of this study was to establish at rest, Doppler echocardiographic criteria for assessing the patency of a LITA composite graft, when it is revascularizing LAD and another LCS branch. The specific objective was to identify the sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) of the DPV/SPV and DVTI variables for determining composite graft patency, using a diastolic fraction (DF) ≥ 0.5 as the reference value.

METHODS

This study was carried out in two groups: control and study group. None of the patients included or excluded from the study group were part of the control group.

Control Group

In the control group, 40 bypass patients were studied; 20 had single grafts, and 20 had composite grafts. A single graft is when LITA is anastomosed to LAD only and a composite graft is when a segment of the valveless saphenous magna vein (SMV) is anastomosed in "Y" shape in a single graft with a distal anastomosis to another branch of the LCS. Patients with simple and composite grafts, who had their graft patency confirmed by angiography, underwent TDE in order to record two flow variables: the DVTI, and the ratio of diastolic peak velocity to systolic peak velocity (DPV/SPV). For each flow variable, cutt-off points were established to

identify composite grafts by analyzing the Receiver Operator Characteristic (ROC) curves. Patients whose LITA was not adequately seen due to technical limitations were excluded.

Study Group

In the study group, 159 examinations were evaluated, corresponding to 159 subjects, 27% of which were female patients. The mean age was 63.4 years, ranging from 36 to 82 years. All patients had undergone CABG with a composite graft in which the LITA was grafted to the LAD and to another LCS artery by a saphenous vein segment in "Y" anastomosis without cardiopulmonary bypass (CPB).

All Doppler studies were performed by one echocardiographer (MCAL). The average time interval between surgery and examination was approximately 12.9 months, ranging from 2 to 96 months. The examinations were done and collected for the last 10 years and the preparation of the database occurred between December 2010 and January 2011.

Patients were excluded from the study group because of the following reasons: a LITA that could not be visualized, when LITA provided blood flow to more than two vessels of the LCS; and patients who were submitted to the Vineberg procedure, LITA single grafts, LITA sequential grafts, and on-pump operations. Tests performed during the first two months after CABG were also excluded because as outpatients it's easier to avoid unstable conditions that could be presented during hospitalization period. The concern was to get an uniform group.

In this phase, the Doppler criteria obtained from the cutoff points in the control group were applied to these 159 patients. They were tested in the real world. The rate of true-positives, false-positives, false-negatives and true-negatives were calculated. Sensitivity, specificity, PPV and NPV, were determined with their respective confidence intervals of 95%.

The reference pattern for patency was the diastolic fraction of ≥ 0.5 which is considered by meta-analysis the Doppler gold standard for assessment of single graft patency with LITA. There is no one criterion yet for patency of composite grafts with LITA. The fact that all patients in the control group had FD ≥ 0.5 supports its use.

The Doppler examinations were conducted at the Unimed Regional Hospital (Hospital Regional da Unimed). The operations were performed at these four hospitals: Unimed Regional Hospital (Hospital Regional da Unimed), Monte Klinikum Hospital (Hospital Monte Klinikum), São Raimundo Hospital (Hospital São Raimundo), and the Walter Cantídio Hospital at the Federal University of Ceará (Hospital Walter Cantídio da Universidade Federal do Ceará). This study was approved by the Research Ethics Committee of Federal University of Ceará (CONEP - Comitê de Ética em Pesquisa) on October 12, 2010, protocol no. 315/10 and letter no. 349/10.

Description of technique

The equipment used was the Toshiba and GE Vivid7. The

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transducer was a nonlinear 5 MHz frequency. The patient was placed in the dorsal decubitus position and the transducer placed on the left supraclavicular region. Using color Doppler, the LITA leaving the subclavian artery was visualized. Subsequently, a pulsed Doppler was applied to obtain the spectral curve and measurement of the variables. Angle adjustment was not necessary for aligning the Doppler cursor with LITA flow [8].

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences® for *Windows* (v.16, SPSS Inc. Chicago, IL) statistical package. None of the quantitative variables had normal distributions according to the Kolmogorov-Smirnov test. As a result, parametric tests could not be used and the variables were described by medians and interquartile ranges. The nonparametric Mann-Whitney test was used to compare the medians in relation to the type of graft configuration (single or composite) in the control group phase.

The cutoff points for the DPV/SPV and DVTI variables during the standardization phase were defined using the ROC curve. In the study group phase, TDE criteria for composite graft patency determined by the cutoff points were put in a 2x2 contingency table, designed using the DF as the reference for graft patency. Subsequently, sensitivity, specificity, PPV, and NPV were calculated, with 95% confidence intervals. The results were expressed in tables. A probability of type I error of 5% was established 5% for every analysis, being considered statistically significant the value of *P*<0.05.

RESULTS

Control Group

The cutoff points obtained from the ROC curves for identifying composite grafts were 0.71 for DPV/SPV (Figure 1) and 0.09m for DVTI (Figure 2). The median values and the respective interquartile ranges for DPV/SPV and DVTI were also calculated. In the control group, the patients with composite grafts had significantly higher values (*P*< 0.0001) than those with single grafts (Table 1). All patients of the control group with composite graft showed FD>0.5.

Study Group

Table 1 shows the median values and interquartile range of the variables in the control group and study group considering the type of graft performed.

Table 2 shows the performance of our criterion DSV/SPV ≥0.71 in the assessment of patency of LITA composite grafts. Because DF is the most accurate criterion according to the literature of LITA graft, it was our reference standard for validation of our two patency criteria for composite grafts. This table displays the rates of true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) findings for the criterion DPV/SPV ≥ 0.71. Among the 159 patients of the study group, 59 were TP: they had DSV/SPV ≥ 0.71 and patency was confirmed by DF ≥ 0.05. Eleven were TN, they neither reached the patency criterion for LITA composite graft we were testing nor achieved the reference pattern. 89 were FN: our criterion had detected as non-patent or non-composite graft but they had DF ≥ 0.05.
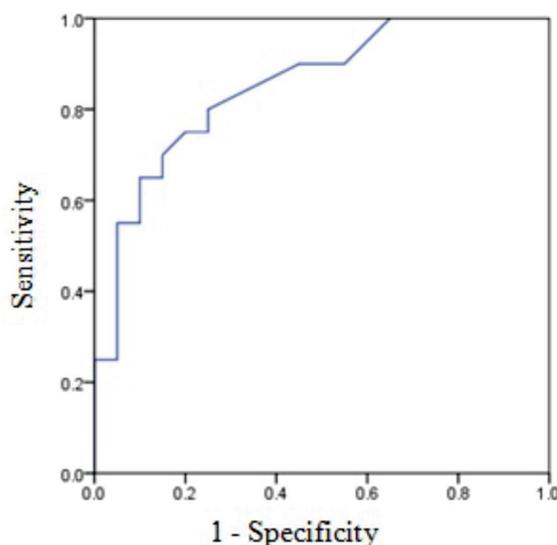
Area Under the Curve

Area	Standard error	Confidence Interval 95%	
		Lower Limit	Upper Limit
,851	,060	,734	,969

Fig. 1 – ROC curve in the control group to determine the best cutoff point for the variable VPD/VPS in evaluating the patency of composite graft

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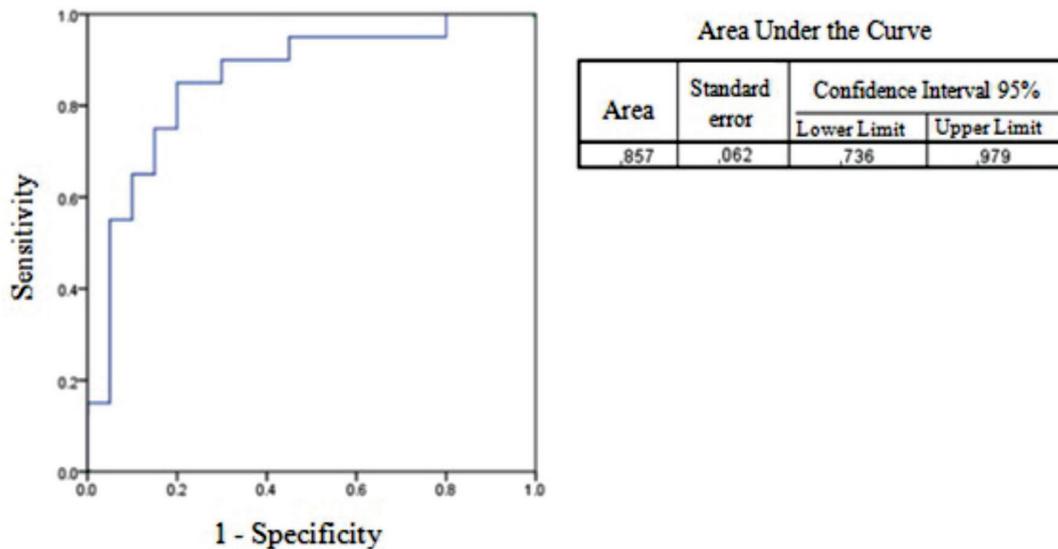*Rev Bras Cir Cardiovasc 2013;28(2):167-75*

Fig. 2 – ROC curve in the control group to determine the best cutoff point for the variable VTId in evaluating the patency of composite graft

Table 1. The medians and interquartile ranges (lower and upper quartiles) of the variables analyzed during the standardization and validation phases by type of graft used.

	Control Group				
	Simple graft (n=20)		Composite graft (n=20)		
Variables	Median	Interquartile range	Median	Interquartile range	Statistical significance
DPV/SPV	0.64	0.45 – 0.69	0.87	0.69 – 1.05	*P<0.0001***
DVTI (m)	0.06	0.04 – 0.08	0.12	0.09 – 0.16	*P<0.0001***

	Study Group	
Variables	Composite graft (n=159)	
	Median	Interquartile range
DPV/SPV	0.64	0.45 – 0.69
DVTI (m)	0.08	0.06 – 0.10

DPV/SPV = Peak diastolic velocity/peak systolic velocity; DVTI = Diastolic velocity integral

Table 2. Detecting composite graft patency (present or absent) using DPV/SPV, with DF as the gold standard. Data obtained from 38 patients.

	Patency – DF (gold standard)		
Patency – DPV/SPV	DF ≥ 0.5 (present)	DF < 0.5 (absent)	Total
DPV/SPV ≥ 0.71 (present)	True-positives 59	False-positives —	59
DPV/SPV< 0.71 (absent)	False-negatives 89	True-negatives 11	100
Total	148	11	159

DPV/SPV = Peak diastolic velocity/peak systolic velocity; DF = Diastolic fraction

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Table 3 shows the same for the criterion DVTI ≥ 0.09m. The number of TP was 54: they had DVTI ≥ 0.09m and patency was confirmed. There were also eleven TN. 94 patients, out of a total of 159, were FN, meaning our criterion had detected as non-patent or non-composite graft but they had DF ≥ 0.05. There was no FP with our two criteria: no graft detected as patent composite graft had DF lower than 0.05.

In Table 4, we can see the percentages of sensitivity, specificity, positive and negative predictive values calculated for our patency criteria of the composite grafts, all of them with confidence interval of 95%. For both criteria, DPV/SPV ≥ 0.71 and DVTI ≥ 0.09m, the specificity and positive predictive value were 100%.

DISCUSSION

The prognosis of the CABG patients depends on demonstration of an efficient by pass function. This study is one of

the first contributions to finding criteria to establish patency of composite graft of LITA and SMV revascularizing LAD and another branch of the LCS, using TDE at rest; a totally noninvasive diagnostic method which is part of the routine clinical practice [17].

It is important to mention that all patients in the control group had their graft patency confirmed by CA. This is meaningful because it corroborates the efficiency of the criteria we applied in the study group. In the study group phase, an actual practical application of these criteria occurred in a considerable sample of 159 patients with composite graft. This sample is consistent with the reality of the routine follow-up of CABG patients. This evaluation is not easy because these patients can present atypical symptoms and nonspecific, or even inconclusive, changes in some exams, such as exercise stress test for example.

There are controversies regarding some variables measured by Doppler, but the integral of the mean velocity/time (VTI) is well accepted as an indicator of patency [6-13].

Table 3. Detecting composite graft patency (present or absent) using DVTI, with DF as the gold standard. Data obtained from 38 patients.

| Patency – DVTI | Patency – DF (gold standard) | | Total |
	DF ≥ 0.5 (present)	DF < 0.5 (absent)	
DVTI ≥ 0.09 m (present)	True-positives 54	False-positives —	54
DVTI< 0.09 m (absent)	False-negatives 94	True-negatives 11	105
Total	148	11	159

DVTI = Diastolic average velocity-time integral; DF = Diastolic velocity integral

Table 4. Validation criteria for using DPV/SPV to detect composite graft patency, with DF as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the associated 95% confidence intervals were calculated.

DPV/SPV			
Parameter	Value	95% confidence interval	Significance
Sensitivity	0.3986 (39.86%)	0.3192 to 0.4823	
Specificity	1.0000 (100.00%)	0.7151 to 1.0000	
PPV	1.0000 (100.00%)	0.9394 to 1.0000	
NPV	0.1100 (11.00%)	0.0562 to 0.1883	
DVTI			
Parameter	Value	95% confidence interval	Significance
Sensitivity	0.3649 (36.49%)	0.2874 to 0.4479	
Specificity	1.0000 (100.00%)	0.7151 to 1.0000	
PPV	1.0000 (100.00%)	0.9340 to 1.0000	
NPV	0.1048 (10.48%)	0.0535 to 0.1797	

DPV/SPV = Peak diastolic velocity/peak systolic velocity; DVTI = Diastolic velocity integral; PPV = Positive Predictive Value; NPV = Negative Predictive Value

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The VTI is calculated by using the mean velocity, mapping the Doppler spectral curve point to point rather than at punctual time. That's why it quantifies the flow with more reliability than the peak velocity. It's simple and reproducible.

Peak velocity is affected by the intravascular resistance and pressure and is a measure of the maximum velocity at one moment during systole or diastole. Even so, Shimizu et al. [18] and Dubey et al. [19] have shown that the graft diameter, its degree of obstruction, and its flow, are proportional to DPV [20]. A DPV/SPV ratio greater than 1 [21] is associated with good angiographic findings and can provide sensitivity up to 100% and a specificity of 58% for detecting graft patency [12].

The DF expresses how much the diastolic flow represents in relation to the total (systolic plus diastolic) flow and it can be calculated using VTI (m) or the blood flow (ml/min). When VTI is used, the diastolic VTI fraction is obtained by dividing the DVTI by the sum of the VTI in systole plus VTI in diastole. When blood flow is used, the diastolic fraction is the diastolic blood flow divided by the sum of diastolic and systolic blood flow. Blood flow is obtained from the product of three variables: VTI, cross-sectional vessel area, and heart rate. For this reason, blood flow is more susceptible to interoperator variations and to the status of the patient at the time of the exam. The diastolic fraction calculated using the velocity integral has shown a good correlation with cardiac catheterization results. A DF value lower than 0.5 is predictive of graft stenosis [16,22].

The specificity of the two criteria evaluated in this study was 100%, meaning that all of the composite grafts that were not patent were correctly classified by the cutoff points. Thus, DPV/SPV and DVTI values greater than or equal to the cutoffs were a strong indicators of composite graft patency. Despite the 100% specificity, the possibility of false-positives cannot be ruled out. During the surgical report collection phase, it was observed that some single grafts had a surprisingly high diastolic flow to LAD at rest. In these cases, patients even with obstruction of the SMV graft to the other LCS branch would meet the patency criteria for patent composite grafts established in this study.

A large number of patients did not meet our criteria for patency of the composite graft, but they had DF ≥ 0.5; the FN. LITA flow was suggestive of obstruction at rest. Several factors can affect the LITA graft flow and may explain these data. One of the grafts in the configuration of the composite graft could be obstructed; however, what we could observe more frequently was the latent flow. The latency of the flow when there is no obstruction in the graft but rather a reduced demand is described in the literature. Understanding flow competition is extremely important to grasp the complex anatomy and pathophysiology of coronary flow. LAD flow competition is associated with a reduction in LITA diastolic velocity. Invasive studies have shown that residual flow in the recipient artery, when the obstruction is not severe, can compete with the flow of the patent LITA, thereby reducing blood flow in the graft. In addition, collateral circulation resulting from the total obstruction of a vessel, also called a physiological bridge, can lead to flow competition within the LITA bypass [18]. As the coronary disease progress es in the native or collaterals, the flow of the graft increases considerably. It is described in the literature and we can notice it in everyday practice. LITA has the ability to restore its patency after apparent occlusion in the progression of the coronary disease. Other conditions can influence LITA flow, including severe dysfunction of the left ventricle [6], coronary microcirculation disease, hypertrophy, fibrosis and myocardial viability [24,25]. TDE at stress can be very helpful in these situations and it can avoid a more invasive test [23]. The increased demand will enhance the velocity of the graft flow and confirm that it was a false negative and the graft is patent. The realization that there is graft malfunction with TDE can't be done unless the graft flow has been previously registered and its patency established.

There was a sensitivity of 39.86% for DPV/SPV and 36.49% for DVTI. One may think that the detection rate is low, yet as sensitivity represents the ability to identify patent composite grafts among those that are truly patent, it is not a low rate. It is even audacious if in 40% of CABG patients with composite grafts coming for an echocardiogram with three more minutes we are able to affirm that their grafts are patent. Moreover, TDE is not expensive and totally noninvasive. It can be repeated frequently in routine or forward to a change in clinical status, providing the possibility of comparison of data during follow ups. Actually, it is much more important to compare previous Doppler measurements in a given patient than isolated ones.

Final considerations

Studying resting coronary graft flow with Doppler echocardiography in a completely noninvasive manner is challenging. The coronary vessel pattern is similar to a fingerprint and then, there are unlimited normal anatomical variations. Coronary heart disease involves a large number of other pathophysiological conditions that can affect the flow through the coronary arteries and their grafts. Similar to other exams, Transthoracic Doppler echocardiography requires accurate interpretation, and the multifactorial context must be considered.

It is significant that Transthoracic Doppler echocardiography at rest can be performed at any time deemed necessary to evaluate bypass patients because of its noninvasive nature. Additionally, this technique compares the current and previous values rather than obtaining an absolute value from a single observation [16]. When reduction in these patency criteria is observed, it is possible that part of the composite graft is obstructed. A stress TDE is suggested to measure the coronary

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flow reserve and notice its potential increase. Values equal or greater than the cutoffs are probably indicators of composite graft patency. These cases do not require additional testing beyond the resting TDE, although the medical decision making always depends on the clinical setting. One of the mains contributions of this study is briefly illustrated in Figure 3.
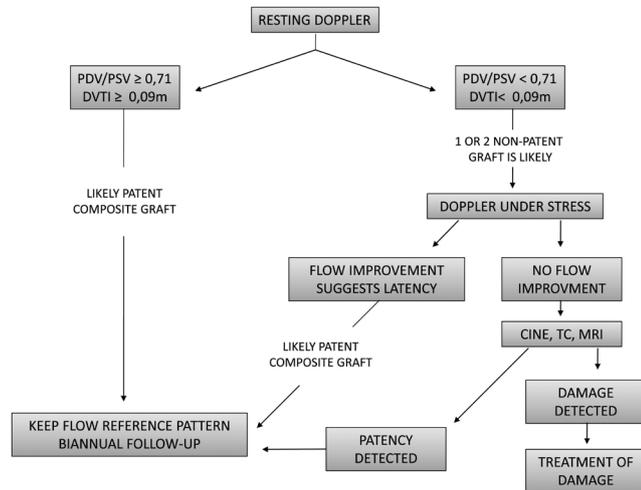

Fig. 3 – Follow-up algorithm for bypass patients with composite LITA grafts that are grafted to the LAD and another LCS branch (1100% specificity for both, 39.86% sensitivity for DPV/SPV, 36.49% sensitivity for DVTI, 100% PPV for both, 11% NPV for DPV/SPV, and 10.48% NPV for DVTI)

Study and technique limitations

The Doppler imaging may not have visualized the LITA for anatomical or operator-dependent reasons. The anatomical reasons include unfavorable configurations of the rib cage, the position and diameters of the LITA graft, and the mobility of the heart [6-22]. The overlap of vessels in the supraclavicular block may also have impaired the visualization of LITA.

In the quantitative evaluation of the graft flow, the LITA diameter was considered to be equal during systole and diastole because of the technical difficulty in measuring this difference.

This study did not obtain data on comorbidities, the medications used by the patients, previous coronary anatomy, or the segmental and overall myocardial contractility, all of which are factors that can affect LITA flow.

CONCLUSION

Values equal or greater than those established by the criteria DPV/SPV ≥ 0.71 and DVTI ≥ 0.09m suggest high probability of patency of the composite graft. Lowers values present a large number of false negatives, not being conclusive to patency and needing further evaluation.

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