Fractional flow reserve of pedicled internal thoracic artery and saphenous vein grafts 6 months after bypass surgery

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Abstract

Background: Although the internal thoracic artery was proven superior to saphenous vein graft in long-term patency, it is thought to be a more resistive conduit than the vein graft. Moreover, patency studies comparing both left and right internal thoracic arteries have provided results favoring the former. Fractional flow reserve is an established functional index of coronary blood flow. Methods: To compare the fractional flow reserve between both internal thoracic arteries and saphenous vein grafts, 43 bypass grafts were studied 6 months after revascularization. Intra-graft pressures were measured during cardiac catheterization using a pressure-wire advanced to the first distal anastomosis of 12 left internal thoracic arteries (ITAs), 10 right ITAs and of 21 vein grafts. Pressure gradients between the aorta and the graft were measured at baseline and during a maximal hyperemia. Results: At baseline, pressure gradient was recorded in the left ITA (2.9 ± 2.2 mmHg), in the right ITA (1.2 ± 1.2 mmHg) and in the vein graft (0.4 ± 0.7 mmHg). During maximal hyperemia, pressure gradient increased to 9.6 ± 3.2 mmHg in left ITA, to 4.5 ± 2.0 mmHg in the right ITA (p < 0.001 vs left ITA) and to 3.3 ± 2.7 mmHg in vein (p < 0.001 vs left ITA; NS vs right ITA). Fractional flow reserve was 0.90 ± 0.04 in left ITA, 0.95 ± 0.03 in right ITA (p < 0.01 vs left ITA) and 0.96 ± 0.03 in vein (p < 0.001 vs left ITA). Conclusion: Internal thoracic arteries and saphenous vein grafts allow myocardial revascularization with minimal resistance to maximal blood flow. The resistance appears significantly higher in left ITA compared to both the right ITA and venous grafts.

1. Introduction

The superiority of the internal thoracic artery (ITA) over the saphenous vein (SV) coronary graft has been demonstrated by several clinical and angiographic follow-up studies [1–3]. Consequently, the use of this arterial conduit is considered an essential part of bypass surgery, particularly when the left anterior descending (LAD) coronary artery is involved. The superiority of the ITA is thought to result from favorable biological properties protecting this vessel against the atherosclerotic process, possibly due to a more effective release of nitric oxide and prostacyclin from endothelial cells [4,5].

Left ITA is most commonly grafted on the LAD whereas the right ITA is preferred for the marginal branches, either used pedicled or used within a Y-graft configuration. The long-term patency of the left ITA has always been found superior to that of the right ITA, even when implanted on the LAD [6,7]. Since the two ITA’s are supposed to be identical in terms of anatomy and physiology, this difference has been mainly explained by differences in the quality of the run off of the targeted vessel [8].

The concept of pressure-derived fractional flow reserve (FFR), calculated as the ratio of distal coronary pressure (Pd) divided by aortic pressure (Pa) during maximal hyperemia (FFR = Pd/Pa) [9], has been developed to assess the physiological significance of coronary stenosis [10]. The larger the resistance to blood flow, the larger is the decline in pressure and the smaller FFR value. In the absence of resistance along a coronary vessel or by analogy, along a graft conduit, there is no pressure decline and FFR equals one.
Previous studies have shown that a FFR value <0.75 discriminates functionally significant coronary lesions susceptible to justify revascularization.

The present study was designed to evaluate more specifically the difference of resistance between both ITA and venous grafts, assuming that venous grafts are the reference conduits that offers the lowest resistance to blood flow. For that purpose, the pressure drop across these different type of grafts was measured in basal conditions and during maximal hyperemia induced by a bolus injection of adenosine. From pressure measurements, the FFR, calculated as the ratio of distal intragraft pressure divided by ostial graft pressure, was determined as an index of the resistance along the grafts.

2. Methods

2.1. Patients

Twenty-three consecutive patients (20 men, 3 women) were studied during cardiac catheterization. All had undergone coronary artery bypass surgery for chronic stable angina >6 months (range 6—8 months) before the study and had been enrolled in a prospective study consisting in a systematic angiographic and functional follow-up evaluation. At time of evaluation, patients were asymptomatic and did not show evidence of myocardial ischemia during maximal exercise testing.

In each patient, one or several grafts were selected for the study based on the characteristics of the graft and on the selectivity of the ostial cannulation by the angiographic catheter in order to allow a safe progression of the pressure wire within the graft. Criteria for inclusion were as follow: (a) the absence of major tortuosities of the graft, (b) perfect patency of all anastomoses with a good run off flow to the grafted arterial segments and (c) absence of severe wall motion abnormality in the reperfused area of myocardium.

The study protocol was approved by the Ethics Committee of our institution. All patients gave informed consent at the time of bypass surgery and before the angiographic investigations.

2.2. Study protocol

Patients underwent cardiac catheterization by a standard femoral approach 24 h after discontinuation of all vasoactive medications. Selective catheterization of the ostium of both ITAs or SV was achieved by using 5F guiding catheters without side holes. This catheter was connected to a fluid-filled pressure transducer zeroed at mid-chest level. After intragraft administration of 1 mg of isosorbide dinitrate, a biplane angiogram of the graft was obtained. A 0.014-in. electronic sensor tipped wire (PressureWire 5, Radi Medical Systems, Uppsala, Sweden) was advanced to the tip of the guiding catheter to ensure that the pressures recorded in the ostium of the graft through the fluid-filled catheter and the pressure wire were identical. The wire was then advanced in the distal part of the graft, the pressure sensor being carefully positioned within the last centimeter before the first distal anastomosis on the coronary vessel. The pressures were simultaneously measured at baseline, in the ostium of the graft through the fluid-filled catheter and in the distal part of the graft using the electronic pressure sensor. Coronary arteriolar vasodilation was then induced by a bolus of 40 μg of adenosine inside the graft to produce a transient maximal hyperemia. Pressure signals were recorded continuously until distal pressure returned to baseline values. An example of pressure recording is illustrated in Fig. 1. When the pressure sensor was pulled back in the guiding catheter, pressures were checked again to exclude any drift of the transducers.

2.3. Angiographic and pressure data analysis

Graft and coronary angiograms were reviewed by two independent investigators and encoded for the coronary territory, the number of distal anastomoses, the number of major coronary branches opacified by each graft and the quality of the run off. Three categories of run off were determined by consensus (Table 1). Angiograms were quantitatively analyzed using the CAAS II system (Pie Medical, Maastricht, The Netherlands) as previously described [5].

Pressures recorded at different measurement points are compared in basal condition and during maximal hyperemia. The difference in mean intra-graft pressure between the ostium and the distal part of each graft are expressed in absolute values. From pressure measurements obtained during maximal hyperemia, FFR is computed as an index of resistance to blood flow of the different types of grafts. In the absence of resistance along a vascular segment, there is no pressure decline and FFR equals one. The larger the resistance to blood flow of a graft segment, the greater the drop in perfusion pressure across this segment and thus the smaller FFR.

Fig. 1. Pressure recording (phasic pressure signal and mean values) in the ostium (Pa) and in the distal part of a saphenous vein graft (Pd) after intragraft injection of 40 μg of adenosine. A transient decrease in distal perfusion pressure results from the adenosine-induced coronary arteriolar vasodilation resulting in a maximal pressure drop of 3 mmHg across the graft. This gradient reflects the resistance opposed by the graft to maximal blood flow, corresponding to a FFR of 0.96.
FFR was considered in relation with the following variables: type of the graft (SV or right ITA or left ITA), revascularized coronary vascular bed, number of distal anastomoses per graft, quality of the run off, number of major coronary branches opacified per graft, severity of the stenosis of the grafted vessel, luminal diameter of the graft, of the coronary artery immediately distal to the graft and minimal luminal diameter of the anastomosis (Table 2).

2.4. Statistical analysis

Data are expressed as mean ± SD. Pressure drops across various types of grafts before and after adenosine injection were compared using paired Student’s t-test. Differences in pressure gradients between different types of grafts were assessed using unpaired Student’s t-test. In bivariate analyses, the association of independent variables with each outcome was tested with Student’s t-test for independent samples (binary variables) or nonparametric Spearman correlation (ordinal and continuous variables). A multiple linear regression model was then build with a stepwise approach (p in < 0.05 and p out < 0.10), to obtain a parsimonious, clinically sound model. Since the distribution of outcome variables was skewed, logarithmic transformation was also used. No change occurred in the regression model when transformed variables were used. All p-values are two-tailed.

The SPSS software (release 11.5) was used in the statistical analysis.

3. Results

Forty-three grafts were evaluated in 23 patients. Twelve left ITA were implanted on the LAD system (mean: 1.3 ± 0.5 anastomoses per graft), 10 right ITA were implanted on the left circumflex (LCX) system (mean: 1.2 ± 0.3 anastomoses per graft) and 21 SV were implanted on the LAD in two cases, the LCX in nine cases and the right coronary artery (RCA) in 10 cases with a mean of 1.3 ± 0.6 anastomoses per graft.

In basal conditions, a small pressure gradient between the ostium and the distal part of the graft was recorded in four SV (28%), in six right ITA (60%) and 10 left ITA (83%) (Fig. 2). The pressure gradient through the grafts averaged 2.9 ± 2.2 mmHg for left ITA, 1.2 ± 1.2 mmHg for right ITA (p < 0.05 vs left ITA) and 0.4 ± 0.7 mmHg (p < 0.005 vs left ITA; NS vs right ITA) for SV. Adenosine injection resulted in a consistent increase in pressure drop, the maximal pressure gradient during maximal adenosine-induced hyperemia being higher for left ITA (9.6 ± 3.2 mmHg) than for both right ITA (4.5 ± 2.0 mmHg; p < 0.001 vs left ITA) and SV (3.3 ± 2.7 mmHg; p < 0.001 vs left ITA and NS vs right ITA) (Fig. 3).

FFR averaged 0.90 ± 0.04 in left ITA, reflecting a minimal resistance to flow during maximal hyperemia. Mean values of FFR were significantly higher in right ITA (0.95 ± 0.03; p < 0.01 vs left ITA) and in SV (0.96 ± 0.03; p < 0.001 vs left ITA and NS vs right ITA). All individual values were superior to 0.75 in every type of graft.

In univariate analyses, maximal pressure gradient was significantly correlated with the variables: left ITA graft, LAD territory, LCX territory with a positive relationship and with the variables: run off and SV graft with a negative relationship (Table 3). Similarly FFR was significantly correlated with...
the variables: left ITA graft, LAD territory, LCX territory with a negative relationship and with the variables: run off and SV graft with a positive relationship (Table 3).

In multivariate analysis, after inclusion of the variable ‘left ITA versus other graft’, which was the main predictor of both maximal pressure gradient and FFR, no significant correlation remained between neither maximal pressure gradient nor FFR and any other variables.

4. Discussion

The efficacy of a coronary graft is related to its capacity to supply blood flow to the myocardium while opposing only minimal resistance. This translates in a distal perfusion pressure as close as possible to the aortic blood pressure, even during periods of maximal blood flow demand. The pressure drop across a graft in a given configuration is affected by the anatomic and physiologic characteristics of the conduit but also by the importance of the revascularized myocardial territory.

In the present study, we evaluated the resistances of different graft configurations by measuring the pressure drop during maximal hyperemia and the pressure-derived FFR. In coronary arteries without focal stenosis at angiography, De Bruyne et al. [9] reported FFR values of 0.97 in patients without atherosclerosis and 0.89 in patients with a remote focal angiographic stenosis. We recently reported a FFR of 0.91 in arterial Y-grafts revascularizing the whole left coronary system in a 6-months follow-up study after bypass surgery [11]. The values of FFR observed in left ITA in the present study are close to those previously reported in these Y-graft configurations. As it was the case in our previous study, FFR was superior to 0.75, the cutoff for inducible ischemia in all individual cases.

The main message of the present study is that the resistance of the left ITA appears significantly higher than that of the right ITA or of the SV. This is reflected by a smaller FFR and by a higher drop in perfusion pressure through the left ITA than through the right ITA or a SV graft during...
maximal hyperemia. Several factors could contribute to this finding. First, the territory of the LAD on which the left ITA is preferentially implanted is likely to require a larger blood flow supply than that of the other territories for which SV or right ITA are more often used. Second, differences in the three-dimensional configuration of various types of grafts could affect the transmission of the pressure wave; curvatures of the proximal left ITA could result in some damping of the pressure waveform that could explain a resistance to phasic pulsatile flow superior to that of the right ITA whose configuration is more rectilinear because of its anatomic course into the tranverse sinus. Third, differences in length and lumen diameter of graft conduits are parameters directly affecting their resistance to flow.

The relative contribution of these factors cannot be directly extrapolated from our data since clinical practice has associated specific graft conduits with specific territories with different anatomic and physiologic characteristics. In our institution, SV grafts and right ITA are preferentially used for distal RCA and LCX territories respectively. Conversely, given the well demonstrated superiority of the left ITA over SV grafts in long-term patency and its impact on survival [1–3], the left ITA is the conduit of choice for the left anterior descending territory. This preferential association of one type of graft with one coronary vascular bed precludes any definitive conclusion about the influence of the conduit or the reperfused territory. Although left ITA was the variable most strongly associated with pressure drop during hyperemia and a lower FFR, the higher resistance of left ITA demonstrated in the present study must be interpreted only considering its preferential use for the LAD territory. However, although the preferential use of either ITA or SV grafts to revascularize different territories may be viewed as a theoretical limitation of our study, only the type of graft — left ITA versus other grafts — significantly predicted FFR and pressure drop when all parameters were considered in the multivariate analysis.

Since all individual values of FFR were higher than 0.75, the resistance of the left ITA graft appears low enough to allow an adequate reperfusion of the LAD territory in all cases. The small differences in resistance between grafts are thus unlikely to have clinical consequences on the capacity of these grafts to prevent ischemia. They could however reflect differences in the adaptive mechanisms to chronic changes in blood flow. The pressure drop across a vessel is the direct consequence of the interaction between the blood flow and the vessel wall. Frictional forces on the endothelial surface created by flowing blood contribute to dissipate the mechanical driving force; they also stimulate biological adaptive mechanism controlling vasomotion and vessel remodeling. Nitric oxide and prostacyclin are released from endothelial cells in response to shear stress; these vasodilator agents contribute to flow-mediated vasodilation but are also known to inhibit platelet adhesion and aggregation which are key factors in atherothrombosis. In addition, chronic flow increase induce a remodeling of the vessel resulting in an anatomical enlargement of the lumen. Both flow-mediated vasodilation and chronic vessel remodeling are dependent on the integrity of the endothelium and contribute to normalize longitudinal shear stress [12–15].

When compared to other types of grafts, the higher-pressure drop through the left ITA reflects larger interactions between flow and vessel wall and larger frictional forces likely to induce a more effective release of endothelial factors. A more effective stimulation of these endothelial mechanisms in left ITA graft, as a combined result of superior endothelial cell function and favorable hemodynamic conditions, could contribute to the better long-term results of this conduit over the right ITA in coronary bypass surgery.

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References

Functional assessment of bypass grafts by fractional flow reserve

In an interesting paper published in the present issue of the journal, Glineur et al. describe systematic measurements of fractional flow reserve in coronary bypass grafts [1]. These data are important because they tell us more about the function of normal grafts both at rest and during maximum hyperemia, corresponding with physiologic exercise in true life.

Fractional flow reserve (FFR) is the gold standard for functional assessment of coronary arteries. It is an index which is exclusively calculated during maximum coronary and myocardial hyperemia and expresses maximum achievable blood flow in a particular conduit (native or graft) as a fraction of normal maximum blood flow to the same myocardial territory in case the patient would be completely healthy [2,3].

FFR can be easily calculated during cardiac catheterization by the ratio of distal coronary pressure (or distal bypass graft pressure) compared to aortic pressure after administration of a sufficient hyperemic stimulus, mostly adenosine.

In normal coronary arteries, fractional flow reserve equals 1.0 even under conditions of maximum hyperemia [4]. This indicates that resistance in a normal coronary artery is negligible. A value of FFR < 0.75 indicates inducible ischemia with a specificity and sensitivity of more than 90% [2,3]. In the last 10 years, FFR has been validated repeatedly in many physiologic and pathologic conditions.

In fact, FFR can also be considered as an inverse measure of resistance of a particular conduit. If there is no resistance at all along the conduit, the pressure distal in the conduit and proximal in the conduit should be equal, even at maximum blood flow. With increasing resistance, decline of pressure will be more pronounced.

Until recently, only few data have been available for FFR in bypasses. It has been suggested that resistance in a mammalian artery graft (ITA) would be higher than in saphenous venous grafts. In earlier studies, it has even been suggested that resistance in an ITA graft would be so high that myocardial ischemia could result, especially shortly after the operation before hyperplasia has occurred and especially in case of a large myocardial territory depending on the graft.

The present study by Glineur does not allow us to assess this latter point quantitatively but at least it enables us to establish the functional capacity of bypass grafts 6 months after surgery [1]. The authors show that even in a mammalian bypass graft, often long and sometimes tortuous, and even if placed on a normal viable anterior wall representing a large perfusion territory, the resistance to blood flow is small (although not negligible) under maximum hyperemic conditions. A value of fractional flow reserve of 0.90 ± 0.04 for the left ITA and 0.95 ± 0.03 for the right ITA indicates that, although mild resistance is present, the function of such a graft is far above the threshold at which myocardial ischemia might occur.

Glineur et al. [1] also show that a normal venous bypass graft has a resistance, which is completely negligible (FFR = 0.96 ± 0.03) and therefore is comparable in this respect to a normal coronary artery.

A strong issue in their paper is the fact that the study was not performed in patients with complaints but in well functioning patients with angiographically normal grafts. So, it can be presumed that these data are truly representative for normal bypass grafts.

A minor point of criticism is that it would have been better to use intravenous adenosine as hyperemic stimulus in their study, allowing a pressure pull-back recording which could show that the minimal decline of pressure along the course of the ITA graft was uniformly distributed along that graft.

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