Comparison of the Rheologic Parameters in Left Internal Thoracic Artery Grafts With Those in Saphenous Vein Grafts

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Background Left internal thoracic artery (LITA) grafts have superior patency to saphenous vein grafts (SVG). Because shear stress augments the release of nitric oxide throughout the LITA endothelium, shear stress and shear rate in coronary artery bypass grafts (CABG) may play an important role in the higher patency, so the aim of the present study was to evaluate and compare the rheologic parameters in CABG using LITA and SVG.

Methods and Results Rheologic examinations were done in 197 patients using a vacuum-suction glass tube viscometer after CABG surgery was completed. Shear stress and shear rate were calculated from the geometry of the graft, blood flow in the graft and blood viscosity. Of 197 patients, 177 underwent LITA grafting to the left anterior descending artery (LAD) and 160 had SVG anastomosis to coronary arteries. Mean wall shear stress in the LITA grafts to the LAD (13.8±1.0 dyne/cm²) was nearly 4–6-fold larger than that in the SVG grafts. Mean shear rate (559.1±57.0 s⁻¹) of LITA–LAD grafts was approximately 2–3-fold higher than that of SVG.

Conclusion These results suggest that high wall shear stress and shear rate play an important role in the higher patency rate of LITA grafts. (Circ J 2005; 69: 700–706)

Key Words: Coronary artery bypass grafting; Left internal thoracic artery graft; Saphenous vein graft; Shear rate; Wall shear stress

Methods

Study Population
From December 1995 to March 1999, 197 patients with coronary artery disease (151 males, 46 females) underwent elective CABG surgery after autologous blood storage. Blood viscosity, plasma viscosity and hematocrit were determined in all patients immediately after the operation was completed. Mean age (± SD) of the patients was 66±8 years. Mean blood viscosity (µB), mean plasma viscosity and mean hematocrit were 2.12±0.41 mPa.s, 1.26±0.14 mPa.s and 25.7±5.7%, respectively. Patients with associated congenital heart disease, valvular disease, and complications secondary to myocardial infarction were excluded (Table 1).

The CABG surgery used 431 grafts in the 197 consecutive patients using LITA and SVG.

Table 1 Patient Characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>197 (151 men, 46 women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66±8</td>
</tr>
<tr>
<td>Total no. of grafts</td>
<td>431 grafts</td>
</tr>
<tr>
<td>1 graft 44 patients</td>
<td>44 grafts</td>
</tr>
<tr>
<td>2 grafts 85 patients</td>
<td>170 grafts</td>
</tr>
<tr>
<td>3 grafts 55 patients</td>
<td>165 grafts</td>
</tr>
<tr>
<td>4 grafts 13 patients</td>
<td>52 grafts</td>
</tr>
<tr>
<td>LITA-LAD</td>
<td>179 grafts</td>
</tr>
<tr>
<td>SVG-LAD</td>
<td>10 grafts</td>
</tr>
<tr>
<td>SVG-Diag</td>
<td>52 grafts</td>
</tr>
<tr>
<td>SVG-OM</td>
<td>79 grafts</td>
</tr>
<tr>
<td>SVG-RCA</td>
<td>26 grafts</td>
</tr>
<tr>
<td>SVG-PD</td>
<td>45 grafts</td>
</tr>
<tr>
<td>SVG-PL</td>
<td>40 grafts</td>
</tr>
</tbody>
</table>

LITA, left internal thoracic artery; SVG, saphenous vein graft; LAD, left anterior descending artery; Diag, diagonal branch; OM, obtuse marginal branch; RCA, right coronary artery; PD, posterior descending artery; PL, posterolateral branch.
Rheologic Parameters in LITA and SVG

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Rheologic Methods

When blood streams as a steady laminar flow in the coronary bypass graft (radius: \( \rho \), diameter: \( D \), blood velocity: \( u \)), then, supposing that there is a hypothetical blood stream column ABCD (radius: \( r \), length: \( L \), pressure gradient between A and B (length \( L \)): \( \Delta P \)) in the blood flow of the coronary bypass graft, the shear stress \( \tau \) toward the reversed direction of blood flow acts parallel according to the law of rheologic mechanics. Wall shear stress \( \tau_w \) is shown as \( \tau_w = \frac{\Delta P D}{4L} \) from the equilibrium of the forces working on every side of the column ABCD (Fig 1).

\[ \tau_w = \frac{\Delta P D}{4L} \]

Wall shear stress and shear rate were calculated using equation (3) and (4) respectively.

Statistical Analysis

All parameters of blood rheology, geometry and hemodynamics in the coronary bypass grafts are expressed as mean±SEM. Comparisons among the rheologic parameters were made by analysis of variance (ANOVA) with more than 3 parameters and the t-test with 2 parameters. Statistical significance was set at \( p<0.05 \).

Results

Geometric Parameters

The mean diameter (D) of the LITA grafts was 0.23±0.02 cm, compared with that of SVGs of 0.44±0.01 cm in the diagonal branch, 0.43±0.01 cm in the OM, 0.44±0.01 cm in the RCA, 0.44±0.01 cm in the PD, 0.43±0.01 cm in the PL, and 0.45±0.02 cm in the LAD. The diameter of the SVGs to each branch in each patient was almost the same, because autogenous SVs were used as the grafts in each patient. The mean diameter of the SVGs was approximately twice that of the LITA grafts and
statistical analysis showed that the mean diameter of the LITA grafts was significantly less than that of the SVGs (Fig 2A, Table 2).

The average cross-sectional area (A) of the LITA grafts was 0.043±0.001 cm², compared with that of SVGs of 0.015±0.001 cm² in the diagonal branch, 0.014±0.001 cm² in the OM, 0.015±0.001 cm² in the RCA, and 0.016±0.001 cm² in the LAD. Therefore, the average cross-sectional area of the SVGs was approximately 3–4-fold greater than that of the LITA grafts (ie, the mean cross-sectional area of the LITA grafts was significantly smaller than that of the SVGs to each branch of the coronary artery. The mean cross-sectional area of the SVGs is nearly 3–4-fold bigger than that of the LITA grafts. (C) Mean blood flow in the LITA grafts is much less than that in the SVGs to each branch of the coronary artery. The highest flow of all the bypass grafts is in SVGs to the LAD and the lowest is in the LITA grafts to the LAD. LITA, left internal thoracic artery; SVG, saphenous vein graft; LAD, left anterior descending artery; Diag, diagonal branch; OM, obtuse marginal branch; RCA, right coronary artery; PD, posterior descending artery; PL, posterior lateral branch.
A. Wall Shear Stress in Coronary Bypass Grafts

The mean blood flow in the LITA grafts was 34.4±1.6 ml/min, compared with that in the SVGs of 62.0±4.3 ml/min in the diagonal branch, 76.2±4.4 ml/min in the OM, 64.3±6.1 ml/min in the PL, 78.9±7.2 ml/min in the PD, 98.2±8.2 ml/min in the RCA, and 135.2±22.8 ml/min in the LAD. Mean blood flow in the SVGs to the LAD was approximately 4-fold greater than that in the LITA grafts to the LAD, and the mean blood flow in the SVGs to the RCA was approximately 3-fold greater than that in the LITA grafts. Moreover, the mean blood flow in the SVGs to the OM and PD was approximately 2-fold greater than that in the equivalent LITA grafts. Therefore, the mean blood flow in the SVGs was much greater than that in the LITA grafts (Fig 2C, Table 2).

B. Shear Rate in Coronary Bypass Grafts

The mean blood flow velocity in the LITA grafts to the LAD was 13.1±0.7 cm/s and that in the SVGs was 12.9±1.9 cm/s. The mean blood flow velocity in the SVGs to the diagonal branch was 7.3±0.6 cm/s, to the OM was 9.0±0.6 cm/s, to the RCA was 10.8±1.1 cm/s, to the PD was 10.0±1.4 cm/s, and to the PL was 10.0±1.1 cm/s. Of all the bypass grafts the mean blood flow velocity was highest in the SVGs to the diagonal branch.

Rheologic Parameters

The mean wall shear stress (\(\tau_w\)) in the LITA grafts to the LAD was 13.8±1.1 dyne/cm², compared with that in the SVGs of 3.7±0.6 dyne/cm² in the LAD, 2.1±0.6 dyne/cm² in the diagonal branch, 2.6±0.2 dyne/cm² in the OM, 3.4±0.4 dyne/cm² in the RCA, 2.9±0.8 dyne/cm² in the PD, and 2.1±0.3 dyne/cm² in the PL.

The mean wall shear stress in the LITA grafts was approximately 4–6-fold greater than that in all the SVGs and the greatest mean wall shear stress was in LITA grafts to the LAD, followed by SVGs to the LAD, and the least in SVGs to the diagonal branch or PL. The mean wall shear stress in LITA grafts was significantly greater than that in the SVGs (Fig 3A, Table 2).

The mean shear rate (\(\dot{\gamma}\)) of the blood flow in LITA–LAD grafts was nearly 2–3-fold greater than that in the SVGs and the highest mean shear rate was in LITA–LAD grafts (559.1±57.0 s⁻¹ in LITA–LAD grafts vs 244.9±42.7 s⁻¹ in SVGs to the LAD, 212.7±25.3 s⁻¹ in the RCA, 189.8±15.3 s⁻¹ in the OM, 169.2±23.6 s⁻¹ in the PL, 168.6±20.3 s⁻¹ in the PD, and 158.1±20.0 s⁻¹ in the diagonal branch). The highest mean shear rate of blood flow was in LITA–LAD grafts and the least was in SVG–diagonal branch. The mean shear rate of the blood flow in...
LITA–LAD grafts was significantly greater than that in SVGs (Fig 3B, Table 2).

**Early Graft Patenty of LITA and SVG**

In this study, the early graft patenty of LITA grafts and SVGs was 99% and 97%, respectively, estimated by angiography at 2–3 weeks after operation (not a statistically significant difference).

**Discussion**

A randomized controlled trial is the best method for testing the hypothesis that the use of an ITA as a bypass conduit to the LAD increases both the survival and patency rate above those of subjects who have had revascularization with vein grafts only, even in patients with multivessel disease. However, such a trial is very difficult to conduct in daily clinical practice. Therefore, it is necessary to conduct a major controlled study to collect the various data required in order to get accurate evidence regarding long-term graft patenty after CABG.

**Patency of ITA and SV Grafts**

The patency of SVGs is influenced by several variables related to surgery: the state of the grafted vein, the state of the coronary arteries for anastomosis, the surgical techniques, revascularization of the myocardium, the intraoperative graft flow and hemo-rheologic factors.

According to nonrandomized and retrospective studies, the cumulative patency of LITA grafts is much better, both at 1 year (ITA graft: 88.5% vs SVG: 76.4%) and 10 years (ITA: 84.1% vs SVG: 52.8%) after operation; and these results have been confirmed in postoperative angiographic studies. Grondin et al demonstrated that atheromatous changes were frequent in SVGs (43.9%) and uncommon in ITA grafts (5.2%); and on the serial arteriograms studied by Lytle et al in long-term (5–12 years) follow-up of ITA and SV grafts, the patency rates of the ITA grafts were much better than those of the SVGs at both 5 years (ITA: 97% vs SVG: 82%) and 12 years (ITA: 95% vs SVG: 55%).

**Survival Rate of ITA and SV Grafted Group**

Loop et al have reported that the 10-year survival rate was 86.6% in the ITA grafted group compared with 75.9% in the SVG group. Moreover, the 10-year survival rate of patients with 1-veessel disease was 93.4% in the ITA grafted group compared with 88.0% in the SVG group; that of patients with 2-veessel disease was 90.0% compared with 79.5%, respectively, and that of patients with 3-veessel disease was 82.6% vs 71.0%. These differences of survival between the 2 groups were statistically significant. According to a 20-year clinical follow-up study by Cameron et al, cumulative survival rates were 38% for SVGs, 50% for a single ITA graft and 63.5% for bilateral ITA grafts.

**Histological Differences Between SV and ITA Grafts**

Examination of the endothelium of the SV and ITA has confirmed the known susceptibility of the SV to endothelial cell loss during its preparation for grafting, in contrast to the minimal cell loss in the ITA. ITA endothelial cells are smaller and thicker, and have significantly more and deeper processes than those of the SVG. These morphological features are believed to play a role in endothelial attachment and may account for the differing susceptibility of the 2 vessels to endothelial damage during graft preparation.

**Alteration of the Grafted Vessels**

During an early phase after grafting there is a change in the grafted vessel in its response to both injuries and the new environment of pressure and rapid blood flow. The intima shows areas of endothelial sloughing, and leukocytes and fibrin can be seen on the denuded surface of the underlying basement membrane. Edema, focal hemorrhage, and smooth muscle cell necrosis occur in the media and the fragmented adventitia remains separated from the surrounding tissue bed. Early regeneration is common and the intimal luminal surface will undergo a fibrous transformation and a decrease in the relative number of smooth muscle cells within 6 weeks. Longer term evaluation of vein grafts demonstrates a variety of well-developed pathologic changes after more than 1 to 2 months. A characteristic proliferation of intimal hypertrophy is well recognized in aortocoronary vein grafts and has been termed arterialization. These changes are considered to be a response to the high intraluminal pressure and in severe cases may lead to graft occlusion. The fibrous nature of the proliferative process leads to the early designation of intimal fibrous proliferation. The luminal surface of the thickened layer becomes lined with endothelial cells, although the appearance of these cells is altered by the irregular underlying surface of hyperplastic tissue. The pathogenesis of the process is not fully understood, but it has been suggested that it is caused by the arterial pressure and shear stress, the concentration of serum lipids and immunological injury or the release of proliferating factors from blood particles.

**Relationship Between Endothelium-Derived NO and Graft Patenty**

There is clear evidence that an improved late clinical outcome correlates with the superior late patenty of ITA grafts when compared with that of SVGs. However, the mechanisms that account for the excellent patenty of ITA grafts are not fully understood. According to bioassays, endothelium-derived relaxing factor (EDRF) released by the ITA graft could be a factor because the EDRF induces vasodilation and also inhibits platelet adhesion, platelet aggregation, and atherogenesis. Chello et al demonstrated that less neutrophil adhesion to the endothelium of the ITA is a consequence of enhanced release of NO at this level and enhanced release of NO in the endothelium of ITA grafts could be responsible for the better early and long-term patenty of this conduit over SVG in CABG. Furthermore, the release of endothelium-derived NO and prostacycline from the endothelium into the lumen, particularly during hypoxemia, could promote vasodilation of distal coronary artery beds, enhancing myocardial perfusion.

Thus, endothelium-derived NO functions as an endogenous nitro-vasodilator and plays an important physiological role in the protection of blood vessels against vasospasm and thrombosis. Moreover, blood flow in an ITA graft early after operation is characterized by a higher velocity than that in a vein graft flow because of the smaller diameter of ITA graft and this high velocity maintains flow volume at baseline conditions.

**Relationship Between Endothelium-Derived NO and Wall Shear Stress**

Miller et al have demonstrated that chronically increased
shear stress in canine femoral arteries augments the release of endothelium-derived NO and increases blood flow. The endothelium is subject to a wide range of hemodynamically generated shear stress forces throughout the vascular system and endothelial cells change their morphology and biochemistry in response to laminar flow shear stress, varying the K⁺ selective, shear-stress-activated ionic current as a function of shear stress. Shear stress causes a Ca²⁺-mediated ATP-independent transient release of NO, thus regulating vascular tone. Thus, the effect of chronic fluid shear stress on the endothelial constitutive NO synthase (eNOS) concentration may be important in the control of vessel tone. Increased eNOS concentration as the endothelial response to prevailing blood flow may be the mechanism for chronic regulation of vessel diameter. Koller and Huang have documented that in the arterioles of the gracilis muscle of spontaneously hypertensive rats, the attenuated shear stress-induced dilatation seems to be caused by the lack of NO synthesis or release in response to shear stress.

**Relationship Between Wall Shear Stress, NO Production and Graft Patency in ITA and SV Grafts**

A relationship between wall shear stress and NO production has been reported in ITA and SV grafts; namely, increased shear stress augments the release of endothelium-dependent NO in both types of grafts. Others have also reported a relationship between NO production and graft patency, showing a significantly greater release of NO in ITA grafts than in RA grafts and an inferior mid-term patency rate for RA grafts, midway between those of ITA grafts and SVG, compared with ITA grafts. On the other hand, NO production has been shown to be identical in ITA and GEA grafts and the patency rate of GEA grafts is similar to that of ITA grafts. Because the histological and morphological features are identical in these 3 grafts (ITA, RA, GEA), we consider that graft patency is related to wall shear stress and subsequent release of NO.

**Study Limitation**

We measured the external diameter of the grafts to calculate wall shear stress and shear rate, but to be more accurate we should determine from the internal diameter because wall thickness will influence the result. However, it was difficult to measure the internal diameter of the midportion of the grafts during operation, so we substituted the external diameter.

**Conclusions**

Although the previous studies of shear stress-induced NO-dependent vascular dilatation are all in vitro and in vivo experimental studies, our present clinical data demonstrate that both shear stress and shear rate in LITA grafts are markedly increased compared with SVGs. These results suggest that the increased wall shear stress-induced endothelial-dependent dilatation of the LITA graft may play an important role in the superior long-term patency of the graft over that of SVGs.

**References**


