The right internal mammary artery and the great saphenous vein used for left anterior descending artery revascularization in patients whose left internal mammal artery cannot be used: a study based on transit-time flow measurement.

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left descending artery, transit-time flow measurement, internal mammal artery, great saphenous vein
Abstract

Background: Owing to the high patency, the use of the left internal mammary artery (LIMA) for left anterior descending artery (LAD) grafting has been a cornerstone of coronary artery bypass graft surgery (CABG). However, for some patients whose LIMA cannot be used, surgeons have to choose the other conduit materials to revascularize the LAD. The purpose of this study was to explore the difference of different conduit materials used for LAD in the parameters measured by transit-time flow measurement (TTFM) and the early graft patency detected by computed tomography angiography.

Methods: We retrospectively collected the data of 410 patients who undergoing isolated primary OPCAB with intraoperative TTFM data. According to the strategy of the left descending artery (LAD) revascularization, 410 patients were assigned to three groups: a left internal mammal artery (LIMA) group (n=333), a right IMA group (n=34) and a great saphenous vein (SVG) group (n=43). The baseline and perioperative blood parameters were compared for the three groups, as well as the early graft patency rates.

Results: Compared with the LIMA-LAD group, the SVG-LAD group had a significantly higher mean graft flow volume (37.15±23.29 vs 29.71±20.94 ml/min, P=0.036), however, a lower pulsatility index (2.07±0.62 vs 2.65±1.01, P=0.001). There was no significant difference between the two groups in DF (P=0.05). Compared with the RIMA-LAD group, the SVG-LAD group just had a lower pulsatility index (2.07±0.62 vs 2.56±0.96, P=0.029). However, there was no significant difference between the two groups in MGF and DF (P=0.05). Compared with the LIMA-LAD group, the RIMA-LAD group had a bit lower DF (70.76±11.87 vs 74.06±7.09, P=0.018), while there was no difference in MGF and PI between the two groups (P=0.05). The patency rate of the LIMA-LAD group was 98.72% (309/313), the RIMA-LAD group was 97.06% (33/34), and the SVG-LAD group was 100%. There was no difference among the three groups in patency rate (P=0.405).
Conclusions: We conclude that in patients whose LIMA cannot be used, the in-suit RIMA and the SVG are comparable and even better than the LIMA in the blood flow parameters measured by TTFM. In our study, the early patency before discharge of RIMA-LAD and SVG-LAD are comparable with the LIMA-LAD.

Background:
Coronary artery disease remains the most common cause of death worldwide, responsible for about one in every seven deaths[1]. Since Robert Goetz first performed and published the coronary artery bypass graft surgery in humans in 1961, now CABG has become an important revascularization methods of coronary heart disease[2]. Since the mid-1980s, owing to the high patency, the use of the left internal mammary artery (LIMA) for left anterior descending artery (LAD) grafting has been a cornerstone of CABG surgery[3]. However, owing to stenosis or occlusion of LIMA or harvested damage, surgeons have to choose the other conduit materials to revascularize the LAD. Transit-time flow measurement (TTFM) has been increasingly applied to judge the quality of anastomosis and blood flow during CABG, because TTFM is less invasive, more reproducible, and less time consuming[4]. The purpose of this study was to explore the difference of different conduit materials used for LAD in the parameters such as pulse index (PI), the mean graft flow (MGF) and diastolic flow fraction (DF) measured by TTFM.

Material And Methods:

Study population:
Data for isolated CABG were retrospectively collected from October 1, 2017 to October 31, 2019, from the Peking University People’s Hospital database. There were 629 patients who underwent CABGs; we excluded 10 who underwent redo surgeries, 55 who underwent concomitant additional procedures, 134 who underwent on-pump CABGs and 20 without
intro-operative TTFM data (Figure 1). We included 410 patients who undergoing isolated primary OPCAB with intro-operative TTFM data. According to the strategy of the LAD revascularization, 410 patients were assigned to three groups: a LIMA group (n=333), a RIMA group (n=34) and a great saphenous vein (SVG) group (n=43). As shown in Table 1, patients in the RIMA group were younger and were less likely to have a history with diabetes than the other two group. This study was approved by our institutional Review Board /Ethics Committee. Consent for individual use of data was waived because of the nature of the study and previous approval for the use of such data at the time of operative consent.

**Surgical methods**

All patients underwent OPCAB through a median full sternotomy. Heparin was given to reach an activated clotting time > 300s. The central temperature was maintained above 36°C. The pericardium was opened and suspended to expose the heart and the heart was displaced using a posterior pericardial stitch and gauze swabs. Patients lacking good presentation of the target arteries on the lateral and inferior aspect of the heart were placed in a gentle right decubitus Trendelenburg position to assist in visualization. Stabilization of the target coronary arteries was accomplished with a tissue stabilizer (Octopus, Medtronic Corporation, Minneapolis, MN). An intra-coronary shunt (Medtronic Corporation, Minneapolis, MN) was used during grafting in most operations. An Enclose (Novare Surgical Systems Inc., CA, USA) or even “no-touch” aorta technique was available when moderate to severe ascending aortic sclerosis or calcification was detected. In situ or free RIMA and SVG are used considering the patients’ age, state of cardiac function and the surgeons’ preference. The graft anastomosis was secured using a 7-0 or 8-0 polypropylene suture.

**Preoperative internal mammary artery ultrasonography examination**
Preoperative blood flow parameters of IMAs were measured by transthoracic doppler ultrasonography machine (APLIO500 TUS-A500, Probe: PLT-704SBT and PVT-712BT). All preoperative internal mammal artery ultrasonography was performed by the same senior ultrasonologist.

**Intraoperative transit time flow measurement**

The transit time flow of the grafts was measured by The VeriQ system TTFM device (MediStim Inc., Oslo, Norway), equipped with 2, 3 or 4-mm probes, depending on the size of the graft, under stable haemodynamic conditions without the support of a mechanical device such as cardiopulmonary bypass or an intra-aortic balloon pump. The parameter yielded by TTFM system including (i) the mean graft flow volume (MGF, ml/min), (ii) the PI, calculated as (maximum flow volume—minimum flow volume)/(mean flow volume) and (iii) the DF, calculated as (flow volume of the diastolic phase)/(flow volume of the systolic phase + flow volume of the diastolic phase). Satisfactory blood flow parameters criteria: 1, ACI ≥ 50%; 2, The shape of blood flow waveform is stable and repeatable; 3, PI ≤ 5 < MGF ≤ 15 ml/min. If sufficient graft flow was not obtained, graft revision was considered and performed until diastolic graft flow was confirmed.

**Postoperative management**

Postoperatively, aspirin, nitroglycerine and β-blocker were prescribed on postoperative day 1. The patients were routinely examined by cardiac CT scanning prior to discharge from the hospital unless they had grade 3 or more chronic kidney disease.

**Statistical Analysis**

The database was established by EpiDate3.1 software, the data were input twice in parallel. The final analysis database is formed after logical error checking and sorting of the input data and analysis and processing of outliers. Continuous variables were expressed as means ± SDs; if the data conformed to a normal distribution, the two groups
were compared using an independent samples t test, and multiple groups were compared using variance analysis. The least significant difference (LSD) was used for pairwise comparisons among those with intragroup differences. For nonnormally distributed data, Wilcoxon rank-sum tests were used for comparisons between two groups, and Kruskal-Wallis H tests were used for comparison between multiple groups. Categorical variables were described as percentages (rates); comparisons between two groups were performed using chi-square tests, and comparisons between multiple groups were performed using crosstabulation analysis. P<0.05 was considered statistically significant. All analyses were performed in SPSS version 23.

Results

As shown in Table 1, patients in the RIMA group were younger and were less likely to have a history with diabetes than the other two group. There was no difference in the other data.

The comparison of preoperative blood flow parameters between LIMA and RIMA

Compared with LIMA, the RIMA had a bit larger diameter (1.97±0.19 vs 1.96±0.17 mm, P=0.008), bigger mean graft flow volume (18.68±8.75 vs 16.48±7.13 ml/min, P<0.001), but a smaller pulsatility index (3.97±1.20 vs 4.13±1.36, P=0.002) (Table 2).

Compared with preoperative mean graft flow volume examined by ultrasonography, the intraoperative mean graft flow volume measured by TTFM of LIMA (29.71±20.94 vs 16.48±7.13 ml/min, P<0.001) and RIMA (29.03±22.73 vs 18.68±8.75, P=0.011) are both higher but the values of PI are both lower (P<0.001) (Table 2).

The comparison of blood flow parameters examined by TTFM of different conduit grafting used for LAD revascularization.

Compared with the IMAs-LAD group (LIMA-LAD+RIMA-LAD), the SVG-LAD group had a significantly higher mean graft flow volume (37.15±23.29 vs 29.65±21.08 ml/min,
P=0.033), however, a lower pulsatility index (2.07±0.62 vs 2.64±1.00, \(P<0.001\)). There was no significant difference between the two groups in DF (\(P>0.05\)) (Table 3).

Compared with the LIMA-LAD group separately, the SVG-LAD group also had a significantly higher mean graft flow volume (37.15±23.29 vs 29.71±20.94 ml/min, \(P=0.036\)), however, a lower pulsatility index (2.07±0.62 vs 2.65±1.01, \(P<0.001\)). There was no significant difference between the two groups in DF (\(P>0.05\)) (Table 3).

Compared with the RIMA-LAD group separately, the SVG-LAD group just had a lower pulsatility index (2.07±0.62 vs 2.56±0.96, \(P=0.029\)). However, there was no significant difference between the two groups in MGF and DF (\(P>0.05\)) (Table 3).

Compared with the LIMA-LAD group, the RIMA-LAD group had a bit lower DF (70.76±11.87 vs 74.06±7.09, \(P=0.018\)), while there was no difference in MGF and PI between the two groups (\(P>0.05\)) (Table 3).

**The results of the CT angiography examined before discharge of the three groups.**

A total of 406 patients (313 patients in the LIMA-LAD group, 34 patients in the RIMA-LAD group and 43 patients in the SVG-LAD group) were examined for coronary CT angiography before discharge. Table 4 lists the coronary CT angiographic results. The patency rate of the LIMA-LAD group was 98.72% (309/313), the RIMA-LAD group was 97.06% (33/34), and the SVG-LAD group was 100%. There was no difference among the three groups in patency rate (\(P=0.405\)).

**Discussion**

The strategy of in situ LIMA grafting to the LAD (LIMA-LAD) is considered the “gold standard” of coronary revascularization[5]. However, in some circumstances, such as the stenosis or occlusion of LIMA and harvested damage, surgeons have got to choose the other conduit materials to revascularize the LAD. There is no consensus on which conduit
is better for LAD under the un-useable LIMA circumstance. In situ or free RIMA and SVG are used considering the patients’ age, state of cardiac function and the surgeons’ preference. Previous study results demonstrated that revascularization of the LAD using an in situ RIMA resulted in excellent mid-term graft patency and clinical outcomes[6]. The major focuses of the utilization of RIMA conduit include how to place it and where to place it. Several other studies reported an easily reproducible and technically less demanding surgical strategy for RIMA grafting, i.e., retrosternal crossover in situ RIMA grafting to the LAD (RIMA-LAD)[7, 8]. And, this strategy was reported to have positive impacts on the long-term clinical outcomes [9, 10]. SVG are still widely used because of their several advantages, including ease of access, ease of operation, sufficiency of length for transplantation, and short harvest time. However, saphenous vein grafts (SVGs) have a greater rate of both early and late occlusion compared with arterial grafts, which has been proved to affect the patients’ long-term outcome[11–13]. Since the beginning of the 1990s Souza D. have been using a technique for SV preparation in which the vein is harvested with a pedicle of surrounding tissue: the “no-touch (NT) technique”. This has been shown to reduce the risk of spasm and the need for dilatation and therefore preserve vessel wall integrity[14].A study of the longest observation showed that patency of SVGs using the No-touch technique was comparable with that of thoracic artery grafts after 16 years[15]. The SVGs using the No-touch technique may be a choice for LAD revascularization for patients whose LIMA cannot be used.

This study analyzed the preoperative ultrasound data of LIMA and RIMA, and found that the RIMA had a bit larger diameter, bigger mean graft flow volume, but a smaller pulsatility index than the LIMA. The possible explanation may be that Chinese people are mainly right-handed and the muscles and blood vessels on the same side developed better than the left side. However, there was no difference of the MGF and PI assessed by TTFM
intro-operatively between the LIMA-LAD and the RIMA-LAD group. This study proved that in-suite RIMA used for LAD revascularization was comparable with the LIMA in blood parameters.

This study also compared the blood flow parameters of IMAs between examined preoperatively and assessed intro-operatively, and the results demonstrated that compared with the preoperative data, the MGF of both LIMA and RIMA has improved, the PI of both LIMA and RIMA has decreased (P<0.001). The internal mammary artery arises from the undersurface of the first portion of the subclavian artery, and its distal end is the capillary network of the chest wall. Blood flow in un-grafted LIMA occurs mainly during systole similar to the flow in peripheral arteries, like in the subclavian artery. Once grafted to the coronary network, the IMA flow pattern instantly adapts to the left ventricular hemodynamic. The diastolic flow velocity of the LIMA increases after CABG as the result of the physiologically decreased resistance in the coronary circulation. This “diastolisation” of the IMA blood flow is also related to the low resistance and large capacitance of the coronary artery network and to the IMA self-regulated property on vascular tone. [16, 17].

The analysis of intro-operative blood flow parameters of different strategy of the LAD revascularization, and showed that compared with IMAs (LIMA + RIMA), LIMA-LAD and RIMA, the SVG-LAD group has higher MGF and lower PI. The SVG has larger diameters and often not likely affected by the vasoactive drugs and neurohumoral fluids than the arterial conduits[18]. The SVG anastomosed directly to the ascending aorta has higher pressure and higher low-gradient, which caused the larger mean blood flow volume.

The pulsatility index(PI), calculated as (maximum flow volume−minimum flow volume)/(mean flow volume), is one of the TTFM measurements parameters that used for conduit evaluation during operation[19]. The results of Di Giammarco et al study showed
that the PI may be an independent risk factors of graft dysfunction. Higher PI values indicate that there may be greater negative flow or lower average flow.[20]. The results of this study demonstrated that the PI of both LIMA-LAD group and RIMA-LAD group are higher than the SVG-LAD group (P<0.001). We also found that in this study, the proportion of negative flow less than 10 ml/min was larger in arterial conduit group (P < 0.001), suggesting that there was more negative blood flow, i.e., competitive flow, in the early systolic in arterial conduit group. While the venous conduits have fewer smooth muscle, and with low elasticity and small cyclical deformation of pipe diameter with pressure. Therefore, it is impossible to accommodate the reverse flow by adjusting the diameter of the conduits, and the probability of the occurrence of competitive flow may be relatively low[3]. In our study, the early patency before discharge of RIMA-LAD and SVG-LAD are comparable with the LIMA-LAD.

Limitations

Several limitations of our study should be recognized. The first and most important limitation of this study was its descriptive nature, using a relatively small cohort of patients at a single institution. Second, blood flow parameters measured by TTFM and early prior to discharge graft patency do not reflect the all advantage of effect of grafting strategy, as well as major cardiovascular and cerebrovascular adverse events, revascularization events and the long-term graft patency that can reflect the advantage of grafting strategy to LAD, and these other indicators were not included in this study.

Conclusions

We conclude that in patients whose LIMA cannot be used, the in-suit RIMA and the SVG are comparable and even better than the LIMA in the blood flow parameters measured by TTFM. In our study the early patency before discharge of RIMA-LAD and SVG-LAD are
comparable with the LIMA-LAD.

Abbreviations

LIMA
left internal mammary artery
LAD
left anterior descending artery
CABG
coronary artery bypass graft surgery
TTFM
transit-time flow measurement
PI
pulse index
MGF
mean graft flow
DF
diastolic flow fraction
SVG
great saphenous vein
CTA
computed tomography angiography

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

We received explicit consent from the patient.

Availability of data and material

Data will be made available on request.

Competing interests

The authors declare that they have no competing interests
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Authors' contributions
Zhou Zhao is the corresponding author. Guodong Zhang conceived of the study and participated in its design and coordination. Yu Chen, Gang Liu and Shenglong Chen helped to draft the manuscript. All authors read and approved the final manuscript.

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Not applicable

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Tables

|                              | LIMA-LAD (333) | RIMA-LAD(341) | SVG-LAD(431) | P     |
|------------------------------|----------------|---------------|--------------|-------|
| Male (n, %)                  | 241(72.37)     | 29(85.29)     | 30(69.77)    | 0.110 |
| Age                          | 64.27±10.70    | 56.85±11.01   | 70.47±10.2   | 0.000 |
| BMI                          | 26.64±20.25    | 25.55±2.51    | 23.79±3.09   | 0.616 |
| Hypertension (n, %)          | 209(62.76)     | 21(61.76)     | 27(62.79)    | 0.152 |
| Diabetes (n, %)              | 141(42.34)     | 13(38.24)     | 17(39.53)    | 0.036 |
| Hyperlipidemia (n, %)        | 145(43.54)     | 15(44.12)     | 19(44.19)    | 0.455 |
| Previous stroke (n, %)       | 50(15.01)      | 9(26.47)      | 6(13.95)     | 0.158 |
| COPD (n, %)                  | 7(2.10)        | 1(2.94)       | 2(4.65)      | 0.451 |
| PVD (n, %)                   | 40(12.01)      | 6(17.65)      | 3(8.82)      | 0.723 |
| Previous infarction (n, %)   | 65(19.52)      | 6(17.65)      | 7(16.28)     | 0.730 |
| PCI                          | 49(14.71)      | 6(17.65)      | 8(18.60)     | 0.719 |
| Number of anastomosis        | 3.04±0.94      | 2.78±0.87     | 3.24±1.07    | 0.121 |
| NYHA                         | 2.30±0.51      | 2.33±0.60     | 2.28±0.51    | 0.911 |
| LVEF (%, ±s)                 | 62.87±25.18    | 62.81±9.50    | 61.40±8.78   | 0.927 |
| LVEDd(cm, ±s)                | 50.69±7.034    | 50.25±6.201   | 51.43±6.64   | 0.741 |

BMI, body mass index; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular diseases; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic dimension; LIMA, left internal mammary artery; SVG, great saphenous vein; RIMA, left internal mammary artery; LAD, left anterior descending artery
Table 2. The blood flow parameters of LIMA and RIMA

| Items            | Group A                  | Group B                  | P    |
|------------------|--------------------------|--------------------------|------|
|                  | Preoperative LIMA        | Preoperative RIMA        |      |
| PI               | 4.13±1.36                | 3.97±1.20                | 0.002|
| MGF (ml/min)     | 16.48±7.13               | 18.68±8.75               | 0.000|
| Diameters (mm)   | 1.96±0.17                | 1.97±0.19                | 0.008|
|                  | Preoperative LIMA        | Intraoperative LIMA      |      |
| PI               | 4.13±1.36                | 2.65±1.01                | 0.000|
| MGF (ml/min)     | 16.48±7.13               | 29.71±20.94              | 0.000|
|                  | Preoperative RIMA        | Intraoperative RIMA      |      |
| PI               | 3.97±1.20                | 2.56±0.96                | 0.011|
| MGF (ml/min)     | 18.68±8.75               | 29.03±22.73              |      |

LIMA, left internal mammary artery; SVG, great saphenous vein; RIMA, left internal mammary artery; MGF, mean graft flow; PI, pulsatility index; DF, diastolic flow fraction

TABLE 3. Intraoperative blood flow parameters of the three groups

| Items            | Group A                  | Group B                  | P    |
|------------------|--------------------------|--------------------------|------|
|                  | IMAs-LAD(367)            | SVG-LAD(43)              |      |
| PI               | 2.64±1.00                | 2.07±0.62                | 0.000|
| MGF (ml/min)     | 29.65±21.08              | 37.15±23.29              | 0.033|
| DF (%)           | 73.75±7.71               | 71.85±8.38               | 0.146|
|                  | LIMA-LAD(333)            | RIMA-LAD(34)             |      |
| PI               | 2.65±1.01                | 2.56±0.96                | 0.642|
| MGF (ml/min)     | 29.71±20.94              | 29.03±22.73              | 0.859|
| DF (%)           | 74.06±7.09               | 70.76±11.87              | 0.018|
|                  | LIMA-LAD(333)            | SVG-LAD(43)              |      |
| PI               | 2.65±1.01                | 2.07±0.62                | 0.000|
| MGF (ml/min)     | 29.71±20.94              | 37.15±23.29              | 0.036|
| DF (%)           | 74.06±7.09               | 71.85±8.38               | 0.091|
|                  | RIMA-LAD(34)             | SVG-LAD(43)              |      |
| PI               | 2.56±0.96                | 2.07±0.62                | 0.029|
| MGF (ml/min)     | 29.03±22.73              | 37.15±23.29              | 0.102|
| DF (%)           | 70.76±11.87              | 71.85±8.38               | 0.551|

LIMA, left internal mammary artery; SVG, great saphenous vein; RIMA, left internal mammary artery; MGF, mean graft flow; PI, pulsatility index; DF, diastolic flow fraction
Table 4 Graft Patency of three groups

| Items         | LIMA-LAD              | RIMA-LAD       | SVG-LAD       | P       |
|---------------|-----------------------|----------------|---------------|---------|
| CTA           | 94.00(313/333)        | 100(34/34      | 93.02(40/43)  | 0.381   |
| Patency rate (%) | 98.72(309/313)        | 97.06(33/34    | 100(40/40)    | 0.405   |

LIMA, left internal mammary artery; SVG, great saphenous vein; RIMA, left internal mammary artery; CTA, computed tomography angiophy