Original Article

An Experimental Study of the Effects of IABP on Coronary Artery Bypass Graft Flow Waveform

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Purpose: Graft evaluation after coronary artery bypass grafting (CABG) is still not sufficient. This study analyzed the flow waveform of coronary arteries and grafts during intra-aortic balloon pumping (IABP) assist.

Methods: Subjects were eight pigs that underwent off-pump CABG. Using transit-time flow measurement (TTFM) and occluder, blood flow waveforms were recorded while changing the degree of stenosis of Seg.6 and the left internal thoracic artery (LITA) and analyzed by percentage of reverse flow component to the total blood flow (R/T) and the ratio of diastolic blood flow of IABP operative and IABP inoperative (D1/D0).

Result: Reverse flow of the LITA was reduced when stenosis of Seg.6 increased and R/T decreased. The average diastolic blood flow of Seg.8 and the LITA increased with IABP on showing a D1/D0 of 1 or more. R/T of the LITA increased when stenosis of Seg.6 was fixed and increasing the degree of LITA stenosis. D1/D0 increased up to a 75% LITA stenosis and is decreased in more severe stenosis.

Conclusion: R/T is significantly higher in the antagonist or stenosis during IABP assist and was able to confirm the effectiveness of the graft as a functional assessment of graft. D1/D0 is useful as an indicator of the effectiveness of IABP on coronary blood flow.

Keywords: coronary artery bypass grafting, graft flow wave, intra-aortic balloon pumping, ischemic heart disease

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Introduction

Coronary artery bypass grafting (CABG) is routinely performed as a surgical method for ischemic heart disease. In Japan, CABG procedures exceed 12000 cases per year and a good mortality rate of 0.81% has been achieved for an initial elective CABG.¹⁾ However, in recent years, elderly patients and patients with cardiac dysfunction, diabetes, or renal dysfunction, among others, are increasingly undergoing CABG surgery owing to the advances in percutaneous coronary intervention (PCI).²⁾ The long-term patency is considerably affected by the quality of graft anastomosis in severe cases and, therefore, accurate evaluation of graft function is essential. It is possible to increase long-term graft patency if the quality of the graft anastomosis can be evaluated during surgery. However, in clinical practice, objective and quantitative assessment of graft function is still not sufficient. Coronary angiography has conventionally been performed to evaluate grafts, showing the shape of the graft lumen as the flow of the contrast agent is pushed through. Nevertheless, this procedure has its drawbacks, and only two dimensions can be evaluated without providing hemodynamic information; hence, quantitative evaluation is not sufficient.³⁾ Other methods of evaluating graft anastomosis during surgery exist, including intraoperative echocardiographic imaging⁴⁾ and fluorescent imaging using indocyanine (SPY system).^{5,6)} However, these visual and costly assessments lack reliability because they are not subjective or quantitative. Among intraoperative evaluation methods, transittime flow measurement (TTFM) is considered convenient and reproducible, and not affected by vascular diameter, hematocrit value, or the probe angle.⁷⁾ Therefore, unlike other methods, TTFM has been attracting attention as a method that can objectively and quantitatively assess the graft anastomosis.7-9)

Intra-aortic balloon pumping (IABP) is the earliest clinically popular mechanical assist device, and its effectiveness has been well reported.⁸⁻¹²⁾ However, few studies investigate the effect of IABP on the blood flow waveform of CABG grafts. This is especially the case for CABG using the left internal thoracic artery (LITA) because the graft is long it creates a time difference in the blood flow, and the diastolic advantage of the graft blood flow is not clear, making it difficult to evaluate the effectiveness of the graft.

We previously created an experimental model that allows us to freely set the stenosis of coronary arteries and graft anastomosis, and have performed detailed graft flow waveform analysis immediately after CABG using TTFM.¹³⁾ The present study analyzed the flow waveform of coronary arteries and grafts during IABP assist using this experimental model, and examined in detail the effects of IABP on graft flow rate and coronary blood flow.

Materials and Methods

The subjects used were eight male pigs weighing 45 ± 3 kg. The subjects were sedated using Midazolam 0.1 mg/kg via intramuscular injection, and anesthetized using Propofol 0.5 mg/kg administered through the ear vein. After muscle relaxation using Vecuronium 0.1 mg/kg, the pigs were tracheotomized, breathing set to 200–300 mL/kg/min, and general anesthesia maintained with Sevoflurane

2%. An IABP balloon was inserted through the femoral artery (Senko Medical Instrument Mfg. Co., Tokyo, Japan), the tip of the balloon was fixed in the descending aorta 2 cm from the left subclavian artery inlet.

Measurement of average blood flow and flow waveforms in the pre-group before bypass

The LITA was harvested using the skeletonization technique. The left anterior descending (LAD) branch was peeled off from Seg.6 to Seg.8. Seg.6, Seg.8, and the LITA were fitted with TTFM (Transonic Systems Inc., Ithaca, NY, USA), and the average blood flow and flow waveforms of Seg.6, Seg.8, and the LITA measured as the control blood flow. Next, a vascular stenosis (VO-5/ Unique Medical Co., Ltd., Tokyo, Japan) (inner diameter 4 mm, width 7 mm, thickness 2 mm) was attached to Seg.6. Using the vascular stenosis (occluder), a 0% reduction in the control blood flow at Seg.6 was modified to a 25% reduction, 50% reduction, 75% reduction, and a 90% reduction. The flow waveform at Seg.6 and Seg.8 was measured in real time for each reduction in blood flood; these measurements were made in the pregroup before bypass. In this study, the rate of change in the blood flow is expressed as the rate of decrease in blood flow. This measures the actual blood flow and indicates the amount of decrease in blood flow compared to the control, unlike the stenosis rate that is usually evaluated by two-dimensional vascular diameter in angiography. For evaluating the cross-sectional area of the blood vessels, a stenosis rate of 50% corresponds to a blood flow reduction rate of 75%. The stabilizer was released during flow waveform measurement, and blood pressure measured while keeping the heart rate within the normal range. The measurement results are based on the analysis software Acknowledge (BIOPAC Systems Inc., Santa Barbara, CA, USA) and were recorded in six channels: aortic pressure, left ventricular pressure, electrocardiogram, Seg.6 flow, Seg.8 flow, and LITA flow.

Measurement of average blood flow and flow waveforms after CABG in the post-bypass group

After heparinization, the LAD was fixed using a stabilizer, and the LITA was end-to-side anastomosed to Seg 7 with Prolene 8-0. We reattached the vascular stenosis device to Seg.6, 2 cm central from the anastomotic end, and to the LITA, 0.5 cm central from the anastomotic end. We also mounted TTFM probes on Seg.6 and Seg.8, 1 cm central from the anastomotic end, and on the LITA, 1 cm central from the anastomotic end (**Fig. 1**). Using



Fig. 1 Coronary artery measurement models in Protocols 1 and 2 (upper) and R/T, D1/D0 calculation methods (lower). IABP: intra-aortic balloon pumping; LAD: left anterior descending; LITA: left internal thoracic artery

the stenosis device attached to Seg.6 and the LITA, the blood flow volume of Seg.6 and the LITA was changed according to each protocol, and the flow waveforms of Seg.6, Seg.8, and the LITA measured and during bypass in real time. Recording was performed on six channels using Acknowledge as in the previous group.

Experimental Protocols

The data were measured and recorded according to the following two protocols.

(1) Protocol 1 (Experimental stenosis model of the coronary artery) (**Fig. 1**)

After blocking the blood flow of the LITA, the stenosis was performed so that the blood flow reduction rate of Seg.6 was 0%, 25%, 50%, 75%, and then 90%. When the blood flow became stable, the blockade of LITA was released. When the blood flow stabilized again, the flow waveforms of Seg.6, Seg.8, and the LITA were measured and recorded. These steps and measurements were repeated for each blood flow reduction rate of Seg.6.

(2) Protocol 2 (Experimental stenosis model of graft) (Fig. 1)

With the LITA clamped, Seg.6 was fixed at a blood flow reduction rate of 75% or 90%. When the blood flow stabilized, the LITA clamp was released, and the LITA blood flow reduction rate narrowed to 0%, 25%, 50%, 75%, and 90%. For each LITA blood flow reduction rate, the flow waveform of Seg.6, Seg.8, and the LITA were measured and recorded.

Two indices were calculated for each protocol, and it was examined whether or not these were appropriate as indices for evaluating graft function. The first is an index that we previously proposed, which indicates the graft function and is the ratio of the regurgitant component (R) to the total flow component (T), R/T14) (**Fig. 1**). The other is the ratio D1/D0 of the diastolic blood flow (D1) when IABP is activated to the diastolic blood flow (D0) when IABP is not activated (**Fig. 1**).

Statistical analysis

The Kruskal–Wallis test was performed for comparison between the five groups from 0% to 90%, and p <0.05 was considered significant.

Results

Pre-group before bypass

The LITA showed a flow waveform similar to a normal arterial waveform, mainly flowing during systolic period, whereas coronary blood flow occurs mainly during the diastolic period. Seg.6 and Seg.8 matched the



Fig. 2 Flow wave pattern in Protocol 1. IABP: intra-aortic balloon pumping

left chamber and during the contraction period a momentary reflux waveform was seen. This is a physiological phenomenon (coronary slosh phenomenon) caused by the blood flow of the intracardiac coronary vessel bed into the coronary artery by contraction of the myocardium. The reflux waveform was also observed in LITA, coinciding with the early systolic contracting period during the operation with IABP activated. This is because the balloon rapidly squeezes in the early systolic phase, causing apparent negative pressure on the LITA inlet portion close to the position of the balloon tip as the blood flow is temporarily drawn from LITA to the aorta. In both cases, the effect of diastolic augmentation of IABP increases the coronary blood flow during diastole.

(1) Protocol 1 (Experimental Stenosis Model of Coronary Artery)

(a) Flow waveform of Seg.6, Seg.8, and the LITA after bypass (**Fig. 2**)

After bypass when the blood flow reduction rate of Seg.6 was 0%, blood flow from Seg.6 to the LITA was observed during early systole after the coronary slosh phenomenon. Following this, Seg.6 blood flow became antegrade and the LITA blood flow retrograde. Later, with the increase in antegrade blood flow of LITA, retrograde blood flow from LITA to Seg.6 was observed. As a result, the flow waveform of Seg.6 and LITA showed a

symmetric pattern centered on 0 mL/min. This demonstrated that bloodstream antagonism occurs between Seg.6 and LITA. This phenomenon is due to the entrance of the LAD being closer to LITA. In addition, when IABP was activated at 0% blood flow reduction rate of Seg.6, the blood flow of Seg.6 and Seg.8 increased compared to when it was inactive, and reflux that was not inactivated during LITA blood flow was observed. This can be explained due to IABP increasing the pressure in the aorta during early diastole, increasing coronary blood flow and causes blood flow from Seg.6 to the LITA. After this, as the blood flow of LITA increases a little later, the forward blood flow waveform appears. This diastolic LITA reflux occurred only when there was no stenosis of Seg.6, and was not seen when Seg.6 has a blood flow reduction rate of more than 25%. This was due to the reduction of Seg.6 flow rate compared to the LITA flow rate. As the blood flow reduction rate of Seg.6 was gradually increased, the antagonism of Seg.6 and LITA also decreased gradually as visible in the flow waveform. In other words, the flow rate of Seg.6 decreases gradually, and the flow rate of LITA increases. When Seg.6 had a blood flow rate of 75% and 90%, retrograde flow waveforms were observed in Seg.6 during the diastolic period. These waveforms were observed because the blood flow of the LITA is relatively high due



Fig. 3 R/T and D1/D0 in Protocol 1. IABP: intra-aortic balloon pumping; LITA: left internal thoracic artery

to the high stenosis of Seg.6 and flows from LITA to Seg.6. During the procedure with IABP, we observed that as the blood flow reduction rate of Seg.6 increased, the blood flow antagonism between Seg.6 and the LITA during the expansion period decreased at 0% blood flow reduction rate of Seg.6, and disappeared at 90%. Also, when Seg.6 had a reduction greater than 25%, the IABP procedure significantly increased LITA's forward blood

flow, increasing the blood flow of LITA to Seg.8. This demonstrated the diastolic augmentation effect of IABP.

(b) R/T of Seg.6, Seg.8, and LITA (Fig. 3)

When IABP was off, R/T of Seg.8 was 5.69 ± 2.33 (p = 0.035) when the blood flow reduction rate was 50%, 2.33 ± 3.17 (p = 0.031) when 75%, and 0.89 ± 1.22 when 90% (p = 0.018). When IABP was on, R/T of Seg.8 was 7.48 ± 4.81 (p = 0.017) when Seg.6 had a blood flow



Fig. 4 Flow wave pattern in Protocol 2. IABP: intra-aortic balloon pumping; LITA: left internal thoracic artery

reduction rate of 50%, 5.95 ± 5.60 (p = 0.032) when 75%, and 6.91 ± 5.44 when 90% (p = 0.019).

When IABP was off, R/T of LITA was 4.47 ± 2.33 (p = 0.013) when Seg.6 had a blood flow reduction rate of 50%, 2.21 ± 3.17 (p = 0.017) when 75%, and 1.21 ± 1.22 (p = 0.026) when 90%; significantly lower than 27.87 ± 19.96 when 0%. When IABP was on, R/T of LITA was 7.78 ± 4.80 (p = 0.027) when Seg.6 had a blood flow reduction rate of 50%, 6.02 ± 5.60 (p = 0.030) when 75%, and 6.96 ± 5.44 (p = 0.022) when 90%, which was significantly lower than 40.19 ± 11.30 when 0%.

(c) D1/D0 of Seg.6, Seg.8, and LITA (**Fig. 3**)

When there was little or no blood flow reduction rate of Seg.6 (0%, 25%), D1/D0 of LITA was 0.76 ± 0.13 , 1.03 ± 0.12 , and D1/D0 of Seg.8 was 1.02 ± 0.29 . No significant difference was found. However, when Seg.6 had a blood flow reduction rate of 75%, D1/D0 of LITA was 1.30 ± 0.05 , when 90% it was 1.38 ± 0.09 , and D1/D0 of Seg.8 was 1.22 ± 0.14 when 50%, 1.40 ± 0.07 when 75%, and 1.45 ± 0.12 when 90%. The difference between 0% and 90% was statistically significant (p = 0.015).

(2) Protocol 2 (Experimental Stenosis Model of Graft)

(a) LITA flow rate waveform when the blood flow reduction rate of Seg.6 was fixed at 75% and 90% (Fig. 4)

When Seg.6 was fixed at 75%, some diastolic blood flow of the LITA can be observed, up to a LITA blood flow reduction rate of 0-50%; however, this becomes significant at 75–90%. It drops obviously. Also, with the activation of IABP, the diastolic blood flow was observed to increase.

When Seg.6 was fixed at 90%, the diastolic blood flow of the LITA, with a blood flow reduction rate of 0-25%, was increased compared to when Seg.6 was fixed at 75%. When the LITA blood flow reduction rate was 50% or more, the diastolic blood flow became almost flat. With IABP open, an increase in diastolic blood flow is observed when the blood flow reduction rate of LITA was 0-50%, but between 75 and 90%, there is almost no flow, even with IABP.

(b) R/T of Seg.6, Seg.8, and the LITA (Fig. 5)

As the LITA's blood flow was decreased, the R/T of LITA increased. With Seg.6 fixed at 75%, the R/T of the LITA when LITA blood flow reduction rate of 0% was 3.11 ± 4.02 , when 75% it was 31.69 ± 13.15 (p = 0.031), and when 90% it was 60.66 ± 10.11 (p = 0.027). The same trend was observed with IABP open: the R/T of the LITA with a LITA blood flow reduction rate of 0% was 12.17 ± 12.34 , when 75% it was 39.02 ± 13.71 (p = 0.033), and when 90% it was 55.59 ± 4.66 (p = 0.024). Similarly, the R/T of Seg.8 also increased with a decrease in the LITA blood flow rate. When Seg.6 was fixed at 75%, the R/T of Seg.8 with a LITA blood flow reduction rate



Fig. 5 R/T and D1/D0 in Protocol 2. IABP: intra-aortic balloon pumping; LITA: left internal thoracic artery

of 0% was 1.28 ± 1.35 , it was 9.96 ± 7.28 (p = 0.011) when 75%, and 9.94 ± 6.10 (p = 0.009) when 90%. Similarly with IABP on, the R/T of Seg.8 with a LITA blood flow reduction rate of 0% was 5.90 ± 6.67 , when 75% it was 16.55 ± 17.24 (p = 0.038), and when 90% it was 12.63 ± 13.58 (p = 0.017). (**Fig. 4**; middle). These phenomena indicate antagonism of blood flow, suggesting graft dysfunction due to anastomotic stricture. In

addition, as IABP increases regurgitation in early systole, the R/T when IABP is on is generally higher than that when it is off. When Seg.6 was fixed at 90%, the R/T of the LITA with a LITA blood flow reduction rate of 0% was 7.74 ± 7.04 , when 75% it was 27.64 ± 23.74 (p =0.017), and when 90% it was 47.45 ± 21.29 (p =0.028). With IABP off, the R/T of the LITA with a LITA blood flow reduction rate of 0% was 11.91 ± 6.24 , when 75% it

was 53.04 ± 19.63 (p = 0.030), and when 90% it was 73.87 ± 17.84 (p = 0.029). R/T of Seg.8 was 4.71 ± 3.98 when the LITA blood flow reduction rate was 0%, when 75% it was 3.59 ± 1.80 (p = 0.015), and when 90% it was 3.77 ± 3.33 (p = 0.017). With IABP activated, the R/T of Seg.8 with a LITA blood flow reduction rate of 0% was 16.08 ± 12.69 , when 75% it was 5.11 ± 1.91 (p = 0.044), and when 90% it was 7.07 ± 4.69 (p = 0.034).

(c) D1/D0 of Seg.6, Seg.8, and LITA (Fig. 5)

The D1/D0 showed an increasing trend with blood flow reduction rate of the LITA up to 75%. When the blood flow reduction rate of LITA was 0%, D1/D0 of Seg.8 was 0.88 ± 0.38 , when 50% it was 1.27 ± 0.36 , and when 75% it was 1.30 ± 0.36 . Similarly, the D1/D0 of LITA was 0.81 ± 0.25 when 0%, 1.40 ± 0.15 when 50%, and 1.69 ± 0.31 when 75%, increasing up to a 75% stenosis. In contrast, when the anastomotic stenosis rate was 90%, the D1/D0 decreased in both Seg.8 and the LITA, and the difference with the D1/D0 of the other stenosis rates (25%-75%) was statistically significant.

Discussion

When considering the indication for CABG on preoperative coronary artery imagine, it may be assumed that a stenosis of 75% or more is observed; however, the representation of the stenosis rate is based on a two-dimensional image and may not necessarily be an accurate evaluation of blood flow reduction. Blood flow evaluation of coronary arteries is unreliable, and, to our knowledge, no study has examined how bypassed grafts exhibit function. Generally, early graft patency is 98% and high,¹⁴⁾ and the opportunity to sufficiently analyze how graft function is reduced by anastomosis stenosis is very small at present. Therefore, we have created an experimental model that can freely set the stenosis rate of coronary arteries and graft anastomosis, and have analyzed data on the blood flow waveform of the coronary arteries and grafts.¹³⁾ Additionally, many reports support the utility of IABP in ischemic heart disease,10-12) owing to the observed effect of IABP increasing the coronary blood flow. Hence, as there are few studies of the effects of CABG on grafts,⁷) in the present study, we examined the effects of IABP on coronary blood flow and grafts experimentally.

In Protocol 1 of this study, when the bypass was performed, and the blood flow reduction rate of the mid-LAD stenosis was 0%, there was little change in the flow waveform of Seg.8. The flow waveform of Seg.6 and the LITA showed a symmetric figure centered at 0 mL/min, and retrograde blood flow from Seg.6 to the LITA was observed in the early systolic period. This phenomenon was observed because the LITA became a blood outflow route from Seg.6 when the waveform of Seg.6 became antegrade, and a retrograde waveform was, unusually, observed in LITA. Later, due to the phase shift in terms of arterial pressure on the coronary artery and the LITA, with the increase in antegrade blood flow through the LITA, retrograde blood flow from LITA to Seg.6 might be increased. At this time, it was suggested that blood flow competition occurred between the LAD and the LITA. Therefore, we consider that the amplitude of the retrograde waveform (R) observed in the LITA blood flow waveform reflects the degree of blood flow competition between the two. When R becomes larger, the blood flow of Seg.8 decreases, and the rate of R to total flow rate component (T), R/T, is considered effective for the evaluation of graft function 1.6)

The results of Protocol 1 show that the degree of blood flow conflict between LAD and LITA nearly disappeared at a blood flow loss rate of 50% or more because the R/T decreased and disappeared when the stenosis rate of Seg.6 was increased and the blood flow decrease rate was more than 50%. Hence, a sufficient graft flow rate is obtained when the blood flow reduction rate of the coronary artery bypassed is at least 50% or more, and the graft has been shown to function effectively. Furthermore, when IABP is on in Protocol 1, the diastolic period has an increased flow rate, and as the balloon of the IABP is rapidly squeezed in early systole the blood flow is temporarily drawn from LITA to the aorta. We consider that there was no change in the R/T because the reflux from the systolic period is also increased. In addition, at 0% blood flow reduction rate in Seg.6, the flow rate to Seg.6 increases earlier in the diastolic period, because it flows back to the LITA. Even if IABP is activated when there is no stenosis in the coronary artery, the blood flow antagonist between Seg.6 and the LITA occurs more frequently and the effect of the graft and IABP was not observed at all. When Seg.6 had a mild blood flow reduction rate, the D1/D0 of the LITA and Seg.8 showed less difference in blood flow from 1.0, but the D1/D0 of the LITA and Seg.8 increased significantly when the Seg.6 blood flow reduction rate was 75% or more. The fact that D1/D0 is one or more indicates that diastolic blood flow is increased during the IABP procedure, and therefore the diastolic augmentation effect is thought to be observed in grafts with IABP for a blood flow reduction rate of 75% or more.

Based on the results of Protocol 1, Protocol 2 fixed the blood flow reduction rate of Seg.6 to 75% and 90% to evaluate changes in the anastomotic stenosis rate of the LITA. An increase in R/T was observed when graft dysfunction due to anastomotic stenosis was increased. When the anastomotic stenosis rate was increased, the flow rate waveform decreased significantly when IABP is off compared to when it was activated. It was suggested that the graft does not function properly as a blood supply tube when the blood flow reduction rate of the LITA is 75% or more. Interestingly, the LITA and Seg.8 had a D1/D0 of 1 or more when the blood flow reduction rate of LITA was 25%-75%, and it was considered that the anastomotic stricture might be hidden by the effect of IABP. Considering the above, it was suggested that the retrograde component area ratio (R/T) of the graft flow rate waveform could be a reliable quantitative index for estimating graft function. Therefore, we consider that the consistency and validity of the graft anastomosis can be judged intraoperatively, the function of the graft can be evaluated, and the anastomotic stricture occurring immediately after the operation can be predicted. Moreover, as the effect of IABP increases coronary diastolic blood flow and may mask anastomotic stenosis, the intraoperative graft blood flow should always also be evaluated when IABP is off.

Conclusion

When the blood flow reduction rate in LITA was in a range of 25–75%, LITA and Seg 8's D1/D0 was 1 or higher, in which effects of IABP may conceal anastomotic stenosis. Thus, it was indicated that retrograde component area ratio (R/T) on graft flow analysis could serve as a reliable and quantitative index to estimate graft functions. Using this index, it is possible to evaluate integrity and appropriateness of the graft during surgery. In addition, graft function assessment can be performed. Moreover, it is possible to predict anastomotic stenosis which may occur immediately after surgery. Finally, effects of IABP may increase diastolic blood flow of the coronary artery and may mask anastomotic stenosis. Accordingly, the evaluation of graft blood flow during surgery should be conducted while IABP is turned off.

Disclosure Statement

None of the authors have any conflicts of interest associated with this study.

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