A 10-year angiographic follow-up of competitive flow in sequential and composite arterial grafts

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Abstract

Objective: Physiological reaction to competitive flow is considered as the primary mechanism of arterial graft occlusion. Reopening of graft lumen had been also reported, but details remain unknown. We sought to delineate the effect of management of the moderately stenotic targets on the occurrence of competitive flow and clinical results. Methods: Clinical records and angiograms of 3263 bypass grafts in 852 patients, who underwent off-pump coronary revascularization using the internal thoracic artery (ITA) and radial artery without aortic manipulation since 2000, were examined. Dominant flow direction was graded as antegrade, competitive, and no flow (occlusion). Late angiography was performed in 157 patients with 561 bypass grafts for clinical reasons. The follow-up period was 55.5 ± 31.1 months. Results: The early graft patency rate was 98.0% (3197/3263). The rate of antegrade flow was 91.5% (2986/3263), while competitive flow was detected in 6.5% (211/3263). The actuarial patency rates of bypass grafts with antegrade flow were significantly higher than those with competitive flow (87.9% at 5 years and 71.3% at 8 years, vs 25.8% at 5 years and 9.2% at 8 years, p < 0.0001). In the univariate and multivariate analyses for 852 patients, territory of right coronary artery (odds ratio (OR) = 2.20, p = 0.0002), composite radial artery (OR = 1.90, p = 0.03), and the distal end of the graft (OR = 2.90, p = 0.0003), were identified as the significant predictors of competitive flow from the target with 51–75% stenosis. Individual grafting inversely correlated with occurrence of competitive flow (OR = 0.48, p = 0.04). Reopening of the graft lumen associated with progression of native stenosis was not observed in these patients. Conclusions: Competitive flow can be efficiently avoided by appropriate graft arrangement and patients’ selection. Selection of the target of the graft end would be crucial to achieve antegrade bypass flow and long-term patency of entire sequential bypass grafts. For the composite graft, functional recovery of the occluded graft would be extremely rare.

Keywords: CABG; Off-pump CABG; Arterial graft; Radial artery; Angiography

1. Introduction

When the bypass flow is not sufficient, the most important advantage of the arterial graft disappears [1,2]. It has been believed that competitive flow is relatively frequent in the sequential and composite bypass grafts, as compared with individual grafting. This would be the primary reason for reluctance to use this technique, irrespective of its benefits, such as avoidance of aortic manipulation and efficient use of graft materials [3,4]. In addition, it is also still controversial whether and how often the narrowed or occluded graft restores its luminal patency and function, when the native coronary stenosis develops.

Angiographic flow grading has been introduced since 2000. This grading system significantly correlated with mid-term angiographic patency, and would be useful in the evaluation of various graft configurations and combinations of the target branches [5]. In the present study, we sought to examine the effect of bypass flow and graft configurations on the early and late angiographic outcomes, and to establish optimal management of the target coronary branch with moderate stenotic lesion.

2. Materials and methods

Between April 2000 and April 2010, 852 patients underwent off-pump coronary artery bypass grafting (CABG) using internal thoracic artery (ITA) and radial artery, and following early postoperative angiography. This retrospective observational study was approved by our institutional review board. Our standard strategy for CABG has been total arterial off-pump revascularization without aortic manip-
The follow-up period was 55.5 months in patients with 561 bypass grafts for clinical reasons. The mean late angiography was performed in 157 (18.4%) patients. When graft occlusion or progression of native coronary lesion was suspected, the invasive angiography was performed during hospitalization, and had been routinely performed for patients aged less than 80 years without considerable risk until 2007, bypass grafts were assessed by their anatomical patency and flow direction as antegrade, competitive or no flow. Since 2008, contrast-enhanced computed tomography was used for early and late angiographic assessment. The early graft patency rate was 98.0% (3197/3263). "Sequential proximal" meant sequential anastomosis in a side-to-side fashion, besides anastomosis at the graft end. We judged as "patent", when there was complete continuity of the graft lumen from the subclavian artery to the target coronary branch, irrespective of the flow direction. Whenever the bypass flow from an in situ ITA graft to the target coronary branch was interrupted at any level, it was defined as no flow (occlusion). Competitive flow was defined as a situation in which the target branch was slightly opacified or was not opacified from the ITA injection, and the bypass graft was opacified by retrograde flow from the native coronary injection. Reverse flow in our previous study [5] was included in competitive flow in this study.

We especially focused on the management of the target branches with moderate stenosis. The significance of correlations between competitive flow and features of the bypass grafts and target branches with 51—75% stenosis was examined.

3. Statistical analysis

The continuous variables are expressed as the mean values ± standard deviation (SD). The data of two independent groups were compared using Fisher's exact probability test. Longitudinal data were estimated by the Kaplan-Meier method and the difference of two groups was compared with the log-rank method. Logistic regression analysis was used to examine the significance of the variables. The differences were considered statistically significant when the p value was less than 0.05.

4. Results

The early graft patency rate was 98.0% (3197/3263). Competitive flow was found in 211 (6.5%) bypass grafts. Of
these, 49.8% (105/211) occurred in the RCA region, while 60/211 (28.4%) and 46/211 (21.8%) occurred in the LCX and LAD regions, respectively. Of the target branches causing competitive flow, 85.3% (180/211) had 51—75% stenosis, and 90.0% (190/211) were anastomosed with the graft end (Table 2).

Fifty-two bypass grafts with competitive flow in the early angiography were reevaluated by the repeated angiography. Of these, 39/52 (75.0%) were occluded (Table 3). The cumulative patency rates of the bypass grafts with competitive flow were significantly lower than those with antegrade flow (25.8% at 5 years and 9.2% at 8 years, vs 87.9% at 5 years and 78.8% at 8 years, \( p < 0.0001 \)) (Fig. 1). In the univariate and multivariate analyses for 852 patients, territory of RCA (odds ratio (OR) = 2.20, \( p = 0.0002 \)), composite radial artery (OR = 1.90, \( p = 0.03 \)), and the distal end of the graft end were independent risk factors for competitive flow.

4.1. Analyses of 852 patients, regarding management of bypass grafts to target vessels with 51—75% stenosis

For the target vessels with 51—75% stenosis, the early graft patency rate was 97.7% (1379/1412), while the rate of competitive flow was 12.7% (180/1412) (Table 2). The cumulative patency rates of bypass grafts with antegrade flow were significantly higher than those with competitive flow (81.4% at 5 years and 41.2% at 8 years, vs 21.5% at 5 years and 9.6% at 8 years, \( p < 0.0001 \)) (Fig. 2). In the univariate and multivariate analyses for 852 patients, territory of RCA (odds ratio (OR) = 2.20, \( p = 0.0002 \)), composite radial artery (OR = 1.90, \( p = 0.03 \)), and the distal end of the graft end were independent risk factors for competitive flow.
OR = 2.90, \( p = 0.0003 \), were identified as the significant predictors of competitive flow from the target with 51–75% stenosis anastomosed at the graft end.

### 4.2. Relation between severity of native coronary stenosis and anastomosis at graft end or sequential proximal

As shown in Fig. 3, the incidence of competitive flow at the graft end was significantly higher than that of competitive flow at sequential proximal (20% vs 3.3%, \( p < 0.0001 \)). For the targets with 91–100% stenosis, there was no significant difference in the rates of competitive flow and occlusion between the graft end and the sequential proximal (Fig. 3).

For the targets with 51–75% stenosis, the cumulative patency rates of the graft end were significantly lower than those of sequential proximal (59.0% vs 74.8% at 5 years, \( p = 0.001 \)). There was no significant difference in the patency rates between the graft end and the sequential proximal for the bypass grafts to 76–90% (\( p = 0.19 \)) and 91–100% (\( p = 0.95 \)) (Fig. 4).
5. Discussion

Recent studies suggested limitations of angiographic estimation of moderately stenotic lesions. Hamilos and colleagues mentioned that angiographic assessment was not sufficient for decision making about the need for surgical revascularization [6]. Tonino and colleagues reported that functional assessment of coronary artery lesions did not coincide with angiographic visual assessment. Approximately two-thirds of 50–70% stenotic lesions and one-fifth of 71–90% stenotic lesions were functionally insignificant [7]. Pijls and colleagues reported that fractional flow reserve significantly correlated with exercise test, thallium scan, stress echocardiography and clinical results, and was useful in the detection of functional significance of moderate stenosis, rather than the angiography [8]. Fractional flow reserve may be practical for prediction of failure of arterial grafts. The 1-year patency rate of the bypass grafts for functionally significant lesions was significantly higher than that of the bypass grafts for functionally insignificant lesions [9]. Moreover, the minimal luminal diameter [10] and combinations of the targets in sequential anastomoses [11] or combinations of the bypass grafts in the left coronary artery [12] may be possible predictors of insufficient flow and/or early graft failure.

When intracoronary pressure is comparable with graft pressure, competitive flow occurs. As even aortocoronary radial artery will present string sign, when the native coronary stenosis is not sufficiently severe [13], more severe stenosis is required for the composite radial artery [14]. As pressure at the proximal portion of the graft is presumably higher than pressure at the graft end, a more severely stenotic target is suitable for the graft end, than for the proximal site of the conduit. Glineur and colleagues reported that the in situ ITA had some resistance in itself, even when it was not stenotic at all. The pressure gradient between the proximal and distal portion of the in situ ITA increased along with increase of bypass flow, induced by reduction of vascular resistance in the myocardial tissue [15]. In the Y-graft, fractional flow reserve at the distal anastomotic site of ITA to LAD was about 0.9 with decrease of pressure by 9 mmHg, as compared with the origin of ITA [15]. Therefore, avoidance of anastomosis of the target with moderate stenosis is considered reasonable.

Our present study demonstrated that bypass grafting at the graft end significantly correlated with competitive flow, and individual grafting inversely correlated. In addition, as shown in Fig. 3, inferior results of the graft end were obvious exclusively in the bypass grafts to the moderately stenotic target, whereas no significant disadvantage of grafting at the graft end was found for the target with severe stenosis. We presume that avoidance of anastomosis of the graft end to the moderately stenotic branch will dramatically decrease competitive flow and improve graft patency. In other words, when the graft end is anastomosed to the target with severe stenosis, entire patency of the sequential graft can be highly expected. In addition, as shown in Fig. 3, occurrence of graft occlusion presented a tendency similar to occurrence of competitive flow. Not only technical failure and thrombus formation, but also insufficient bypass flow may be mechanism of relatively early failure of the arterial graft.

Limitations of this study are as follows. The present study was not prospective and not randomized. This retrospective study proved necessity of avoidance of insufficient flow. When competitive flow is predicted, using the aortocoronary venous graft can be reasonable [16]. Factors, which are possibly associated with the amount of bypass flow, may be perfusion capacity of bypass grafts, selection of graft materials, design of configurations, the strength of native coronary flow and peripheral vascular resistance in the myocardial tissue. Previous studies described that not only growth of the arterial graft, but also adaptability of peripheral vasculature played an important role in increase of bypass flow after operation [17,18]. In the present study, we examined graft configurations and the native coronary stenosis. However, peripheral vascular resistance could not be taken into account at all. This would be the next concern in the future.

There were several reports of recovery of graft lumen after string sign or diffuse narrowing. In the present series, none of the bypass grafts, which had presented competitive flow in the early angiography and occluded in the follow-up angiography, restored luminal patency afterward. However, during the same period, recovery of the ITA graft was seen in one patient. To our experience, functional recovery may be specific to the ITA graft.

In conclusion, our 10-year observation of angiographic bypass flow confirmed that the arterial graft with competitive flow would close its own lumen and become non-functioning in a few years. For the composite graft, reopening the lumen can be hardly expected, indeed. The graft configuration should be adjusted to the features of each coronary system so as to minimize competitive flow. For patients, who do not have the target vessel with moderate stenosis, or whose target vessel with moderate stenosis can be appropriately managed, composite and sequential grafting is sufficiently reliable.

References

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Appendix A. Conference discussion

**Dr L. Hamilton** (Newcastle Upon Tyne, UK): You have tackled four controversial topics in one paper: off-pump surgery, total arterial revascularization, composite grafts, and sequential grafts. Now, all of these have their advocates, but they haven’t achieved universal acceptance, and I am one of those that haven’t adopted all these techniques. So it is always good to hear a paper that confirms one’s own prejudices.

Now, I have two questions for you. First on patient selection. In your paper you have covered about 85 patients per year. I assume your program does grafts on more patients than that. How do you select your patients? Because in your manuscript you mention some selection criteria: you don’t re-angio patients if they are over 80, and you choose bilateral IMAs if the patients do not have any comorbidity.

And my second question really relates to the slides in your presentation on the FAME study. We heard it discussed yesterday, and the suggestion is that we should all be using FFR (fractional flow reserve). I want to know if you are going to bring that into your practice. So two questions, one on patient selection and, two, the use of FFR in selection of patients.

**Dr Nakajima**: Our patient selection: at the beginning of this period we applied this sequential composite graft technique to all patients as our standard technique. Postoperative angiography was almost routinely performed for patients less than 80 years old.

Recently when competitive flow has been highly predicted, we have performed the modification of our standard design of the bypass grafts, and we occasionally choose aortocoronary bypass to achieve antegrade flow. Consequently, our angiography patency rate at five years became better than that of the early period.

Inclusion criteria of this study were patients who underwent aorta no-touch total arterial grafting and early postoperative angiography. Patients who had a saphenous vein or gastroepiploic artery bypass were excluded.

For the second question, I am very interested in the FFR study, because competitive flow is caused by the competitive intraluminal pressure of the bypass graft and the native coronary artery. We believe that the measurement of intracoronary pressure at rest and hyperemic restoration in FFR study will contribute to the optimal management of a moderately stenotic target and prevention of competitive flow.

In addition, FFR is suitable for evaluation of bypass grafts even without structural stenosis; a previous FFR study showed that a composite graft had significant decline of intraluminal pressure from subcoronary artery to the LAD anastomotic site by about 10 mmHg even without structural stenosis. So FFR will be informative regarding the preoperative assessment of moderate stenosis.

**Dr W. Gomes** (São Paulo, Brazil): A question goes back to the FAME study. By the data raised in the FAME study, the cardiologists are now pushing us to graft these angiographically moderate lesions. Would you recommend grafting these moderate stenotic lesions? What is your recommendation regarding that?

**Dr Nakajima**: Our data suggests that the moderately stenotic target should be bypassed at the sequential proximal anastomosis, combined with the near-occluded target at the end. When the end of sequential grafting is anastomosed to the severely near-occluded target, the entire patency of sequential grafting can be expected. Consequently, we consider that improved patency will be achieved, as compared with individual grafting to a moderately stenotic target. Combinations of targets would be our concern in this study.