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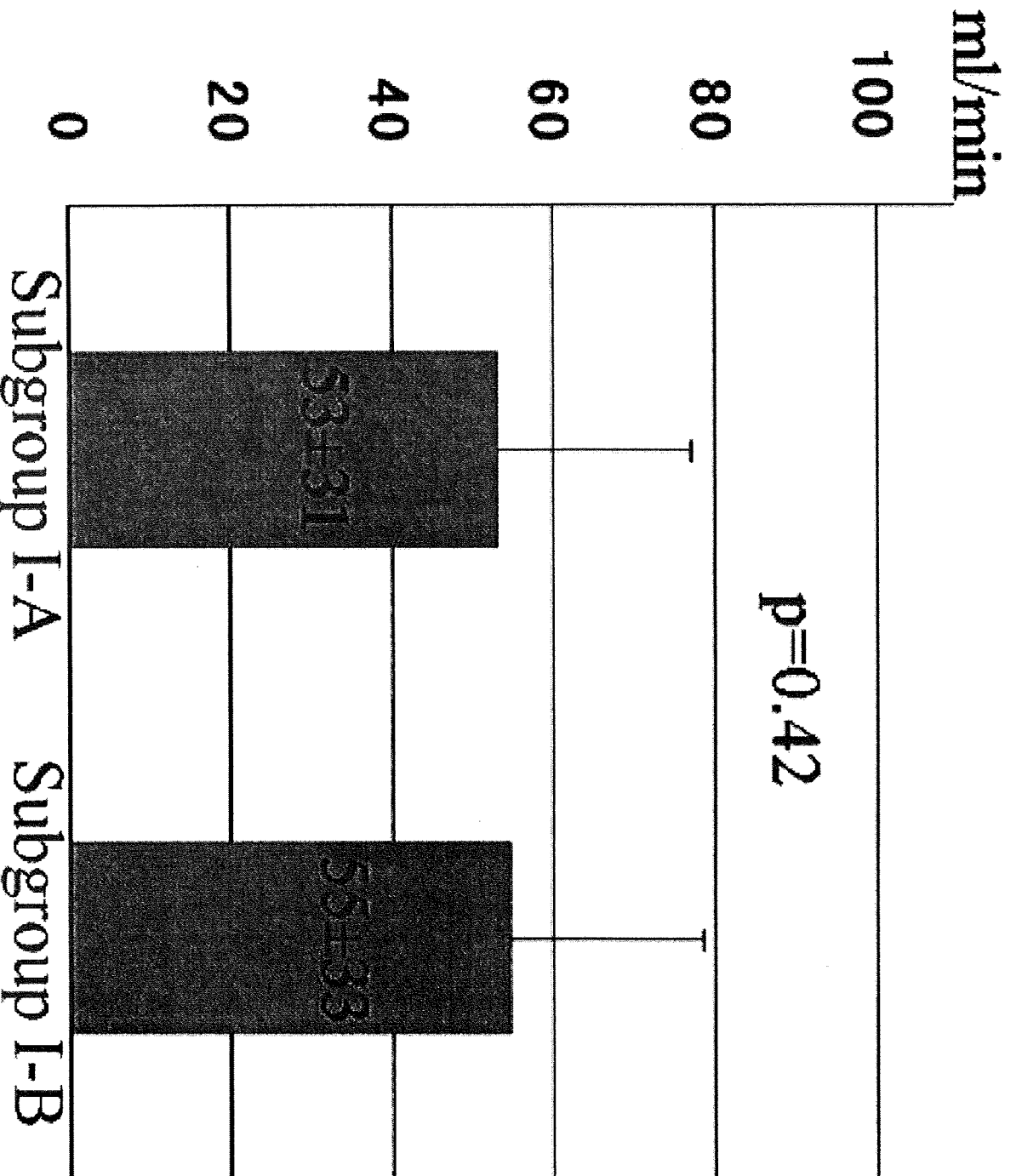
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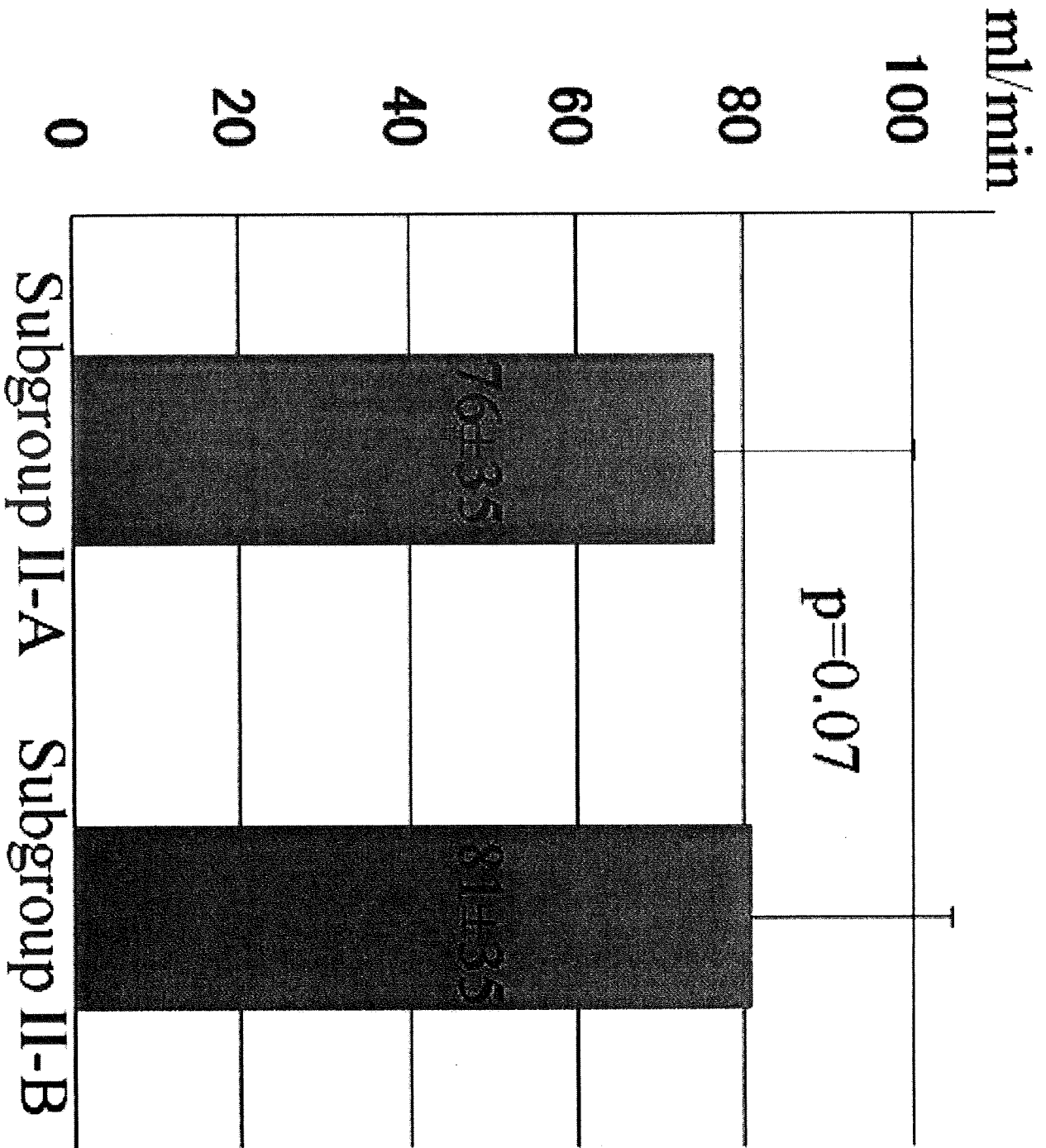
Figure 1,

Comparison of the amount of intraoperative bypass flow: subgroup I-A versus subgroup I-B.

Figure 2,

Comparison of the amount of intraoperative bypass flow: subgroup II-A versus subgroup II-B.





Patency rate of the internal thoracic artery to the left anterior descending artery bypass is reduced by competitive flow from the concomitant saphenous vein graft in the left coronary artery

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Abstract

Objective: In coronary artery bypass grafting (CABG), insufficient bypass flow can be a cause of occlusion or string sign of the internal thoracic artery (ITA) graft. A patent saphenous vein (SV) graft from the ascending aorta can reduce the blood flow through the ITA graft, and may affect its long-term patency. In the present study, we examined the impact of the patent SV graft to the left coronary artery on the long-term patency of the ITA to left anterior descending (LAD) artery bypass. **Methods:** We reviewed the coronary angiograms of 313 patients who had two bypasses to the left coronary artery including 1 in situ ITA to LAD graft between March 1986 and December 2006. Patients who had occlusion of either bypass grafts to the left coronary artery in the early angiography, were excluded. In 64 patients (20.4%), bilateral ITAs were individually anastomosed to the LAD and the second target branch in the left coronary artery (BITA group), while 249 patients (79.6%) had the ITA to LAD bypass and the SV graft to the second target branch in the left coronary artery (ITA/SV group). The mean follow-up period was 6.8 ± 4.9 years. **Results:** The cumulative patency rate of ITA-LAD bypasses at 10 years was 100% in the BITA group and 81.4% in the ITA/SV group. The ITA to LAD bypass was occluded in 14 (5.6%) patients of the ITA/SV group. In the ITA/SV group, the cumulative graft patency rate of the ITA to LAD bypass in patients who had severe ($\geq 76\%$) native coronary stenosis between the two anastomotic sites was 98.6% at 5 years, and was significantly higher than that of 82.3% in patients without severe stenosis ($p < 0.0001$). **Conclusions:** Long-term patency of the ITA-LAD bypass was affected by the presence of the patent SV graft to the left coronary artery, particularly when the native coronary stenosis between the two anastomotic sites was not severe. Competitive flow from SV graft could play an important role in occlusion of the in-situ arterial graft.

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Keywords: Coronary artery bypass grafting; Internal thoracic artery; Saphenous vein graft; Competitive flow; Graft arrangement

1. Introduction

The utilization of an internal thoracic artery (ITA) in coronary artery bypass grafting (CABG) has decreased the operative mortality without increasing the operative complications [1,2]. The ITA to the left anterior descending artery (LAD) in coronary revascularization has been proven to have a superior long-term patency rate [3], and it improves the long-term mortality and morbidity in patients with coronary artery disease [4–8] as compared to use of vein grafts to the LAD.

On the other hand, a current issue regarding the ITA graft is that competitive flow in the ITA graft causes graft occlusion

or 'string sign', which represents the narrowing of the artery along its whole length [9]. In previous reports, competitive flow usually arose when native coronary stenosis was not severe, and the patency rate of the ITA graft inversely correlated with severity of native stenosis [10–12].

Recently, various grafts such as ITA, radial artery, gastroepiploic artery, and saphenous vein (SV) graft are applied and designed in various configurations. There are several reports investigating the hemodynamic features of bypass grafts. Kawasuji and colleagues compared the flow capacities of arterial grafts and SV graft and demonstrated that the flow capacity of the in situ ITA graft which represented diastolic blood pressure, was less than that of SV graft, whose proximal anastomosis was placed on the ascending aorta [13]. When the in situ ITA and the SV graft were connected to the same coronary artery system, the patent SV graft may affect the in situ ITA graft. Such

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interactions between the SV graft and arterial bypass grafts have not yet been delineated.

The purposes of this study are to examine the effects of the graft material, for the circumflex or diagonal branch on the long-term patency of the ITA to LAD graft, and to delineate the interactive effect between the bypass grafts aiming at establishing appropriate usage of the SV graft and strategy for optimal graft arrangement in CABG.

2. Materials and methods

We reviewed the coronary angiograms of 313 patients who underwent CABG with two bypasses to the left coronary artery including one in situ ITA to LAD graft and early postoperative angiography between March 1986 and December 2006. Of these, 263 were male and 50 female with a mean age of 60.9 ± 8.9 years and a mean follow-up period of 6.8 ± 4.9 years. In our institution, early postoperative coronary and graft angiography was routinely performed about 2 weeks after surgery, except for patients with renal insufficiency, severe atherosclerosis in the aorta or aged more than 80 years. Late coronary angiography was done when patients suffered from chest pain or recurrence of angina pectoris was suspected by electrocardiogram or other clinical symptoms. Late coronary angiograms were carried out on 133 patients in this series (42.5%; 133/313). All coronary angiograms were independently evaluated by cardiologists for coronary artery stenosis and graft patency. Stenoses were grouped as 51–75% and 76–100% by a precise measurement of the minimal luminal diameter and labeled as 'moderate' and 'severe', respectively in the present study.

The in situ ITA graft or the SV graft as an aorto-coronary bypass was exclusively used in an individual fashion for these patients. The patients who did not undergo early postoperative angiography, who had graft occlusion in either of two bypass grafts to the left coronary artery in the early angiography, and who had a gastroepiploic artery, radial artery, sequential or composite graft, were excluded from this study. Patients whose bypass graft to the right coronary artery was occluded, but both bypass grafts to the left coronary artery were patent in early angiography, were included. Ninety-three patients had two bypass grafts in the left coronary artery, and 220 patients had two bypass grafts in the left coronary artery and 1 in the right coronary artery. The second target site in the left coronary artery was the left circumflex artery (LCX) in 270 patients and the diagonal branch (Dx) in 43 patients.

Patients were divided into two groups based on the graft selection for the second target site in the left coronary artery. The BITA group comprised 64 patients in whom the bilateral in situ ITAs were individually anastomosed to the LAD and the second target site (Fig. 1). In the ITA/SV group, 249 patients had a single in situ ITA to LAD and the SV graft to the second target site in the left coronary artery (Fig. 2). Characteristics of both groups are shown in Table 1. In addition, the ITA/SV group was divided into two subgroups based on the severity of native left coronary stenosis between two distal anastomotic sites, which was referred from preoperative coronary angiography (Fig. 3). The subgroup S comprised 189 patients who had

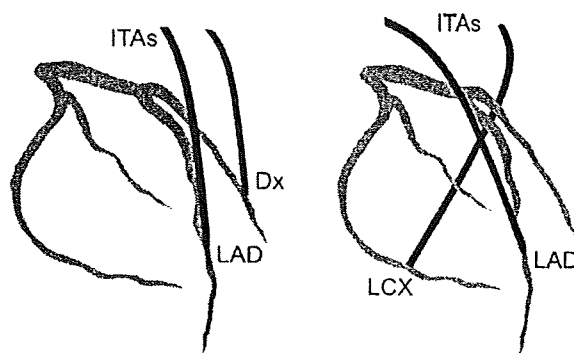


Fig. 1. In the BITA group, bilateral ITAs were individually anastomosed to LAD and the diagonal or circumflex artery. Solid lines indicate the in situ ITA. ITA: internal thoracic artery; LAD: left anterior descending; Dx: diagonal branch; LCX: left circumflex artery.

severe (76–100%) stenosis between two anastomotic sites, while the subgroup M consisted of 60 patients who had moderate (51–75%) or less stenosis between two anastomotic sites. For example, the subgroup S included patients who had severe stenosis at the origin of LAD or circumflex, and the subgroup M included patients with the stenotic lesion localized in the left main trunk.

3. Operative technique

Our current operative technique has been described previously [14]. In brief, our standard technique since 2000 was off-pump CABG without aortic manipulation. Additionally, we preferably use the bilateral in situ ITAs when we place two bypass grafts to relatively large branches in the left coronary artery region in patients without considerable operative risk, such as chronic obstructive pulmonary disease or an advanced age of more than 75 years. A suction-type stabilizer and an apical heart positioner were used for off-pump CABG. The surgical field was maintained by a CO₂ blower and an intracoronary shunt.

Before introduction of an off-pump operation, conventional CABG was performed with ascending aortic and bicaval cannulations. The core temperature was maintained between

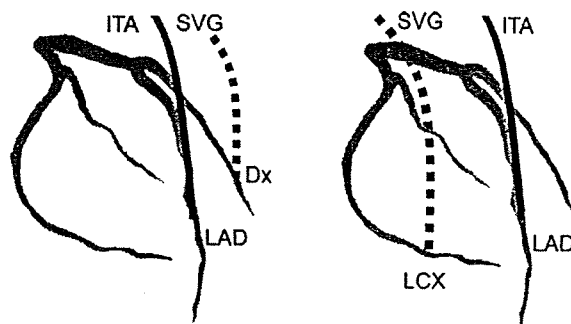


Fig. 2. In the ITA/SV group, an in situ ITA was anastomosed to LAD and the SV graft were anastomosed to Dx or LCX as an aorto-coronary bypass. Solid lines and dash lines indicate ITA and SV graft, respectively. ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; Dx: diagonal branch; LCX: left circumflex artery.

Table 1
Baseline characteristics in both groups

Characteristics	BITA	ITA/SV	p value
Number of patients	64	249	
Age	59.8 ± 8.7	61.2 ± 8.9	0.30
Follow-up period (years)	4.6 ± 4.4	7.3 ± 4.9	<0.0001
Male/female	59 (92%)/5 (8%)	204 (82%)/45 (18%)	0.046
Hypertension	40 (63%)	117 (47%)	0.03
Hypertipidemia	38 (59%)	126 (52%)	0.34
Diabetes mellitus	30 (47%)	109 (44%)	0.66
LVEF (%)	50.4 ± 12.2	52.8 ± 13.5	0.26
Operative procedure			
On-pump/off-pump	29 (45%)/35 (55%)	248 (99.6%)/1 (0.4%)	<0.0001
Second target branch in the left coronary artery			
Dx/LCX	6 (9%)/58 (91%)	37 (15%)/212 (85%)	0.26
+ Bypass graft to RCA	19 (30%)	201 (81%)	<0.0001

Mean ± standard deviation. LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting; LAD: left anterior descending artery; Dx: diagonal branch; LCX: left circumflex artery; ITA: internal thoracic artery; RCA: right coronary artery; SV: saphenous vein.

32 °C and 34 °C. Intermittent tepid blood cardioplegia was infused antegradely and retrogradely.

The ITA was harvested in either conventional (combined with vein and fascia), semiskeletonized (partially combined with vein) or skeletonized fashion [14]. All distal portions of ITA grafts were greater than 1.5 mm in diameter assessed by insertion of a 1.5-mm flexible probe.

4. Long-term patency rate of the ITA to LAD bypass

We analyzed the long-term patency of the ITA to LAD bypass and examined the effects of graft materials anastomosed to the second target site in the left coronary artery and severity of the native coronary stenosis between two distal anastomotic sites.

5. Statistical analysis

The continuous variables are expressed as mean values ± standard deviations and compared between the two groups by using Wilcoxon rank-sum test. The data of two independent

groups were compared using Fisher's exact probability test. The Kaplan–Meier method was used to determine the cumulative graft patency rate and log-rank test was used to compare two groups. The differences in the outcomes were considered statistically significant at a probability value of <0.05.

6. Results

The baseline rate of off-pump CABG in the BITA group was significantly higher than that in the ITA/SV group. Male and hypertensive patients were included in the BITA group with a significantly higher rate as compared to the ITA/SV group. On the other hand, the population of CABG with three distal anastomoses was significantly higher in the ITA/SV group than in the BITA group.

In the ITA/SV group, 14 bypass grafts were occluded during the follow-up period (5.6%; 14/249), whereas, all the ITA-LAD bypasses remained patent in the BITA group. The cumulative patency rate of the ITA-LAD bypass in the ITA/SV group was 94.9% at 5 years and 81.4% at 10 years (Fig. 4).

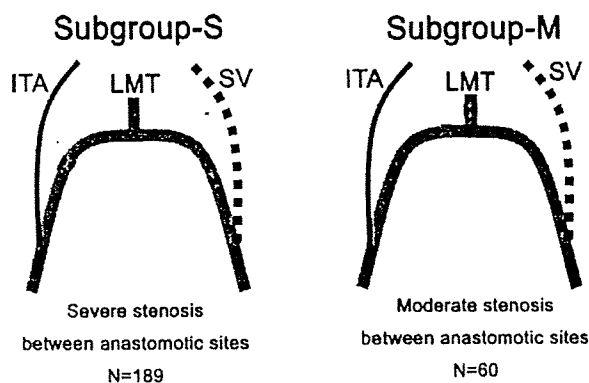


Fig. 3. Patients in the ITA/SV group were divided into two subgroups in regard to severity of the native coronary stenosis between two anastomotic sites (solid line: ITA; dash line: SV graft). ITA: internal thoracic artery; SV: saphenous vein; LMT: left main trunk.

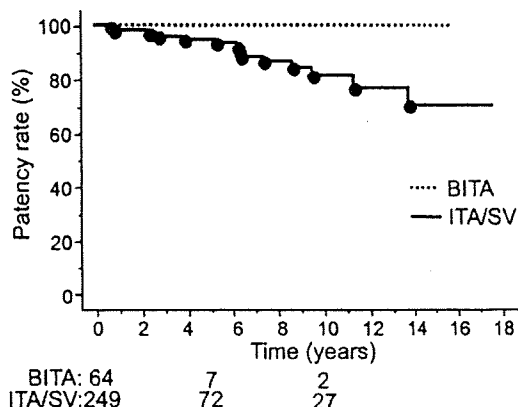
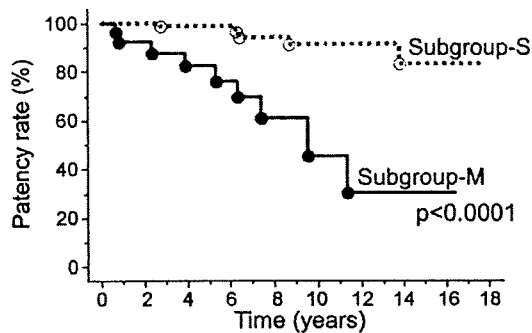


Fig. 4. The cumulative patency rate of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 100% in the BITA group and 81.4% in the ITA/SV group. Number at risk is described below the x-axis.



Subgroup-S: 189 58 24
 Subgroup-M: 60 14 3

Fig. 5. The cumulative patency of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 91.2% in the subgroup S and 45.6% in the subgroup M ($p < 0.0001$). Number at risk is described below the x-axis.

In a comparison of two subgroups of the ITA/SV group, the ITA to LAD bypass graft was occluded in five patients of the subgroup S (2.6%; 5/189) and in nine patients of the subgroup M (15%; 9/60). The cumulative patency rate of the ITA to LAD bypass in the subgroup S were 98.6% at 5 years and 91.2% at 10 years, whereas those in the subgroup M were 82.3% at 5 years and 45.6% at 10 years ($p < 0.0001$) (Fig. 5).

The early and late coronary angiograms of 14 patients with occlusions of the ITA to LAD bypass were carefully reviewed. In 4 out of 14 patients, there were no stenoses of the ITA-LAD bypasses in the early angiograms. However, through SV graft injection of the late angiograms, strong bypass flow from SV graft opacified not only the left circumflex artery but also LAD. In addition, the ITA grafts were visualized by retrograde flow and exhibited 'string sign' (Fig. 6).

7. Discussion

Significant differences in hemodynamic characteristics between the ITA graft and the SV graft have been reported.

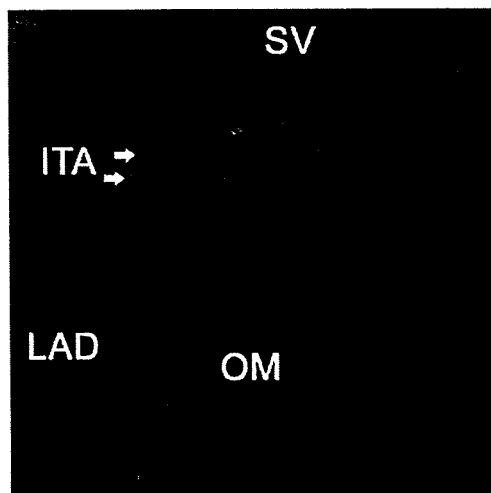


Fig. 6. The distal portion of the ITA graft was visualized by retrograde flow from the SV graft injection (arrows). ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; OM: obtuse marginal branch.

The SV graft as the aorto-coronary bypass has higher flow capacity than the in situ ITA graft [13] owing to higher blood pressure directly from the ascending aorta and its greater diameter of the SV graft, as compared with those of the in situ ITA graft. Therefore, we presumed that if the patent SV graft to the left coronary artery was present, it might decrease the blood flow in the in situ ITA graft, and diminish its advantage as arterial materials.

In the present study, we attempted to prove the interactive effect between the individual bypass grafts with the different blood source, investigating from a viewpoint of blood flow and patency of arterial grafts. To minimize a bias associated with the bypass grafts and coronary arteries, only patients who had a simple graft arrangement and coronary artery lesions were included. In particular, to eliminate procedural differences, such as on-pump versus off-pump and technical failure, which would be one of the most fundamental biases, patients who had early occlusion of the bypass graft to the left coronary artery were entirely excluded. We focused on the patency of the ITA to LAD bypass, because it is clinically important for survival after CABG.

The results of this study demonstrated that the presence of the patent SV graft anastomosed to the second target site in the left coronary artery reduced the patency rate of the ITA to LAD graft, particularly when the native coronary stenosis between the two distal anastomoses in the left coronary artery was not severe. It was suspected that a mechanism of occlusion of the ITA-LAD bypass was associated with competitive flow from the SV graft by our careful observation of the late coronary angiogram about string of the ITA-LAD bypass.

We previously investigated competitive and reversal flow in sequential and composite arterial grafts, and identified that some specific situations, which were related to two or more coronary branches and arrangement of bypass grafts, significantly increased the incidence of competitive and reversal flow [15]. Moreover, we reported that the graft arrangement with maximized antegrade bypass flow in the arterial grafts played an important role in achieving the advantages of arterial materials and minimizing the incidence of cardiac events after CABG [16]. Since arterial graft occlusion due to insufficient bypass flow mostly occurs within 1 or 2 years [10,16], the long-term prognosis could be jeopardized. We believe that this interactive effect from the SV graft should be avoided as far as possible to achieve the advantage of the arterial graft.

Schmidt and colleagues recommended the use of arterial graft to the second target branch in the left coronary artery because of the superior survival rate [17]. Importance of the circumflex artery over the right coronary artery and inferior patency of the venous graft [18] are considered as primary reasons for the superiority. Results of our study may suggest that interactions of the SV graft on the in situ ITA may be another possible explanation for the superiority of arterial grafting to the second target site in the left coronary artery. We suppose that the use of the SV graft in the right coronary artery region hardly affects the bypass flow in the ITA to LAD graft.

Implications of this study are as follows: patency rate of the ITA to LAD bypass had been believed similar, irrespective

of graft arrangement for the second target branch in the left coronary artery. However, the results of this study strongly suggested that the in situ ITA to LAD bypass only, bilateral ITA grafting, sequential grafting and the composite Y graft to the LAD and the second target branch will provide the higher patency rate of the ITA to LAD bypass than the use of the SV graft to the circumflex or diagonal branch, when the stenosis between the two anastomotic sites in the native left coronary artery is moderate or less. Even in patients unsuitable for bilateral ITA harvest, the avoidance of the SV graft from ascending aorta should be considered.

We suggest that, on the contrary, the in situ ITA to LAD bypass concomitant with the aorto-coronary bypass is suitable when the left coronary and circumflex artery is remarkably large or a large amount of bypass flow is required. The isolated ITA to LAD can be a reasonable option of choice in patients with a localized lesion in the left main trunk. For the concomitant diagonal branch, Dion and colleagues reported excellent long-term patency of sequential grafting with the in situ ITA [19]. According to our previous study, when the circumflex artery is almost occluded and the stenosis in LAD is moderate, the composite Y graft is not recommended, because of the high incidence of competitive flow in the ITA to LAD bypass graft [15]. The severity and location of stenoses in the native coronary artery, the size of the target branch, the distance between and positional relationship of the two target sites, quality of the ITA graft, anticipated flow demand and atherosclerosis of the aorta, etc., should be taken into account for decision of strategy for the second target branch in the left coronary artery.

Limitations of the present study are as follows: first, because this study was retrospective and non-randomized, some differences regarding the characteristics of the BITA and ITA/SV groups were noted. Furthermore, the sample size was considered relatively small. However, the influence of these differences on the late angiographic results could be minimized, because early angiography confirmed that all 313 patients had patent grafts to the left coronary artery, and 133 (42.5%) patients underwent late angiography. Since more than 85% of patients after CABG underwent early angiography in our institution between 1986 and 2006, we considered that the selection bias for angiography was not so significant. Second, although the follow-up period was not enough for development of vein graft disease and ischemia in the left coronary artery region, it would be sufficient for examining correlations between the insufficient flow and arterial graft occlusion, as compared with previous studies [10,16]. In addition, progression of native coronary artery disease during the follow-up period, the length and the location of the stenotic lesion, the size of the circumflex coronary artery could not be taken into account. Moreover, peripheral vascular resistance in the myocardial tissue, and flow demands could also have important roles in the coronary perfusion. However, these factors could not be quantified by reliable methods. The effects of diabetes, hypertension, hyperlipidemia, aspirin and statin medical therapy may be the next concern in the future.

It may be controversial in management of 'string sign', which differs from graft occlusion. Several previous reports documented that the ITA graft with string sign could recover its own lumen when the native coronary artery disease

became severe [20,21]. In the statistical analyses of this study, graft occlusion probably associated with string sign was not separated from the other graft occlusion. The reasons for this were as following: (1) contrast medium from the ITA injection did not reach LAD, (2) reversibility is not guaranteed for all ITA grafts presenting string sign, (3) the purpose of this study is to delineate the effect of the abundant blood flow from the SV graft, and (4) it is generally accepted that both graft occlusion and string sign are commonly associated with the abundant native coronary flow.

When we use the combination of the in situ arterial and in situ aorta-coronary venous grafts, it would be necessary to pay attention not to place influence on the patency of the important bypass especially created with the in situ ITA graft. This study is not conclusive in nature and is hypothesis generating only. Further investigations for interactive effects and considerations for the appropriate usage of the SV graft are necessary to establish the strategy for graft arrangement.

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Letter to the Editor

Fractional flow reserve: a reliable tool in bypass strategy

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Keywords: Fractional flow reserve; Intermediate coronary stenosis; Coronary bypass strategy

I read with interest the article by Kawamura et al. entitled 'Patency rate of the internal thoracic artery to the left anterior descending artery bypass is reduced by competitive flow from the concomitant saphenous vein graft in the left coronary artery' [1]. The authors proved that long-term patency of the internal thoracic artery (ITA) left anterior descending (LAD) coronary bypass was affected by the presence of the patent saphenous vein graft (SVG) to the left coronary artery, particularly when the native coronary stenosis between the two anastomotic sites was not severe.

I agree that the greater diameter of the SVG as compared with the in situ ITA graft can be associated with lower flow resistance. It was proved by pressure wire measurements by Glineur et al. who found significantly higher resistance in left ITA compared to venous grafts [2].

However this lower resistance could cause significant competitive flow only in case of non-significant flow limitation between the two distal anastomoses. Kawamura et al. drew attention to the anticipated flow demand of the second target branch in the left coronary artery, but they doubted that this factor could be quantified by reliable methods. Here I would like to argue for the intracoronary pressure wire measurement during induced maximal hyperemia as a practical tool for reliable assessment of the functional severity of coronary stenoses. Botman et al. evaluated the patency of bypass grafts in relation to the preoperative angiographic and functional severity of the coronary lesions assessed by fractional flow reserve (FFR) determination. They found 21.4% occlusion rate of the bypass grafts on functionally non-significant lesions (FFR > 0.75) in contrast to 8.9% among those on functionally significant lesions (FFR ≤ 0.75) [3].

In our institute we plan the surgical revascularization strategy on the basis of extensive consultation with the invasive cardiologists. In our routine the FFR measurements give valuable information in the decision about grafting vessels with intermediate lesions [4]. Integrating these functional data into bypass strategy helps to avoid the inappropriate use of grafts [5]. In my opinion, careful evaluation of functional consequences of coronary lesions can contribute to find the right strategy in multiple coronary grafting.

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Reply to the Letter to the Editor

Reply to Maros

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Keywords: Coronary artery bypass strategy; Competitive flow; Fractional flow reserve

We thank Dr Maros [1] for his meaningful comments, and agree with the importance of fractional flow reserve (FFR) in coronary revascularization strategy. FFR is calculated as the ratio of blood pressure in the proximal and distal sites of the coronary stenosis after induced hyperemia [2], and has been generally accepted as a reliable method for detecting myocardial ischemia and assessing functional severity of coronary stenosis. Particularly, FFR is considered useful for decision making of bypass grafting to the intermediate stenosis lesion to avoid creating non-functioning bypass, which will be occluded in association with flow insufficiency [2].

One of the major issues regarding selecting graft material is that the situations, which truly necessitate the saphenous vein graft, have not been fully delineated. The venous graft as the aorto-coronary bypass has higher intraluminal pressure and lower resistance of the conduit itself than the in-situ internal thoracic artery (ITA) graft [3]. It is widely considered that ITA grafting can give rise to hypoperfusion syndrome and residual myocardial ischemia in spite of graft patency when its flow capacity is insufficient for huge flow demand of the myocardium. We, therefore, believe that assessment of peripheral vascular resistance and flow demands in the myocardium would be valuable for appropriate usage of the venous graft.

Most of previous studies about FFR focused on management of the intermediate stenosis, not on predicting shortage of flow capacity of the ITA graft, nor necessity of the venous graft. In addition, we suggested complicated mechanism of competitive flow, which was found in the ITA to left anterior

descending artery graft and caused by the venous graft to the circumflex branch [4]. As Botman and colleagues mentioned previously [5], we consider that usefulness of FFR in selection of graft materials, including in patients with left main trunk or proximal left coronary artery disease, has not been proved, and may be the next concern in the future.

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Letter to the Editor

Priming of cardiopulmonary bypass: effect on renal function

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Keywords: Anaesthesia; Cardiac, other; Congenital, cyanotic; Extracorporeal circulation

I have read with interest the work by Loeffelbein et al. regarding the use of high colloid pressure priming on cardiopulmonary bypass (CPB) [1].

The benefits of such therapeutic actions are important. However I would disagree with some of their conclusions.

The authors state in the conclusion that '*...does not affect renal function more severely than in paediatric patients undergoing cardiac surgery on CPB with blood priming*', moreover in the discussion they mention that '*According to our results, renal damage on CPB may be a temporary effect, which normalises quickly*'.

It has been reported that in some paediatric populations undergoing CPB with blood priming, renal function does not deteriorate; on the contrary some of the specific tests used to study renal function in those patients show that renal function is well preserved [2].

As in adults, CPB in paediatric patients has not been shown to be an independent risk factor for renal dysfunction or acute renal failure [3]. The focus should be the postoperative period with all the haemodynamic changes and the therapeutic manoeuvres that patients go through. To our knowledge there is no study, so far, showing specific data from that complex surgical period.

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* The authors of the original paper [1] were invited to reply to this Letter to the Editor but they did not respond.

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経皮的冠動脈形成術の既往が冠動脈バイパス術に及ぼす影響

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Nakajima H, Kobayashi J: Negative effects of previous PCI on outcomes of coronary artery bypass grafting. J Jpn Coron Assoc 2009; 15: 78-80

I. はじめに

虚血性心疾患においては、狭窄を有する冠動脈に対して血液の供給を増加させ虚血を改善することが治療であり、これを安全かつ効果的に達成され、持続性のある治療方法が選択される。本来、遠隔期も含めた生命予後の良い治療法が選択されるべきであるが、現状においては、カテーテルによる低侵襲な治療(percutaneous coronary intervention; PCI)の対象となり得るかがまず検討され、その適応から外れた症例が冠動脈バイパス術(coronary artery bypass grafting; CABG)へと外科に送られてくることがしばしばである。PCIは、CABGとの比較において、治療そのもののリスクが圧倒的に低く、低侵襲で入院期間が短く、疼痛など身体的な負担が軽い。これらの理由から患者側のPCIを受けることへの抵抗感が小さいことなどがこの背景にある。

PCIの及ぼすCABGへの影響については、これまでもしばしば議論の対象となってきた。特に、大規模な前向き試験や登録研究のsubstudyとして結果が公表されてきており、活発になってきている。

II. これまでの知見について

まず、これまでに報告された関連する文献の詳細について整理した。2008年IMAGINE試験の副研究として公表されたChocronらの論文によれば、PCIの既往を有するCABG施行例430例と既往のない2059例の比較、治療前背景による補正、多変量Cox hazards regression model解析により、PCIの既往は、心事故の独立した危険因子であるとの結果を示している¹⁾。IMAGINE試験は、左室駆出率が40以上のstable patientsを対象として行われた、ACE(angiotensin-converting enzyme)阻害剤の効果を調べるためのrandomized placebo-controlled試験であり、PCIの影響をみるための試験ではない。

Hassanらの論文では、初回CABGの約6000例(そのう

ちPCI後は約900例)を対象としている。術前PCI施行群は、合併症が少なく、比較的低位リスク群でありながら、一方で緊急と有症状例が多いなど、CABG前患者背景の違いに特徴がある²⁾。これらを補正後、また、propensity-matchした2群間の比較により、PCIの既往は早期死亡の独立した危険因子であるというものである。最終的に、PCIの既往は、独立した危険因子であると結論している。これについての合理的な理由付けとして、彼らは、PCI後にCABGとなる症例は再狭窄を生じるなど動脈硬化の進行が著しいこと、PCIの成功が側副血行路の発達を妨げることが緊急例や症状の発現にかかわっていること、最終的にCABGを行うこととなっても、はじめからCABGを行うこととした場合に想定されるより、より末梢の小さな血管との吻合を強いられ、環流される領域は狭くなると考えられることなどを挙げている。

また、Barakateらも、PCI後のCABG群(361例)と初回CABG群(11909例)とを比較した³⁾。結論としては、両群間に早期死亡率、合併症の発生率に有意な差は認められないものの、CABGが先延ばしになることによる検査やPCIなどのコストがかさむことを指摘し、現状の大きな問題点としている。一見、先のHassanらの結果と相反するものようであるが、この論文ではコストの面に主眼を置いており、術前PCIの医学的な効果についての検討は十分ではなく、術前因子の違いに対する統計学的な補正などは行われておらず、必ずしも相反しているとはいえない。

Bairらによる5年以上のフォローアップ期間を有する多枝病変に対するCABGとPCIの大規模登録研究によれば、治療前背景をadjustした後の両者の比較では、これも、間接的なデータではあるものの、患者群の全体としてはPCIよりCABGの予後のほうが良好であったが、今回治療前にPCIが行われている患者に限定すると、PCIのほうがCABGより治療後の生存率が良好であった⁴⁾。

III. どのような機序によるものか

PCIの既往を有することが、どのような機序でCABGへ悪影響を及ぼしているのかについて、十分解明されてい

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ない。

想定される機序の一つは、PCIを行うことによって起こる心臓および冠動脈への直接の変化である。ステントの植え込みが成功であると評価されても、変性の進行した冠動脈への血管形成により、形態的な変化を来し、これによりおもな枝の内腔が保持されてもしばしば標的以外の枝の閉塞や、末梢への debris の塞栓などの可能性がある。さらに、Hassan らの指摘にもあるように、再狭窄を生じた際には、PCIを行わずに CABG を行った場合と比較して、一般に、より末梢の小さな血管との吻合が必要と予想され、吻合の確実性の低下や還流される領域は狭くなることの影響が考えられる。

開存するステントに対する CABG の悪影響として報告されている事柄としては、外科的な操作に伴うステントの kinking や変形による狭窄の可能性も指摘されている⁵⁾。おそらく頻度は高くないものの、前下行枝領域や回旋枝領域ではこれが生じやすく、右冠動脈ではまれであるとされている⁶⁾。当然のことながら、この末梢にいわば予防的にグラフト吻合を行えば、開存ステントからの血流とバイパス血流の競合 (competitive flow) により、比較的早期の graft failure の懸念が大きくなる。

もう一つ想定される機序としては、PCIを行うこと、もしくは PCI 後に再狭窄が起こることなどが、患者群をふるいにかけている可能性がある。植え込まれたステントの内部に狭窄が出現するかどうか、本当に動脈硬化のアグレッシブな進行や CABG の効果を弱めることの指標となり得るのかについては明らかでない。Shishebor らは、ステント内狭窄を有する例とパテントステントを有する群とで Cleveland Clinic での CABG 後の予後の比較を行っている⁷⁾。このなかでは、興味深いことにステント内狭窄の有無にかかわらずステントされた冠動脈枝にはバイパス吻合を行っている。ステント内の狭窄の有無にかかわらずバイパス吻合された結果、ステント内狭窄の有無は予後と関連しなかった。ステントが植え込まれた枝には両群間に差があり、症例数も十分ではないが、このデータについて別の見方をすると、ステント内の再狭窄の有無は必ずしも動脈硬化の進行度や CABG の治療効果の大小、CABG 後の予後不良群であることを反映しているとはいえないことを示唆していると考えられる。開存ステントに対する CABG は、competitive flow によるグラフト閉塞などを引き起こすと思われる。もともと一般的には行われませんが、今後、DES により再狭窄率が低下するとバイパス吻合の必要性が低下し、反対に competitive flow など CABG のネガティブな部分が大きくなると予想される。

また、ステント内狭窄の発現とグラフトの開存性との関連をみた Gaudino らの報告によれば⁸⁾、ステント内の再狭窄例では、動脈硬化の進行性が著しく、ステント内とグラフト内で同様の機序が働くと推測され、静脈グラ

フトの開存率が低く、NO 分泌などの点で動脈グラフト優位性を述べているが、症例数などの点から説得力は十分ではない⁸⁾。

さらには、もともと CABG の適応でありながら全身状態不良などにより、これを回避し PCI を施行してみたものの、やはり狭窄の再発や病変の進行により、CABG へと回ってくる症例も実際にはあり得る。この場合、PCI の既往を有する群はハイリスク群となると予想される。Hassan らの患者背景はこれには当てはまらない。

IV. 当センターでの成績

当センターにおいては、全動脈グラフトによる off-pump での完全血行再建を標準術式としている。2001 年以降の当センターでの成績をみると、これまでのところ、早期成績と PCI の既往の有無とは有意な関連は認めなかった。また、術後早期のカテーテル検査の結果では、グラフトの開存率、competitive flow の頻度には差がなかった。ただし、手術中に計測したグラフト流量をみると、PCI の既往なしの群は、PCI の既往ありの群との比較において有意にグラフト流量が多かった (図 1)。このことは、先に述べたような、PCI を行うことによる還流域の低下や、flow demand の低下などを引き起こしていることを示唆するものである。遠隔期成績では、PCI の既往ありの群はなしの群と比較し有意に心事故の発生が多かった (図 2)。ただし、術前背景に有意差がある。

V. まとめ

PCI の既往が CABG に与える影響の解明を主目的とした論文はなく、これまでのところ十分に議論が尽くされているとはいえない。今後、先行する PCI がどのような患者群でどのような機序により悪影響を生じるか、PCI

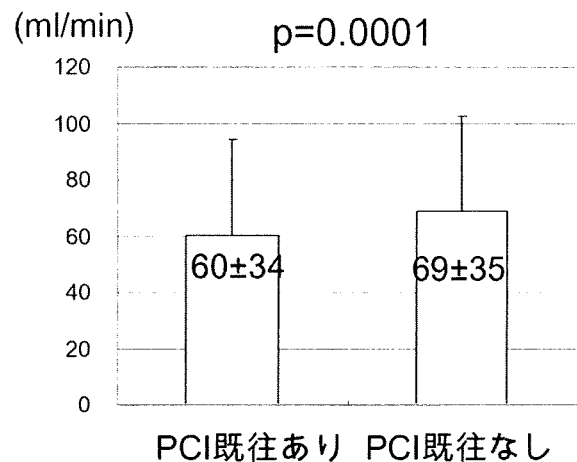


図 1 Total graft flow by intraoperative measurement.

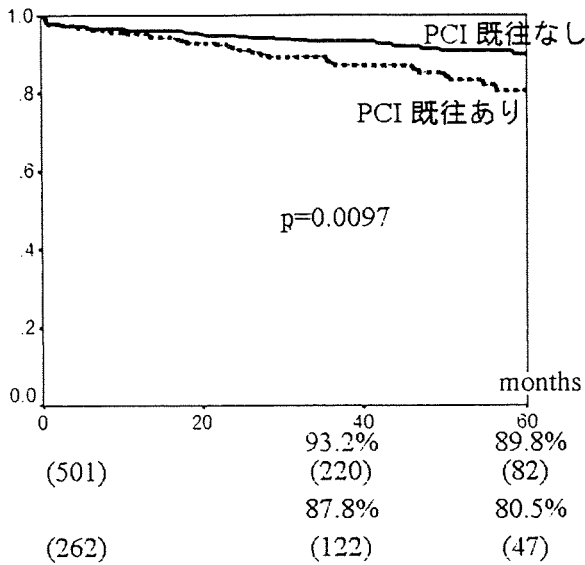


図2 CABG 術後心事故回避率
PCIの既往の有無により予後に差が認められるが、術前の患者背景に有意差がある。

およびCABGの適応決定にどのように加味すべきかを明らかにし、議論を深めていくことには大きな意義があり、焦点を絞って研究を重ねていく必要がある。

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2) 高リスク症例（糖尿病，透析患者，再手術，COPDなど）に対する治療戦略

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はじめに

近年，冠動脈バイパス術（CABG）の手術リスクは軽減し，標準術式としてoff-pump CABGが広く認知されるとともに，一般にハイリスク例の割合が増加している。高齢化に伴う肺疾患や腎障害など他臓器の障害の合併例が増加し，また，動脈グラフトの多用や上行大動脈の粥状硬化など，手術適応や術式選択に際して考慮すべき要因も多様化し，一概に議論することはできない。ここでは，ハイリスクとされる

要因について，どのように外科治療方針に反映させるべきかについて，過去の文献から確立されてきた治療指針に，当センターにおける経験や最新のデータを踏まえての今後の展望について考察を加味し，まとめた。

低左心機能

低心機能例は，全身状態が不良な例も多く，正常心機能例と比較すると当然ながら手術死亡率が高い。Off-pump CABGが一般的にハイリスク症例に対する手術リスクを軽減しているが，人工心肺が必要か，off-pumpが可能かで手術リスクに大きく差があると考えられる。そして，術中にoff-pump CABGから，緊急にon-pumpへconversionすることは，当初からon-pump CABGで施行した症例，off-pump CABGを完遂した症例より合併症の発生率が高く，術

前の十分な評価と適切な手術計画が重要である^{1,2)}。

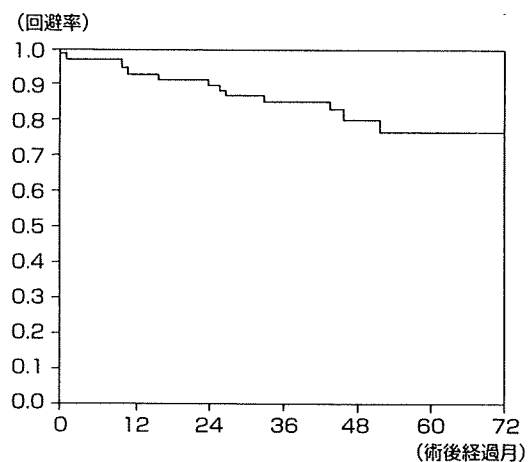
心拡大、駆出率の低下と共に左室瘤を有する場合には、人工心臓のリスクや上行大動脈の性状などの状況が許せば、左心室の形成術を行うことで左室駆出率と予後の改善を期待し得る。また、虚血性僧帽弁閉鎖不全症の存在は、CABG術後の心不全や死亡のリスクとされており、予後を悪化させ得る。このため、Ⅲ度以上の重度の逆流に対しては、CABGと同時に僧帽弁手術を行うことが、現時点では標準的な治療戦略といえる³⁻⁶⁾。一方で、僧帽弁閉鎖不全症に対して、CABG単独とCABGプラス僧帽弁手術の術後生存率には差がないとする報告もある⁷⁾。逆流がⅡ～Ⅲ度の中等度逆流に対して僧帽弁手術を同時に行うかについてはさらに議論の余地がある。積極的な僧帽弁手術により予後の改善が得られるとする報告と、変わらないとする報告とがある。これらの遠隔成績は、on-pump CABGとCABGプラス僧帽弁手術との比較であり、わが国で標準的となっている複数の動脈グラフトを使用したoff-pump CABGとon-pump CABGプラス僧帽弁手術の2つの戦略の比較ではない。人工心臓の使用、非使用にかかわらず、外科的な血行再建は着実に達成しつつ、さらに、僧帽弁手術を付加するかどうかを、僧帽弁閉鎖不全の重症度や心不全の既往のみから決断することには限界がある。

さらに近年は、動脈グラフトの多用により僧帽弁に対しての再手術となった際には、開存グラフトの存在により困難が予想されることも十分あり得る。このため、冠血行再建と同時に、軽度から中等度逆流に対して僧帽弁形成術をより積極的に行うことも妥当と思われる。当センターの成績によれば、左室機能が低下した症例に対しても単純CABGについては、off-pump CABGの対象であり、最近10年間に施行されたoff-pump CABGのうち、約6.5%は左室駆出率

が30%以下の超低左心機能症例であった。これらはいずれも僧帽弁閉鎖不全は中等度以下で、十分完遂可能である。このことは、ハイリスク例の手術成績の向上に寄与している。しかしながら、退院後左室remodelingと共に、虚血性僧帽弁閉鎖不全が発症する症例があり、平均3.8年のフォロー期間において5年後の僧帽弁閉鎖不全の累積回避率は約75%であった(図1)。虚血性僧帽弁閉鎖不全症の進行の的確な予測が必要となってくるが、これらの症例では、心筋梗塞部位や、左室拡大の程度や駆出率は、虚血性僧帽弁閉鎖不全の重症化の予測には有用とはいえなかった。これには、乳頭筋および左心室の形態や機能の評価が必要と思われ、僧帽弁手術への適切な症例の選択方法は、今後検討すべき課題である。

腎機能障害

腎機能障害は近年増加している合併症の1つである。術後の人工透析は手術死亡と高率に関連し⁸⁾、術前の腎機能障害も手術死亡のリスクと考えられている。また、術前慢性透析の患者は、CABG術後の死亡率で約3倍、縦隔炎や脳梗塞など重篤な合併症のリスクも増加する⁹⁾。



■ 図1 冠動脈バイパス術後の虚血性僧帽弁閉鎖不全の累積回避率

これに対して, 人工心肺使用を回避するoff-pump CABGは周術期合併症の軽減に有効とされる¹⁰⁾.

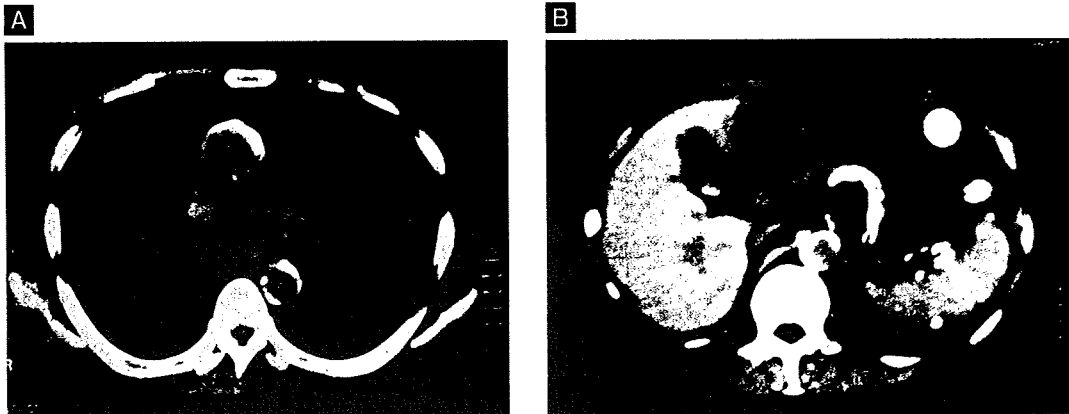
腎不全例については, グラフト選択がしばしば問題となる. やはり, 少なくとも片側内胸動脈の使用は標準的であるが, 橈骨動脈は基本的に使用できない. また, 透析症例や糖尿病性腎症の場合には, 両側内胸動脈の使用には創治癒遅延などの合併症の懸念があり, 多枝バイパスを動脈グラフトのみで行うことは困難なことも多い. しかしながら, 上行大動脈の石灰化 (図2A) や腹部分枝の石灰化 (図2B) などにより, 全身状態に比して両側内胸動脈など過大な侵襲ともなり得る術式を選択せざるを得ないことも多い.

最近約10年間の当センターにおける慢性透析症例に対するCABGの経験からは, まずグラフトに関しては, 胃大網動脈の性状にやや難があることが特徴で, その他の内胸動脈および静脈グラフトの開存率は非透析症例と同等で良好であった. しかしながら手術成績については, 1カ月以内の死亡がやはり約4%と比較的高く, 早期合併症としては, 低心拍出量と縦隔炎や腸管虚血などが認められている. また, 遠隔死亡

の半数は, 心臓以外の原因の呼吸不全や腸管の合併症によるものであった. このことから, 術前に全身の評価を行い, 手術に際しては侵襲を最小限とし, 感染や腸管の合併症を念頭に置いた上での術式やグラフトの選択, さらに周術期管理を行う必要がある.

呼吸機能低下

呼吸機能障害のうち, 心疾患にしばしば合併するのは慢性閉塞性肺疾患 (chronic obstructive pulmonary disease ; COPD) である. COPDは, CABGの死亡率, 合併症率を増大させ, 入院も長期化しやすい. 従来術式では, 人工心肺の使用が炎症性サイトカインを活性化させ, 肺機能に悪影響を与えることが原因と考えられてきた. 近年, off-pump CABGが標準的となっても, CABGのリスク因子として考えられているものの, 人工心肺の使用の有無で比較すると, 術後の呼吸機能の回復や, 人工呼吸期間, ICU滞在日数などの短縮にoff-pump CABGは有効であった. 特に胸骨を切開しないMIDCAB (minimally invasive direct coronary artery bypass grafting) では影響が最も少ないとされている^{11, 12)}. この術式は, 標的冠動脈枝が左前下行枝領域に



■ 図2 狭心症に対して冠動脈バイパス術の適応となった慢性透析の単純CT画像

橈骨動脈の使用はできず, さらに上行大動脈が著明に石灰化し, 腹部動脈にも著明な石灰化が連続している. 静脈グラフトの中樞吻合を上行大動脈に行うことも胃大網動脈の使用もできない.



■ 図3 MIDCABによる左内胸動脈-左前下行枝バイパスの術後造影
 外科的血管再建の最大のメリットを最小限の皮膚切開で提供することが可能である。

限定している例では、疼痛の軽減や出血量の減少、入院日数の短縮などメリットがある(図3)。

脳血管障害

脳障害は、CABG術後の最も忌むべき合併症の1つである。発症の頻度は定義により幅広いが、術前の脳梗塞の既往は周術期の脳障害発症の危険因子である。

術後脳神経障害はType1, Type2の2つに区別される。Type1は局所症状を伴う脳神経障害、昏睡昏迷と関係し重篤である。Type2は知的機能の低下や記憶障害で、双方に共通する

危険因子は高齢者(70歳以上)と高血圧である。

まず、Type1の危険因子は、上行大動脈の粥状硬化、脳障害の既往、大動脈内バルーンポンピングの使用、糖尿病などであった。上行大動脈の粥状硬化は最も強い危険因子で、心臓手術の手術操作と関連が強い。このため、CABGに際しては、術前CTによる評価は必須で、石灰化が認められる症例については、上行大動脈への人工心肺カニューラ挿入、大動脈遮断、partial clampによる静脈グラフトの中枢吻合など、上行大動脈への手術操作を回避することが必要である。そのための方法として、大腿動脈や鎖骨下動脈の使用、心室細動下の心臓操作や、人工心肺そのものの使用の回避があり、静脈グラフトの中枢吻合デバイスや自動吻合器も有効と考えられている。次に、Type2については、機序としては微小な塞栓などが想定されており、その危険因子として術前の飲酒や不整脈、再手術例などがあり、必ずしも上行大動脈の性状との関連は強くないとされている。

これまでの報告によれば、off-pump CABGは、大動脈への操作を回避することに有用で、結果としてoff-pump CABGは脳合併症の発生を減少させる¹³⁾。また、Type2の脳障害についても、off-pump CABGは発生が低く有用であるとする報告が多い¹⁴⁻¹⁶⁾。国内の主要施設が共同で行ったrandomized studyによれば、術後CKMBの上昇、輸血量などとともに、neuron-specific enolase値、S-100蛋白値などで有意にoff-pump CABGが良好な結果となっている¹⁷⁾。

超高齢者(80歳以上)

社会全体の高齢化と心臓手術の安全性の向上が相まって、手術対象における高齢者の割合は増加している。当センターにおいても手術適応の拡大とともに高齢者の増加が目立つ。高齢者に対しても、内胸動脈の使用は標準的であり、非使用に比べて生命予後が良好で、左内胸動脈