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Original Article

The Risk Factor Analysis for the Late Graft Failure of Radial Artery Graft in Coronary Artery Bypass Grafting

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Objective: The aim of this retrospective study was to investigate the early operative results and detect the factors influencing the fate of radial artery grafts (RAGs) by evaluating the mid-term patency.
Methods: We retrospectively reviewed 410 patients who underwent isolated coronary artery bypass grafting using RAG. RAGs were anastomosed to 526 coronary arteries. Mid-term angiography was performed in 214 patients at an average 4.9 years after the operation.
Results: The early patency of RAGs was 97.6%. Cumulative 5-year patency was 86.5% for RAG, 94.1% for LITA graft, and 81.0% for saphenous vein graft (SVG). RAG was significantly superior to SVG in mid-term patency. Individual grafting (not sequential grafting) (hazard ratio [HR]: 2.535; 95% confidence interval [CI]: 1.293–5.281; p = 0.006) and grafting to the target coronary artery with ≤75% proximal stenosis (HR: 1.947; 95% CI: 1.090–3.484; p = 0.025) were found to be independent risk factors influencing late RAG patency.
Conclusions: The patency of RAGs was superior to that of SVGs in the studied population. When using RAGs, grafting to the target vessel with severe proximal stenosis is favorable. The RAG is suitable for sequential grafting.

Keywords: radial artery graft, coronary artery bypass grafting, graft patency

Introduction

Long-term outcome after coronary artery bypass grafting (CABG) is associated with the patency of the grafts used. Because of its good long-term patency, left internal thoracic artery (LITA) grafting is acknowledged as the gold standard in CABG for revascularization of the left anterior descending coronary artery. In addition to LITA grafts, several types of arterial grafts have been used in CABG.

Among the various arterial grafts, the use of the radial artery graft (RAG) in CABG was reported by Carpentier and coleagues.[1] Initial angiographic studies revealed that the follow-up patency was not favorable. However, RAGs have been included in arterial graft since the revival of its use was reported by Acar et al.[2] Since then, RAG patency rates have been reported to range from 74% to 98% at ≥5 years after CABG.[3–6] Although early results of radial artery grafting are encouraging, issues remain with regard to long-term results. Furthermore, there remains a

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lack of consistent and robust clinical study about long-term patency comparing the RAG and the saphenous vein graft (SVG). From results of previous clinical data, the patency of the RAG may be affected by patient characteristics, anatomical characteristics of the coronary artery, and other factors. Thus, although RAGs are easily harvested and versatile and have excellent handling characteristics, some factors that potentially influence its patency remain a concern. This retrospective study was designed to investigate the early operative results of CABG using RAGs and to detect the factors influencing the fate of the RAG by evaluating its mid-term patency.

Patients and Methods

Patients

We retrospectively reviewed 410 patients who underwent primary CABG using RAGs. Operations were performed from January 1997 to December 2015. The patients' profiles are summarized in **Table 1**. In this study, there were 1462 distal anastomoses in total: 418 anastomoses were constructed with LITA grafts, 526 with RAGs, 473 with SVGs, 26 with the right internal thoracic artery, 15 with the right gastroepiploic artery, and 4 with the inferior epigastric artery. The distal anastomotic sites were summarized in **Table 2**. The mean number of distal anastomoses per patient in CABG was 3.6 ± 1.0. There were 65 (15.9%) emergent or urgent cases. Off-pump CABG was performed in 55 cases (13.4%). The mean operation time was 354.6 ± 80.6 min. In on-pump CABG cases, mean extracorporeal circulation time was 161.6 ± 42.8 min and aortic clamping time was 124.1 ± 32.4 min.

Table 1 Patients' profile

Male:female	336:74
Age (years)	64.6 ± 8.6
Obesity	80 (19.5)
Hypertension	287 (70.0)
Dyslipidemia	258 (62.9)
Diabetes mellitus	217 (52.9)
Smoking	245 (59.8)
Serum Creatinine >2.0 mg/dL	8 (2.0)
Hemodialysis	2 (0.5)
Peripheral arterial disease	45 (11.0)
History of CVA	52 (12.7)
PCI history	119 (29.0)
CCS 3, 4	156 (38.0)
NYHA III, IV	81 (19.8)
LVEF <40%	62 (15.1)
Left main trunk disease	130 (31.7)
Three-vessels disease	315 (76.8)
Two-vessels disease	84 (20.5)
One-vessel disease	11 (2.7)
Preoperative IABP	41 (10.0)

Values are expressed as mean ± standard deviation or patient number (percentage). CVA: cerebrovascular accident; PCI: percutaneous coronary intervention; CCS: Canadian cardiovascular society functional class; NYHA: New York heart association functional class; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pumping

Surgical technique

We have harvested RAGs as a skeletonized graft. The RAG was usually harvested from the non-dominant forearm. Distal anastomosis was conventionally constructed in a parallel configuration on an individual grafting. Side-to-side anastomoses in sequential RAGs were constructed in a diamond shape, and end-to-side anastomoses in sequential RAGs were constructed in a right angle or a parallel configuration depending on the graft and the coronary artery axis. The target vessel and graft arteriotomy length in the diamond configuration were tailored to prevent a "seagull" deformity. Conventionally, proximal anastomoses of RAGs were constructed on the ascending aorta. In patients whose proximal anastomoses of RAGs were constructed on the LITA in a parallel configuration.

Graft management

An Allen's test and preoperative ultrasonographical assessment of the radial artery were routinely performed.[7] After harvesting, 10 mL of papaverine solution (0.2 mg/mL in heparinized arterial blood) was injected intraluminally, and the RAG was stored in the same solutions until ready for grafting.

During intensive care unit stay, continuous drip infusion of diltiazem chloride was used (0.5 µg/kg/min) until the administration of oral drug commenced. Oral diltiazem chloride was used routinely in patients with RAGs unless contraindicated by hypotension or bradycardia. The patients with SVGs received oral warfarin potassium for 6 months.

Angiographic studies

Early postoperative coronary angiography was performed in 356 patients. Follow-up coronary angiography or multi-slice computed tomography angiography was conducted to assess graft patency in 214 patients who gave their informed consent. There were 48 symptomatic patients (22.4%). In all, 117 coronary angiographies

Table 2 Anastomotic sites

	LITA	RAG	SVG	Other
LAD	409	93	74	20
LAD	378	8	1	11
D	31	85	73	9
LCX	9	229	248	5
OM	1	113	88	2
PL	8	116	160	3
RCA	0	204	151	20
#3RCA	0	29	18	6
#4PD	0	143	78	11
#4AV	0	32	55	3
Total	418	526	473	45

LITA: left internal thoracic artery; RAG: radial artery graft; SVG: saphenous vein graft; LAD: left anterior descending; D: diagonal branch; LCX: left circumflex artery; OM: obtuse marginal artery; PL: posterolateral artery; RCA: right coronary artery; PD: posterior descending artery; AV: atrioventricular node branch

Table 3 Early operative results

Mean ICU stay (days)	1.9
Low output syndrome	15 (3.7)
Perioperative MI	6 (1.5)
Prolonged ventilation	28 (6.8)
Re-exploration for bleeding	5 (1.2)
Multiple organ failure	2 (0.5)
Cardiac tamponade	3 (0.7)
Hemodialysis	11 (2.7)
Cerebral infarction	2 (0.5)
Deep sternal infection	7 (1.7)
Hospital death	5 (1.2)

Values are expressed as patient number (percentage) except for mean ICU stay. ICU: intensive care unit; MI: myocardial infarction

and 211 multi-slice computed tomography scans were included in this study. These studies were performed at a mean 4.9 ± 3.4 years after surgery. Both studies were reviewed and evaluated by interventional cardiologists. A coronary graft was considered to be a failure in cases of high stenosis (>75%) or complete occlusion of the graft and/or an anastomosed coronary artery, or in cases of string sign. In sequential grafting, both anastomotic sites were counted as an occlusion in cases of an occluded proximal side of the graft and patent distal anastomotic sites.

Statistical analysis

All data were obtained by retrospective review of medical records. Statistical analysis was performed with the JMP 11 software package (SAS Institute Inc., Cary, NC, USA). Categorical variables are expressed as direct number and percentage are given where appropriate. Continuous variables are expressed as mean and standard deviation unless otherwise stated. Cumulative patency curves were constructed using the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were used to detect independent risk factors influencing late RAG patency. The significant factors in univariate analysis ($p < 0.05$) were forward analyzed with multivariate analysis to identify the independent risk factors. In all analyses, a value of $p < 0.05$ was considered significant.

Results

Operative results and early patency

The early operative results are summarized in **Table 3**. There were five hospital deaths (1.2%), the causes of which were low output syndrome in two cases, uncontrollable ventricular fibrillation in one case, mediastinitis in one case, and cerebral infarction in one case.

In 356 patients (86.8%), postoperative coronary angiography was performed (with informed consent) during postoperative hospitalization. The early patency was 99.2% (365/368 anastomoses) for LITA grafts, 97.6% (448/459 anastomoses) for RAGs, 96.4% (398/413 anastomoses) for SVGs, and 97.1% (34/35 anastomoses) for other arterial grafts.

Follow-up patency

Cumulative 5-year patency rates were 94.1% for LITA grafts, 86.5% for RAGs, and 81.0% for SVGs (**Fig. 1**). The follow-up patency of the LITA grafts was significantly superior to that of the other two grafts ($p < 0.01$) while that of RAG was significantly superior to SVG ($p = 0.04$).

Risk factor for mid-term RAG patency

Upon univariate Cox regression analysis, three factors were detected as a risk for late patency (**Table 4**): individual grafting (not sequential grafting) (hazard ratio [HR]: 2.999; 95% confidence interval [CI]: 1.595–6.046; $p < 0.001$), grafting to the target coronary artery with ≤75% proximal stenosis (HR: 1.828; 95% CI: 1.026–3.263; $p = 0.041$), and grafting to the right coronary artery (HR: 2.278; 95% CI: 1.282–4.075; $p = 0.005$). Multivariate

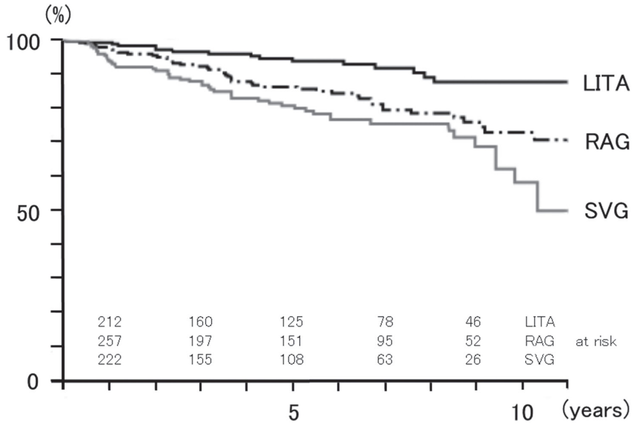

Fig. 1 Cumulative graft patency of the LITA graft, RAG, and SVG. Cumulative 5-year patency rates were 94.1% in the LITA graft, 86.5% in the RAG, and 81.0% in the SVG. LITA: left internal thoracic artery; RAG: radial artery graft; SVG: saphenous vein graft

analysis after univariate analysis identified two significant independent factors influencing late RAG patency: individual grafting (HR: 2.535; 95% CI: 1.293–5.281; $p = 0.006$) and grafting to the target coronary artery with ≤75% proximal stenosis (HR: 1.947; 95% CI: 1.090–3.484; $p = 0.025$).

Discussion

The early operative results of several studies have indicated that the RAG can be used as a useful arterial graft in CABG.[2,8,9] The present study also demonstrates low operative mortality and good early patency (97.6%). These results suggest that there are no technical difficulties in anastomosis and graft arrangement when using RAG. Although early results of radial artery grafting are encouraging, issues remain with regard to long-term results. Some clinical follow-up data showed good CABG results when using RAG in comparison with SVGs.[6,10] On the other hand, some studies reported lower RAG patency.[11] Therefore, it is difficult to draw a definite conclusion regarding long-term graft patency. When evaluating graft patency many factors should be considered, such as patient's clinical profile, medication, operative method, and target coronary artery condition and run-off. There remains a lack of well-organized clinical analysis of long-term patency comparing RAGs and SVGs that take into account the numerous factors potentially influencing the long-term patency of the grafts. Meanwhile, knowledge of the factors that may influence the patency of each graft is important.

During this studied period, RAGs were used as a second arterial graft in our institute. We found their midterm patency to be superior to that of SVGs. Multiple arterial coronary artery grafting improves long-term survival compared with single arterial CABG, but the best second arterial conduit to be used with the LITA remains undefined.[12] Another possible alternative as a second graft is the right internal thoracic artery. Bilateral internal thoracic artery has reportedly achieved good outcomes in CABG. We therefore also used the right internal thoracic artery in patients without a high risk of sternal complications during the studied period. However, the right internal thoracic artery was not frequently used during the studied period since a RAG can be used for more distal territory than in situ right internal thoracic artery graft and it is used for sequential multiple grafting. In recent years, the number of patients who underwent CABG using right internal thoracic arteries is increasing in our institute using as a free graft. The free right internal thoracic arteries also can be used for sequential graft, but their superiority to RAG regarding long-term graft patency has not yet been established.[6,13] According to the society of thoracic surgeons clinical practice guidelines on arterial conduits for CABG, as an adjunct to LITA, a second arterial graft (right internal thoracic artery or RAG) should be considered in appropriate patients.[13] Further systematic comparative studies on the issue are necessary.

The RAG can be used as a free graft and is suitable for use in sequential grafting. Schwann and colleagues[14] mentioned that sequential RAG patency compares favorably with their previously reported single RAG patency in symptomatic patients.[15] Although the sample size was relatively small, Emir and colleagues[16] also proposed sequential radial artery grafting as a method of choice for maximizing arterial graft survival and patency. Improved patency in a sequential versus single SVG configuration has been reported and widely accepted[17] although superiority of sequential RAG in comparing with single RAG in late patency is yet to be established. However, the flow dynamics reported in sequential SVGs may have a similar favorable effect on RAGs since sequential grafting decreases total resistance to graft flow.[18] When performing sequential grafting, the target vessel condition and graft arrangement are crucial factors influencing graft patency. Likewise in sequential radial artery grafting, careful graft arrangement is important in minimizing concerns about coronary steal and graft flow reversal.[19] Severity of stenosis in the most distal target was reported to have a significant impact on prevention of competitive

Table 4 Univariate analysis of the risk factor for radial artery graft patency

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
Age (/year)	1.016	0.982–1.052	0.377			
Female gender	0.757	0.288–1.655	0.511			
Obesity	1.052	0.454–2.146	0.898			
Hypertension	1.304	0.723–2.445	0.384			
Hypercholesterolemia	0.711	0.398–1.306	0.265			
Diabetes mellitus	0.655	0.366–1.168	0.150			
Smoking history	1.305	0.726–2.422	0.379			
Serum creatine level (/mg)	1.617	0.278–4.231	0.830			
Peripheral artery disease	1.211	0.631–2.519	0.578			
History of CVD	2.082	0.790–4.566	0.127			
NYHA	1.038	0.768–1.377	0.805			
LV ejection fraction (/%)	0.994	0.977–1.015	0.567			
Operation time (/minute)	0.998	0.995–1.002	0.329			
Coronary stenosis ≤75%	1.828	1.026–3.263	0.041	1.947	1.090–3.484	0.025
Individual grafting	2.999	1.595–6.046	<0.001	2.535	1.293–5.281	0.006
Grafted to RCA	2.278	1.282–4.075	0.005	1.721	0.939–3.186	0.079
Composite	2.281	0.783–5.305	0.120			

HR: hazard ratio; CI: confidence interval; CVD: cerebrovascular disease; NYHA: New York heart association functional class; LV: left ventricular; RCA: right coronary artery

flow and long-term patency in all targets.[20] The graft arrangement regarding target coronary artery condition, run-off and severity of proximal stenosis may contribute to good patency of sequential RAGs. As indicated above, since sequential RAG patency is thought to be favorable, sequential radial artery grafting can facilitate maximization of the number of arterial graft reconstructions.

In the present study, severity of proximal target vessel stenosis was also found to be a risk factor for late RAG patency. Proximal stenosis of the target vessel of >75% is preferable for late patency. Previous studies suggested that grafting to a target vessel with more severe proximal stenosis improved the graft patency[4,21,22] although the reported threshold of proximal stenosis severity varies. Hata et al.[4] demonstrated that target vessel stenosis <75% was a risk for RAG patency. In some studies, stenosis of ≥90% was defined as severe proximal stenosis while other recommended stenosis of >80% in grafting to the right coronary artery.[4,21,22] Regardless of the extent of proximal stenosis, severe stenosis is important for RAG patency. Miwa et al. reported that very high-grade proximal lesions was also associated with a much lower incidence of diffuse narrowing, known as string sign.[23] Adaptive narrowing of the RAG in the setting of flow competition may lead to graft occlusion. It was previously suggested that reduced flow in arterial conduits may lead to low shear stress, inducing graft dysfunction.[24] By contrast, some reports reported a reversal of the arterial graft string sign.[25,26] While the relation between the string sign and graft occlusion is unclear, the string sign was included in graft occlusion in this study.

Target location may also affect the patency of grafts. Some studies reported that RAGs to targets of the right coronary artery appear to be at high risk of graft failure.[27,28] Gaudino and colleagues, however, found that the location of the distal anastomotic site does not influence long-term RAG patency.[29] However, other factors such as site (proximal or distal), size, and degree of proximal stenosis seem to have more influence on the late patency of RAG when grafted to the right coronary artery. In the present study, grafted to the right coronary artery was detected as a risk factor for graft failure in univariate analysis, while not being an independent risk factor in multivariate analysis. The reason for this result is that sequential grafting was used more frequently for circumflex arterial territory revascularization than for the right coronary territory in our study population. Sequential grafting may more strongly affect late RAG patency than target location.

Our study has several limitations. This study is subject to the limitations inherent to retrospective observational data studies. Although the study cohort is from a single surgical group, graft selection was at the discretion of the surgeon and subject to bias. Renal dysfunction was suggested to impair RAG patency.[30] However, in general, RAG was not used for patients with severe renal dysfunction in our institute, to enable a future shunt for hemodialysis. Selection of the target location for the RAG was also at the discretion of the surgeon. Because RAGs are shorter than SVGs, they can be difficult to use for grafting to the distal branch of the circumflex artery in some cases. This fact might affect the result that RAGs were used both in circumflex and right coronary artery almost equally, whereas SVGs were used more for the circumflex territory than right coronary artery in this study (**Table 2**). Small target vessel size may affect late patency. However, the size of the target vessel was not considered in this study because vessel size was not recorded in all patients. Finally, during follow-up, there were no assessments of patients' status, such as lipid levels, glycemic control, or smoking or medication compliance.

Conclusion

Early patency and operative results of CABG using RAG are favorable. RAG patency was superior to that of SVGs in this studied population. RAG represents a viable alternative for arterial grafting in CABG. When using RAGs, grafting to the target coronary artery with >75% proximal stenosis is favorable. Furthermore, RAGs are suitable for sequential grafting.

Disclosure Statement

None of authors had a conflict of interest concerning this study, and none received outside support for this research.

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