

ORIGINAL ARTICLE

Midterm Follow-up of Coronary Artery Bypass Grafting with 64-Slice Multi-detector Computed Tomography: Identification of Risk Factors Affecting Graft Patency

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Key words: coronary artery bypass graft; computed tomography; cardiovascular risk factor; graft vessel patency

Objective To identify the risk factors that are associated with the midterm coronary artery bypass grafting (CABG) functionality by assessing patency of left internal mammary artery (LIMA) graft and saphenous vein (SV) graft with 64-slice multi-detector computed tomography (64-MDCT).

Methods Patients who underwent CABG operation and postoperative 64-MDCT follow-up examinations from August 2012 to December 2015 were included. The graft patent status was classified into patent and poor patent according to MDCT findings predominantly on 3D reconstructed images by two radiologists. The clinical data and imaging findings of the patients were collected and compared between the patent group and poor patent group. Univariate analysis and the multivariate logistic regression analysis were performed to identify the risk factors that affect graft patency.

Results Among 341 patients in the study, there were 330 LIMA grafts [326 anastomosed to the left anterior descending artery (LAD), 4 to right coronary artery (RCA)] and 564 SV grafts (SVG) [100 anastomosed to the diagonal branch (D), 226 to the obtuse marginal branch (OM), and 238 to the RCA territory]. The approximal vessel stenosis exceeding 90% occurred in 268 of 292 patent LIMA grafts, and in 1 of 34 poor patent grafts ($\chi^2=167$, $P<0.001$). The patency rate was higher when SVG was anastomosed to OM (85.4%) or RCA territory (81.9%) than to D (69.0%) ($\chi^2=15.471$, $P=0.004$). The proximal target vessel stenosis $< 90\%$ ($OR=0.015$, 95% $CI: 0.01-0.14$, $P=0.000$) was independently associated with the closure risk of LIMA grafts, the dyslipidemia ($OR=1.52$, 95% $CI: 1.0-2.5$, $P=0.048$), history of diabetes ($OR=1.28$, 95% $CI: 0.90-2.26$, $P=0.045$) and typical angina symptoms ($OR=1.81$, 95% $CI: 1.33-4.15$, $P=0.003$) were independently associated with the closure risk of SVG.

Conclusions The proximal LAD stenosis less than 90% was adversely associated with graft patency in LIMA recipients; dyslipidemia, diabetes and angina symptoms were associated with the midterm failure in SVG recipients. The choice of the target anastomosis sites may affect the patency of SVG.

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CORONARY artery bypass grafting (CABG) is one of the most effective treatments to ensure myocardial re-perfusion for the advanced coronary artery atherosclerotic heart disease. More than 9 800 patients with coronary heart disease accept CABG operation annually in China.¹ Some patients present with symptoms after operation, such as recurrent angina or effort dyspnea. It was reported that graft stenosis and closure occurred in 20%-30% of patients within 3 years after CABG operation.² Therefore, it is imperative to accurately assess the graft patency after CABG operation.

Invasive cardiac angiography (ICA) has been the gold standard to evaluate graft patency; however, despite its invasive nature, the procedures also accompany with complications, such as thrombosis, dissection, arrhythmia, myocardial infarction and stroke.³ In recent years, 64 slice multi-detector computed tomography (MDCT) has emerged as an alternative to ICA in evaluating the graft and native coronary arteries for its diagnostic potentials, low cost and safety.⁴ Some studies⁵⁻⁸ have shown that 64-MDCT has high sensitivity, specificity, positive predictive value and negative predictive values in evaluation of graft patency in patients with CABG operation compared with ICA.

In the meantime, there hasn't sufficient data to identify the risk factors that affect the graft patency. A few studies reported conflicting findings.⁹⁻¹² Levisman JM *et al*⁹ found that the comorbidity of diabetes had no significant impact on the graft failure. However, Yanagawa B and Singh SK *et al*^{10, 11} found that diabetes was a potential clinical predictor for the development of graft failure. Choi JS *et al*¹² reported that diabetes mellitus did not affect the early and midterm postoperative outcome. Although the type of graft (i.e. vein or artery) was also reported to affect the long-term outcome of CABG,¹³ little has been known regarding the impact of distant anastomosis site on graft patency. As a result, in the present study, we aimed to evaluate the CABG graft patency in different graft types and different distant anastomosis site by using 64-slice MDCT, and secondly, to identify the risk factors that affect the midterm graft failure among the clinical and imaging characteristics of the patients.

MATERIAL AND METHODS

Patients and information collection

The retrospective study was approved by the insti-

tutional ethic review board, and the consents from patients were waived. From August 2012 to December 2015, consecutive patients with history of CABG who underwent postoperative follow-up examination using 64-MDCT to determine the outcomes of grafts in our institute were reviewed. Subjects who didn't undergo postoperative MDCT angiography due to renal dysfunction, arrhythmia, allergic to iodinated contrast media, or failed to accomplish a 15-second breath hold were excluded. Subjects who had poor MDCT image quality due to remarkable artifacts were also excluded. We collected the basic information of the enrolled patients, including age, gender, height, weight, symptoms at the MDCT examination, comorbidities of type 2 diabetes, hypertension, dyslipidemia, history of smoking, and cerebrovascular disease, ongoing medication, date of coronary artery bypass graft surgery, date of 64-MDCT examination, preoperative quantitative coronary angiography results. The operative notes were carefully reviewed to extract the information on the graft type, number of all graft conduits, and the target anastomosis for analysis.

Coronary artery imaging

Coronary CT angiography(CTA) was performed on a 64-slice CT scanner (SOMATOM Sensation Cardiac 64, Siemens Medical System, Forchheim, Germany). Each patient received 85ml contrast media (Omnipaque 350 mg I/ml, GE Healthcare, Pewaukee, WI) intravenously at a rate of 5ml/s, followed by 40ml saline solution at the same rate. Bolus tracking technique was used to monitor the intensity of aortic root and trigger the scan protocol automatically when the CT attenuation of aortic root reached 150 HU. Scanning field was set from thoracic inlet to costophrenic angles. For patients with heart rates less than 65bpm, CTA was performed using a prospective ECG-triggering protocol with tube voltage 120kV, effective tube current 195mAs. Otherwise, a retrospective ECG-triggering protocol was used with parameters of 0.33 s/r, 120kV, eff.900mAs, pitch 0.18, slice collimation 64x0.6 mm, thickness 0.75 mm. Axial images were reconstructed using standard reconstruction algorithm with a slice thickness of 1 mm (increment of 0.6 mm) at the optimal ECG-phases when the minimum motion artifacts presented on the images for optimal delineation of each coronary artery bypass graft and main branch of the coronary arteries.

Post-processing and analysis of images

For each patient, the axial image data were transferred to an Advanced Workstation (Circulation 2 workstation,

Siemens, Forchheim, Germany) for post-processing and vessels reconstruction. The CABG was reformatted with Volume Render (VR), maximum intensity projection (MIP), multi-planar reconstruction (MPR) or curved planar reconstruction (CPR). MPR and CPR images were predominantly used to assess the CABG patency.

Two experienced radiologists reviewed the MDCT images independently to identify the graft patency with reference of brief operation records on graft number and anastomosed location. The graft patency status was classified into 2 categories according to the imaging findings: patent (excellent visualization, luminal stenosis <50%), and poor patent (visualized with significant stenosis, luminal stenosis $\geq 50\%$, or totally occluded).¹³ Luminal stenosis was quantified by the formula: $(\text{diameter}_{\text{proximal normal lumen}} - \text{diameter}_{\text{stenosed lumen}}) / \text{diameter}_{\text{proximal normal lumen}}$. In case of sequential bypass graft with multiple target anastomoses, each sequential bypass graft was considered as isolate grafts. The graft targets were divided into three territories: left anterior descending branch (LAD), including the diagonal branch (D); left circumflex coronary artery (LCX), including obtuse marginal branch (OM); right coronary artery (RCA), including posterior descending artery (PDA) and posterior lateral branch (PLB). For any discrepancy in interpreting, a consensus was achieved by discussion between the two radiologists.

Statistical analysis

The clinical characteristics of patients, including age, gender, history of diabetes, hypertension, dyslipidemia, smoking, cerebrovascular disease, ongoing medical therapy as well as graft type and target territories, were compared between patients with patent grafts and those with poor patent grafts. Continuous variables were described as mean $\pm$ standard deviation and compared using *t* test; categorical variables were described as percentages and analyzed using chi-square test. Univariate analysis and multivariate logistic regression analysis were performed to identify the risk factors that were associated with graft failure. A two-tailed *P* value of <0.05 was considered statistically significant. All the statistical analyses were conducted by SPSS (version 19.0, SPSS Inc, Chicago, IL).

RESULTS

Clinical characteristics

A total of 379 consecutive patients with history of

CABG and having completed 64-MDCT follow-up examinations were initially included in this study. All the patients were not referred to redo the CABG. There were 38 patients with 59 bypass grafts excluded for remarkable artifacts on CT images (metal clip in 22 segments, calcification inducing blooming in 5, motion artifact in 21) or deficient contrast enhancement (11 CABG segments). So a total of 894 grafts in 341 patients (mean 2.62 grafts per patient) were included in the study, with 273 males and 68 females, mean age of 62.6 ± 10.2 , ranged from 32 to 85 years old. The mean interval time between CABG operations and MDCT examinations was 30.2 ± 17.0 months.

The clinical characteristics of patients who had patent grafts and poorly patent grafts were shown in **Table 1**. All patients received postoperative antiplatelet medication after CABG surgery, including aspirin (100 mg, daily) and clopidogrel (75 mg, daily) regularly. The adjuvant medication other than antiplatelet were beta blocker, angiotensin-converting-enzyme (ACE) inhibitor, statin and calcium channel blocker. Fifty-four out of 341 (15.8%) patients were symptomatic at the time of MDCT. The symptoms included discomfort of the precordial area, chocking sensation in chest, or short of breath.

Patency of left internal mammary artery (LIMA) graft and saphenous veins (SV) graft

Of 894 grafts in 341 patients, there were 330 LIMA grafts and 564 SV grafts. Among the 330 LIMA grafts, 326 grafts were anastomosed to the left anterior descending artery (LAD), 4 to the right coronary artery (RCA). Assessed by the MDCT examination, there were 294/330 LIMA grafts (89.1%) being patent (**Fig. 1**), of which 292 were anastomosed to LAD and 2 to RCA; there were 36/330 LIMA grafts being poor patent, of which 34 were anastomosed to LAD and 2 to RCA. In 326 LIMA grafts that were anastomosed to LAD, pre-operative quantitative coronary angiography showed that the significant luminal stenosis exceeding 90% of proximal target vessel occurred in 268 of 292 patent grafts, while in only 1 of 34 poor patent grafts, the proximal target vessel showing significant luminal stenosis exceeding 90% ($\chi^2=167$, $P<0.001$).

The MDCT examination revealed that, of 564 SV graft, 457 were patent (81.03%) (**Fig. 1**), and 107 were poor patent (**Fig. 2**). The patency rates of SV graft that were anastomosed to the diagonal branch(D), the obtuse marginal(OM) branch and

Table 1. Clinical characteristics of patients who had patent grafts or poorly patent grafts at the time of MDCT examination ($n=341$)[§]

Clinical characteristics	Patient groups		In total	<i>t</i> or χ^2 value	<i>P</i> value
	Patent grafts (<i>n</i> =231)	Poor patent grafts (<i>n</i> =110)			
Sex					
Male, <i>n</i> (%)	188(81.4)	85(77.3)	273	0.79	0.37
Female, <i>n</i> (%)	43(18.6)	25(22.7)	68		
Age, years	62.7±10.3	62.5±10.0	62.6±10.2	0.42	0.87
Bypass grafts, <i>n</i> (%)	574	320	894		
Body Mass Index	30.1±5.8	30.5±6.1	30.2±5.9	0.55	0.45
History of					
Diabetes, <i>n</i> (%)	72(31.2)	41(37.3)	113	1.25	0.26
Hypertension, <i>n</i> (%)	157(68.0)	61(55.5)	218	5.06	0.025
Dyslipidemia, <i>n</i> (%)	58(25.1)	38(34.5)	96	3.28	0.07
Smoking, <i>n</i> (%)	118(51.1)	48(43.6)	166	1.65	0.20
Cerebrovascular disease, <i>n</i> (%)	28 (12.1)	26 (23.6)	54	7.41	0.006
Post-operative adjuvant medication					
Beta blocker, <i>n</i> (%)	101(43.7)	48(43.6)	149	0.00	0.98
ACE inhibitor, <i>n</i> (%)	58(25.1)	27(24.5)	85	0.01	0.9
Statin, <i>n</i> (%)	107(46.3)	49(44.5)	156	0.10	0.76
Calcium channel blocker, <i>n</i> (%)	21(9.1)	9(8.2)	30	0.08	0.78
Symptomatic, <i>n</i> (%)	39(16.9)	15(13.6)	54	0.59	0.44

§: Plus and minus values are means $\pm$ SD; MDCT: multi-detector computed tomography; ACE: angiotensin-converting-enzyme.

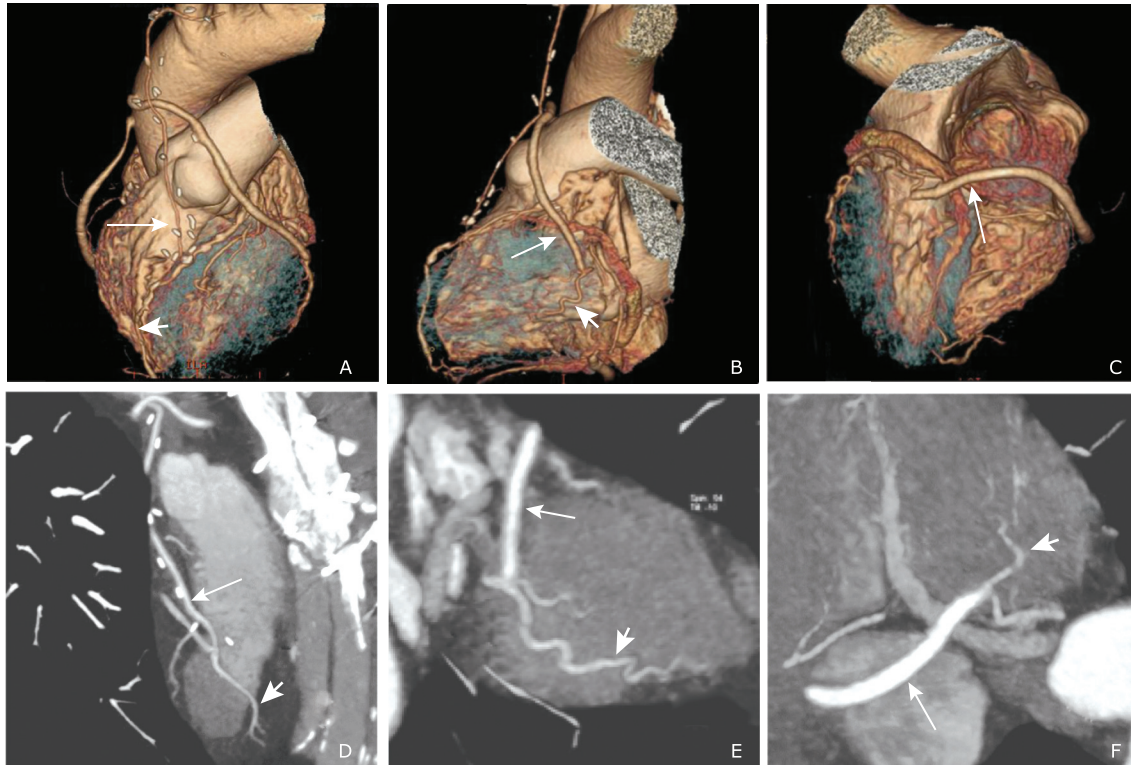


Figure 1. Volume rendering (VR) and Multi-planar reconstruction (MPR) images of a 72-year-old male who had coronary artery bypass graft (CABG) operation one year ago show the grafts were all patent. A and D, the left internal mammary artery graft (long arrow) was anastomosed to the left anterior descending artery(short arrow); B and E, the saphenous veins graft (long arrow) was anastomosed to the obtuse marginal branch (short arrow); C and F, another saphenous vein graft (long arrow) was anastomosed to the left ventricular posterior branch (short arrow).

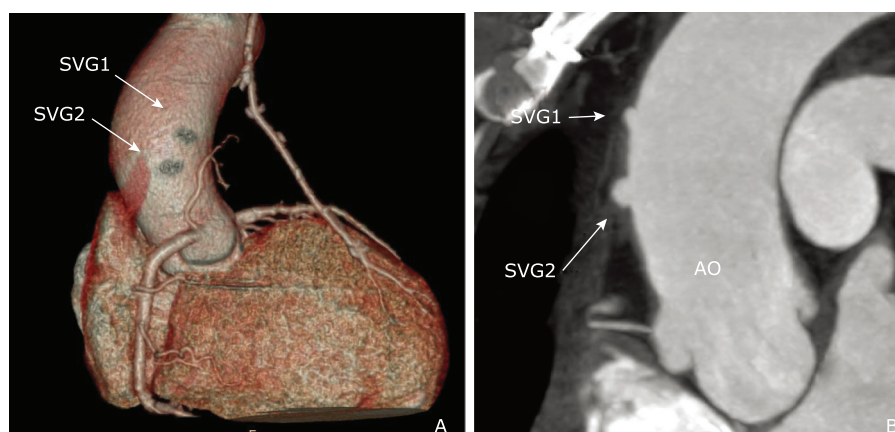


Figure 2. MPR image and VR image of a 54-year-old male who had coronary artery bypass graft operation 15 months ago. VR image (A) and MPR image (B) show the two saphenous vein grafts (white arrows) were all occluded. SVG: saphenous vein graft; AO: aorta.

the right coronary artery(RCA) were 69%(69/100), 85%(193/226) and 82%(195/238), respectively. The distribution of patency rates among all the territories of target vessels were statistically different ($\chi^2=15.471$, $P=0.004$) (**Table 2**).

Risk factors affecting patency of LIMA and SV grafts

Independent-samples *t*-test showed that the mean ages of patients with patent graft and poor patent graft were not significantly different for neither LIMA grafts (62.6 ± 10.1 vs. 63.4 ± 10.3 years, $t=-0.45$, $P=0.65$), nor SV grafts (62.8 ± 10.1 vs. 62.4 ± 10.3 years, $t=-0.39$, $P=0.70$). Univariate analysis for LIMA and SV graft patency (**Table 3**) showed that the gender, history of cerebrovascular disease, as well as luminal stenosis of proximal target vessel exceeding 90% were significantly associated to LIMA patency; the history of diabetes, hypertension, being symptomatic, and dyslipidemia were significantly associated to SV graft patency. Multivariate logistic regression analysis of graft patency showed the luminal stenosis of proximal tar-

get vessel of less than 90% was the independent risk factor for LIMA closure ($OR=0.015$, 95% CI : 0.01-0.14, $P=0.000$), and the history of diabetes, dyslipidemia, and being symptomatic were the independent risk factors for SV grafts closure (**Table 4**).

DISCUSSION

In this study we used 64-MDCT to follow up the midterm outcomes of CABG. There were three major findings: firstly, the patency rate of CABG was higher in SV graft that was anastomosed to the OM or to RCA territory than that to the diagonal branch; secondly, the closure risk of LIMA graft was relatively high in patients whose luminal stenosis of proximal target vessel was less than 90%; thirdly, the occlusive risks of SV graft graft were relatively high in patients with history of dyslipidemia, diabetes, as well as those postoperatively experiencing typical anginal symptoms such as chest pain or dyspnea.

The impact of distant anastomosis site of bypass

Table 2. Distribution of LIMA and SV grafts patency among anastomosed vessels/territories of CABG

Graft type	Target vessel	Patent, <i>n</i> (%) (<i>n</i> =751)	Poor patent, <i>n</i> (%) (<i>n</i> =143)	In total (<i>n</i> =894)
LIMA*		294(89.1)	36(10.9)	330
	LAD	292(89.6)	34(10.4)	326
	RCA	2(50.0)	2(50.0)	4
SV**		457(81.0)	107(19.0)	564
	D	69(69.0)	31(31.0)	100
	OM	193(85.4)	33(14.6)	226
	RCA territory	195(81.9)	43(18.1)	238

*statistical analysis was not applicable; **chi-square test: $\chi^2=15.471$, $P=0.004$.

LIMA:left internal mammary artery; SV:saphenous venous; LAD:left anterior descending branch; RCA:right coronary artery; D:diagonal branch; OM:obtuse marginal branch; RCA:right coronary artery.

Table 3. Univariate analysis of factors that related to patency of LIMA grafts and SV grafts

Variates	Patency of LIMA grafts				Patency of SV grafts			
	Patent <i>n</i> =294	Poor patent, <i>n</i> =36	χ^2	<i>P</i> value	Patent <i>n</i> =457	Poor patent <i>n</i> =107	χ^2	<i>P</i> value
Male, <i>n</i> (%)	266(90.5)	29(80.6)	6.85	0.03	372(81.4)	82(76.6)	1.22	0.27
Hypertension, <i>n</i> (%)	259(88.1)	33(91.7)	0.68	0.71	383(83.8)	79(73.8)	8.06	0.005
Dyslipidemia, <i>n</i> (%)	259(88.1)	32(88.9)	2.53	0.28	340(74.4)	91(85.0)	3.56	0.04
Diabetes, <i>n</i> (%)	267(90.8)	32(88.9)	1.08	0.58	345(75.5)	89(83.2)	4.39	0.036
Smoking, <i>n</i> (%)	268(91.2)	31(86.1)	2.76	0.25	376(82.3)	84(78.5)	1.36	0.24
Cerebrovascular disease, <i>n</i> (%)	230(78.2)	33(91.7)	10.47	0.005	366(80.1)	86(80.4)	0.00	0.98
Symptomatic, <i>n</i> (%)	255(86.7)	32(88.9)	0.57	0.75	326(71.3)	88(82.2)	5.18	0.023
Proximal target vessel stenosis >90%, <i>n</i> (%)	290(98.6)	14(38.9)	169	<0.001	NA	NA	NA	NA

NA: not applicable.

Table 4. Logistic regression analysis for the closure risk of LIMA grafts and SV grafts

Risk factors	LIMA graft closure (<i>n</i> =330)		SV graft closure (<i>n</i> =564)	
	Odds ratio (95% CI)	<i>P</i> value	Odds ratio (95% CI)	<i>P</i> value
Gender	3.82(0.73-20.05)	0.11	1.38 (0.77-2.50)	0.28
Hypertension	1.99(0.39-10.05)	0.41	0.61(0.38-0.98)	0.04
Dyslipidemia	1.48 (0.30-7.37)	0.64	1.52(1.00-2.5)	0.048
Diabetes	0.14(0.02-1.32)	0.09	1.28(0.90-2.26)	0.045
Smoking	0.53(0.10-2.93)	0.47	0.96(0.59-1.57)	0.88
Cerebrovascular disease	2.55(0.41-15.93)	0.32	1.0(0.53-1.88)	1.00
Symptomatic	1.01(0.09-11.25)	0.99	1.81(1.33-4.15)	0.003
Proximal target vessel stenosis <90%	0.015(0.01-0.14)	0.000	NA	NA

graft on its patency has rarely been reported in the literature. A previous study reported that the grafts anastomosed to LAD had better patency than those to RCA,⁹ but subgroup analysis to delineate the ideal usage of each graft type wasn't carried out. In this study, we delineated the graft type that was anastomosed to LAD territory, LCX territory and RCA territory, and found that the SVGs conduit to the LCX and RCA territory showed a significantly better patency than those to the D. This finding implied that the selection of the target anastomosis sites may influence on the graft patency. Histologically, the D has a smaller diameter of vessel than OM, RCA, PDA and PLB, therefore the mismatch of graft-target vessels size might account for the low patency rate of the SV graft anastomosed to the D.

Our study showed that the proximal LAD target vessel stenosis of less than 90% was adversely associated with LIMA patency. Otherwise, flow competition from native vessel would result in LIMA graft failure. This was consistent with previous study findings that

the poor patency of LIMA graft might be caused by the vessels spasm or flow competition.¹⁴

It was believed that the failure of SV graft was caused by thrombosis, intimal hyperplasia or graft atherosclerosis.^{13, 15} Thrombosis mainly accounts for the graft failure in the first month after CABG, while intimal hyperplasia and graft atherosclerosis were regarded to associate with the delayed graft failure.¹⁶

This study found that suffering from type 2 diabetes, dyslipidemia, and being symptomatic of CHD yielded significant higher failure rate for SV graft, but not for LIMA graft. Yanagawa B *et al*¹⁰ and Singh SK *et al*¹¹ also suggested that diabetes had significant impact on the SV graft failure. When comparing the study for radial arteries between the patients with diabetes and non-diabetic patients, there was no significant difference.¹¹ Noyez L regarded that dyslipidemia and diabetes could promote the progress of atherosclerosis in the graft vessel, which is one of the main reasons for SV graft failure.¹⁶ We also found that symptomatic patients after SV graft operation

had lower patency rate than those without symptom. This result is consistent with the findings in the study of Harskamp *et al*, where acute SV graft closure was found to lead to adverse coronary events, whereas slow-onset of SV graft failure did not. This is possibly because the developed collateral circulations take over the blood supplying.¹⁷ Interestingly, we found that hypertension for patients who had SV graft might be a protective factor against its occlusion.

Our study showed female, history of cerebrovascular disease was associated with an increased risk of LIMA graft failure. In this study, the mean diameter of patent LIMA in female patients was shown to be less than that in male patients. Vessels with small diameter are not amendable to complete surgical revascularization, which may contribute to the grafts failure of LIMA in female. The history of cerebral vascular disease was shown to be a risk factor for graft failure in this study. Since cerebrovascular disease is usually associated with atherosclerosis, patients with cerebrovascular disease may have diffuse small-vessel coronary disease, which is not amendable to complete surgical revascularization and thus cause grafts failure.

There are several limitations in this study. Firstly, due to the experience and the preference of surgeons in our hospital, the number of patients with LIMA graft anastomosed to RCA was too small to perform statistical analysis. Secondly, as this is a retrospective observational study, the diameters of target vessels and the grafts could not be re-evaluated accurately. Thirdly, since 64-MDCT has been applied as routine to evaluate graft patency in our hospital for its well-recognized high accuracy,¹⁸ coronary angiography was not obtainable to double-confirm the MDCT observation in this study.

In conclusion, this retrospective study investigated patients of CABG who underwent midterm follow-up for the assessment of graft patency using 64-slice MDCT. It is concluded that the proximal LAD target vessel stenosis of less than 90% was adversely associated with LIMA graft patency; type 2 diabetes, dyslipidemia, being anginal symptomatic were associated with the midterm failure of SV grafts, and selecting the target vessels for anastomosis may affect the patency of SV graft.

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