Ann Thorac Cardiovasc Surg 2024: 30; 23-00066
Online July 19, 2023
doi: 10.5761/atcs.oa.23-00066

Original Article

Impact of Graft Velocity on Saphenous Vein Graft Atherosclerosis after Coronary Artery Bypass Grafting

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Purpose: Saphenous vein grafts (SVGs) sometimes occur as vein graft stenosis or failure in coronary artery bypass grafting. The purpose of this study was to detect the factors affecting vein graft atherosclerosis.
Methods: We performed two analysis. In the first analysis, we enrolled 120 grafts using conventionally harvested saphenous vein graft (C-SVG) and followed-up with multiple coronary computed tomography angiography (CCTA). We examined the factors that contribute to the graft atherosclerosis defined by graft failure at subsequent CCTA or substantial progression of graft stenosis (a decrease of ≥0.6 mm in diameter). In the second analysis, 66 grafts using no-touch harvested saphenous vein graft (N-SVG) were compared with those in the first analysis using C-SVG, focusing on the differences in intraoperative factors using propensity score-matched analysis.
Results: In the first analysis, graft atherosclerosis+ group comprised 27 grafts, which had a larger SVG diameter, lower graft velocity, and higher graft/native ratio in diameter than the graft atherosclerosis– group. In the multivariable analysis, slow graft velocity and graft/native ≥2 in diameter were independently associated with the graft atherosclerosis. In the second analysis, the N-SVG group had a much greater graft velocity than the C-SVG group.
Conclusion: Lower graft velocity and higher graft/native ratio in diameter were associated with the graft atherosclerosis. The N-SVG group had increased graft velocity, which may contribute to prevent the graft atherosclerosis.
(Trial registration: UMIN Clinical Trial Registry no. UMIN000050482. Registered 3 March 2023, retrospectively registered.)

Keywords: vein graft disease, vein graft atherosclerosis, conventional harvest SVG, no-touch harvested SVG, graft velocity, CABG

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Received: April 16, 2023; Accepted: June 23, 2023
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Introduction

Saphenous vein grafts (SVGs) are still commonly used in coronary artery bypass grafting (CABG) because of their relative versatility and ease of handling. Problems with conventionally harvested saphenous vein graft (C-SVG), a skeletonized and manually dilated SVG, include a lower graft patency rate than that of other arterial grafts.[1] The graft occlusion rate is about 3%–12% before hospital discharge, 8%–25% at 1 year, and only 50%–60% remaining patent after a decade.[2]

There could be a number of reasons for the low graft patency of SVG. In the early stages (from surgery to 1 month post-surgery), there are problems of thrombosis and technical failure; in the mid-to-long stage (1 month to a year), problems include neointimal hyperplasia and vein graft arteriosclerosis; and beyond a year, there can be the so-called vein graft disease (VGD), causing subsequent graft stenosis and obstruction.[2–4] Various causes of the VGD have been cited. Coronary risk factors include dyslipidemia, diabetes, and renal dysfunction.[1,5] Other causes of vein graft failure are SVG and native coronary artery characteristics, such as SVG diameter, and the ratio of SVG diameter and native coronary artery (G/N ratio).[6,7] A no-touch harvested saphenous vein graft (N-SVG), a pressure-controlled harvest with preservation of surrounding fat tissue, has received attention in recent years because of its good rate of graft patency: 83% in 16 years.[8] The mechanism behind good graft patency and the exact means of preventing the VGD remain controversial, but multiple factors have been proposed.[9–13]

Graft angiography after CABG often has a large graft diameter compared with the native coronary artery and slow velocity in C-SVG, while N-SVG has a small graft diameter and high velocity.[14] Blood velocity and wall shear stress are generally correlated, and slower velocity decreases the wall shear stress, causing intraluminal stenosis through a pathophysiological pathway.[3,15,16] The mean graft flow (MGF) and graft diameter are reportedly associated with graft patency,[6,17,18] but there are no reports on graft patency in relation to graft velocity. We hypothesized that a higher graft velocity might be associated with prevention of the graft atherosclerosis. This study evaluates whether the initial graft velocity affects the graft atherosclerosis and whether C-SVG and N-SVG have different graft velocities.

Materials and Methods

Ethical statement

This single-center retrospective cohort study was approved by the Wakayama Medical University Institutional Review Board (approval number 3546). The need for informed consent was waived because of the retrospective and observational nature of this study, but the study was conducted in accordance with the principles of the Declaration of Helsinki.

Study design and participants

This study comprised of two distinct analyses, the patient flowcharts of which are shown in **Supplementary Fig. 1**. (The supplementary files are available online.)

Analysis 1: Retrospective analysis of conventional harvest SVGs to detect the factors affecting the graft atherosclerosis

At Wakayama Medical University Hospital, Japan, 424 patients underwent CABG with SVG (except for patients with acute myocardial infarction) between January 2010 and December 2017. To investigate the graft patency, postoperative coronary computed tomography angiography (CCTA) follow-up was undertaken on 271 grafts (215 patients) within 3 months. Among these, 14 grafts (7.4%) were occluded. A further 137 grafts (50.6%) were not examined with subsequent CCTA due to the progression of chronic kidney disease (estimated glomerular filtration rate [eGFR] <45), failure to properly perform CCTA, or lack of consent to the CCTA. The first analysis thus included 120 grafts in 96 patients. The graft atherosclerosis was defined as graft failure shown by subsequent CCTA or decrease of ≥0.6 mm in lumen diameter of SVG in subsequent CCTA compared with the early postoperative CCTA (<3 months postoperatively), as described below. The group with graft atherosclerosis, henceforth referred to as "graft atherosclerosis+ group" comprised 27 grafts, and the group without graft atherosclerosis, henceforth referred to as "graft atherosclerosis− group" comprised 93 grafts. All SVGs were conventionally harvested.

Analysis 2: Propensity score-matched analysis of MGF and graft velocity measurement between C-SVG and N-SVG

Between June 2019 and December 2021, 121 patients underwent CABG with SVG, excepting those with acute myocardial infarction. Postoperative CCTA follow-up was undertaken for 71 grafts (57 patients) within 3 months to identify the graft patency, among which, five grafts (7.0%) were occluded. The second analysis therefore included 66 grafts in 52 patients. During this period, the harvest method was changed from C-SVG to N-SVG as described below. The C-SVG 120 grafts included in our first analysis and N-SVG 66 grafts were enrolled in our second analysis. These groups differed in baseline characteristics (**Supplementary Table 1**), so a propensity score-matched analysis was conducted to account for imbalances in baseline risk. The C-group and the N-SVG group each had 54 grafts, and the two groups were compared with respect to intraoperative graft measurements and postoperative CCTA characteristics within 3 months.

SVG harvest technique

Between January 2010 and December 2017 and included in our first analysis, SVGs were conventionally

harvested; the surrounding fatty tissue was removed and skeletonized to the venous adventitia only. SVGs were manually pressure extended with a syringe to detect the venous branch and dilated to facilitate anastomosis to the coronary artery. Between June 2019 and December 2021, the N-SVG technique was used, preserving about 3–5 mm of fat tissue around the graft to keep the vasa vasorum and the nerves around vein graft intact as described previously.[14,19] Harvested grafts were gradually dilated for 10 min after harvest using an infusion drip line in which pressure was controlled at around 120 mmHg. After flushing thrombi from the grafts, the harvested SVGs were stored in a normal saline solution with heparin. SVGs were harvested from below the knee except for those with diameter <2 mm or a lot of SVG branches that were not appropriate as a graft. All grafts included in this study were anastomosed to the ascending aorta as the graft inflow.

Intraoperative graft flow measurement

Intraoperative graft flow measurement was performed using a transit time flow meter (TTFM; VeriQ System, Medistim, Oslo, Norway). Graft flow assessment was performed just before chest closure, and after hemodynamic stabilization, systolic blood pressure was controlled around 120 mmHg and the heart rate was controlled from 60 to 80 bpm. The parameters evaluated with TTFM were MGF (mL/min) and pulsatility index (PI; absolute value, maximal flow − minimal flow/mean flow). We routinely measured MGF and PI with a 3-mm probe and checked the flow pattern and acoustic coupling index (ACI; as a correlate of the quality or reliability of the TTFM measurements) >30%.[20] If we thought inappropriate measurements, we changed the probe to a 2- or 4-mm probe as appropriate and checked good flow pattern and ACI >30%.

All grafts were evaluated with intraoperative fluorescence graft imaging with Photodynamic Eye (Hamamatsu Photonics K.K., Shizuoka, Japan) to check whether or not the grafts were successful.

Postoperative CCTA

Postoperative graft evaluation was performed with CCTA. Betablockers and isosorbide mononitrate were used to ensure adequacy of the images. Postoperative CCTAs were performed within 3 months of surgery except for chronic kidney disease (eGFR <45) or if there was allergy to the contrast agent. Subsequent postoperative CCTA graft evaluations at 3 months, 1 year, 5 years, and 10 years after surgery were planned for patients irrespective of whether they had symptoms. Curved planar reconstruction images of the grafts were created from the images obtained by CCTA, and the vessel diameters 1 cm before central and peripheral anastomosis, and their midpoints were measured (using proximal anastomosis if sequential bypass). The average of these three points was taken as the mean vessel diameter and was used to calculate the mean cross-sectional area. The native diameter of the grafted coronary artery was also measured by CCTA. The graft and native coronary artery diameter ratio (G/N ratio) was calculated using the diameter of the graft vessel 1 cm before the peripheral anastomosis and the diameter of the native vessel 1 cm peripherally.

Graft velocity calculated from TTFM and CCTA

The graft velocity (cm/sec) was calculated from the MGF (mL/min) and the average cross-sectional area (mm^2) was obtained by postoperative CCTA within 3 months because the graft velocity was not actually measured during surgery. This calculated velocity is a hypothetical average velocity.

Graft velocity (cm/sec) = MGF (mL/min)/average cross-sectional area (mm^2)/60.

Definition of the graft atherosclerosis

The pathogenesis of VGD is composed of three distinct processes: thrombosis, intimal hyperplasia, and atherosclerosis.[2–4] Early failure is attributed to technical failure (graft trauma during harvesting, anastomotic deficiencies), or conduit-related (mismatch in conduit size or preexisting graft pathology) or extrinsic factors (hypercoagulability) causing acute thrombosis.[2] Intimal hyperplasia typically occurs after the early phase, which may reduce the lumen area by up to 25%,[3] while atherosclerosis tends to occur beyond the 1-year point. This study focuses upon intimal hyperplasia and atherosclerosis, which are important for the long-term patency of SVG, so we included SVGs except for early graft failure and compared the mean cross-sectional area obtained by the first and subsequent CCTA. The graft atherosclerosis was defined as a decrease of ≥0.6 mm in lumen diameter at one or more of three points (proximal, mid, and distal) or graft failure at the subsequent CCTA as previously described (**Fig. 1**).[21]

Statistical analysis

Continuous variables are presented as median and interquartile range or average and standard deviation (SD). Categorical variables are presented as numbers and percentages. To compare the two groups, Student's t test or Wilcoxon rank sum test was used for continuous

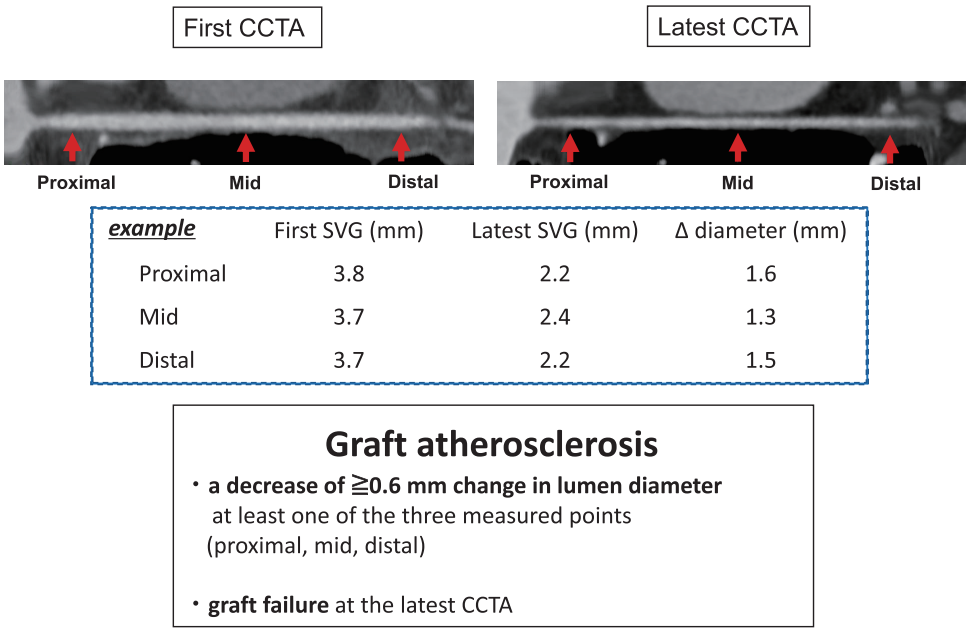

Fig. 1 Vein graft atherosclerosis defined by CCTA. Curved planar reconstruction images of the grafts were created from the images obtained by CCTA, which showed the same patient's SVG. These panels show the graft diffuse stenosis after the operation over a period of years. We measured three points of the graft diameter (1 cm before central and peripheral anastomosis, and their midpoint). Compared with the first CCTA, vein graft atherosclerosis was defined as a decrease ≥0.6 mm in the lumen diameter at least at one of the three measured points or graft failure in the latest CCTA. The example shows impressive diffuse stenotic change in the diameter of three points compared with the latest CCTA (7 years). Δdiameter shows the difference in SVG diameter between the first and the last CCTA. CCTA: coronary computed tomography angiography; SVG: saphenous vein graft

variables, and Pearson's chi-square test or Fisher's exact test was used for categorical variables as appropriate. Univariate and multivariate logistic regression models were used to assess the association between intraoperative measurements and the graft atherosclerosis. The multivariate logistic model used predefined adjusters (selected based on the literature and clinical judgment) that would be risk factors of graft failure. These adjusters focusing on intraoperative measurements included MGF <20 mL/min,[22,23] mean SVG diameter ≥3.5 mm,[6] native diameter <1.5 mm,[3,24] and G/N ratio ≥2.[2,7] The graft velocity cutoff value was determined as median velocity of 120 grafts. To date, there have been no reports on the optimum velocity to maintain the long-term graft patency. No statistical sample size calculations were conducted because of the retrospective nature of this study. The multivariate model used variables that had *P* value <0.05 in the univariate model. In our second analysis, propensity score-matched analysis was performed to adjust the patient background and reduce selection bias. A nearest neighbor algorithm was used to match 1:1, without replacement, those who use C-SVG with those who use N-SVG by using a caliper width of 0.2 SD of the logit of the propensity score. The 16 factors using this analysis were age, sex, body mass index, hypertension, chronic kidney disease, hemodialysis, diabetes mellitus, insulin use, dyslipidemia, diagnosis, emergent operation, angiographic stenosis, target vessel location, wall motion abnormality of grafted lesion, above-knee SVG use, and sequential bypass use. A standardized difference of <0.25 suggests adequate variable balance after propensity matching.[25]

JMP Pro software (version 16; SAS Institute, Cary, NC, USA) was used in all analyses. A two-sided *P* value <0.05 was considered to be statistically significant.

Results

The results of our first analysis, which explored the factors affecting the graft atherosclerosis, are shown in **Table 1**. Patient characteristics and grafted lesion characteristics were not significantly different between the

Table 1 Patient characteristics

	Graft atherosclerosis+ (n = 27)	Graft atherosclerosis– (n = 93)	*P* value
Patient characteristics			
Age, y, ±SD	67.8 ± 10.1	67.2 ± 9.5	0.77
Male, n (%)	18 (67)	63 (68)	0.92
Body mass index, kg/m^2, ±SD	23.9 ± 3.2	23.4 ± 3.7	0.54
Hypertension, n (%)	25 (93)	82 (91)	0.60
Chronic kidney disease (eGFR <60), n (%)	7 (26)	34 (37)	0.30
Hemodialysis, n (%)	4 (15)	18 (19)	0.59
Diabetes mellitus, n (%)	15 (56)	49 (53)	0.79
Insulin use, n (%)	5 (19)	19 (20)	0.83
Dyslipidemia, n (%)	21 (78)	65 (70)	0.42
History of smoking, n (%)	12 (44)	45 (48)	0.72
Diagnosis			0.27
Old myocardial infarction, n (%)	14 (52)	35 (38)	
Angina pectoris on exertion, n (%)	8 (30)	26 (28)	
Unstable angina pectoris, n (%)	5 (18)	32 (34)	
Emergent operation, n (%)	2 (7)	6 (6)	0.86
Off-pump surgery, n (%)	19 (70)	65 (70)	0.96
Concomitant surgery	3 (11)	6 (6)	0.42
Ejection fraction, %, ±SD	48.3 ± 10.0	52.2 ± 11.1	0.10
Lesion characteristics			
Angiographically severe stenosis ≥90%, n (%)	17 (63)	56 (60)	0.80
Target lesions			0.28
Right coronary artery, n (%)	13 (48)	56 (60)	
Left coronary artery, n (%)	14 (52)	37 (40)	
Wall motion abnormality, n (%)	16 (59)	45 (48)	0.32

SD: standard deviation; eGFR: estimated glomerular filtration rate

graft atherosclerosis + and the graft atherosclerosis – groups. **Table 2** shows the intraoperative and CCTA characteristics within 3 months after surgery. In the graft atherosclerosis+ group, the SVG diameter was larger, the graft velocity was slower, and the G/N ratio was higher compared with those in the graft atherosclerosis– group. There was no significant difference in MGF. In the graft atherosclerosis+ group, two grafts were occluded at subsequent CCTA, and above-knee SVGs were used more frequently because the diameter of below-knee SVGs was less than 2 mm or there were multiple branches in below-knee SVGs. The cross-sectional area of SVG at subsequent CCTA in the graft atherosclerosis+ group was reduced to 69.6% compared with postoperative CCTA within 3 months (mean follow-up period: 5.6 years).

In the multivariate logistic regression model that adjusted the influence of predefined confounders about intraoperative and postoperative CCTA within 3 months (**Table 3**), low graft velocity and high G/N ratio were significantly associated with the graft atherosclerosis (adjusted odds ratio [aOR] 5.0, 95% confidence interval [CI] 1.4–18.6, $P = 0.016$; aOR 6.6, 95% CI 1.9–23.6, $P < 0.01$, respectively). The SVG diameter was also considered to be an important factor, but without statistically significant difference.

The results of our second analysis, comparison of C-SVG and N-SVG are shown in **Supplementary Table 1**. Differences were observed across most covariates before matching. After propensity score matching, baseline characteristics were almost well balanced between the two groups except for concomitant surgery, and there was no significant difference in patients, lesion, or SVG characteristics. The C-SVG group and the N-SVG group both had 54 grafts. Regarding intraoperative measurements and postoperative CCTA within 3 months (**Table 4**), the N-SVG group had much more MGF (40.0 [25.0–53.3] vs 27.5 [16.0–37.0], $P < 0.01$), lower PI (2.0 [1.4–2.5] vs 2.3 [1.6–3.5], $P = 0.03$), and higher graft velocity (9.0 [6.0–12.2] vs 5.8 [3.7–7.1], $P < 0.01$) than the C-SVG group, although there was no significant difference in the SVG diameter and the G/N ratio at 3 months.

Table 2 Intraoperative and postoperative characteristics

	Graft atherosclerosis+ (n = 27)	Graft atherosclerosis– (n = 93)	*P* value
Intraoperative characteristics			
Above knee SVG, n (%)	**3 (11)**	**0 (0)**	**<0.01**
Sequential bypass, n (%)	5 (19)	23 (25)	0.50
MGF, mL/min, median [IQR]	20.0 [14.0–35.0]	26.0 [15.0–34.5]	0.57
PI, median [IQR]	2.7 [1.9–4.0]	2.3 [1.6–3.4]	0.45
Postoperative CCTA within 3 months characteristics and calculated graft velocity			
SVG diameter, mm, ±SD	**3.3 ± 0.5**	**3.0 ± 0.5**	**0.019**
SVG cross–sectional area, mm², ±SD	**8.5 ± 2.5**	**7.3 ± 2.2**	**0.036**
Graft velocity, cm/sec [IQR]	**4.3 [3.4–5.9]**	**6.1 [3.8–7.7]**	**0.016**
Native coronary artery diameter, mm, ±SD	1.8 ± 0.4	1.9 ± 0.5	0.13
G/N ratio, ±SD	**1.9 ± 0.5**	**1.6 ± 0.3**	**<0.01**
Postoperative subsequent CCTA characteristics			
SVG diameter, mm, ±SD	**2.7 ± 0.7**	**3.1 ± 0.5**	**<0.01**
SVG cross-sectional area, mm², ±SD	**6.0 ± 2.5**	**7.5 ± 2.5**	**<0.01**
ΔSVG cross sectional area (%)	**69.6 ± 18.9**	**103.6 ± 14.1**	**<0.01**
Mean follow-up, y, IQR	5.6 [3.0–7.4]	4.3 [3.2–5.6]	0.23
SVG failure, n (%)	**2 (7)**	**0 (0)**	**<0.01**

SVG: saphenous vein graft; CCTA: coronary computed tomography angiography; MGF: mean graft flow; IQR: interquartile range; PI: pulsatility index; SD: standard deviation; G/N ratio: graft and native coronary artery diameter ratio; ΔSVG cross-sectional area: percentage change in SVG cross-sectional area of postoperative CCTA within 3 months and subsequent CCTA

Table 3 Impact for graft atherosclerosis in multivariable analysis

	Univariable OR (95% CI)	*P* value	Multivariable OR (95% CI)	*P* value
Graft velocity <5.64, cm/sec	**3.8 [1.5–9.8]**	**<0.01**	**5.0 [1.4–18.6]**	**0.016**
MGF<20, mL/min	1.3 [0.53–3.0]	0.59		
SVG diameter ≥3.5, mm	**3.6 [1.4–9.6]**	**<0.01**	2.9 [0.91–9.4]	0.073
Native diameter <1.5, mm	1.5 [0.54–4.0]	0.46		
G/N ratio ≥2	**5.7 [2.2–14.9]**	**<0.01**	**6.6 [1.9–23.6]**	**<0.01**

OR: odds ratio; CI: confidence interval; MGF: mean graft flow; G/N ratio: graft and native coronary artery diameter ratio; SVG: saphenous vein graft

Table 4 Intraoperative measurements and postoperative CCTA characteristics within 3 months after propensity score matching

	C-SVG (n = 54)	N-SVG (n = 54)	*P* value
MGF, mL/min, median [IQR]	**27.5 [16.0–37.0]**	**40.0 [25.0–53.3]**	**<0.01**
PI, median [IQR]	**2.3 [1.6–3.5]**	**2.0 [1.4–2.5]**	**0.03**
SVG diameter, mm, ±SD	3.2 ± 0.47	3.0 ± 0.43	0.11
SVG cross sectional area, mm², ±SD	8.0 ± 2.2	7.3 ± 2.1	0.10
Graft velocity, cm/sec [IQR]	**5.9 [3.7–7.1]**	**9.0 [6.0–12.2]**	**<0.01**
Native diameter, mm, ±SD	1.9 ± 0.37	1.8 ± 0.37	0.22
G/N ratio, ±SD	1.7 ± 0.42	1.7 ± 0.36	0.88

CCTA: coronary computed tomography angiography; SVG: saphenous vein graft; C-SVG: conventionally harvested saphenous vein graft; N-SVG: no-touch harvested saphenous vein graft; MGF: mean graft flow; IQR: interquartile range; PI: pulsatility index; SD: standard deviation; G/N ratio: graft and native coronary artery diameter ratio

Discussion

In our first analysis, low graft velocity and high G/N ratio were associated with progression of the graft atherosclerosis in the C-SVG group. In the second analysis, graft velocity and MGF of N-SVG were much higher than those in the C-SVG group.

The relationship between graft velocity and shear stress is an important consideration in the graft atherosclerosis. The magnitude of the shear stress can be estimated in most of the vasculature by Poiseuille's law, which states that shear stress is proportional to blood velocity and is inversely proportional to the third power of the internal radius.[26] Low-wall shear stress is known to promote development of atherosclerosis through the loss of endothelial cell alignment in the direction of the flow, to promote increase in low-density lipoprotein (LDL) cholesterol accumulation, and to promote transmigration of macrophages, which lay the foundation for atherosclerotic plaque formation.[16] Atherosclerotic plaque formation progress leads to significant intraluminal stenosis. Intraluminal stenosis causes stagnant flow, further reducing the flow velocity and creating a vicious cycle. Khan et al. reported the role of shear stress in the graft atherosclerosis using patient-specific computational fluid dynamics; stenosis formation was associated with low-wall shear stress.[16] In our first analysis, low graft velocity was associated with the graft atherosclerosis in the multivariate analysis, suggesting that low graft velocity contributes to low shear stress and atherosclerosis. Motwani et al. suggested that the clinical impact of vein graft atheroma had a marked increase 5–7 years postoperatively,[3] and that further graft atherosclerosis progression and increase in diseased vein grafts should be noted. G/N ratio ≥2 was also a significant predictor of the graft atherosclerosis in multivariate analysis (aOR 6.6 [1.9–23.6], P <0.01). This factor is important in terms of thrombus formation and intimal hyperplasia due to flow disturbance.[2,15] Reducing the graft and native coronary artery diameter mismatch by selecting the appropriate graft size and avoiding excessive dilatation may be beneficial.

In our second analysis, which compared C-SVG with N-SVG in propensity score-matched analysis, graft velocity and MGF of N-SVG were much greater than those of C-SVG. In general, graft velocity depends on graft flow and graft diameter. Jiang et al. reported that N-SVG was associated with higher MGF than C-SVG, and this was the result of less spastic features and less intimal endothelium damage due to the SVG harvest procedure and intraluminal pressure.[13,21] More MGF are associated with higher graft velocity, which contributes to increased shear stress, endothelial nitric oxide synthase, and other shear stress-dependent factors, especially in the intimal endothelium-preserved N-SVG.[16,21] These mechanisms may lead to less spastic graft and intimal thickening regression, i.e., antiatherosclerotic effect, and provide short- and long-term patency comparable to those of arterial grafts.[8,23,27] The blood flow to the SVG wall is mainly supplied from the intraluminal blood through the vasa vasorum, and this is also important in the long-term patency of N-SVG, which is the preserved vasa vasorum.[9] In our second analysis, the diameter of N-SVG did not have a significant difference compared with that of C-SVG detected by postoperative CCTA within 3 months. In our experience, graft angiography after CABG tends to have a large graft diameter compared with N-SVG, but vasodilation may have been affected by premedication during CCTA because N-SVG was more responsive to the drugs.[10]

In addition to surgical techniques, postoperative pharmacotherapy and control of coronary risk factors are also important in the suppression of the graft atherosclerosis.[2,28] The American Heart Association (AHA) recommends the use of antiplatelet therapy for life, and dual antiplatelet therapy over monotherapy with aspirin to improve graft patency in off-pump CABG. The SVG occlusion due to intimal hyperplasia and atheromatous plaque is related to increased levels of LDL cholesterol, so the AHA recommends that all CABG patients receive statin therapy. Focusing on VGD, White et al. previously reported that more steady blood flow leads to less SVG remodeling.[29] In our study, aspirin was administered for all patients, and statins, beta-blocker use, and diabetes mellitus control were not thought to contribute to the graft atherosclerosis suppression in our first analysis (**Supplementary Table 1**); however, they remain important in the prevention of graft atherosclerosis.

Limitations

This study has several limitations. First, it is a single-center retrospective study that focuses on the patients who had CCTA within 3 months and subsequent CCTAs. Only half of the eligible patients were actually evaluated (**Supplementary Fig. 1**) due to discharge to other hospitals for rehabilitation. We routinely performed CCTA in

outpatient follow-up, but half of the patients were lost to follow-up beyond that. Second, we did not focus on patients who had chronic kidney disease (eGFR <45) except for those undergoing hemodialysis, so the relationship between chronic kidney disease and the graft atherosclerosis remains unknown. Also, the median observation period for this study was 5.8 years for the graft atherosclerosis+ group and 4.2 years for the graft atherosclerosis– group, with fewer patients in the graft atherosclerosis+ group. Shah et al. reported that graft failure increased more than 5 years postoperatively,[6] so further investigation is needed. Third, we did not measure the graft velocity intraoperatively, so we used the calculated value with intraoperative MGF and cross-sectional area of the SVG in CCTA within 3 months. Although the relationship between slow graft velocity and the graft atherosclerosis was revealed, the appropriate cutoff value of practical vein graft velocity remains unknown. Fourth, some grafts may be outer remodeling due to VGD and were not included as the graft atherosclerosis in this study. Fifth, the postoperative medication was not controlled because of retrospective nature (**Supplementary Table 2**). Finally, while we could report that N-SVG had faster vein graft velocity, the relationship between N-SVG and long-term patency should be continuously followed.

Conclusion

Slow graft velocity and high G/N ratio were associated with the graft atherosclerosis in the conventional harvest, and N-SVG increased MGF and graft velocity. N-SVG is suggested to be a good long-term quality graft comparable to other arterial grafts, and the graft velocity may be a reason for the prevention of graft atherosclerosis.

Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Author Contributions

RN and KH designed the study and are entirely responsible for its content. RN drafted the manuscript. KH, YN, and KA critically revised the manuscript. HK and TF helped to draft the manuscript. All authors have read and approved the final manuscript.

Acknowledgments

We acknowledge proofreading and editing by Benjamin Phillis at the Clinical Study Support Center at Wakayama Medical University.

Disclosure Statement

None declared.

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