

The expansion of no-touch harvesting sequential vein graft after off-pump coronary artery bypass grafting

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Funding information

National Natural Science Foundation of China, Grant/Award Numbers: 81570373, 81770412; Beijing Hospital Authority Project, Grant/Award Number: PX2018027

Abstract

Background and Aim of the Study: Many studies support that the no-touch (NT) procedure can improve the patency rate of vein grafts. However, it is not clear that the sequential vein graft early expansion in the NT technique during off-pump coronary artery bypass grafting (CABG). This study will explore this issue.

Methods: This was a prospective single-center randomized controlled clinical trial. A total of 100 patients undergoing off-pump CABG with the sequential saphenous graft were randomly assigned to two groups: the NT and conventional (CON) groups. Perioperative and postoperative data were collected during the hospital stay. The mean diameter of sequential grafts was measured using cardiac computed tomography angiography 3 months after the operation.

Results: There was a significant difference in the average diameter of sequential grafts between the two groups (NT: $[2.98 \pm 0.42]$, CON: $[3.26 \pm 0.51]$, $p = .005$). There was no difference in occlusion of sequential venous grafts between the two groups (NT: 4/48 [8.3%], CON: 5/49 [10.2%], $p = 1.000$). There were differences in surgery time between the two groups (NT: 220 [188,240], CON: 190 [175,230], $p = .009$).

Conclusions: The sequential graft early expansion in the NT technique is not as pronounced as that in the conventional technique, which may have a long-term protective effect on the grafts.

KEYWORDS

cardiac computed tomography angiography (CCTA), conventional saphenous vein graft harvesting, coronary artery bypass grafting (CABG), no-touch saphenous vein graft harvesting, off-pump CABG, sequential saphenous vein grafting

Abbreviations: BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; CCTA, cardiac computed tomography angiography; CON, conventional saphenous vein graft harvesting; Cr, creatinine; HbA1c, glycosylated hemoglobin; IABP, intra-aortic balloon pump; ICU, intensive care unit; IQR, interquartile range; LVEDD, left ventricular end diastolic; LVEF, left ventricular ejection fraction; NT, no-touch saphenous vein graft harvesting; PCI, percutaneous coronary intervention; SVG, saphenous vein graft; TnI, troponin I.

Clinical trial registration: Registered 1 November 2018, [ClinicalTrials.gov](https://clinicaltrials.gov) NCT03729531, <http://www.clinicaltrials.gov>.

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1 | INTRODUCTION

Coronary artery bypass surgery is an effective way to treat multi-vessel disease, complex lesions, and severe left main coronary heart disease.¹⁻³ The graft materials are mainly the combination of the left internal mammary artery and saphenous vein graft.⁴ Early graft failure after coronary artery bypass grafting (CABG) was present in up to 12% of grafts.⁵ The low patency rate of the saphenous vein remains a major challenge.⁶ Therefore, it is essential to determine how to improve the patency rate of the venous grafts.

In 1996, the Swedish expert Souza's team initiated the no-touch (NT) technology, which retained part of the tissue surrounding the vein; the vein did not dilate manually after harvesting it. This reduced the damage to the vein's intima, decreased vascular smooth muscle cell activation, and protected against distension-induced damage.^{7,8} After 16 years of follow-up, the patency rate of venous grafts in the NT group was found to be comparable to that of the left internal mammary artery.⁹⁻¹² It is not clear that the sequential vein graft early expansion in the NT technique during off-pump coronary artery bypass surgery. The more obvious degree of vein dilation, the greater damage to the vein. This study aimed to test the expansion of NT technology in off-pump CABG in sequential venous grafts.

2 | MATERIALS AND METHODS

2.1 | Medical ethics

The study was approved by the Ethics Committee of Beijing Anzhen Hospital and Capital Medical University (Approval Numbers:

2018036X) and informed consent was taken from all individual participants.

2.2 | Study design

This was a single-center, randomized controlled study testing the expansion of NT technology in off-pump CABG in sequential venous grafts. The enrollment of participants was determined by selecting random envelopes. The flow chart and study design schedule are presented in Figure 1.

2.3 | Participants

This study recruited 100 patients who underwent off-pump coronary artery bypass grafting in cardiac surgery center China, from December 2018 to October 2019.

The inclusion criteria were as follows: (a) aged 18–80 years; (b) at least three-vessel coronary artery disease; and (c) voluntarily joined the study and signed the informed consent form. The exclusion criteria were as follows: (a) simultaneous operations (such as heart valve or lung or abdominal surgery); (b) emergent surgery; (c) ejection fraction $\leq 35\%$; (d) complicated with interventricular septal perforation and ventricular aneurysm; (e) redo CABG; (f) internal diameter of great saphenous vein ≤ 0.20 cm, varicose great saphenous vein, or venous tortuosity; (g) complicated with severe malignant tumor or other serious systemic diseases; (h) severe renal insufficiency (creatinine >200 $\mu\text{mol/L}$); (i) dual antiplatelet taboo; (j) severe peripheral vascular disease; (k) allergy to the radio-contrast agent; (l) participation in other clinical trials at the same time.

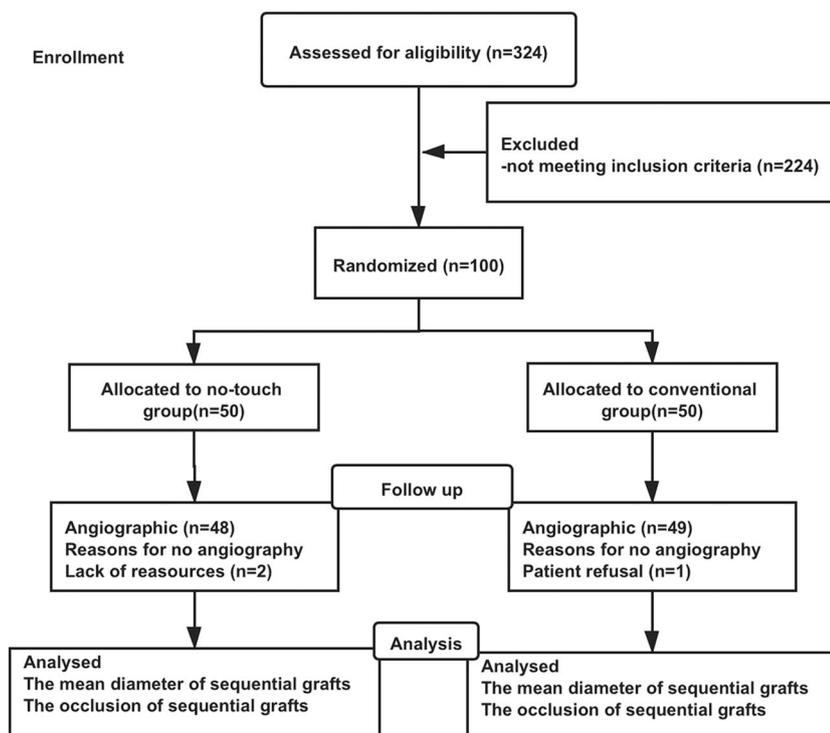


FIGURE 1 The flow diagram of enrolled patients

2.4 | Randomization

Participants will be randomly assigned (at a 1:1 ratio) to the NT and conventional saphenous vein graft harvesting (CON) groups with a random permuted block length of four patients per block to ensure that trial groups at each block are balanced. The specific scientific research secretary kept and facilitated the random drawing of lots. The study patients were blinded.

2.5 | Interventions

2.5.1 | Surgical techniques

All patients were examined using bilateral great saphenous vein ultrasonography and marked before the operation. The patients received off-pump coronary artery bypass surgery with only one sequential venous graft.

2.5.2 | NT group

The leg incision was cut longitudinally along the ultrasound mapping line made before the operation, and the trunk of the vein was exposed. When the trunk of the vein was dissociated, approximately 2 mm of the surrounding tissue was retained on both the left and right sides. The vein was not dilated after harvesting. After removal, the vein was stored in a mixture containing heparinized saline and papaverine hydrochloride. The vein was fully predilated by aortic pressure and then examined for leakage.

2.5.3 | Control group

The leg skin was cut longitudinally along the preoperative ultrasound marking line to expose the trunk and separate the visible branches. When the trunk of the vein dissociated, the surrounding tissue was not retained. The vein was dilated using a syringe filled with heparinized saline, checked for leakage, and placed in a mixture of heparinized saline and papaverine. Other operational processes were similar to those in the NT group.

2.6 | Follow-up

All patients underwent cardiac computed tomography angiography (CCTA) 3 months after the operation.

2.7 | Outcome measures

1. The average diameter of sequential grafts at 3 months

The preoperative sequential graft diameter was measured by venous ultrasound. We used CCTA to compare the average diameter of the sequential graft of the two groups at 3 months after the surgery. The CCTA was used to measure the diameter of the sequential grafts in the proximal, middle, and distal segments, and then the average diameter of the grafts was calculated as shown in Figures 2–4.

2. The occlusion rate of sequential vein grafts 3 months after the operation

This was detected using CCTA as shown in Figure 5. Evaluation of graft failure: the number of failures was calculated by distal anastomosis. The graft and anastomotic failure were evaluated according to the

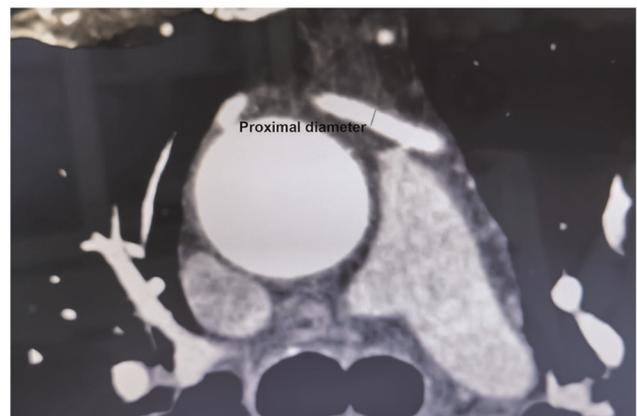


FIGURE 2 The measurement diameter of proximal segment of sequential graft



FIGURE 3 The measurement diameter of middle segment of sequential graft

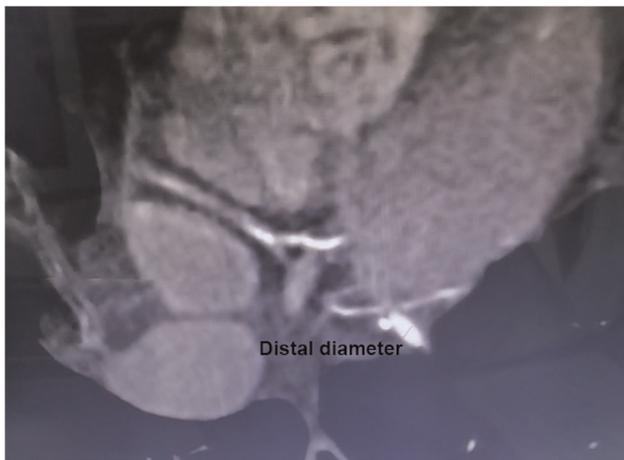


FIGURE 4 The measurement diameter of distal segment of sequential graft

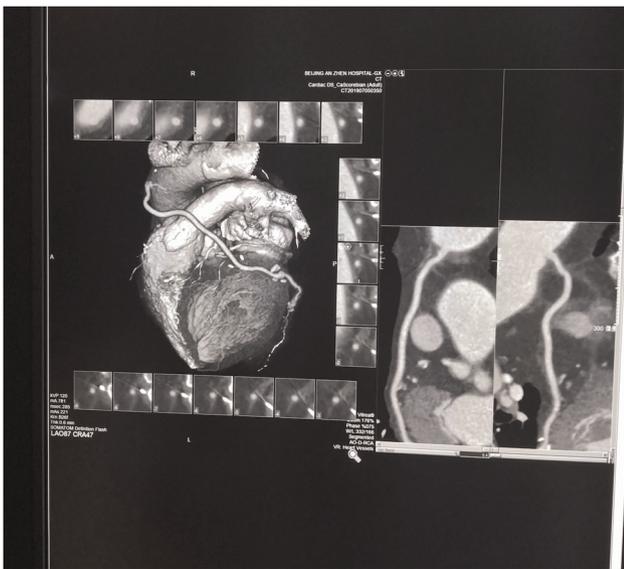


FIGURE 5 The patency of sequential vein grafts by CCTA. CCTA, cardiac computed tomography angiography

FitzGibbon classification system.¹³ FitzGibbon-A refers to a wide range of unobstructed grafts or less than 50% narrow grafts; FitzGibbon-B is a limited flow graft with a narrowing higher than 50%. FitzGibbon-O refers to an occlusive graft without blood flow. In this study, FitzGibbon-A/B was used for patency, and FitzGibbon-O was used for graft failure. The diseased graft was also regarded as a lesion if the lesion was located at the proximal/distal anastomosis site or the graft trunk. To determine the effectiveness of the sequential grafts more early, CCTA detection was carried out in advance 3 months after the operation.

3. Surgical data and postoperative mortality

Number of grafts, total number of distal anastomoses, left main disease, surgical duration, acute renal failure, atrial

fibrillation, intra-aortic balloon pump (IABP) implantation, blood transfusion, bleeding reoperation, ventilation time, and intensive care unit (ICU) stay were analysed.

2.8 | Statistical methods

SPSS 22.0 for Mac (IBM SPSS Statistics) was used for statistical analyses. Continuous variables are reported as the mean \pm SD or median (interquartile range) (IQR). Categorical variables were reported as the absolute frequency and as a percentage. The Student *t* test was applied for continuous data with equal or unequal variances. The Mann-Whitney *U* test was applied for continuous data that were not normally distributed. Pearson's χ^2 and Fisher's exact tests were used for categorical data. Statistical significance was accepted at *p* less than .05.

3 | RESULTS

3.1 | Patients

A total of 324 patients were recruited from December 2018 to April 2020 in Beijing Anzhen Hospital China. Finally, a total of 50 patients were randomly assigned to the NT group and 50 patients to the CON group. A total of 97 patients (48 patients in the NT group and 49 patients in the CON group) received a CCTA follow-up survey. The flow of patients through the trial up to 3 months of follow-up is shown (Figure 1). The groups were well matched in age, sex, body mass index, smoking, left ventricular ejection fraction, previous medical history, and so on (Table 1). Intraoperative and postoperative data are shown in Tables 2 and 3.

3.2 | Follow-up

In the surgical arm, (NT: 48, CON: 49) underwent CCTA. There was a 100% clinical follow-up.

3.3 | Outcomes

3.3.1 | The average diameter of sequential grafts

Among the 100 patients, 2 in the NT group and 1 in the CON group failed the follow-up CCTA examination. The diameters of sequential grafts measuring 48 and 49 were determined in the NT group and the CON group, respectively. There was a significant difference in the average diameter of sequential grafts between the two groups (NT: [2.98 \pm 0.42], CON: [3.26 \pm 0.51], *p* = .005) as shown in Figure 6. The detailed results are shown in Table 4.

TABLE 1 Characteristics of the patients at baseline

Characteristic	NT group (N = 50)	CON group (N = 50)	p Value
Age (year), mean \pm SD	61.0 \pm 8.7	59.8 \pm 7.8	.463
Male, n (%)	46 (92.0)	47 (94.0)	1.000
Body-mass index (kg/m ²) >25, n (%)	31 (62.0)	30 (60.0)	.838
Smoking, n (%)	26 (52.0)	28 (56.0)	.688
Hypertension, n (%)	29 (58.0)	30 (60.0)	.839
Diabetes mellitus, n (%)	18 (36.0)	20 (40.0)	.680
Hyperlipidemia, n (%)	12 (24.0)	11 (22.0)	.812
Peripheral vascular disease, n (%)	14 (28.6)	14 (28.6)	.950
Previous stroke, n (%)	4 (8.0)	5 (10.0)	1.000
Previous myocardial infarction, n (%)	23 (46.0)	22 (44.0)	.841
Previous PCI, with or without stent, n (%)	6 (12.0)	6 (12.0)	1.000
LVEF (%), median (IQR)	60 (55, 65)	60 (56, 67)	.521
LVEDD (mm), mean \pm SD	49.9 \pm 5.1	49.6 \pm 5.8	.813
Euroscore II median (IQR)	0.98 (0.69, 1.41)	0.91 (0.55, 1.28)	.195
BNP (pg/ml), median (IQR)	62 (31, 113)	62 (37, 150)	.687
Tnl (ng/ml), median (IQR)	0.01 (0.00, 0.06)	0.01 (0.00, 0.02)	.461
Cr (μ mol/L), median (IQR)	66.5 (57.1, 82.0)	73.1 (66.2, 80.1)	.067
HbA1c (%), median (IQR)	6.3 (5.6, 7.6)	6.4 (5.6, 7.2)	.950

Abbreviations: BNP, B-type natriuretic peptide; CON, conventional saphenous vein graft harvesting; Cr, Creatinine; HbA1c, glycosylated hemoglobin; IQR, Interquartile range; LVEDD, left ventricular end diastolic; LVEF, left ventricular ejection fraction; NT, no-touch saphenous vein graft harvesting; PCI, percutaneous coronary intervention; Tnl, troponin I.

TABLE 2 Surgical characteristics

Variable	NT group (N = 50)	CON group (N = 50)	p Value
Number of grafts, n (%)			
In situ internal thoracic artery	49 (98.0)	48 (96.0)	1.000
Double sequential	39 (78.0)	36 (72.0)	.488
Triple sequential	-	-	-
Total number of distal anastomoses	161	164	-
Left coronary territory	107 (66.5)	108 (65.9)	.908
Right coronary territory	-	-	-
Left main disease, n (%)	15 (30.0)	12 (24.0)	.499
Surgical duration (min) median (IQR)	220 (188, 240)	190 (175, 230)	.009

Abbreviations: CON, conventional saphenous vein graft harvesting; IQR, interquartile range; NT, no-touch saphenous vein graft harvesting.

3.3.2 | The occlusion rate of sequential vein grafts 3 months after the operation

There was no difference in occlusion of sequential venous grafts between the two groups (NT: 4/48 (8.3%), CON: 5/49 (10.2%), $p = 1.000$) as showed in Table 4.

3.3.3 | Surgical data and postoperative mortality

There were differences in surgery time between the two groups (NT: 220 [188, 240], CON: 190 [175, 230], $p = .009$) as showed in Table 2. There was no difference in the number of grafts, total number of distal anastomoses, left main disease, acute renal

Variable	NT group (N = 50)	CON group (N = 50)	p Value
Postoperative mortality, n (%)			
Bleeding reoperation	1 (1.1)	0 (0)	1.000
Acute renal failure	2 (4.0)	1 (2.0)	1.000
Atrial fibrillation	14 (28.0)	10 (20.0)	.349
IABP implantation	2 (4.0)	1 (2.0)	1.000
Blood transfusion	7 (14.0)	12 (24.5)	.185
Postoperative duration, median (IQR)			
Ventilation time (h)	14.7 (12.4, 20.7)	16.0 (13.2, 19.3)	.586
ICU stay, (h)	22.0 (17.0, 41.0)	22.5 (20.3, 29.4)	.722

TABLE 3 Comparison of early results in hospital

Abbreviations: CON, conventional saphenous vein graft harvesting; IABP, intra-aortic balloon pump; ICU, intensive care unit; IQR, interquartile range; NT, no-touch saphenous vein graft harvesting.

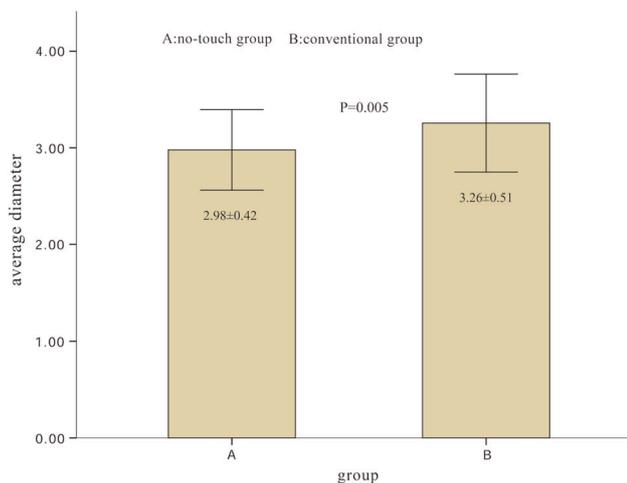


FIGURE 6 Comparison of average diameter of sequential grafts

failure, atrial fibrillation, IABP implantation, blood transfusion, bleeding reoperation, ventilation time, and ICU stay as showed in Tables 2 and 3.

4 | DISCUSSION

This study aimed to explore the sequential vein graft early expansion in the NT technique during off-pump coronary artery bypass surgery. The results showed that the sequential graft early expansion in the NT technique is not as pronounced as that in the conventional technique.

One of the characteristics of NT technology is that the vein is not manually expanded after harvesting. The expansion of the vein graft depended entirely on the blood pressure of the aorta. In this case, the degree of postoperative expansion of the graft obtained using NT may be weaker than that of the conventional

Variable	NT group (N = 48)	CON group (N = 49)	p Value
Diameter (mm), mean ± SD			
Preoperative diameter of sequential graft	2.62 ± 0.47	2.71 ± 0.78	.517
Diameter of proximal segment of sequential graft	3.34 ± 0.49	3.47 ± 0.64	.275
Diameter of middle segment of sequential graft	2.91 ± 0.48	3.17 ± 0.53	.014
Diameter of distal segment of sequential graft	2.68 ± 0.48	3.11 ± 0.75	.002
Average diameter of sequential graft	2.98 ± 0.42	3.26 ± 0.51	.005
Vein grafts occlusion, n (%)	4(8.3)	5(10.2)	1.000

TABLE 4 Comparison of average diameter and occlusion of sequential grafts at 3 months

Abbreviations: CON, conventional saphenous vein graft harvesting; NT, no-touch saphenous vein graft harvesting.

group. Therefore, CCTA was used to compare the average diameter of the sequential graft of the two groups 3 months after surgery. The results indicate that the average diameter of veins in the NT group was significantly less than that in the conventional group (Figure 6). This suggested that NT technology reduced the damage caused by vein expansion while ensuring the safety and effectiveness of the surgery. This milder vein expansion may have a protective effect on the long-term patency of sequential grafts. We only find that the change of vein dilation from the morphology by CCTA, and we need to explore the pathophysiological changes of vein graft in future, so as to draw a more reliable conclusion.

There was no difference in occlusion of sequential venous grafts between the two groups. The milder vein expansion in NT group did not lead to higher patency rate. On the one hand, the sample is small, on the other hand, our follow-up period is too short. Larger sample size and longer-term follow-up need to be implemented, which may lead to more meaningful results.

There were differences in surgery time between the two groups. In the actual operation process, the NT harvesting process needs to be more careful to prevent tissue and vein graft damage. In addition, due to the pedicle of the vein graft, it is necessary to carefully identify the direction of the vein during the anastomosis, and carefully examination of the venous branches is required for bleeding. All of these will prolong the operation time.

Previous studies showed that the vein grafts obtained by NT technology were mostly single vein grafts, and the most common surgery was on-pump CABG.^{9,12,14,15} This is different from our study; we used all sequential vein grafts, and all procedures were off-pump CABG. Sequential vein grafts can preserve vein length, and off-pump bypass grafting can accelerate postoperative recovery and reduce the incidence of postoperative complications.¹⁶ Many studies have shown that there is no substantial difference between single vein and sequential vein grafts.¹⁷⁻¹⁹

There were limitations in this study. The study was a single-center study; the sample is small. A multicentre, large sample, prospective randomized controlled study may be carried out in the future, which can provide more definitive evidence for the effect of NT technology. Our follow-up period is too short. It is necessary to explore the pathophysiology of vein graft, and more convincing conclusions can be drawn from molecular biology.

5 | CONCLUSIONS

The sequential graft early expansion in the NT technique is not as pronounced as that in the conventional technique, which may have a long-term protective effect on the grafts.

ACKNOWLEDGMENTS

This work was supported by funding of the Beijing Hospital Authority Project (PX2018027) and the National Natural Science Foundation of China (Grant Nos.: 81570373 and 81770412).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Ran Dong and Jubing Zheng were responsible for the design, supervision of the study, and revision of the manuscript. Xuejian Hou drafted the manuscript. Kui Zhang and Bangrong Song designed a statistical plan. Yang Li and Taoshuai Liu participated in the revision of the manuscript and the coordination of the study. Yang Zhao, Shijun Xu, and Zhuhui Huang participated in data acquisition. All authors read and agreed to the final manuscript.

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How to cite this article: Hou X, Zhang K, Liu T, et al. The expansion of no-touch harvesting sequential vein graft after off-pump coronary artery bypass grafting. *J Card Surg.* 2021; 36:2381-2388. <https://doi.org/10.1111/jocs.15577>