Sequential Vein Bypass Grafting is Not Associated with an Increase of Either In-hospital or Mid-term Adverse Events in Off-pump Coronary Artery Bypass Grafting

Fucheng Xiao, Jian Wang, Hengchao Wu, Hansong Sun

Department of Cardiovascular Surgery, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital and Cardiovascular Institute, National Center for Cardiovascular Diseases, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100037, China

Abstract

Background: The impact of sequential vein bypass grafting on clinical outcomes is less known in off-pump coronary artery bypass grafting (CABG). We aimed to evaluate the effects of sequential vein bypass grafting on clinical outcomes in off-pump CABG.

Methods: From October 2009 to September 2013 at the Fuwai Hospital, 127 patients with at least one sequential venous graft were matched with 127 patients of individual venous grafts only, using propensity score matching method to obtain risk-adjusted outcome comparison. In-hospital measurement was composite outcome of in-hospital death, myocardial infarction (MI), stroke, requirement for intra-aortic ballon pump (IABP) assistance and prolonged ventilation. Major adverse cardiac events (MACEs: Death, MI or repeat revascularization) and angina recurrence were considered as mid-term endpoints.

Results: No significant difference was observed among the groups in baseline characteristics. Intraoperative mean blood flow per vein graft was 40.4 ml in individual venous grafts groups versus 59.5 ml in sequential venous grafts groups ($P < 0.001$). There were no differences between individual and sequential venous grafts groups with regard to composite outcome of in-hospital mortality, MI, stroke, IABP assistance and prolonged ventilation (11.0% vs. 14.2%, $P = 0.45$). Individual in-hospital measurement also did not differ significantly between the two groups. At about four years follow-up, the survival estimates free from MACEs (92.5% vs. 97.3%, $P = 0.36$) and survival rates free of angina recurrence (80.9% vs. 85.5%, $P = 0.48$) were similar among individual and sequential venous grafts groups with a mean follow-up of 22.5 months. In the Cox regression analysis, sequential vein bypass grafting was not identified as an independent predictor of both MACEs and angina recurrence.

Conclusions: Compared to individual vein bypass grafting, sequential vein bypass grafting was not associated with an increase of either in-hospital or mid-term adverse events in patients undergoing off-pump CABG.

Key words: Coronary Artery Bypass; Sequential Grafting; Surgery

Introduction

Although the arterial grafts have superior long-term patency rates, especially for left internal mammary artery to left anterior descending artery,\(^1\) saphenous vein grafts continue to be the backbone of daily coronary revascularization practice. The sequential vein bypass grafting is a frequently used technique in coronary surgical revascularization whereby more than one distal anastomosis is constructed per segment of conduit used. The major advantages of sequential vein bypass grafting includes saving graft material, reduction of the number of proximal anastomoses and more importantly, higher graft flow\(^2\) and thereby, increased graft patency rates.\(^3\)\(^-\)\(^5\) Furthermore, by allowing anastomoses to smaller coronary arteries in patients with diffuse coronary disease, sequential vein bypass grafting is thought to achieve a more complete revascularization, which theoretically should translate into better clinical outcomes.\(^6\)

In the present era of coronary artery surgery, an increasing volume of patients with diffuse coronary disease and patients requiring re-do coronary artery bypass grafting (CABG) with limited available graft material are being referred to surgical revascularization since the number of patients who underwent CABG over the past four decades is relatively huge and patients with focal coronary artery lesions or even simple multi-vessel coronary diseases are being successfully treated with percutaneous coronary intervention (PCI). Under this situation, sequential vein bypass grafting is likely to increase. However, there are inconsistent and limited
evidences with regard to clinical outcomes of sequential vein bypass grafting.[7‑13] Moreover, most of those studies were conducted two decades ago in patients undergoing on-pump CABG[7,9,11‑13] and no longer reflect contemporary coronary surgical management. Less is known about the impact of sequential vein bypass grafting on clinical outcomes in off-pump CABG. So the objective of this study is to provide a present-day assessment of the effects of sequential vein bypass grafting on in-hospital and mid-term clinical outcomes following off-pump CABG.

**Methods**

**Patient population**

A cohort of 920 consecutive patients, who underwent isolated off-pump CABG from October 2009 to September 2013, operated by one surgical team at the Fuwai Hospital (Beijing, China), was obtained. Sequential venous graft was defined as a venous graft with the number of distal anastomoses exceeding the number of its proximal anastomoses. Of those 920 patients, there were 165 patients with at least one sequential venous graft (sequential venous grafts group) and the remainder with individual venous grafts only (individual venous grafts group). We propensity-matched 127 out of 165 patients receiving at least one sequential venous graft to 127 out of 755 patients with individual venous graft only. This study was approved by the Institutional Review Board of Fuwai Hospital with patient informed consent waived.

**Surgical procedure**

Because off-pump CABG is technically more demanding, and expertise in constructing a sequential anastomosis is perhaps among the major determinants of graft patency or clinical outcomes, the present study only includes patients operated by one surgical team to minimize the surgical variability. The heart was exposed through a median sternotomy in all the patients. An Octopus stabilizer (Medtronic, Minneapolis, MN), a humidified carbon dioxide blower (Medtronic DLP, Grand Rapids, MI) and intracoronary shunts (CardioThoracic System, Cupertino, CA, USA) were used routinely to facilitate the anastomoses distally or proximally. The number of distal anastomoses is generally two on one sequential venous graft in our current policy. The remaining anastomoses were made on another segment of graft. The distal anastomosis on a sequential graft was done in end-to-side fashion and middle ones were done in side-to-side fashion. Side-to-side anastomoses were performed in a crossing fashion and in a diamond-shape, and end-to-side ones were done parallel to the native coronary vessel axis. All distal anastomoses were done using double-armed 7–0 polypropylene sutures with a continuous sutureting technique. Proximal anastomoses were stitched to the ascending aorta with continuous double armed 6–0 polypropylene sutures during partial-clamping of the aorta. When hemodynamics were stable after completion of all the anastomoses, the graft blood flow and pulsatility index were measured by flow meter to confirm patency of the grafts (Veri-Q, Medistim, Oslo, Norway). The proximal segment of the graft was chosen as the measuring site.

**Clinical outcomes and definition**

The in-hospital measurement of our study was composite outcome of in-hospital death, myocardial infarction (MI), stroke, the need for intra-aortic balloon pump (IABP) assistance and prolonged ventilation. Major adverse cardiac events (MACEs: death, MI or repeat revascularization) and angina recurrence during follow-up were considered as mid-term endpoints. In-hospital death was defined as death regardless of cause during hospitalization. Perioperative MI was documented by the following criteria: The creatine kinase MB must be ≥5 times the upper limit of normal or development of new Q waves in two or more contiguous electrocardiograph leads.[14] Stroke was defined as a central neurologic deficit persisting postoperatively for >72 hours.[15] We excluded confused states, transient events, and intellectual impairment to avoid any subjective bias. Postoperative IABP requirement is defined as low cardiac output state requiring newly IABP assistance. Prolonged ventilation was defined as duration of ventilation great than 24 hours. Death during follow-up was defined as all-cause mortality after patient’s discharge. MI during follow-up was defined a new Q wave in two or more contiguous leads on electrocardiography, or significant increase of cardiac enzyme levels (great than the upper limit of the normal) combined with electrocardiographic or clinical or angiographic evidence of MI. Repeat revascularization was defined as PCI or CABG. Recurrence of angina was defined as occurrence of chest pain or distress due to myocardial ischemia after discharge.

**Clinical follow-up**

The postoperative results were assessed in all patients at discharge and during follow-up. Patients diagnosed with hyperlipemia resumed statins therapy postoperatively and during follow-up, and beta-blocker and aspirin were generally taken in all the patients except for few patients with respective contraindications. All patients had been followed up at least three months since discharge from hospital with the exception of patients who were lost to follow-up. Follow-up involved review of outpatient and (or) inpatient medical records and structured telephone interviews. The medical records in outpatient clinics of those who reported any adverse events after discharge were reviewed for further confirmation. When any major adverse event was reported by another hospital, patients were requested to mail a copy of all relevant medical information. Follow-up was 95.7% (243/254) complete with a mean follow-up of 22.5 months (with a median follow-up of 23.6 and 21.6 months for MACEs and angina recurrence respectively).

**Statistical analysis**

To minimize potential selection bias in the comparisons of outcomes between the two groups, a propensity score matching using multivariate logistic regression model was performed to match patients of sequential venous grafts with patients of
individual venous grafts only in a 1-to-1 fashion. Variables selected for inclusion in the propensity score were core patients’ characteristics, including age, sex, insulin-dependent diabetes, hypertension, body mass index, left ventricular ejection fraction, previous cardiac surgery, numbers of vessels grafted and extent of coronary disease as previously described. Left ventricular end diastolic diameter was also included because of significant difference among the two groups before matching. The receiver operating characteristics curve was used to estimate the area under the curve of the model, predicting the probability of being included in any of the two groups. The C statistic, which is equivalent to the receiver operating characteristic curve, for this model was 0.86. Using a greedy matching algorithm, patients of sequential venous grafts were matched with patients of individual venous grafts only on an identical propensity score in a higher-digit priority order, namely a five-digit to a four-, three-, two-, or one-digit match. If more than one patient of individual venous grafts only were matched to patient of sequential venous grafts, patient with individual venous grafts only was selected randomly among those patients and eventually, 127 well-matched pairs of patients were obtained.

Continuous data are shown as mean ± standard deviation. The Student’s t-test was used to measure the differences for variables with a normal distribution and equal variances. The Wilcoxon rank sum test was used for variables not normally distributed. Categorical data are displayed as frequencies and percentages and comparisons were made with Chi-square tests (Fisher exact tests if appropriate). P < 0.05 was considered statistically significant. Kaplan-Meier product limit curves for event-free survival were constructed and compared with the log-rank test. The hazard ratio (HR) with 95% confidence interval (CI) was derived from the Cox proportional hazards model. All statistical analyses were performed using Statistical Analysis System (SAS) for Windows version 9.1 (SAS Institute, Cary, NC).

**RESULTS**

**Baseline and procedural characteristics**

The baseline characteristics of the propensity-matched patients with sequential or individual vein bypass grafting respectively are given in Table 1. Both groups were well matched with the only significant difference being that patients receiving sequential grafts had lower rates of preoperative angina (P = 0.03). Detail of grafts and flow measurement are presented in Table 2. No significant difference was observed between the two groups in distal anastomoses, graft pulsative index and blood flow per distal anastomoses. The mean number of sequential anastomoses, graft pulsative index and blood flow per distal anastomoses was 2.0 ± 0.1 in sequential grafts group. Despite of fewer proximal anastomoses (P < 0.001), patients with sequential grafts had a higher blood flow per vein graft (P < 0.001), especially per sequential vein graft (P < 0.001).

**In-hospital outcomes**

Results of in-hospital outcomes are shown in Table 3. No significant differences was present in in-hospital composite endpoints, with 14 (11.0%) total events in individual venous grafts group versus 18 (14.2%) in sequential venous grafts group (P = 0.45). Also, there were no significant differences between individual venous grafts and sequential venous grafts group with regard to the individual outcome of in-hospital mortality (0.8% vs. 0.0%, P = 1.00), MI (0.8% vs. 0.8%, P = 1.00), stroke (0.8% vs. 0.8%, P = 1.00), IABP assistance (0.0% vs. 0.8%, P = 1.00) and prolonged ventilations (10.2% vs. 13.4%, P = 0.44).

**Mid-term outcomes**

Major adverse cardiac events occurred in six (4.7%) patients (two deaths, two MIs and two PCIs) in individual venous grafts group and two (1.6%) patients (two MIs) in sequential venous grafts group. The Kaplan-Meier MACE-free survival estimates at about four years were 92.5% and 97.3% in the individual and sequential venous grafts group respectively (P = 0.36; Figure 1a). The HR for sequential vein bypass grafting was estimated at 0.21 (95% CI, 0.03–1.85, P = 0.16). The survival rates free of angina recurrence at about 4 years was 80.9% in patients receiving individual venous grafts only versus 85.5% in patients receiving sequential venous grafts (P = 0.48; Figure 1b), with HR for sequential vein bypass grafting at 0.70 (95% CI, 0.27–1.83, P = 0.47).

![Figure 1](image-url): Event-free Kaplan-Meier Estimates for individual venous grafts group and sequential venous grafts group respectively. Shown are percent survival free from MACE (a) and survival free of angina recurrence (b). MACE: Major adverse cardiac events.
Table 1: Baseline characteristics of propensity-matched patients based on sequential venous grafts

| Characteristics                      | Individual grafts (n = 127) | Sequential grafts (n = 127) | P     |
|--------------------------------------|-----------------------------|-----------------------------|-------|
| Age (years), (mean ± SD)             | 62.1 ± 9.3                  | 61.3 ± 8.3                  | 0.34  |
| Female, n (%)                        | 32 (25.2)                   | 27 (21.3)                   | 0.46  |
| BMI (kg/m²), (mean ± SD)             | 25.7 ± 3.2                  | 25.6 ± 3.1                  | 0.84  |
| Diabetes mellitus, n (%)             | 42 (33.1)                   | 42 (33.1)                   | 1.00  |
| Hypertension, n (%)                  | 84 (66.1)                   | 89 (70.1)                   | 0.50  |
| Renal dysfunction, n (%)             | 0 (0)                       | 2 (1.6)                     | 0.50  |
| COPD, n (%)                          | 3 (2.4)                     | 2 (1.6)                     | 0.65  |
| Carotid artery stenosis, n (%)       | 26 (20.5)                   | 35 (27.6)                   | 0.19  |
| History of PCI, n (%)                | 14 (11.0)                   | 16 (12.6)                   | 0.70  |
| Cerebrovascular disease, n (%)       | 16 (12.6)                   | 14 (11.0)                   | 0.70  |
| Hyperlipidaemia, n (%)               | 73 (57.5)                   | 74 (58.3)                   | 0.90  |
| Angina pectoris, n (%)               | 123 (96.9)                  | 115 (90.6)                  | 0.03  |
| Myocardial infarction, n (%)         | 44 (34.7)                   | 54 (42.5)                   | 0.20  |
| Ejection fraction, %, (mean ± SD)    | 58.3 ± 11.8                 | 59.2 ± 10.9                 | 0.57  |
| LVEDD (mm), (mean ± SD)              | 49.0 ± 8.6                  | 49.4 ± 7.7                  | 0.95  |
| RWMA, n (%)                          | 50 (39.4)                   | 52 (40.9)                   | 0.80  |

Mitral regurgitation, n (%)
- None, n (%) 116 (91.3) 111 (87.4) 0.55
- Mild, n (%) 10 (7.9) 14 (11.0) 
- Moderate, n (%) 1 (0.8) 2 (1.6) 
- Atrial fibrillation, n (%) 2 (1.6) 5 (3.9) 0.45
- Prior cardiac surgery, n (%) 1 (0.8) 1 (0.8) 1.00
- Preoperative IABP 1 (0.8) 0 (0.0) 
- Coronary artery disease, n (%)
  - Single-vein disease, n (%) 2 (1.6) 1 (0.8) 0.73
  - Two-vein disease, n (%) 3 (2.4) 6 (4.7) 
  - Three-vein disease, n (%) 72 (56.7) 69 (54.3) 
- Left main, n (%) 50 (39.4) 51 (40.2) 
- LIMA, n (%) 127 (100) 124 (97.6) 0.25
- NYHA, n (%)
  - 1 20 (15.8) 11 (8.7) 0.20
  - 2 93 (73.2) 103 (81.1) 
  - 3 13 (10.2) 13 (10.2) 
  - 4 1 (0.8) 0 (0.0) 

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; IABP: Intra-aortic balloon pump; LIMA: Left internal mammary artery; LVEDD: Left ventricular end diastolic diameter; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention; RWMA: Regional wall motion abnormality; SD: Standard deviation.

Table 2: Procedural characteristics of propensity-matched patients based on sequential venous grafts

| Characteristics                      | Individual grafts (n = 127) | Sequential grafts (n = 127) | P     |
|--------------------------------------|-----------------------------|-----------------------------|-------|
| Distal anastomoses                   | 3.8 ± 0.5                   | 3.8 ± 0.5                   | 0.90  |
| Proximal anastomoses                | 2.8 ± 0.5                   | 1.9 ± 0.5                   | <0.001|
| Sequential anastomoses              | 0 ± 0.0                     | 2.0 ± 0.1                   | <0.001|
| Blood flow per distal anastomoses   | 35.3 ± 13.3                 | 33.7 ± 13.0                 | 0.34  |
| Blood flow per VG (ml)              | 40.4 ± 16.6                 | 59.5 ± 27.0                 | <0.001|
| Pulsatile index per VG              | 1.9 ± 0.6                   | 1.9 ± 0.7                   | 0.44  |
| Blood flow per SVG or IVG (ml)      | 40.4 ± 16.6                 | 69.7 ± 32.3*                | <0.001|
| Pulsatile index per SVG or IVG      | 1.9 ± 0.5*                  | 1.9 ± 0.6*                  | 0.70  |

*Values for SVG and IVG respectively. IVG: Individual vein graft; SVG: Sequential vein graft; VG: Vein graft.

Table 3: In-hospital outcomes of propensity-matched patients based on sequential venous grafts

| Variables                      | Individual grafts (n = 127) | Sequential grafts (n = 127) | P     |
|-------------------------------|-----------------------------|-----------------------------|-------|
| Composite in-hospital outcome, n (%) | 14 (11.0)                  | 18 (14.2)                   | 0.45  |
| In-hospital mortality, n (%)  | 1 (0.8)                     | 0 (0.0)                     | 1.00  |
| Myocardial infarction, n (%)  | 1 (0.8)                     | 1 (0.8)                     | 1.00  |
| Stroke, n (%)                 | 1 (0.8)                     | 1 (0.8)                     | 1.00  |
| IABP, n (%)                   | 0 (0.0)                     | 1 (0.8)                     | 1.00  |
| Prolonged ventilation, n (%)  | 13 (10.2)                   | 17 (13.4)                   | 0.44  |

IABP: Intra-aortic balloon pump. Composite in-hospital outcome includes in-hospital mortality, myocardial infarction, stroke; IABP requirement and prolonged ventilation.

DISCUSSION

This retrospective analysis of 127 propensity-matched pair of patients is performed in an attempt to assess the impact of sequential vein bypass grafting on both in-hospital and mid-term clinical outcomes in the setting that there was limited and inconsistent data concerning clinical outcomes of sequential vein bypass grafting and that published reports on this subject were conducted mostly in patients undergoing on-pump CABG and failed to exclude the impact of different level of surgical expertise with sequential grafting technique. The present study suggests that sequential vein bypass grafting technique was not independently associated with increased risk of composite or individual outcomes of in-hospital mortality, MI, stroke, IABP assistance and prolonged ventilation in patients undergoing off-pump CABG. Moreover, mid-term MACEs and angina recurrence was also comparable between sequential venous grafts group and individual venous grafts group.

Sequential grafting was introduced by Flemma et al.[19] in 1970s. A single vein used as sequential graft can revascularize whole heart as a snake graft. The sequential bypass grafting technique is a widely used surgical technique in myocardial revascularization.[10,12,20] The key concept of sequential grafts is decreased total resistance to graft flow by having more than one target per segment. Indeed, the resistance in a sequential circulation is decreased with two or more distal anastomoses because the size of vascular bed is increased so that flow increase. This notion was supported by our observation that blood flow in sequential vein graft was significantly increased compared with individual vein graft, which was in line with the results reported by Nordgaard et al.[3] Through this higher flow the main bypass trunk stays open and may assist in maintaining patency of side-to-side anastomoses to arteries with a poor runoff.[3-5] One recent meta-analysis[21] by Li et al., which included 12 studies and compared 6838 sequential grafts towards 3285 individual vein grafts, reported that the mid-term and long-term risk of occlusion in
sequential grafts was lower than that in individual grafts (risk ratio 0.67, 95% CI 0.60–0.74, \(P < 0.0001\)).

Studies regarding the effect of sequential vein bypass grafting on clinical outcome in on-pump CABG had yielded inconsistency results. Early favorable results from the study by Bigelow et al.[7] involving 130 patients, revealed benefits of better survival with sequential vein bypass grafting, compared to multiple individual grafts. Garatti et al.[8] recently reported the results of an observational study to evaluate the effect of sequential vein bypass grafting on early and long-term clinical outcomes in 452 propensity matched patients. They observed that sequential vein bypass grafting group was even comparable to total arterial revascularization group in in-hospital mortality, long-term survival, repeat PCI, MI and even reappearance of angina during a mean follow-up of 14 ± 4 years.

Despite purported benefits, the use of sequential vein bypass grafting is variable among surgeons. Sequential grafting typically puts all the eggs in one basket. Concerns have centered on the dependence of multiple distal anastomoses on a common inflow with the possibility of catastrophic consequences in the event of a proximal occlusion, thus leading to the patient’s life at stake. After having followed up 428 patients in 15 years following a coronary revascularization procedure, van Brussel et al.[9] found although more complete revascularization was obtained in patients with sequential vein grafts only, more events (death, MI and reintervention), especially MI, occurred in these patients than in patients with individual vein grafts only. Likewise, Mehta et al.[10] recently reported in a subanalysis of the PREVENT IV trial that patients with sequential vein bypass grafting were more likely to have grafts failure, a trend towards higher death, acute MI or repeated revascularization in the 5 years following surgery.

All those studies concerning the effect of sequential vein bypass grafting on clinical outcomes were done using patients who had on-pump CABG. Off-pump CABG is now gaining increasing recognition, especially in Asian countries, which account for at least 60% of all the CABG operations.[22] The safety and efficacy of this procedure have been well documented.[23] However, the impact of sequential vein bypass grafting is seldom investigated in off-pump CABG. Compared to on-pump CABG, sequential vein bypass grafting in off-pump CABG is technically more demanding due to its increased difficulty of conduit manipulation and complexity of certain distal anastomoses during beating heart surgery. Such feature of off-pump CABG may exert great impact on the quality of constructing the anastomoses and eventually on clinical outcomes.

The present study shows that compared to individual vein bypass grafting, sequential vein bypass grafting was not associated with an increase of either in-hospital or mid-term adverse events in patients undergoing off-pump CABG and additionally, the hazard of proximal occlusion of a sequential grafts, leading to severely adverse cardiac events, might be overestimated. Findings from Christenson et al.[11] also failed to detect significant survival benefits with sequential vein bypass grafting and suggested that a proximal occlusion of a sequential bypass resulted in renewed angina without infarction or sudden death in most instances. It is possible that a proximally occluded sequential vein graft will function as a large collateral vessel, provided that the terminal anastomosis is connected to a large coronary vessel with high blood flow. Similarly, our findings corresponded well to both studies described by Meeter et al.[12] and Ouzounian et al.,[13] who demonstrated in their study that sequential grafting was not found to be an independent predictor of short-term and long-term adverse events after adjusting for baseline difference in patients receiving on-pump CABG. It might appear strange that although the mid-term survival rate free from MACEs and angina recurrence is higher in sequential venous grafts group in the present study, the purported benefits of sequential vein bypass grafting did not necessarily translate into statistically significant difference of those clinical outcomes. A reason, as we speculated, might be that the period of follow-up of the present study may be not long enough to detect any significant group difference of mid-term outcome. Moreover, this finding could be explained in part by the fact that incomplete sequentialization of distal venous anastomosis (69%, 255 sequential venous anastomoses in 369 distal venous anastomoses) in sequential venous grafts group might have also diluted the beneficial effect of sequential vein bypass grafting.

The results of this study support the use of either grafting technique for venous conduits by surgeons at their discretion. Sequential grafting should be preferably considered in the following clinical scenarios: Patients with athero-aortic disease with the desire to limit manipulation of the proximal aorta; patients with limited length of graft material and small target vessels and patients with special requirement for reducing hypoperfusion time of certain organs during operation; younger patients with the need for total arterial grafting. However, further studies are needed to validate the safety of sequential grafting technique for total arterial revascularization.

There are limitations in the present study. One major limitation was that it was a retrospective study which possesses limitations due to the inherent biases that exist in nonrandomized, unblinded studies, thus limiting the generalizability of our conclusions. Although propensity matching method, which is by far the best method of comparison in observational settings, was used, the unknown variables that affect the outcomes of interest could not be fully eliminated. Moreover, the sample size in our study was relatively small because we only included patients operated by one surgical team to minimize the surgical technique and expertise viability which probably was among the major determinants of graft patency or clinical outcomes. Finally, direct assessment of graft patency by means of angiographic data or coronary computed tomography was lacking to verify whether the
adverse cardiac events during follow-up were resulted from grafts failure. Therefore, a further study, especially randomized controlled trial, with increasing sample size and longer follow-up is needed to confirm our results, a large multi-center, randomized, controlled trial is needed to yield high-level evidence on this issue. However, there is, so far, no clinical trial available comparing the outcome between the sequential vein bypass grafting and individual vein bypass grafting.

Compared to individual vein bypass grafting, sequential vein bypass grafting was not associated with an increase of either in-hospital or mid-term adverse events in patients undergoing off-pump CABG. The results of this study support the use of either grafting technique. However, in view of widely reported benefit of higher patency rate associated with sequential vein bypass grafting, we recommended the use of sequential vein bypass grafting when feasible.

REFERENCES

1. Hillis LD, Smith PK, Anderson JL, Butil JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. J Am Coll Cardiol 2011;58:e123-210.

2. Nordgaard H, Vitale N, Haaverstad R. Transit-time blood flow measurements in sequential saphenous coronary artery bypass grafts. Ann Thorac Surg 2009;87:1409-15.

3. O’Neill MJ Jr, Wolf PD, O’Neill TK, Montesano RM, Waldhausen JA. A rationale for the use of sequential coronary artery bypass grafts. J Thorac Cardiovasc Surg 1981;81:686-90.

4. Meurala H, Vallee M, Hekali P, Somer K, Frick MH, Harjola PT. Patency of sequential versus single vein grafts in coronary bypass surgery. Thorac Cardiovasc Surg 1982;30:147-51.

5. Gronidin CM, Limet R. Sequential anastomoses in coronary artery grafting: Technical aspects and early and late angiographic results. Ann Thorac Surg 1977;23:1-8.

6. Garcia S, Sandoval Y, Roukoz H, Adabag S, Canoniero M, Yannopoulos D, et al. Outcomes after complete versus incomplete revascularization of patients with multivessel coronary artery disease: A meta-analysis of 89,883 patients enrolled in randomized clinical trials and observational studies. J Am Coll Cardiol 2013;62:1421-31.

7. Bigelow JC, Bartley TD, Page US, Krause AH Jr. Long-term follow-up of sequential aortocoronary venous grafts. Ann Thorac Surg 1976;22:507-14.

8. Garatti A, Castelvecchio S, Canziani A, Corain L, Generali T, Mossuto E, et al. Long-term results of sequential vein coronary artery bypass grafting compared with totally arterial myocardial revascularization: A propensity score-matched follow-up study. Eur J Cardiothorac Surg 2014;46:1006-13.

9. van Brussel BL, Plokker HW, Voors AA, Ernst JM, Kelder JC, Knaepen PJ, et al. Different clinical outcome in coronary artery bypass with single and sequential vein grafts: A fifteen-year follow-up study. J Thorac Cardiovasc Surg 1996;112:69-78.

10. Mehta RH, Ferguson TB, Lopes RD, Haffey GE, Mack MJ, Kouchoukos NT, et al. Saphenous vein grafts with multiple versus single distal targets in patients undergoing coronary artery bypass surgery: One-year graft failure and five-year outcomes from the Project of Ex-Vivo Vein Graft Engineering via Transfection (PREVENT) IV trial. Circulation 2011;124:280-8.

11. Christenson JT, Simonet F, Schmuziger M. Sequential vein bypass grafting: Tactics and long-term results. Cardiovasc Surg 1998;6:389-97.

12. Meeter K, Veldkamp R, Tijsen JG, van Herwerden LL, Bos E. Clinical outcome of single versus sequential grafts in coronary bypass operations at ten years’ follow-up. J Thorac Cardiovasc Surg 1991;101:1076-81.

13. Ouzouian M, Hassan A, Yip AM, Bath KJ, Baskett RJ, Ali IS, et al. The impact of sequential grafting on clinical outcomes following coronary artery bypass grafting. Eur J Cardiothorac Surg 2010;38:579-84.

14. Cao L, Silvestry S, Zhao N, Dietl J, Sun J. Effects of preoperative aspirin on cardiocerebral and renal complications in non-emergent cardiac surgery patients: A sub-group and cohort study. PLoS One 2012;7:e30094.

15. STS General Thoracic Data Specifications, version 2.081. September 5, 2008. Accessed February 16, 2014 at http://www.sts.org/sites/default/files/documents/pdf/ndb/General Thoracic Data Specs V2081.pdf.

16. Jacob M, Smedira N, Blackstone E, Williams S, Cho L. Effect of timing of chronic preoperative aspirin discontinuation on morbidity and mortality in coronary artery bypass surgery. Circulation 2011;123:577-83.

17. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29-36.

18. Parsons LS. Reducing bias in a propensity score matchedpair sample using greedy matching techniques. In: Proceedings of the Twenty-Sixth Annual SAS Users Group International Conference, Long Beach, CA. Cary, NC: SAS Institute Inc.; 2001.

19. Flemming RJ, Johnson WD, Lepley D Jr. Triple aorto-coronary vein bypass as treatment for coronary insufficiency. Arch Surg 1971;103:82-3.

20. Christenson JT, Schmuziger M. Sequential venous bypass grafts: Results 10 years later. Ann Thorac Surg 1997;63:371-6.

21. Li J, Liu Y, Zheng J, Bai T, Liu Y, Wang X, et al. Thepatency of sequential and individual vein coronary bypass grafts: A systematic review. Ann Thorac Surg 2011;92:1292-8.

22. Taggart DP, Altman DG. Off-pump vs. on-pump CABG: Are we any closer to a resolution? Eur Heart J 2012;33:1181-3.

23. Polomsky M, He X, O’Brien SM, Puskas JD. Outcomes of off-pump versus on-pump coronary artery bypass grafting: Impact of preoperative risk. J Thorac Cardiovasc Surg 2013;145:1193-8.