

# Mid-Term Clinical Outcome of Patients Undergoing Coronary Artery Bypass Grafting with Valvulotomized Vein Grafts

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## ABSTRACT

**Background:** The lower patency rate of vein grafts (VG) in comparison to arterial grafts may be related to vein valves, which favor turbulences and thrombosis that lead to graft failure. The aim of this study was to determine the outcome of patients with valvulotomized VG after coronary artery bypass grafting (CABG) procedure.

**Methods:** From 2007 to 2014, 233 patients with a mean age of  $67 \pm 9$  years had CABG or combined CABG and valve procedures. Valvulotomized saphenous VG and arterial grafts were used. Clinical follow-up and outcome were evaluated after  $6.3 \pm 2$  years. The graft patency was rated with multislice computed tomography in 57 patients and coronary angiography in 29 patients  $3.1 \pm 2$  years postoperatively.

**Results:** Overall, 168 patients had segregated CABG surgery, and 65 patients received additional procedures, with mean  $2.7 \pm 1$  arterial and  $1.5 \pm 0.7$  venous anastomoses. The 30-day-mortality in isolated CABG patients was 2%. Survival at five years was 80%. Major adverse cardiac and cerebrovascular events (MACCE) free rate at five years was 80%. At the last follow up (mean 6.3 years), 94% of the patients were in Canadian Cardiovascular Society (CCS) class 0. The quote of patent valvulotomized VG was 96.1% compared to a patency rate of 96.7% for the arterial grafts in the subgroup undergoing angiography or computed tomography of the heart.

**Conclusion:** Our data demonstrate good mid-term results of graft patency, and comparable clinical results in patients undergoing CABG with valvulotomized VG. A longer follow-up period and a higher number of bypass graft imaging examinations are necessary to affirm our results.

## INTRODUCTION

One of the biggest advantages of coronary artery bypass grafting (CABG) is the longevity and patency of grafts. The Syntax trial showed that CABG is the norm of care for patients with multi-vessel or left main coronary artery disease, with

superior results in terms of major adverse cardiac and cerebrovascular events (MACCE) compared to percutaneous coronary intervention (PCI) [Mohr 2013]. In the Syntax trial, a large number of patients had a bypass operation using an internal thoracic artery and additional saphenous vein (SV) graft. During the last 17 years, several studies report an increased usage of arterial grafts for CABG, due to its survival benefit [Glineur 2012; Taggart 2001; Calafiore 2000; Lytle 1999].

The ideal choice for the second graft in CABG is still a controversial issue, as studies on this topic with randomized trials and a significant number of patients are lacking. A 90% patency rate for VG at five years is described in a randomized study by Hayward and colleagues [Hayward 2010]. However, the disadvantages of venous conduits are obvious, including diameter mismatch and vein valves [Mills 1989]. Mills characterizes the vein valves as “bad guys” in CABG that might have an influence on hemodynamic relevant narrowing [Mills 1989]. The work of Lajos and coworkers may show enhanced patency of valvulotomized VG in “horseshoe grafts” [Lajos 2007].

In this study we aimed to analyze patency data and clinical outcomes of patients who received CABG with valvulotomized vein graft (VG) at the University Hospital Frankfurt am Main.

## MATERIALS AND METHODS

CABG with valvulotomized VG was performed on 233 patients from 2007 to 2014 at the University Hospital Frankfurt am Main. During this period, 4737 isolated CABG and 1142 CABG and concomitant procedures were performed. Patients who received valvulotomized VG in our center were included. All VGs were valvulotomized except when they were already free of vein valves. The preoperative patient data are characterized in Table 1. Patients were an average of  $67 \pm 9$  years old.

The area of the anterior wall was always provided with the left internal mammary artery (LIMA). A valvulotomized VG was bypassed to the right coronary artery (RCA). The circumflexus area was revascularized depending on graft disposability (with radial artery [RA], or right internal mammary artery [RIMA]), and the risk criterion of the patient. The RA was used when the target vessel had a profound stenosis (>80%). We avoided bilateral use of internal mammary artery (BIMA) in patients with chronic obstructive pulmonary disease (COPD) or insulin dependent diabetes mellitus. Retrospective and follow up clinical data were collected. Our institutional ethics committee permitted the study.

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Table 1. Patient Characteristics

Variable list	
n (%)	233
Age	67 ± 9
Female	27
Male	206
CCS II-III	205 (89%)
NYHA II -III	211 (91%)
Former myocardial infarction	34 (15%)
Cardiogenic shock	2 (0.9%)
PCI/stent	42 (18%)
Hypertension	191 (82%)
Hypercholesterolemia	106 (45%)
COPD	22 (9%)
pad	18 (8%)
Renal insufficiency	40 (17%)
Diabetes mellitus	73 (31%)
Coronary artery disease	
Left main stenosis	87 (37%)
One-vessel disease	6 (3%)
Two-vessel disease	27 (11%)
Three-vessel disease	200 (86%)
EF (%)	54 ± 1
Previous heart operation	4 (2%)

CCS indicates Canadian Cardiovascular Society Angina Classification; NYHA, New York Heart Association classification; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; pad, peripheral artery disease; EF, ejection fraction.

### Operative Technique

The standard approach in CABG was median sternotomy. Preparation of IMA was done as a veno-arterial pedicle [Wimmer-Greinecker 1999]. The artery was rinsed with spasmolytic solution. The radial artery (RA) harvesting technique has been published elsewhere [Risteski 2006]. The great SV was taken gently from the lower limb, preserving the enclosed adventitia. The vein preparation has been described elsewhere [Monsefi 2016]. Cannulation of the vein at the distal end was performed, and tagging of venous valves was done by probing. Then, valvulotomy was undertaken using valve scissors (Ulrich medical, Ulm, Germany) before distal anastomoses were performed with the reversed vein [Monsefi 2016].

In detail, the venous graft harvesting was performed, the vein was removed, and the vein valves were then valvulotomized with a small valvulotomy scissor that was inserted gently into the inflated vein. When vein valves were present, their resistance could be felt when penetrating them gently

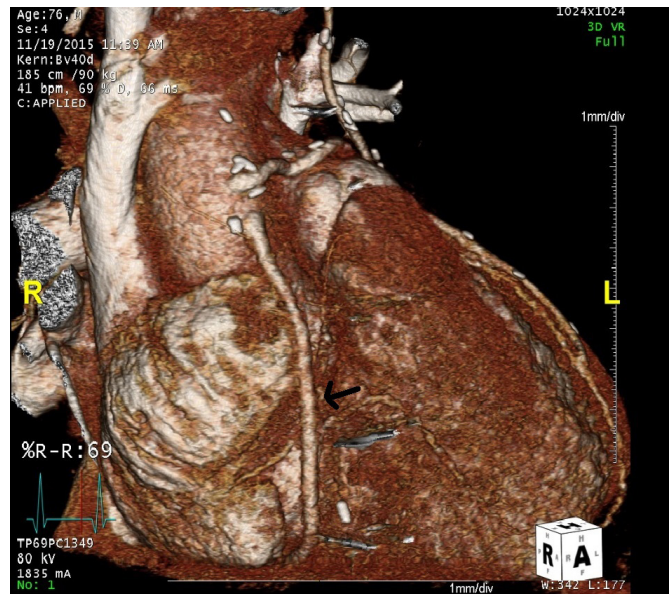


Figure 1. Computer tomography (CT) of the heart, with black arrow indicating the patent valvulotomized venous bypass graft to the right coronary artery (RCA).

with the valvulotomy scissors. When they were cut, the scissors were pushed forward in the vein until the complete length of the vein was valvulotomized. The vein flush solution consisted of a buffered saline solution loaded with papaverine and heparin.

The decision of placing the conduits to the recipient coronary was dependent on the amount of vessel disease, graft availability, and the grade of stenosis of the coronary vessel. LIMA was always used for the left anterior wall revascularisation (LAD). Another arterial graft (RIMA or radial artery) was used for the next territory (ramus circumflexus [RCX] or right coronary artery [RCA]). The radial artery was only used when the destination vessel had profound stenosis (>80%). For the third territory, the valvulotomized vein was used (RCX or RCA). Typically, we applied two arterial and one venous graft for CABG in cases of three diseased vessels.

The majority of CABG cases (n = 219, 94%) were performed on-pump. Calafiore solution was applied for myocardial protection [Calafiore 1996]. Distal anastomoses were done with 7/0 or 8/0 Prolene (Ethicon, Norderstedt). Lastly, proximal anastomoses to the aorta were finalized.

### Postoperative Follow-Up

Clinical follow up (6.3 ± 2 years) of the patients was assessed by phone call or letter, and was completed in 99% of patients. NYHA and CCS statuses were evaluated. Survival and MACCE were analyzed. MACCE was specified as all sources of death, myocardial infarction, cerebrovascular incident, and recurrent revascularization. Coronary angiography results from assigning cardiologists were also collected. In cases of atypical chest pain, patients were examined with multislice computed tomography of the heart (MSCT) for testing graft patency (Figure 1).

Table 2. Perioperative Results and Surgical Procedures

Variable list	
On pump	219 (94%)
CPB time mean (min)	151 ± 42
Cross-clamp time mean (min)	102 ± 31
Number of anastomoses (mean)	4.2 ± 1
Arterial	2.7 ± 1 (mean)
Venous	1.5 ± 0.7 (mean)
Number of grafts (number of anastomoses)	933
LIMA to anterior wall	215, with 135 sequential (total 350)
RIMA to CX	113, with 62 sequential (total 175)
Radial artery to CX	40, with 20 sequential (total 60)
Saphenous vein graft total	348
Saphenous vein graft to RCA	195, with 55 sequential (total 250)
Saphenous vein graft to CX	66, with 32 sequential (total 98)
Concomitant procedures in 65 patients	
Aortic valve replacement	25
Mitral valve repair	11
Tricuspid valve repair	6
Aorta ascendens replacement	8
Ablation	15
ICU stay (d)	2 ± 3
Ventilation time (h)	20 ± 27
Neurological event (stroke)	1 (0.4%)
Myocardial infarction	1 (0.4%)
Reangiography/stent	1 (0.4%)
Reoperation (bypass revision)	1 (0.4%)
30-d mortality (all procedures)	10 (4%)
30-d mortality (isolated CABG)	5 (2%)

CPB indicates cardiopulmonary bypass; LIMA, left internal mammary artery; RIMA, right internal mammary artery; ICU, intensive care unit; CX, circumflexus; RCA, right coronary artery; CABG, coronary artery bypass graft.

**Statistical Analysis**

Statistical analysis was performed using BIAS 11.06 software (Frankfurt, Germany). Continuous parameters are indicated as mean ± standard deviation, and categorical information as numbers and percentages. The survival curve and the MACCE free curve were evaluated using the Kaplan-Meier method. For comparison of the patency between the conduits, the chi-square or fisher’s exact test was applied.

Table 3. Follow-Up Data

Myocardial infarction	2 (1%)
Coronary reangiography	29 (12%)
CCS 0	150 (94%)
CCS I	9 (5%)
NYHA I	133 (83%)
NYHA II	24 (15%)
NYHA III	2 (1%)
Neurological event (stroke)	4 (2%)
Reoperation	0
Late mortality	63 (28%)
CT scan of the heart	57 (25%)
Results of 29 reangiographies and 57 CT scans in 86 patients	
Patency rate of venous BG to the RCA	94.8% (4/77 occluded)
Patency rate of venous BG to the CX	94.1% (1/17 occluded)
Patency rate of venous anastomoses	95.7% (5/117 occluded)
Patency rate of all venous BG	96.1% (5/94 occluded)
Patency rate of LIMA graft to anterior wall	97.6% (2/84 occluded)
Patency rate of RIMA graft to CX	94.2% (3/52 occluded)
Patency rate of radial artery graft to CX	100% (0/14 occluded)
Patency rate of arterial anastomoses	97.9% (5/242 occluded)
Patency rate of arterial BG	96.7% (5/150 occluded)

(mean 6.3 ± 2 years; 99% completed)

CCS indicates Canadian Cardiovascular Society Angina Classification; NYHA, New York Heart Association classification; TNM, temporary neurological deficit; CT, Computed tomography; BG, bypass graft; RCA, right coronary artery; CX, circumflexus.

**RESULTS**

As displayed in Table 2, 168 patients underwent single CABG, and 65 patients had concomitant procedures. The mean number of anastomoses was 4.2 ± 1, with a trend for increased arterial anastomoses (2.7 ± 1). There was one case of myocardial infarction perioperatively due to bypass kinking (LIMA-LAD) that lead to early bypass revision. There were no operative deaths. The 30-day-mortality was 2% (n = 5) in isolated CABG, and 4% (n = 10) in total: three patients suffered from multi organ failure (two of them urgent cases due to acute coronary syndrome), three died unexpectedly after uneventful recovery, two died of heart failure (one was in cardiogenic shock preoperatively), one patient suffered sepsis due to pneumonia, and one died of brain death due to stroke and cerebral edema.

Follow up data are presented in Table 3. In the follow up period, 63 patients died: 16 patients died of cancer, eight suffered from sepsis, six had terminal renal failure, four had a fatal fall, two died of multi organ failure, one died of sustained

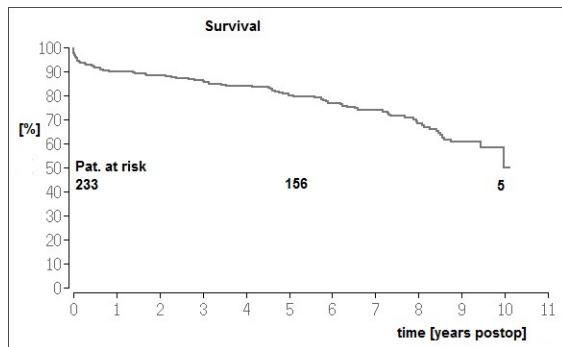


Figure 2. Kaplan-Meier-curve for survival.

rupture of a duodenal ulcer, two had ischemia of the bowel, two sustained fulminant stroke, three suffered from pneumonia, one from creutzfeldt jakob disease, and one from pulmonary edema. Ten patients had cardiac-related events like heart failure ( $n = 7$ ), myocardial infarction ( $n = 1$ ), cardiac arrest ( $n = 1$ ), and low cardiac output syndrome ( $n = 1$ ). In seven patients, the cause of death was unidentified. Kaplan-Meier survival at five years was 80% (Figure 2). MACCE free rate at five years was 80%, and 45% at ten years (Figure 3).

Twenty-nine re-angiographies and 57 MSCT scans were used for the assessments of graft patency in 86 patients; five patients had an occlusion of the VG. Two patients had an occlusion of the LIMA graft to the anterior wall, and three patients had an occlusion of the RIMA graft to the RCX. Two patients received stents in the RCX territory, one because of de-novo stenosis, and the other because of RIMA graft dysfunction. We analyzed a 96.1% patency rate for the valvulotomized VG with 94.8% for the RCA territory; specifically, a 92.6% patency rate (4/54 occluded) for VG to RCA, 100% (0/23 occluded) for VG to PDA ( $P = .23$ ), and 96.7% for the arterial grafts in the subgroup ( $n = 86$ )  $3.1 \pm 2$  years postoperatively. At the last follow up (mean of 6.3 years), 94% of the patients were in CCS class 0, and 83% were in New York Heart Association (NYHA) class I.

We compared the patency rates of the different conduits and found that there was no significant difference: Arterial versus venous BG patency,  $P = .33$ ; RIMA versus LIMA graft patency,  $P = .28$ ; radial artery versus RIMA graft patency,  $P = .48$ ; radial artery versus LIMA graft patency,  $P = .73$ ; radial artery versus venous graft patency,  $P = .49$ ; RIMA versus venous graft patency,  $P = .59$ ; LIMA versus venous graft patency,  $P = .27$ .

## DISCUSSION

The Syntax trial has emphasized that CABG should be the standard of treatment for patients with complex lesions, as MACCE was significantly better than PCI in their patient group [Mohr 2013]. Although there is a trend towards full arterial revascularization, the ideal choice for the second graft in CABG is still a controversial issue [Buttar 2017; Naik 2003]. Athanasiou and colleagues presented a meta-analysis of 35 studies that showed a superiority in mid-term (range

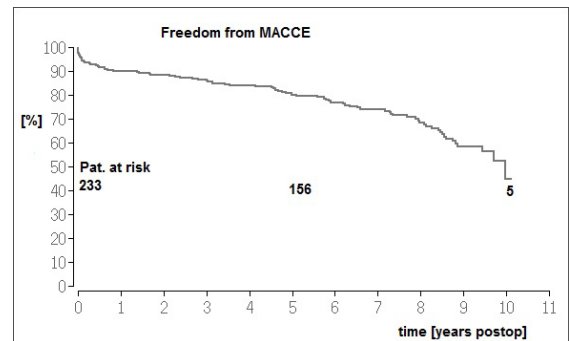


Figure 3. Freedom from major-adverse-cardiac-and-cerebrovascular-events (MACCE) curve.

51%-97%) and long-term patency (85%-94%) for RA conduits in comparison to SV (59%-91% at mid-term and 64%-91% at long-term), despite similar early patency rates of both conduits (50%-100% for RA and 60%-100% for SV conduits) [Athanasiou 2011].

In the small cohort of our study, the mid-term ( $3.1 \pm 2$  years) patency rate of valvulotomized VG was 96.1%, versus 100% in radial artery grafts (Table 3). This is comparable to Athanasiou's findings. Supporters of RA grafts advocate the minimal intimal proliferation and adaption to blood flow compared to SV grafts [Joannides 1995]. However, other studies suggest the use of SV conduits over RA grafts because of better mid-term patency rates of SV versus RA (64% versus 51.3% at a mean of 565 days follow-up) [Khot 2004]. The mid-term patency results of RIMA bypass grafting is 94.2% in our study, which is similar to the patency rate of valvulotomized VG (96%).

Glineur and colleagues examined 152 patients with coronary angiography, and reported the dysfunction of 25.3% of RIMA grafts six months postoperatively. In particular, when RIMA was anastomosed to the intermediate branch or RCA, the prognosis was inferior [Glineur 2009]. In the small cohort of our study (86 patients who received CT scan of the heart/coronaries or reangiography), RIMA graft patency was inferior in comparison to RA and LIMA graft patency, and similar to that of the SV graft at  $3.1 \pm 2$  years follow up (Table 3).

Mukherjee et al found 226 articles on the topic of whether the RIMA achieves an outcome superior to the saphenous VG for revascularization of the RCA. In summary, considering methodological limits and differences in evidence, they showed that the saphenous VG offers an improved outcome for revascularization of the RCA when compared to RIMA BG, and better results in patency, recurrent revascularization, and cardiovascular complication [Mukherjee 2012]. Hayward and colleagues presented data of a randomized trial that compared the patency rate of arterial (RA or RIMA) and saphenous VG as a second graft: At a mean 5.5 year follow-up angiography in mostly asymptomatic patients, the choice of arterial or venous graft for the second conduit did not significantly influence patency [Hayward 2010].

Shah and colleagues investigated the mid-term (3 years) graft patency rates of bypass grafts in randomized studies: the patency rate of the saphenous VG was 90%, similar to

that of the RA graft (91%) when used for the second best region [Shah 2005]. These findings are comparable to our data (Table 3). The valvulotomized VG had similar mid-term patency rates (96.1%) compared to that of arterial grafts in our study (100% for RA and 94.2% for RIMA). A few studies describe the merit of valvulotomized VG: Thubrikar described the pressure trap character as a possible cause of vein graft stenosis in an experimental survey. He showed that the veins opened and closed every cardiac circuit when the venous flow rate decreased under 30 mL/min, and that the blood flow in the segment distal to the venous valve stopped in each cycle [Thubrikar 1994]. Molina used valvulotomized saphenous VG in CABG and described a midterm patency rate of 90% (mean 3.5 years) for valvulotomized VG [Molina 1989]. Lajos et al showed an improvement of patency in valvulotomized “horseshoe grafts” [Lajos 2007].

In a former study, we demonstrated that flow in the venous bypass graft to the RCA increased significantly after valvulotomy, which supports the assumption noted above (+20.2 mL/min;  $P = .02$ ) [Monsefi 2016]. Of course, it is necessary to mention the potential detrimental effect of valvulotomy if it is performed incorrectly. If pushing the valvulotomy scissors in the vein by force, endothelial disruption and graft tear/trauma could occur, which could promote early graft closure. Our experience with valvulotomized saphenous VGs presents a patency rate of 96.1%, versus 96.7% for the arterial grafts after  $3.1 \pm 2$  years postoperatively in the subgroup ( $n = 86$ ). In this subgroup, valvulotomized vein grafts have analog mid-term patency as arterial grafts. However, the patency rates between the different conduits mentioned in the results section did not differ significantly in our study. We think that a longer follow up period and a higher sample size is necessary to reveal the long term effects of valvulotomy, and its effect on patency rate.

Valvulotomy is feasible, and seems to be an effective surgical technique to improve patency rate. The MACCE free rate was 80% at five years in our study, which is comparable to other reported trials [Mohr 2013]. However, long-term follow-up investigations and a larger volume of MSCTs and angiographies are needed to confirm our results.

## STUDY LIMITATIONS

About 86 of 233 (37%) patients in this study had a CT scan or coronary re-angiography of the heart. A higher volume of valvulotomized vein grafts cases, and more CT scans with a longer follow up period could provide clearer and more reliable results. Another limitation is the surgeons' experience, which plays an important role and affects also outcome. Finally, a randomized controlled survey or a propensity matched analysis that distinguishes between valvulotomized and non-valvulotomized VG would provide interesting data.

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