Long-term Graft Patency of Saphenous Vein Grafts after Endoscopic Harvest in Aortocoronary Bypass Surgery

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Abstract: Endoscopic vein harvest of the greater saphenous vein for aortocoronary bypass grafting presents a relatively newer and less invasive mode of vein harvest that has become a more popular approach used in the field of cardiac surgery. This study aimed to compare the long-term patency of saphenous vein grafts and clinical outcomes (a minimum of 10 years) after endoscopic harvest with open vein harvest in patients after isolated surgical myocardial revascularization. Fifty patients (25 after endoscopic and 25 after open harvest) who underwent isolated myocardial revascularization between 2009 and 2011 assessed. The study comprised two phases: completion of questionnaires assessing recurring symptoms of ischemic heart disease and visualisation of vein grafts via coronary computed tomography angiography to assess graft patency.
The primary outcome showed higher patency rates after open vein harvest (76.1 vs. 68.8%); without significant statistical difference (p=0.873). Differences in clinical outcomes were not statistically significant regarding recurring angina (28% endoscopic group, 32% open group, p=0.519), dyspnea (24 vs. 16%, p=0.817) and myocardial infarctions with catheter-based revascularization of vein grafts (8% endoscopic group, 16% open, p=0.734). Redo surgery was not reported in neither group. Endoscopic and open vein harvest yielded comparable long-term patency rates both angiographically and clinically. That strenghtens endoscopic approach as a non-inferior mode to the traditional approach in patients undergoing surgical myocardial revascularization.

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Introduction

Coronary artery bypass grafting (CABG) refers to a surgical treatment modality for ischemic heart disease that resolves obstructive coronary artery disease by re-routing and restoring optimal oxygenated blood flow to compromised parts of the myocardium. The ultimate goal of surgical revascularization of the myocardium is to achieve long-term improvement of the quality of life of patients with chronic or acute ischemic heart disease, symptomatic or asymptomatic with hemodynamically significant stenotic or totally occluded coronary arteries, with respect to the elimination of the occurrence or recurrence of angina pectoris, prevention of acute myocardial infarction, prevention of life-threatening ischemia-related ventricular arrhythmias, improving exercise tolerance, and preventing sudden death (Ivaniuk et al., 2016). Arterial or venous graft patency plays an important role in achieving long-term clinical outcomes of CABG. The greater saphenous vein (GSV) is widely known to be one of the most common and readily accessible conduits employed in surgical myocardial revascularization. Currently, two common approaches to vein harvest exist: the traditional open vein harvest (OVH) and the more recently introduced endoscopic vein harvest (EVH). Unlike conventional OVH, which requires a long incision corresponding to the length of the needed graft, EVH is a minimally invasive video-assisted approach for harvesting the. Since the inception of EVH, extensive comparative studies of leg wound morbidity between OVH and EVH have been conducted, has been proven to manifest significantly lower leg-wound morbidity rates after CABG (Aziz et al., 2005; Chiu et al., 2006; Yokoyama et al., 2021). However, few studies have evaluated long-term graft patency after EVH with its associated clinical outcomes. Some studies have documented an association between EVH and a higher incidence of early graft failure via vascular endothelial damage, triggering an inflammatory response and the subsequent activation of the coagulation cascade, thus facilitating early graft failure.

This study aimed to angiographically assess and compare the long-term graft patency, a minimum of 10 years after CABG, between saphenous vein grafts (SVGs) after EVH and OVH, and also comparing the clinical outcomes after bypass surgery.

Material and Methods

Study design

This was an observational, retrospective single-centre study approved by the local ethics Committee of the University Hospital; ethical approval number: 402/2020, project protocol number: 01/RVO-FNOs/2020. All cohorts were selected in chronological order from the date of CABG via the database of the Department of Cardiac Surgery, University Hospital Ostrava. This study retrospectively examined patients to assess vein graft patency via radiological imaging and subsequent clinical outcomes at a minimum follow-up time of 10 years after CABG.

Inclusion criteria

Adult patients between the ages of 18–85 years who had undergone isolated CABG from 2009 to 2011 with at least one saphenous vein graft and consenting participants.

Exclusion criteria

Moderate to severe chronic renal impairment as a relative contraindication for application of intravenous contrast material for radiographic imaging methods, non-consenting patients, deceased patients, conversion of EVH to OVH, and CABG with only arterial grafts, including MIDCAB (minimally invasive direct coronary artery bypass) procedure, a minimally-invasive method of myocardial revascularization of the left anterior descending artery (in some cases, diagonal branches of the left anterior descending [LAD] artery) via left-sided anterolateral thoracotomy within the fourth or fifth intercostal space.

Through telephone contacts extracted from the hospital database, the purpose of the study was extensively explained to the patients or relatives, and an invitation for examination was extended to free willing participants.

Methods

Two hundred and eighty-three patients who underwent isolated CABG, regardless of the urgency of surgery, from November 2009 to March 2011 were enrolled from the departmental surgery records in chronological order. After CABG, all patients were encouraged to use a combination of antiaggregation therapy (for at least 1 year) and cholesterol-lowering drugs. Fifty-eight patients were confirmed to have died by relatives and from the hospital database. Ninety-six patients refused follow-up examinations, and 74 could not be traced. Fifty-five patients agreed to be examined and were enrolled in the study (28 OVH and 27 EVH). Two written consent forms were required and signed by all cohorts for: enrolment into the study and radiological examination using coronary computed tomography angiography (CCTA). One patient in the OVH group was excluded from the study because of refusal of administration of intravenous contrast material upon arrival. Blood

Table 1: Pre- and perioperative patient characteristics and demographics

		Endoscopic vein harvest (n=25)	Open vein harvest (n=25)	P-value
Age in years (mean ± SD)		72.9 ± 7.33	72.8 ± 6.08	0.950
Gender	male, n (%)	19 (76)	21 (84)	0.981
	female, n (%)	6 (24)	4 (16)	0.817
BMI > 30 kg/m^2, n (%)		9 (36)	5 (20)	0.519
LV EF < 55%, n (%)		9 (36)	7 (28)	0.882
COPD, n (%)		5 (20)	8 (32)	0.666
Previous MI, n (%)		10 (40)	9 (36)	–
Diabetes mellitus, n (%)		13 (52)	12 (48)	–
Hypertension, n (%)		24 (96)	24 (96)	–
Dyslipidemia, n (%)		21 (84)	21 (84)	–
Tobacco use	non-smokers, n (%)	11 (44)	9 (36)	0.909
	ex-smokers, n (%)	8 (32)	9 (36)	–
	current smokers, n (%)	6 (24)	7 (28)	–
Use of ECC, n (%)		21 (84)	18 (72)	0.883
Urgency of surgery	planned, n (%)	24 (96)	16 (64)	0.463
	urgent, n (%)	1 (4)	5 (20)	0.265
	emergent, n (%)	0 (0)	4 (16)	0.158

SD – standard deviation; BMI – body mass index; LV EF – left ventricular ejection fraction; COPD – chronic obstructive pulmonary disease; MI – myocardial infarction; ECC – extracorporeal circulation

was drawn to complete renal function tests of all study cohorts upon arrival. Two patients from each group were excluded because of elevated creatinine levels upon completion of renal function tests before CCTA. The total study population comprised of 50 patients. Baseline patient characteristics and preoperative and perioperative demographics are highlighted in Table 1. During this period, EVH was performed using VirtuoSaph® Plus Endoscopic Harvest System coupled with a Terumo® endoscope (Terumo Cardiovascular Systems Corporation, MI, USA). At the time of surgery, EVH approach was via a 2–3 cm incision at the medial aspect of the knee above the GSV identified and marked using ultrasound prior to surgery. OVH was performed using a traditional surgical incision from the medial aspect of the ankle, above the saphenous vein. All vein grafts were always interrupted at least 5 minutes after systemic administration of heparin intravenously. All side branches of the vein grafts were either ligated or clipped off, dilated with a mixture of heparinized Ringer's solution and subsequently preserved and the same solution at room temperature pending anastomosis either as single or sequential grafts. Both modes of harvesting were performed by experienced cardiac surgeons with over two years experience in EVH. The cohorts, who were selected in chronological order of the date of surgery, were categorised into two groups: 25 patients (48 total vein grafts) after EVH and 25 patients (46 total vein grafts) after OVH. All patients in the EVH group underwent complete endoscopic harvesting of the SVG, without conversion to OVH. The study comprised of two phases. The first phase involved filling out questionnaires that assessed the clinical outcomes of patients with respect to angina symptoms and subsequent treatment, medical or surgical, indicative of ischemic heart disease, and risk factors of ischemic heart disease. The second phase involved the assessment of vein graft patency using CCTA as an imaging method of choice to quantify the degree of stenosis, CCTA being preferred because of its reliability, usage of low-dose radiation and noninvasiveness (Richards and Obaid, 2019). Patients were examined at a mean follow-up time of 10.67 years. We defined significant stenosis of the vein grafts as luminal occlusion greater than 49% of the total graft thrombosis.

Coronary computed tomography angiography

Computed tomography (CT) imaging was performed using a Siemens Somatom Force, double-source CT scanner with 66 ms temporal resolution and EKG-gated scanning. The software employed for image reconstruction and evaluation was Syngovia, Siemens Healthcare GmbH, CT cardiac dedicated software, and coronary vessel evaluation for semiautomatic

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vessel course identification. A virtual line along the long axis of the center of the bypass graft was created, which allowed for the evaluation of vessel length, diameter, plaque size, residual lumen diameter and area.

Image analysis: All CT examinations were evaluated twice by the same radiologist for using the operative protocol to confirm the revascularized target vessels.

Statistical analysis

Results were calculated using standard statistical methods for continuous variables (*t*-test, Kruskal-Wallis test – for categorical variables using the chi-square test). Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as percentages. Statistical significance was set at $p<0.05$.

Results

Approximately 26% of the recruited cohorts were untraceable putting the estimated survival rate at least 53.36% (34.98% OVH vs. 18.37% EVH). All-cause mortality accounted for at least 20.49%. Angiographic findings estimated the overall vein graft patency within the study population at a minimum follow-up time of 10 years at 72.3%. The primary outcome showed higher patency rates in the OVH group (76.1%) than in the EVH group (68.8%), but with no statistically significant difference at a follow-up of a minimum of 10 years after CABG within both groups (p=0.873) (Table 2).

Similarly, the secondary endpoints (Table 3), with respect to the clinical manifestations of ischemic heart disease, were as follows:

Recurring angina symptoms CCS (Canadian Cardiovascular Society) III–IV were comparable between the groups (p=0.519). Two patients in each group with totally occluded grafts did not present with recurrent angina symptoms. Recurring dyspnea on exertion were comparable in both groups p=0.058. Non-fatal myocardial infarctions after CABG were observed in 12% (6 of 50 patients) of the study cohorts, with double rates occurring within the OVH group, 16% (4 of 25 patients) than in the EVH group (2 of 25 patients), and comparable rates in both groups (p=0.734). The same figures were accounted for with respect to patients undergoing percutaneous coronary intervention (PCI) in both groups. In fact, the patients who suffered myocardial infarctions (MIs) resultant of vein graft occlusion were the same as those who underwent PCI of the grafts. With respect to individual grafts, PCI rates within OVH were 11.6% (5 of 46 grafts) versus EVH 4.35% (2 of 48 grafts), but with no statistically significant difference (p=0.256). In-stent restenosis was present in the vein graft of one patient in each group. None of the patients included in the study required repeat CABG at the time of the examination. It is important to note that all patients after CABG were treated with antiaggregation therapy (a minimum of one year) and cholesterol-lowering drugs many statins. At the time of examination, one patient in each group reported discontinuation of statins (the patient in the EVH group also reported discontinuation of

Table 2: Angiographic findings by coronary computed tomography angiography assessing saphenous vein graft occlusion at a minimum of 10 years after surgical myocardial revascularization

	Endoscopic vein harvest (n=48)	Open vein harvest (n=46)	P-value
0–49% graft stenosis, n (%)	33 (68.8)	35 (76.1)	0.873
≥ 50% – total graft thrombosis, n (%)	15 (31.2)	11 (23.9)	0.706

Table 3: Clinical outcomes of isolated surgical myocardial revascularization after a minimum of 10 years

	Endoscopic vein harvest (n=25)	Open vein harvest (n=25)	P-value
Angina pectoris CCS III–IV, n (%)	7 (28)	8 (32)	0.519
Dyspnea, NYHA III–IV, n (%)	6 (24)	4 (16)	0.817
MI with catheter-based revascularization of vein grafts, n (%)	2 (8)	4 (16)	0.734
Redo surgical myocardial revascularization, n (%)	0 (0)	0 (0)	–

NYHA – New York Heart Association; CCS – Canadian Cardiovascular Society; MI – myocardial infarction

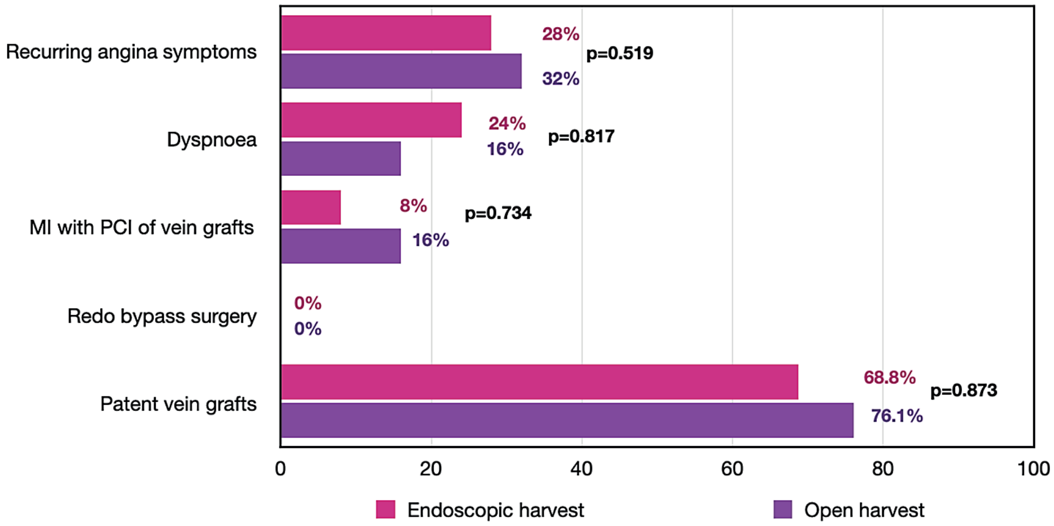

Figure 1: Summary illustrating the primary and secondary outcomes evaluated at a minimum of 10 years after surgical myocardial revascularization. MI – myocardial infarction; PCI – percutaneous coronary intervention.

antiaggregation and/or anticoagulation therapy); both patients had patent SVGs with no recurring angina symptoms. Discontinuation of antiaggregation therapy in one patient after OVH reported with thrombosis of the SVG. The category of patients who reported the use of anticoagulation therapy instead of the antiaggregation concomitantly with statins (5 of EVH and 3 of OVH) all had patent SVGs. The clinical and angiographic outcomes were not influenced by the administration of statins and antiaggregation therapy. Figure 1 summarises of the primary and secondary outcomes of this study.

Discussion

The SVG a commonly used conduit in surgical myocardial revascularization. From an evidence-based standpoint, the overall occlusion rate of the SVG after CABG is estimated to be approximately 8% after surgery, 13% at 1 year, 20% at 5 years, 41% at 10 years, and 45% at more than 11.5 years (Fitzgibbon et al., 1996; Motwani and Topol, 1998). Long-term patency rates at a minimum of 10 years, according to a review analysis, accounts for 50–60% (Gaudino et al., 2017). It is well documented that SVGs are generally more susceptible to accelerated development of atherosclerosis than native coronary arteries, subsequently limiting the duration of patency with possible poor long-term clinical outcomes after CABG. Risk factors influencing SVG disease after CABG, similar to those involved in the development of atherosclerosis in native coronary arteries, include dyslipidemia with increased LDL (low-density lipoproteins) levels and lower HDL (high-density lipoproteins) levels, cigarette smoking, hypertension, and diabetes mellitus.

Long- or short-term patency, whether of arterial of vein grafts, after surgical myocardial revascularization cumulatively depends on several intrinsic and extrinsic determinants, such as patient characteristics and the patients' compliance to treatment regimes after myocardial revascularization, surgeon's experience of both conduit harvest and construction of coronary-graft anastomosis, quality of the target vessels, and development of new hemodynamically significant occlusive lesions of the native coronary arteries after CABG etc. This opens an extensive discussion ranging from patient characteristics, lifestyle, and technical surgical factors to radical treatment strategies to decelerate the atherosclerotic processes of SVGs after CABG. Since the inception of EVH, there has been widespread speculation of relatively more frequent endothelial damage during vein harvest associated with early graft failure compared to OVH. However, every mode of harvest is associated with some degree of shear vascular wall stress from mechanical manipulation and increased distension pressure; hence, some level of endothelial damage is expected. These speculations are however not supported by sufficient clinical trials powered solely to assess long-term vein graft patency following EVH. Without sufficient evidence, a reasonable consensus regarding the safety and efficacy of EVH compared to the traditional approach of vein harvesting cannot be reached. Development and improvement of operators' skills of endoscopic vein harvest has been linked with a steep learning curve during which graft injuries arising from

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thermal assault by the cautery device causing avulsion to the vasa vasorum and adventitia of the saphenous venous subsequently causing segmental vein necrosis (Krishnamoorthy et al., 2016). Overcoming this curve is crucial to reducing graft-related injuries.

According to a conducted study (Manchio et al., 2005), a strong and direct correlation was established between endothelial integrity and graft patency. After comparative histological examination of the grafts after OVH and EVH, thrombosed grafts exhibited higher rates of compromised endothelial integrity than patent vein grafts (Manchio et al., 2005). However, the difference between endothelial disruption and subsequent vein graft failure (VGF) due to thrombosis discovered within the EVH (51.24%) and OVH (49.23%) subgroups was not statistically significant. Hence, early vein graft failure could not be solely attributed to a specific mode of harvest. A histological and immunohistochemical analysis of vein grafts, showed higher rates of endothelial damage within the EVH group than in the OVH group, without any statistical significance (Aboollo et al., 2022).

A more recent follow-up study, initially powered to assess leg-wound morbidity after EVH, evaluated the patency of the SVG at a mean duration of 6.3 years using CCTA. This study showed an increased vein graft failure rate after EVH compared to OVH ($p=0.001$). However, there were comparable rates of recurrent angina symptoms ($p=0.44$), myocardial infarction ($p=0.11$), and all-cause mortality ($p=0.15$) (Andreasen et al., 2015). In this study, angiographic findings did not correlate with overall clinical outcomes. This could imply that with time following CABG, graft patency alone is not a single significant predictive factor for recurrent clinical manifestations of ischemic heart disease.

Another follow-up study from the PREVENT IV trial (Hess et al., 2014), a multicenter randomized controlled trial, powered to evaluate the effects of types of vein graft preservation solutions on graft patency after one year and subsequent clinical outcomes after 5 years, reported that EVH was associated with increased rates of vein graft failure at 12–18 months evaluated angiographically, thereby presenting an independent predictive factor in occlusive graft disease with poor clinical outcomes with regards to acute ischemic cardiac events, repeat CABG, and death. Interestingly, there was a significant difference in terms of race, that is, there were more people of African descent than Hispanics and a higher number of hypertensive patients enrolled in the EVH group than in the OVH group. This is not a coincidence, as it has been documented that the incidence of hypertension is higher among people of African descent. This may further emphasise the influence of hemodynamic pathophysiology on graft patency, with hypertension being one of the risk factors accelerating the development of atherosclerosis rather than the mode of harvest. At 3 years, EVH was also associated with poor clinical outcomes associated with EVH with respect to higher rates of myocardial infarction and repeat CABG. The PREVENT IV trial has however been associated with the poor overall graft patency therefore so many questions can be raised about attributing graft failure solely to EVH.

Results from the ROOBY trial (Zenati et al., 2011), primarily powered to compare the efficacy of on-pump and off-pump bypass grafting at 1-year angiographic follow-up, showed that grafts after EVH were associated with a higher incidence of SVG occlusion in at least one vein graft (43.1 vs. 28% after OVH, $p<0.0001$). However, the 30-day composite outcomes (repeat revascularization, cardiac arrest, and stroke) were comparable between the groups ($p=0.60$). The 1-year composite outcome showed no statistically significant difference between the cohorts that underwent OVH and EVH ($p=0.061$). However, the repeat revascularization rates were higher in the EVH group ($p=0.033$). Similar to the follow-up of the PREVENT IV trial, the clinical outcomes did not correlate with the angiographic findings, further emphasising that long-term clinical outcomes do not depend on graft patency alone.

Results from a study (Jarrett et al., 2023) showed that at 5 years, ischemia-driven revascularization of the myocardium was significantly higher in the EVH group (11.5 vs. 6.7%, $p=0.047$). However, the graft occlusion rates (9.7 vs. 5.4%, $p=0.054$) and the composite of death, myocardial infarction, and stroke (17.4 vs. 20.9%, $p=0.27$) at 5 years were similar between the OVH and EVH groups.

Angiogenesis of collateral blood supply or the presence of LIMA grafts, which significantly or partially compensates for occluded grafts, is capable of relieving angina symptoms to some extent in cases where new hemodynamically significant stenosis of the native coronary arteries is absent. This could partially explain why some patients with total thrombosis of the SVGs do not present with recurrent angina symptoms. On the other hand, new atherosclerotic plaques of the coronary arteries causing significant obstructive flow could account for the recurring symptoms of ischemic heart disease in patients with fully patent grafts after CABG. Reduction in the intensity of physical exertion due to old age could also mask angina symptoms in patients with new atherosclerotic plaques.

As mentioned earlier, another important and uncontrollable factor, which is patient compliance to treatment regimens with a combination of hypolipidemics such as statins, antiaggregation therapy and antihypertensives, adequate management of other co-morbidities, lifestyle changes such as cessation of smoking that aim at controlling the rate of thrombogenesis, and atherosclerosis play a crucial role in ensuring long-term graft patency, arterial or venous. Over the years, technological enhancements in various EVH systems have facilitated the improvement of perioperative surgical conditions and outcomes of CABG. Moreover, EVH is skill-dependent with a steep learning curve. A study conducted assessing the impact of the learning curve of EVH on graft quality and early graft failure (Desai et al., 2011) showed that inexperienced technicians performing EVH are more likely to cause intimal and deep vessel injury to the SVG, increasing graft failure risk and concluded that growing surgical experience in the EVH might be associated with better outcomes.

Vein graft patency is closely linked to the target artery caliber and the lesion complexity reflected in the SYNTAX score (Ong et al., 2006). A higher SYNTAX score (>33) is associated with more diffuse and complex coronary artery disease (CAD), CABG requiring multiple vein grafts to achieve complete revascularization offers superior long-term outcomes compared to PCI. The SYNTAX study also showed that SVG to the LAD have higher failure rates compared to arterial grafts in the same position, whereas vein grafts to the right coronary artery or obtuse marginal branches often have relatively better patency rates largely attributed to differences in vessel caliber, flow dynamics, and competitive flow (Ong et al., 2006). These factors must be considered when selecting the optimal revascularization strategy, reinforcing the importance of individualized surgical planning.

Conclusion

Despite speculations regarding EVH causing endothelial damage, thereby influencing early and/or late graft failure, at a minimum follow-up time of 10 years, no significant difference in graft patency rates between EVH and OVH was found. Similarly, the long-term clinical outcomes were comparable between the two groups. Considering the multiple factors that influence overall graft patency, it would be erroneous to attribute reduced long-term graft patency solely to a specific mode of harvest. Based on the results of this study, considering the added advantages of lower leg wound morbidity EVH over OVH, we conclude that EVH, if performed carefully with minimal structural damage to the SVG, is a non-inferior method of vein harvest, comparable to the long-term graft patency rates of vein grafts after OVH. We propose that for aortocoronary anastomoses, EVH should be considered, especially in diabetic and obese patients who fall into the high-risk group for general surgical wound complications and higher leg-wound morbidity rates.

Study limitations

All patients after isolated CABG were initially not followed up routinely with the intention of assessing graft patency and/or clinical outcomes after EVH; therefore, many patients were eventually lost to follow-up after 10 years. This study size was not optimal. Follow-up of patients, especially after 10 years, is was quite demanding. A number of patients died of unknown causes due to the inability to access the database of other hospitals so exact percentages of all-cause mortality and cardiovascular-related deaths could not be estimated. A significant number of patients refused follow-up examination likely due to being addled with old age and limiting comorbidities.

Data availability

The data of this research is only accessible within the University Hospital Ostrava servers in accordance with patient privacy laws of the Czech Republic. However, anonymized data can be extracted and made available by the corresponding author upon reasonable request.

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