

## ORIGINALNI NAUČNI RADOVI ORIGINAL STUDIES

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### PATENCY OF INTERNAL THORACIC ARTERY AND VEIN GRAFTS ACCORDING TO REVASCULARIZED CORONARY ARTERY PROPERTIES

*PROHODNOST UNUTRAŠNJE GRUDNE ARTERIJE I VENSKIH GRAFTOVA U ODNOSU NA OSOBINE REVASKULARIZOVANE KORONARNE ARTERIJE*

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**Summary** – Long-term results of surgical myocardial revascularization are determined by the quality of grafts and the progression of atherosclerosis in coronary arteries. The aim of the study was to evaluate the patency rate of internal thoracic artery and great saphenous vein grafts in relation to the hemodynamic properties of revascularized coronary artery. The patency of internal thoracic artery and great saphenous vein grafts was analyzed in relation to the degree of coronary stenosis estimated by angiography and the diameter of distal portion of coronary artery assessed intra-operatively. The long-term patency of great saphenous grafts depends on the distal coronary artery diameter but not on the degree of coronary artery stenosis. The patency of internal thoracic artery graft depends on the degree of coronary artery stenosis but not on the distal coronary artery diameter. The internal thoracic artery is the superior graft in coronary surgery, but the low patency rate in case of moderate coronary artery stenosis emphasizes the importance of selective approach.

**Keywords:** Coronary Artery Bypass; Myocardial Revascularization; Graft Occlusion, Vascular; Mammary Arteries; Internal Mammary - Coronary Artery Anastomosis; Vascular Patency; Coronary Stenosis

#### Introduction

Long-term results of surgical myocardial revascularization are determined by the quality of implanted grafts and the progression of atherosclerosis in native coronary arteries (CA). The process of atherosclerosis is multi-factorial and a rigorous control of risk factors must be imposed in order to slow down this process. On the other hand, the proper selection and preparation of implanted grafts can prolong the graft patency and postpone the need for reoperation [1].

For decades, venous grafts have been predominantly used grafts in coronary surgery. Several studies have established the superior long-term patency rate for arterial conduits. Ten years after the implantation, vein conduits are more likely to develop significant stenosis or occlusion (30-50%) compared to the arterial conduits (5-12%). This has led to a widespread expansion of arterial grafts in the contemporary coronary surgery [2-4]. Because of its superiority over other grafts, the internal thoracic artery (ITA) as *in situ* graft is considered as a graft of choice for revascularization of the left anterior descending artery. What causes 10% of arterial graft malfunction in long-term studies remains unknown. In addition to ITA atherosclerosis, which is rare, other causes are still unclear. Some studies indicate that moderate native CA stenosis is the most impor-

tant factor that leads to dysfunction of the ITA graft [5,6]. The significant blood flow through the native CA with a moderate proximal stenosis (<75%) or the developed collateral circulation may create an effect of competitive flow in relation to the implanted graft. Arterial grafts are more sensitive to the presence of competitive flow in contrast to the venous grafts [7]. On the other hand, diffuse distal atherosclerotic changes and small CA diameter may influence the blood flow through the graft by reducing it, which, in turn, may lead to a graft occlusion [8].

The aim of this study was to examine the influence of hemodynamic characteristics of CA on the patency of arterial (ITA) and venous (great saphenous vein - GSV) conduits.

#### Material and method

The study was designed and implemented as a retrospective one at the Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica. The study analyzed the patency of GSV and ITA grafts in patients who had undergone surgical myocardial revascularization in the period July, 1992 – July, 2008 and subsequently, underwent re-angiography due to recurrent angina or positive treadmill test. The surgical technique, pre- and post-operative patient treatment was consistent throughout the observed period.

### Abbreviations

CA	– Coronary artery
ITA	– Internal thoracic artery
GSV	– Great saphenous vein
CDUS	– Color doppler ultrasound
CABG	– Coronary artery bypass surgery
FFR	– Fractional flow reserve

In relation to the angiographic patency rate, the grafts were classified as: occluded grafts, grafts with hemodynamically significant stenosis (estimated stenosis over 75%) and grafts without hemodynamically significant narrowing (estimated stenosis under 75%). The patency of GSV and ITA grafts was analyzed in relation to the hemodynamic characteristics of the target CA. The hemodynamic characteristics included the degree of proximal stenosis assessed by angiography and the intra-operatively verified diameter of revascularized CA. According to the degree of CA stenosis, the grafts were divided into two groups: group I – the grafts on the target CA with moderate stenosis (< 75%) and group II – the grafts on the target CA with significant angiographic stenosis (≥ 75%). In relation to the intra-operatively verified peripheral diameter of the target CA, the grafts were divided into the grafts on the target CA with the diameter smaller than 1.5 mm (group III) and the grafts on CA with the diameter ≥ 1.5 mm (group IV).

Numerical variables are presented as the arithmetic mean and standard deviation (SD). The categorical variables, expressed as absolute values or percentages, are shown in a summary form of distribution frequency. The characteristics of patients and grafts were compared by using univariate analysis, t - tests for the continuous variables and chi-square test for categorical variables. The level of statistical significance was set at the level of 0.05. The statistical analysis was performed with statistical package SPSS.

### Results

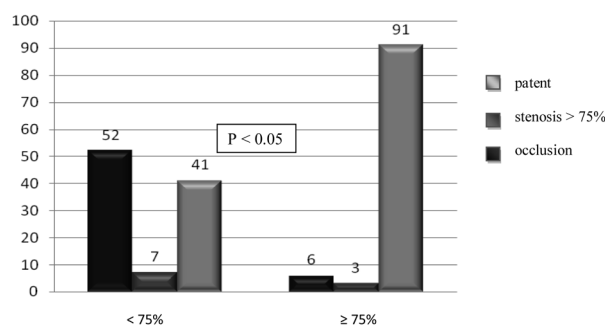
The study included 383 patients and 913 grafts (185 ITA grafts and 728 GSV grafts). The average follow-up period for ITA grafts was 60 months. The left anterior descending artery with stenosis of less than 75% was revascularized with 44 ITA grafts (24%), while the CA with stenosis greater than 75% was revascularized with 141 ITA grafts (76%). For the ITA grafts on the target CA with moderate stenosis (<75%) (group I) the average follow-up period was 58 months, while for the ITA grafts on the target CA with significant stenosis (≥ 75%) (group II) the average period from surgery to angiography was 61 month. The CA with diameter smaller than 1,5 mm were revascularized with 22 ITA grafts (12%) while the CA with diameter 1,5 mm and more were revascularized with 163 grafts (88%) (**Table 1**). The average follow-up period of the third and fourth group of ITA grafts was 54 months and 61 months, respectively. Out of 44 ITA grafts on the target CA with moderate stenosis, 23 grafts (52%) were occluded, 3 grafts (7%) were significantly narrowed, while 18 grafts (41%) were pa-

**Table 1.** Distribution of ITA and GSV grafts according to the hemodynamic characteristics of target coronary artery

**Tabela 1.** Distribucija graftova ATI\* i VSM\* u odnosu na hemodinamske karakteristike ciljane koronarne arterije

Group I Ste- nosis < 75%	Group II Ste- nosis ≥ 75%	Group III Diameter of co- ronary artery < 1,5 mm	Group IV Diameter of co- ronary artery ≥ 1,5 mm
Grupa I Stenoza < 75%	Grupa II Stenoza ≥ 75%	Grupa III Dijametar koronarne arterije < 1,5 mm	Grupa IV Dijametar koro- narne arterije ≥ 1,5 mm
44	141	22	163
GSV	167	113	615

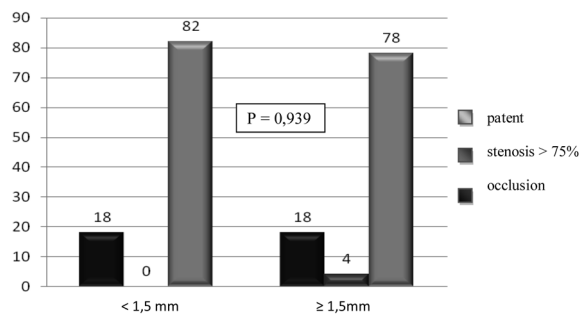
\*ATI - a. thoracica interna, VSM - v. saphena magna



**Fig. 1.** Patency of ITA grafts according to the degree of coronary artery stenosis.

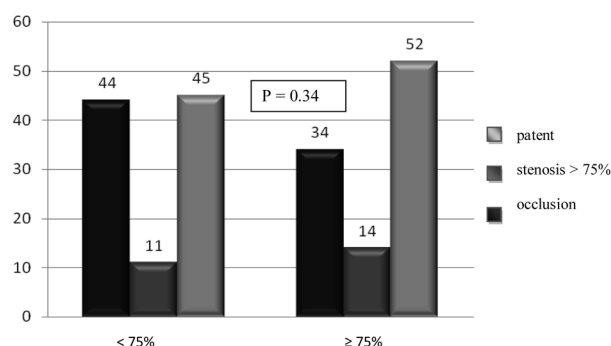
**Slika 1.** Prohodnost ITA graftova u odnosu na stepen stenozе koronarne arterije

ent. Out of the ITA grafts on the target coronary arteries with significant stenosis, 9 grafts (6%) were occluded, 4 grafts (3%) had stenosis greater than 75%, while 128 grafts (91%) were patent. The analysis of ITA graft patency in relation to the degree of proximal CA stenosis showed that the ITA graft group on the target CA with moderate stenosis had the significantly lower patency rate compared to the ITA grafts on CA with significant stenosis ( $p < 0.05$ ) (**Figure 1**). Out of 22 ITA grafts on the target CA with the diameter smaller than 1.5 mm, 4 grafts (18%) were occluded, while 18 grafts (82%) were patent. In the ITA graft group on the target CA with the diameter 1.5 mm and more, 29 grafts (18%) were occluded, 7 grafts (4%) were significantly narrowed, while 127 grafts (78%) were patent. In relation to the



**Fig. 2.** Patency of ITA grafts according to the peripheral diameter of target coronary artery

**Slika 2.** Prohodnost graftova ATI u odnosu na dijametar periferne ciljane koronarne arterije

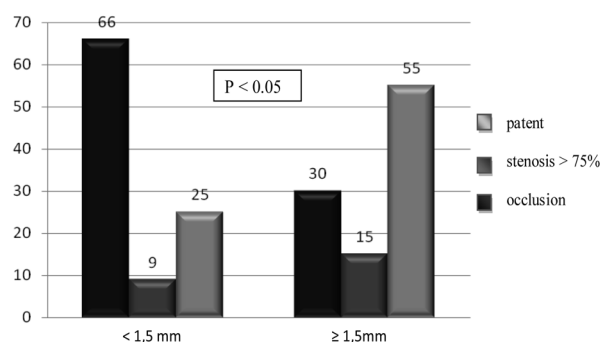


**Fig. 3.** Patency of GSV grafts according to the degree of coronary artery stenosis.

*Slika 3. Prohodnost VSM grafta u odnosu na stepen stenoze koronarne arterije*

diameter of the target CA there was no significant difference in the ITA graft patency rate ( $p=0.939$ ) (**Figure 2**). This result has relative significance since the number of ITA grafts on CA with diameter smaller than 1.5 mm is insufficient to obtain statistically valid data.

The average follow-up period for the GSV grafts was 84 months. CA with moderate stenosis were revascularized with 167 GSV grafts (22%) while the CA with severe stenosis were revascularized with 561 GSV grafts (78%) (Table 1). For the GSV grafts on the target CA with moderate stenosis (<75%) (group I) the average follow-up period was 80 months, while for the GSV grafts on the target CA with significant stenosis ( $\geq 75\%$ ) (group II) the average period from the surgery to angiography was 85 months. CA with intra-operatively measured diameter smaller than 1.5 mm were revascularized with 113 GSV grafts (15%), while the CA with diameter 1.5 mm and larger were revascularized with 615 GSV grafts (85%) (**Table 1**). The average follow-up period for the third and fourth group of GSV grafts was 75 months and 76 months, respectively. Out of 167 GSV grafts on the target CA with moderate stenosis, 73 grafts (44%) were occluded, 19 grafts (11%) had stenosis greater than 75%, while 75 grafts (45%) were patent. Out of the GSV grafts on the target CA with significant stenosis, 191 grafts (34%) were occluded, 80 grafts (14%) had stenosis greater than 75%, while 290 grafts (52%) were patent. There was no significant difference in the GSV graft patency rate according to the degree of target (CA stenosis ( $p = 0.34$ )) (**Figure 3**). Out of 113 GSV grafts on the target CA with diameter smaller than 1.5 mm, 75 grafts (66%) were occluded, 10 grafts (9%) were significantly narrowed, while 28 graft (25%) were patent. In the group of GSV grafts on the target CA with diameter 1.5 mm and larger, 185 grafts (30%) were occluded, 91 grafts (15%) had stenosis greater than 75%, while 335 grafts (55%) were patent. In relation to the diameter of the target CA, there was a significant difference in the GSV graft patency rate with a lower patency rate in the group of GSV grafts on the



**Fig. 4.** Patency of GSV grafts according to the peripheral diameter of target coronary artery.

*Slika 4. Prohodnost VSM graftova u odnosu na dijama tar periferne ciljne koronarne arterije*

target CA with diameter smaller than 1.5 mm ( $p < 0.05$ ) (**Figure 4**).

### Discussion

The diameter and quality of the periphery of the target CA ("run off") have a significant impact on the long-term venous graft patency. This sensitivity of the venous graft in relation to the run off is influenced by the graft to CA diameter mismatch that results in a slower flow of blood through the graft, and possible consequent graft thrombosis due to a poor run off.

In one of the largest published studies aimed at examining graft patency after coronary revascularization, Shah et al [8] reviewed 3715 angiograms of 1607 patients who had undergone coronarography and graftography due to recurrent angina following coronary artery bypass surgery (CABG). The average period from the operation to coronary re-angiography was 99 months. The graft with stenosis greater than 80% was considered dysfunctional. The results of this study indicate that the size of proximal stenosis of the target CA does not affect the graft patency ( $p = 0.18$ ). The venous graft "resistance" to a competitive flow is interpreted as the absence of auto-regulating mechanisms and lower tendency to spasm. A significant correlation between the venous graft patency and the diameter of the peripheral segment of the revascularized CA was confirmed, which explains the influence of the diameter of CA on the run off and the speed of flow through the graft [8].

The lower patency of ITA grafted on the CA with moderate stenosis (<75%) indicates the sensitivity of this particular graft to the competitive flow. The reason for this may be the influence of the autonomous regulation and ITA spasm in the presence of a competitive flow and compromised in-flow of blood in the target CA.

Native ITA is predominantly characterized by the systolic blood flow. When used as a graft, a proximal segment of the ITA has bi-phase (systolic-diastolic) blood flow [9]. During systole the blood fills the proximal segment of the ITA without myocardial

perfusion. In diastole, with the decrease of vascular resistance, the blood enters the distal part of ITA in the target CA and myocardium [9,10]. The poor quality of the target CA with a pronounced competitive flow is a cause of a reduction of the diastolic flow through the graft [11,12].

Dincer and Barnar reported a rare case of spontaneous recanalization of the previously occluded ITA due to the progression of stenosis in the proximal target CA and the reduction of competitive flow [13]. A diffuse narrowing of distal ITA ("string sign") is seen in the cases with the "low grade" stenosis of the target CA [14]. Villareal and Mathur have found in their study that the competitive flow directly influences the development of diffuse spasm of ITA graft [15]. Other possible causes of the ITA graft malfunction include: venous graft anastomosis in the ITA irrigation zone; ITA graft stenosis [16] ITA "steal" phenomenon [17], poor myocardial contractility in the area of the target CA caused by myocardial infarction [18].

Nasu and associates based their research on the intravascular Doppler assessment of flow through the ITA graft. They found that the flow through the graft was compromised in the case of border proximal stenosis in contrast to significant stenosis or occlusion of the target CA. Similar to other investigations, the competitive blood flow is recognized as a cause of reduced flow through the ITA graft [4].

Madaric et al investigated the functionality of the ITA graft using colour-duplex ultrasound (CDUS) in 452 patients of whom 111 had undergone subsequent control angiography due to the anginous pain or positive stress tests. The data were interpreted in relation to the findings of preoperative angiography where CA stenosis greater than 50% was considered as borderline stenosis, and stenosis over 60% as significant. Revascularization of CA with borderline stenosis was identified as a possible cause of ITA graft malfunction. CDUS is a useful non-invasive diagnostic tool that can functionally assess ITA graft [19].

By comparing the ITA graft patency verified by angiography one year after CABG with the severity of CA stenosis verified preoperatively by Fractional Flow Reserve (FFR), the authors established 91.1% graft patency (target CA with significant stenosis) compared to 78.6% graft patency (target CA with borderline stenosis [20].

The ITA grafts, as opposed to the venous grafts, are not sensitive to the size of the lumen of the target CA. This can be interpreted by the comparable diameter between ITA graft and coronary blood vessel. On the other hand, the ITA graft with its inherited autonomous flow regulation has the ability to adapt to the native CA peripheral flow.

After the introduction of percutaneous interventions in the treatment of coronary disease, the profile of patients undergoing CABG significantly changed. Cardiac surgeons are frequently faced with the diffuse atheromatous lesions of the CA, which are more technically demanding and increase both operative

and postoperative early and late morbidity and mortality.

The quality of the CA, which are designated for surgical revascularization, progressively deteriorates, which is detected by preoperative angiography (minor, poorly visible periphery, diffuse distal atheromatous changes). In this group of patients, the operative mortality is increased while the long-term survival is shortened [21]. Corbineau and associates observed diffuse distal CA disease with minor lumen and poor run off as predictors of the operative mortality [22]. For this reason, angiographic findings should be scored according to the severity of CA pathology. One such scoring model is based on the intra-operatively verified size of the CA distal to anastomosis and characteristics of distal lesions, which are estimated by means of angiography [23]. Increased mortality in the group of patients with small coronary arteries is explained by the increased risk of coronary thrombosis, technical challenge in creating the anastomosis of small CA, and the short- and long-term graft patency. CASS (Coronary Artery Surgery Study) study found that the operative mortality was in invert relation to the mean diameter of CA [24].

Shah and associates analyzed the factors that influence the long-term ITA graft patency in order to optimize the surgical approach. According to 2117 analyzed grafts (1482 ITAs and 635 RITAs), there is no significant influence of either graft or the native CA diameter on the long-term graft patency [25].

All published studies aimed at analyzing the ITA patency by means of clinical parameters, angiographic and ultrasound examinations unanimously confirmed its superiority even in patients with smaller diameter of coronary arteries and diffuse distal coronary disease. In this group of patients, vein grafting is characterized by the low short-term and long-term graft patency and increased operative and early and late postoperative morbidity and mortality.

### Study limitations

The retrospective nature of this study with all the disadvantages of patient selection and possible bias is a major limiting factor. The higher percentage of occluded grafts and grafts with significant stenosis compared to literature data is explained by the fact that only the patients with postoperative anginous pain and positive stress tests were scheduled to undergo coronary and graft angiography.

### Conclusion

The long-term venous graft patency is partly influenced by the diameter of the peripheral segment of the target coronary artery. There is a significantly higher percentage of occluded venous grafts in the group of patients with diffuse distal coronary disease and diameter of the peripheral segment of the revascularized coronary artery less than 1.5 mm. The degree of stenosis of proximal native coronary



artery has no significant influence on the venous graft patency. There is no statistically significant difference in the long-term patency of internal thoracic artery graft in relation to the diameter of the peripheral segment of the target coronary artery. In the new era of coronary surgery, when the patients with diffuse distal coronary disease not suitable for stenting are referred to cardiac surgeons, internal thoracic artery is

a graft of choice. On the other hand, it has been documented that the internal thoracic artery graft patency is significantly lower in the case of revascularization of the target coronary artery with moderate stenosis, which indicates the importance of the selective approach in the implementation of internal thoracic artery graft.

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### Sažetak

#### Uvod

Dugogodišnji rezultati hirurške revaskularizacije miokarda uslovljeni su kvalitetom implantiranih graftova i brzinom progresije ateroskleroze na nativnim koronarnim arterijama. Cilj ove studije bio je da ispita uticaj hemodinamičkih karakteristika koronarnih arterija na prohodnost grafta a. thoracicae internae i grafta v. saphenae magnae.

#### Materijal i metode

Retrospektivnom analizom je obuhvaćeno 383 bolesnika podvrgnuta koronarnoj hirurgiji i postoperativnoj reangiografiji. Prohodnost graftova a. thoracicae internae i v. saphenae magnae je analizirana u odnosu na angiografski verifikovan stepen stenozе i intraoperativno verifikovan dijametar revaskularizovane koronarne arterije. Graftovi su podeljeni u četiri grupe: grupa I – stenozа ciljne koronarne arterije < 75%, grupa II – stenozа koronarne arterije > 75%, grupa III – dijametar koronarne arterije < 1,5 mm, grupa IV – dijametar koronarne arterije > 1,5 mm.

**Ključne reči:** Bypass koronarne arterije; Miokardijalna revaskularizacija; Okluzija vaskularnih graftova; Mamarne arterije; Anasto-moza mamarije interne i koronarne arterije; Vaskularna prohodnost; Koronarna stenozа

#### Rezultati

Studijom je analizirano 913 graftova (185 graftova a. thoracicae internae i 728 graftova v. saphenae magnae). Prohodnost graftova v. saphenae magnae grupe I i II je bila 45% (75/167), odnosno 52% ( $p=0,34$ ). Prohodnost graftova a. thoracicae internae grupe I i II je bila 41% (18/44), odnosno 91% (128/141) ( $p<0,05$ ). Prohodnost graftova v. saphenae magnae grupe III i IV bila je 25% (28/113) i 55% (335/611) ( $p<0,05$ ). Prohodnost graftova a. thoracicae internae grupe III i IV bila je 82% (18/22) i 78% (127/163) ( $p=0,095$ ).

#### Zaključak

Dugoročna prohodnost graftova v. saphenae magnae je uslovljena dijametrom periferije ciljne koronarne arterije. Na dugoročnu prohodnost graftova a. thoracicae internae značajan uticaj ima stepen stenozе revaskularizovane koronarne arterije. Graftovi a. thoracicae internae se smatraju superiornim u koronarnoj hirurgiji, međutim niska prohodnost u uslovima granične stenozе koronarne arterije ističe značaj selektivnog pristupa u njihovoj primeni.

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