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Coronary Revascularization in Stable Coronary Artery Disease. State of the Art

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Abstract

In the present review, we have discussed the fundamental issues of coronary revascularization in stable coronary artery disease and shown the pivotal differences between percutaneous coronary intervention and coronary artery bypass grafting regarding the long-term prognosis and clinical profiles. The analysis of the latest publications has demonstrated the advantages of open heart surgery due to the long-term survival and prevention of adverse events in specific groups of patients.

Keywords: Coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, myocardial revascularization

Introduction

The uncompromising competition between coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) has been ongoing for over 25 years, with the first comparative randomized controlled trial (RCT) taking place in the 1960s. This, of course, is supported by the high prevalence and cardiovascular disease mortality worldwide[(1)]. CABG, as the historical first method of coronary revascularization (CR), became possible in the 1960s due to advanced achievements in clinical medicine[(2)]. PCI, as an alternative method, emerged in 1978[(3)] and quickly gained a dominant position because of its low invasiveness, irreplaceability in acute CA disease (CAD), and good reproducibility[(4)].

Nowadays, treatment of patients with myocardial infarction (MI) is directed toward reducing symptoms,

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lowering the risk of cardiovascular events, and improving survival. The essential component of treatment is optimal medical therapy (OMT) with beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), aspirin and statins[1]. The objective of these invasive techniques is to restore adequate blood flow to the myocardium[5]. Currently, there is no doubt that CR plays a key role for treating patients with acute myocardial ischemia, and PCI has priority in this regard[6]. The current situation regarding stable CAD is less clear.

Many studies have demonstrated the high effectiveness of both CABG and PCI in reducing angina symptoms, decreasing the need for antianginal medications, increasing tolerance to physical activity, and improving quality of life[7]. However, the impact of CR on the prognosis of stable CAD from the standpoint of evidence-based medicine has remained unclear.

With the accumulated data on long-term outcomes in several major studies, two sobering conclusions were made. First, for PCI in stable CAD, there has been no improvement in survival or a significant reduction in the rate of new MI cases, regardless of the type of stent used[8]. Second, improved survival and decreased rate of new MIs were consistently demonstrated in CABG, but this effect was not always evident and depended on the severity of CAD[9] and, possibly, on the presence of diabetes mellitus (DM)[10].

At first glance, these conclusions may seem paradoxical, as both procedures provide revascularization and should, at least, lead to similar results[5]; however, this does not happen in reality. Understanding this phenomenon becomes clear if we consider the fundamental differences between the two CR methods. CAs are bypassed in the less compromised distal site during open surgeries, creating a new myocardial blood flow (“surgical collateralization”)[11]. PCI is focused on the local elimination of coronary blood flow obstruction by stenting the CA site with maximum stenosis. In the long term, a working conduit provides stable blood flow to the CA and prevents myocardial ischemia during the possible growth of atherosclerotic plaque (ASP) and its destabilization in the stenosis area. PCI is not secure from thrombotic complications in the stent implantation area or around it with further disease development[12]. Significant differences also include evidence that ASPs, which do not cause hemodynamically significant restrictions in CA blood flow, are a cause of many severe cardiovascular complications (“major cardiovascular events” - MACE). Endothelial dysfunction after stent implantation and the inability to achieve the necessary completeness of CR play a negative role in PCI. A significant challenge in CABG remains to achieve graft patency from a long-term perspective, and this can be solved by improving CABG technology and implementing an autoarterial CR[13,14].

Long-term survival in CAD can be achieved primarily through the prevention of spontaneous MI, which cannot be underestimated. This goal can only be achieved by preventing the destabilization of stable CAD because of the treatment[15].

Thus, recent clinical studies have largely changed the modern view on the CR from the standpoint of evidence-based medicine. The purpose of this review is to update the current data regarding the definition of optimal invasive strategies in various groups of patients with stable CAD.

Research Results

Randomized Comparison of CABG and Everolimus-Eluting Stent Implantation In the Treatment of Patients with Multivessel CAD (BEST) Trial

The trial was conducted to demonstrate the equivalence of endovascular intervention using everolimus-eluting stents and CABG (Table 1)[16]. The inclusion criteria were two or more stenoses of the left main CA (LMCA) and/or the left anterior descending CA >70% (Table 2). The mean SYNTAX score (24.2 points for PCI and 24.6 points for CABG) indicated the absence of severe CAD, but 66% of patients in the PCI group and 79% in the CABG group had a score of 33 or higher (Table 3). The primary combined endpoints were non-periprocedural acute MI, repeated PCI of the ischemia-driven artery, and stroke (Table 1). The frequency of complete revascularization was significantly lower in the PCI group, whereas the frequency of composite endpoint events was higher in this group at 2 years (11% vs. 7.9%, respectively; p=0.32) and at 4.6 years (15.3% vs. 10.6%, respectively; p=0.04). Statistically significant increases in the frequency of repeated hospitalizations and revascularization were observed in the PCI group (19.9% vs. 13.3%, respectively; p=0.01), but the frequency of stroke was comparable. Thus, the initial hypothesis of the non-inferiority of PCI to CABG was not confirmed(17).

Evaluation of Xience vs CABG for Effectiveness of Left Main Revascularization (EXCEL) Trial

The results of endovascular intervention using XENCE stents compared with CABG for LM stenosis and moderate to severe CAD were evaluated(18). Almost 29.1% of the participants had DM. The study was based on the hypothesis of comparable mortality, the frequency of stroke, MI, or repeated CR within a 5-year follow-up period (Table 1). Initially, the frequency of events of the combined primary endpoint over a 3-year follow-up was indeed found to be equivalent, which was later heavily criticized for using the definition of periprocedural MI based on the criterion of increasing the enzymatic cardiomyocytes activity, putting CABG in a deliberately unequal position(28). A significant disadvantage of RCT was the absence of repeated RM in the combined primary endpoint(29). In 2019, the results were revised(30) using the fourth universal definition of MI. Additional assessment of baseline coronary lesions revealed an underestimation with 25% of patients having a SYNTAX score of ≥32, which was previously defined as an exclusion criterion(31). Ultimately, it was concluded that there was a higher frequency of the combined primary endpoint events over a 4-year follow-up in the PCI group, mainly due to

Table 1. Trials and studies included into analyses

Author/study, year	N and profile of patients, inclusion criteria	Type of study	Primary endpoints	DM
BEST(16), 2015	880 patients with stable CAD and multivessel CAD. Mean SYNTAX Score 24	RCT, 27 centers, Southeast Asia, prospective	Combined endpoint (death, MI or CR of ischemia driven CA at 2 years of randomization)	Yes (40%)
EXCEL(18), 2016	1905 patients with stable CAD and LMCA. SYNTAX Score less 32	RCT, 126 centers, Europe, prospective	Combined endpoint (death from any cause, stroke, MI at 3 years)	Yes (30%)
NOBLE(19), 2016	1200 patients with stable CAD and LMCA. Mean SYNTAX Score 22	RCT, 36 centers, Europe, prospective	Combined endpoint (death from any cause, stroke, non-procedural MI, repeated CR)	No
FREEDOM, FREEDOM-Follow-on(20,21), 2019	943 patients with stable CAD and multivessel. CAD and DM	RCT, 25 centers, international, prospective	Death from any cause at 7.5 years	Yes
Bianco et al.(22), 2020	2,869 patients with stable CAD and multivessel. CAD and. DM	Single center, retrospective, PSM analysis	Combined endpoint (death from any cause, MI, stroke)	Yes
Head et al.(23), 2018	11,528 patients with stable CAD and LMCA or multivessel. CAD Mean SYNTAX Score 22	Meta analysis of 11 RCTs	Death from any cause at 5 years	Yes
Gallo et al.(24), 2022	4,595 patients with stable CAD and LMCA	Meta analysis of 5 RCTs	Combined endpoint (death from any cause, stroke, MI, repeated CR)	Yes
De Filippo et al.(25), 2021	6,296 patients with stable CAD and LMCA	Meta analysis of 3 RCTs, 6 studies	Combined endpoint (death from any cause, stroke, MI, repeated CR)	Yes
Gaudino et al.(26), 2023	12,334 patients with stable CAD	Meta analysis of 20 RCTs	Spontaneous MI	Yes
Sun et al.(27), 2020	12,113 patients with stable CAD and reduced LV EF	Retrospective cohort study, Canada	Death from any cause	Yes (52.5%)

CAD: Coronary artery disease, CA: Coronary artery, LMCA: Left main coronary artery, LV: Left ventricle, MI: Myocardial infarction, RCT: Randomized clinical trial, DM: Type 2 diabetes mellitus, LVEF: Left ventricle ejection fraction mortality (9.4% vs. 6.5% respectively; p=0.02), with a comparable frequency of stroke.

Nordic-Baltic-British Left Main Revascularization Study (NOBLE)

The trial compared the strategies of CR in the case of LM disease in stable CAD (Table 1)[19]. Exclusion criteria included complex lesions, and the primary endpoint, in addition to mortality from any cause, non-surgical MI, stroke included repeated MR. 14% of enrolled patients had DM. The CABG group proved to be predominant in terms of stroke frequency during the first 30 days after surgery, but with further follow-up, the indicator shifted toward PCI, mainly due to hemorrhagic stroke (5% vs. 2%, respectively; p=0.073). The obvious reason was antiplatelet therapy. Five-year follow-up revealed an increase in the frequency of adverse outcomes after PCI with any assessment on the SYNTAX score, mainly due to mortality and repeated CR, which allowed us to have a better prognosis after CABG with LM CAD, regardless of the severity of the CA lesion.

Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) Follow-on Study

Important findings regarding the influence of DM on the results of CR with CABG or PCI with sirolimus and paclitaxel-eluting stents have been obtained (Tables 1, 2)[20]. The incidence of MACE in the mid-follow-up of 3.8 years was higher in the PCI group, whereas a statistically significant reduction in mortality was observed in the CABG arm (16.3% vs. 10.9%, respectively; p=0.049). However, the frequency of stroke in the early postoperative period was higher by 3% in the CABG group.

The FREEDOM follow-on study that was extended in 25 centers for up to 13.2 years (the average follow-up is 7.5 years) showed an even greater divergence in mortality: 24.3% in the PCI group compared with 18.3% in the CABG group (p=0.01). The mortality

Table 2. Baseline patients's characteristics

Author/study, year	Type of revascularisation	Mean age, years	Female, %	BMI, kg/m²	Smokers, %	DM, %	Insulin, %	Prior stroke/TIA, %	Prior MI, %	HF, %	Prior PCI, %	Prior CABG, %	EF, %
BEST[16], 2015	PCI	64	30.6	24.7	20.1	40.4	4.6	8.4	5.7	3.7	6.8	N/A	59.1
	CABG	64.9	26.5	25.5	20.1	42.1	4.1	7.5	6.6	2.7	8.6	N/A	59.9
EXCEL[18], 2016	PCI	66	23.8	28.6	23.4	30.2	7.7	5.5	17.8	7.1	18.4	0	57.0
	CABG	65.9	22.5	28.8	20.2	28	7.7	7.0	16.8	6.2	15.9	0	57.3
NOBLE[19], 2016	PCI	66.2	20	27.9	19	15	N/A	N/A	N/A	N/A	19.6	0.7	60
	CABG	66.2	24	28.1	22	15	N/A	N/A	N/A	N/A	19.6	0.3	60
Head et al.[23], 2018	PCI	63.6	23.9	28.1	22.3	38.5	12.9	5.4	28	16.1	N/A	N/A	N/A
	CABG	63.7	23.8	28.3	22.3	37.7	11.9	6.2	27.5	15.3	N/A	N/A	N/A
FREEDOM, FREEDOM-Follow-on[20,21], 2019	PCI	63.2	26.8	29.6	14.8	100	33.8	3.9	26.2	3.3	N/A	N/A	65.7
	CABG	63.1	30.5	29.8	16.6	100	30.9	3.0	25	1.7	N/A	N/A	66.6
												N/A	
Bianco et al.[22], 2020	PCI	67	34.05	31	53	100	N/A	N/A	71	20.07	N/A	N/A	50
	CABG	66	36.20	31	57	100	N/A	N/A	84	22.58	N/A	N/A	50
Sun et al.[27], 2020	PCI	66.5	20.5	28.5	33.1	52.4	N/A	N/A	25.8	100	N/A	N/A	<35
	CABG	66	19.9	28.1	32.7	51.9	N/A	N/A	25.8	100	N/A	N/A	<35
Gaudino et al.[26], 2023	PCI	61.6	28%	N/A	N/A	54	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	CABG	61.6	29%	N/A	N/A	53	N/A	N/A	N/A	N/A	N/A	N/A	N/A

BMI: Body mass index, CABG: Coronary bypass surgery, MI: Acute myocardial infarction, DM: Diabetes mellitus, TIA: Transient ischemic attack, PV: Ejection fraction, CHF: Chronic heart failure, PCI: Percutaneous coronary intervention, N/A: No data curves of PCI and CABG began to diverge as early as the second year of observation[21], with the benefits of CABG not being influenced by the severity of CAD. Additional data on the frequency of MI and stroke in confirmation of the benefits of open-heart surgery were obtained in 17 centers: MI, 4.0% in CABG compared with 4.7% in PCI; stroke, 1.5% in CABG compared with 2.3% in PCI. From a long-term perspective, the FREEDOM study demonstrated solid benefits of CABG for DM and multivessel CAD regardless of SYNTAX Score assessments.

Single-center Retrospective Study Bianco et al.[22]

A comparative assessment of the impact of DM on the results of CR was performed using propensity score matching (PSM)[22]. The analysis of 30-day mortality did not reveal any differences, but the 1-year (CABG - 92.5%, PCI - 85%; p=0.023) and 5-year (PCI - 65.97%, CABG - 79.01%; p<0.004) survival in CABG patients was higher. The PCI group showed a higher frequency of repeated readmissions characteristic both within the first year (PCI - 16.49%, CABG - 9.32%; p<0.011) and within the 5-year follow-up (PCI - 19.71%, CABG - 11.83%; p<0.025). Additionally, the PCI group had a higher incidence of major adverse cardiovascular and cerebrovascular events (MACCE) over 5 years of follow-up (PCI - 32.97%; CABG - 21.51%; p<0.002) mainly due to repeated CR (PCI - 6.45%, CABG - 2.51%; p=0.024) and MI.

Meta-analysis by Head et al.[23]

The meta-analysis included patients from 11 RCTs with a SYNTAX Score of 26 points or more (Tables 1, 2), and 22.1% of them had scores higher than 33 points[23]. Mortality from all the causes after 5 years of follow-up in PCI was higher (11.2% vs. 9.2%, respectively; p=0.0038), and the significance of the differences increased in the case of DM (15.5% vs. 10%, respectively; p=0.0004). The advantages of CABG CS increased with an increase in the severity of CAD lesions.

Meta-analysis by Gallo et al.[24]

Based on the study of 5 RCTs, data on LM CAD were obtained (Table 1)[24]. Over the 5-year follow-up in the PCI group, the frequency of MI and repeated CR was higher

Table 3. Coronary arteries characteristics

Author/study, year	Type of revascularisation	LM bifurcation n, %	EuroSCORE	Mean SYNTAX Score
BEST[16], 2015	PCI CABG	57.5 58.8	2.9 3.0	24.2 24.6
EXCEL[18], 2016	PCI CABG	81.3 77.4	2 2	32.2 (<22), 42.8 (<23-32), 25.1 (>33) 39.3 (<22), 37.3 (<23-32), 23.4 (>33)
NOBLE[19], 2016	PCI CABG	N/A N/A	2 2	22.5 22.4
Head et al.[23], 2018	PCI CABG	N/A N/A	N/A N/A	37.6 (<22), 41.1 (<23-32), 21.3 (>33) 39.1 (<22), 38.1 (<23-32), 22.8 (>33)
FREEDOM, FREEDOM-Follow-on[20,21], 2019	PCI CABG	22.3 20.9	2.7 2.8	26.2 26.1
Bianco et al.[22], 2020	PCI CABG	N/A N/A	N/A N/A	N/A N/A
Sun et al.[27], 2020	PCI CABG	N/A N/A	N/A N/A	N/A N/A
Gaudino et al.[26], 2023	PCI CABG	N/A N/A	N/A N/A	N/A N/A

PCI: Percutaneous coronary intervention, CABG: Coronary bypass surgery, N/A: No data than that in the CABG group; however, there were no statistically significant differences in terms of mortality and stroke between CABG and PCI during the 5-year follow-up.

Meta-analysis by De Filippo et al.[25]

A meta-analysis showed the effect of localization of the LM CA lesion site on the results of CR (Table 1)[25]. In 36.1% of patients, LMCA lesions were localized in the ostial or proximal third and in 62.8% - in its distal part. It was concluded that PCI in the distal third of the LM is associated with an increased risk of developing MACE during the 5-year follow-up, whereas there was no difference in PCI and CABG in patients with ostial LMCA involvement.

Meta-analysis by Gaudino et al.[26]

The authors evaluated the impact of revascularization strategies on the incidence of spontaneous MI in 20 RCTs (Table 1)[26]. A statistically significant difference from the prevalence in the PCI group was revealed in 7 (35%) patients. In addition, PCI was associated with a statistically significant increase in mortality from all causes (odds ratio: 1.13; 95% confidence interval: 1.01-1.28). When analyzed in subgroups, a statistically significant improvement in survival was only observed for CABG and only in studies that showed a statistically significant decrease in the incidence of spontaneous MI in the open-heart surgery group.

Multicenter Retrospective Study by Sun et al.[27]

The results of RM in chronic heart failure (CHF) and low left ventricular ejection fraction (LVEF) were compared (Table 1)[27]. With an average follow-up of 9.2 years, the rate of primary endpoint events over 5 years, including mortality (30% vs. 23.3%, respectively), BCVS (50.9% vs. 32.1%. respectively), repeated RM (27.4% vs. 8.6%, respectively), repeated MI (17.8% vs. 6.4%, respectively), and hospitalizations for decompensated CHF (25.8% vs. 20.1%, respectively) were statistically significantly higher in the PCI group and did not depend on the type of stents used and the presence of DM (see Table 2). The incidence of stroke was lower in the PCI group (4.0% vs. 6.1%, respectively). The benefits of CABG over long-term survival have been confirmed.

Discussion

First and foremost, it is important to emphasize that the results of clinical studies can only be relevantly applied to clinical practice when considering the severity of CAD (higher SYNTAX Score make the benefits CABG more significant), only if the recommended OMT is fully used (systematic non-compliance with the benefits of CABG compared to PCI may be nullified)[28-32], and if all patient clinical profile data that affect the long-term prognosis of the procedure are considered (Table 4).

Left Main CAD

Hemodynamically significant stenoses of LMCA are classified as high-risk and require careful consideration when deciding on CR[33]. In the EXCEL and NOBLE studies[18,19], unequal results were obtained, but the frequency of events of the primary endpoint for individual components was still similar in favor of CABG. The NOBLE study showed the superiority of CABG in terms of the frequency of the combined primary endpoint events regardless of the severity of CAD. The frequency of stroke in this study was initially higher in the CABG group, but after 5 years, the situation reversed. The frequency of MI increased equally over a 5-year follow-up period in both studies. Discrepancies between studies were due to several circumstances[34]. First, repeated CRs were excluded from the combined primary endpoint in the EXCEL study. Second, periprocedural MI was included in the combined primary endpoint criteria in the EXCEL study and was omitted in the NOBLE study. An incorrect definition of periprocedural MI in the EXCEL study had a particularly negative impact on the evaluation of the results[30]. Third, the assessment of the severity of CAD in the same RCT population was initially underestimated. Fourth, the MACE curves reached statistically significant deviation only by the third year of observation. Perhaps the shorter

Table 4. Features of coronary revascularization

Author/ study, year	Type of revascu-larisation	Aspirin, %	Ticagrelor, %	Statins, %	Beta-blockers, %	ACEi/ ARB, %	Calcium channel blockers, %	Number of lesions	Complete revascu-larisation, %	DES, %	Left IMA, %	BIMA, %	Off pump CABG, %	No. of grafts		
														Total	Arterial	Au-toveno-sus
BEST[16], 2015	PCI CABG	97.0 96.6	N/A N/A	83.1 83.5	68.5 42.8	44.5 25.3	58.0 46.4	N/A N/A	53.9 71.8	100 -	- 99.3	- N/A	- 64.3	- 3.1	- 2.1	- 1.0
EXCEL[18], 2016	PCI CABG	95.9 92.1	6,9 0,2	94.7 88.0	81.8 88.1	55.7 40.1	N/A N/A	1.9 2.6	N/A N/A	100 -	- 94.9	- 27.7	- 28.3	- 2.6	- 1.4	- 1.2
NOBLE[19], 2016	PCI CABG	91.0 N/A	N/A N/A	18.6 N/A	N/A N/A	N/A N/A	N/A N/A	2.0 2.0	91.7	100 -	N/A N/A	N/A N/A	N/A N/A	N/A N/A	N/A N/A	N/A N/A
Head et al.[23], 2018	PCI CABG	97.3 95.5	N/A N/A	88.1 83.0	79.1 76.2	63.7 46.9	27.7 21.8	N/A N/A	N/A N/A	73.4 -	- 96.2	- 18.7	- 27.5	- N/A	- N/A	- N/A
FREEDOM, FREEDOM-Follow-on[20,21], 2019	PCI CABG	95.3 95.4	N/A N/A	91.4 89.9	82.6 82.8	80.2 60.2	28.4 24.8	5.7 5.7	N/A N/A	N/A -	- 94.4	- N/A	- 17.4	- 2.9	— N/A	— N/A
Sun et al.[27], 2020	PCI CABG	N/A N/A	N/A N/A	N/A N/A	N/A N/A	N/A N/A	N/A N/A	N/A N/A	- 81.4	N/A -	- N/A	- N/A	- N/A	- 3.3	- N/A	- N/A

BIMA: Bilateral internal mammary artery, ARB: Angiotensin II receptor blockers, ACE: Angiotensin converting enzyme, LIMA: Left internal mammary artery, DES: Drug eluting stents, N/A: No data

follow-up period in the EXCEL study (3 years vs 5 years) was the reason for the advantage of PCI; however, the 4-year results, especially for mortality, favored CABG. Meta-analysis by Gallo et al.[24], with the inclusion of both RCTs, convincingly demonstrated an association between CABG and a lower incidence of MI and repeated hospitalizations over a 5-year follow-up period. The publication by De Filippo et al.[25] demonstrated the long-term benefits of CABG in distal LMCA disease relative to MACCE, mortality, and repeated CRs. Summing up the data, CABG is superior in terms of long-term outcomes for LMCA disease regardless of the severity of CAD.

Multivessel CAD

RCT BEST revealed similar results for PCI according to the "non-inferiority" criteria compared with CABG[16]. Similar results were obtained in the FREEDOM study for this type of lesion and DM, where the superiority of CABG was clearly demonstrated in terms of combined primary endpoint events, including death from any cause, MI, and stroke[20]. The initial prevalence of stroke incidence after CABG was leveled for 7.5 years: all-cause mortality after CABG remained lower than that in the PCI group, whereas the positive effect of CABG was higher among smokers and younger patients. Meta-analysis by Head et al.[23] was particularly noteworthy, which demonstrated the clear advantages of CABG in survival in this group of patients based on the study of individual results of 11,518 cases of CR.

SYNTAX Score

The COR for PCI in LMCA stenosis and low SYNTAX Score remains high (IIa), but it should not be forgotten that these guidelines were based on the results of subgroup analyses of the SYNTAX trial (705 patients)[35], LE MANS (100 patients)[36], PRECOMBAT (600 patients)[37], and Boudriot et al.[38] (201 patients). In fact, these studies were not designed to evaluate outcomes of unprotected LMCA stenosis, and the usefulness of the SYNTAX Score was only considered in them as a secondary (post-hoc) analysis of the data[39], and not during randomization. In contrast, the results of a large NOBLE trial[19] with a wellplanned design clearly demonstrated the advantages of CABG regardless of the severity of CAD assessed by the SYNTAX Score. It is also important to note a significant feature of the SYNTAX trial, which is that the incidence of combined primary end point events constantly increased over time only in the PCI group, but not in the CABG group. This suggests that the severity of CAD is a risk factor exclusively for PCI. This also implies that the main factor underlying the differences in all-cause mortality is a reduction in the probability of developing MI.

In the FREEDOM trial[20], a low SYNTAX score was not associated with improved PCI outcomes in multivessel CAD[40]. Conversely, this indicator was an independent predictor of MACCE in the PCI group but not in the CABG group in several studies. A possible explanation is the dependence of CABG outcomes on the state of the distal anastomosis zone and independence from the severity of the proximal lesion, as determined by the SYNTAX score. Therefore, many authors do not consider the SYNTAX Score to be a determining factor in the indications of CABG.

Type 2 DM

Co-existing DM predisposes to generalization of the process in CAs with diffuse and multivessel involvement and frequent involvement of the LMCA. The plaque burden is higher and more prone to rupture with an increased vasculitic process and a lower ability to form collaterals[41,42]. DM also triggers a change in platelet receptor sensitivity and aggregational activity, leading to an increase in in-stent restenosis[41,42]. All this together enhances the advantages of CABG in diabetic patients, which has been clearly demonstrated by the BARI[43], BEST[16], and FREEDOM[20,21], as well as the meta-analysis by Head et al.[23]. Moreover, the FREEDOM trial results emphasized that performing CABG in stable multivessel CAD in diabetic patients provides better long-term outcomes regardless of the SYNTAX Score. Bianco et al.[22], confirming the findings of the RCT, emphasized the importance of DM management as an important component of improving the outcomes of CR.

Spontaneous MI

Currently, the long-term protective effect of CABG in relation to mortality in CAD is associated with the possibility of preventing spontaneous MI by bypassing the area of greatest lesion or «surgical collateralization», which was first demonstrated in a meta-analysis by Gaudino et al.[26]. In contrast to PCI, a new pathway of blood supply in CABG allows the securement of to secure not only the initial lesions of the CAs but also all future CA lesions proximal to the coronary anastomosis zone (Figure 1).

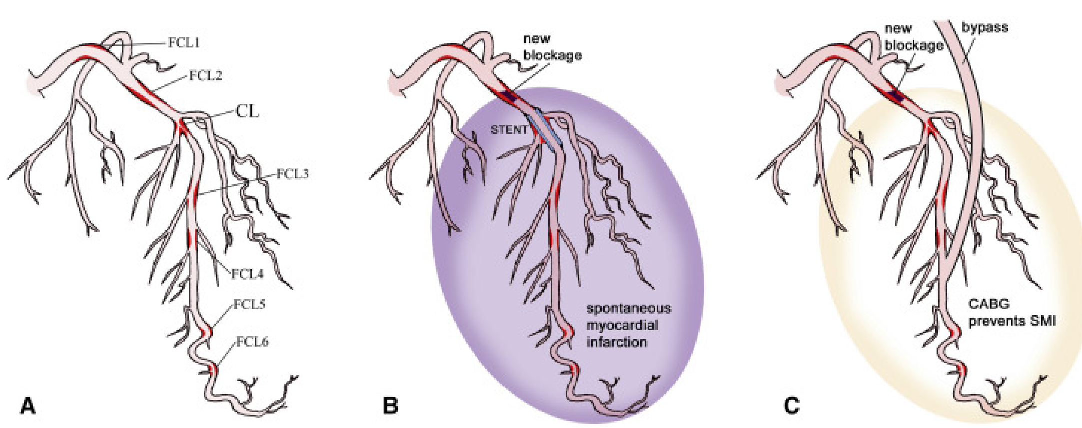

Figure 1. Benefits of surgical collateralization adapted from[57]
A) Myocardial ischemia is caused by a flow-restricting "culprit" lesion (CL), but other "future culprit" lesions (FCL) also exist. **B)** When a new blockage occurs at another lesion later, spontaneous MI (SMI) may develop despite the previously implanted stent. **C)** Alternatively, the blood supply from the bypass graft would prevent SMI

It should also be noted that the concept of "surgical collateralization" calls into question the expediency of shunting stenoses only with hemodynamic significance proven on the basis of the fractional reserve of blood flow; however, the issue requires further study[44]. It should also be noted that the concept of "surgical collaterization" calls into question the feasibility of bypassing only hemodynamically significant lesions based on fractional flow reserve; however, this issue requires further study[44].

Ischemic Cardiomyopathy and Heart Failure

The development of ischemic cardiomyopathy (ICMP) significantly worsens the prognosis of CAD[45]. The role of CR in the treatment strategy in this case is not fully defined, but the restoration of coronary blood flow in the areas of hibernating myocardium, the relief of myocardial ischemia, and especially the prevention of recurrent MI, prevents the progression of heart failure[46], heart failure[46], while determining the volume of viable myocardium may be crucial[1].

STICH and STICHES[47,48] previously showed a 16% survival advantage of CABG over OMT during follow-up to 9.8 years, but the 30-day mortality after CABG was quite high - 3.6%. Later on, a meta-analysis by Wolff et al.[49] revealed better outcomes in CABG in terms of survival, reduction in the incidence of MI, and repeated CR with a mid-follow-up of 3 years. Bangalore et al.[50] did not find these differences over a 3-year period, but a 2-fold increase in the incidence of MI and repeated hospitalizations was observed in the PCI group. The SCAAR registry[51] confirmed the benefits of CABG in long-term survival in 2509 patients. A recent study by Sun et al.[27] reported optimistic results of CABG over 9.2 years, which the authors associate with the effectiveness, completeness of CR, and prevention of MI[49]. Note that recent studies[52] demonstrated a positive effect of combined LV reconstruction in CABG in patients with postinfarction aneurysms in terms of improving survival, in contrast to earlier studies[47,48].

Available publications associate CABG with improvement in long-term outcomes in ICMP and define it as the preferred method of treatment if the risk and benefit of intervention are adequately assessed[46].

Multiarterial Grafting

Only retrospective studies comparing Multiarterial Grafting (MAG) with PCI are available. Thus, Habib et al.[53], based on PSM analysis of 546 pairs of patients, concluded that the survival rate after MAG was higher for up to 9 years. Similar results were obtained by Raja et al.[54]. A large multicenter study by Rocha et al.[55] (3,600 patients underwent MAG and 2,187 patients underwent PCI) was associated with a higher 5-year survival rates (96.8% vs. 94.5%, respectively) with arterial revascularization, whereas a lower incidence of recurrent MI (1.4% vs. 6.9%, respectively) and repeated CR (4.1% vs. 24.2%, respectively) was observed. The accumulated data allows us to assume (Table 4) that the findings of RCTs regarding CABG would be even more convincing if the frequency of complete arterial CRs in them were higher (in the EXCEL study - 24%, in NOBLE - 2%).

Discussion

Despite almost 45 years of development of endovascular techniques and the emergence of new generations of stents, PCI has not been able to surpass CABG. This is due to several reasons: 1) PCI, unlike CABG, violates the physiology of the CA and excludes the positive effect of endothelial vasodilating substances; 2) arterial conduits have a patency of more than 90% over 20 years and possess protective qualities against atherosclerosis progression in distal areas of grafted vessels; 3) PCI implies incomplete CR[56]; 4) CABG, unlike PCI, prevents spontaneous MI in the long term, due to the effect of "surgical collateralizat ion"[11,49,57,58].

Extensive data obtained by methods of evidence-based medicine should have determined a higher COR for CABG for treating patients with stable CAD, but the statistics of CR indicate the opposite, and PCI continues to prevail.

Such an inadequate practice of CR is due to many factors, including the following: 1) external attractiveness of PCI due to low invasiveness; 2) the lack of proper informing of patients about the objective results of CR; 2) a formal approach to the work of the "Heart Team"; 3) conflicts of interest when choosing a method of CR; 4) problems of organizing relevant treatment technologies; 5) the lack of fully reliable clinical guidelines that appropriately reflect the results of recent clinical studies, and the inability to use these recommendations adequately according to the clinical profile of a particular patient. The latter was clearly reflected when the American Association of Thoracic Surgeons refused to accept the latest guidelines of ACC/AHA/SCAI 2021[59]. They significantly reduced the COR for CABG, based on the findings of the ISCHEMIA trial, in which CABG was clearly underestimated[60].

The current situation with the choice of the method of CR clearly requires a change. Statistics show that a patient after coronary angiography always receives more recommendations for PCI, even if there are clear indications for CABG prescribed in the guidelines[61]. This happens because if the patient is not informed that only coronary bypass surgery will save his life in the long term, then the choice will always be PCI - a method with less invasiveness. Distortion of existing scientific facts about CR leads to errors in the management and non-constructive work of the "Heart Team". If there are clear indications for CABG in patients with chronic CAD, PCI should only be performed if the surgical risk is high or if the patient's predicted life expectancy is clearly limited because of comorbidities.

Conclusion

Recent studies have indicated the advantages of CABG in improving the long-term prognosis of life in stable CAD. It can be stated that with multivessel CAD, LMCA stenosis, and concomitant DM, CABG is the "gold standard" of CR. For patients with CHF and reduced LVEF, open heart surgery is the first-line method if the surgical risk is acceptable compared with its benefit. The advantages of CABG are determined by the reliability and completeness of CR compared with PCI. It is necessary to consider the available information about the benefits of MACR.

Ethics

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Concept: Popova NV, Popov VA, Revishvili AS, Design: Popova NV, Popov VA, Revishvili AS, Data Collection and/or Processing: Popova NV, Popov VA, Revishvili AS, Analysis and/or Interpretation: Popova NV, Popov VA, Revishvili AS, Literature Search: Popova NV, Popov VA, Revishvili AS, Writing: Popova NV, Popov VA, Revishvili AS.

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