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REVIEW

RESEARCH ARTICLES

CASE REPORT

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Journal: Sawhney N, Anousheh R, Chen WC, Narayan S, Feld GK. Five-Year Outcomes After Segmental Pulmonary Vein Isolation for Paroxysmal Atrial Fibrillation. Am J Cardiol 2009; 104(3):366–72.

Book: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS. Gleen's thoracic and cardiovascular surgery. 1st ed. London: Appleton&Lange; 1991.

Book Chapter: Weinberg PM. Aortic arch anomalies. In: Allen HD, Clark EB, Gutgesell HP, Driscoll DJ (eds). Moss and Adams' heart disease in ınfants, children, and adolescents. 1st ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 707-735.

Conference Paper: Davis L, Lee M, Sheridan B, et al. Berlin Heart EXCOR support in the first year of life. In: 32nd EACTS Annual Meeting; 18-20 October, 2018; Milan, Italy.

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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/m^2	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
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	97.0	N/A	83.1	68.5	44.5	58.0	N/A	53.9	100	-	-	-	-	-	-
	CABG	96.6	N/A	83.5	42.8	25.3	46.4	N/A	71.8	-	99.3	N/A	64.3	3.1	2.1	1.0
EXCEL[18], 2016	PCI	95.9	6,9	94.7	81.8	55.7	N/A	1.9	N/A	100	-	-	-	-	-	-
	CABG	92.1	0,2	88.0	88.1	40.1	N/A	2.6	N/A	-	94.9	27.7	28.3	2.6	1.4	1.2
NOBLE[19], 2016	PCI	91.0	N/A	18.6	N/A	N/A	N/A	2.0	91.7	100	N/A	N/A	N/A	N/A	N/A	N/A
	CABG	N/A	N/A	N/A	N/A	N/A	N/A	2.0		-	N/A	N/A	N/A	N/A	N/A	N/A
Head et al.[23], 2018	PCI	97.3	N/A	88.1	79.1	63.7	27.7	N/A	N/A	73.4	-	-	-	-	-	-
	CABG	95.5	N/A	83.0	76.2	46.9	21.8	N/A	N/A	-	96.2	18.7	27.5	N/A	N/A	N/A
FREEDOM, FREEDOM-Follow-on[20,21], 2019	PCI	95.3	N/A	91.4	82.6	80.2	28.4	5.7	N/A	N/A-	-	-	-	-	—	—
	CABG	95.4	N/A	89.9	82.8	60.2	24.8	5.7	N/A		94.4	N/A	17.4	2.9	N/A	N/A
Sun et al.[27], 2020	PCI	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-	N/A	-	-	-	-	-	-
	CABG	N/A	N/A	N/A	N/A	N/A	N/A	N/A	81.4	-	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 well-

planned 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).

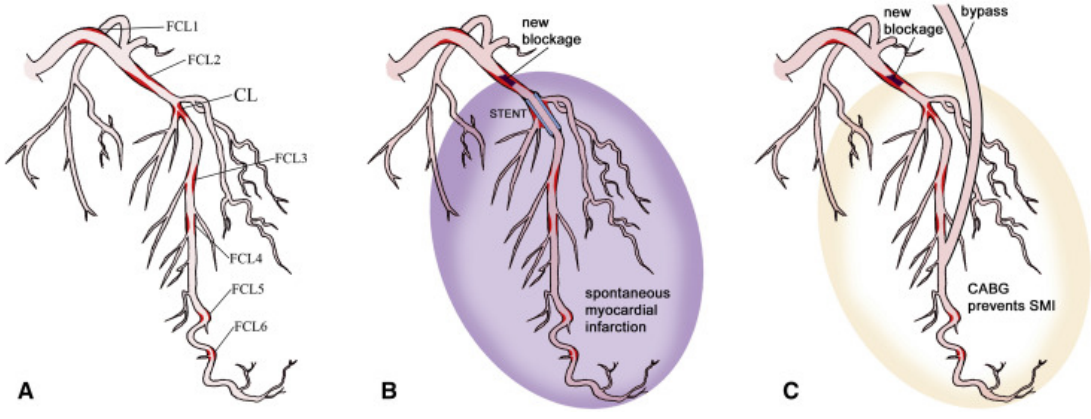

Figure 1. Benefits of surgical collateralization adapted from[57]
A) Myocardial ischemia is caused by a flow-restricting "culprit" lesion (CL), but other "future culprit" lesions (FCL) also exist. **B)** When a new blockage occurs at another lesion later, spontaneous MI (SMI) may develop despite the 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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Indicators of Hospital Mortality in Patients Aged 80 Years with Acute Coronary Syndrome

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Abstract

Objectives: In modern times, life expectancy is increasing. At the same time, the burden of care and treatment for elderly patients is increasing. Against this background, we analyzed the factors influencing and contributing to mortality in patients aged 80 years with acute coronary syndromes.

Materials and Methods: This was an observational study of 250 patients with acute coronary syndrome. Clinical presentation, laboratory values, echocardiographic and electrocardiographic parameters, vital signs, thrombolysis in myocardial infarction (MI) scores, Killip class on admission, treatment options, and complications during hospitalization were analyzed.

Results: In our study, reducing the effect of invasive treatment on mortality was evident in this age group. From the data collected at first hospital presentation, the presence of diabetes and heart failure in the medical history, deterioration of vital signs, type of acute coronary syndrome, and presence of mitral regurgitation or segmental wall motion defect on echo were statistically significant for association with higher mortality in this age group. For laboratory analysis, lower HDL and higher troponin and creatinine levels on admission were also associated with higher mortality. In-hospital episodes of ventricular tachycardia or ventricular fibrillation, heart failure, acute renal failure, cardiac arrest, cardiogenic shock, and recurrent MI were indicators of worse prognosis and higher mortality. In our study, the in-hospital mortality rate was 11%. It would be reasonable to expect our mortality rate to be higher because our study group was 80 years or older. However, there was no statistically significant association between mortality and gender. We hypothesize that acute MI is

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Abstract

more common in male patients because of the protective effects of hormonal mechanisms in females. We found that the incidence of low EF, mitral regurgitation, and segmental wall motion defect was significantly higher in those who died. Many studies have also supported this finding. In our study, as in other studies, invasive treatment was superior to medical treatment, which is an indication that coronary angiography should be considered as the first treatment for acute coronary syndrome in octogenarians.

Conclusion: Many factors affect mortality in patients aged 80 years. Because the incidence of mortality in invasive procedures is low in these patients, it is advisable to prophylactically treat patients with invasive procedures when the treatment protocol is decided.

Keywords: Acute coronary syndrome, elderly, mortality

Introduction

Developments in technology and science have had a major impact on medicine, raising awareness of the importance of maintaining good health. Expected life expectancy has increased, and the proportion of older people in society has begun to rise[1]. It is projected that 10.8%, 13.6%, and 17.3% of the total population in Turkey will be over 65 years of age in 2030, 2040, and 2050, respectively[2]. Given that cardiovascular causes are the most common cause of death in the advanced age group and that the population is aging, more studies are needed in this age group. Because of advances and improvements in the management of acute myocardial infarction (AMI), deaths from cardiovascular disease have decreased significantly in recent decades[3]. While the in-hospital mortality rate was 29% at the end of the 1960s, it has fallen below 10% since 2015[4,5]. In studies to date, 1-year mortality has been associated with age, sex, and comorbidities, whereas treatment modality affects 30-day mortality. However, the effect of additional treatments is controversial[1,6].

In this study, we aimed to compare invasive and medical treatment with respect to mortality and identify other factors that influence in-hospital mortality in patients aged 80 years.

Materials and Methods

The study was an observational study of 250 patients aged 80 years hospitalised for acute coronary syndrome (ACS). Patients' age, sex, complaint of hospital admission, clinical presentation [unstable angina pectoris (USAP), ST segment elevation MI (STEMI), non-STEMI (NSTEMI)], laboratory values [hemoglobin (HGB), platelets (PLT), fasting glucose, creatinine, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerideand troponin], current risk factors for ACS, comorbidities, 12-lead electrocardiogram (ECG) and transthoracic follow-up were recorded, comorbidities, 12-lead ECG and transthoracic echocardiography findings, thrombolysis in MI (TIMI) risk score results calculated from available data, vital parameters (blood pressure and pulse rate), Killip class, preferred treatment option, if invasive treatment was chosen, the responsible lesion, additional treatments after treatment, in-hospital complications and the effect of all these on mortality. We calculated TIMI score in STEMI patients with history (age, concomitant diseases like hypertension, diabet, angina), physics examination findings (systolic blood plessure, heart rate, Killip class, weight), presentation (anterior ST elevation or left bundle branch block, time to reperfusion) findings. For other USAP/NSTEMI patients, are calculated with age, coronary artery disease risk factors, known coronary artery disease, use of acetyl

salicylic acid, angina, and ECG changes. Ejection fraction (EF), valve status, and segmental wall motion in the left ventricle were evaluated by echocardiography.

Treatment options were adjudicated between medical and invasive treatments by two experienced cardiologists. In addition to antiischemic treatment, medical treatment included thrombolytic and antithrombotic therapy. Patients who did not want to participate in the study for any reason, those who did not have chest pain compatible with ACS, and those with inoperable malignancies were excluded from the study.

Ethical approval was received from the University of Health Sciences Turkey, Antalya Training and Research Hospital Clinical Research Ethics Committee (approval no: 13/04, date: 21.09.2017).

Results

There were 250 patients in the follow-up, 23 died, and 227 were discharged. When comparing these two groups of patients, there were no significant differences between the age and sex of the patients (Table 1).

In terms of comorbidities, heart failure and diabetes were significantly different between the two groups. Diabetes was in 89 (39.2%) surviving patients and in 16 (69.6%) deceased patients (p=0.005). Heart failure was in 36 (15.9%) of the surviving patients and in 10 (43.5%) of the deceased patients (p=0.003). There were no significant differences between the two groups in terms of other chronic diseases or medical history (Table 2).

In the analysis of vital parameters, systolic blood pressure, diastolic blood pressure, and heart rate were significantly lower in the patients who died (p<0.001; p<0.001, p=0.003, respectively). The mean EF of the patients was 46.6±13.6; the mean EF of the patients who survived was 48.3±12.9, and the mean EF of the patients who died was 30.2±9.5%. In our study, the EFs of patients who died were significantly lower (p<0.001).

The mean TIMI score of the patients was 5.3±2.1, the mean TIMI score of the patients who survived was 5.1±1.9 and the mean TIMI score of the patients who died was 6.9±2.6. In our study, the TIMI scores of patients

Table 1. Distribution of patient groups by age and sex

	Overall, n (%)	Surviving (n=227), n (%)	Deceased (n=23), n (%)	p-value
Female	108 (43.2)	101 (44.5)	7 (30.4)	0.195
Male	142 (56.8)	126 (55.5)	16 (69.6)	
Age	84.4±3.9	85.4±4.0	84.3±3.9	0.184

Table 2. Association between comorbidities and mortality

		Overall n (%)	Surviving (n=227) n (%)	Deceased (n=23) n (%)	p-value
Hypertension		194 (77.6)	179 (78.9)	15 (65.2)	0.135
Diabetes mellitus		105 (42)	89 (39.2)	16 (69.6)	0.005
Hyperlipidemia		104 (41.6)	93 (41)	11 (47.8)	0.525
History of coronary angiography (CAG) or coronary revascularization		85 (34)	80 (35.2)	5 (21.7)	0.193
Family history		72 (28.9)	62 (27.4)	10 (43.5)	0.106
PCI/CABG in patients with a history of coronary revascularization	PCI	45 (67.2)	41 (66.1)	4 (80)	0.776
	CABG	19 (28.4)	18 (29)	1 (20)	
Smoking		50 (20)	43 (18.9)	7 (30.4)	0.183
Heart failure		46 (18.4)	36 (15.9)	10 (43.5)	0.003
Atrial fibrillation		41 (16.5)	35 (15.5)	6 (26.1)	0.233
History of AMI		38 (15.2)	34 (15)	4 (17.4)	0.761
Chronic renal failure (CRF)		15 (6)	13 (5.7)	2 (8.7)	0.636
History of cerebrovascular events		10 (4)	9 (4)	1 (4.3)	>0.999

who died were significantly higher (p=0.003). When the patients included in the study were examined in terms of Killip class, 75 (30%) of the patients were classified as stage 1, 113 (45.2%) as stage 2, 42 (16.8%) as stage 3, and 20 (8%) as stage 4. In our study, the mortality rate of stage 3 and 4 patients was significantly higher (p<0.001) (Table 3).

When analyzing patients' admission complaints, no significant difference in mortality was observed between typical angina, atypical angina, and other angina equivalents. Considering the preliminary diagnoses at admission, no mortality was observed in USAP in our study, whereas the mortality rate was higher in STEMI (p=0.008) (Table 4).

Another significant difference was observed in treatment decisions. Medical treatment was chosen in 42 (16.8%) of the 250 patients in our trial, and invasive treatment was chosen in 208 (83.2%) of the patients. It was found that 10 (23.8%) of the patients who received medical treatment alone and 13 (6.3%) of the patients who received both medical and invasive treatment died (Table 5).

No significant difference in mortality was observed when comparing lesions in patients who preferred the invasive approach (Table 6).

Echocardiograms of patients were also examined for the presence of segmental wall motion abnormalities and mitral regurgitation. Both were significantly associated with mortality (Table 7).

Ventricular tachycardia (VT)- Ventricular fibrillation (VF) developed during CAG in 15 patients (7.2%), CHF in 161 (64.7%), haemorrhage in 54 (21.6%), and bleeding in 4 (1%), 6%) recurrent MI, 29 (11.6%) shock, 26 (10.4%) cardiac arrest, 1 (0.4%) cerebrovascular incident(CVI, 54 (21.6%) acute renal failure (ARF) and 35 (14%) contrast nephropathy. The incidence of complications was higher in patients who were excised. Development of VT-VF, haemorrhage, recurrent MI, shock, cardiac arrest, HF and ARF during CAG were significantly associated with mortality. The incidence of SVI and contrast nephropathy was similar in living and excised patients (Table 8).

When the blood parameters of the patients are examined at the time of admission, it is seen that creatinine, HDL cholesterol, and troponin have a statistically significant effect on mortality. There was no significant association between other parameters and mortality (Table 9).

Table 3. Relationship between vital parameters and ejection fraction (EF) and mortality

	Overall Mean ± SD	Surviving (n=227) Mean ± SD	Deceased (n=23) Mean ± SD	p-value
Systolic blood pressure	132.7±25.9	137.2±22.8	88.9±9.3	<0.001
Diastolic blood pressure	76.5±11.3	78.4±10	57.7±5.7	<0.001
Pulse rate	76.5±15	77.4±13.5	67.7±24.3	0.003
EF	46.6±13.6	48.3±12.9	30.2±9.5	<0.001

Table 4. Association between preliminary diagnosis and mortality

	Overall n (%)	Surviving (n=227) n (%)	Deceased (n=23) n (%)	p-value
USAP	52 (20.8)	52 (22.9)	0	0.008
NSTEMI	147 (58.8)	133 (58.6)	14 (60.9)	
STEMI	51 (20.4)	42 (18.5)	9 (39.1)	

Table 5. Association between the treatment modality and mortality

	Invasive (n=208) n (%)	Medical treatment alone (n=42) n (%)	p-value
Deceased	13 (6.3)	10 (23.8)	<0.001
Surviving	195 (93.8)	32 (76.2)	

Table 6. Association between lesion characteristics and mortality in patients undergoing CAG

		Overall n (%)	Surviving n (%)	Deceased n (%)	p-value
Culprit lesion	Single vessel	74 (35.2)	68 (34.5)	6 (46.2)	0.128
	Multivessel	88 (41.9)	81 (41.1)	7 (53.8)	
Lesion location	LAD	114 (54.5)	106 (54.1)	8 (61.5)	0.601
	Cx	82 (39.2)	75 (38.3)	7 (53.8)	0.265
	RCA	84 (40.2)	76 (38.8)	8 (61.5)	0.105
	LMCA	8 (3.8)	6 (3.1)	2 (15.4)	0.081
Calcified lesion		74 (35.4)	67 (34.2)	7 (53.8)	0.229
Bifurcation lesion		37 (17.7)	33 (16.8)	4 (30.8)	0.253

Table 7. Association between the presence of mitral regurgitation and segmental motion defects and mortality

		Overall n (%)	Surviving (n=227) n (%)	Deceased (n=23) n (%)	p-value
Mitral regurgitation	None	29 (11.6)	29 (12.8)	0 (0)	<0.001
	Mild	79 (31.6)	78 (34.4)	1 (4.3)	
	Moderate	73 (29.2)	67 (29.5)	6 (26.1)	
	Severe	69 (27.6)	53 (23.3)	16 (69.6)	
Segmental wall motion defect	Present	176 (70.4)	154 (67.8)	22 (95.7)	0.005

Table 8. Assosiation between complications and mortality

	Overall n (%)	Surviving (n=227) n (%)	Deceased (n=23) n (%)	p-value
Development of VT/VF during CAG	15 (7.2)	4 (2.1)	11 (84.6)	<0.001
Heart failure	161 (64.7)	138 (61.1)	23 (100)	<0.001
Bleeding	54 (21.6)	54 (23.8)	0	0.006
Recurrent AMI	4 (1.6)	1 (0.4)	3 (13)	<0.001
Cardiogenic shock	29 (11.6)	6 (2.6)	23 (100)	<0.001
Cardiac arrest	26 (10.4)	4 (1.8)	22 (95.7)	<0.001
Cerebrovascular event	1 (0.4)	0	1 (4.3)	0.092
Acute renal failure	54 (21.6)	41 (18.1)	13 (56.5)	<0.001
Contrast nephropathy	35 (14)	32 (14.1)	3 (13)	>0.999

Table 9. Relationship between laboratory parameters and mortality

	Overall Mean ± SD	Surviving (n=227) Mean ± SD	Deceased (n=23) Mean ± SD	p-value
HGB	12.1±2	12.1±2	11.5±2.3	0.142
PLT	251.9±121	253±124.6	241.7±77.1	0.687
FG	133.4±60.1	130.6±57.6	161.1±76.8	0.062
Creatinine	1.3±0.8	1.3±0.7	1.8±0.8	0.001
Total cholesterol	179.5±49	180.6±48.2	168.9±56.7	0.278
LDL	111.2±40.1	112.2±39.3	101.5±47.3	0.223
HDL	46.1±13.3	46.5±12.7	41.9±18.3	0.008
Triglyceride	115.6±64.8	114.4±65.6	127.7±56.3	0.141
Troponin	701.7±1283.1	605.3±1184.4	1652.9±1783.7	<0.001

Discussion

The most common cause of death in patients over 65 years of age worldwide is coronary heart disease and related complications[6,7]. Considering today's increasingly aging society, we could not find any study in the literature that investigated the factors influencing in-hospital mortality after ACS in the patient group aged 80 years and older. Long-term follow-up of antithrombotic management patterns in ACS patients (EPICOR) stated that age is one of the most important factors for one-year mortality in patients[8]. In a study published in 2023 by Bianco et al.[9] was mortality rate 6.2% and invasive strategy of ACS in elderly patients seems safe and effective. In Thomachan et al.[10] published in JACC, it was reported that an invasive strategy in oncogenes was very effective in reducing long-term mortality. In the latest ESC ACS guideline, octogerian patients with NSTEMI reported superiority of an invasive vs. a conservative strategy in the reduction of the composite of MI, need for urgent revascularization, stroke, and death. In STEMI, primary percutaneous coronary intervention has drastically improved outcomes for all ages including elderly patients[11]. In a recent article published in the American Heart Association, the choice of medical treatment in octogenarians is stated as follows:

• A loading dose of aspirin 325 mg followed by a daily dose of 81 mg should be administered before an invasive approach to management to reduce ischemic events.

• A loading dose of a P2Y12 inhibitor should be administered after the anatomy is known in patients proceeding to PCI.

• Clopidogrel is the preferred P2Y12 inhibitor because of its significantly lower bleeding profile than ticagrelor or prasugrel; however, for patients with STEMI or complex anatomy, the use of ticagrelor is reasonable[12].

Arat et al.[13] found in their study that in-hospital mortality was 24% in patients with AMI over 70 years of age. Öner et al.[14], in their study conducted in all age groups, found that the in-hospital mortality rate was 18.4% and that the rate increased above 65 years of age. In their study, Haase et al.[15] found the mortality rate to be 11.2% in patients under 75 years of age, 26.4% in those over 75 years of age, and 33.6% in those over 80 years of age. In our study, the in-hospital mortality rate was 11%. It would be reasonable to expect our mortality rate to be higher because our study group was 80 years or older. Although the in-hospital mortality rate is related to the clinical status of the patient, we believe that it may be related to both the technical and medical quality of the hospital. In addition, considering that our study was conducted in patients aged 80 years, we believe that there is no difference between the groups after this period, as age is associated with a high risk of mortality.

Gierlotka et al.[5] found that AMI was more common in men and that mortality in these patients was similar in both sexes. McNamara et al.[4] reported that women in their study had higher in-hospital mortality. Mirić et al.[16] reported that although the mortality of patients undergoing coronary intervention was lower in both sexes than in those receiving medical treatment alone, the mortality rate was higher in women. In our study, there was no statistically significant association between mortality and gender. We hypothesize that AMI is more common in male patients because of the protective effects of hormonal mechanisms in females. We believe that the protective effect of the sex difference was removed because the study was conducted in older patients, in whom female patients are postmenopausal.

In our study, no association was found between mortality and HT, HPL, history of CAG or revascularization, history of PCI/CABG, smoking, atrial fibrillation, AMI, CRF, and cerebrovascular events. The incidence of DM and HF was significantly higher in patients who died. We believe that mortality is higher in patients with DM because of the deterioration of many organ systems, especially the vascular bed. We believe that HF may increase mortality because it predisposes patients to AMI and accelerates disease progression.

Hypotension and abnormalities in pulse rate, which are included in the GRACE classification used to show in-hospital mortality, are indicators of poor prognosis[17,18]. Ali et al.[19] reported that although blood pressure was lower in patients with high in-hospital mortality, there

was no difference in heart rate. In our study, systolic blood pressure, diastolic blood pressure, and heart rate were significantly lower in patients who died. We believe that the vital parameters were low because of cardiogenic shock and fatal arrhythmias in the patients who died.

Our study confirmed that Killip and TIMI scores were successful in predicting mortality. In their study, De Luca et al.[20] found that long-term mortality was also high in patients with a high Killip score.

In Sladojevic et al.[21] a higher percentage of patients who died had impaired left ventricular function. In the EPICOR study, he found that EF was the second most important factor for long-term mortality in patients[8]. In our study, we found that the incidence of low EF, mitral regurgitation, and segmental wall motion defect was significantly higher in those who died.

In terms of treatment options, coronary interventions were found to reduce mortality in studies by Degano et al.[22]. Many other studies have found that invasive treatment is better than medical treatment alone in terms of mortality[5,15,17]. In our study, 83.2% of patients underwent an invasive procedure, and the mortality rate was significantly higher in patients who received only medical treatment. The superiority of the interventional approach over medical management in advanced age should encourage cardiologists. In this group, the standard of care is interventional.

When assessing blood parameters, Salisbury et al.[23] reported that the degree of anemia increased mortality in patients with AMI. Sattur et al.[24] reported that there was no association between mortality and anemia in patients undergoing PCI. In our study, although the HGB level was lower in the high mortality group, no statistical difference was observed. Oylumlu et al.[25] reported that total cholesterol and HGB had no effect on mortality, whereas PLT, HDL, LDL, triglycerides, and creatinine had an effect on mortality. Gibson et al.[26] found that renal function was a risk factor for in-hospital mortality and attributed this to the fact that abnormalities in renal function impair the fibrinolytic effect. The same study found that troponin was also affected in patients with impaired renal function, which increased mortality. Other studies confirm that high creatinine and troponin levels are indicators of poor prognosis[18,19]. In our study, no difference was found between the groups in terms of HGB, PLT, FPG, total cholesterol, LDL, and triglycerides. HDL levels were found to be significantly higher in the surviving patients and troponin and creatinine levels were found to be significantly higher in the deceased patients.

Conclusion

Today, society's average life expectancy is increasing because of improved welfare and accelerated medical development. As a result, geriatric cardiology is a field that will become increasingly important in the future. Because cardiovascular disease is one of the most common causes of death in people over the age of 80, it is necessary to determine the optimal treatment and follow-up for cardiovascular disease.

In our study, we found that the invasive approach reduced mortality in this patient group and should be the standard approach in the elderly age group.

We also found that the presence of diabetes and heart failure in the patient's medical history at the time of admission, deterioration of vital parameters, type of ACS, and presence of mitral regurgitation or segmental wall motion abnormalities on echocardiography were predictive of mortality. In hospital episodes of VT or VF, development of heart failure, development of acute renal failure, cardiac arrest, cardiogenic shock, and recurrent MI were indicators of poorer prognosis and higher mortality. When evaluating blood parameters, HDL, troponin, and creatinine levels were found to be predictive of mortality. In conclusion, in patients over 80 years of age with ACS, attention to these factors in the follow-up and treatment process is valuable in minimizing mortality. Further studies are needed on AMI in this age group.

Ethics

Ethics Committe Approval: Ethical approval was received from the University of Health Sciences Turkey, Antalya Training and Research Hospital Clinical Research Ethics Committee (approval no: 13/04, date: 21.09.2017).

Informed Consent: My article is original, patient rights have been protected by observing Helsinki ethical rules.

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Authorship Contributions

Concept: Arslan GY, Çağırıcı G, Design: Arslan GY, Çağırıcı G, Data Collection and/or Processing: Arslan GY, Çağırıcı G, Analysis and/or Interpretation: Arslan GY, Çağırıcı G, Literature Search: Arslan GY, Çağırıcı G, Writing: Arslan GY, Çağırıcı G.

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How Does the New Hemodynamic Definition Affect the Prevalence of Pre-capillary PH?

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Abstract

Objectives: The current 2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) pulmonary hypertension (PH) guidelines suggest mean pulmonary artery pressure (mPAP) >20 mmHg, pulmonary vascular resistance (PVR) >2 Wood Unit (WU), and pulmonary arterial wedge pressure (PAWP) ≤15 mmHg as the new hemodynamic definition of pre-capillary PH. In this study work, we aimed to analyze how the new ESC/ERS 2022 PH definition would affect the prevalence of pre-capillary PH in daily practice.

Materials and Methods: We searched the right heart catheterization (RHC) procedure performed at our institution between 2017 and 2023. When defining pre-capillary PH, both 2015 and 2022 ESC/ERS PH guidelines were used.

Results: One hundred and twenty-three catheter procedures were performed over in a 6-year period. Most of them were female (72.4%). Right heart catheterization (RHC) was clinically indicated for various reasons, with 43.9% of patients exhibiting suspicion of idiopathic pulmonary arterial hypertension (PAH), 32.5% having congenital heart disease-associated pulmonary arterial hypertension PAH (APAH-CHD), 17.9% presenting with PH due to left heart disease, and 5.7% diagnosed with chronic thromboembolic pulmonary hypertension PH (CTEPH). The mean age of the study population was 53.1±16.6 years. The RHC results revealed a mean PAP of 35.4±17.8 mm Hg, PAWP of 13.3±6.0 mm Hg, and PVR of 5.2±6.3 WU. According to the previous guidelines, the number of patients diagnosed with pre-capillary pulmonary hypertension PH was 35 (28.5%), whereas while with the new definition, this number increased to 47 (38.2%). Almost 10% of patients had pre-capillary PH according to the new hemodynamic PH definition criteria that who was not

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Abstract

able to be classified as having pre-capillary PH according to previous guideline. There was 24.4% patients (n=30) had combined pre and post-capillary PH according to current guideline. Finally, 15.4% of patients had undefined PH, defined as mPAP >20 mmHg, but PVR <2 WU, which was a novel definition for the first-time mentioned in 2022 guideline.

Conclusion: The current ESC/ERS guidelines for the diagnosis and treatment of PH is going to increase almost 10% in our pre-capillary PH population.

Keywords: Pre-capillary PH, hemodynamic definition, ESC/ERS PH guideline, current evidence, PAH

Introduction

Increased right ventricle (RV) afterload due to pulmonary vascular injury associated with negative remodeling is the underlying mechanism of pulmonary hypertension (PH), and if it is not diagnosed and treated early, it is characterized by increased mortality risk due to RV failure[1]. The World Heart Organization suggested 5 PH groups that classified disease with similar pathophysiology, clinical presentation, and treatment strategy under same umbrella[2]. Among these groups, left heart disease (group 2), lung disease (group 3), and chronic thromboembolism (group 4) are the most common pathologies that might be associated with PH[3]. Group 1 PH, which is called pulmonary arterial hypertension (PAH), is the most rare group, but drugs tested in randomized clinical trials and approved for this indication are used only in this group. Early diagnosis and quick initial up-front combination therapy according to the patient's risk strata prevent RV function and improve survival.

PH has been defined as a mean pulmonary artery pressure (mPAP) is ≥25 mmHg at rest in the supine position during right heart catheterization (RHC) since the 1st World Symposium of PH (WSPH)[4]. This definition was maintained without any change until the 6th WSPH (2018)[2]. Data accumulated from healthy individuals showed that a normal mPAP at rest is 14.0±3.3 mmHg. Therefore, during the 6th WSPH, the revised mPAP threshold for defining PH was set at >20 mmHg. Meanwhile, the cut-off points for pre-capillary PH remained unchanged, with pulmonary capillary wedge pressure (PCWP) <15 mmHg and pulmonary vascular resistance (PVR) >3 WU[2]. The upper limit of normal PVR in healthy volunteers, and the lowest prognostically relevant threshold for PVR, is approximately ~2 WU. Consequently, the definition of pre-capillary PH was once again updated in the 2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) PH guidelines as mPAP >20 mmHg, PCWP ≤15 mmHg, and PVR >2 WU[3].

In this study, we analyzed how the new ESC/ERS 2022 PH definition would affect the prevalence of pre-capillary PH in daily practice.

Materials and Methods

The results of RHC performed using various clinical indications at our institution between 2017 and 2023 were analyzed. The most common indication of RHC was differential diagnosis among various PH etiologies. RHC was performed via the right femoral vein route under local regional anesthesia. For all incident patients, coronary angiography and left heart catheterization were also performed using the same procedure. Swan-Ganz balloon catheter, multipurpose, and pigtail catheters are the most preferred catheters during procedures according to availability. All hemodynamic data were obtained in the supine position at rest. Medical reports were examined to record patient demographics, clinical history, and

comorbidities. Hemodynamic data (mPAP, PAWP, PVR) were collected from RHC reports. Both 2015 and 2022 ESC/ERS PH guidelines were used to identify patients with PH. This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients before the procedure.The retrospective study was approved by the Istanbul University-Cerrahpasa Institute of Cardiology Ethic Committee (number: E-96241115-904-6852, date: 11.01.2023).

Statistical Analysis

For statistical analyses, we used SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). If the variable is continuous mean ± standard deviation or median (minimum-maximum), it was used. Categoric variables are expressed as counts and percentages. Normality was tested with the Kolmogorov-Smirnov test. While Student's t-test or the Mann-Whitney U test were used to compare continuous variables, for categorical data, the chi-square test was used. A p-value <0.05 was set as significant.

Results

One hundred and twenty-three RHC procedures were performed over a 6-year period. Most were female (72.4%). The mean age was 53.1±16.6 years. After initial diagnostic evaluation, patients with intermediate or high probability of PH underwent RHC. It was clinically indicated for various reasons, with 43.9% of patients exhibiting suspicion of idiopathic PAH, 32.5% having congenital heart disease-associated PAH, 17.9% presenting with PH due to left heart disease, and 5.7% diagnosed with chronic thromboembolic PH (Figure 1) [5].The RHC results revealed a systolic PAP of 54.2±26.3 mmHg, mPAP of 35.4±17.8 mmHg, diastolic PAP of 23.8±14.0 mmHg PAWP of 13.3±6.0 mmHg, PVR of 5.2±6.3 WU and cardiac index of 2.8±1.2 L/per minute/m^2 (Table 1).

According to the previous guidelines, the number of patients diagnosed with pre-capillary PH was 35 (28.5%), whereas with the new definition, this number increased to 47 (38.2%). Almost 10% of patients had pre-capillary PH according to the new hemodynamic PH definition criteria that could not be classified as having pre-capillary PH according to previous guidelines. There were 24.4% patients (n=30) had combined pre and post-capillary PH according to current guidelines. Finally, 15.4% of patients had undefined PH, defined as mPAP >20 mmHg, but PVR <2 WU, which was a novel definition for the first-time mentioned in 2022 guideline (Table 2)[5].

Discussion

Data collected from healthy individuals suggest 14.0 14.0±3.3 mmHg as a normal mPAP at rest and 0.3-2.0 WU as a normal PVR. First during 6th WSPH the cut-off mPAP value for PH definition was updated as >20 mmHg[2]. Then, the PVR threshold for the diagnosis of

Table 1. Hemodynamic data of study population

Hemodynamic variable	Mean
sPAP (mmHg)	54.2±26.3
mPAP (mmHg)	35.4±17.8
dPAP (mmHg)	23.8±14.0
PCWP (mmHg)	13.3±6.0
PVR (WU)	5.2±6.3
CI (L/per minute/m^2)	2.8±1.2

CI: Cardiac index, PAP: Pulmonary artery pressure, PCWP: Pulmonary capillary wedge pressure, PVR: Pulmonary vascular resistance

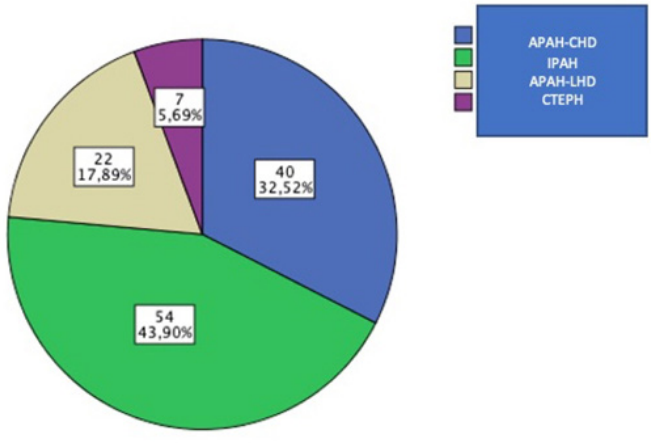

Figure 1. Indications of RHC
RHC: Right heart catheterization

Table 2. The comparison of the prevalence of pre, post and combined pre, post-capillary PH patients according to the 2015 and 2022 ESC/ERS PH guideline

Definition	2015 ESC/ERS PH Guideline, n (%)	2022 ESC/ERS PH Guideline, n (%)
Pre-capillary PH	35 (28.5%)	47 (38.2%)
Ipc-PH	0	2 (1.6%)
Cpc-PH	20 (16.3%)	30 (24.4%)
Undefined PH	-	19 (15.4%)
No PH	25 (20.3%)	

Cpc-PH: Combined pre- and post-capillary pulmonary hypertension, ERS: European Respiratory Society, ESC: European Society of Cardiology, Ipc-PH: Isolated post-capillary pulmonary hypertension, PH: Pulmonary hypertension

pre-capillary PH in 2022 ESC/ERS guideline on diagnosis and management of PH was redefined as >2 WU, while the PCWP cut-off remained unchanged as 15 mmHg[3]. Based on the results of this new hemodynamic definition, it is obvious that the number of pre-capillary PH patients we will diagnose in daily practice will increase. This definition makes it easier for us to diagnose PH early, especially in patients with systemic sclerosis who are at high risk for PAH and have a poor prognosis. Our study showed that the new hemodynamic definition would affect the prevalence of pre-capillary PH by approximately 10%. In our previous study, there was 12.1% increase in our PH patient population after 6th WSPH PH definition[6].

Nevertheless, the PH diagnostic algorithm is triggered by clinical suspicion. For individuals exhibiting symptoms, risk factors, and clinical signs indicative of PH, the primary approach in the diagnostic algorithm involves assessing the likelihood of PH through echocardiography. The thresholds for tricuspid regurgitation velocity corresponding to low, intermediate, and high probabilities of PH have not changed (<2.8 m/s, 2.9-3.4 m/s, >3.4 m/s, respectively).

While the incidence of pre-capillary PH diagnoses is on the rise, the randomized controlled trials that led to the approval of PAH-specific treatments used the old definition. Consequently, these medications have not undergone rigorous testing and approval for both efficacy and safety in individuals falling under this evolving diagnostic category. It is crucial to bear in mind this circumstance. In the future, if PAH-specific drugs receive approval for use in this patient cohort, early detection and swift initiation of initial combination therapy could safeguard RV function and enhance life expectancy.

Conclusion

After the release of the most recent PH guidelines, our pre-capillary PH population will increase by almost 10%. Although we struggle with more pre-capillary PH patients, we need evidence from randomised clinical trial before treating these patients.

Ethics

Ethics Committee Approval: The retrospective study was approved by the Istanbul University-Cerrahpasa Institute of Cardiology Ethic Committee (number: E-96241115-904-6852, date: 11.01.2023).

Informed Consent: Informed consent was obtained from all patients before the procedure.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Sinan ÜY, Concept: Sinan ÜY, Design: Sinan ÜY, Küçükoğlu MS, Data Collection and/or Processing: Engin K, Analysis and/or Interpretation: Sinan ÜY, Literature Search: Sinan ÜY, Writing: Sinan ÜY.

Conflict of Interest: The authors declare no conflicts of interest concerning the authorship or publication of this article.

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Reconstruction of External Iliac Vein for an Iatrogenic Venous Hypertension due to Iatrogenic Vein Injury, A Case Report

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Abstract

Iatrogenic major vessel injuries are rare but life-threatening complications for oncologists. Although the procedures for arterial reconstruction are clear and precise, venous repair techniques are controversial. In case of excessive exanguination, prompt surgical intervention is required. Repair techniques such as venorrhaphy, patching, and end-to-end anastomosis should be considered. If ligation is performed in the major vein, clinical signs of venous hypertension, such as swelling and edema, may occur. We performed interposition between the femoral vein and common iliac vein using a 10-mm dacron graft. Graft interposition is a safe and effective surgical procedure when necessary to restore venous blood flow. Our aim is to contribute to the literature on this gray area with the surgical intervention we applied in such a complicated case.

Keywords: Femoral vein, iliac vein, reoperation, vascular system injuries, veins

Introduction

Lower extremity edema can develop due to many reasons such as kidney failure, heart failure, pericarditis, thyroid disease, malnutrition syndromes, pregnancy, adverse drug effects, liver failure, obesity, and vascular diseases[1]. Bilateral edema is frequently caused by systemic reasons[1]. However, unilateral edema is commonly seen due to primary or secondary venous and

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lymphatic diseases[1]. Additionally, acute swelling, with a duration of swelling less than 72 h, is seen in deep vein thrombosis, trauma, and infectious circumstances[1]. Doppler ultrasound, computed tomography, magnetic resonance imaging, and venography are imaging techniques that clarify the diagnosis[1]. Treatment options change by diagnosis. Occlusive disease occurring hours after the surgical procedure makes us think of surgical complications. Cessation of blood flow by ligation can be a life-saving option in life-threatening uncontrolled bleeding[2]. If the ligated vessel is a vein and the other veins that will provide drainage of the region are insufficient or underdeveloped, swelling and tension in the region may be seen in the acute period because adequate venous drainage cannot be provided. Possible diagnoses are clarified using imaging methods. Doppler ultrasound is the first option imaging technique, and computed tomography (CT), magnetic resonance imaging, and venography are other options[1]. If clinical suspicion of vessel damage is supported by imaging, treatment is considered to be repair of vessels for required flow at reoperation. Compression therapy may also be considered after surgical repair and blood flow restoration.

Case Presentation

A 63-year-old male patient with diabetes, benign prostatic hyperplasia, and hypertension was admitted to the general surgery department with abdominal pain and bloating. Physical examination revealed a mass in the left lower quadrant. CT imaging revealed a mass adjacent to the iliac artery and iliac vein associated with the ileum and descending colon. Wide excision of the mass was performed by general surgeons using a median incision, sparing the ureter. One hour after the operation, sudden swelling, tension, and pain in the left leg were observed, and imaging was performed using venous Doppler ultrasound. Afterwards, the tension and swelling in the leg gradually increased. According to the ultrasound report, there was partial thrombus in the common femoral artery but no flow; there was also no flow and no thrombus in the deep femoral vein, superficial femoral vein, and no thrombus in the popliteal vein and calf veins, and there was no arterial problem. The general surgery department consulted the vascular surgery team regarding the ultrasound report. As a vascular surgery team, we recommended reoperation and venous repair (Figure 1). The midline incision was reopened, and access to the iliac artery and vein was achieved. Common iliac artery pulsation was observed. It was observed that the integrity of the external iliac vein was impaired. Flow was not observed in the external iliac vein, but it was observed that it was ligated. Simultaneously, the inguinal vertical incision was opened by the second vascular surgery team, and the femoral artery and vein were found and prepared. Saphenous vein

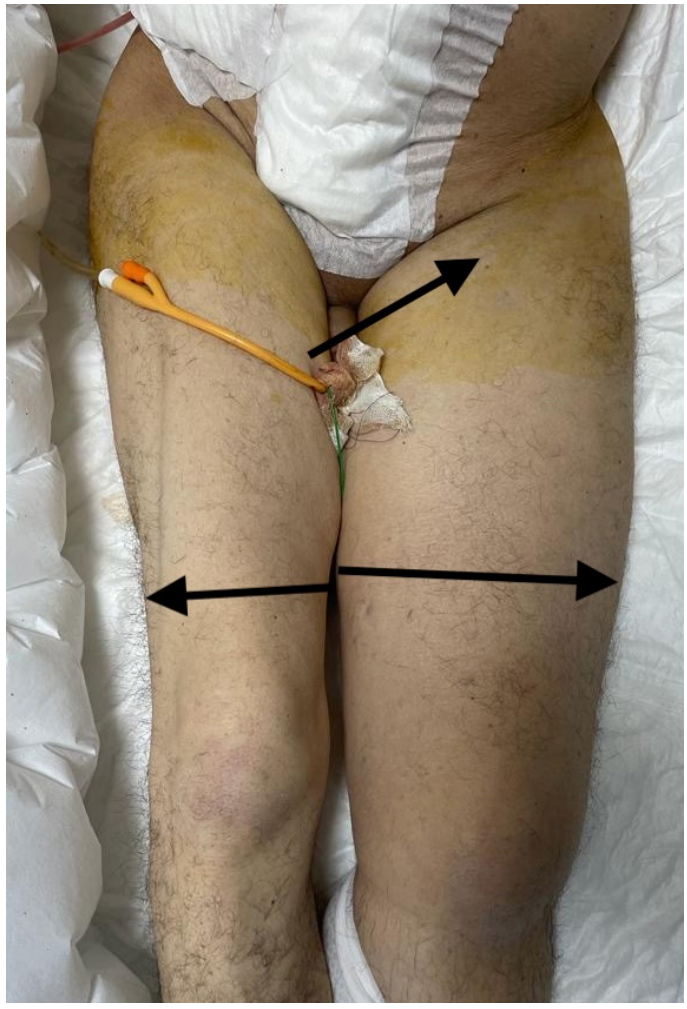

Figure 1. Comparison of both left and right legs before surgery, without the left inguinal operative scar of the vascular surgery team

diameter was found to be insufficient. A larger diameter synthetic graft was preferred to prevent occlusion caused by narrowing. An end-to-side anastomosis was performed between the femoral vein and the intact common iliac vein with a 6-0 prolene running suture (Figure 2). The skin and subcutaneous tissues were closed in the standard fashion after bleeding control was accomplished.

For anticoagulation, we used standard heparin intravenously on the first day and then low-molecular-weight heparin subcutaneously. Also, in the left leg, we observed a significant decrease in calf diameter after reoperation. Left calf diameter calculated 44 cm, right calf diameter calculated 32 cm before interposition. After the venous interposition, the left calf diameter was calculated as 38 cm and the right calf diameter was 31 cm. Tension and swelling were noticeably reduced (Figure 3). Compression therapy with elastic bandage was applied routinely in the postoperative period. CT venography could not be performed because the patient had acute renal failure. Ultrasound imaging performed 1 week after the operation revealed that the graft was open, and no thrombus was detected. He was discharged as a mobilizable patient 2 weeks after the operation.

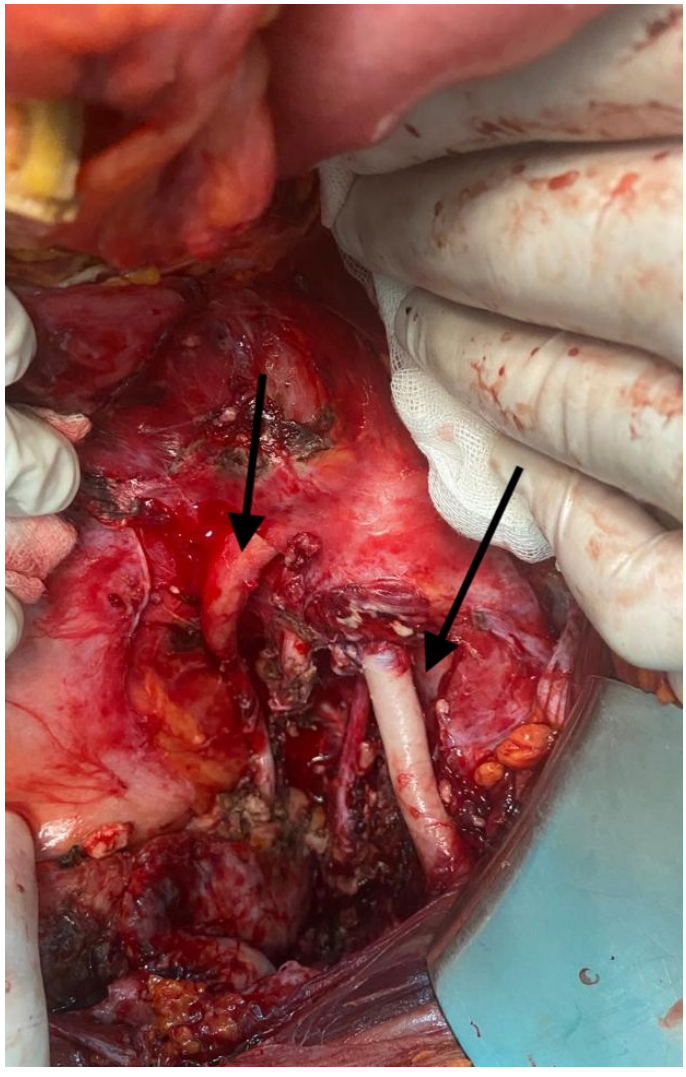

Figure 2. Intraoperative shoot of the interposition space

Discussion

As vascular surgeons, damage control and bleeding are important aspects of our lives. In some situations, elective operations also require vascular surgeons in

Figure 3. Comparison of both left and right legs after surgery with a surgical drain tube

cases of existing vascular injuries[3]. These injuries may cause life threading complications, especially in vessels with low pressure and high flow such as inferior vena cava, portal vein, and internal iliac veins[3]. It is stated that owing to the development of cancer surgery and therapies, radical oncologic resections may result in more iatrogenic vascular injuries, which could be encountered more commonly[3]. Because the great vessels carry a large amount of blood, the amount of blood loss can create life-threatening causes such as hypotension and shock[3]. It also requires a large amount of transfusion even if bleeding is stopped. In addition, bleeding without a vascular surgeon results in more blood loss[3]. In addition, in severe or inoperable patients, there is an increased risk for the probability of a major vein injury due to radical surgical procedures[3]. Therefore, major vessel injuries should be repaired immediately, especially in hemodynamically unstable patients[4]. Oderich et al.[3] reported that they applied vein ligation in only 1 of 44 studies. According to Oktar[4], ligation should be the last option to stop active bleeding. In addition, after exsanguination is controlled in the acute period, venous reconstruction is recommended as soon as possible[4]. However, ligation of the common iliac vein is an option to life threading exsanguination[2]. Furthermore, Timberlake et al.[5] stated that they believe that edema after vein ligation is temporary and that postoperative leg elevation prevents long-term functional loss; venous hypertension has dramatic and life-lowering complications. In a recent study on the same subject, Matsumoto et al.[6] compared ligation and repair. According to their study, the venous ligation group was associated with significantly higher rates of secondary amputation and longer hospital stay and fasciotomy than the venous repair group[5]. If a hemodynamically unstable situation exists, ligation is recommended[5,6]. On the other hand, in hemodynamically stable circumstances, repair and reconstruction are suggested[5,6]. Although there is an endovascular treatment option for iliac artery and vein injuries, this option is only possible if there is complete vascular integrity that can be accessed intravascularly[7]. According to our opinion, to maintain venous flow, interposition with a wide-sized Dacron graft is one of the most important therapies. Demirdas et al.[8] have declared in their study, which is about an interposition via 10 mm Dacron graft, similar to us, between the brachiocephalic vein to the atria. Their study is very similar to ours in terms of graft type, graft size, and the aim of interposition[8].

It is clear that choosing the appropriate size and type of graft and suture is a multivariate equation that is possible with the surgeon's experience and profit-loss consideration. In our opinion, timely consultation with an experienced and competent vascular surgery team in iatrogenic vascular injuries is life-saving and the most beneficial approach to the patient. In venous injuries, interposition of grafts with appropriate sizes is a safe and effective treatment method, especially in complicated cases.

Ethics

Informed Consent: Informed consent was obtained.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

All authors contributed equally to the article.

Conflict of Interest: The authors declare no conflicts of interest concerning the authorship or publication of this article.

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