



MEDICAL UNIVERSITY - PLEVNA

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ABSTRACT OF DISSERTATION

for the award of the academic degree of "Doctor"

**Bifurcation optimization technique combining
proximal balloon optimization and kissing
balloon inflation for the treatment of patients
with coronary bifurcation stenoses**

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ABBREVIATIONS USED:

In Bulgarian:

АН – артериално налягане

ДАН – диастолично артериално налягане

ДББ – десен бедрен блок

ДК – дясна камера

ДКА – дясна коронарна артерия

ДП – дясно предсърдие

ЗД – захарен диабет

ЗСЛК – задна стена на ЛК

ИБС – исхемична болест на сърцето

ИТМ – индекс на телесна маса

КБ – коронарна болест

ЛАД – лява предна десцендентна артерия

ЛББ – ляв бедрен блок

ЛК – лява камера

ЛП – ляво предсърдие

ЛЦх – лява циркумфлексна артерия

МИ – миокарден инфаркт

МКП – междукамерна преграда

МР – митрална регургитация

ОСА – обструктивна сънна апнея

ПМ – предсърдно мъждене

ПКИ – перкутанна коронарна интервенция

РИМ – интермедиерен клон

САН – систолично артериално налягане

СН – сърдечна недостатъчност

СС – сърдечно-съдов

СЧ – сърдечна честота

ТДР – теледиастолен размер

ТСР – телесистолен размер

ФИ – фракция на изтласкване

ХОББ – хронична обструктивна белодробна болест

In the Latin alphabet:

BMS – bare-metal stent

CABG – coronary artery bypass grafting

CI – confidence intervals

СК-МВ – creatine kinase-MB

CR – percutaneous coronary intervention

DES – drug-eluting stent

FFR – fractional flow reserve

GFR – glomerular filtration rate

KBI – Kissing balloon inflation

MACE – major adverse cardiovascular event

МВ – distal main vessel

MLD – minimum lumen diameter

MV – proximal main vessel

NC – non-compliant balloon

OCT – optical coherence tomography

OR – odds ratio

PES – paclitaxel-eluting stent

PMS – propensity score

POBA – percutaneous balloon angioplasty

POCE – patient-oriented adverse cardiovascular event

POKI – proximal balloon optimization and kissing balloon inflation technique

POT – proximal optimization technique

PCI – percutaneous coronary intervention

PTCA – percutaneous transluminal coronary angioplasty

QCA – quantitative coronary angiography

SD – standard deviation

SB – side branch

SES – sirolimus-eluting stent

TAPSE – tricuspid annular systolic excursion

TLR – target lesion revascularization

TVR – target vessel revascularization

%DS – percentage diameter stenosis

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1. INTRODUCTION

Coronary bifurcation lesions account for approximately 20–25%, depending on the definition, of all percutaneous coronary interventions (PCI) (1). Invasive procedures for this subgroup of coronary lesions present a technical challenge with a high incidence of early and late complications (2–4). PCI for bifurcation stenoses can be performed using various techniques, depending on the distribution of plaque in the main and side branches and the geometry of the bifurcation (5). The geometry of coronary bifurcations results in a certain discrepancy in diameters between the proximal main vessel (MV) and the daughter branches—the distal main vessel (main branch, MB) and the side branch (SB). (6) Various optimization techniques have been introduced during percutaneous intervention to improve procedural outcomes in the treatment of these complex lesions. (7) The kissing balloon inflation (KBI) technique (simultaneous dilation of two balloons in the main and side branches) was one of the first techniques proposed for stent optimization specific to bifurcation lesions. (8) This technique continues to play a significant role in bifurcation PCI by optimizing stent geometry and improving access to the side branches. However, performing KBI requires advancing a guidewire into the side branch after stenting the main vessel, which adds additional procedural and fluoroscopic time, as well as contrast agent volume. It also requires a certain level of operator expertise, particularly in cases of side-branch occlusion following stenting. Additional disadvantages of KBI include elliptical deformation of the proximal main vessel, which may further compromise long-term outcomes. (9) The proximal optimization technique (POT, balloon inflation in the main vessel proximal to the bifurcation) has been proposed as a stent optimization technique that can adapt the tubular design of the coronary stent to the natural anatomy of the bifurcation. (10) It was expected that POT could correct the stent position by accommodating the fractal anatomy of the vessel without compromising, and even improving, the patency of the SB. However, studies have shown that to preserve SB patency without compromising functional vascular blood flow, additional balloon dilation of the SB is necessary. (11) The optimal outcome of POT depends largely on precise balloon positioning, and inaccurate placement can lead to incomplete adherence of the stent to the lateral wall of the SB. (12,13) In addition, data indicate that even a correctly positioned balloon for POT (according to current criteria(4) may cause additional elliptical deformation at the SB ostium, thereby further stenosing it. (14) Optimization techniques following stent placement in patients with bifurcation lesions require refinement. A technique combining KBI and POT may lead to better procedural outcomes and better long-term clinical outcomes in these patients.

2. AIM and OBJECTIVES

2.1 AIM

The aim of this dissertation is:

To analyze the efficacy and safety of the new bifurcation optimization technique – POKI, compared to the standard kissing balloon inflation technique in patients with coronary bifurcation stenoses.

2.2 OBJECTIVES

To achieve our aim we set the following objectives:

1. To form a cohort of patients based on predefined criteria.
2. To analyze the demographic characteristics of the study population—gender, age, and risk factors.
3. To analyze the main clinical indicators, comorbidities, and findings from invasive and non-invasive diagnostic methods in both study groups.
4. To compare immediate angiographic results following treatment with the POKI technique and the KBI technique.
5. To compare the incidence of procedural complications in the two groups after treatment with the POKI technique and the KBI technique.
6. To assess mortality overall and cardiovascular mortality.
7. To compare the incidence of major cardiovascular events (cardiovascular mortality, non-fatal myocardial infarction, stroke, and revascularization of the target vessel) and the incidence of patient-oriented cardiovascular events between the two groups.
8. To identify significant factors influencing patient survival in both groups, including demographic indicators, risk factors, comorbidities, and indicators from non-invasive and invasive diagnostic methods.
9. To assess the impact of the POKI technique on patient survival and the incidence of adverse cardiovascular events.

3. MATERIALS and METHODS

Patient Selection

This dissertation includes 511 patients who met the inclusion criteria. They were recruited between 2021 and 2024 at the Specialized Hospital for Cardiology Medica Cor in Ruse. All patients were hospitalized at the clinic. Information on the participants was collected at the time of their hospitalization, as well as from accompanying documentation. Follow-up of the patients included in the study was conducted through contact with them and their relatives, review of their medical records, and verification of their health insurance status with the National Revenue Agency.

Definitions

Coronary artery disease is defined as a history of myocardial infarction, a history of aortocoronary bypass surgery and/or percutaneous intervention, or the presence of significant coronary artery stenosis ($\geq 50\%$).

Survival was calculated based on the number of months survived after discharge. Overall mortality is classified as cardiovascular mortality, death from another disease unrelated to the cardiovascular system, and death from an unspecified cause. Overall mortality is defined as death of cardiovascular and non-cardiovascular origin. (143)

For cardiovascular mortality, we included deaths resulting from:

- fatal MI;
- HF leading to a fatal outcome;
- sudden cardiac death;
- cardiovascular complications, such as stroke, hemorrhage,
- periprocedural complications;
- death from another cardiovascular-related condition, such as peripheral arterial disease;
- death from an unknown cause.

For major adverse cardiovascular events (MACE), we included cardiovascular death and non-fatal myocardial infarction. For Patient-Oriented Adverse Cardiovascular Events (POCE),

we included cardiovascular death, non-fatal myocardial infarction, and target vessel revascularization (TVR). (143)

For non-cardiovascular mortality, we included deaths resulting from:

- cancer;
- pulmonary diseases;
- infection, sepsis;
- trauma;
- organ failure other than cardiovascular.

We defined chronic kidney disease as the presence of a glomerular filtration rate (GFR, calculated using the MDRD formula) below 60 ml/min/1.73 m² for at least 3 months. Renal function was classified according to glomerular filtration rate (GFR, calculated using the MDRD formula) into 5 stages (Kidney Int 2007;72:247):

- Stage I – GFR > 90 ml/min/1.73m²;
- Stage II – GFR 60–89 ml/min/1.73 m²;
- Stage III – GFR 30–59 ml/min/1.73 m²;
- Stage IV – GFR 15–29 ml/min/1.73 m²;
- Stage V – GFR < 15 ml/min/1.73 m² or dialysis.

Bifurcation lesions are classified according to the Medina classification, with “1” denoting stenosis >50% and “0” denoting stenosis <50% in the main vessel, main branch, and side branch, respectively (Figure 4).

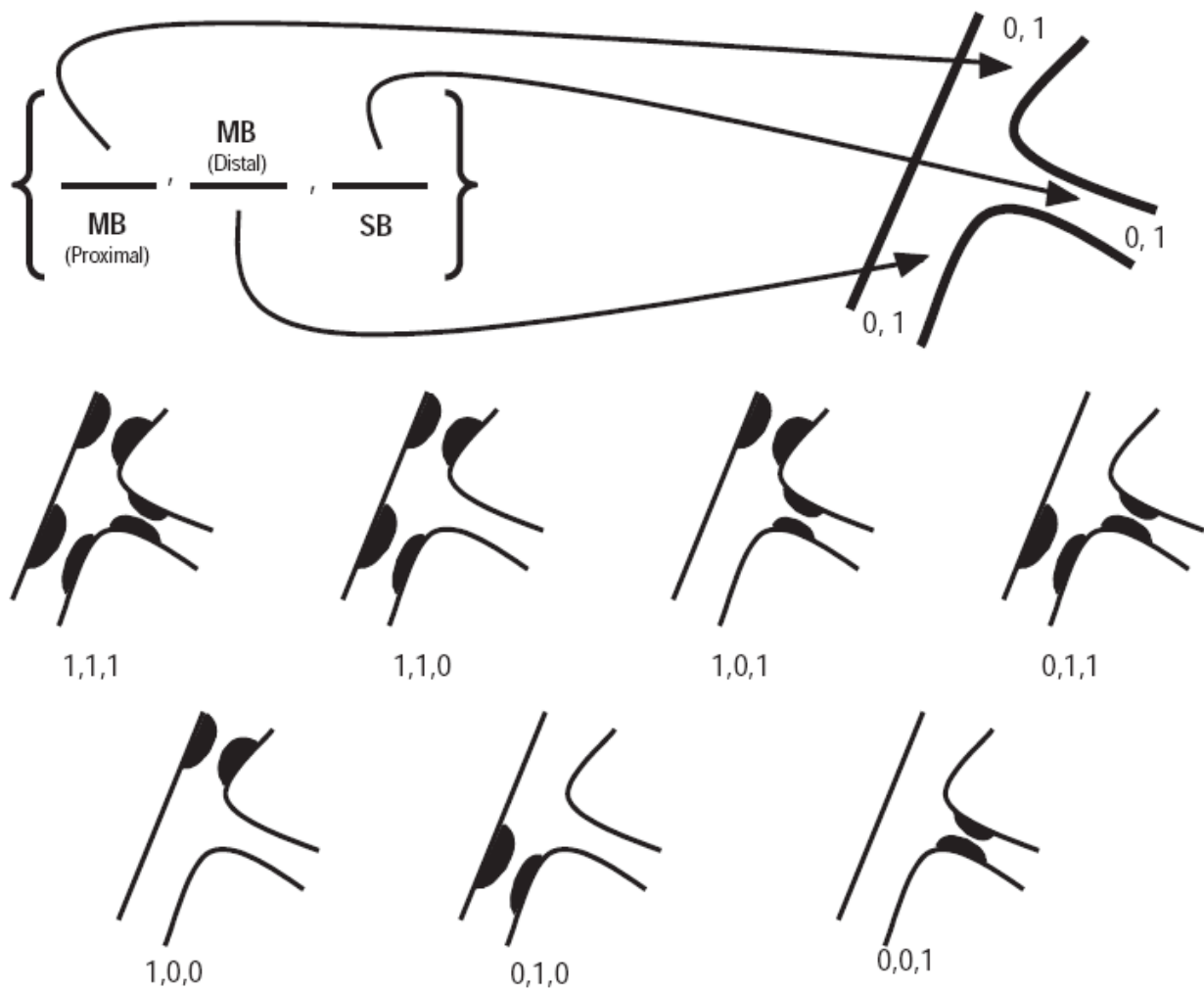


Figure 4. Medina classification of bifurcation lesions – an index of 1 or 0 is assigned based on the presence or absence of stenosis greater than 50%.

Informed Consent

After a detailed explanation of the procedures involved in the study, all patients sign an informed consent form to participate in the study. The informed consent form used for the purposes of the study is attached at the end of the dissertation.

Inclusion criteria:

1. Patients with stable angina pectoris who are candidates for invasive coronary angiography.
2. Patients with an angiographically confirmed bifurcation lesion in a native coronary artery with a percentage of diameter stenosis (%DS) greater than 50% in the MV.
3. The bifurcation lesion is in a native coronary artery with a diameter ≥ 2.5 mm and ≤ 4.5 mm and an SB diameter ≥ 2.0 mm
4. Signed informed consent.
5. Patients over 18 years of age.

Exclusion criteria:

1. Acute coronary syndrome.
2. Hemodynamic instability.
3. Acute respiratory failure.
4. Acute renal failure or end-stage chronic kidney disease.
5. Refusal to sign the informed consent form.
6. Cancer with an expected life expectancy of < 1 year.
7. Age under 18 years.
8. Pregnancy.

Methods

The methods used in this dissertation can be divided into two main groups: non-invasive and invasive methods. Non-invasive methods include: medical history, physical examination, electrocardiogram, echocardiography, and laboratory tests. Invasive methods include selective coronary angiography.

Medical History

Medical history data were collected from all patients regarding their current clinical condition, past and concomitant medical conditions, risk factors for cardiovascular disease, demographic factors, and family history.

Physical Examination

All study participants underwent a comprehensive physical examination by system, with the information recorded in the patient's medical records. The physical examination of each patient included measurement of blood pressure in both arms, auscultation of the lungs and heart, assessment for peripheral signs of heart failure, and assessment for peripheral vascular pulsations.

Electrocardiogram

All participants underwent a complete 12-lead ECG recording (peripheral and precordial leads) at a speed of 25 mm/s. The parameters included were: determination of heart rhythm, electrical position of the apex, QRS complex width, presence of ST-segment elevation/depression, Q-wave, presence of LBBB (defined according to the criteria set forth in the European guidelines), RBBB, and LBBB.

Laboratory tests

A full set of standard laboratory parameters was tested in the study participants—complete blood count, serum electrolytes (potassium, sodium), liver enzymes, creatinine, cardiovascular markers such as creatine phosphokinase, creatine phosphokinase-MB fraction, high-sensitivity troponin T, lipid profile, and coagulation status. The parameters were analyzed at the Clinical Laboratory of SHATC Medica Cor, Ruse.

Echocardiography

Echocardiography is a primary noninvasive method used to perform a comprehensive assessment of cardiac function. In this study, a Philips Affinity 70 device was used. In adult patients, an echocardiography transducer emitting ultrasound waves between 4–7 MHz is used. Standard echocardiographic positions include: parasternal long-axis, parasternal short-axis, apical four-, two-, and three-chamber views, and subxiphoid view. The main dimensions of the cardiac chambers – left ventricle, left atrium, right ventricle, right atrium, and aorta – were

measured using two-dimensional echocardiography (2D method). Segmental abnormalities in LV kinetics were defined as hypokinesis, akinesis, and dyskinesis. Left ventricular diastolic function was calculated according to established guidelines using PW Doppler echocardiography. At the level of mitral valve coaptation, peak velocities of early (E-peak, m/s) and late (A-peak, m/s) diastolic flow, their ratio (E/A), and the deceleration time of early diastolic filling were measured. It also includes measurement of tissue Doppler parameters and determination of the E/e' ratio. Left atrial dimensions and volume are calculated from four- and two-chamber views. Measurements also include determination of indexed LA volume via two- and four-chamber measurements and LA area. Right ventricular function is assessed by measuring right ventricular dimensions in the parasternal long-axis and four-chamber views. Tricuspid annular systolic excursion (TAPSE) is measured using M-mode echocardiography. Pulmonary artery pressure was determined by measuring the blood flow velocity through the tricuspid valve using CW Doppler echocardiography.

Coronary angiography and angioplasty

The study utilized vascular access via the radial or femoral artery with local anesthesia at the puncture site. Selective imaging of the left and right coronary arteries was performed using an iodine-based contrast agent (Iomeron 350 mg/ml). At least two views were obtained for each coronary artery. PCI was performed in accordance with current guidelines. (142) Provisional stenting was the default PCI procedure for all patients included in the study. All lesions were stented with second-generation DES. Angiographic success is defined as %DS at the end of the procedure in the MV <20% and stenosis in the SB <50% without significant dissection or impairment of blood flow. Procedural success includes angiographic success in the absence of in-hospital MACE (death and non-fatal myocardial infarction). All patients received dual antiplatelet therapy with aspirin 75–100 mg and a P2Y2 inhibitor (clopidogrel, prasugrel, or ticagrelor).

Proximal Balloon Optimization and Kissing Balloon Inflation (POKI)

After stent placement in the MV (sized according to the diameter of the distal vessel), the POKI technique involves the following steps: (1) proximal optimization using a noncompliant (NC) balloon sized according to the proximal diameter of the MV; (2) crossing the SB with a guidewire and removing the snagged guidewire; (3) Inflation of a kissing balloon with an NC balloon in the SB, with the balloon's proximal marker within the stent, and an NC POT balloon in the MV, with the balloon's distal marker positioned parallel to the tip of the carina(Figure 5)

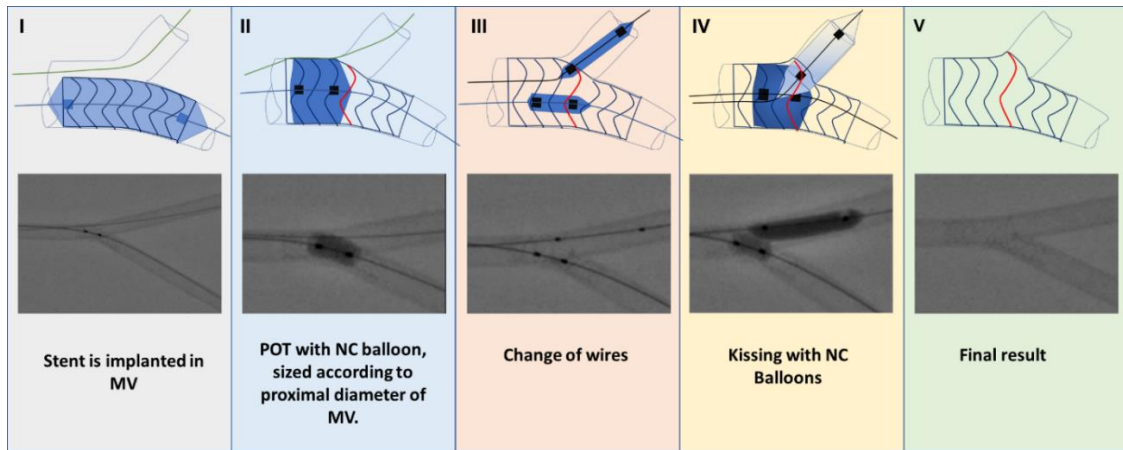


Figure 5. POKI procedure

MV- main vessel; POT – proximal optimisation technique; NC – non-compliant.

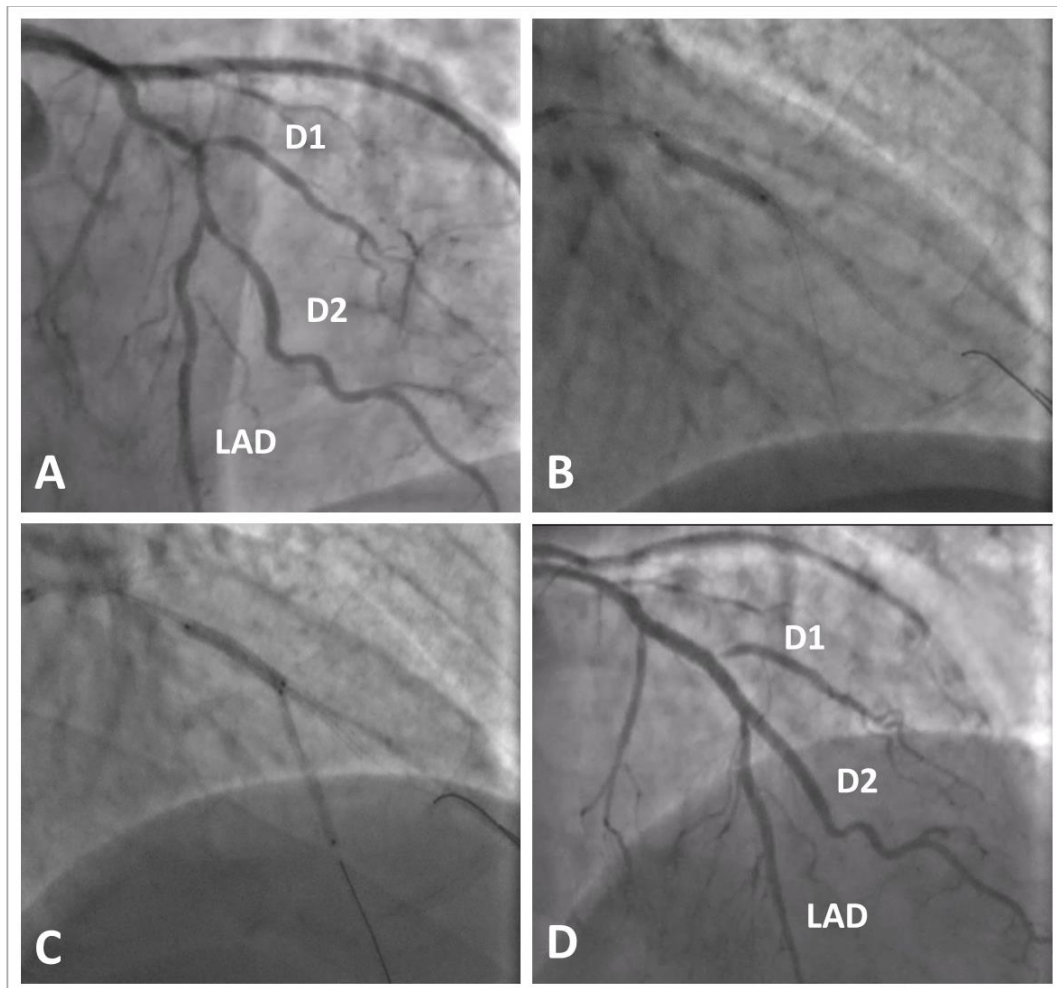


Figure 6. Clinical case involving a POKI procedure – A) Baseline angiography showing significant stenosis of the LAD – D1; B) POT; C) Kissing balloon dilation; D) Final angiography with excellent angiographic result. LAD – left anterior descending artery; D1 – first diagonal branch; D2 – second diagonal branch.

Angiographic Analysis

A specialized analysis of bifurcation quantitative coronary angiography (QCA) was performed in accordance with the consensus recommendations on QCA methods for bifurcation lesions, using General Electric QCA software and MicroDicom QCA software. (144) True bifurcation lesions were defined as those with stenosis (%DS) >50% in the SB. The minimum luminal diameter (MLD), reference vessel diameter (RVD), and %DS were measured for each segment of the bifurcation (i.e., proximal and distal MV and SB) before and after the intervention. Lesion length was measured from the proximal main vessel to the distal main branch (i.e., we considered the starting and ending points where the stent would hypothetically be implanted). The length of the SB lesion was measured from the ostium to the first normally appearing portion of the vessel. All analyses were performed by two investigators, and in cases of disagreement, a consensus was reached through additional analysis by an experienced expert.

Statistical Methods

1. Descriptive Statistics

Quantitative variables are represented by statistical measures: mean, median, standard deviation (SD), minimum, and maximum values; The results for categorical variables are summarized using absolute (n) and relative (%) frequencies.

2. The Kolmogorov-Smirnov test (One-Sample Kolmogorov-Smirnov test) is used to test the shape of the frequency distribution. The test was performed against the normal distribution.

3. Chi-square test or Fisher's exact test – when examining relationships between descriptive (categorical) data with two or more categories.

4. Independent-Samples t-test – used when comparing two independent groups with a normal distribution of the variable under study.

5. Mann-Whitney nonparametric test when comparing two independent groups – used for ordinal data or when the shape of the frequency distribution differs from that of a normal distribution.

6. When there are more than two groups in a given parameter, an analysis of variance (ANOVA) is performed—a one-way ANOVA test.

7. Binary Logistic Regression – for a quantitative assessment of the factor dependence of a binary dependent variable on independent factor variables (categorical

or quantitative). The resulting statistic—the odds ratio (OR)—indicates the magnitude and direction of the effect of the studied factor on the binary dependent variable.

8. Univariate and multivariate Cox regression analysis—to identify independent predictors of mortality. Using the proportional hazard method—hazard ratio—the predictive power of the factors on the change in risk is assessed

9. Kaplan-Meier analysis—to estimate the survival curve (function) until the occurrence of the events under study.

10. Log-rank test – to compare survival curves among two or more independent groups.

11. Propensity Matching Score – nearest neighbor method – to select patients from the control group (group treated with kissing balloon inflation) with clinical characteristics similar to those of patients in the test group (the group treated with POKI). The clinical characteristics used for the analysis are as follows: gender, age, prevalence of hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, left ventricular ejection fraction, cerebrovascular disease, neoplastic disease, renal insufficiency, atrial fibrillation, SYNTAX score. The analysis allows for pseudo-randomization to balance the baseline risk profile between the two groups.

Statistical significance is considered at $p < 0.05$.

The specialized statistical package SPSS (Statistical Package for the Social Sciences) version 23.0 and R Studio Statistical Software v.3.4. (R Foundation for Statistical Computing, Vienna, Austria) were used to process the study data.

The statistical analysis was conducted in several stages:

I. Descriptive statistics of the patients included in the study—demographic and clinical characteristics, risk factors, results of invasive and non-invasive tests.

II. Conducting a propensity-score matching analysis to select two groups with a similar baseline risk profile – a test group (treated with the POKI technique) and a control group (treated with the KBI technique).

III. Comparison of demographic and clinical characteristics and risk factors in the two groups—test and control.

IV. Comparison of immediate angiographic results and the incidence of complications in the two groups—test and control.

V. Comparison of the incidence of major cardiovascular events (in-hospital and during follow-up) in the two groups – test and control.

VI. To determine the clinical predictors of the listed endpoints, a multiple regression analysis was performed using stepwise backward elimination, with an inclusion criterion of $p < 0.1$ and retention in the model at $p < 0.05$ – logistic or Cox regression analysis when a recorded time was available for a given outcome. This identified the independent predictors for the occurrence of major adverse cardiovascular events.

4. RESULTS

4.1 Study population

Between January 2021 and January 2024, 511 patients underwent percutaneous coronary intervention for a bifurcation lesion. Of these, 403 patients were treated with the KBI technique, and 108 patients with the POKI technique (Figure 7). This cohort of patients constituted the study's overall population. Following a detailed analysis of the overall population, a propensity score matching was performed to balance the two study groups. Thus, the final study population consisted of a total of 216 patients – 108 patients in the POKI group and 108 patients in the KBI group—who were matched for risk factors and clinical characteristics.

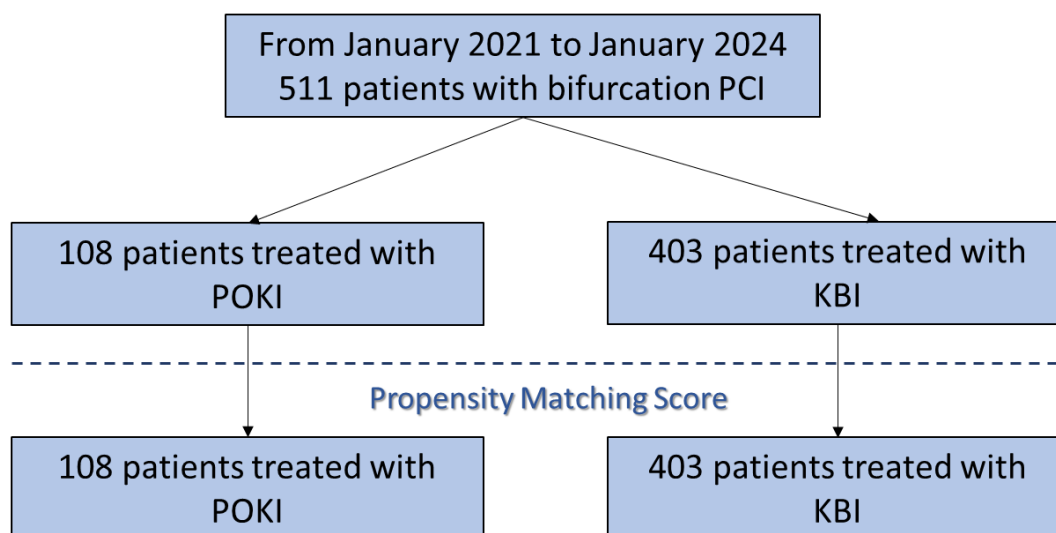


Figure 7. Patient enrollment process for the study

POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique.

4.2 Demographic and clinical characteristics of the overall population

The mean age of the patients included in the study was 66.5 ± 9.9 years. 72% (n=369) of all patients were men. 98% (n=505) of the patients had hypertension, and 95% (n=485) had dyslipidemia. 33% of the population (n=166) were smokers. 40.5% (n=206) of the patients had diagnosed diabetes, and 19% (n=20) had atrial fibrillation and were receiving anticoagulant

therapy. A total of 53% (n=273) of the population had pre-existing coronary artery disease. Of these, 29% (n=150) had a history of myocardial infarction. The clinical characteristics and risk factors of patients in the general population are described in Table 5. The demographic characteristics of the population indicate a high prevalence of risk factors for atherosclerosis, which is associated with more advanced and severe coronary artery disease.

Table 5. Demographic and clinical characteristics of the overall population. BMI – body mass index; COPD – chronic obstructive pulmonary disease; PCI – percutaneous coronary intervention; MI – myocardial infarction

Characteristics Total = 511	Total = 511
Age, years (mean \pm sd) 66.5 \pm 9.9	66.5 \pm 9.9
Male, n (%) 369 (72)	369 (72)
BMI, mean \pm sd 28.5 \pm 4.8	28.5 \pm 4.8
Hypertension, n (%) 505 (98)	505 (98)
Family history, n (%) 47 (23.4)	47 (23.4)
Dyslipidemia, n (%) 485 (95)	485 (95)
Diabetes mellitus, n (%) 206 (40.5)	206 (40.5)
Chronic kidney disease, n (%) 12 (6)	12 (6)
Neoplasm, n (%) 33 (6.5)	33 (6.5)
Smoking, n (%) 166 (33)	166 (33)
Atrial fibrillation, n (%) 20 (19)	20 (19)
Cerebrovascular disease, n (%) 70 (13.7)	70 (13.7)
Peripheral arterial disease, n (%) 60 (12)	60 (12)
COPD, n (%) 57 (11)	57 (11)
Previous PCI, n (%) 273 (53)	273 (53)
Previous MI, n (%) 150 (29.4)	150 (29.4)

4.3 Echocardiographic characteristics of the general population

Most patients in the study had preserved left ventricular (LV) systolic function—74% (n=382), while 12% (n=61) had mildly reduced LV systolic function, and 14% (n=69) had reduced LV systolic function, Table 6. The mean ejection fraction for the entire population was $52.6 \pm 9.7\%$. Abnormalities in left ventricular kinetics—hypo-, a-, or dyskinesia—were observed in 199 patients (39%). Mild mitral regurgitation was observed in 52% (n=268) of patients, and mitral regurgitation \geq grade 2 in 21% (n=107). Left ventricular hypertrophy was found in 68% (n=137) of patients, with mean measurements of the interventricular septum at 12.7 ± 1.8 mm and of the left ventricular posterior wall at 12.1 ± 1.6 mm.

Table 6. Echocardiographic characteristics of the overall population

IVS – interventricular septum; LVSW – left ventricular posterior wall; EF – ejection fraction.

Characteristics Total N = 511	Total N = 511
LVEDD, mm (mean \pm SD) 12.7 ± 1.8	12.7 ± 1.8
LVEDV, mm (mean \pm SD) 12.1 ± 1.56	12.1 ± 1.56
EF, % (mean \pm SD) 52.6 ± 9.7	52.6 ± 9.7
Patients with mildly reduced EF, n (%) 61 (12)	61 (12)
Patients with reduced EF, n (%) 69 (14)	69 (14)
Mitral regurgitation \geq grade 2 22 (21)	22 (21)
Kinetic abnormalities, n (%) 199 (39)	199 (39)

4.4. Laboratory results for the entire population

Analysis of the laboratory parameters for the entire population revealed a mean serum creatinine level prior to the invasive examination of 98.7 ± 39.4 $\mu\text{mol/L}$; a total of 6% (n=12) of the population had an eGFR below 60 ml/min and, accordingly, had some degree of chronic kidney disease. The mean total cholesterol level was 4.48 ± 1.29 mmol/L, and the mean LDL level was 2.59 ± 1.08 mmol/L. The laboratory parameters of patients in the general population are described in Table 7.

Table 7. Laboratory characteristics of the overall population

LDL – low-density cholesterol; *HDL* – high density cholesterol; *eGFR* – estimated glomerular filtration

Characteristics	Total N= 511
Hemoglobin, % (mean ± sd)	136.4 ± 16.0
Red Blood Cells, (mean ± sd)	4.89 ± 2.12
White Blood Cells, (mean ± sd)	8.0 ± 2.2
Platelets, (mean ± sd)	257.5 ± 69.6
Total Cholesterol, mmol/l (mean ± sd)	4.48 ±1.29
LDL, mmol/l (mean ± sd)	2.59 ± 1.08
HDL, mmol/l (mean ± sd)	1.12 ± 0.3
Triglycerides (mean ± sd)	1.78 ± 1.08
Creatinine, mcmol/L (mean ± sd)	98.7 ± 39.4
eGFR, (mean ± sd)	74.5 ± 24.4
eGFR< 60 ml/min, n (%)	12 (6)
Creatin phosphokynase, (mean ± sd)	116.2 ± 85.6
Creatin phosphokynase – MB, (mean ± sd)	17.0 ± 12.2
Troponin – T, (mean ± sd)	0.12 ± 0.61

4.5 Angiographic and procedural characteristics of the general population

The mean procedure time during the study was 99.3 ± 36.1 min, and the mean fluoroscopy time was 25.1 ± 11.2 min. At the same time, the average amount of contrast medium used during the study was 232.1 ± 118.6 mL (Table 8). The higher amount of contrast medium compared to that reported in the literature is likely related to the complex nature of the treated lesions.

In a total of 64% (n=324) of the population, the target vessel undergoing coronary revascularization was the left anterior descending artery (LAD); in 20% (n=101), the intervention was performed on the left circumflex artery (LCA). The right coronary artery (RCA) was the target vessel in 13% (64) of the population, and the remaining 3% (n=19) of patients underwent intervention on an intermediate branch (RIM), (Figure 8). The mean number of stents implanted in the entire population was 1.9 ± 0.9 , with a mean stent length of 53.8 ± 28.8 mm and a mean stent diameter of 3.15 ± 0.36 mm. (Table 8). The large total length of the stents used is another characteristic indicating the complex nature of the stenoses that were treated.

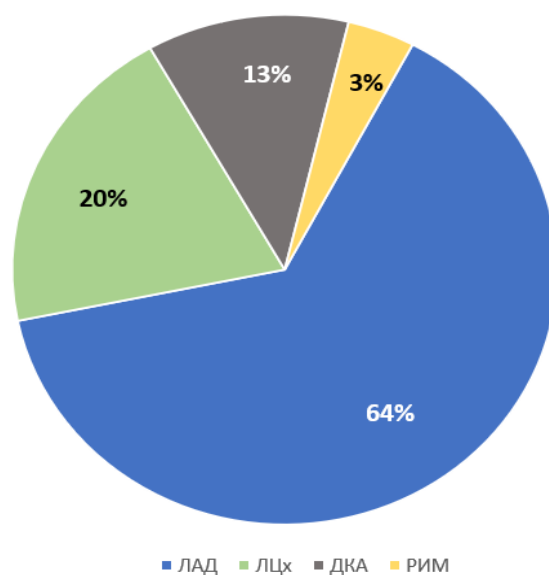


Figure 8. Anatomy of the target vessel undergoing intervention

LAD – left anterior descending artery; LCI – left circumflex artery; RCA – right coronary artery; IBA – intermediate branch.

Table 8. Procedural characteristics

LAD – left anterior descending artery; LCI – left circumflex artery; RCA – right coronary artery; IBA – intermediate branch.

Characteristics	Total N= 511
Procedure time, min, (mean ± sd)	99.3 ± 36.1
Fluoroscopy time, min, (mean ± sd)	25.1 ± 11.2
Contrast volume, mL, (mean ± sd)	332.1 ± 118.6
Target vessel: <ul style="list-style-type: none"> • LAD, n (%) • LCx, n (%) • RCA, n (%) • RIM, n (%) 	<ul style="list-style-type: none"> • 324 (63.6) • 101 (19.8) • 64 (12.8) • 19 (3.8)
Number of stents implanted, (mean ± sd)	1.9 ± 0.9
Length of implanted stent, mm, (mean ± sd)	53.8 ± 28.8
Diameter of implanted stent, mm, (mean ± sd)	3.15 ± 0.36

Angiographic analysis of the coronary lesions included in the study revealed a mean lesion length in the main branch of 40.7 ± 19.9 mm and a mean lesion length in the side branch of 8.3 ± 5.1 mm. (Table 9). The mean SYNTAX score, providing the most comprehensive information on the complexity of coronary artery disease, was 15.5 ± 7.2 points.

Analysis using quantitative coronary angiography (QCA) allowed for a detailed characterization of the bifurcation lesions in the segments of the proximal main branch (MV), distal main branch (MB), and side branch (SB). The analysis revealed mean baseline stenosis values in all three bifurcation segments >50%, indicating significant obstruction. The highest mean baseline stenosis was observed in the distal main branch segment—%DS MB— $64.9 \pm 26.7\%$, (Figure 9). QCA analysis following the interventional procedure revealed low post-procedural stenoses in all three segments of the coronary bifurcation, respectively: final %DS

MV – $7.59 \pm 12.6\%$, final %DS MB - $6.07 \pm 9.37\%$, and final %DS SB - $13.5 \pm 18.8\%$ (Figure 10).

Table 9. Angiographic characteristics of the overall population

MB – distal main branch; SB – side branch; %DS – percentage of vessel stenosis; MV – proximal main branch.

Characteristics	Total N= 511
Lesion length - MB, mm, (mean \pm sd)	40.7 ± 19.9
Lesion length - SB, mm, (mean \pm sd)	8.3 ± 5.1
SB RVD, mm (mean \pm sd)	2.5 ± 0.36
SYNTAX score, (mean \pm sd)	15.5 ± 7.2
Bifurcation coronary artery disease, n (%)	134 (26)
Trifurcation coronary artery disease, n (%)	251 (49)
Baseline %DS MV, %, (mean \pm sd)	55.7 ± 28.4
Baseline %DS MB, %, (mean \pm sd)	64.9 ± 26.7
Baseline %DS SB, %, (mean \pm sd)	58.3 ± 29.2
Final %DS MV, %, (mean \pm sd)	7.59 ± 12.6
Final %DS MB, %, (mean \pm sd)	6.07 ± 9.37
Final %DS SB, %, (mean \pm sd)	13.5 ± 18.8

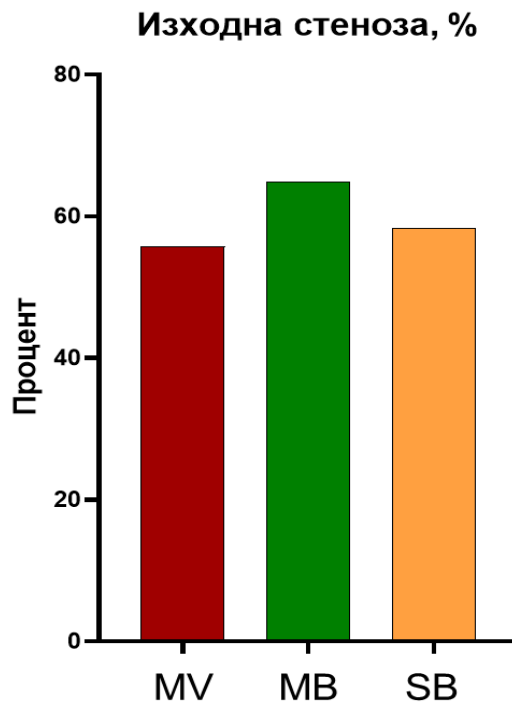


Figure 9. Graph showing the initial stenosis in the three segments of the bifurcation. MB – distal main branch; SB – side branch; MV – proximal main branch

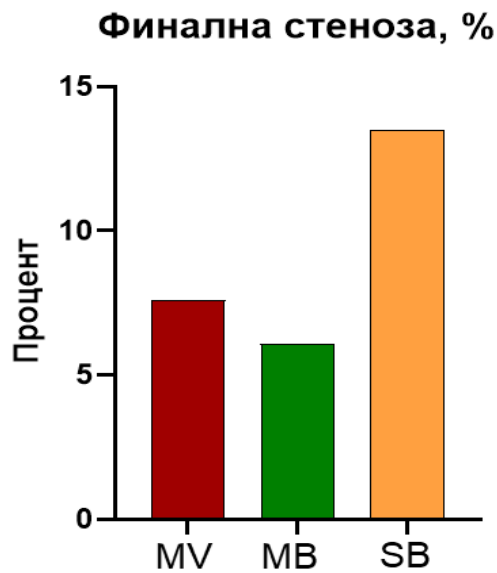


Figure 10. Graph showing the final stenosis in the three segments of the bifurcation. MB – distal main branch; SB – side branch; MV – proximal main branch

4.6 Analysis of the two groups following Propensity Matching Score (PMS) – a nearest-neighbor method – to select patients from the control group (KBI) with clinical characteristics similar to those of the test group (the group treated with POKI). PMS was performed, matching the groups on the following indicators: gender, age, prevalence of hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, left ventricular ejection fraction, cerebrovascular disease, neoplastic disease, renal insufficiency, atrial and SYNTAX score. This resulted in two groups with an equal number of patients (108 patients each) and a balanced baseline risk profile between the two groups (Figures 11–13).

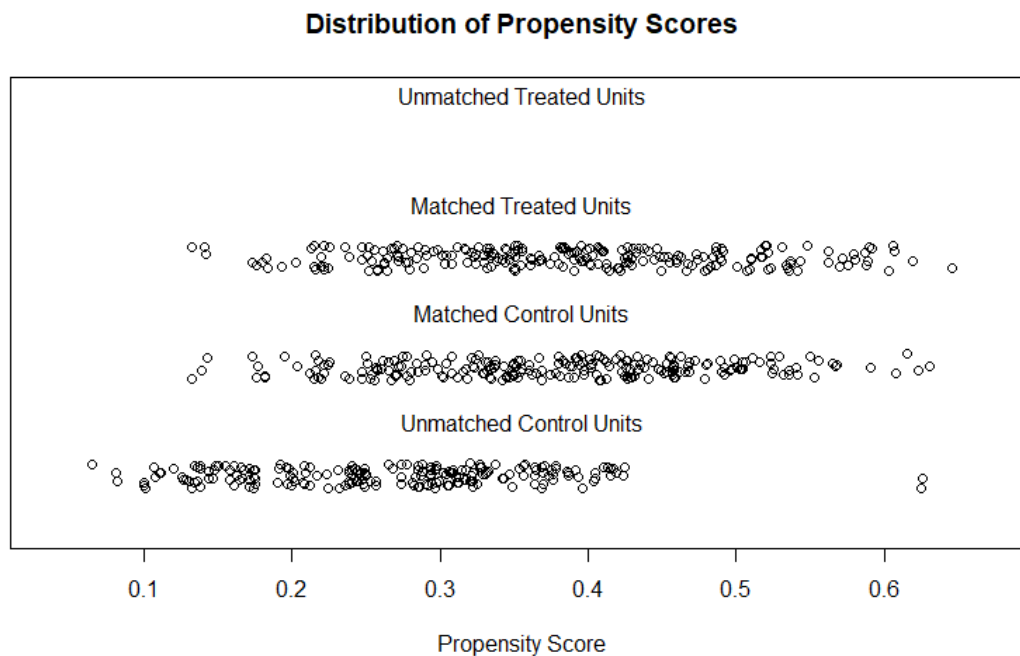


Figure 11. Distribution of patients by characteristics (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, left ventricular ejection fraction, cerebrovascular disease, neoplastic disease, renal failure, SYNTAX score) in the treated patient group (POKI) and in the control group (kissing-balloon inflation) — before and after matching patients by the listed characteristics.

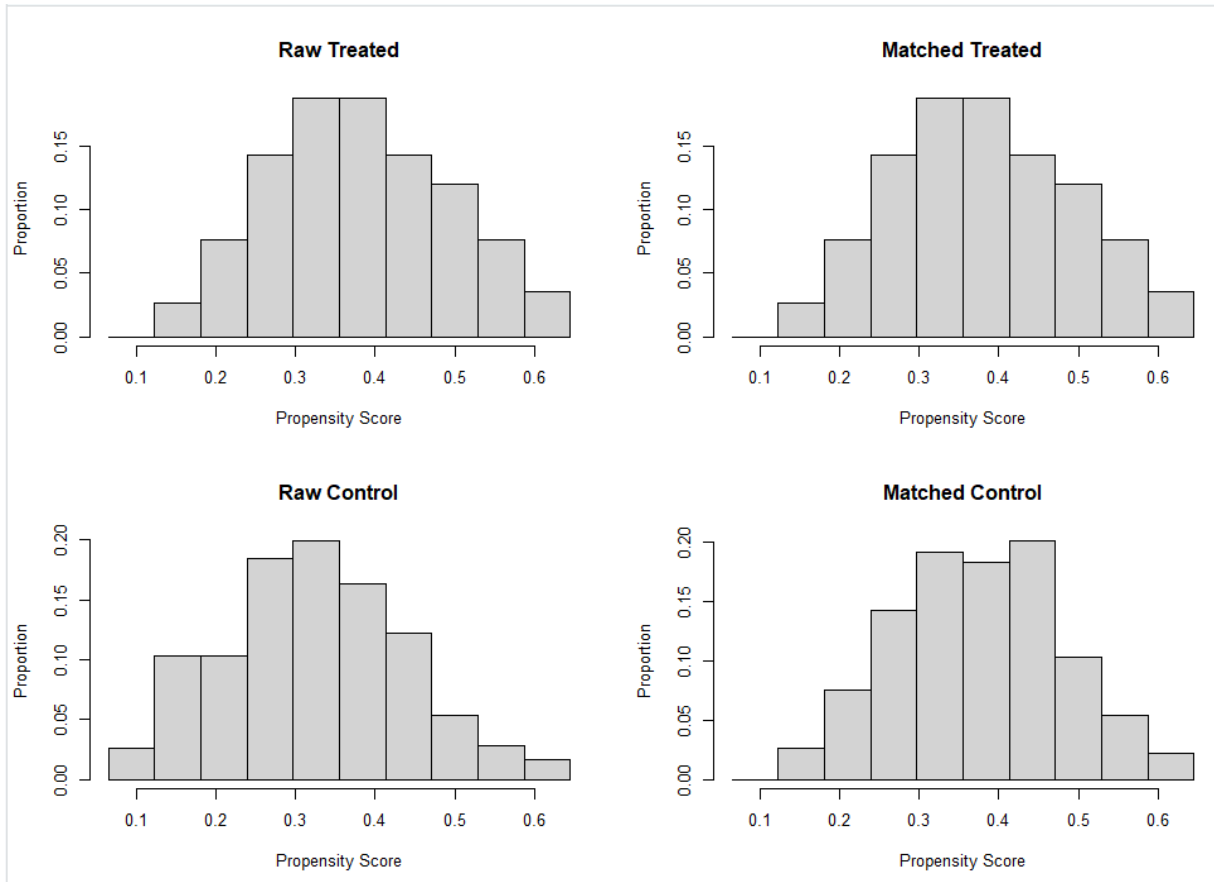


Figure 12: Histograms showing the distribution of patients by characteristics (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, left ventricular ejection fraction, cerebrovascular disease, neoplastic disease, renal failure, SYNTAX score) in the treated patient group (POKI) and in the control group (kissing-balloon inflation) — before and after matching patients by the listed characteristics.

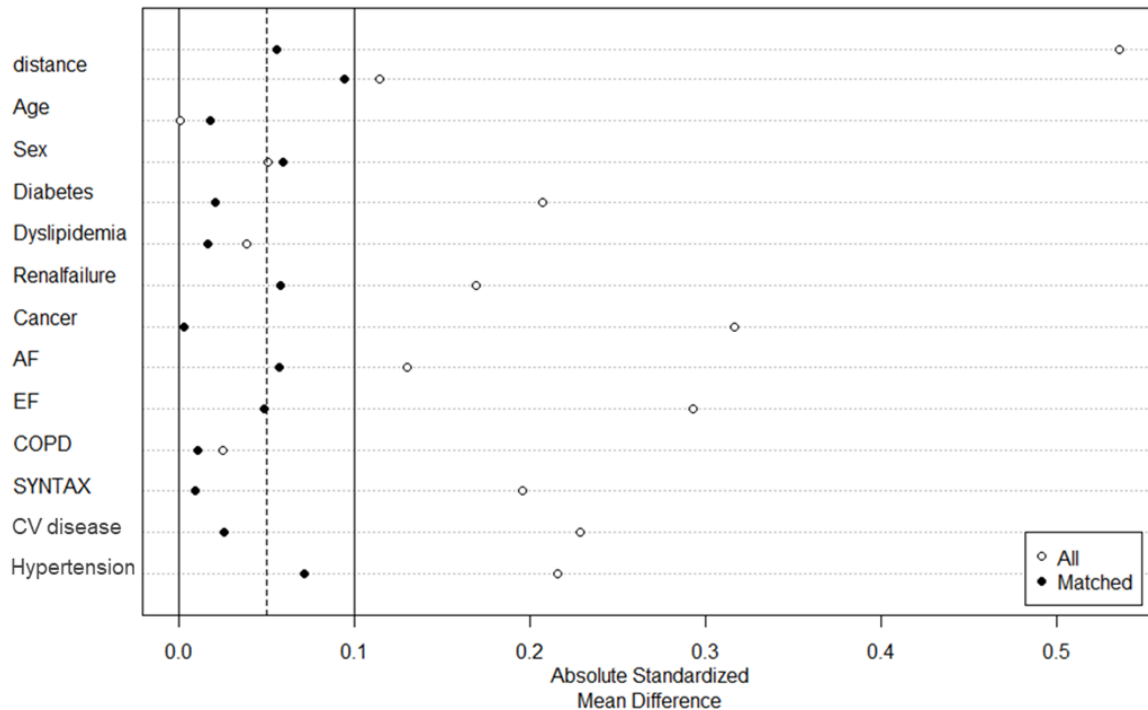


Figure 13. Histograms showing the distribution of patients by characteristics (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, left ventricular ejection fraction, cerebrovascular disease, neoplastic disease, renal failure, atrial fibrillation, SYNTAX score) in the treated patient group (POKI) and in the control group (kissing-balloon inflation) — before and after matching patients by the listed characteristics.

When comparing the populations in the two groups after performing PSM, there was no significant difference in the demographic and clinical characteristics of patients treated with POKI and those with KBI, respectively: age— 67.1 ± 9.7 years versus 66.8 ± 9.2 years, $p = 0.478$; hypertension – 100% vs. 99%, $p = 0.784$; diabetes mellitus – 33% vs. 38.9%, $p = 0.069$; cerebrovascular disease – 11.1% vs. 12%, $p=0.803$, as well as in the other characteristics described in Tables 10 and 11. The data in the tables show good alignment of characteristics across the groups, allowing for independent analysis of the differences identified in further comparisons.

Table 10. Demographic and clinical characteristics

POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique

Characteristics	POKI N= 108	KBI N= 108	Total N= 216	P-value
Age, years (mean ± sd)	67.1 ± 9.7	66.8 ± 9.2	66.5 ± 9.9	0.478
Male, n (%)	75 (69.4)	82 (76)	157 (73)	0.219
BMI, mean ± sd	29.3 ± 5.4	28.2 ± 4.4	28.5 ± 4.8	0.432

Table 11. Clinical characteristics of the patients

POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique

Characteristics	POKI N= 108	KBI N= 108	Total N= 216	P-value
Hypertension, n (%)	108 (100)	107 (99)	215 (99.5)	0.784
Dyslipidemia, n (%)	105 (97)	103 (95)	208 (96.3)	0.622
Diabetes mellitus, n (%)	36 (33)	42 (38.9)	78 (36.1)	0.069
Chronic kidney disease, n (%)	35 (32.4)	33 (31)	12 (6)	0.719
Neoplasm, n (%)	4 (3.7)	5 (4.6)	9 (4.2)	0.866
Smoking, n (%)	40 (37)	35 (32)	75 (34.7)	0.091
Atrial fibrillation, n (%)	19 (17.6)	23 (21)	20 (19)	0.074
Cerebrovascular disease, n (%)	12 (11.1)	13 (12)	25 (11.6)	0.803
Peripheral arterial disease, n (%)	11 (10.2)	9 (8.3)	20 (9.3)	0.113
COPD, n (%)	4 (3.7)	10 (4.2)	14 (9.3)	0.306
Previous PCI, n (%)	54 (50)	59 (55)	273 (53)	0.081
Previous MI, n (%)	29 (27)	33 (30)	150 (29.4)	0.092
FI, % (mean ± sd)	49.1 ± 9.8	51.1 ± 9.1	52.6 ± 9.7	0.268

Analysis of the invasive examination data for patients in both groups revealed that the POKI procedure was associated with significantly shorter procedural and fluoroscopic times, specifically POKI versus KBI: procedural time 91.5 ± 27.3 min vs. 105 ± 38.8 min, $p = 0.004$; fluoroscopy time – 22.7 ± 10.2 min vs. 27.4 ± 12.2 min, $p = 0.006$. In addition, the results showed that the amount of contrast used during POKI was significantly lower – 285.7 ± 84 mL vs. 360.7 ± 129 mL, $p < 0.001$ (Table 12). Table 13 details the characteristics of the balloons used for dilation of the main and side branches in the POKI procedure group (Figures 14 -19). The results indicate that POKI shortens the duration of the procedure and, consequently, requires a smaller amount of contrast.

Table 12. Procedural Characteristics

POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique

Characteristics	POKI N= 108	KBI N= 108	Total N= 216	P-value
Procedure time, min, (mean \pm sd)	91.5 ± 27.3	105 ± 38.8	99.3 ± 36.1	0.004
Fluoroscopy time, min, (mean \pm sd)	22.7 ± 10.2	27.4 ± 12.2	25.1 ± 11.2	0.006
Contrast volume, (mean \pm sd)	285.7 ± 84	360.7 ± 129	332.1 ± 118.6	<0.001
Target vessel:				0.105
LAD, n (%)	69 (64)	67 (62)	136 (63.2)	
LCx, n (%)	23 (21)	21 (19)	43 (20)	
RCA, n (%)	12	15 (14)	28 (13)	
RIM, n (%)	(11.2) 4 (3.8)	5 (5)	19 (3.8)	
Number of stents implanted, (mean \pm sd)	1.57 ± 0.7	1.98 ± 1.11	1.8 ± 0.9	0.001
Length of implanted stent, mm, (mean \pm sd)	46.8 ± 23.0	61.9 ± 31.8	58.6 ± 28.2	<0.001
Diameter of implanted stent, mm, (mean \pm sd)	3.2 ± 0.43	3.2 ± 0.3	2.7 ± 0.35	0.943

Table 13. Characteristics of the balloons used during the POKI procedure. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique; MB – distal main branch; SB – side branch; %DS – percentage stenosis of the vessel; MV – proximal main branch

Characteristics	Total N= 108
POKI MB Balloon length, mm, (mean ± sd)	10.1 ± 4.6
POKI MB Balloon diameter, mm, (mean ± sd)	3.71 ± 0.54
POKI SB Balloon length, mm, (mean ± sd)	17.6 ± 5.5
POKI SB Balloon diameter, mm, (mean ± sd)	2.56 ± 0.4

Table 14. Angiographic characteristics. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique; MB – distal main branch; SB – side branch; %DS – percentage of vessel stenosis; MV – proximal main branch

Characteristics	POKI N= 108	KBI N= 108	Total N= 216	P-value
Lesion length - MB, mm, (mean ± sd)	34.4 ± 17.2	41.1 ± 17.7	39.8 ± 17.5	0.006
Lesion length - SB, mm, (mean ± sd)	9.04 ± 4.26	8.44 ± 5.46	8.7 ± 5.1	0.371
SYNTAX score, (mean ± sd)	19.1 ± 7.3	17.6 ± 6.8	18.3 ± 7.2	0.179
Baseline %DS MV, (mean ± sd)	58.1 ± 16.9	45.2 ± 29.8	55.7 ± 28.4	<0.001
Baseline %DS MB, (mean ± sd)	49.8 ± 21.7	53.6 ± 36.5	52.1 ± 26.7	0.347
Baseline %DS SB, (mean ± sd)	43.6 ± 30.5	57.1 ± 22.4	54.3 ± 29.2	<0.001
Final %DS MV, (mean ± sd)	16.3 ± 13.1	16.1 ± 14.1	7.59 ± 12.6	0.918
Final %DS MB, (mean ± sd)	11.7 ± 8.0	14.1 ± 11.0	6.07 ± 9.37	0.070
Final %DS SB, (mean ± sd)	8.59 ± 7.3	19.0 ± 13.4	13.5 ± 18.8	<0.001

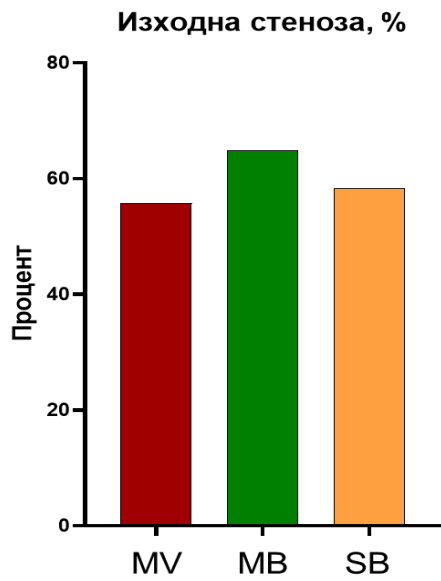


Figure 14. A graph depicting the initial stenoses in the three segments of the bifurcation. MV – proximal main branch; MB – distal main branch; SB – side branch

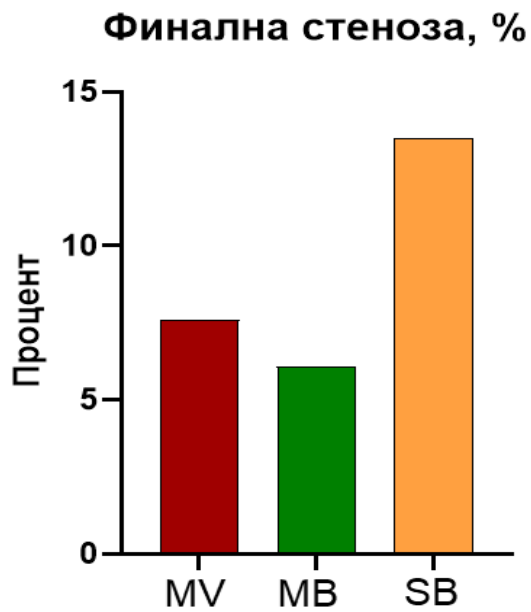


Figure 15. Graph showing the final stenoses in the three segments of the bifurcation. MV – proximal main branch; MB – distal main branch; SB – side branch

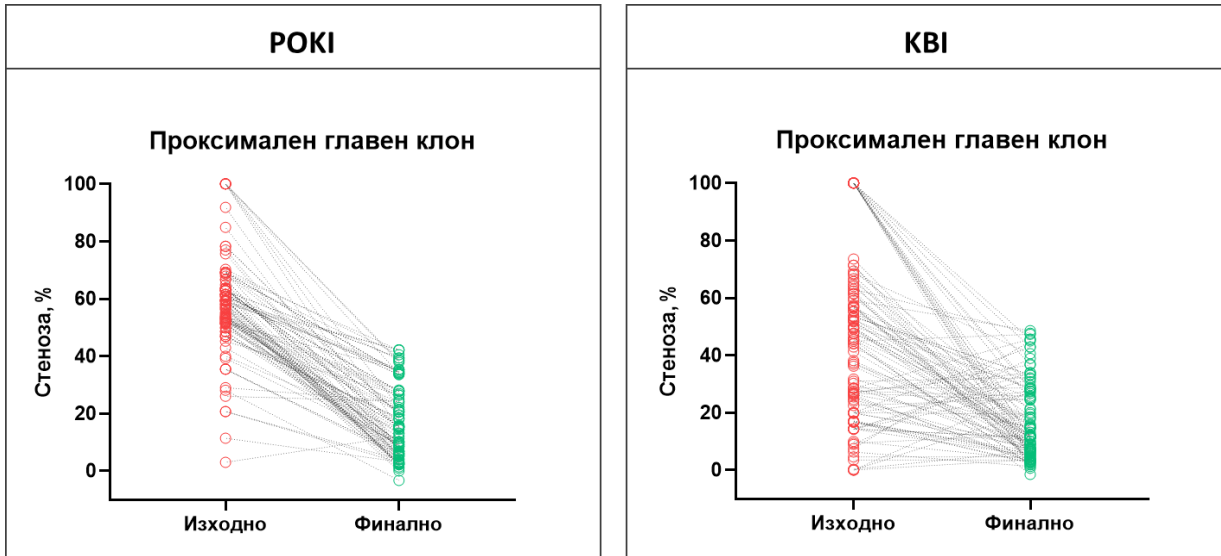


Figure 16. Visualization of the initial and final stenosis in a proximal main branch using the POKI technique and the KBI technique. The initial stenosis is shown in red, and the final stenosis in the proximal branch is shown in green

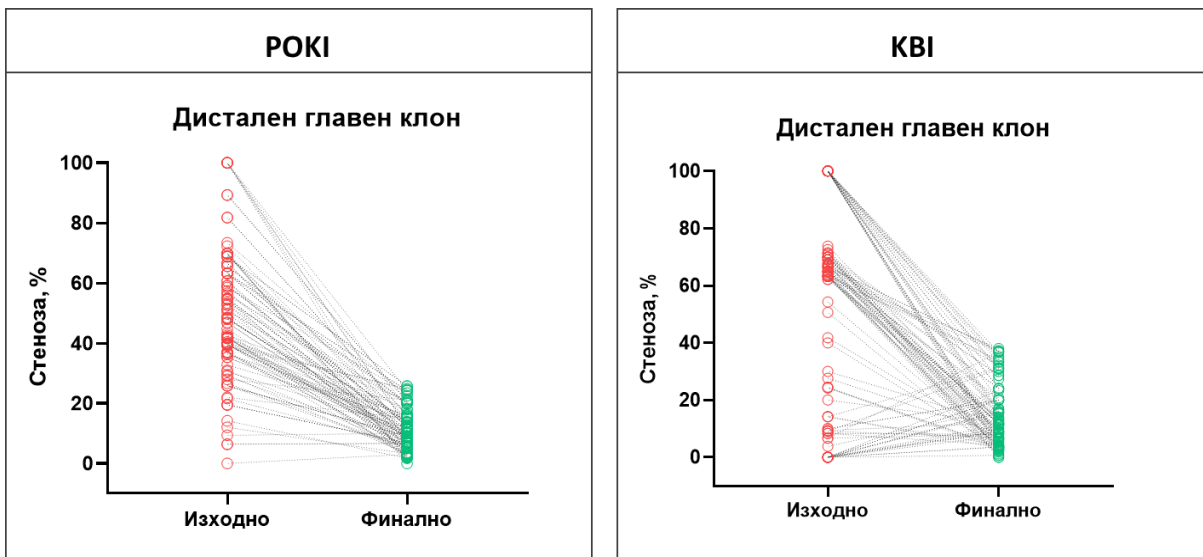


Figure 17. Visualization of the initial and final stenosis in a distal main branch using the POKI technique and the KBI technique. The initial stenosis is shown in red, and the final stenosis in the distal main branch is shown in green

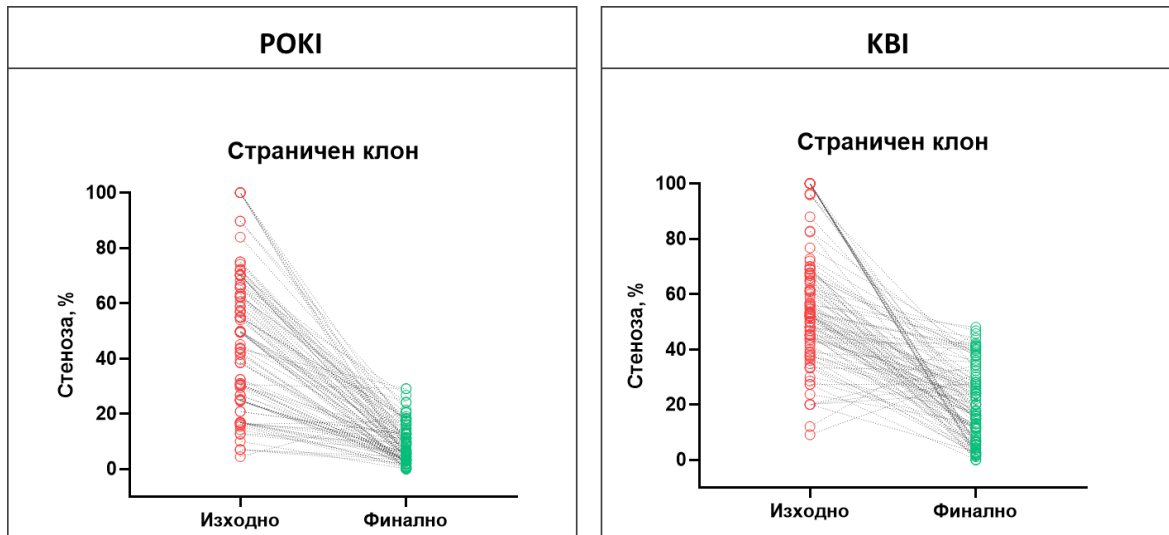


Figure 18. Visualization of the initial and final stenosis in a lateral branch using the POKI technique and the KBI technique. The initial stenosis is shown in red, and the final stenosis in the lateral branch is shown in green

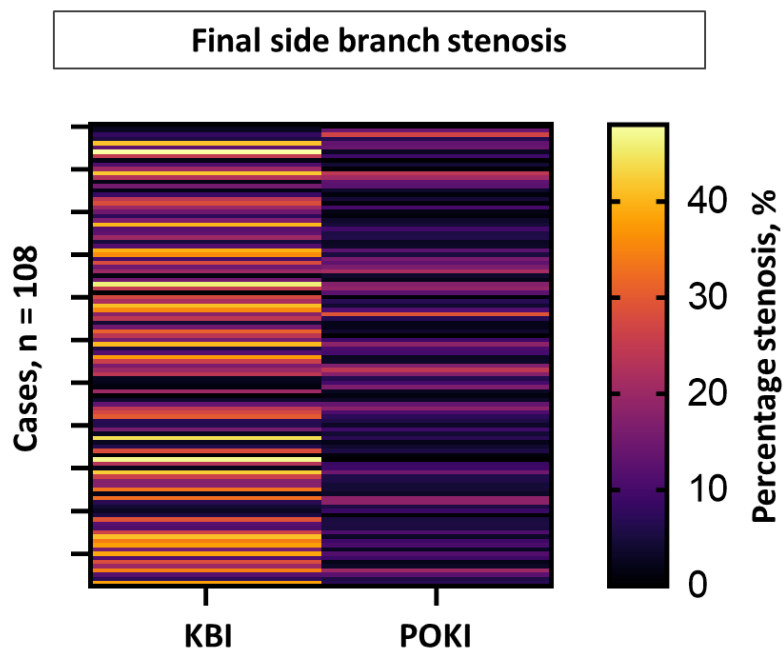


Figure 19. Color-coded visualization of final stenosis in the lateral branch using the KBI technique and the POKI technique. The figure illustrates the generally lower rate of final stenosis in the lateral branch among patients treated with the POKI technique (shown in a darker purple color)

4.7 Comparison of immediate angiographic results between the group of patients treated with POKI and those treated with KBI

Using the definition of angiographic success—a post-procedural stenosis in the MV <20% and a final stenosis in the SB <50%—it was found that 85% (n=92) of the patients in the POKI group achieved complete angiographic success, whereas in the KBI group, only 72% (n=77) achieved angiographic success, $p < 0.001$ (Table 15, Figures 20 and 21). This means that the POKI technique provides a better final angiographic outcome, mainly due to a better final result in the lateral branch and the distal main branch.

Table 15. Angiographic success. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique; MB – distal main branch; SB – side branch; %DS – percentage of vessel stenosis; MV – proximal main branch

Characteristics	POKI N= 108	KBI N= 108	P - value
Patients with a final %DS \geq 20%, n (%)	16 (15)	27 (25)	<0.001
Patients with a final %DS SB \geq 50%, n (%)	0 (0)	4 (3.7)	0.006
Angiographic success, n (%)	92 (85)	77 (72)	<0.001

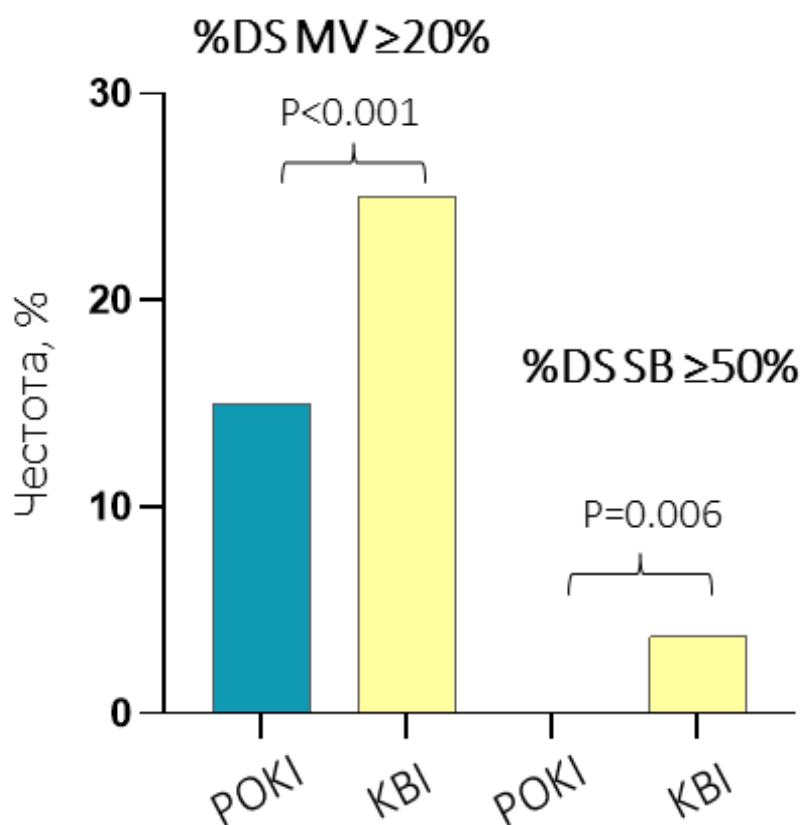


Figure 20. Post-procedural angiographic results. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique; MB – distal main branch; SB – side branch; %DS – percentage of vessel stenosis; MV – proximal main branch. The figure shows the frequency of patients with residual stenosis in the proximal main branch $\geq 20\%$ among patients after POKI (in blue), which is statistically significantly lower than the frequency of patients with such stenosis after the KBI procedure (in yellow)

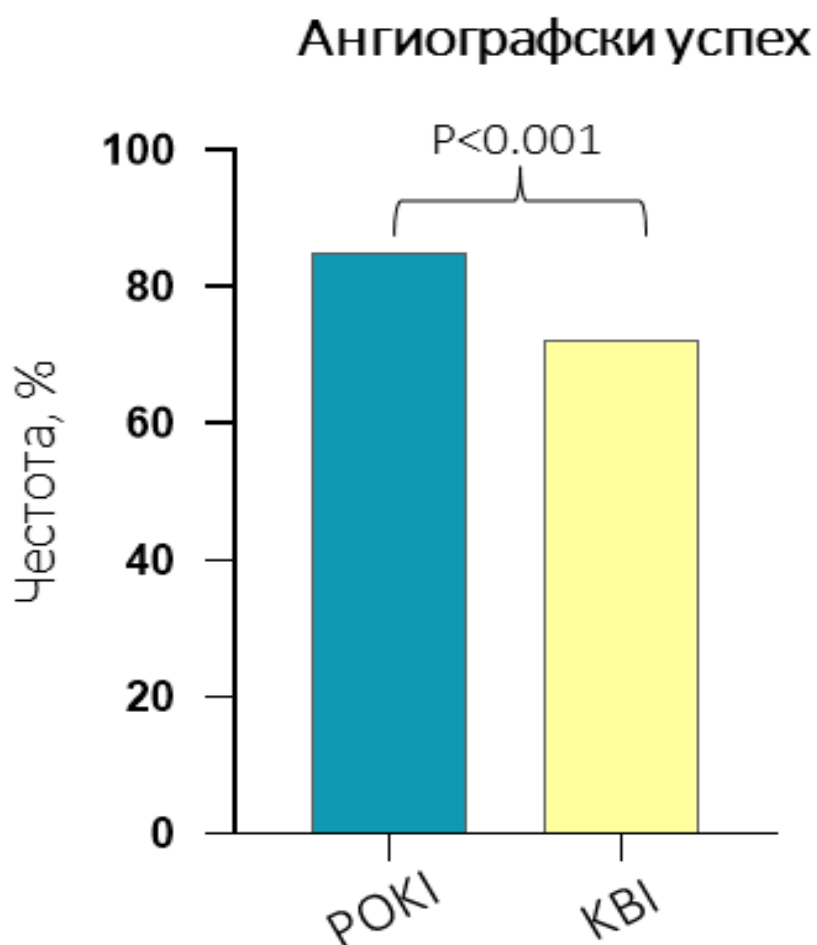


Figure 21. Angiographic success. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique. The figure shows the rate of angiographic success in patients following POKI—85% (blue), which is statistically significantly higher than the rate of angiographic success in patients following the KBI procedure—72% (yellow), $p < 0.001$.

4.8 Analysis of Perioperative Complications

A total of 16 (7.5%) peri-procedural complications were recorded in the entire population. Puncture-site complications were recorded in a total of 7 patients (3.2%), and iatrogenic dissection of the target vessel was recorded in four patients (1.9%). Rhythm and conduction disturbances were reported in five patients (2.3%) during the procedure. No cases of coronary perforation, acute heart failure, or death were reported in the entire population.

When comparing the incidence of different types of complications between the two study groups, the overall incidence of periprocedural complications was 6.5% ($n=7$) in the POKI

group and 8.3% (n=9) in the KBI group, p=0.096. A significantly higher incidence of puncture site-related complications was observed in patients in the KBI group compared to the POKI group—1.9% (n=2) versus 4.6% (n=5), p=0.032 (Table 16).

Table 16. Incidence of peri-procedural complications. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique.

Parameter	Total (N = 216)	POKI (N = 108)	KBI (N = 108)	P- стойност
Periprocedural complications, n (%)	16 (7.5)	7 (6.5)	9 (8.3)	0.096
Coronary dissection, n (%)	4 (1.9)	2 (1.9)	2 (1.9)	1.0
Rhythm and conduction disorders, n (%)	5 (2.3)	3 (2.8)	2 (1.9)	0.118
Complications at the puncture site, n (%)	7 (3.2)	2 (1.9)	5 (4.6)	0.032

4.9 Analysis of Mortality and Major Cardiovascular Events

During the patient follow-up period of 14 [10–21] months, a total of 20 patients (20/216, 9.3%) died. Of these, 7.4% (n=16) died of cardiovascular causes, and 1.9% (n=4) died of non-cardiovascular causes. Three (1.4%) patients experienced a non-fatal MI. A total of 18 patients (8.3%) experienced a major adverse cardiovascular event (MACE). In 11 patients (5.1%), subsequent revascularization of the target vessel was performed, and patient-oriented events (POCE) occurred in a total of 13.4% (Figure 22).

Cardiovascular events

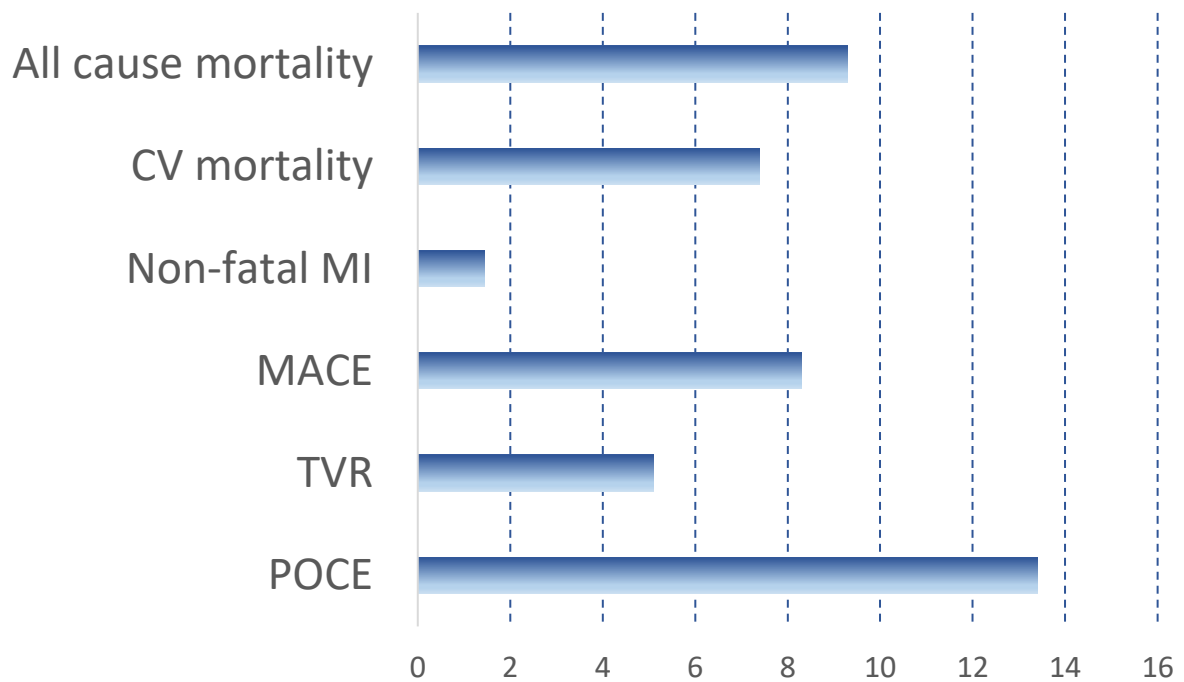


Figure 22. Incidence of adverse cardiovascular events. CV – cardiovascular; MI – myocardial infarction; MACE – major adverse cardiovascular events; TVR – target lesion revascularization; POCE – patient-oriented cardiovascular events.

With regard to demographic and clinical characteristics, no significant differences were found between the deceased and the living in terms of gender distribution, prevalence of chronic kidney disease, or history of myocardial infarction. The analysis revealed a significantly higher age (71 ± 8 vs. 64 ± 12 , $p=0.001$), a higher prevalence of diabetes mellitus (41% vs. 35%, $p=0.012$), and a lower left ventricular ejection fraction (43.5 ± 11.9 vs. 50.8 ± 8.2 , $p=0.001$) among deceased patients compared to living patients (Table 17). The results show that deceased patients were older, more frequently diabetic, and had reduced LVEF (Figure 23).

Table 17. Clinical characteristics of patients—survivors and deceased. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique; LVEF – left ventricular ejection fraction.

Parameter	Deceased (n=20)	Alive (n=196)	P-value
Gender, male, n (%)	15 (75)	145 (74)	0.652
Age, years, (mean ± sd)	71 ± 8	64 ± 12	0.001
Diabetes mellitus, n (%)	8 (41)	67 (35)	0.012
Chronic kidney disease, n (%)	7 (37)	59 (30)	0.032
History of myocardial infarction	6 (28)	59 (30)	0.261
LVEF, %	43.5 ± 11.9	50.8 ± 8.2	0.001

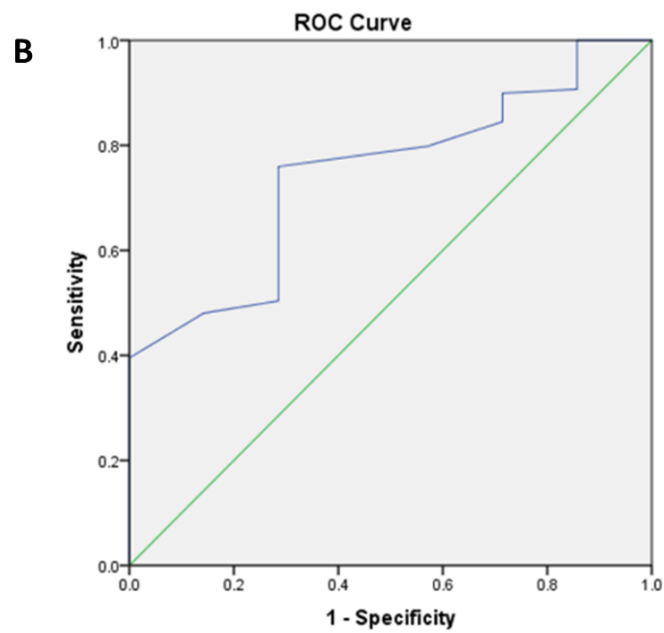
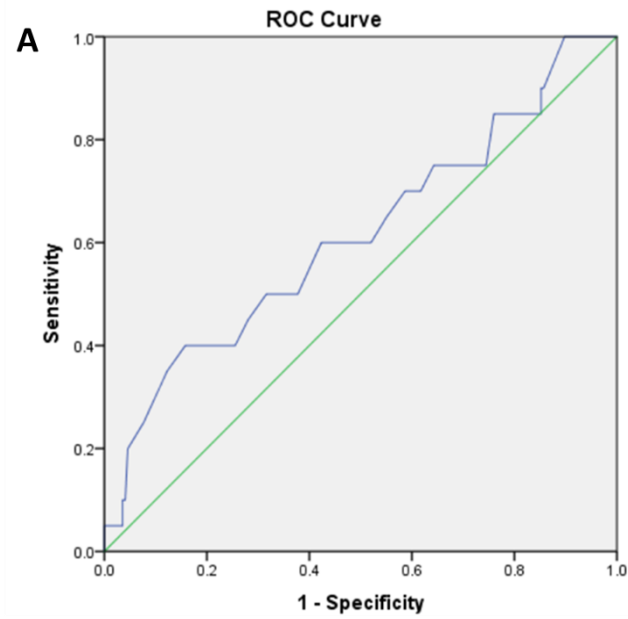


Figure 23. ROC curves defining the cutoff values for the parameters from the univariate analysis associated with the occurrence of death. A) Change in age and mortality values, C -statistic = 0.613, $p = 0.096$. Cutoff value: age 65 – sensitivity 50%, specificity 82%; B) LV ejection fraction, $c = 0.745$, $p = 0.030$, cutoff value: EF < 55%, sensitivity 76%, specificity 72%.

A comparison of procedural characteristics revealed no significant differences between deceased and surviving patients regarding baseline stenosis in the bifurcation segments or SYNTAX scores. However, the results showed a significantly higher final stenosis in the side branch in the group of deceased patients— $20.4 \pm 13.9\%$ versus $13.1 \pm 11.6\%$, $p=0.028$. The analysis also revealed a significantly higher frequency of POKI technique use in surviving patients (52% vs. 30%, $p=0.008$), (Table 18). An interesting finding is that although deceased patients had more severe final stenoses, the length of the lesions was shorter. It should be noted that in both groups, the mean stenosis length was less than 10 mm.

Table 18. Procedural characteristics of patients—deceased and alive. MB—distal main branch; SB—side branch; %DS—percentage of vessel stenosis; MV—proximal main branch.

Parameter	Deceased (n=20)	Alive (n=196)	P-value
Procedure time, min, (mean \pm sd)	104.5 \pm 32.3	99.2 \pm 30.4	0.093
Fluoroscopy time, min, (mean \pm sd)	27.6 \pm 11.1	25.3 \pm 12.0	0.068
Contrast volume, (mean \pm sd)	315.7 \pm 91	339.7 \pm 118	0.109
Lesion length - MB, mm, (mean \pm sd)	35.3 \pm 13.9	37.9 \pm 18.1	0.517
Lesion length - SB, mm, (mean \pm sd)	6.65 \pm 2.78	8.95 \pm 5.02	0.046
Baseline %DS MB, (mean \pm sd)	40.1 \pm 30.1	52.9 \pm 29.8	0.082
Baseline %DS SB, (mean \pm sd)	56.0 \pm 23.2	49.8 \pm 27.8	0.211
SYNTAX score, (mean \pm sd)	19.0 \pm 6.1	18.3 \pm 7.1	0.209
POKI technique, n (%)	6 (30)	102 (52)	0.008
Final %DS MV, (mean \pm sd)	16.8 \pm 18.9	16.1 \pm 13.0	0.822
Final %DS MB, (mean \pm sd)	9.1 \pm 8.3	13.3 \pm 9.8	0.081
Final %DS SB, (mean \pm sd)	20.4 \pm 13.9	13.1 \pm 11.6	0.028

4.10 Impact of the POKI Technique on Survival and Cardiovascular Events

In the group of patients who underwent a POKI procedure, a total of 6 patients (5.6%) died, and in all cases the cause of death was cardiovascular. One of the deceased patients had a non-fatal MI (Table 19). Therefore, 5.6% of patients experienced a major adverse cardiovascular event (MACE). An additional 4 patients (3.7%) underwent repeat revascularization of the target vessel. Consequently, patient-oriented events occurred in a total of 9.3% (n=10).

In the group of patients treated with KBI, death was recorded in a total of 14 patients (13%), and in 10 (9.3%) of them, it was of cardiovascular origin. Non-fatal myocardial infarction was recorded in two patients (1.9%). Consequently, 11% of patients experienced a major adverse cardiovascular event (MACE). In addition, 7 patients (6.5%) underwent repeat revascularization of the target vessel. Thus, patient-oriented events occurred in a total of 17.6% (n=19) of the group undergoing KBI.

Table 19. Incidence of adverse cardiovascular events. POKI – proximal-optimization and kissing technique; KBI – kissing-balloon inflation technique. MACE – major adverse cardiovascular events; POCE – patient-oriented adverse cardiovascular events.

Parameter	Общо (N = 216)	POKI (N = 108)	KBI (N = 108)	P value
Overall mortality, n (%)	20 (9.3)	6 (5.6)	14 (13.0)	0.036
Cardiovascular mortality, n (%)	16 (7.4)	6 (5.6)	10 (9.3)	0.195
Non-fatal MI, n (%)	3 (1.4)	1 (0.93)	2 (1.85)	0.558
Revascularization of the target vessel, n (%)	11 (5.1)	4 (3.7)	7 (6.5)	0.264
MACCE, n (%)	18 (8.3)	6 (5.6)	12 (11)	0.078
POCE, n (%)	29 (13.4)	10 (9.3)	19 (17.6)	0.032

When comparing the incidence of cardiovascular events in the two study groups, a significantly lower overall mortality rate of 5.6% versus 13% ($p = 0.036$) was observed in the POKI group compared to the KBI group. At the same time, the incidence of cardiovascular mortality, non-fatal MI, target vessel revascularization, and MACE, although not statistically significant, was numerically lower in the POKI group. It is important to note that when analyzing the composite patient-oriented outcome (POCE) measure, a significantly lower incidence of POCE was observed in the POKI group compared to the KBI group, specifically 9.3% versus 17.6%, $p=0.032$ (Figures 24–29).

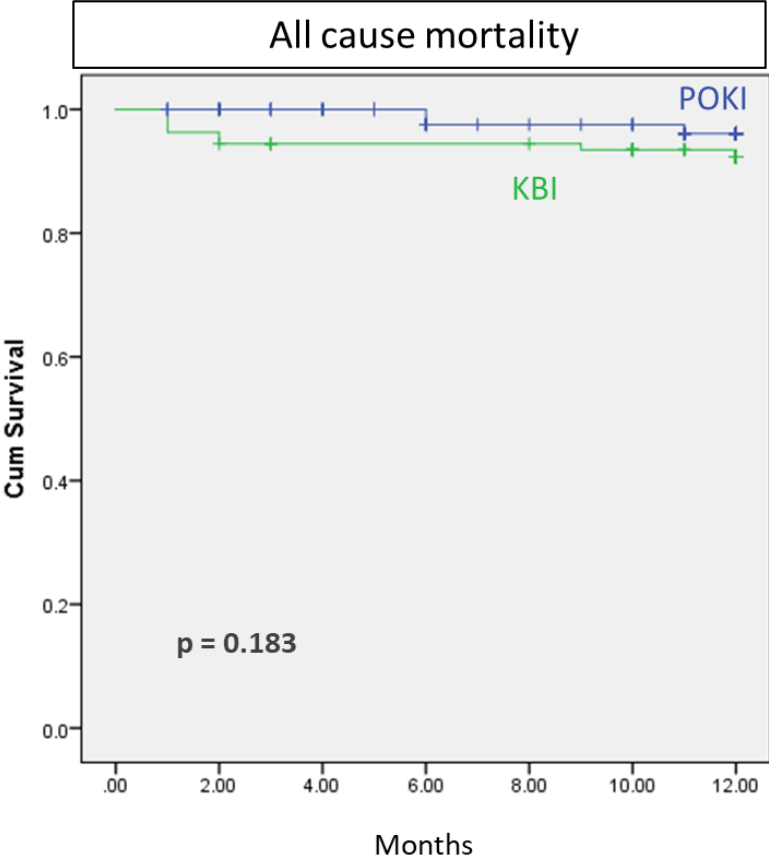


Figure 24. Kaplan-Meier curve illustrating the difference in overall mortality rates between the groups treated with the POKI technique and the KBI technique. A significantly lower overall mortality rate was observed in the POKI group (5.6%) compared to the KBI group (13%), $p=0.036$

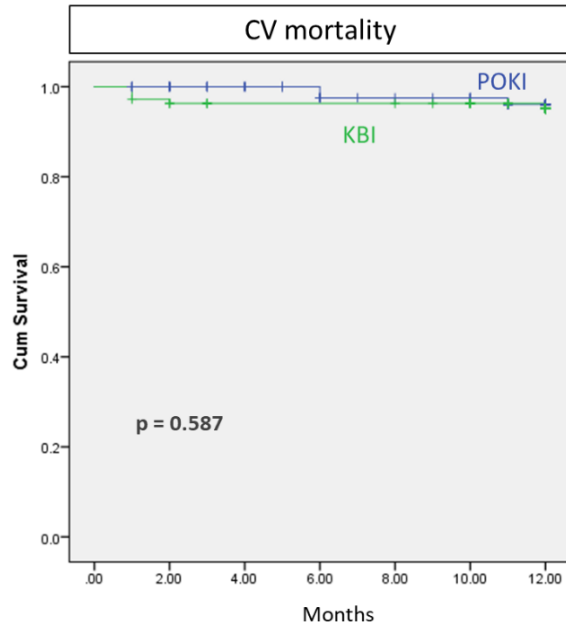


Figure 25. Kaplan-Meier curve illustrating the difference in the incidence of cardiovascular mortality between the groups treated with the POKI technique and the KBI technique. A lower rate of cardiovascular mortality was observed in the POKI group (5.6%) compared to the KBI group (9.3%), $p=0.195$.

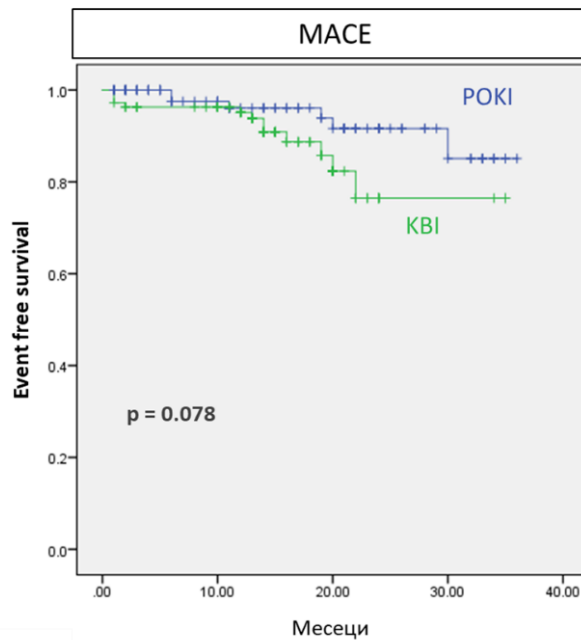


Figure 26. Kaplan-Meier curve illustrating the difference in the incidence of major adverse cardiovascular events between the groups treated with the POKI technique and the KBI technique. A lower incidence of MACE was observed in the POKI group (5.6%) compared to the KBI group (11%), $p=0.078$.

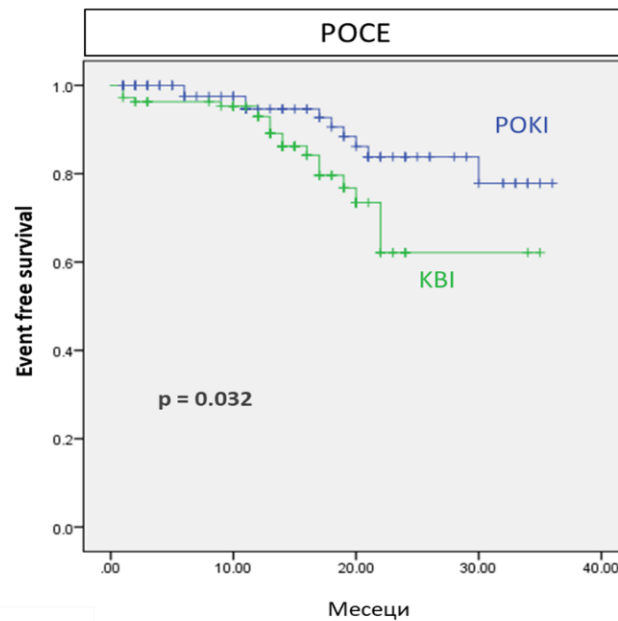


Figure 27. Kaplan-Meier curve illustrating the difference in the incidence of patient-oriented cardiovascular events between the groups treated with the POKI technique and the KBI technique. A significantly lower incidence of POCE was observed in the POKI group (9.3%) compared to the KBI group (17.6%), $p=0.032$.

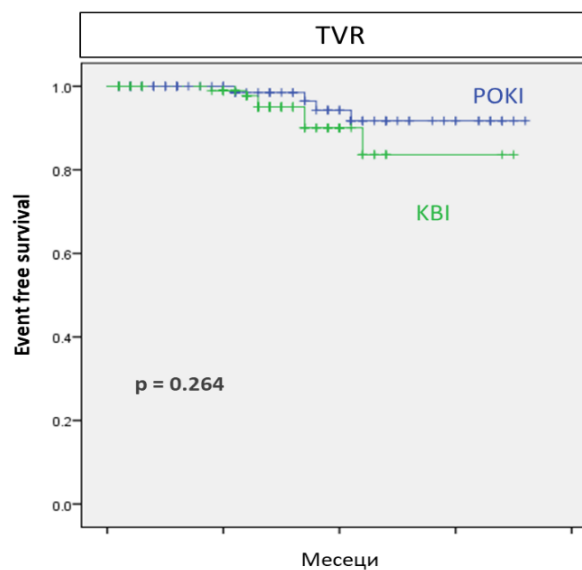


Figure 28. Kaplan-Meier curve illustrating the difference in the rate of target lesion revascularization between the groups treated with the POKI technique and the KBI technique. A lower frequency of TVR was observed in the POKI group (3.7%) compared to the KBI group (6.5%), $p=0.264$.

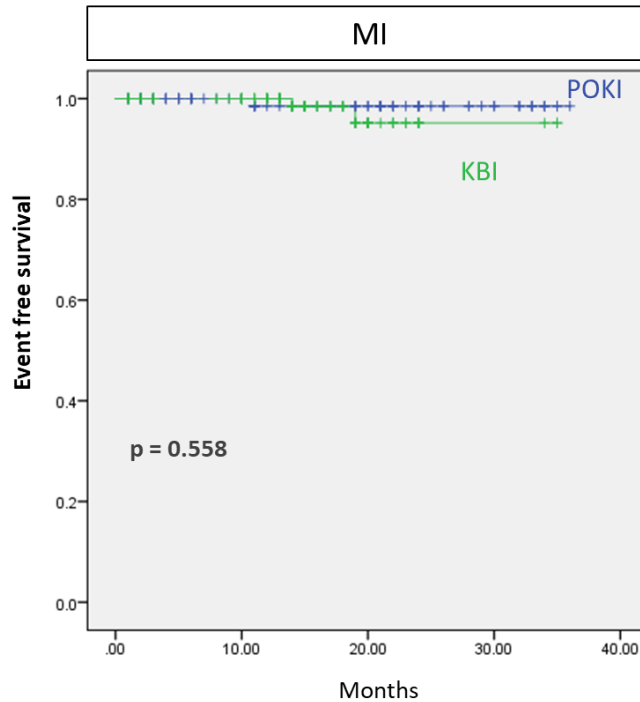


Figure 29. Kaplan-Meier curve illustrating the difference in the incidence of myocardial infarction between the groups treated with the POKI technique and the KBI technique. A lower incidence of myocardial infarction was observed in the POKI group (0.93%) compared to the KBI group (1.85%), $p=0.558$.

4.11 Predictors of mortality

A univariate regression analysis was performed, incorporating demographic, clinical, and angiographic characteristics of the patients, to identify independent predictors of mortality. The factors that showed significant predictive value were included in a multivariate Cox regression analysis (Table 20 and Figure 30).

The variables that showed significant predictive value in the univariate analysis were as follows:

- patient age – HR 1.26, 95% CI 1.11–1.47, $p=0.019$;
- smoking – HR 1.14, 95% CI 1.05–1.49, $p=0.029$
- presence of diabetes mellitus – HR 1.09, 95% CI 1.02–1.20, $p=0.019$;
- non-use of the POKI technique – HR 2.49, 95% CI 1.84–5.22, $p=0.001$;
- SYNTAX score – HR 1.42, 95% CI 1.09–1.79, $p=0.036$ (Table 21)

Multivariate Cox regression analysis revealed the use of the POKI technique as the only significant predictor of cardiovascular death—HR 2.9, 95% CI 1.06–7.90, $p=0.001$), Figure 29.

Table 20. Univariate and multivariate Cox regression analysis of predictors of cardiovascular mortality.

Промениви	Univariate analysis of mortality			Multivariate Cox regression analysis		
	HR	95% CI	p	HR	95% CI	p
Age, yeats	1.26	1.11 - 1.47	0.019	1.00	0.99 - 1.1	0.068
Gender, male	0.73	0.65 - 1.29	0.102	-	-	-
Dyslipidemia	0.92	0.61-1.38	0.695	-	-	-
Smoking	1.14	1.05 -1.49	0.029	0.95	0.78-1.33	0.102
Atrial fibrillation	0.97	0.79-1.42	0.114	-	-	-
CKD eGFR < 60 ml/min	1.43	0.84-2.19	0.293	1.5	0.61-3.6	0.810
Diabetes	1.09	1.02 - 1.20	0.019	1.3	0.52 – 1.26	0.219
Neoplasm	1.19	0.92 – 2.19	0.074	-	-	-
Ejection fraction	1.55	0.98-2-28	0.060	-	-	-
Absence of POKI	2.49	1.84-5.22	0.001	2.9	1.06-7.9	0.001
SYNTAX	1.42	1.09-1.79	0.036	1.0	0.95-1.1	0.071

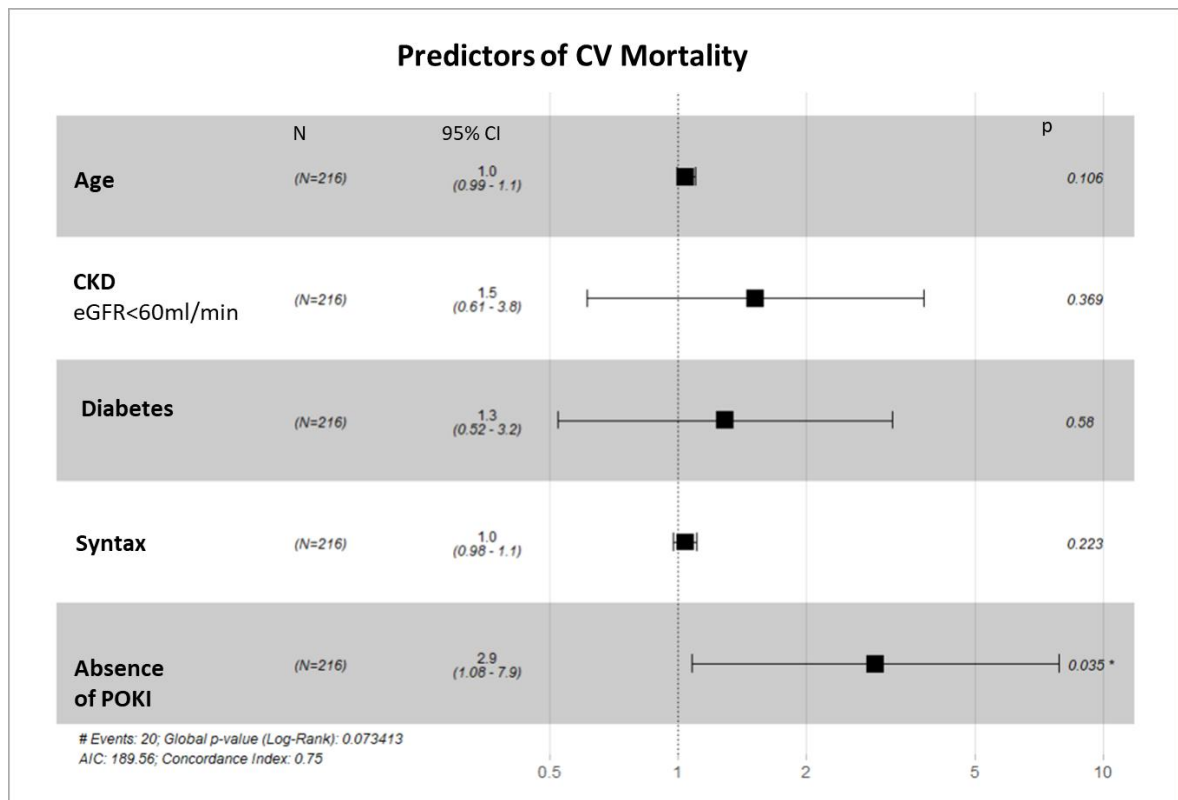


Figure 30. A Forest plot depicting a Cox regression model for predictors of cardiovascular mortality. The only significant independent predictor of cardiovascular mortality is the absence of the POKI technique (OR 2.9, 95% CI 1.08–7.9, $p = 0.035$).

4.12 Predictive value of the POKI technique for the occurrence of repeat revascularization and patient-oriented events.

A univariate regression analysis was performed, incorporating demographic, clinical, and angiographic characteristics of the patients, to identify independent predictors of patient-oriented cardiovascular events (POCE). The factors that demonstrated significant predictive value were included in a multivariate Cox regression analysis to create a predictive model. The variables that demonstrated significant predictive value in the univariate analysis were as follows: patient age – HR 1.34, 95% CI 1.19–1.59, $p=0.010$; presence of atrial fibrillation – HR 2.01, 95% CI 1.10–5.12, $p=0.03$; non-use of the POKI technique – HR 2.18, 95% CI 1.13–4.92, $p=0.001$; SYNTAX score – HR 1.66, 95% CI 1.09–2.29, $p=0.009$. Table 20 The multivariate Cox regression analysis revealed the absence of the POKI technique as the sole significant predictor of patient-oriented outcomes—HR 2.3, 95% CI 1.05–5.20, $p=0.036$), (Figure 31).

Table 21. Univariate and multivariate Cox regression analysis of predictors for the occurrence of patient-oriented adverse cardiovascular events

Променливи	Univariate regression analysis			Multivariate Cox – regression analysis		
	HR	95% CI	p	HR	95% CI	p
Age, years	1.34	1.19 - 1.59	0.010	1.00	0.97 - 1.1	0.493
Male, gender	0.73	0.65 - 1.29	0.102	-	-	-
Dyslipidemia	0.92	0.61-1.38	0.695	-	-	-
Smoking	1.14	1.05 -1.49	0.029	-	-	-
Atrial fibrillation	2.01	1.10-5.12	0.034	2.2	0.95 - 4.9	0.066
CKD eGFR < 60 ml/min	1.34	0.80-2.05	0.313	-	-	-
Diabetes	1.18	0.92 - 1.34	0.079	-	-	-
Neoplasm	1.19	0.92 – 2.19	0.074	-	-	-
Ejection fraction	1.55	0.98-2-28	0.060	-	-	-
Absence of POKI technique	2.18	1.13-4.92	0.001	2.3	1.05-5.2	0.036
SYNTAX	1.66	1.09-2.29	0.009	1.0	0.99-1.1	0.060

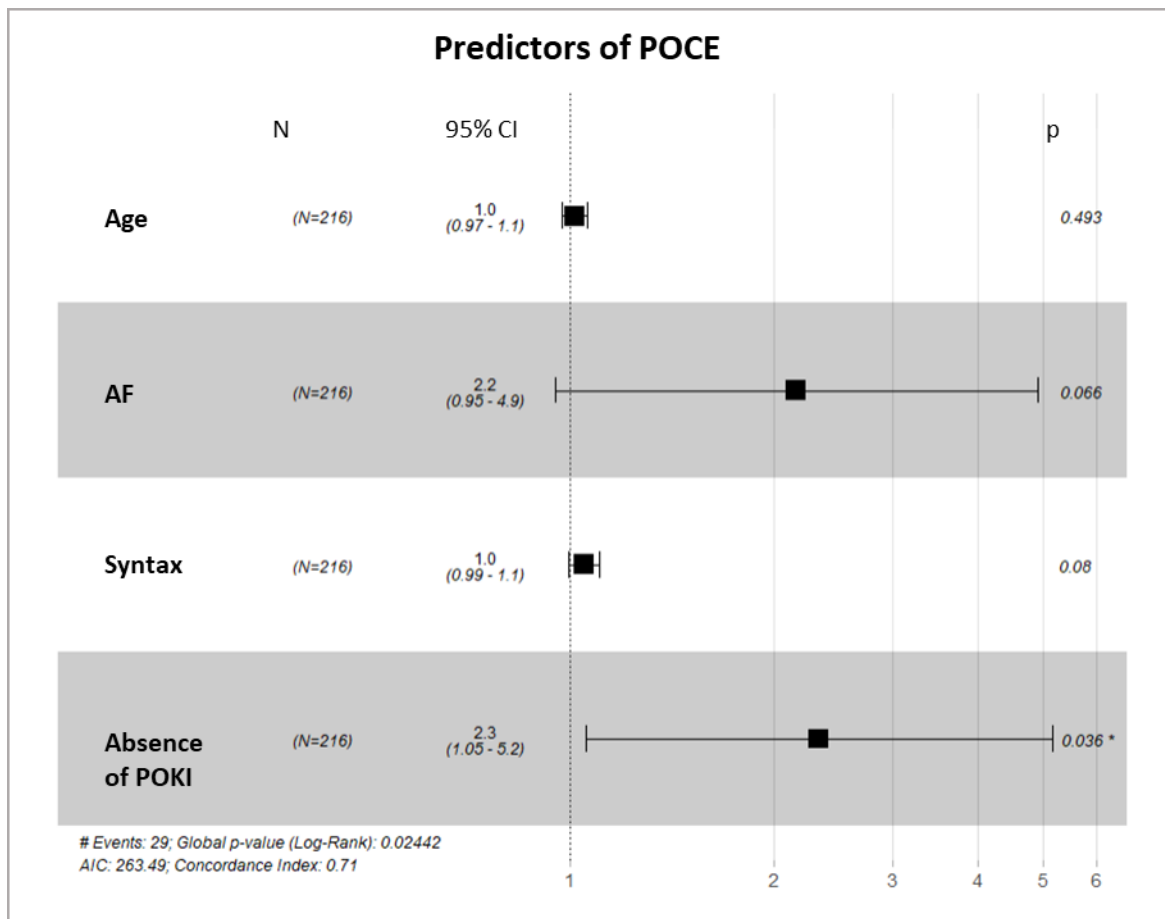


Figure 31. A Forest plot depicting a Cox regression model for predictors of patient-oriented adverse cardiovascular events. The only significant independent predictor of POCE occurrence is the absence of the POKI technique OR 2.3, 95% CI 1.05–5.2, $p = 0.033$.

POCE – patient-oriented clinical events; AF – atrial fibrillation.

4.13 A practical algorithm for selecting and applying a bifurcation optimization technique

After analyzing the data obtained from our study, we developed a simplified algorithm for selecting a specific optimization technique and applying it in the treatment of coronary bifurcation stenoses (Figure 32). The first step of the algorithm involves placing coronary guidewires in the main and side branches. After stenting the main branch, a proximal optimization technique (POT) is performed. The next step is to evaluate the side branch. If any of the following factors are present (%DS of the side branch $\geq 50\%$, TIMI flow < 3 , or significant

dissection of the side branch ostium), the coronary guidewires are crossed, followed by dilatation of the side branch and performance of POKI. If none of the described factors are present, proceed to final POT.

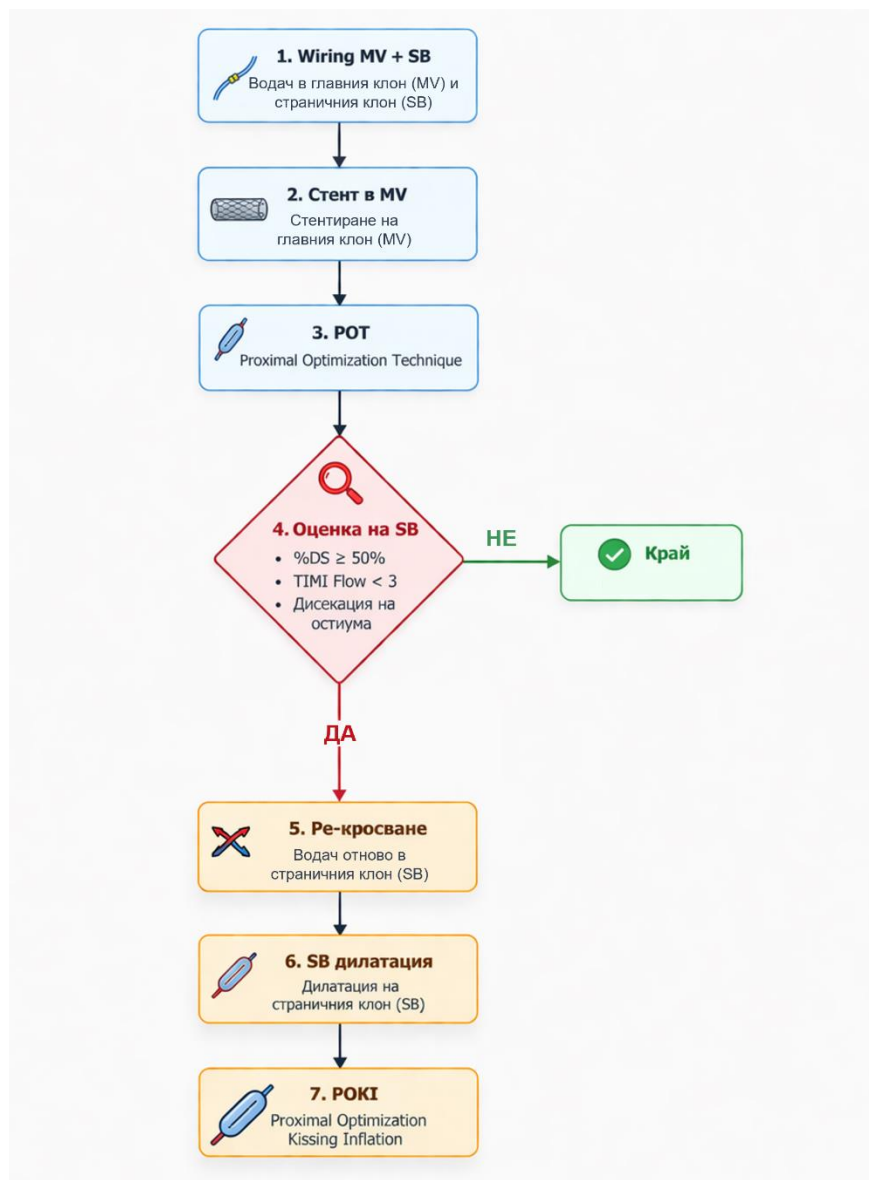


Figure 32. Practical algorithm for selecting a bifurcation optimization technique. MV – proximal main branch; SB – side branch; POT – proximal optimization technique; %DS – percentage of stenosis diameter; POKI – proximal optimization technique with kissing inflation

5. DISCUSSION

The POKI technique is an innovative bifurcation optimization technique that combines proximal balloon optimization and kissing balloon inflation. The technique was developed and first introduced by Prof. Dobrin Vasilev and colleagues. (146) The method was developed specifically for the treatment of patients with coronary bifurcation stenoses with the aim of combining the advantages of already established optimization techniques while achieving better post-procedural outcomes. The current study is the first of its kind to analyze the efficacy and safety of the innovative POKI technique, comparing it with the standard kissing balloon inflation (KBI) technique, in a large group of patients with coronary bifurcation stenoses.

Demographic and clinical characteristics of the population

An analysis of the demographic and clinical characteristics in our population reveals a notably higher-risk patient profile compared to populations in other studies examining bifurcation interventions. In our study, the mean age of patients was 66.5 ± 9.9 years, with 98% having hypertension, 95% having dyslipidemia, and as many as 40.5% having diabetes. In publications on various bifurcation techniques, the prevalence of diabetes ranges from 12% (NORDIC series of studies) to approximately 30% in registries from Japan, China, and South Korea (130, 135).

By comparison, in the general population of the PROPOT study, only 74% have hypertension, 72% have dyslipidemia, and 35% have diabetes mellitus. In our population, 29% of patients have a history of myocardial infarction, whereas in PROPOT, patients with a prior MI account for 13%. (142) Data from the Korean COBIS III registry present similar patient characteristics, with a mean patient age of 62.5 ± 10.6 (140), a mean prevalence of hypertension of 57%, dyslipidemia of 26%, and diabetes mellitus of 32%.

It is important to emphasize this difference in the baseline risk profile of our population and those from the major studies published to date, with a view to the subsequent interpretation of clinical outcomes. Given the markedly higher-risk profile of our patients, it would not be appropriate to compare the absolute rates of cardiovascular events between our patients treated with POKI and those undergoing other techniques but from a population with a lower baseline risk. To assess the actual benefit of the POKI technique, a comparison with a population having a similar risk profile is necessary, as was done in our study.

Procedure and scopic time, contrast

It is well known that interventional procedures involving the revascularization of coronary bifurcation stenoses are associated with longer procedural and imaging times. (2,4) The prolongation of the procedure is likely due, to some extent, to the time required to apply optimization techniques aimed at improving the final procedural outcome. In the PROPOT study, no significant differences in procedural and imaging time were found between the POT and KBI groups. (142) The authors report a mean procedure time of 70.0 [55.0–85.0] min in the POT group and 67.5 [55.0–85.0] min in the KBI group. On the other hand, in the NORDIC III study, which compared a bifurcation PCI technique with and without KBI in a total of 477 patients, significantly longer procedural and fluoroscopy times were observed in the group using KBI: procedural time – 61 ± 28 min vs. 47 ± 22 min, $p < 0.0001$; fluoroscopy time – 16 ± 12 min vs. 11 ± 10 min, $p < 0.0001$.

The prolonged duration of the interventional procedure in bifurcation stenoses is often associated with a greater amount of contrast medium used. The PROPOT study demonstrated lower contrast medium usage in the KBI group (174 ± 76.4 mL) compared to 201 ± 80.2 mL in the POT group. Similarly, in the NORDIC III study, the group of patients treated with KBI showed a significantly higher amount of contrast used— 235 ± 97 mL compared to 200 ± 92 mL, $p < 0.0001$. (146)

By comparison, in our study, the mean procedure time in the KBI group was 105 ± 38.8 min, and a significantly shorter procedure time was observed in the POKI group— 91.5 ± 27.3 min. At the same time, the fluoroscopy time in the PROPOT study was 28.5 [20–40] min in the POT group and 28.0 [19.0–38.8] min in the KBI group. In our study, the mean scan time was 27.4 ± 12.2 minutes for the KBI group and, again, significantly lower for the POKI group— 22.7 ± 10.2 minutes. In addition, our study found a significantly lower amount of contrast used with POKI— 285.7 ± 84 mL compared to 360.7 ± 129 mL with KBI, $p < 0.001$. The results described demonstrate a significant advantage of the POKI technique. The shorter durations and reduced contrast volume are associated with both less harm to the patient and the operator, as well as lower costs associated with patient care.

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Angiographic results

The first study introducing the POKI technique was published in 2022 and presented data from tests using silicone bifurcation models, as well as data from real-world clinical practice in patients with bifurcation stenoses. (145). A total of 41 patients (41 vessels) were evaluated in the study. The predominant type of bifurcation lesion was Medina 1-1-1 (62.6%). The mean length of the MV lesion was 38.6 ± 20.5 , and the mean length of the SB lesion was 9.18 ± 2.24 . The baseline stenosis of the proximal MV was $60.0 \pm 23.7\%$, the distal MV DS% was $58.8 \pm 28.9\%$, and the SB DS% was $53.0 \pm 32.0\%$. The measured residual stenosis after the

intervention in the proximal MV was $11.5 \pm 15.4\%$, distal MV — $6.6 \pm 9.3\%$, and SB — $22.9 \pm 28.5\%$. These first published data demonstrated encouraging results regarding the immediate angiographic outcomes following the POKI technique. Comparing residual stenosis in all three segments of the bifurcation with published data from other studies reveals that the POKI technique resulted in better immediate angiographic outcomes. In the PROPOT study, in the group of patients treated with POT, residual stenosis in the MV segment was $12.7 \pm 9.3\%$, in the MB segment $13 \pm 9.7\%$, and in the SB segment $26.2 \pm 19.8\%$. Residual stenoses in the group treated with KBI were $12.2 \pm 9.1\%$ for the MB, $13.2 \pm 7.1\%$ for the MV, and $24.2 \pm 17.4\%$ for the SB. In addition, data from the current study confirm these better immediate angiographic results following the POKI technique: final stenosis in the MV— $16.3 \pm 13.1\%$, final restenosis in the MB — $11.7 \pm 8.0\%$, and final restenosis in the SB — $8.59 \pm 7.3\%$.

To a large extent, unsatisfactory outcomes following bifurcation PCI, which are associated with target lesion failure and stent thrombosis, are due to suboptimal stent expansion and improper stent placement. (1) It is precisely for this reason that modern interventional practice employs stent optimization techniques to prevent these events. (5) Current expert guidelines consider the proximal optimization technique (POT) a mandatory step in bifurcation PCI, as it is believed to improve stent apposition in the proximal main branch and reduce stent deformation (5)

However, data indicate that inappropriate distal positioning of the POT balloon carries a risk of displacement of the stent toward the lateral branch. On the other hand, incorrect proximal positioning of the balloon may lead to stent malposition and insufficient expansion near the carina. A study involving 135 bifurcation lesions in 134 patients evaluated the effect of the POT technique using optical coherence tomography (OCT). (147) The results show a lower rate of successful re-crossing with the guidewire in the POT group (65%) compared to the non-POT group (72%, $p=0.44$). In addition, a numerically higher eccentricity index in the proximal main branch was noted in the POT group. At the same time, no significant differences were found in stent expansion and the frequency of incomplete stratum apposition between the two groups. The authors note that a possible reason for the lack of advantage of the POT technique is the incorrect positioning of the POT balloon, which leads to incomplete stent expansion in the carina region. The analysis shows that reduced expansion in the region of the proximal main branch was associated with a lower rate of successful recrossing and a higher rate of incomplete strut apposition. (147)

Another study compared three different stent-optimization strategies using artificial bifurcation models and computational modeling methods. (148) It demonstrated that standalone POT can be a source of additional ostial stenosis of the side branch due to stretching of the ostium and causing elliptical deformation. (14, 148)

These published data emphasize the importance of precise positioning of the POT balloon to achieve optimal results. The POT balloon should be positioned so that the distal arm lies exactly in the plane of the carina. (149) It should be noted that, in addition to good practical training, this also requires excellent knowledge of the balloon's specific characteristics. The problem is further complicated by parallax when precisely locating the balloon marker and the tip of the carina. Another important aspect is that balloons from different manufacturers have different locations for the so-called balloon shoulder—the point where the balloon's diameter begins to decrease. Even when the marker is located at the same point on balloons from different manufacturers, the location of this transition can vary significantly, and in the case of the carina, even 1 mm is of great importance. The POKI technique facilitates balloon positioning by performing precise dilation and achieving optimal results. When positioning the balloons for POKI, the distal marker of the balloon in the main branch touches the tip of the carina, and the balloon in the side branch is positioned with the proximal marker exactly at the edge of the stent. Thus, the proximal markers of the SB balloon and the MV balloon are positioned in a parallel plane for optimal technique execution. The operator need not worry about subsequent displacement of the carina, as the SB ostium is dilated simultaneously. Furthermore, visualization of the SB balloon's proximal marker at the stent margin provides a reliable marker for the carina's position and facilitates balloon positioning in the main vessel.

Regarding carotid displacement, a study by Derimay et al., examining bifurcation models using optical coherence tomography (OCT), demonstrated the superiority of the KBI technique over POT followed by balloon dilation of the side branch. (149) Theoretically, the KBI technique provides access to the side branch and optimizes stent architecture. (115) Balloon dilation of the side branches or the KBI technique may lead to adverse outcomes in the main branch. A study using intravascular ultrasound in a total of 23 patients with bifurcation lesions, treated with the single-stent technique, demonstrated a significantly reduced stent cross-sectional area in the main branch immediately after side-branch separation (from $5.9 \pm 1.2 \text{ mm}^2$ baseline to $5.2 \pm 1.2 \text{ mm}^2$ after dilation, $p < 0.05$). This area does not return to its initial value even after KBI application— $5.6 \pm 1.2 \text{ mm}^2$. (150)

In addition, balloon dilatation of the side branch, as well as KBI, may affect local hemodynamic conditions. Analysis using computational fluid dynamics shows that intervention on the side branches does not improve fluid dynamics and demonstrates that overdilation of the proximal segment of the main branch associated with KBI would lead to additional blood flow disturbances. (151) Using computer simulation, a study by Mortier et al. demonstrated that the classic KBI technique carries a risk of elliptical deformation of the stent in the proximal portion of the main vessel. (148) In turn, this elliptical deformation of the stent showed a significant association with thrombosis formation in a study using optical computed tomography in 53 bifurcation lesions. (152)

Clinical outcomes following optimised bifurcation techniques

In addition, randomized clinical trials comparing outcomes of percutaneous coronary interventions with or without KBI have not reported any advantage of KBI in terms of clinical outcomes. (146, 153) The NORDIC III study included a total of 477 patients with bifurcation lesions who underwent interventional treatment. (146) Of these, 238 patients underwent KBI following stenting of the main branch, while 239 patients did not undergo KBI following stenting. Clinical outcomes at 6-month follow-up showed 2.1% MACE (cardiovascular death, non-procedural myocardial infarction, revascularization of the target lesion, stent thrombosis) in the KBI group and 2.5% MACE in the non-KBI group. In addition, the rate of restenosis in the entire bifurcation region at 8 months post-procedure was 11.0% in the KBI group versus 17.3% in the non-KBI group ($p=0.11$).

Another randomized study (CORPAL Kiss Trial) (153) compared 1-year clinical outcomes in patients following bifurcation PCI, with 124 patients randomized to KBI after stenting and 120 patients randomized to the non-KBI group. Similar to the data from NORDIC III, the incidence of major cardiovascular events (death, revascularization of the target lesion, and acute myocardial infarction) did not differ significantly between the two groups—9% in the KBI group versus 6% in the non-KBI group at 1-year follow-up.

Last but not least, when comparing clinical outcomes between KBI and POT techniques with subsequent SB dilatation in the PROPOT study, no significant advantage of either technique over the other could be identified. (142) Over a median follow-up period of one year, neither group experienced any deaths or stent thrombosis. In the KBI group, one patient

experienced a non-fatal myocardial infarction, and revascularization of the target lesion occurred in one patient from each group (1/51, 2% in POT and 1/52, 1.9% in KBI, $p>0.05$).

In the multicenter e-Ultimaster registry, an analysis was performed on a group of 35,839 patients undergoing PCI, stratified according to the complexity of the procedure and further according to the number and type of complex characteristics. (143) Patients with complex PCI ($n=9,793$, 27.3%) were associated with an increased hazard ratio for the composite endpoint at one year (target lesion failure [TLF]: 1.41 [1.25; 1.59]), due to an increased risk of cardiovascular death (1.28 [1.05; 1.55]), myocardial infarction (1.48 [1.18; 1.86]), and clinically indicated revascularization of the target lesion. In addition, the registry shows higher intervention rates for lesions with stent restenosis (7.5% vs. 4.5%), as well as for bifurcation lesions (20.3% vs. 8.6%) and ACC/AHA B2/C lesions (47.2% vs. 39.3%) in the complex PCI group. Complex lesions required longer stents, both per patient (48.3 ± 26.7 mm vs. 24.5 ± 10.3 mm) and per lesion (30.0 ± 18.3 mm vs. 23.3 ± 9.6 mm).

It is important to note that in our study, we observed a significantly higher overall incidence of adverse cardiovascular events. The most logical explanation for this observation is the higher-risk profile of our population, as discussed earlier.

Over a mean follow-up period of 14 [10–21] months, a total of 20 patients (9.3%) died in our study. Of these, 7.4% ($n = 16$) died of cardiovascular death, and three (1.4%) patients experienced a non-fatal MI. A total of 18 patients (8.3%) experienced a major adverse cardiovascular event (MACE), with 11 patients (5.1%) undergoing subsequent revascularization of the target vessel. Comparing the incidence of cardiovascular events in the two study groups, a significantly lower overall mortality rate of 5.6% versus 13% ($p = 0.036$) was observed in the POKI group compared to the KBI group. At the same time, the incidence of cardiovascular mortality, non-fatal MI, revascularization of the target vessel, and MACE, although not statistically significant, was numerically lower in the POKI group. It is important to note that when analyzing the composite endpoint of patient-oriented events, a significantly lower incidence of POCE was observed in the POKI group compared to the KBI group, specifically 9.3% versus 17.6%, $p=0.032$. Given the extremely high-risk profile of the overall population, the POKI technique results in a significantly lower incidence of adverse cardiovascular events.

Limitations

This study has several limitations. First, our study is a prospective registry. Despite the lack of randomization in one of the two groups, we performed multivariable propensity score matching, which balanced demographic and clinical differences between the two groups.

Another limitation of this study is the lack of intravascular imaging. The use of intravascular imaging would have allowed for confirmation of the findings regarding better angiographic outcomes after POKI compared to conventional optimization techniques.

Finally, it is important to note the relatively short period of clinical follow-up of patients in our study. A follow-up analysis with longer-term follow-up will be able to demonstrate the long-term outcome of the procedure.

Conclusion

The results of this study have important clinical implications. The innovative POKI optimization technique combines the benefits of the previously known POT and KBI methods. On the one hand, the technique reduces procedure time and the amount of contrast agent used by combining the techniques within a single-step approach. In addition, the study demonstrates that the technique can provide better immediate angiographic outcomes and a better clinical prognosis in patients following percutaneous intervention for bifurcation lesions. A subsequent randomized study with a longer follow-up period could confirm the findings regarding the advantage of the POKI technique.

6. CONCLUSIONS

- 6.1 The patient population with coronary bifurcation stenoses represents a group with a very high baseline risk profile.
- 6.2 The bifurcation optimization technique combining proximal balloon optimization and kissing balloon inflation (POKI) is applicable for the treatment of patients with coronary bifurcation stenoses.
- 6.3 The POKI technique is associated with shorter procedural and fluoroscopic times compared to the kissing balloon inflation (KBI) technique.
- 6.4 The POKI technique is associated with a lower amount of intra-procedural contrast used compared to KBI.
- 6.5 Patients in the group treated with the POKI technique had significantly fewer complications at the puncture site.
- 6.6 The POKI technique leads to better immediate angiographic results compared to KBI.
- 6.7 The POKI technique leads to better procedural success compared to KBI.
- 6.8 The POKI technique is associated with significantly lower mortality and a lower incidence of patient-oriented adverse cardiovascular events compared to KBI.
- 6.9 The absence of treatment with the POKI technique emerged as the sole significant predictor of cardiovascular death and the occurrence of patient-oriented cardiovascular events.

7. CONTRIBUTIONS

Of a scientific and theoretical nature

- 7.1 Patients with coronary bifurcation stenoses are at high risk.
- 7.2 Failure to apply the POKI technique is the only significant predictor of cardiovascular death and patient-oriented cardiovascular events.

With an applied nature

- 7.3 With a median follow-up period of over one year, the POKI technique is associated with better clinical outcomes in patients with coronary bifurcation stenoses compared to the standard optimization technique—KBI.
- 7.4 The POKI technique is associated with a lower incidence of complications at the puncture site.

Of a confirmatory nature

- 7.5 We confirmed the initial findings of excellent immediate angiographic results following the POKI technique.
- 7.6 We confirmed that the POKI technique is associated with shorter procedure and fluoroscopy times, as well as a lower volume of contrast medium used.

Original contributions

- 7.7 The current study is the first of its kind to analyze the efficacy and safety of the innovative POKI technique, comparing it to the standard KBI technique in a large patient population.
- 7.8 Based on the results obtained, a practical algorithm was developed for the selection and application of a specific bifurcation optimization technique.

8. PUBLICATIONS AND PRESENTATIONS AT CONFERENCES RELATED TO THE DISSERTATION

8.1 Publications:

1. **Panayotov P**, Mileva N, Vassilev D. Current Challenges in Coronary Bifurcation Interventions. *Medicina (Kaunas)*. 2024 Sep 3;60(9):1439. doi: 10.3390/medicina60091439. PMID: 39336480; PMCID: PMC11434469.
2. Vassilev D, Mileva N, **Panayotov P**, Rigatelli G, Gil RJ. Management of side branch stenosis with pre-dilatation in coronary bifurcation disease. Author's reply. *Kardiol Pol*. 2024;82(6):681-682. doi: 10.33963/v.phj.101169. Epub 2024 Jun 18. PMID: 38887785.
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8.2 Participation in scientific conferences:

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2. Mileva N.¹, Velikov T.¹, **Panayotov P.**¹, Vassilev D.¹, SHATC Medica Cor, Ruse, Bulgaria. Combined obstruction of mitral valve. World Congress of Echocardiography 2023, Sofia.
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