

Immediate versus Staged Complete Revascularization in Multi-Vessel Coronary Artery Disease Patients with ST-Elevation Myocardial Infarction Uncomplicated by Cardiogenic Shock

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ABSTRACT

Background: Although Primary Percutaneous Coronary Intervention (PPCI) has been established as the best treatment for ST-Elevation Myocardial Infarction (STEMI), there is a gap in the evidence about the optimal time when non-Infarct Related Artery (IRA) lesions should be revascularized.

Objectives: The first primary outcome was defined as death within a timeframe of one year from the complete revascularization. The second primary outcome was a composite of Major Adverse Cardiac and Cerebrovascular events (MACCE) within a year following complete revascularization. Overall, the study aimed to compare the two study groups (patients with multi-vessel coronary artery disease (MVD) presenting with STEMI uncomplicated by cardiogenic shock, in which complete revascularization was attained using either complete revascularization during the PPCI (group A) or during the same hospital admission (group B)) regarding the occurrence of the above-mentioned outcomes. **Methods:** This single-center, retrospective study aimed to review the outcomes in two groups, each consisting of 50 consecutive MVD patients with STEMI uncomplicated by cardiogenic shock. The patients included in the trial underwent successful culprit-lesion Percutaneous Coronary Intervention (PCI) between 1 January 2017 and 1 June 2019. Then, they underwent complete revascularization with either PCI of all angiographically significant non-culprit lesions in the index PPCI procedure (group A) or during a second procedure that took place during the same hospital admission (group B).

Results: The first primary outcome was observed in 4% of the whole study population (n = b2, P = 0.98), while the second primary outcome was detected in 6% of the patients (n = 3, P = 0.97). The results revealed no significant difference between the two groups concerning the outcomes.

Conclusions: Among the MVD patients with STEMI uncomplicated by cardiogenic shock, there was no significant difference regarding the outcomes when using the complete revascularization of non-culprit lesions during PPCI and in a second PCI session at the same hospital admission.

1. Background

Patients presenting with ST-Elevation Myocardial Infarction (STEMI) can be effectively treated by Primary Percutaneous Coronary Intervention (PPCI), which restores blood flow to the Infarct-Related Artery (IRA)

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(1). Among patients presenting with acute STEMI, 20-50% have multivessel coronary artery disease (MVD) (2, 3). Several studies; i.e., "Preventive Angioplasty in Acute Myocardial Infarction" (PRAMI) (4), "Complete Revascularisation versus Treatment of the Culprit Lesion only in Patients with ST-Segment Elevation Myocardial Infarction and Multivessel Disease" (DANAMI-3-PRIMULTI) (5), "Complete Versus Lesion-Only Primary PCI Trial" (CvLPRIT) (6), "Comparison Between

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Fractional Flow Reserve (FFR)-Guided Revascularization Versus Conventional Strategy in Acute STEMI Patients With Multivessel disease" (COMPARE-ACUTE) (7), and "Complete Versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease After Early PCI for STEMI" (COMPLETE) (8), have shown benefits in terms of a lower rate of Major Adverse Cardiac and Cerebrovascular Events (MACCE) in patients undergoing the complete revascularization strategy compared to those undergoing an IRA-only PCI strategy, thus causing a shift in guidelines towards the complete revascularization strategy in patients with MVD.

2. Objectives

To the best of our knowledge, no study has been conducted on the head-to-head comparison of outcomes in different strategies for attaining complete revascularization in these patients. Some studies completed the revascularization during the PPCI (PRAMI and COMPARE-ACUTE) and some others in subsequent sessions (DANAMI-3-PRIMULTI and CvLPRIT). There is also a gap in the evidence body regarding the optimal time when non-IRA lesions should be revascularized. Hence, in case a staged procedure strategy is applied, the interval between the PPCI and completion of the revascularisation process is not known.

3. Patients and Methods

This single-center, retrospective trial aimed to compare the complete revascularization strategy (consisting of PCI of all suitable non-culprit lesions) during the index PPCI to that in a second PCI session during the same hospital admission as the PPCI among MVD patients with STEMI uncomplicated by cardiogenic shock who had undergone successful culprit-lesion PPCI. The researchers reviewed the charts and procedures of the patients who presented between 1 January 2017 and 1 June 2019 to the hospital with the diagnosis of STEMI uncomplicated by cardiogenic shock (n = 427) and underwent successful culprit-lesion PCI followed by complete revascularisation of all nonculprit lesions either in the index PPCI or staged in a second procedure done before discharge (n = 105). The patients were assigned to either group A (n = 50) and received complete revascularization during the PPCI or group B (n = 50) and underwent complete revascularization in a staged procedure (Figure 1).

The eligible patients had MVD, which implied that a minimum of an angiographically significant non-culprit stenosis in a vessel larger than 2 mm in diameter, different from the IRA, was present and could be treated employing PCI. The non-culprit lesions that caused more than 75% stenosis by visual estimation on angiography (or 50% in the left main coronary artery) and those ranging from 50% to 74% associated with an FFR below 0.8 were considered to be significant. The inclusion and exclusion criteria have been listed in Table 1.

The patients in both groups benefited from guideline-based medical therapy. Drug Eluting Stent (DES) was preferred for all PCI procedures, while Bare Metal Stent (BMS) was only used in case of the unavailability of the DES dimension. The techniques used for bifurcation stenosis treatment

Figure 1. The Study Flow-Chart



IRA, infarct related artery; MVD, multivessel coronary disease; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; STEMI, ST elevation myocardial infarction.

Table 1. The Inclusion and Exclusion Criteria				
Inclusion Criteria	1. Men and women with successful PCI (preferably using a drug eluting stent) for culprit lesions for STEMI (PCI for STEMI should be primary PCI in the first 12 hours after the onset of symptoms) and complete revascularization of non-culprit lesions during the index PPCI procedure or during a different procedure performed before index hospital discharge.			
	2. Multi-vessel disease defined as at least one additional non-infarct-related coronary artery lesion measuring at least 2.5 mm in diameter that has not been stented as a part of the primary PCI, is amenable to successful treatment with PCI, and has at least 75% diameter stenosis (visual estimation) or at least 50% diameter stenosis (visual estimation) with FFR \leq 0.80.			
	3. Age between 18 and 90 years			
	4. Signing the written informed consent form			
Exclusion criteria	1. Rescue PCI for failed fibrinolysis or a combination strategy where PCI is performed routinely 3-12 hours after fibrinolysis			
	2. Cardiogenic shock			
	3. Non-cardiovascular known comorbidity reducing life expectancy to < 2 years			
	4. Any factor precluding the one-year follow-up			
	5. Prior CABG surgery			
	6. A different operator from the previously designated one			
	7. Inability to provide consent for any reason			

Abbreviations: FFR, fractional flow reserve; IRA, infarct-related artery; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

included provisional stenting, TAP, Culotte, and DK-Crush. Provisional stenting was the preferred technique whenever possible. All the procedures included simultaneous kissing balloon and the final proximal optimization technique according to the catheterization laboratory protocols. All procedures were done by a single operator, thus eliminating the operator bias.

The data on the patients' clinical characteristics, medications, angiography, FFR, and PCI were manually extracted after reviewing all the available records. Clinical outcomes were investigated either through telephone interview with the patients and/or medical records review.

The study protocol was approved by the Ethics Committee of the hospital where the patients had been admitted. The protocol was also registered in an international clinical trial database (NCT04582175). All the study procedures were conducted according to the good clinical practice guidelines and in line with the principles stipulated in the Declaration of Helsinki. Furthermore, written informed consent was attained from each study participant.

3.1. Null Hypothesis and Outcomes

The authors hypothesized that there would be no difference in the one-year outcomes in the two groups. The first primary outcome was all-cause mortality, while the second primary outcome was a composite of all-cause mortality, new myocardial infarction, stroke, and symptomdriven revascularization at one year. Myocardial infarction was defined using the criteria from the fourth universal definition of myocardial infarction and was further subdivided according to the territory involved as it appeared on the ECG. The patients' medical records were rigorously reviewed to evaluate the outcomes one month and one year after the completion of the revascularisation process.

Considering the power of 80% and using the IBM SPSS

Statistics, version 1.0.0.1447, 64 patients were found to be required in each study group. However, due to a lower-than-expected number of cases enrolled, two equal groups of 50 patients were settled for a calculated power of 70%.

3.2. Statistical Analysis

Categorical data have been reported as number (percentage), and Pearson chi-squared test was used for group comparisons. On the other hand, continuous variables have been presented as mean \pm Standard Deviation (SD). The central tendency of the baseline characteristics and end points of the two groups were compared using t-test for normally distributed continuous variables and Mann-Whitney rank sum test for non-normally distributed ones. Moreover, the Kaplan-Meier method was employed to assess the time to the primary endpoints and to determine the survival estimate. Chi-square test was also used to compare the outcomes in the two groups. A p-value < 0.05 was considered statistically significant. All statistical analyses were done using Medcalc Software, version 19.8 (MedCalc Software Ltd, Ostend, Belgium; https://www. medcalc.org; 2021).

4. Results

The results revealed no significant difference between the two groups regarding the baseline characteristics, except for a greater number of DESs used in group B (4.14 ± 1.8) than in group A (3.3 ± 1.5) (P = 0.01) and Left Ventricular Ejection Fraction (LVEF) (P = 0.03). Detailed baseline characteristics have been presented in Table 2. Accordingly, 12% of the patients had one or more BMSs implanted. Additionally, one patient in group B had only BMSs but no DESs implanted. There was no significant difference between the two groups regarding the mean number of BMSs implanted (0.38 vs. 0.16, P = 0.191).

Table 2. Baseline Characteristics					
Characteristics	Group A	Group B	P-value		
Number of cases (%)	50 (50%)	50 (50%)	1		
Type of STEMI (%)					
Anterior	22 (44%)	18 (36%)	0.416		
Inferior	22 (44%)	30 (60%)	0.111		
Lateral	4 (8%)	2 (4%)	0.402		
Posterior	2 (4%)	0 (0%)	0.155		
Number of diseased vessels including IRA (%)					
2	31 (62%)	27 (54%)	0.420		
3	13 (26%)	10 (20%)	0.478		
4	5 (10%)	11 (22%)	0.103		
5	1 (2%)	2 (4%)	0.559		
Bifurcation lesion (%)	10 (20%)	16 (32%)	0.173		
Number of DESs used (mean ± SD)	3.3±1.5	$4.14{\pm}1.8$	0.014		
Number of BMSs used (mean)	0.38	0.16	0.191		
Syntax (mean ± SD)	21.76±9.32	21.53±7.06	0.688		
Left ventricular ejection fraction on admission (%)	42.04 (39.77 to 44.30)	45.12 (43.43 to 46.81)	0.031		
Presence of CTOs (%)	5 (10%)	3 (6%)	0.463		
Left main PCI (%)	8 (16%)	10 (20%)	0.604		
Successful CTO PCI procedures (%)	80%	67%	0.700		
FFR-guided PCI	5 (10%)	6 (12%)	0.750		

Abbreviations: BMS, bare metal stent; CTO, chronic total occlusion; DES, drug eluting stent; FFR, fractional flow reserve; IRA, Infarct related artery; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction.

The results indicated no statistically significant difference between the two groups concerning the type (territory) of infarction, presence of Chronic Total Occlusion (CTO) lesions, number of vessels involved (reflecting the sum of the vessels including the IRA), bifurcation lesions, and involvement of the left main coronary artery (Figures 2, 3, and 4; Table 2).

The mean baseline LVEF (%) was significantly higher in the patients in group B compared to those in group A (42%; 95% CI: 39.77 to 44.30 vs. 45%; 95% CI: 43.43 to 46.81) (Figure 5).

In this study, the mean Syntax score was not significantly higher in group A compared to group B (21.76 vs. 21.53; P =0.688). The patients were included in the trial regardless of a high Syntax score if they opted for interventional complete revascularisation after the PPCI done according to one of the two arms of the trial. Yet, Coronary Artery Bypass Graft (CABG) surgery is the gold standard in this case (9).

Based on the results, there were eight CTOs in eight patients (none of the patients presented two or more CTOs). Four CTOs were in the Left Anterior Descending (LAD) artery and four in the Right Coronary Artery (RCA). Out of these patients, five were in group A (two LAD CTOs and three RCA CTOs) and three were in group B (two



Figure 2. The Relative Frequency of the Vessels with Significant Angiographic Stenosis in Group



Figure 4. Comparison of the Two Groups regarding the Prevalence of Different Infarction Types

LAD CTOs and one RCA CTO). In both groups, the PCI of the RCA CTO was not successful and was finished with subintimal plaque modification technique as an investment procedure. Moreover, PCI of chronic total occlusions was attempted in all the patients. Successful CTO PCI was achieved in 80% of the cases in group A and 67% of those in group B (95% CI: -37.28% to 61.87%, P = 0.700).

The results revealed the first primary outcome in two cases in the whole study population (n = 50), representing 4% of the patients in group A and 4% of those in group B (Hazard Ratio (HR): 0.97; 95% CI: 0.13 to 6.95; P = 0.983) (Figure 6). Additionally, the second primary outcome was detected in three cases (accounting for 6% of the patients in each group) (HR: 0.96; 95% CI: 0.19 to 4.80; P = 0.969) (Figure 7). Overall, there was no significant difference between the two groups regarding the outcomes.

The two groups were homogeneous with respect to the survival at one year and the MACCE. However, the rate of stroke was higher in group A than in group B although the difference was not statistically significant (P = 0.332). On the other hand, the incidence of symptom-driven revascularization was higher in group B compared to group A, but the difference was not statistically significant (P = 0.307) (Table 3). There were no incidents of stent thrombosis,



Figure 3. The Relative Frequency of the Vessels with Significant Angiographic Stenosis in Group



Figure 5. Comparison of the Two Groups regarding the Mean Left Ventricular Ejection Fraction

Table 3. Major Adverse Cardiac and Cerebrovascular Outcomes One Year after Primary Percutaneous Coronary Intervention (PPCI)						
Event Name	Group A	Group B	P-value *			
All-cause mortality at one year (%)	2 (4%)	2 (4%)	1			
MI (%)	0 (0%)	0 (0%)	1			
Symptom-driven PCI (%)	0 (0%)	1 (2%)	0.307			
Stroke (%)	1 (2%)	0 (0%)	0.332			

*MedCalc uses the 'N-1' chi-square test, as recommended by Campbell (2007) and Richardson (2011).



Figure 6. Kaplan-Meier Curves Comparing the Two Groups regarding the First Primary Outcome; i.e., Survival at One Year



Figure 7. Kaplan-Meier Curves Comparing the Two Groups regarding the Second Primary Outcome; i.e., Incidence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) at One Year

major bleeding, or Contrast Induced Nephropathy (CIN) at the one-year follow-up. CIN was defined as a 25% rise in the serum concentration of creatinine from the baseline value within 72 hours of the PCI.

5. Discussion

The study findings showed no significant difference between the two groups regarding all-cause mortality and a composite of all-cause mortality, stroke, myocardial infarction, and symptom-driven revascularization at one year. However, there was a non-significantly better survival with complete revascularization during the PPCI strategy at one month (P = 0.155). In contrast, Tarantini G et al. disclosed that the best results, both early and late, were achieved through staged MV-PCI. The difference might result from the difference in the inclusion/exclusion criteria or the study design (both prospective and retrospective trials were included in the meta-analysis). Upon analyzing the studies included in the aforementioned meta-analysis, the results of one trial was similar to those of the current research. Ochala A. et al. (10) reported no significant difference between the two types of complete revascularization under investigation. Unfortunately, that trial was also underpowered, reflecting the difficulty of including a large number of patients in an interventional trial with a design entailing a single operator. All the other trials included in that meta-analysis had more than one

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operator performing the PCIs.

The present study findings revealed a non-significantly higher incidence of stroke in complete revascularization during PPCI, while the staged PCI group presented a higher, albeit not significant statistically, risk of symptom-driven revascularization. The higher incidence of stroke could possibly be linked to a higher incidence of anterior wall infarction in group A. Due to the fact that the trial was underpowered, such an assumption could not be made. Nevertheless, the association between anterior wall infarction and post-STEMI stroke was reported by Hachet O. et al., as well (11).

Although the present trial was under-powered, the results indicated no significant difference between the complete revascularization at the time of PPCI and the staged procedure during the same hospital admission among the MVD patients presenting with STEMI uncomplicated by cardiogenic shock undergoing successful IRA PPCI defined as Thrombolysis in Myocardial Infarction (TIMI) 3 flow and Myocardial Blush Grades (MBG) 2 or 3 (12).

The results of the current study were in agreement with those of the PRAMI and CvLPRIT trials in terms of the incidence of all-cause mortality at one year (4% vs. 5.1% vs. 1.3%; P = 0.666 and P = 0.090), MI (1% vs. 1.3% vs. 2.99%; P = 0.813 and P = 0.276), and symptom-driven revascularization (1% vs. 5.12% vs. 4.7%; P = 0.076 and P = 0.093). "Ad-hoc" CTO PCI was not indicated (there was a 48-72 h timeframe for procedural set-up in group B), especially in the setting of STEMI. However, this study aimed to compare the two strategies for attaining complete revascularization the MVD patients presenting with STEMI uncomplicated by cardiogenic shock. Thus, the presence of CTOs was not considered an exclusion criterion. This subset of lesions is frequently present in patients with MVD and STEMI. Therefore, not including this particular high-risk category in the trial could have caused an important selection bias. Other trials such as COMPLETE that dealt with complete revascularization in the setting of STEMI also included patients with CTOs. Additionally, the procedural time and the contrast media use were not assessed in this study. Nonetheless, in order to limit the possible harmful effects, radiation dose was kept under 7 Gy for the whole procedure (CTO plus non-CTO lesions) and the contrast media use was maintained under 5X body weight (kg)/serum creatinine (mg/dL) according to cathlab's protocols. Moreover, prevention methods including good hydration, statin, and Acetylcysteine (ACC) use were routinely employed for reducing CIN. There were no reports in the reviewed files regarding CIN requiring renal replacement therapy, radiation-induced skin lesions, or bleeding complications in any of the patients (presenting or not with a CTO). An interesting finding was that group A (complete revascularization of all non-IRA significant stenoses during PPCI), in which "ad-hoc" CTO-PCI was performed had a higher success rate (80%) compared to group B (67%) (complete revascularization of non-IRA significant stenoses during a staged PCI procedure that took place during the index hospitalization). However, these findings have no statistical bearing and result from the small number of patients with this type of lesion analyzed in the study. Thus, treating CTOs in the context of STEMI needs further investigations and is not advisable at this moment.

FFR measurement was employed in 11% of the cases in the current trial. Functional assessment was employed whenever a stenosis was considered intermediate on Quantitative Coronary Angiography (QCA), thus reducing overstenting or understenting. Therefore, unnecessary non-culprit lesion PCIs can be reduced by an FFR-guided strategy. However, it is safe to say that the influence of FFR-based treatment decisions are minimal in this specific case. Several studies have also raised the question whether FFR in the setting of STEMI produces reliable results. To the best of our knowledge, most of them have favored an FFR-driven revascularization in this subset of patients (13-15). DANAMI 3, PRIMULTI, and COMPARE ACUTE trials also employed an FFR-guided revascularization in the setting of STEMI.

5.1. Limitations

The main limitation of this trial was the small number of patients (n = 100), which is related to the fact that averagely 450 STEMIs are annually treated in the study center and the workload is shared among three independent operators. Since only 20 - 50% of patients had CMV and the patients with cardiogenic shock as well as those suited for CABG (9) were not eligible for the trial, approximately 50 cases were treated annually by each operator. In view of the fact that different operators have different skillsets and experiences, all procedures were done by a single operator to eliminate the operator bias. However, this approach entailed several limitations regarding the external validity of this singlecenter study. Yet, the operator who performed the procedures included in this trial as well as the center in which the study took place fall in the category of high-volume operators/ centers (>100 PCI/year/operator and > 200 PCI/ year/center) according to the National Cardiovascular Data Registry. Hence, similar results can be expected in further studies by other operators in other centers falling in the same work volume category. Furthermore, an FFR-guided nonculprit PCI strategy was employed in a relatively small number of cases in this trial (11%). It is up for discussion if the physiological evaluation of non-culprit stenosis on a wider scale impacts the trial results. Finally, this study was a retrospective one in nature, thus presenting some disadvantages over a prospective trial regarding the need for very large sample sizes for rare outcomes, which could not be attained due to being single-center and including a single operator. Yet, attempts were made to eliminate the selection bias by enrolling consecutive cases.

5.2. Conclusion

The study findings revealed no significant difference between the two groups in terms of MACCE and mortality at one year. The researchers are encouraged to review a larger number of patients and possibly include other operators in order to achieve adequate power for the trial. Although small, this trial could contribute to the idea that immediate complete revascularization was not inferior to staged complete revascularization in MVD patients presenting with STEMI uncomplicated by cardiogenic shock. The abovementioned hypothesis has been investigated in two ongoing trials; i.e., "Direct Complete Versus Staged Complete Revascularization in Patients Presenting With Acute Coronary Syndromes and Multivessel Disease Trial (BioVasc)" and "MULTivessel Immediate Versus STAged RevaScularization in Acute Myocardial Infarction-The MULTISTARS AMI Trial (MULTISTARS AMI)", which bear similarities to the present study.

Overall, the current study results suggest that operators can safely choose the strategy for achieving complete revascularization by considering different factors favoring the deferral of non-culprit lesions for a second procedure or the treatment of all lesions during the index procedure. However, further trials with adequate statistical power are warranted.

5.3. Clinical Trial Registration Code ClinicalTrials.gov Identifier: NCT04582175.

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5.4. Ethical Approval

This study was approved by the Ethics Committee of the Emergency Clinical County Hospital of Oradea (approval No. 20466/08.09.2020).

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Authors' Contribution

Study concept and design: NBMT and MIP; analysis and interpretation of the data: NBMT and DCPC; drafting of the manuscript: NBMT; critical revision of the manuscript for important intellectual content: VP; statistical analysis: NBMT.

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References

- Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal*. 2018;**39**(2):119-77.
- Martí D, Mestre JL, Salido L, Esteban MJ, Casas E, Pey J, et al. Incidence, angiographic features and outcomes of patients presenting with subtle ST-elevation myocardial infarction. *American heart journal*. 2014;168(6):884-90.
- Park D-W, Clare RM, Schulte PJ, Pieper KS, Shaw LK, Califf RM, et al. Extent, location, and clinical significance of non–infarctrelated coronary artery disease among patients with ST-elevation myocardial infarction. Jama. 2014;312(19):2019-27.
- 4. Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, *et al.* Randomized trial of preventive angioplasty in myocardial infarction. *N Engl J Med.* 2013;**369**:1115-23.

- Engstrøm T, Kelbæk H, Helqvist S, Høfsten DE, Kløvgaard L, Holmvang L, *et al.* Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3— PRIMULTI): an open-label, randomised controlled trial. *The Lancet*. 2015;**386**(9994):665-71.
- Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, *et al.* Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *Journal of the American College of Cardiology*. 2015;65(10):963-72.
- Smits P, Omerovic E, Abdel-Wahab M, Klerk BB-d, Lunde K, Neumann F-J, et al. Two year results from the COMPARE-ACUTE trial. Journal of the American College of Cardiology. 2018;71(11S):A1158-A.
- Mehta SR, Wood DA, Storey RF, Mehran R, Bainey KR, Nguyen H, et al. Complete revascularization with multivessel PCI for myocardial infarction. New England Journal of Medicine. 2019;381(15):1411-21.
- 9. Serruys PW, Morice M-C, Kappetein AP, Colombo A, Holmes DR, Mack MJ, *et al.* Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *New England journal of medicine.* 2009;**360**(10):961-72.
- 10. Ochala A, Smolka GA, Wojakowski W, Dudek D, Dziewierz

A, Krolikowski Z, *et al.* Th e function of the left ventricle after complete multivessel one-stage percutaneous coronary interventio n in patients with acute myocardial infarction. *J Invasive Cardiol.* 2004;**16**:699-702.

- Hachet O, Guenancia C, Stamboul K, Daubail B, Richard C, Béjot Y, *et al.* Frequency and predictors of stroke after acute myocardial infarction: specific aspects of in-hospital and postdischarge events. *Stroke.* 2014;45(12):3514-20.
- Hayıroğlu Mİ, Keskin M, Uzun AO, Yıldırım Dİ, Kaya A, Çinier G, et al. Predictors of In-Hospital Mortality in Patients With ST-Segment Elevation Myocardial Infarction Complicated With Cardiogenic Shock. *Heart, Lung and Circulation.* 2019;28(2):237-44.
- Ntalianis A, Sels J-W, Davidavicius G, Tanaka N, Muller O, Trana C, et al. Fractional flow reserve for the assessment of nonculprit coronary artery stenoses in patients with acute myocardial infarction. JACC: Cardiovascular Interventions. 2010;3(12):1274-81.
- Scarsini R, Terentes-Printzios D, De Maria GL, Ribichini F, Banning A. Why, When and How Should Clinicians Use Physiology in Patients with Acute Coronary Syndromes? *Interventional Cardiology Review*. 2020;15.
- 15. Wood DA, Poulter R, Boone R, Owens C, Starovoytov A, Lim I, *et al.* Stability of non culprit vessel fractional flow reserve in patients with St-segment elevation myocardial infarction. *Canadian Journal of Cardiology.* 2013;**29**(10):S291-S2.