GEORGIAN BIOMEDICAL NEWS

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994 VOLUME 1. ISSUE 1. APRIL-JUNE 2023

Comparison of Long-term Preventive Effects of Dual Antiplatelet Therapy vs. Monotherapy in High Cardiovascular Risk Patients After Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA)

Ioseb Sikharulidze,[1] Kakhaber Chelidze,[2] Levan Chelidze,[3] Tamar Kajaia,[4] Irma Bakhlishvili[1]

DOI: 10.52340/GBMN.2023.01.01.31

ABSTRACT

BACKGROUND.
Myocardial infarction with nonobstructive coronary arteries (MINOCA) has similar outcomes to patients with acute MI with obstructive coronary disease for up to 1 year. According to existing evidence, dual antiplatelet therapy (DAPT) was not significantly better than aspirin alone in lowering 1-year MACCEs in different cardiovascular risk patients with non-obstructive coronary artery disease.

OBJECTIVES
In the present study, we aimed to compare the long-term preventive effect of DAPT to aspirin alone in high cardiovascular-risk patients over 5 years.

METHODS
For the long-term observation, 34 MINOCA patients with a high 10-year risk of atherosclerotic cardiovascular disease (ASCVD ≥20%) were randomly distributed among the DAPT group (15 patients on aspirin plus clopidogrel therapy) and the MAPT group (19 patients on aspirin alone). The decision about prolonged DAPT was made through the case-by-case evaluation of the bleeding and ischemic risks via the DAPT score calculator.

RESULTS
By Kaplan-Meier survival analysis, the mean survival time for the DAPT group (4.7±0.048 years 95% CI [4.60 to 4.79]) was significantly longer than the mean survival time for the APMT group (4.5±0.049 years 95% CI [4.41 to 4.61]), with p-value less than 0.0001.

CONCLUSIONS
Long-term dual antiplatelet therapy effectively and safely reduces major adverse cardiovascular and cerebrovascular events (MACCEs) in patients after myocardial infarction with nonobstructive coronary arteries (MINOCA).

KEYWORDS
Atherosclerotic cardiovascular disease (ASCVD) risk; dual antiplatelet therapy (DAPT); major adverse cardiovascular and cerebrovascular events (MACCEs); myocardial infarction with nonobstructive coronary artery (MINOCA) disease.

BACKGROUND

Myocardial infarction with nonobstructive coronary arteries (MINOCA), a disorder with heterogeneous pathophysiology, has similar outcomes to patients with acute MI with obstructive coronary disease for up to 1 year.[1-4]

The prevalence of MINOCA varies between 5 to 15% depending on the observed population and is associated with younger age (<55 years), female gender, genetic predispositions, and mental stress.[5-9]

Growing evidence indicates that nonobstructive coronary artery disease (NOCAD) is linked with a significant risk of future major adverse cardiovascular and cerebrovascular events (MACCEs), primarily due to nonobstructive plaque erosion and subsequent thrombosis.[10-13] Therefore, antiplatelet therapy becomes especially important in patients with NOCAD. However, the efficacy of various antiplatelet therapy regimens for preventing MACCEs in individuals with nonobstructive coronary artery disease remains unclear.[14]

According to existing evidence, dual antiplatelet therapy (DAPT) was not significantly better than aspirin alone in lowering 1-year MACCEs in different cardiovascular risk patients with NOCAD.[15-18]

The same results were found in our recent cohort study of secondary prevention DAPT (aspirin plus the P2Y12 receptor antagonist clopidogrel) was not significantly better than aspirin alone in lowering 1-year MACCEs.[19]

In the present observational cohort study, we aimed to compare the long-term preventive effect of DAPT to aspirin alone in high cardiovascular-risk patients over 5 years.

METHODS

Patient population

Overall, 115 of 1018 antiplatelet-naive patients without previous revascularization admitted to the Coronary Care Unit of Tsinamdzgvrishvili Center of Cardiology LTD (Tbilisi, Georgia) and categorized as MINOCA were included in the research between March 2018 and August 2019. For the long-term observation, 34 MINOCA patients with a high 10-year risk of atherosclerotic cardiovascular disease (ASCVD ≥20%) were randomly distributed among the DAPT group (15 patients on aspirin plus clopidogrel therapy) and the MAPT group (19 patients on aspirin alone). The decision about prolonged DAPT was made through the case-by-case evaluation of the bleeding and ischemic risks via the DAPT score calculator.[25]

Periprocedural full blood count, renal and liver function, electrolytes, glycated hemoglobin (HbA1c), high-sensitive C-reactive protein, coagulation screen and D-dimer, lipid profile, serial cardiac troponin, N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) and infection screening were performed in all study patients. In addition, echocardiography was performed in all patients. The CRUSADE score calculator was used to assess post-MI major bleeding risk.

Diagnosis of MINOCA

All study patients meet the criteria for a diagnosis of MINOCA criteria, such as acute myocardial infarction with nonobstructive (≤50%) infarct-related epicardial stenosis during angiography and absence of overt alternative systemic cause (Tab.1).[5,22]

Cardiovascular risk estimation

The 10-year Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimator Plus (designed for persons aged 40 to 79) was used to predict the risk of myocardial infarction, stroke, or cardiovascular mortality.[23]

Follow-up

A five-year follow-up period was used in both groups to determine a six-point MACCE, including all-cause mortality, myocardial infarction, stroke, hospitalization for heart failure, coronary revascularization, and atrial fibrillation (AF). In addition, the registration of bleeding associated with antiplatelet therapy was performed using the bleeding severity classification developed by the Thrombolysis in Myocardial Infarction (TIMI) study group.[24] Spontaneous gross hematuria, spontaneous hematemesis, or observed bleeding with a decrease in hemoglobin ≥3 g/dl but ≤15% was classified as minor bleeding, and intracranial bleeding or overt bleeding with a decreased in hemoglobin ≥5 g/dl or decrease in hematocrit ≥15% was classified as major bleeding.[24] The DAPT risk score calculation results were used to decide whether to keep or stop DAPT.[25]

Statistical analysis

IBM SPSS version 26.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. The descriptive statistics, nonparametric Mann-Whitney U test, Kaplan-Meier survival analysis, linear and quantile regression analysis, Pearson correlation, ANOVA test, Z-scores, and B coefficients were employed to examine differences between development and validation cohorts. $p<0.05$ was used for assessing statistical significance.

RESULTS

Baseline characteristics of study patients

Table 1 represents the baseline characteristics of study patients.

TABLE 1. Baseline characteristics of MINOCA patients with a high 10-year risk for ASCVD randomly distributed by the regimen of antiplatelet therapy

	DAPT, n=15	*AMPT, n=19*	*P-value*
Mean age, year, M±SD	65.8±0.78	67.58±1.84	**<0.0001**
Female, n (%)	12 (80)	9 (47)	0,111
Mean BMI, kg/m^2, M±SD	28.3±3.20	27.6±2.98	0.391
Current smoking , n (%)	6 (40)	6 (32)	0.681
Hypertension, n (%)	15 (100)	18 (95)	0.811
History of ASCVD, n (%)	2 (13)	2 (11)	0.891
History major bleeding, n (%)	0 (0)	0 (0)	0
History of AF, n (%)	3 (20)	4 (21)	0.973
Hoistory of COPD, n (%)	0 (0)	2 (11)	0.607
Current AF, n (%)	0 (0)	0 (0)	0
Mean 10-year ASCVD score, M±SD	30.25±9.64	30.28±8.59	0.846
Mean CRUSADE score, M±SD	20.87±3.04	20.63±2.83	0.550
Mean EF, %, M±SD	45.4±5.80	44.16±5.46	0.639
Mean RBC, 10^9/l, M±SD	4.14±0.54	4.05±0.67	0.647
Mean Hb, g/dL, M±SD	13.87±0.76	13.67±0.77	0,674
Mean Hct,%, M±SD	40.7±2.47	40.4±3.10	0.381
Mean MCV, µm^3, M±SD	86.6±4.42	86.8±3.95	0.404
Mean Plt, 10^9/l, M±SD	272.1±56.6	266.7±50.7	0.688
Mean WBC, 10^9/l, M±SD	7.32±1.54	7.67±1.68	0.498
Mean HbA1c, M±SD	7.59±1.58	8.30±1.99	0.253
Mean hs-CRP, mg/L, M±SD	2.37±0.66	2.65±0.63	0.938
Mean AST, U/L, M±SD	30.9±3.95	30.2±4.22	0.825
Mean ALT, U/L, M±SD	36.9±9.45	36.3±7.90	0.504
Mean serum Na, mmol/L, M±SD	138.8±3.69	138.8±3.36	0.590
Mean serum K, mEq/L, M±SD	4.3±0,62	4.5±0.65	0.517
Mean PT, seconds, M±SD	11.93±0,48	11.98±0,49	0.765
Mean aPTT, seconds, M±SD	36.53±3.14	34.42±3.95	0.178
Mean D-dimer, ng/mL, M±SD	201.1±25.3	200.3±25.4	0.984
Mean TC, mg/dL, M±SD	229±27.46	231±19.84	0.823
Mean HDL-C, m/dl, M±SD	37±5.97	35±5.86	0.786
Mean GFR, mL/min/1.73 m^2, M±SD	75.4±14.88	78.7±12.65	0.202
Meat cTnI, microg/L, M±SD	0.47±0.24	0.55±0.21	0.697
Mean NT-pro-BNP, pg/mL, M±SD	82.1±19.3	77.0±20.6	0.620
Previous ACIs/ARBs, n (%)	13 (87)	15 (79)	0.706
Previous BBs, n (%)	3 (20)	6 (32)	0.584
Previous CCBs, n (%)	3 (20)	4 (21)	0.973
Previous Statins, n (%)	11 (73)	15 (79)	0.784

Abbreviations: ACIs, angiotensin converting enzyme inhibitors; AF, atrial fibrillation; ALT, alanine transaminase; APMT, antiplatelet monotherapy; aPTT, partial thromboplastin time; ARBs, angiotensin receptor blockers; ASCVD, atherosclerotic cardiovascular disease; AST, aspartate aminotransferase; BB, beta-blockers; BMI, body mass index; CCB, calcium channel blockers; COPD, chronic obstructive pulmonary disease; cTnI, cardio troponin I; DAPT, dual antiplatelet therapy; EF, left ventricle ejection fraction; GFR, glomerular filtration rate; Hb, hemoglobin; HbA1c, hemoglobin A1c; Hct, hematocrit; HDL-C, high density lipoprotein cholesterol; hs-CRP, highly sensitive C-reactive protein; K, potassium; M±SD, mean ± standard deviation; MCV, mean corpuscular volume; MINOCA, myocardial infarction with nonobstructive coronary arteries; Na, sodium; No-DAPT, antiplatelet monotherapy; NT-pro-BNP, N-terminal pro-B-type natriuretic peptide; Plt, platelets; PT, prothrombin time; RBC, red blood cells; TC, total cholesterol; WBC, white blood cells.

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

There was no statistically significant difference between the groups by baseline characteristics, except for mean age, which was higher in the APMT group patients compared to DAPT group patients (67.58±1.84 vs. 65.8±0.78, p<0.0001).

Follow-up

Table 2 represents the annual cumulative incidence of MACCEs in DAPT and APMT groups during the five-year follow-up period.

TABLE 2. Annual cumulative incidence of MACCEs in DAPT and APMT groups during the five-year follow-up period

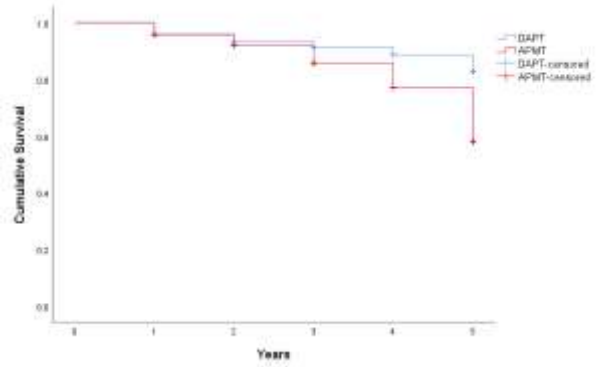
	Chi-Square	Significance
1st year cumulative MACCEs	0.034	0.811
2nd year cumulative MACCEs	0.630	0.427
3rd year cumulative MACCEs	8.258	**0.004**
4th year cumulative MACCEs	9.034	**0.003**
5th year cumulative MACCEs	11.539	**0.001**
5-year cumulative MACCEs	18.365	**<0.0001**

Abbreviations: APMT, antiplatelet monotherapy; DAPT, dual antiplatelet therapy; MACCEs, major adverse cardiovascular and cerebrovascular events

Our previous study showed that DAPT had no secondary preventive effect on one-year cumulative MACCEs in MINOCA patients with high cardiovascular risks.[19] The neutral effect of dual antiplatelet therapy was observed during the second follow-up year; however, from the third year until the end of the follow-up, the preventive effect of DAPT on cumulative MACCEs significantly exceeded the effect of antiplatelet monotherapy with aspirin.

By Kaplan-Meier survival analysis, the mean survival time for the DAPT group (4.7±0.048 years 95% CI [4.60 to 4.79]) was significantly longer than the mean survival time for the APMT group (4.5±0.049 years 95% CI [4.41 to 4.61]), with p-value less than 0.0001 (Fig.1).

FIGURE 1. Kaplan-Meier survival functions for 5-year MACCEs in study groups



	Chi-Square	df.	Sig.
Log Rank (Mantel-Cox)	18.365	1	.000

Abbreviations: *APMT, antiplatelet monotherapy; DAPT, dual antiplatelet therapy; MACCEs, major adverse cardiovascular and cerebrovascular events.*

When the effect of different antiplatelet regimens on individual components of MACCEs was evaluated, DAPT was found to have a more substantial preventative effect on all of them; however, only a decrease in the incidence of myocardial infarction (RR=0.45, 95% CI [0.23 to 0.87], z statistic=2.372, p=0.02, NNT[Benefit]=6.196 95% CI [3.51 to 26.58]) and revascularization (RR=0.32, 95% CI [0.14 to 0.73], z statistic=2.677, p=0.007, NNT[Benefit]=5.793, 95% CI [3.51 to 16.62]) was statistically significant (Tab.3).

TABLE 3. Survival analysis of 5-year all-cause mortality, myocardial infarction, stroke, heart failure hospitalization, revascularization, and atrial fibrillation in comparator groups

MACCEs components	Study groups	Mean survival time (M±SD)	95% CI	Chi-square	p-value
All-cause mortality	DAPT	4.86±0.093	4.68 to 5.04	1.895	0.169
	APMT	4.65±0.112	4.43 to 4.87		
Myocardial infarction	DAPT	4.55±0.15	4.26 to 4.85	5.436	**0.02**
	APMT	4.35±0.13	4.08 to 4.61		
Stroke	DAPT	4.67±0.13	4.41 to 4.92	2.898	0.089
	APMT	4.42±0.13	4.16 to 4.68		
Hospitalization for heart failure	DAPT	4.49±0.15	4.20 to 4.78	1.176	0.278
	APMT	4.451±0.12	4.27 to 4.74		
Revascularization	DAPT	4.77±0.11	4.56 to 4.99	7.676	**0.006**
	APMT	4.40±0.13	4.14 to 4.66		
Atrial fibrillation	DAPT	4.82±0.98	4.63 to 5.01	0.739	0.390
	APMT	4.78±0.87	4.61 to 4.95		

Abbreviations: *APMT, antiplatelet monotherapy; DAPT, dual antiplatelet therapy; MACCEs, major adverse cardiovascular and cerebrovascular events.*

The predictive correlation between age, female gender, 10-year atherosclerotic cardiovascular disease (ASCVD) score, and 5-year cumulative MACCEs was evaluated by the multivariate linear regression analysis. The only correlation between a 10-year ASCVD score and the cumulative MACEs was statistically significant (unstandardized/standardized coefficients B=0.749; zero-order correlation=0.728; partial correlation=0.738; part correlation=0.736; p<0.0001).

There were no cases of major bleeding in comparator groups during the 5-year follow-up. However, four and five cases of minor bleeding were observed in the DAPT and APMT groups, respectively (OR=1.014, 95% CI [0.26 to 3.02], z statistic=0.02, p=0.98).

DISCUSSION

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is not benign pathology with comparable outcomes with acute myocardial infarction due to obstructive coronary artery disease.[4]

MINOCA generally is highly associated with younger age (<55 years), female sex, genetic disorders, and physiological stress.[7-9]

The existing scanty evidence shows that treatment with statins and angiotensin-converting enzyme inhibitors (ACEi)/angiotensin receptor blockers (ARBs) has a long-term

The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

beneficial effect, and with beta-blockers has a positive effect on outcomes in patients with MINOCA.[15,26]

Despite the neutral effect on 1-year outcomes, dual antiplatelet treatment (12 months followed by a lifetime single agent) is advised since plaque disruption is considered one of the primary substrates for MINOCA.[15-18,27]

Our prior research results support previously published data on the lack of a secondary preventative effect of DAPT on one-year MACE in MINOCA patients with different cardiovascular risks.[19,28]

Pending trial evidence about the usefulness of DAPT in MINOCA patients from ongoing MINOCA-BAT trial,[29] we decided to compare the long-term preventive effect of dual antiplatelet therapy with a monotherapy regimen in high cardiovascular risk (10-year ASCVD ≥20%) MINOCA patients.

Thirty-four high cardiovascular-risk MINOCA patients were distributed among two groups with different antiplatelet therapy regimens: 15 patients in dual antiplatelet therapy with aspirin and clopidogrel (DAPT group) and 19 patients in antiplatelet monotherapy with aspirin (APMT group). All study patients were initially evaluated regarding post-MI major bleeding risk using a CRUSADE score calculator. After the first follow-up year, the DAPT risk score calculation was used to decide whether to keep or stop DAPT. Even though the DAPT Risk Calculator was designed for post-PCI procedure patients without having a major bleeding or ischemic event on DAPT and who were not on chronic oral anticoagulation,[25] we had to use this application for our study patients, due to the lack of an alternative.

The neutral impact of dual antiplatelet treatment was found during the first two years of follow-up; however, from the third year to the end of the study, the preventative effect of DAPT on cumulative MACCEs considerably outperformed the effect of antiplatelet monotherapy with aspirin. The relative risk for 5-year cumulative MACCEs was 0.49, 95% CI [0.36 to 0.68] and NNT(Benefit)=9.7 95 CI [6.75(Benefit) to 0.67(Benefit)].

Analyzing each component of 5-year MACCEs, we found a decrease in cumulative cases in the DAPT group compared to the APMT group. However, only a reduction in myocardial infarction and revascularization incidence was statistically significant (p=0.02 and p=0.006, respectively). For a 5-year myocardial infarction, the relative risk was equal to 0.45, 95% CI [0.23 to 0.87], and NNT=6.2(Benefit), 95% CI [3.5(Benefit) to 26.5(Benefit)]. For 5-year revascularization, the relative risk was 0.32, 95% CI [0.14 to 0.73], and NNT=5.8(Benefit), 95% CI [3.5(Benefit) to 16.6(Benefit)].

Considering the observed efficacy and the favorable safety profile of long-term dual antiplatelet therapy, it may be safe to assume that the primary cause of most MINOCA cases is atherosclerotic plaque erosion/rupture and thrombosis, coronary embolism, or coronary artery dissection.

Finally, we emphasize the primary limitation of the present study, which is the single-center observational design with a small sample size. Furthermore, we did not use intravascular ultrasound (IVUS), optical coherence tomography, or cardiac MRI to distinguish underlying causes of MINOCA. Additionally, only clopidogrel combined with aspirin was used for dual antiplatelet therapy.

CONCLUSIONS

Long-term dual antiplatelet therapy effectively and safely reduces major adverse cardiovascular and cerebrovascular events (MACCEs) in patients after myocardial infarction with nonobstructive coronary arteries (MINOCA). Therefore, long-term DAPT should be considered case-by-case after carefully evaluating the benefits and risks of dual antiplatelet therapy. Further investigations are required to confirm the efficacy of long-term anti-aggregation therapy after myocardial infarction with nonobstructive coronary arteries.

AUTHOR AFILIATION

[1]Batumi Center for Cardiovascular Diseases and Interventional Medicine, Ckubuc "MedCenter" LTD, Batumi, Georgia;
[2]Department of Internal Medicine, Tbilisi State Medical University (TSMU), Tbilisi, Georgia;
[3]Angio-cardiology Clinic “Adapti” LTD, Tbilisi, Georgia;
[4]Department of Interventional Cardiology & Cardio Surgery, LTD Tbilisi Heart Center, Tbilisi, Georgia.

ACKNOWLEDGEMENTS

Special thanks to Prof. Bezhan Tsinamdzgrishvili M.D., Ph.D. head of Tsinamdzgvrishvili Center of Cardiology LTD for his support during the present study.

REFERENCES

1. Gross H, Sternberg WH. Myocardial infarction without significant lesions of coronary arteries. Arch Intern Med 1939;64:249–67.
2. Nordenskjöld AM, Baron T, Eggers KM, et al. Predictors of adverse outcome in patients with myocardial infarction with non-obstructive coronary artery (MINOCA) disease. Int J Cardiol 2018;261:18–23.
3. Safdar B, Spatz ES, Dreyer RP, et al. Presentation, clinical profile, and prognosis of young patients with myocardial infarction with nonobstructive coronary arteries (MINOCA): results from the VIRGO study. J Am Heart Assoc 2018;7:e009174.
4. Robert Sykes, Daniel Doherty, Kenneth Mangion, Andrew Morrow, Colin Berry. What an Interventionalist Needs to Know About MI with Non-obstructive Coronary Arteries. Interventional Cardiology Review 2021;16:e10. DOI:doi.org/10.15420/icr.2021.10
5. Tamis-Holland JE, Jneid H, Reynolds HR, et al. Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease: a scientific statement from the American Heart Association. Circulation 2019;139:e891–908.
6. Scalone G, Niccoli G, Crea F. Editor’s choice – pathophysiology, diagnosis and management of MINOCA: an update. Eur Heart J Acute Cardiovasc Care 2019;8:54–62.
7. Smilowitz NR, Mahajan AM, Roe MT, et al. Mortality of myocardial infarction by sex, age, and obstructive coronary artery disease status in the ACTION registry-GWTG (Acute Coronary Treatment and

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

Intervention Outcomes Network Registry-Get with the Guidelines). Circ Cardiovasc Qual Outcomes 2017;10:e003443.
8. Barrett TJ, Lee AH, Smilowitz NR, et al. Whole-blood transcriptome profiling identifies women with myocardial infarction with nonobstructive coronary artery disease. Circ Genom Precis Med 2018;11:e002387.
9. Nero D, Agewall S, Daniel M, et al. Personality traits in patients with myocardial infarction with nonobstructive coronary arteries. Am J Med 2019;132:374–81.e1.
10. Carl J. Pepine, MD; Keith C. Ferdinand, MD; Leslee J. Shaw, PHD; Kelly Ann Light-McGroary, MD; Rashmee U. Shah, MD, MS; Martha Gulati, MD, MS; Claire Duvernoy, MD; Mary Norine Walsh, MD; C. Noel Bairey Merz, MD. Emergence of Nonobstructive Coronary Artery Disease. A Women's Problem and Need for Change in Definition on Angiography. J Am Coll Cardiol. 2015;66(17):1918-1933.
11. Jespersen L, Hvelplund A, Abildstrøm SZ, et al. Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events. Eur Heart J 2012;33:734–44.
12. Maddox TM, Stanislawski M, Grunwald G, et al. non-obstructive coronary artery disease is not benign: Insights from the VA CART program on the association between non-obstructive disease and cardiac events (abstr). Circ Cardiovasc Qual Outcomes 2014;7:A24.
13. Min JK, Dunning A, Lin FY, et al., for the CONFIRM Investigators. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. J Am Coll Cardiol 2011;58:849–60.
14. Wenjie Chen, Yufeng Jiang, Tan Chen, Yafeng Zhou. Antiplatelet therapy in patients with myocardial infarction with non-obstructive coronary arteries: A clinical perspective. Front Cardiovasc Med. 2022; 9: 1081934. doi: 10.3389/fcvm.2022.1081934.
15. Lindahl B, Baron T, Erlinge D, et al. Medical therapy for secondary prevention and long-term outcome in patients with myocardial infarction with non-obstructive coronary artery (MINOCA) disease. Circulation. 2017;135:1481---9.
16. Paolisso P, Bergamaschi L, Saturi G, D'Angelo EC, Magnani I, Toniolo S, et al. Secondary prevention medical therapy and outcomes in patients with myocardial infarction with non-obstructive coronary artery disease. Front Pharmacol. (2019) 10:1606. doi: 10.3389/fphar.2019.01606.
17. Ciliberti G, Verdoia M, Merlo M, Zilio F, Vatrano M, Bianco F, et al. Pharmacological therapy for the prevention of cardiovascular events in patients with myocardial infarction with non-obstructed coronary arteries (MINOCA): insights from a multicentre national registry. Int J Cardiol. (2021)327:9–14. doi: 10.1016/j.ijcard.2020.11.040.
18. Abdu FA, Liu L, Mohammed AQ, Xu B, Yin G, Xu S, et al. Effect of secondary prevention medication on the prognosis in patients with myocardial infarction with nonobstructive coronary artery disease. J Cardiovasc Pharmacol. (2020) 76:678–83. doi: 10.1097/FJC.0000000000000918.
19. Sikharulidze Ioseb, Chelidze Kakhaber, Mamatsashvili Merab, Chelidze Levan, Kajaia Tamar, Bakhlishvili Irma. Antiplatelet Therapy for Secondary Prevention After Myocardial Infarction in Antiplatelet-Naive High Cardiovascular Risk Patients with Non-Obstructive Coronary Artery Disease. G Biomed N 23 Feb 2023 Volume 1 (Issue 1):32-36
20. Thygesen K, Alpert JS, Jaffee AS, et al. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol 2018;72:2231-64.
21. Agewall S, Beltrame JF, Reynolds HR, et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J 2017;38:143-53.
22. Christina Ekenbäck, Per Tornvall, Stefan Agewall. MINOCA from A to Z. American College of Cardiology. Jan 06, 2022. https://www.acc.org/latest-in-cardiology/articles/2022/01/05/17/41/minoca-from-a-to-z.
23. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 129:S49.
24. Rao AK, Pratt C, Berke A, et al. Thrombolysis in Myocardial Infarction (TIMI) trial—phase I: hemorrhagic manifestations and changes in plasma fibrinogen and the fibrinolytic system in patients Case Report: Risk of Bleeding Complications with Antiplatelet Agents J Am Coll Cardiol 1988;11:1–11, 2004, https://onlinelibrary.wiley.com/doi/10.1002/ajh.10451.
25. American College of Cardiology. DAPT Risk Calculator. 16th October 2017. https://tools.acc.org/daptriskapp/#!/content/calculator/.
26. Choo EH, Chang K, Lee KY, et al. Prognosis and predictors of mortality in patients suffering myocardial infarction with non-obstructive coronary arteries. J Am Heart Assoc 2019;8:e011990.
27. Collet JP, Thiele H, Barbato E, et al. 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021;42:1289–367.
28. Sikharulidze Ioseb, Chelidze Kakhaber, Chelidze Levan, Kajaia Tamar, Bakhlishvili Irma. Comparison of Inflammatory and Oxidative Stress Markers Among Patients with Non-Obstructive vs. Obstructive Coronary Artery Disease. G Biomed N 15 Mar 2023 Volume 1 (Issue 1):48-51.
29. Anna M Nordenskjöld, Stefan Agewall, Dan Atar, Tomasz Baron, John Beltrame, Olle Bergström, David Erlinge, Chris P Gale, Javier López-Pais, Tomas Jernberg, Pelle Johansson, Annica Ravn-Fisher, Harmony R. Reynolds, Jithendra B. Somaratne, Per Tornvall, Bertil Lindahl. Randomized evaluation of beta blocker and ACE-inhibitor/angiotensin receptor blocker treatment in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA-BAT): Rationale and design. American Heart Journal Volume 231, January 2021, Pages 96-104.

https://www.icrjournal.com/articles/what-interventionalist-needs-know-about-mi-non-obstructive-coronary-arteries