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Predictors of Myocardial Infarction with Non-obstructive Coronary Arteries (MINOCA) Among Patients Presenting with Acute Myocardial Infarction

Akut Miyokard Enfarktüsü ile Başvuran Hastalarda Non-obstrüktif Koroner Arterli Miyokard Enfarktüsünün (MINOCA) Prediktörleri

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Abstract

Objectives: Myocardial infarction with non-obstructive coronary arteries (MINOCA) represents a heterogeneous entity with distinct pathophysiological mechanisms compared with myocardial infarction with coronary artery disease (MICAD). Recognizing indicators of MINOCA upon admission may enable prompt diagnosis and customized treatment.

Material and Methods: We retrospectively analyzed 1,163 consecutive patients admitted with acute myocardial infarction (AMI) at a single tertiary cardiology center in Türkiye between January 2015 and December 2020. Patients were classified as MINOCA (n=87) or MICAD (n=1.076) based on coronary angiography findings. Clinical, demographic, and laboratory parameters were compared.

Results: Multivariable analysis identified female gender [odds ratio (OR) 1.417, 95% confidence interval (CI) 1.112-2.018; p=0.048) and lower low-density lipoprotein (LDL) cholesterol (OR 0.992, 95% CI 0.985-0.998; p=0.017) as independent predictors of MINOCA occurrence, whereas age was significant in univariate analysis but lost significance in multivariable analysis.

Conclusion: Female sex and low LDL cholesterol levels independently predict MINOCA in AMI patients within the Turkish population.

Keywords: MINOCA, acute myocardial infarction, predictors

Öz

Amaç: Non-obstrüktif koroner arterli miyokard enfarktüsü (MINOCA), koroner arter hastalığı olan miyokard enfarktüsüne (MICAD) kıyasla farklı patofizyolojik mekanizmalara sahip heterojen bir tablodur. MINOCA belirtilerinin kabul sırasında tanınması, hastalığın teşhis edilmesini hızlandırır ve kişiye özel tedaviyi mümkün kılabilir.

Yöntem ve Gereçler: Türkiye'deki tek bir üçüncü basamak kardiyoloji merkezinde, Ocak 2015 ile Aralık 2020 tarihleri arasında akut miyokard enfarktüsü (AME) tanısıyla yatırılan 1.163 hastayı retrospektif olarak analiz ettik. Hastalar, koroner anjiyografi bulgularına göre MINOCA (n=87) veya MICAD (n=1,076) olarak 2 gruba ayrıldı. Hastaların klinik, demografik ve laboratuvar parametreleri karşılaştırıldı.

Bulgular: Çok değişkenli analiz sonucunda, kadın cinsiyetinin [odds oranı (OO) 1,417, %95 güven aralığı (GA) 1,112-2,018; p=0,048) ve düşük yoğunluklu lipoprotein (LDL) kolesterolünün (OO 0,992, %95 GA 0,985-0,998; p=0,017) MINOCA oluşumunun bağımsız öngörücüleri olduğunu saptamıştır; ancak yaş, tek değişkenli analizde anlamlı iken çok değişkenli analiz sonucunda anlamlılığı kaybetmiştir.

Sonuç: Kadın cinsiyeti ve düşük LDL kolesterol seviyeleri, Türk popülasyonunda AME hastalarında MINOCA'yı bağımsız olarak öngörmektedir.

Anahtar Kelimeler: MINOCA, akut koroner sendrom, prediktörler

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INTRODUCTION

Acute coronary syndrome is a common cause of global mortality and morbidity, affecting a wide range of patients. Acute myocardial infarction (AMI) is diagnosed by evidence of acute myocardial injury in the setting of myocardial ischemia. Coronary angiography (CA) is regarded as the gold standard for assessing anatomical abnormalities in the coronary arteries during AMI (1).

AMI typically arises from thrombus formation at the site of atherosclerotic blockage in the coronary artery (2). Approximately 5-10% of patients with AMI exhibit no significant coronary artery obstruction (normal or less than 50% stenosis); this condition is referred to as myocardial infarction with non-obstructive coronary arteries (MINOCA) (3). MINOCA is a multifaceted condition resulting from diverse etiologies, including coronary plaque rupture, coronary artery spasm, spontaneous coronary artery dissection, and coronary artery embolism or thrombosis. Furthermore, MINOCA may be associated with non-coronary causes, including myocarditis, microvascular spasm, Takotsubo cardiomyopathy, and myocardial oxygen supply-demand imbalance (4-6).

It is clinically significant to distinguish MINOCA from myocardial infarction with coronary artery disease (MICAD), particularly in the early stages, as the evaluation and management of patients with suspected MINOCA differ substantially from those for patients with MICAD (7). Most studies show that MINOCA patients are younger and more often female than MICAD patients within acute coronary syndrome cohorts (8,9). Studies indicate that inflammation significantly contributes to MINOCA, and several inflammatory markers are associated with the condition (10,11). Demographic and biochemical markers present at admission may offer critical insights for identifying patients at risk of MINOCA and informing further diagnostic imaging or treatment strategies.

This study aimed to identify factors associated with MINOCA among Turkish patients with AMI, a subject not previously unexplored, while emphasizing readily available baseline data.

MATERIAL AND METHODS

Study Population and Design

This retrospective observational study encompassed 1,163 patients diagnosed with AMI who underwent CA at a tertiary cardiovascular hospital between January 2015 and December 2020. Patients were eligible if they were between 18 and 90 years old at presentation, were hospitalized for AMI, and underwent CA. Patients with a history of CA, myocardial infarction, percutaneous intervention, coronary artery bypass grafting, or who had absent laboratory parameters were excluded. The study commenced with 1,784 potentially eligible patients. One hundred ninety-seven patients diagnosed with acute coronary syndrome who did not fulfill the criteria for AMI were excluded. After applying the exclusion criteria, 424 patients were excluded, and 1,163 patients with complete clinical data were included in the final analysis. Our extensive data collection included demographic variables, transthoracic echocardiography (TTE) and electrocardiogram (ECG) characteristics, laboratory results, medication administration, CA findings, procedure-specific complications, and follow-up data, all obtained from hospital medical records and national health databases. Our study protocol complied with the Declaration of Helsinki and received clearance from the local ethics board, thereby ensuring the ethical integrity and reliability of our findings.

Definitions

The fourth universal definition of myocardial infarction was used to characterize MINOCA and other AMI variants. AMI is characterized by recent alterations in clinical symptoms or signs, with or without corresponding changes on the 12-lead ECG and with or without acute elevations in cardiac troponin levels, culminating in a diagnosis of AMI or unstable angina. The laboratory diagnosis of myocardial infarction necessitates elevated cardiac biomarkers that exceed the 99th percentile with a rising and/or falling pattern, alongside at least one of the following: ischemic symptoms, ECG alterations indicative of ischemia, new regional wall motion abnormalities on TTE, or angiographic evidence of coronary thrombus. Non-obstructive coronary stenosis is defined as luminal narrowing of less than 50%. Coronary ectasia is defined as a dilatation of ≥50% relative to an adjacent normal segment, whereas coronary sluggish flow is defined as delayed opacification in the absence of severe epicardial coronary artery stenosis (1,2,12,13).

Laboratory Analyses

Laboratory parameters assessed upon admission included full blood counts, liver function tests, renal function tests, electrolytes, lipid profiles, and cardiac biomarkers.

Coronary Angiography

CA was performed using the standard Judkins approach and evaluated by two experienced interventional cardiologists on an Axiom (Siemens Medical Solutions) workstation. This study was approved by İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (decision no: 1272, date: 30.10.2025). Written informed consent was obtained from all patients prior to the procedure.

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test and were presented as mean ± standard deviation for normally distributed data or as median (interquartile range) for non-normally distributed data. Categorical variables were expressed as counts and percentages (%). Comparisons between the MINOCA and MICAD groups were conducted using the Student's t-test or Mann-Whitney U test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables, as appropriate. To identify independent predictors of MINOCA, variables with $p<0.10$ in univariate analyses were entered into a multivariable logistic regression model using the enter method. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Survival analysis was conducted with the Kaplan-Meier method, and differences between groups were assessed using the log-rank test. A two-sided $p<0.05$ was considered statistically significant.

RESULT

The study comprised 1,163 patients, of whom 1,076 (92.5%) had MICAD and 87 (7.4%) had MINOCA. The mean age of patients was significantly higher in the MINOCA group than in the MICAD group (64.5±13.2, 57.4±17.7, $p<0.001$). The percentage of female patients in the MINOCA group was significantly higher than that in the MICAD group (50.6% vs. 32.8%; $p=0.002$). No statistically significant differences were observed in the laboratory data, except for low-density lipoprotein (LDL) cholesterol levels, which were lower in the MINOCA group than in the MICAD group [112 (96-144), 133 (108-165) $p<0.001$]. No substantial differences were observed between the groups in the remaining assessed data. The baseline clinical, demographic, and laboratory features of patients with MICAD and MINOCA are presented and compared in Table 1.

Table 2 summarizes univariate and multivariate models for predicting MINOCA in AMI patients. A univariate regression analysis identified age, female sex, and LDL cholesterol levels as predictors of MINOCA. Multivariate analyses indicated that only female sex and LDL cholesterol levels were independent predictors (OR=1.417, 95% CI 1.112-2.018, $p=0.048$; OR=0.992, 95% CI 0.985-0.998, $p=0.017$). Figure 1 shows the cumulative survival curves of patients with MINOCA and MICAD and demonstrates no statistically significant difference in survival between the two groups (log-rank=0.390, $p=0.532$).

DISCUSSION

Our study of MINOCA patients in the Turkish population identified female sex and low LDL cholesterol levels as independent predictors of MINOCA in the setting of AMI. These findings provide new insights into the literature.

Our finding that female gender is an independent risk factor for MINOCA corroborates prior studies showing that MINOCA predominantly affects women. A recent extensive meta-analysis conducted by Ang et al. (14) revealed that 59.5% of patients with MINOCA were female. Our study determined this ratio to be 50.6%. Vranken et al. (15) determined this ratio to be 51.5%. The MINOCA-TR study, conducted in Türkiye, revealed that MINOCA was considerably more prevalent among women (16). This sex difference is likely multifactorial. Estrogen plays a pivotal role in maintaining endothelial homeostasis by up-regulating nitric oxide synthase and reducing oxidative stress (17). Following menopause, the decline in estrogen levels contributes to endothelial dysfunction and microvascular dysregulation, which can lead to coronary microvascular disease, a well-recognized mechanism in MINOCA pathogenesis (18). Takotsubo syndrome contributes significantly to MINOCA (observed in roughly 1.2-2.2% of AMI patients) and is more prevalent among postmenopausal women (19,20).

Vasospasm or endothelial dysregulation can transiently obstruct coronary flow, a phenomenon that is more prevalent in women (21). Spontaneous coronary artery dissection predominantly occurs in women younger than 50 years (22). These mechanisms underline the importance of considering sex-specific pathophysiological differences when evaluating MINOCA.

Our study showed that MINOCA patients were markedly older than MICAD patients. However, multivariate analysis revealed that older age was not an independent risk factor. This may contradict numerous studies indicating that MINOCA patients tend to be younger (8,14). Nevertheless, the majority of our MINOCA patients are women, and numerous studies have indicated that women with MINOCA are older than men with MINOCA (23,24). This finding may reflect the confounding effect of the sex distribution, because women, who constituted a greater proportion of MINOCA cases, were generally older.

A comprehensive meta-analysis by Pasupathy et al. (25) reported significantly reduced 1-year all-cause mortality in MINOCA patients compared with MICAD patients; however, our study found no significant difference between the two cohorts. This may result from a restricted study population and the higher mean age of the MINOCA group; the latter may contribute to higher mortality.

Table 1. Baseline clinical, demographic, and laboratory characteristics of patients diagnosed with myocardial infarction with non-obstructive coronary arteries (MINOCA) and those with myocardial infarction with coronary artery disease (MICAD)

	Patients with MICAD (n=1076)	Patients with MINOCA (n=87)	p-value
Age, years	57.4±17.7	64.5±13.2	<0.001
Gender, male %	723 (67.2%)	44 (49.4%)	0.002
Body mass index, kg/m^2	28.1 (26.0-29.4)	28.0 (26.2-29.2)	0.647
Hypertension, %	371 (34.5%)	32 (36.8%)	0.664
Diabetes mellitus, %	218 (20.3%)	17 (19.5%)	0.872
Hyperlipidemia, %	728 (67.7%)	55 (63.2%)	0.396
Smoking, %	77 (7.2%)	4 (4.6%)	0.341
Coronary artery ectasia, %	57 (5.3%)	6 (6.9%)	0.463
Coronary slow flow, %	91 (8.5%)	10 (11.5%)	0.353
Atrial fibrillation, %	154 (14.3%)	16 (18.4%)	0.315
Left ventricle ejection fraction, % <30% 30-50% >50%	 108 (10.0%) 251 (23.3%) 717 (66.6%)	 11 (12.6%) 19 (21.8%) 57 (65.5%)	 0.454 0.750 0.832
Hemoglobin g/dL	13.6 (12.0-14.7)	13.1 (11.7-14.7)	0.359
Neutrophils cells/µL	7.50 (5.70-9.00)	7.30 (5.50-9.00)	0.365
Platelets/mm^3	234 (191-273)	224 (190-272)	0.482
Lymphocytes/mm^3	1.8 (1.4-2.5)	1.8 (1.3-2.5)	0.388
Glucose, mg/dL	117 (99-156)	118 (99-157)	0.933
Creatinine, mg/dL	0.90 (0.80-1.20)	0.89 (0.81-1.19)	0.135
AST U/L	25 (19-44)	24 (19-37)	0.557
ALT U/L	20 (16-32)	20 (16-31)	0.623
Triglyceride, mg/dL	131 (105-179)	130 (99-177)	0.562
LDL cholesterol, mg/dL	133 (108-165)	112 (96-144)	<0.001
HDL cholesterol, mg/dL	36 (30-42)	36 (31-45)	0.170
Hs-CRP, mg/dL	3.1 (1.8-4.9)	2.6 (1.6-4.7)	0.171
Hs-troponin, ng/mL	0.39 (0.11-3.40)	0.30 (0.10-1.74)	0.222
TSH, mIU/L	1.2 (0.7-1.7)	1.0 (0.6-1.7)	0.230
Albumin g/dL	3.7 (3.0-3.9)	3.5 (3.0-3.8)	0.242
1-year mortality	96 (8.9%)	6 (6.9%)	0.507

MICAD: Myocardial infarction with coronary artery disease, MINOCA: Myocardial infarction with non-obstructive coronary arteries, BMI: Body mass index, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, Hs-CRP, High-sensitivity C-reactive protein, Hs-troponin: High-sensitivity troponin, TSH: Thyroid-stimulating hormone

Table 2. Univariable analysis and multivariable model for MINOCA occurrence according to admission parameters

Univariable analysis	p-value	OR (95% CI)	Multivariable analysis	p-value	OR (95% CI)
Age	0.003	1.027 (1.012-1.042)	Age	0.071	1.014 (0.989-1.039)
Female gender	0.002	2.002 (1.290-3.105)	Female gender	0.048	1.417 (1.112-2.018)
LDL cholesterol	0.031	0.993 (0.986-0.999)	LDL cholesterol	0.017	0.992 (0.985-0.998)

OR: Odds ratio, CI: Confidence interval, LDL: Low-density lipoprotein

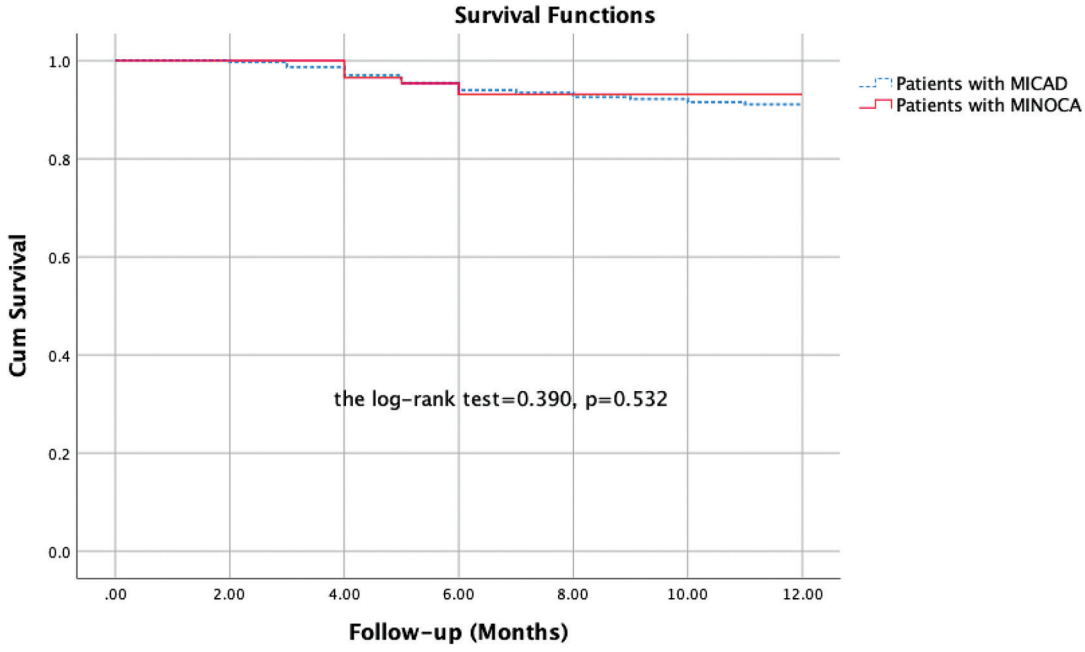

Figure 1. The cumulative survival curves of patients with MINOCA and MICAD
MICAD: Myocardial infarction with coronary artery disease, MINOCA: Myocardial infarction with non-obstructive coronary arteries

Although MINOCA is considered a low-risk condition, some patients may experience adverse outcomes, including death, recurrent myocardial infarction, and heart failure. Multiple studies have demonstrated that negative outcomes are more prevalent among women. This may be particularly evident in postmenopausal elderly populations (23,26).

Patients aged over 90 years were excluded from this study for clinical and methodological reasons. The rationale for this, particularly in patients aged over 90, reflects a marked increase in comorbidities, frailty, polypharmacy, and age-related decline in physiological reserve. Moreover, troponin elevations in older adults are often associated with concomitant non-cardiac diseases. This complicates clinical interpretation for both MINOCA and MICAD diagnoses and may diminish the specificity of biomarkers and invasive diagnostic assessments (27,28).

One novel finding of this study was that low LDL cholesterol levels were an independent risk factor for MINOCA in patients with AMI. Abdu et al. (29) study in a Chinese population identified significantly lower LDL cholesterol levels in MINOCA patients. In a study by Sucato et al. (30), LDL levels were lower in the MINOCA group; however, this difference was not statistically significant. Patients with MICAD typically have a greater extent of atherosclerotic plaque accumulation and more stable plaques. Conventional risk factors, including hypertension, diabetes mellitus, smoking, and hyperlipidemia, are prevalent in this patient population (31). Nonetheless, MINOCA patients typically demonstrate a reduced plaque burden attributable to mechanisms including microvascular dysfunction, coronary spasm, or plaque erosion or fracture (32). Therefore, low LDL cholesterol may serve as an independent risk factor for patients with MINOCA.

Our findings underscore the necessity for sex-specific diagnostic methods and thorough etiological studies in patients with AMI and suspected MINOCA. In the survival analysis, no significant difference in one-year survival was observed between the MINOCA and MICAD groups. Although MINOCA has traditionally been considered to have a more favorable prognosis, our results suggest that MINOCA can lead to adverse outcomes comparable to MICAD, emphasizing that it is not a benign condition. Future studies should focus on amalgamating biochemical, imaging, and hormonal profiles to enhance risk classification and tailor treatment.

Study Limitations

The retrospective design, single-center focus, and restricted sample size of this study constrain the generalizability of the results. Systematic application of advanced imaging techniques, such as cardiac magnetic resonance imaging or intracoronary imaging, was lacking, potentially constraining the identification of certain etiologies. Biomarker values were evaluated solely at baseline and may not reflect temporal variations. Further, meticulously designed prospective multicenter trials are required to validate and enhance our findings.

CONCLUSION

In conclusion, female sex and low LDL cholesterol levels were identified as independent predictors of MINOCA among Turkish patients with AMI. These findings underscore the necessity of examining non-atherosclerotic causes, especially in women with low LDL levels, and of identifying MINOCA as a distinct clinical entity with specific demographic and biochemical characteristics.

*Ethics

Ethics Committee Approval: This study was approved by İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (decision no: 1272, date: 30.10.2025).

Informed Consent: Written informed consent was obtained from all patients prior to the procedure.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.İ., Concept: E.K., Design: K.K., G.İ., Data Collection or Processing: M.Ö., E.K., Analysis or Interpretation: K.K., Literature Search: M.Ö., T.Ç., Writing: K.K., K.G., M.İ.H.

Conflict of Interest: The authors declare no conflict of interest.

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