

Editorial Comment / Editöryal Yorum

Evaluation of demographic and clinical characteristics of female patients presenting with MINOCA

MINOCA ile başvuran kadın hastaların demografik ve klinik özelliklerinin değerlendirilmesi

Merih Kutlu, M.D. 

Department of Cardiology, Karadeniz Technical University School of Medicine, Trabzon, Turkey

Myocardial infarction with non-obstructive coronary arteries (MINOCA), which is a heterogeneous group of cardiovascular disorders, was first reported over 80 years ago.^[1] MINOCA is characterized by clinical evidence of the universal myocardial infarction criteria with less than 50% coronary artery stenosis on coronary angiography. MINOCA is a syndrome with a number of possible pathophysiologic mechanisms suggested, including coronary arterial dissection, coronary microvascular disorder (CMD), coronary arterial embolization, and endothelial dysfunction. MINOCA occurs in 5%-15% in patients with ST-segment elevation MI or non-ST segment elevation MI (NSTEMI).^[2,3] Accurate diagnosis may require additional testing, including intracoronary imaging studies with intravascular ultrasound or optical coherence tomography, echocardiography, cardiac magnetic resonance imaging, and provocative testing for coronary vasospasm.^[4] The prognosis is highly variable, depending on the cause of MINOCA, including increased risk for re-infarction and all-cause mortality. The optimal therapy for patients with MINOCA remains unclear.^[5]

Compared with patients with myocardial infarction with obstructive coronary arteries (MIOCA), patients with MINOCA are more likely to be younger and female and less likely to be associated with traditional coronary artery disease risk factors; including dyslipidemia, hypertension, and diabetes mellitus.^[2,6] In the VIRGO study,^[4] factors associated with MINOCA in-

cluded female sex, younger age (<55 years), genetics, and physiological stress. Data from >750 hospitals in the USA from 2007 to 2014 indicate that MINOCA occurs in more women (10.5%) presenting with myocardial infarction (MI) more than in men (3.4%).^[7]

Female patients with MINOCA may be associated with vasomotor disorders and CMD owing to inflammation, mental stress, and autonomic and neuroendocrine dysfunction, which predispose them to endothelial dysfunction and CMD.^[8] This condition indicates a predominant role of non-atherosclerotic related etiologies and risk factors in patients with MINOCA.

Although the prognosis of patients with MINOCA is better than that of patients with MIOCA, the survival rate of patients with MINOCA is worse than that of healthy individuals.^[6] Female patients with MINOCA may have more adverse cardiac events, including non-fatal acute myocardial infarction (AMI), non-fatal stroke, and heart failure hospitalization than male patients with MINOCA.^[9] In the

Abbreviations:

| | |
|-----------|--|
| AMI | Acute myocardial infarction |
| CMD | Coronary microvascular disorder |
| MI | Myocardial infarction |
| MINOCA | Myocardial infarction with non-obstructive coronary arteries |
| MINOCA-TR | Myocardial Infarction with Non-Obstructive Coronary Arteries in Turkish Population |
| MIOCA | Myocardial infarction with obstructive coronary arteries |
| NSTEMI | Non-ST segment elevation myocardial infarction |



SWEDHEART registry,^[5] 22% of the patients with MINOCA who developed re-infarction died during the 2.3-year follow-up, and half of the deaths were attributed to cardiovascular reasons. Opolski et al.^[10] investigated 38 patients with MINOCA using optical coherence tomography and magnetic resonance and found that MINOCA was often associated with atherosclerotic plaque disruption, thrombosis, and myocardial ischemic injury.

The treatment of MINOCA requires an individualized approach depending on the underlying diagnosis. At present, there are no specific treatment recommendations for MINOCA because of a paucity of data from randomized controlled trials on treatment in MINOCA. The SWEDHEART registry^[11] showed that treating MINOCA with angiotensin-converting enzyme inhibitors/angiotensin receptor II blockers and statins has a long-term effect on favorable outcomes, and beta-blockers demonstrated a positive trend; but no benefits were observed with dual antiplatelet therapy. Bossard et al.^[12] suggested that antiplatelet treatment may be harmful in patients with MINOCA, and therefore, should not be routinely used. The most appropriate treatment should be selected on the basis of etiology.

In this issue of Archives of Turkish Society of Cardiology, Gök et al.^[13] investigated potential demographic and clinical differences between female patients diagnosed with MINOCA and MIOCA. The article is the first study to evaluate clinical and demographic findings of women with MINOCA in a Turkish population and to compare these findings with male patients with MINOCA. This study was a multicenter, observational cohort study conducted in Turkey in 2018, a subgroup analysis of the Myocardial Infarction with Non-Obstructive Coronary Arteries in Turkish Population (MINOCA-TR) study. This study included 477 female patients diagnosed with AMI. Among them, 49 were diagnosed with MINOCA, and 428 had MIOCA. The number of patients in the MINOCA group was higher than in the MIOCA group, and those with MINOCA were younger than those with MIOCA. The frequencies of diabetes mellitus, hyperlipidemia, and hypertension were lower in the MINOCA group than in the MIOCA group. The MINOCA group had higher rates of recent flu history and NSTEMI than the MIOCA group. When clinical characteristics of female patients with MINOCA

were compared with those of male patients with MINOCA, the female patients were older, obese, had lower hemoglobin levels, and higher frequency of hypertension. The rate of smoking in female patients with MINOCA was higher than that in the general female population on the basis of data from the Turkish Statistical Institute.^[14] Female patients with MIOCA were older and had higher rates of hypertension, hyperlipidemia, and diabetes mellitus than female patients with MINOCA. This study showed that traditional coronary artery disease risk factors were lower in female patients with MINOCA than those with MIOCA. In addition, age, diabetes mellitus, hypertension, hyperlipidemia, and NSTEMI were independent predictors of MINOCA.

The increase in age-related cardiovascular risk factors in female patients with MINOCA may be sharper than that in male patients with MINOCA. General, clinical, and demographic characteristics and cardiovascular risk factors in female patients with MINOCA may differ from that of male patients with MINOCA. Tokgözoğlu et al.^[15] have shown that cardiovascular risk factors are higher in the Turkish female population. The EUROASPIRE study^[16] showed that hypertension, diabetes mellitus, obesity, and hyperlipidemia were higher in women than in men. Similar to the EUROASPIRE study, Gök et al.^[13] observed that female MINOCA patients had higher rates of obesity and hypertension. Differently, hyperlipidemia and diabetes mellitus were similar.

As indicated by the authors, important limitations in the subgroup analysis of the MINOCA-TR study, including the very small number of female patients with MINOCA, the lack of a short-term and long-term prognosis, and specific risk factors related to women were not questioned. Furthermore, the treatment and laboratory tests were unknown, and other possible reasons for MINOCA were not assessed using non-invasive and invasive diagnostic modalities. Moreover, this study may not reflect the global perspective.

Additional limitations of this article could be the lack of enrollment of patients according to country population distribution and the significant age difference between the men and women with MINOCA that could affect the results of the sex comparison. The age difference between women with MIOCA and MINOCA probably affects the clustering of risk

factors. In addition, the difference observed in the general population of Turkish women with MINOCA could be owing to the small number of the study population and the age difference.

Although there are significant limitations, this is the first study that investigated the demographic and clinical features of female patients with MINOCA and compare these with that of male patients with MINOCA in a Turkish population. This study also demonstrated that MINOCA is not a benign condition. This trial increased awareness of gender differences in patients with MINOCA and highlighted the need for further studies to investigate the underlying pathophysiologic mechanism and treatment in female patients with MINOCA.

Conflict of interest: None.

REFERENCES

- Gross H, Sternberg WH. Myocardial infarction without significant lesions of coronary arteries. *Arch Intern Med* 1939;64:249-67. [Crossref]
- Tamis-Holland JE, Jneid H, Reynolds HR, Agewall S, Brilakis ES, Brown TM, 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. [Crossref]
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. *J Am Coll Cardiol* 2018;72:2231-64. [Crossref]
- Safdar B, Spatz ES, Dreyer RP, Beltrame JF, Lichtman JH, Spertus JA, 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. [Crossref]
- Nordenskjöld AM, Lagerqvist B, Baron T, Jernberg T, Hadziosmanovic N, Reynolds HR, et al. Reinfarction in patients with myocardial infarction with nonobstructive coronary arteries (MINOCA): coronary findings and prognosis. *Am J Med* 2019;132:335-46. [Crossref]
- Pizzi C, Xhyheri B, Costa GM, Faustino M, Flacco ME, Gulalano MR, et al. Nonobstructive versus obstructive coronary artery disease in acute coronary syndrome: a meta-analysis. *J Am Heart Assoc* 2016;5:e004185. [Crossref]
- Mahajan AM, Gandhi H, Smilowitz NR, Roe MT, Hellkamp AS, Chiswell K, et al. Seasonal and circadian patterns of myocardial infarction by coronary artery disease status and sex in the ACTION Registry-GWTG. *Int J Cardiol* 2019;274:16-20. [Crossref]
- Sedlak TL, Lee M, Izadnegahdar M, Merz CN, Gao M, Humphries KH. Sex differences in clinical outcomes in patients with stable angina and no obstructive coronary artery disease. *Am Heart J* 2013;166:38-44. [Crossref]
- Ciliberti G, Coiro S, Tritto I, Benedetti M, Guerra F, Del Pinto M, et al. Predictors of poor clinical outcomes in patients with acute myocardial infarction and non-obstructed coronary arteries (MINOCA). *Int J Cardiol* 2018;267:4145. [Crossref]
- Opolski MP, Spiewak M, Marczak M, Debski A, Knaapen P, Schumacher SP, et al. Mechanisms of myocardial infarction in patients with nonobstructive coronary artery disease: results from the optical coherence tomography study. *JACC Cardiovasc Imaging* 2019;12:2210-21. [Crossref]
- Lindahl B, Baron T, Erlinge D, Hadziosmanovic N, Nordenskjöld A, Gard A, Jernberg T. Medical therapy for secondary prevention and long-term outcome in patients with myocardial infarction with nonobstructive coronary artery disease. *Circulation* 2017;135:1481-9. [Crossref]
- Bossard M, Yusuf S, Tanguay JF, Faxon DP, Boden WE, Steg PG, et al. Recurrent cardiovascular events and mortality in relation to antiplatelet therapy in patients with myocardial infarction without obstructive coronary artery disease (MINOCA). *Eur Heart J* 2019;40:2387. [Crossref]
- Gök G, Çoner A, Çınar T, Kılıç S, Yenerçay M, Öz A, et al. Evaluation of demographic and clinical characteristics of female patients presenting with MINOCA and differences between male patients: a subgroup analysis of MINOCA-TR registry. *Türk Kardiyol Dern Ars* 2022;50:XX-XX.
- TUIK. Available at: <https://data.tuik.gov.tr/Bulten/Index?p=Istatistiklerle-Kadin-2020-37221>. Accessed July 9, 2021.
- Tokgözoğlu L, Kayıkçioğlu M, Ekinci B. The landscape of preventive cardiology in Turkey: challenges and successes. *Am J Prev Cardiol* 2021;6:100184. [Crossref]
- Tokgözoğlu L, Kayıkçioğlu M, Altay S, Aydoğdu S, Barçın C, Bostan C, et al. EUROASPIRE-IV: Avrupa Kardiyoloji Derneği'nin koroner arter hastalarında yaşam tarzı, risk faktörleri ve tedavi yaklaşımı üzerine çalışması: Türkiye verileri [EUROASPIRE-IV: European Society of Cardiology study of lifestyle, risk factors, and treatment approaches in patients with coronary artery disease: Data from Turkey]. *Türk Kardiyol Dern Ars* 2017;45:134-44. [Crossref]