Clinical Practices Applied To Patients With Myocardial Infarction Non-obstruction Coronary Arteries (Minoca)

RESUMO | Objetivo: Identificar práticas clínicas com resultados favoráveis aos pacientes com diagnóstico de infarto agudo do miocárdio sem obstrução de artéria coronária. Método: Revisão integrativa da literatura pela base de dados National Library of Medicine e Biblioteca Virtual de Saúde de estudos publicados entre 2018 e 2022. Resultados: 87,5% dos estudos encontraram estratégias farmacológicas e destes, 62,5% citaram o uso da dupla antiagregação plaquetária como mais utilizada, apesar de nenhum estudo evidenciar benefícios. Os inibidores do sistema renina-angiotensina-aldosterona comprovaram benefícios em três estudos. 75% dos artigos apontaram que esse grupo de pacientes recebeu menos medicamentos preventivos comparado aos pacientes com infarto por obstrução coronariana. Outros seis estudos revelaram condução clínica variável desses pacientes. Conclusão: O uso de inibidores do sistema renina-angiotensina-aldosterona deve ser considerado por ser a única medicação com redução da mortalidade evidenciada. São necessários estudos maiores para orientar com mais segurança à condução do infarto do miocárdio sem obstrução de coronária.

Descritores: Infarto do miocárdio sem obstrução de artéria coronária; Terapêuticas; Tratamento; Tomada de decisão clínica

ABSTRACT | Objective: To identify clinical practices with favorable results for patients diagnosed with acute myocardial infarction without coronary artery obstruction. Method: Integrative literature review using the National Library of Medicine and Virtual Health Library databases of studies published between 2018 and 2022. Results: 87.5% of the studies found highlighted pharmacological strategies and of these, 62.5% cited the use of dual antiplatelet therapy as the most used, despite no study showing benefits. Inhibitors of the renin-angiotensin-aldosterone system have shown benefits in three studies. 75% of the articles pointed out that this group of patients receive less preventive medication compared to patients with infarction due to coronary obstruction. Another six studies revealed variable clinical management of these patients. Conclusion: The use of renin-angiotensin-aldosterone system inhibitors should be considered as it is the only medication with proven reduction in mortality. Larger studies are needed to guide with more safety the management of myocardial infarction without coronary obstruction.

Keywords: Myocardial infarction without coronary artery obstruction; Therapeutics; Treatment; clinical decision making

INTRODUCTION

Acute myocardial infarction (AMI) is defined as the death of myocardial cells due to prolonged ischemia. To identify ischemia of the myocardial muscle, the elevation of troponin is evaluated, which is an enzyme that has a higher specificity in relation to the cardiac muscle. (1)

The fourth universal definition of myocardial infarction of 2018 by the European
Society of Cardiology (ESC) defined acute myocardial infarction with non-obstructive coronary arteries (Myocardial Infarction Non Obstructive Coronary Arteries - MINOCA). For its diagnosis, it is necessary that the patient presents the clinical criteria for myocardial infarction, in addition to not finding any obstruction greater than or equal to 50% of the lumen of an epicardial artery observed on coronary angiography. MINOCA is an initial diagnosis that has several etiological possibilities. The main ones can be divided into ischemic and non-ischemic causes.

With regard to its epidemiological characteristics, divergences from those found in AMI due to atherosclerotic obstruction are observed. A greater involvement was observed in female, non-white and younger people, under 55 years of age.

It is observed that patients with MINOCA represent a great therapeutic challenge, and their management is based on still limited evidence. It was believed that the patients had a benign prognosis, however, studies carried out with patients who had a heart attack without significant coronary obstruction identified an increased risk of death and of new major adverse cardiovascular events (MACE).

Since there are several possible pathophysiological mechanisms that cause this syndrome, it is not certain that the classic secondary prevention and treatment strategy used for AMI with coronary obstruction is ideal for all patients with MINOCA.

Considering the complexity in etiological identification and the limited consensus regarding diagnostic methods and ideal treatment, the clinical management of these patients is still an unresolved issue. Given these facts, it is necessary for health professionals to keep up to date with regard to therapeutic strategies that have shown better results. This study proposes to investigate such strategies, with the guiding question “what are the differences in clinical practices applied to patients diagnosed with infarction without significant coronary lesions - MINOCA?”

**METHOD**

An integrative literature review was carried out in which the first step was the elaboration of the guiding question according to the PICO strategy, the second consisted of searching or sampling the literature in the databases, the third, the collection of articles, the fourth, critical analysis of the articles included, the fifth, discussion of the results and, finally, the sixth step, which was the presentation of the integrative review.

The research was carried out using the National Library of Medicine (PubMed) database and the Latin American Health Sciences Literature (LILACS) and ScientificElectronic Library Online (SciELO) databases, using the Virtual Health Library metabase (VHL).

The controlled terms (DeCS/MeSH descriptors) and free terms (keywords) selected for the search were “MINOCA”, “Myocardial Infarction with non obstructive Coronary Arteries”, “Therapeutics”, “Treatment” and “Clinical Decision-Making”. The search strategy was elaborated using the Boolean operators OR and AND.

The inclusion criteria adopted were: primary studies in English, Spanish and Portuguese, published in the years 2018 to 2022 and available in full. Exclusion criteria were duplicate studies, those that did not meet the main objective of the review, in addition to studies still in progress.

The selected articles and the Qualis/CAPES of the works are shown in Table 1. The Qualis/CAPES (13) is a scientific production evaluation index used in Brazil, listed from A1 (highest relevance) to C (low relevance). The path of the findings is shown in the flowchart of Figure 01.
RESULTS

The sample of this study consisted of 8 articles as shown in Table 01.

Table 01- Sample of articles selected after analysis of the full text, carried out from September to November 2022

<table>
<thead>
<tr>
<th>Author/ Year/ Country</th>
<th>Therapeutic strategy used in MINOCA and results</th>
<th>Journals/ Qualis</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAFDAR, B. et al., 2018 U.S.A.</td>
<td>Patients diagnosed with MINOCA tend to receive fewer secondary preventive medications and cardiac rehabilitation.</td>
<td>Journal of the American Heart Association A1</td>
<td>Observational Prospective</td>
</tr>
<tr>
<td>PALIOSSO, P. et al., 2019 Italy</td>
<td>RAAS inhibitors provide medium-term beneficial effects on outcomes in MINOCA patients. In contrast, dual antiplatelet, beta-blocker, and statin therapy had no effects on mortality and major adverse cardiovascular events.</td>
<td>Frontiers in pharmacology B4</td>
<td>Observational Prospective</td>
</tr>
<tr>
<td>GAIOR, P. et al., 2020 Poland</td>
<td>Most patients with MINOCA received conventional treatment for AMI. Patients with MINOCA received fewer preventive medications.</td>
<td>Journal of Clinical Medicine B4</td>
<td>Observational Prospective</td>
</tr>
<tr>
<td>SÁ, F.M. et al., 2020 Portugal</td>
<td>Dual antiplatelet therapy (DAPT) was primarily prescribed to patients in MINOCA subgroups who were more prone to thrombotic events</td>
<td>Revista Portuguesa de Cardiologia B3</td>
<td>Prospective Cohort</td>
</tr>
<tr>
<td>REYNOLDS, H.R. et al., 2021 U.S.A.</td>
<td>Multimodal imaging with optical coherence tomography (OCT) and cardiac magnetic resonance imaging (CMR) identified the cause of MINOCA in 84.5% of the women in the study, demonstrating that identification of the cause of MINOCA is feasible and has the potential to guide medical therapy for secondary prevention.</td>
<td>Circulation AHA A1</td>
<td>Observational Prospective</td>
</tr>
<tr>
<td>AHN, J.H. et al., 2021 Korea</td>
<td>ACE was superior to ARBs in reducing the risk of recurrence of infarction in patients with MINOCA, making it the most indicated first-line treatment for this group.</td>
<td>Cardiology Journal B2</td>
<td>Prospective Randomized</td>
</tr>
<tr>
<td>GAO, S. et al., 2021 China</td>
<td>Among patients with MINOCA who received dual antiplatelet therapy, it was found that ticagrelor, compared to clopidogrel, was not associated with a significant difference in the risk of MACE or bleeding events at a median follow-up of 3.5 years.</td>
<td>Frontiers in Cardiovascular Medicine B4</td>
<td>Cohorte Prospectivo</td>
</tr>
<tr>
<td>SMILOWITZ, N.R. et al., 2021 U.S.A.</td>
<td>High variability in prescription of ACE inhibitors, ARBs and Beta-blockers for patients with MINOCA, in addition to caution regarding the routine use of these agents before elucidating the definitive cause of MINOCA</td>
<td>PlosOne A2</td>
<td>Observational Prospective</td>
</tr>
</tbody>
</table>

Source: Research data, 2022.
coronary obstruction. (14-17,20,21) Still in this context, six studies stated that there is variability in the clinical management of these patients. (14-20,21)

In addition, it was possible to verify in 37.5% (n=3) of the studies, a high incidence of patients who were discharged from the hospital without elucidating the underlying cause of MINOCA. (14,16,20) It was also exposed by 75% (n=6) of the articles, that patients with MINOCA may have unfavorable clinical outcomes, with major cardiovascular events that include all-cause mortality, cardiac death, stroke and myocardial reinfarction. (14-17,21,22) Finally, 87.5% (n=7) of the studies stated that larger studies are needed so that the management of patients with MINOCA is more homogeneous and effective. (14-17,19-21)

**DISCUSSION**

In this review, the incidence of MINOCA compared to AMI due to arterial obstruction varied greatly, ranging from 2.94% (15) to 56.48%. (17) Previous studies have already demonstrated divergent incidences. (1,2) It was also observed that, in studies where cardiac catheterization was more frequent and the included population was younger, MINOCA rates were higher. (14,16,18) In the study with the highest incidence, among the participating individuals, the population was composed only of women. (18)

The initial impression in studies involving MINOCA was that subjects had a benign prognosis. (6) It was found that these patients may have major cardiac events in proportions similar to those of patients with AMI due to coronary artery obstruction, and may also develop heart failure, cardiogenic shock, cardiac arrest and even death. (14,15,19)

It was also identified that there is great heterogeneity in the clinical management of these patients. (15-17,21) It has been observed that many cases of MINOCA receive prevention with DAPT less frequently than patients with AMI with coronary obstruction. Patients from subgroups classified as more prone to thrombotic events are the ones who receive the most DAPT in MINOCA, since professionals consider that the anti-platelet aggregation action can be beneficial for this subgroup, but even so, the indication of these agents in patients with MINOCA is not concrete. (17)

Therefore, a study revealed that P2Y12 inhibitors showed similar results in patients who used Ticagrelor and Clopidogrel in terms of prognosis and bleeding events, so there is no specific predilection between them in MINOCA initially. (20)

Still regarding the pharmacological strategy, in the SWEDEHEART REGISTRY study (2019) (2) indicated long-term beneficial effects of treatment with statins and RAAS inhibitors in patients with MINOCA, as well as a trend towards a positive effect of treatment with beta-blockers and a neutral effect of DAPT. (2) In this work, it was identified that RAAS inhibitors were the only drug class that reduced the mortality rate in these patients, (15) being the most indicated ACE inhibitor as it also reduces the risk of recurrent AMI, and should be considered as the first line of treatment. (19)

This work had important limitations. There are few original studies on the therapeutic management of MINOCA, which resulted in a small sample. The studies found were mostly observational and non-randomized, which allows considering the chance of bias in their results. It was not possible to identify clear or standardized evidence regarding therapeutic strategies for MINOCA, which confirms the need to carry out research with larger populations. No studies were found that address other non-drug therapeutic methods and multidisciplinary care for this group of patients.

**CONCLUSION**

The clinical management of patients diagnosed with MINOCA is still heterogeneous, with a tendency to use standardized strategies for cases of AMI with coronary obstruction, even without scientific evidence. It was observed that compared to patients with AMI due to coronary artery obstruction, individuals with MINOCA may be undertreated and receive less preventive medication. The use of RAAS inhibitors should be considered because it is the only medication with a reduction in mortality shown in studies, mainly ACE inhibitors, due to the reduction in the recurrence of acute myocardial infarction. The absence of studies that address non-pharmacological and multidisciplinary strategies favorable to MINOCA indicates an important gap to be explored. Larger, randomized, multicenter studies are needed to guide MINOCA with more confidence.
References


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