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MINOCA - Perhaps a Rare Post-Covid-19 Infection Cardiac Complication in Disguise – A Case Report

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Abstract

Background*: Myocardial infarction with non-obstructive coronary arteries (MINOCA) was first described over 80 years ago* ***(****1****)*** *as a heterogeneous group of conditions that include both atherosclerotic and non-atherosclerotic disease resulting in myocardial damage that is not due to obstructive coronary artery disease* ***(****2, 3****)****. MINOCA is now, referred to as a syndrome characterized by the clinical characteristics of myocardial infarction but with normal coronary arteries or no significant coronary stenosis on coronary angiography* ***(****4****)*** *and no overt cause for the clinical presentation at the time of Coronary Angiography* ***(****6****)****. Major advances in understanding this condition have been made in recent years. However, the precise pathogenesis of MINOCA is still unclear* ***(****9, 10****)****. However, recently during this Covid-19 pandemic, there have been few reports of incidence of MINOCA as a post- Covid-19 infection complication* ***(****10, 11****)****, particularly among female patients. There are also few reports of the occurrence of MINOCA following vaccination against Covid-19 infection. This case report shades light on one of such rare cases encountered in a tertiary care hospital in Bangladesh.*

Case Summary: *A 75-year-old hypertensive and diabetic lady presented with typical complaints indicating acute coronary syndrome. She had a previous history of a severe form of Covid-19 infection about six months back and had an approximate 45% lung involvement. However, following her recovery from Covid-19 infection, she got herself vaccinated against the Covid-19 virus. Following admission, diagnostic tests were run, results of which were found to be within normal range except high sensitive Troponin I which was found to be positive, ECG showed Antero-Inferior Ischemia and Echocardiogram showed hypokinesia of mid inferior wall. Considering the presenting complaints and lab parameters, she was initially suspected as a case of the acute coronary syndrome and was treated as per ACS management guidelines. However, her D. Dimer was found to be exceptionally high.*

For further evaluation, a Coronary Angiogram was performed which revealed normal epicardial coronaries and was recommended for medical management. Keeping in mind her previous history of severe Covid-19 infection and exceptionally high D.Dimer, the suspicion shifted towards excluding the possibilities of MINOCA and a complete investigation panel to exclude MINOCA was performed. Although her coagulation profile was found to be within normal range except D.Dimer, her Doppler study of both lower limbs revealed Deep vein thrombosis in right popliteal and posterior tibial veins along with mild subcutaneous oedema in both distal legs and CT Pulmonary Angiography revealed Pulmonary Thrombosis. These significant findings most certainly confirmed the suspicion towards the diagnosis of Pulmonary embolism.

Discussion: *The discussion of the case is focused on emphasizing the need to exclude MINOCA as one of the potential differential diagnoses whenever managing a case of ACS with normal coronaries in angiography, particularly when dealing with female cases with a history of COVID-19 infection or with a recent history of vaccination against Covid-19 virus. This is because this condition is more prone to develop thrombosis among women and is associated with 2-fold higher mortality. Moreover, it has been seen to occur as an isolated case among the Covid-19 vaccinated population as seen in this case. Thus, patients with MINOCA should receive the same clinical attention as Acute Myocardial Infarction (AMI) patients and should not be merely dismissed as having an insignificant clinical condition.*

Keywords*: ACS, MINOCA, Covid-19 Infection, Pulmonary Thrombosis, Deep vein thrombosis, CTPA.*

Learning Points:

- MINOCA should be excluded as one of the potential differential diagnoses whenever managing a case of ACS with normal coronaries in angiography, particularly when dealing with female cases with a recent history of COVID-19 infection or Covid-19 vaccination.
- MINOCA can present as an isolated case among the Covid-19 vaccinated population.
- Doppler study of both lower limbs, CT Pulmonary Angiography and Cardiac Magnetic Resonance Imaging are the potential diagnostic tools for MINOCA.
- Identifying the underlying cause of this heterogeneous syndrome – MINOCA is vital because that will determine appropriate therapy.
- Although the prognosis of MINOCA strongly depends on the underlying cause, its overall prognosis is serious, with a 1-year mortality of approximately 3.5%.
- Patients suffering from MINOCA should receive the same clinical attention as Acute Myocardial Infarction patients who have coronary artery disease and not merely be dismissed as having an insignificant clinical condition.

Introduction

Approximately 5–15% of the patients presenting with an acute coronary syndrome are found to have non-obstructive coronary arteries, defined as coronary stenosis <50% **(**5**)**. The term myocardial infarction (MI) with non-obstructive coronary arteries (MINOCA) has been assigned for this clinical entity **(**7**)** to emphasize investigating these patients to identify the underlying cause of their AMI presentation which represents a diagnostic and therapeutic dilemma **(**8**)**. Since even though this syndrome has been examined to a deeper extent over the past few years, many uncertainties exist regarding the pathophysiology of the myocardial damage, the clinical features, management and prognosis of these patients **(**8, 12**)**. As a result, the patients are often treated inappropriately or not treated at all **(**13**)**.

This case report aims to portray a case of MINOCA as a rare post-Covid-19 infection complication. The core intention of this piece of the research paper is to stress the importance of considering MINOCA as a dynamic and a potential diagnosis, particularly among female patients with a history of Covid-19 infection or recent intake of Covid-19 vaccination; to summarise the current understanding of MINOCA; to highlight important issues relating to the investigation, diagnosis and management of patients with MINOCA and to propose a clinical diagnostic algorithm which may lead to optimal treatment of this patient cohort.

Case presentation:

Clinical Course

A 75-year-old hypertensive and diabetic lady presented in the emergency department with typical complaints of chest pain along with profuse sweating, vomiting and cough indicating acute coronary syndrome. She was a known case of Lumber spine Spondylosis, Osteoarthritis, hypothyroidism and had a surgical history of Cholecystectomy about 30 years back. She had a history of hospital admission four years back and was treated for post-menopausal bleeding, Urinary tract infection and Vulvovaginitis. She had a previous history of a severe form of Covid-19 infection about six months back having approximately 45% lung involvement with which she was admitted and treated in hospital for almost a month. She was prescribed with anticoagulant Rivaroxaban for two weeks on discharge. However, following her recovery from Covid-19 infection, she got herself vaccinated. Considering these current complaints and past medical history, she was initially suspected as a case of acute coronary syndrome and was treated as per ACS management guidelines in the emergency department and later shifted to the Coronary Care Unit for further evaluation and management. On the following day, her laboratory investigation reports arrived, which revealed a picture that further supported the initial diagnosis of ACS. Her serial samples of high sensitive Troponin I were found to be positive; ECG showed Antero-Inferior Ischemia as shown in Figure 1. An echocardiogram showed regional wall motion abnormalities like hypokinesia of mid inferior wall, good left ventricular systolic function with LVEF – 60%; grade 1 diastolic dysfunction and valvular abnormality like Aortic Sclerosis as shown in Figure 2.

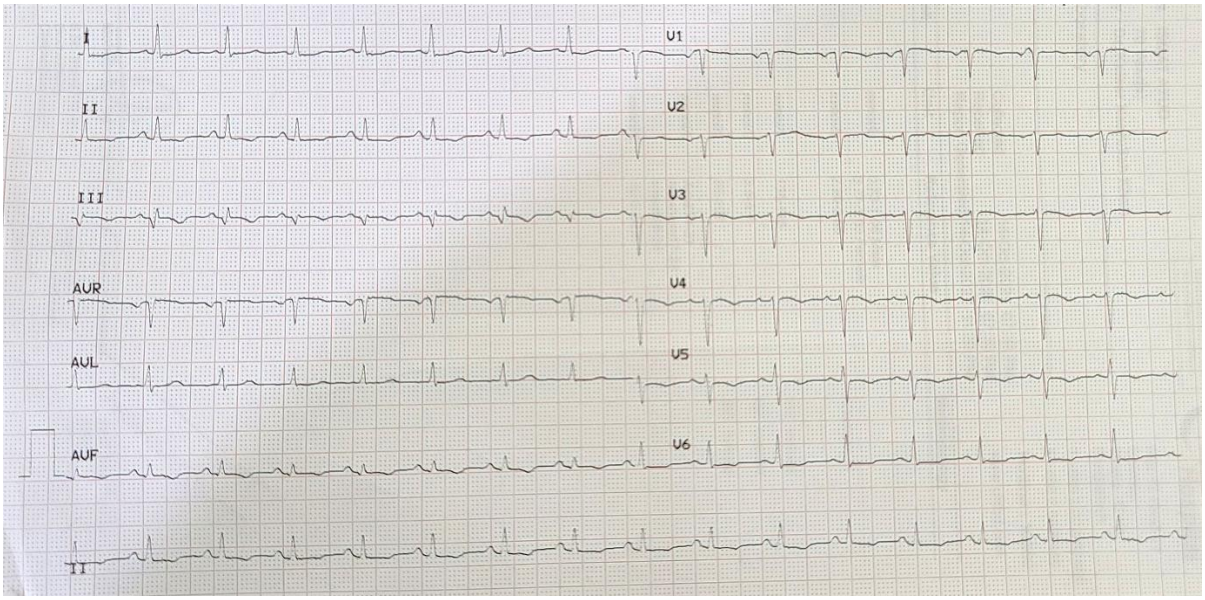


Figure 1: ECG showing Antero-Inferior Ischemia

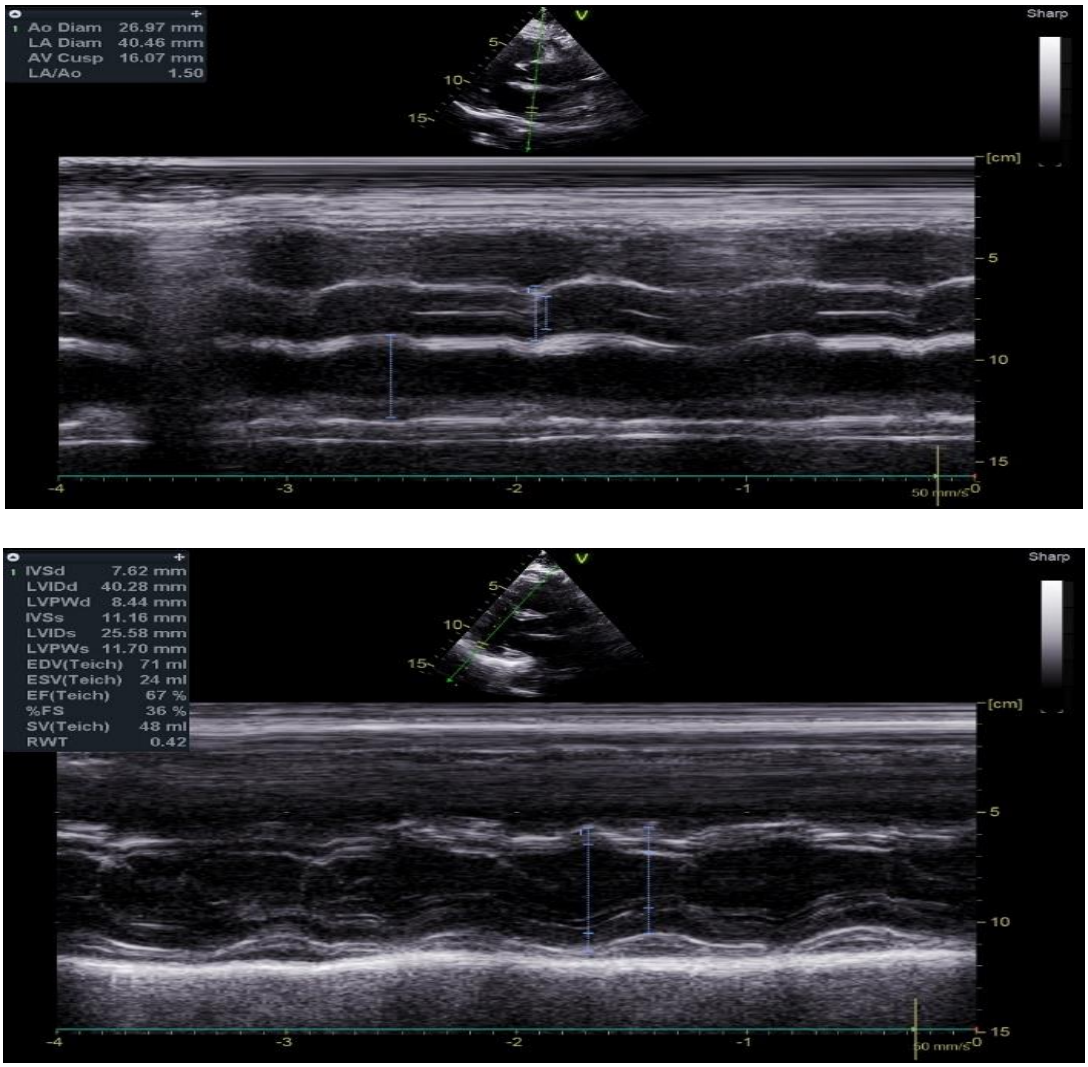


Figure 2: Echocardiogram showing regional wall motion abnormalities - hypokinesia of mid inferior wall, good left ventricular systolic function with LVEF – 60%; grade 1 diastolic dysfunction and valvular abnormality - Aortic Sclerosis

All other laboratory parameters were found within normal range except coagulation marker like the D. Dimer (16000 mcg /mL) which was exceptionally high. For further evaluation of her initial ACS-like symptoms, a Coronary Angiogram was performed on the following day after stabilization. However, despite having serial samples of high sensitive Troponin I positive indicating ACS, her Coronary Angiogram revealed normal epicardial coronaries and was recommended for medical management. Keeping in mind the recent history of severe Covid-19 infection and non-obstructive coronaries in angiogram despite clinical and diagnostic evidence suggesting ACS, now the suspicion shifted towards

excluding the possibilities of MINOCA – Myocardial Infarction with non-obstructive coronary arteries. However, regardless of the CAG outcome, the ongoing management using low molecular weight heparin was continued. In the meantime, a complete investigation panel to exclude MINOCA was performed, which included coagulation profile consisting D.Dimer, Ferritin, FDP, Fibrinogen, Anti-Thrombin III, Protein S, Protein C. Furthermore, imaging such as CT Pulmonary Angiography (CTPA), High-Resolution CT scan of Chest (HRCT-Chest) and Doppler study of both lower limbs were also done. Although her coagulation profile was found to be within normal range except D.Dimer (D.Dimer -16000 mcg /L , Ferritin -92 mcg /L, FDP – 31.34 mcg /mL, Fibrinogen – 4.37 g/L, Anti-Thrombin III – 97%, Protein S – 62%, Protein C -88%) her Doppler study of both lower limbs revealed Deep vein thrombosis in right popliteal and posterior tibial veins along with mild subcutaneous edema in both distal legs as shown in Figure 3 and CT Pulmonary Angiography revealed Pulmonary Thrombosis as shown in Figure 4 and High-Resolution CT scan of Chest revealed bilateral plate atelectatic and emphysematous changes.

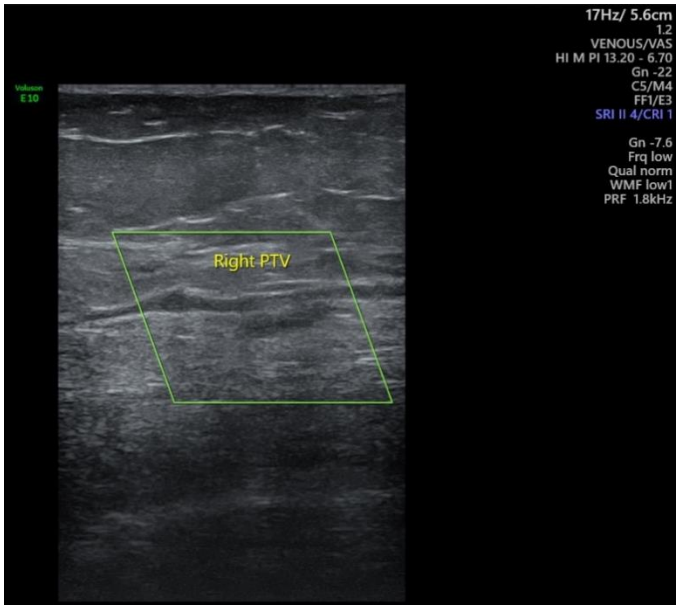


Figure 3: Doppler study of both lower limbs revealed Deep vein thrombosis in right popliteal and posterior tibial veins along with mild subcutaneous edema in both distal legs.

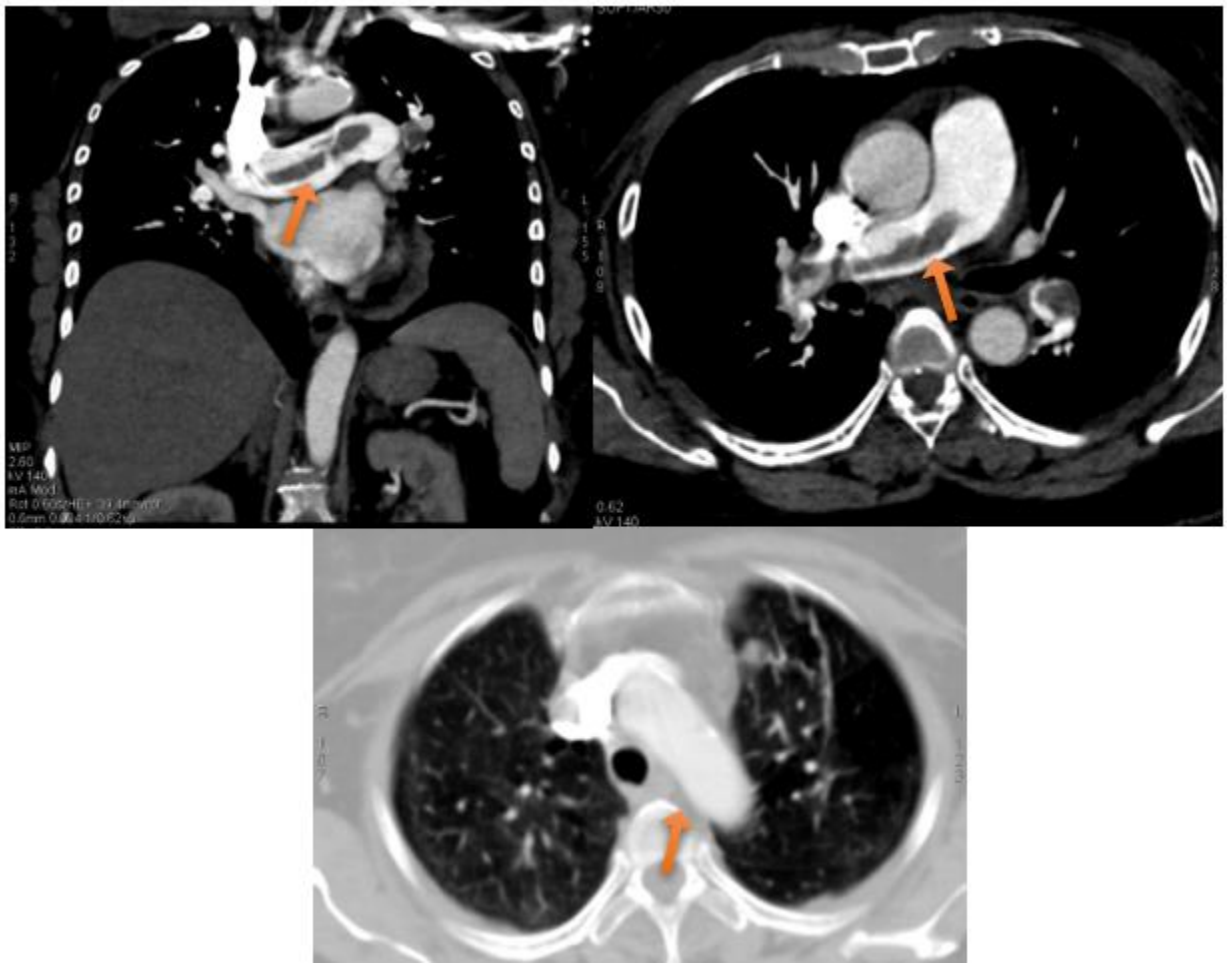


Figure 4: CT Pulmonary Angiography showing Pulmonary Thrombosis

These significant findings in the imaging investigation most certainly confirmed the suspicion towards the diagnosis of Pulmonary embolism which is one of the components of MINOCA. Despite reaching the final diagnosis of MINOCA later in her hospital stay following multiple stepwise arrays of investigation, she was receiving the accurate management for her disease condition using low molecular weight heparin since day one, which was continued up to ten days of hospital stay until the thrombus in her lower extremities became organized. Later, low molecular weight heparin was switched with oral anticoagulant Rivaroxaban and discharged with advice for follow-up after one month with the report of repeat- Doppler study of both lower limbs for tracking the response of the disease progression following treatment.

Discussion:

The discussion of the case is focused on emphasizing the need to exclude MINOCA as one of the potential differential diagnoses whenever managing a case of ACS with normal coronaries in angiography, particularly when dealing with female cases with a recent history of COVID-19 infection or following Covid-19 vaccination. This is because this condition is more prone to develop thrombosis among women **(**13, 14**)** and is associated with 2-fold higher mortality **(**15**)**. Moreover, it has been seen to occur as an isolated case among vaccinated patients of Covid-19 infection as seen in this case. The previous history of COVID-19 infection makes this group of the patient even more vulnerable to adverse consequences as recent studies **(**15, 16**)** have demonstrated a strong susceptibility of Post Covid-19 infection patients to develop pulmonary embolism (PE) with deep vein thrombosis (DVT) and even Ischemic stroke **(**17**)**. Nevertheless, the exact pathophysiology behind the coagulation abnormalities that create a hypercoagulable state in COVID-19 patients is still unclear and there is a potential need for further research in this area.

This case describes the presentation of a typical ACS case without obstructive coronary artery disease. As clinical history portrays, the patient was first admitted to the emergency department for signs of an acute coronary syndrome that was suspected for the rise of High sensitive Troponin I and corresponding ECG changes. Consequently, following stabilization, the patient was taken to the Cath lab for coronary angiography, which, however, showed normal epicardial coronary arteries free from obstructive disease. To exclude MINOCA, CT- Pulmonary Angiography was performed, which revealed Pulmonary Thrombosis and a Doppler ultrasonogram of both lower limbs was performed, which revealed Deep vein thrombosis. It is therefore plausible that the patient's ACS-like symptoms were due to MINOCA. However, due to prompt and appropriate drug therapy, any further serious consequence like Ischemic stroke **(**18**)** was avoided. Non-invasive techniques like Colour Doppler sonography and CTPA have proven to be an accurate and precise investigation tool in detecting the extension of deep venous thrombosis and Pulmonary embolism in this case. However, recent studies, showed that the diagnostic and prognostic impact of cardiovascular magnetic resonance imaging plays a vital role in assessing patients with suspected myocardial infarction with unobstructed coronary arteries **(**12, 19**)**. Therefore, CMR is strongly recommended by the European Society of Cardiology (ESC) **(**15**)**. However, CMR is recommended within 7 days of presentation because delayed imaging can sometimes result in some features no longer being evident **(**15**)**. Nevertheless, in this case, the diagnosis of MINOCA was essentially clinical because of the clear evidence of changes in ECG and a significant increase in the Troponin I in the absence of obstructive coronary artery disease, even though the CMR was not done. Myocardial infarction with non-obstructive coronary arteries (MINOCA) is still a puzzling clinical entity with different mechanisms of pathology. Therefore, it is uncertain whether the established management and prevention guidelines for Myocardial Infarction are optimal for MINOCA patients as well. However, the following are key points

are to be remembered when managing a case of Myocardial infarction with non-obstructive coronary arteries (MINOCA) as per AHA - American Heart Association Scientific Statement **(**20**)**:

- Patients with MINOCA are often younger women and less likely to have dyslipidemia **(**20**)**.
- Diagnosis of MINOCA should be made as per the Fourth Universal Definition of MI as shown in Figure 5, in the absence of obstructive coronary artery disease (no lesion ≥50%) **(**20**)**.

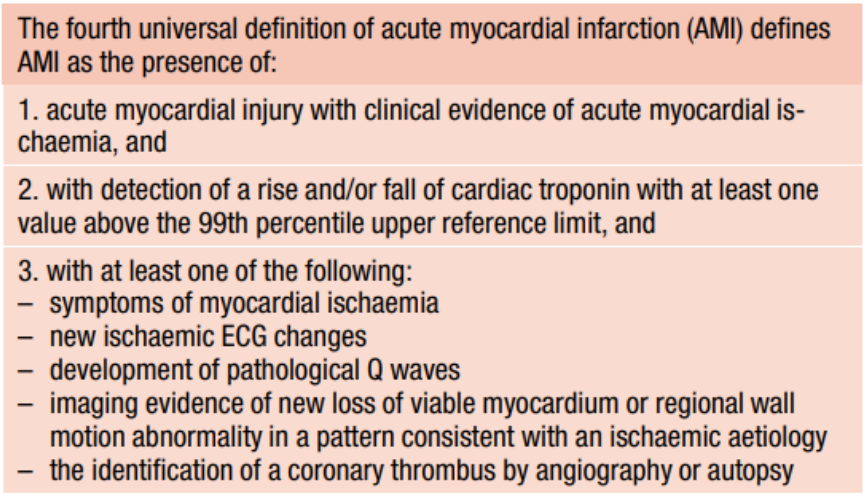


Figure 5: Showing the Fourth definition of AMI

- The diagnosis of MINOCA should exclude the following clinical entities as shown in Figure 6:
- a) Other overt causes for elevated Troponin (e.g., pulmonary embolism, sepsis, etc.),
- b) Overlooked obstructive coronary artery disease (e.g., distal stenosis or occluded small branches)
- c) Non-ischaemic causes for myocyte injury (e.g., myocarditis) **(**20**)**.
- Coronary artery vasospasm is another common cause of MINOCA in which vasoconstriction of an epicardial coronary artery results in compromised coronary blood flow as shown in Figure 6 **(**20**)**.
- Coronary artery microvascular dysfunction may contribute to MINOCA and requires further investigation as shown in Figure 6 **(**20**)**.
- Coronary artery thrombosis or embolism can result in MINOCA, either with or without a hypercoagulable state as shown in Figure 6 **(**20**)**.

- Spontaneous Coronary artery dissection should be considered as a cause of MINOCA **(**20**)**.
- Optical coherence tomography or intravascular ultrasound imaging is recommended in patients with evidence of non-obstructive CAD by angiogram **(**20**)**.
- Medications such as Aspirin, clopidogrel, statin, beta-blockers, angiotensin-receptor blockers should be considered based on the underlying mechanism for MINOCA in each patient **(**20**)**.

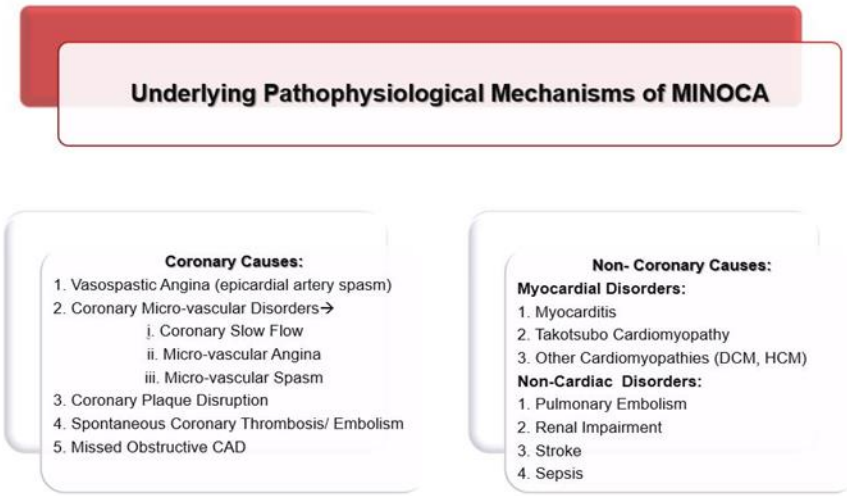
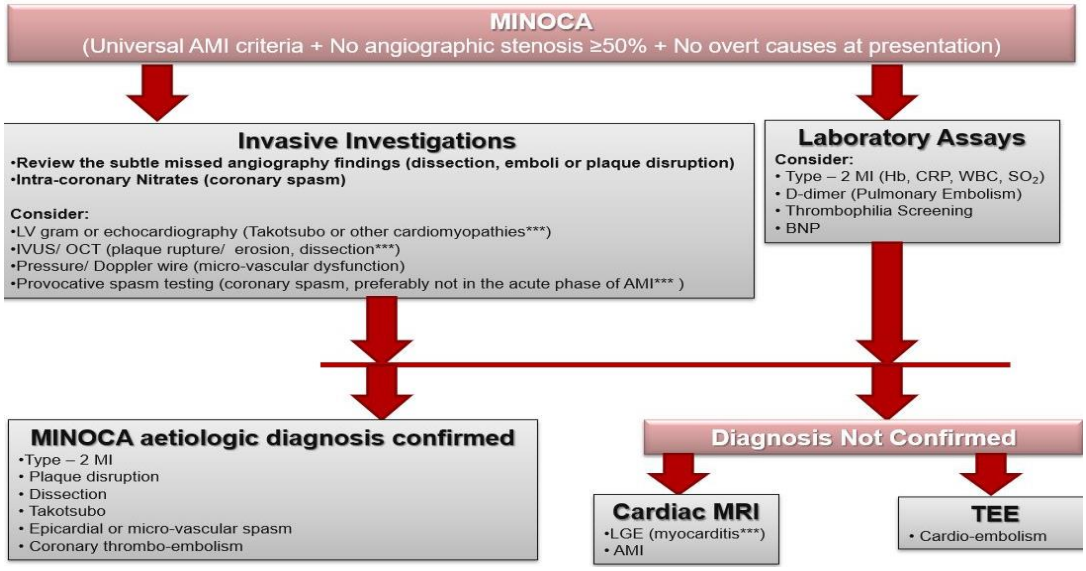


Figure 6: Showing pathophysiological mechanism of MINOCA

The recommended diagnostic and therapeutic algorithm for -MINOCA is as shown in Figure7.



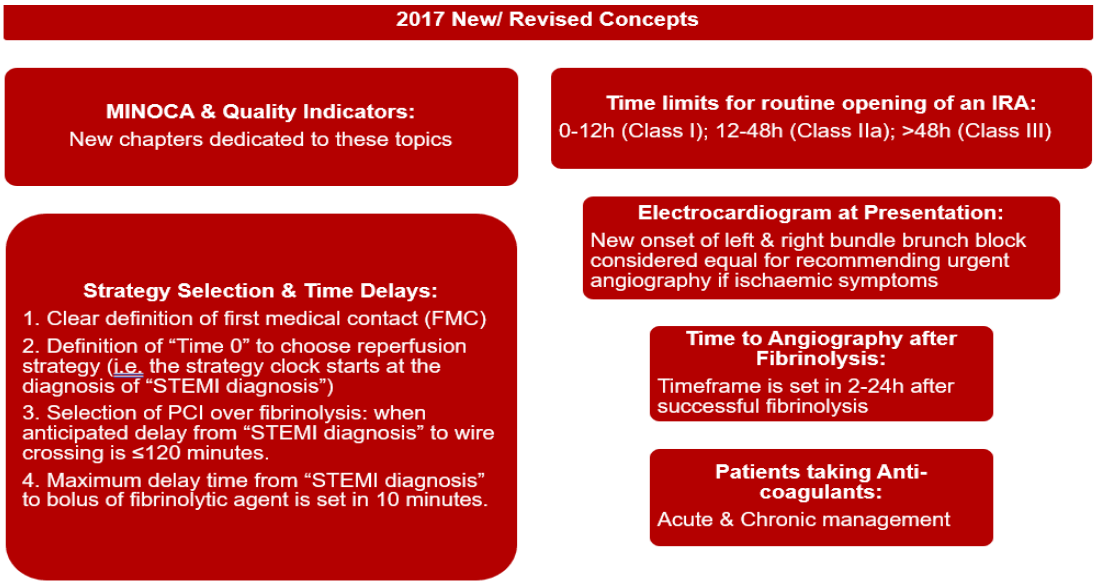


Figure 7: The recommended diagnostic and therapeutic algorithm for MINOCA

Conclusion:

The incidence of MINOCA among Acute Myocardial Infarction patients is about 1–15% and therefore MINOCA should be regarded as a dynamic working diagnosis. Despite having no significant coronary stenosis, MINOCA patients, remain at a high risk of developing adverse cardiovascular events due to variable degrees of heart injury and should be treated with full caution. MINOCA represents many possible aetiologies that can be often challenging to detect. Therefore, clinicians must become familiar with this syndrome sooner than later to ensure that patients are appropriately diagnosed and treated in due time. The optimal evaluation for patients with a diagnosis of MINOCA, should be aimed at determining the specific cause individually for each patient so that targeted therapies can be initiated at an early stage of management. It can be hoped that in light of the currently proposed assessment algorithm there will be a better understanding of the prevalence and treatment of the various conditions that result in MINOCA and improve clinical outcomes in upcoming days. Nevertheless, there is a need for further multicentric clinical trials in the future in order to optimize the management protocol for MINOCA patients as per evidence-based medicine.

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