Thesis

Identification of Acute Coronary Occlusion Using Artificial Intelligence in NSTEMI Patients

submitted by

Matteo Barnaba

In partial fulfilment of the requirements for the degree of

Doktor der gesamten Heilkunde

(Dr. med. univ.)

at the

Medical University of Graz

executed at the

Division of Cardiology

Department of Internal Medicine

under the supervision of

Research Prof. Priv.-Doz. Dr.med. Dr.scient.med. Markus Wallner

and

Research Prof. Priv.-Doz. Dr.med. Gabor Toth, PhD.

Graz, 27.08.2025

Declaration of Academic Integrity

I hereby confirm that the present diploma thesis is the result of my own independent scholarly work. I also confirm that in all cases, where material from the work of others (in books, articles, essays, dissertations, and on the internet) is acknowledged, quotations and paraphrases are clearly indicated. No material other than that cited in the reference list has been used. I have read and understood the Medical University's regulations and procedures concerning plagiarism.

Furthermore, I hereby declare that if artificial intelligence (AI) tools were used to generate and/or correct certain text passages in the preparation of this thesis, this use was carried out in compliance with ethical principles, academic integrity and the guidelines of my university, and that this was subsequently made transparent and labelled in an appropriate manner.

Graz, 27.08.2025 Matteo Barnaba m.p.

Acknowledgment

At this point, I would like to express my sincere thanks to everyone who supported me throughout the journey of writing my diploma thesis.

First, I would like to express my special gratitude to my first supervisor, Research Prof. Priv.-Doz. Dr. med. Dr. scient. med. Markus Wallner, who has always supported me both professionally and personally in the best possible way. His professional expertise and motivating supervision have further strengthened my enthusiasm for scientific research.

I am also deeply grateful to Dr. med. univ. Florian Gallob for his tireless support throughout the process, starting from the data collection to the writing of my diploma thesis. Thanks to his knowledge of this field, I was able to learn a lot during this time.

My biggest thanks go to my family and friends who have been unconditionally supportive and caring thoughout my studies.

Zusammenfassung

Hintergrund: Die derzeitigen STEMI-Kriterien unterscheiden zwischen ST-Strecken-Hebung-Myokardinfarkt (STEMI), der eine akute Koronarangiographie veranlasst, und dem Nicht-ST-Strecken-Hebungs-Myokardinfarkt (NSTEMI), bei dem je nach Risikoklasse eine variable Zeit bis zur invasiven Diagnostik verstreichen kann. Mehrere Studien haben jedoch gezeigt, dass bis zu 25–30 % aller PatientInnen mit NSTEMI einen Totalverschluss einer Koronararterie aufweisen und daher potenziell von einer sofortigen Revaskularisation profitieren würden. Ziel dieser Studie war es, die diagnostische Leistung eines mit künstlicher Intelligenz (KI) unterstützten EKG-Modells (Powerful Medical, Slowakei) bei der Erkennung eines Myokardinfarkts mit Totalverschluss einer Koronararterie (okklusiver Myokardinfarkt; OMI) bei NSTEMI-PatientInnen zu ermitteln.

Methoden: Diese retrospektive Studie umfasste 300 PatientInnen, die im Jahr 2022 an der Universitätsklinik Graz im Rahmen eines NSTEMI eine Koronarangiographie erhielten. Das EKG mit dem kürzesten Zeitintervall bis zur Koronarangiographie wurde mit der KI-untertützten EKG-App von Powerful Medical analysiert und gegen zwei Referenzstandards basierend auf Angiographiebefunden und hs-Troponinwerten verglichen.

Ergebnisse: Die diagnostische Leistung des KI-unterstützten EKG-Modells bei der Erkennung eines okklusiven Myokardinfarktes bei NSTEMI-PatientInnen zeigte je nach Referenzstandard, eine mäßige Spezifität von 70.2 % bzw. 73.2 % sowie einen negativen prädiktiven Wert von 86.6 % bzw. 74.6 %. Die Sensitivität mit 48.1% bzw. 46.3 % und der positive prädiktive Wert mit 25.3 % bzw. 46.3 % waren für beide Definitionen begrenzt. Die Odds Ratios (OR) waren mit 2.18 (95 % CI, 1.19–4.00) und 2.35 (95 % CI, 1.42–3.91) für beide Referenzstandards statistisch signifikant.

Konklusion: Trotz des Potenzials des KI-unterstützten EKG-Modells zur Verbesserung der Erkennung von okklusiven Myokardinfarkten bei NSTEMI-PatientInnen konnten die bisher sehr guten Ergebnisse von vorherigen Studien in unserer NSTEMI-Kohorte nicht nachgewiesen werden. Weitere Untersuchungen sind geplant, um die klinische Anwendbarkeit in dieser Patientengruppe zu evaluieren.

Abstract

Objectives: The current STEMI criteria differentiate between ST-segment elevation myocardial infarction (STEMI), which usually leads to immediate invasive coronary angiography (ICA), and non-ST-segment elevation myocardial infarction (NSTEMI), in which invasive diagnosis may be performed after a variable time depending on the patient´s risk classification. However, several studies have demonstrated that up to 25–30% of all NSTEMI patients have a total occlusion of a coronary artery and would therefore potentially benefit from immediate revascularization. The aim of this study was to assess the diagnostic performance of Powerful Medical's artificial intelligence (AI)-powered ECG model in detecting occlusion myocardial infarction (OMI) in NSTEMI patients.

Methods: This single-center retrospective study included 300 NSTEMI patients who received ICA at the University Hospital of Graz in 2022. The ECG with the shortest time interval prior to ICA was analysed using an AI-powered ECG app and compared against two reference standards based on angiography findings and hs-troponin levels.

Results: The diagnostic performance of the AI-powered ECG model in the detection of occlusion myocardial infarction in NSTEMI patients showed a moderate specifity of 70.2% and 73.2%, depending on the reference standard, and negative predictive value of 86.6% and 74.6%, respectively. The sensitivity of 48.1% and 46.3% as well as positive predictive value of 25.3% and 44.4% were limited for both definitions. The odds ratios (OR) of 2.18 (95% CI, 1.19–4.00) and 2.35 (95% CI, 1.42–3.91) were significant for both reference standards.

Conclusions: Despite the potential of an AI-powered ECG model to improve the detection of occlusion myocardial infarction in NSTEMI patients, the highly favorable results of previous studies could not be replicated in our NSTEMI cohort. Further investigations are planned to evaluate the clinical applicability in this patient group.

Table of Contents

Abbreviations

OMI ..... Occlusion Myocardial Infarction
ICA ..... Invasive Coronary Angiography
95% CI ..... 95% Confidence Interval
ACOMI ..... Acute Coronary Occlusion Myocardial Infarction
ACS ..... Acute Coronary Syndrome
AI ..... Artificial Intelligence
ATO ..... Acute Total Occlusion
AUC ..... Area Under the Curve
BMI ..... Body Mass Index
CABG ..... Coronary Artery Bypass Grafting
CCS ..... Chronic Coronary Syndrome
CHD ..... Coronary Artery Disease
CKD ..... Chronic Kidney Disease
CT ..... Computer Tomography
cTn ..... Cardiac Troponin
cTnI ..... Cardiac Troponin I
cTnT ..... Cardiac Troponin T
CVD ..... Cardiovascular Disease
ECG ..... Electrocardiogram
ESC ..... European Society of Cardiology
i.v. ..... Intravenous
LAD ..... Left Anterior Descending Artery
LBBB ..... Left Bundle Branch Block
LCx ..... Left Circumflex Artery
LM ..... Left Main Coronary Artery
LV ..... Left Ventricular
LVEF ..... Left Ventricular Ejection Fraction
MI ..... Myocardial Infarction
NOMI ..... Non-Occlusion Myocardial Infarction
NPV ..... Negative Predictive Value

NSTE-ACS ..... Non-ST-Segment-Elevation Myocardial Infarction Acute .....Coronary Syndrom

NSTEMI .....Non-ST-Segment-Elevation Myocardial Infarction

OR.....Odds Ratio

PCI .....Percutaneous Coronary Intervention

PPCI.....Primary Percutaneous Coronary Intervention

PPV ..... Positive Predictive Value

RCA .....Right Coronary Artery

ROC .....Receiver Operating Characteristics

SD ..... Standard Deviation

STEMI ..... ST-Segment-Elevation Myocardial Infarction

TIMI..... Thrombolyis in Myocardial Infarction

TO .....Total Occlusion

Trop.....Troponin

UA ..... Unstable Angina

UFH.....Unfractionated Heparin

DAPT ..... Dual Antiplatelet Therapy

ULN.....Upper Limit of Normal

URL.....Upper Reference Limit

List of Figures

List of Tables

1 Introduction

In the last decades, the mortality rate of cardiovascular disease declined significantly. However, cardiovascular disease (CVD) remains the leading cause of death worldwide. (1,2) Furthermore, the worldwide number of deaths from CVD increased from 12.1 million in 1990 to 18.6 million people in 2020, according to the Global Burden of Disease (GBD). (1) The prevalence of myocardial infarction (MI) globally was assessed in a large meta-analysis study from 2023 and is 3.8% in the under-60 age group and 9,5% in the population over-60 years of age. (3) The risk of developing CVD may vary in different countries due to differences in lifestyle, dietary habits, physical activity, and environmental factors. (4) In Europe, 45% of all deaths from CVD in women and 39% in men are attributed to coronary heart disease (CHD). The decline in cardiovascular mortality over the past 30 years varies according to socioeconomic status, from 50% in high-income countries to only 15% in low-income countries. (2)

Acute coronary syndrome (ACS) is often the primary manifestation of coronary heart disease (CHD), typically presenting with sudden onset of chest pain and may be accompanied by ECG changes and elevation of cardiac troponin (cTn). (5,6) Based on clinical signs, laboratory findings, and pathological features acute coronary syndrome (ACS) is divided into three main categories: ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA). This classification system supports the decision on further diagnostic investigations and therapeutic interventions. (7)

NSTEMI and UA are summarized as non-ST-elevation acute coronary syndrome (NSTE-ACS). (8)

1.1 Definition of myocardial infarction

The fourth universal definition of myocardial infarction ,published 2018, defines myocardial infarction as myocardial cell necrosis due to oxygen deficiency accompanied by a dynamic change of cardiac Troponin (cTn) levels exceeding the 99th percentile upper reference limit (URL) and at least one of the following criteria: clinical symptoms of myocardial ischemia that are present at rest; ECG changes indicating ischemia; pathological Q-waves; evidence of myocardial damage in

cardiac imaging or newly identified wall motion abnormalities or the evidence of coronary thrombus by angiography or autopsy. (7)

1.2 Pathophysiology and risk factors of myocardial infarction

Most types of myocardial infarctions are caused by a spontaneous rupture of a vulnerable plaque, which releases procoagulant factors, activates platelets and thus leads to the activation of the coagulation cascade. The resulting thrombus either partially (non-occlusive myocardial infarction) or completely (occlusive myocardial infarction) obstructs a coronary artery. (9) An ECG makes it possible to distinguish between NSTEMI, where according to the previous STEMI paradigm, the coronary artery is not fully occluded and STEMI, which is associated with a fully obstructed coronary artery. However, recent studies have found that in up to a quarter off all patients with NSTEMI have a total coronary occlusion and thus would potentially gain from early revascularization. (10)

Atherosclerotic alterations in the arteries can be found in patients after years of exposure to various risk factors, which can lead to the formation of a plaque that may rupture spontaneously. The main risk factors for developing atherosclerosis are age, hypercholesteremia/dyslipidemia, tobacco use, hypertension, diabetes mellitus, obesity, metabolic syndrome and genetic burden. (2) A healthy lifestyle has a positive impact on many of the main risk factors and should be encouraged before cardiovascular disease (CVD) occurs. (11)

1.3 Clinical classification of myocardial infarction

1.3.1 STEMI

Most cases of acute ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) are caused by coronary plaque rupture leading to thrombotic occlusion of a coronary artery. The differentiation between STEMI, where according to the current STEMI paradigm an acute total occlusion is present, and NSTEMI, which is not associated with total coronary occlusion, is based on ECG findings.(12) On the ECG, this presents as ST-elevation ≥1 mm measured from the J-point in two or more contiguous leads, except in leads V2 or V3, where an elevation of ≥2.5 mm in men under the age of 40, ≥2 mm above the age of 40, and ≥1.5 mm in women (except in the presence of left ventricular

hypertrophy or left bundle branch block). (7) STEMI patients typically experience severe chest pain at rest, which may be accompanied by less specific symptoms such as dyspnea, sweating, nausea, or syncope, and may lead to malign arrhythmia or death. (2,13,14) A severe complication of acute myocardial infarction, with high mortality rates of approximately 35%, is cardiogenic shock, which leads to a decrease in cardiac output and thus to reduced perfusion of vital organs. This can be the result of left ventricular myocardial damage or arrhythmias, which are usually of ventricular but may also be of atrial origin. (15,16) In women, myocardial infarction can often present with symptoms beyond chest pain, such as dyspnea, nausea and vomiting. In addition, women more often experience prodromal symptoms like fatigue days before having a MI. (17) Furthermore, in patients with diabetes mellitus, myocardial infarction is often clinical silent, without typical chest pain. (18,19)

1.3.2 NSTEMI

Non-ST-elevation myocardial infarction (NSTEMI) often appears without pathological ECG changes or unspecific findings, such as horizontal or descending ST-segment depression or T-wave inversion, which do not fulfill the criteria for STEMI. (7,20) Therefore, the determination of high-sensitivity troponin is crucial for the diagnosis of NSTEMI. (14)

1.3.3 Unstable angina

Unstable angina is considered a direct precursor of acute coronary syndrome and usually manifests as intermittent chest discomfort or pain and is clinically indistinguishable from NSTEMI or STEMI. Since cardiac laboratory markers are not elevated in patients with unstable angina, this helps to differentiate it from NSTEMI. (2) Stable angina, on the other hand is characterized by chest pain that occurs during physical exertion or psychological stress and resolves at rest in patients with chronic coronary syndrome (CCS) The incidence of unstable angina has decreased over the past few years and, while the number of NSTEMI has increased due to the implementation of high-sensitive cardiac troponin essays. (21)

1.3.4 Types of myocardial infarction

Based on etiology, pathological criteria, and pathophysiological mechanisms, myocardial infarction (MI) is divided into five types. (7)

1.3.4.1 Type 1

The rupture of a vulnerable plaque often leads to a type 1 myocardial infarction; however, it can also be caused from erosion or dissection of a plaque. This results in the formation of a thrombus that partially or completely occudes the affected artery. (7)

1.3.4.2 Type 2

In type 2 myocardial infarction (MI), there is an imbalance between oxygen supply and demand without evidence of thrombotic occlusion of a coronary artery. This imbalance is typically found in patients with diagnosed stable chronic coronary syndrome (CCS) and is triggered by additional stress factors that either increase oxygen demand, such as tachyarrhythmia, or reduce oxygen supply, as in coronary artery spasm. (7)

1.3.4.3 Type 3

If a patient with symptoms and ECG suggestive of myocardial ischemia dies before cardiac-specific biomarkers can be measured, it is classified as type 3 myocardial infarction. (7)

1.3.4.4 Type 4

Type 4a myocardial infarction: associated with percutaneous coronary intervention (PCI)

According to the 2018 fourth universal definition of myocardial infarction, the diagnosis of a type 4 MI is certain if cardiac troponin (cTn) levels exceed five times the 99th percentile upper reference limit (URL) in patients with normal cTn values before the intervention. However, if the cTn value is already stably elevated before the procedure, an increase of more than 20% above five times the 99th percentile URL after the intervention is required to diagnose type 4a myocardial infarction. Furthermore, one of the following criteria must be met to make a diagnosis of type 4a myocardial infarction: ischemic signs on the ECG, pathological Q-waves,

evidence of ischemia on cardiac imaging, or corresponding findings on angiography. (7)

Type 4b myocardial infarction: stent/scaffold thrombosis associated with PCI

Type 4b myocardial infarction is categorized depending on the timing of stent/scaffold thrombosis: acute type 4 myocardial infarction occurs within the first 24 hours after PCI, subacute appears in the period from 24 hours to 30 days after the intervention, late refers to more than 30 days, and very late is defined as the development of thrombosis more than one year after the procedure. (7)

Type 4c myocardial infarction: restenosis associated with PCI

Type 4c myocardial infarction indicates in-stent restenosis or restenosis after balloon angioplasty in the artery affected by the infarction with no other identifiable cause of thrombus development and an increase of cardiac troponin over the 99th percentile URL. (7)

1.3.4.5 Type 5 myocardial infarction: associated with coronary artery bypass grafting (CABG)

Similar to type 4a myocardial infarction a dynamic increase in cardiac troponin (cTn) levels is essential for the diagnosis type 5 MI, which occurs during coronary artery bypass grafting (CABG) (22). This type is defined by clinical signs of ischemia during CABG and a tenfold increase of cTn levels within the first 48 hours after the procedure compared to the baseline, or when a rise of 20% of cTn values is detected in patients with stably elevated cTn values before the intervention. In this case, the diagnosis of type 5 myocardial infarction can be confirmed by ECG, imaging, and angiography. (7) Cardiac troponin I (cTnI) can rule out type 5 myocardial infarction (MI) with a high degree of certainty. (23)

1.4 Occlusion Myocardial Infarction (OMI) and Non-Occlusion Myocardial Infarction (NOMI) Concept

Currently, acute coronary syndrome (ACS) is categorized into ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) based on the criteria for ST-segment elevation on the ECG recommended in guidelines. (24) The introduction of the STEMI/NSTEMI paradigm was a major improvement in the diagnosis and treatment of myocardial

infarction, driven by the emergence of reperfusion therapy. Today, however, it poses a substantial limitation to improve the detection and management of acute coronary occlusion, mainly due to its focus on the ST segment amplitude. (25–29) Over the past 30 years, STEMI has been associated with acute total coronary occlusion (ATO) with transmural myocardial necrosis requiring immediate reperfusion therapy. (24,28) NSTEMI, on the other hand, was generally associated with subendocardial myocardial infarction without ATO, although a significant proportion of NSTEMI patients also present with ATO in coronary angiography. (24) A 2017 meta-analysis involving 40 777 patients shows that one quarter of all NSTEMI cases have a total occlusion (TO) of the culprit vessel, leading to higher short- and long-term mortality. (10) Although NSTEMI patients with an acute occluded artery and STEMI patients have both occluded arteries, NSTEMI patients with TO experience worse outcomes than STEMI patients. This is presumably, due to delayed reopening of the occluded artery in the NSTEMI group with total occlusion. (30)

However, only 40% of ACS patients with acute total coronary occlusion (ATO) are correctly identified using the STEMI criteria. (31–33) In STEMI patients there are a significantly number of false positive cases without total occlusion, resulting in unnecessary invasive diagnostic procedures and additional costs. These results once again highlight the limitations of the current STEMI criteria. (34–37) The introduction of high-sensitivity cardiac troponin cut-offs has improved the detection of NSTEMI, but ECG interpretation and the patient´s clinical presentation remain fundamental to the management of patients with myocardial infarction (MI) with acute total occlusion (ATO). (38) As reperfusion is delayed In NSTEMI patients with total occlusion (TO), this leads to poorer short- and long-term outcomes than in patients without TO, even though this subgroup of NSTEMI patients has comparable clinical signs, laboratory markers, and echocardiographic findings as STEMI patients with total occlusion (TO). (30,31,39,40) Promising results have been shown in studies on the use of echocardiographic indicators, such as territorial circumferential strain and laboratory markers to support the identification of occlusion myocardial infarction (OMI) and improve timely reperfusion. (41,42)

Due to its simple application, wide accessibility, good reproducibility, and absence of side effects the ECG remains an indispensable tool for the diagnosis of acute coronary syndrome (ACS) and further decision-making. (43,44)

The limited accuracy of detecting ATO using the traditional STEMI criteria led some authors to propose a new classification for acute coronary syndrome, distinguishing between “Occlusion Myocardial Infarction” (OMI) and “Non-Occlusion Myocardial Infarction” (NOMI). (37)

Occlusion myocardial infarction (OMI) refers to a total or nearly total occlusion of the culprit artery, whereas NOMI denotes the absence of a totally occluded coronary artery. Since 25–30% of all NSTEMI patients have an acute total occlusion of a coronary artery, that is not detected by the current STEMI criteria, several studies investigated ECG patterns that are more accurate in detecting myocardial infarction (MI) with acute coronary occlusion than ST-elevation. (10,45) These ECG patterns are presented in Table 1.

1.4.1 ECG patterns for identifying acute coronary occlusion

Table 1: Acute coronary occlusion ECG patterns

Pattern name	Patient group	Criteria	Sensitivity for occlusion	Specificity for occlusion
Modified Sgarbossa-1 (46)	Left bundle branch block (LBBB)	1 of the following criteria in ≥ 1 lead: • Concordant ST-elevation ≥ 1 mm • Concordant ST-depression in V1-V3 ≥ 1 mm • Discordant ST-elevation ST/S ratio > 25%	80%	99%
Modified Sgarbossa-2 (46)	LBBB	Discordant ST-elevation or depression by > 30% of previous S or R wave	64%	98%
Modified Sgarbossa for	Right ventricular pacing	1 of the following criteria in ≥ 1 lead:	67%	99%

paced rhythm (47)		• Concordant ST elevation ≥ 1 mm • Concordant ST Depression in V1-V6 ≥ 1 mm • Discordant ST elevation ST/S ratio > 25% in any lead		
Terminal QRS distortion (48)	Left anterior descending (LAD) occlusion	Loss of S and J wave in V2 or V3	20%	100%
3-Variable formula to differentiate normal ST elevation from subtle LAD occlusion (49)	Differentiation of normal ST elevation from LAD occlusion	• Corrected QT interval (QTc-B) • ST elevation 60 ms after J-point in lead V3 (STE60V3) • R-wave amplitude in lead V4 in mm (RAV4) Formula: 1.196 x STE60V3 + 0.059 x QTc-B – 0.326 x RAV4	86%	91%
4-Variable formula	Same as 3-variable, but not validated	• In addition to 3-variable QRS voltage in V2 (QRSV2) Formula: 0.052 x QTc – 0.151 x QRSV2 – 0.268 x RAV4 + 1.062 x STE60V3	89%	95%
ECG criteria to differentiate acute anterior STEMI from left ventricular aneurysm (50)	ST elevation in V1-V4, either due to acute STEMI or old MI with persistent ST elevation. Q waves usually in V1-V4	T amplitude to total QRS ratio of > 0.36 in one of the leads V1-V4	92%	69%
ST depression in aVL (51)	Suspected inferior acute MI, ST elevation in II, III, aVF	• Exclude patients with Left ventricular hypertrophy (LVH), LBBB,	99%	100%

		delta wave, paced rhythm • ST depression in aVL • ST elevation in inferior leads • Differentiation of persistent ST elevation of old MI and acute MI is not possible		

Source: Miranda, David (2018) (45)

In a retrospective case-control study, the use of OMI-ECG criteria was shown to result in twice the sensitivity of the STEMI criteria (86% vs 41%) in detecting occlusion myocardial infarction (OMI), while maintaining specificity. (52)

1.4.2 Laboratory markers

NSTEMI patients with occlusion myocardial infarction (OMI) have comparable peak troponin levels to STEMI patients with total occlusion (TO). Concentrations are significantly higher than in NSTEMI patients with non-occlusion myocardial infarction (NOMI) and are considered a valuable diagnostic factor. (31) In a cross-sectional observational study, investigators demonstrated that neutrophil levels were significantly higher in patients presenting with occlusion myocardial infarction (OMI) compared to those with non-occlusion myocardial infarction (NOMI), which could therefore serve as an additional diagnostic parameter for the detection of occlusion myocardial infarction (OMI). (53)

1.4.3 OMI Paradigm shift

The OMI paradigm classifies myocardial infarction (MI) based on acute coronary occlusions in contrast to the current STEMI criteria, which are categorized by ST segment changes. Occlusion myocardial infarction (OMI) can occur either with ST elevations that fulfill the STEMI criteria, then it is considered as STEMI positive (+) OMI, or it can present with ECG changes that do not correlate with the STEMI criteria, which is referred to as STEMI negative (-) OMI as shown in Figure 1. (52) On the other hand, non-occlusion myocardial infarction (NOMI) can either appear with false positive ST-elevation on the ECG, which is labeled as STEMI positive

(+) NOMI, or without STEMI findings on the ECG, referred as STEMI negative (-) NOMI (54).

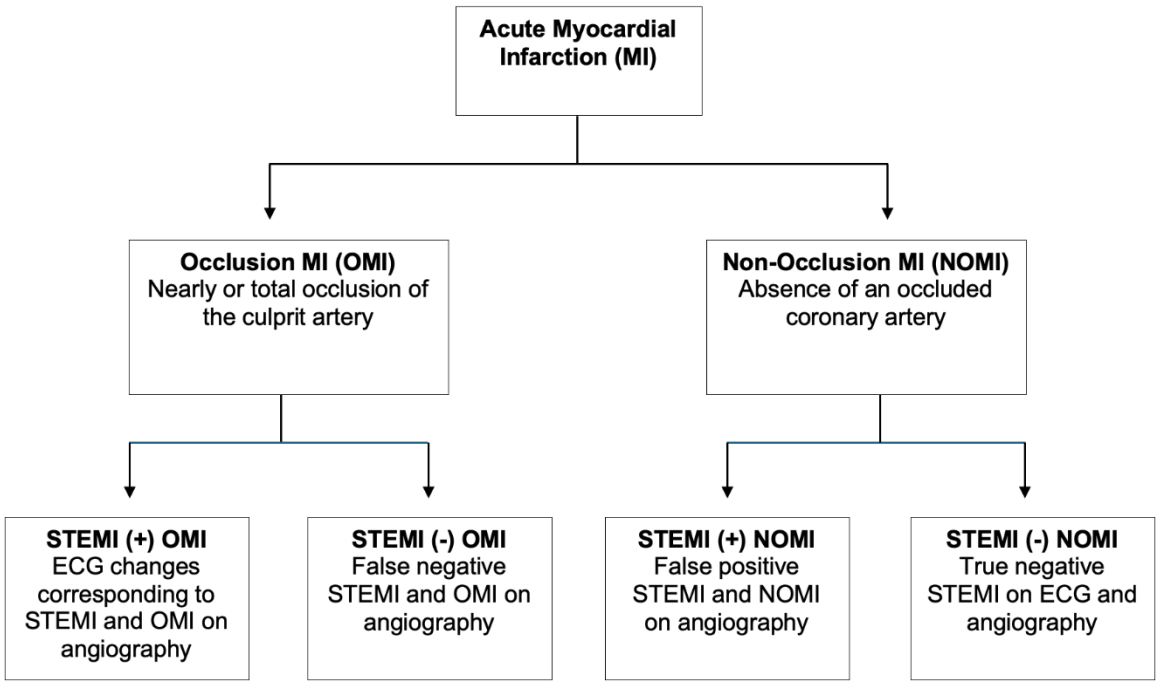

Figure 1: OMI Paradigm shift

Source: McLaren, Jesse (2024) (54)

1.5 Diagnosis of myocardial infarction

1.5.1 History and physical examination

The clinical presentation of patients with acute coronary syndrome (ACS) is diverse. The symptoms range from classic chest pain at rest to non-specific symptoms such as back pain, nausea, and vomiting. The frequency varies between men and women. (55)

Although chest pain is the predominant symptom in patients with acute coronary syndrome (ACS) in both sexes, 40% of men and 49% of women report symptoms that are unspecific for acute coronary syndrome (ACS). (56) In 15–20% of all cases, acute coronary syndrome is asymptomatic, especially in elderly patients and those diagnosed with diabetes mellitus. (2)

A thorough symptom-oriented medical history with simultaneous assessment of vital signs and ECG diagnostics is an efficient approach to identify patients with acute coronary syndrome (ACS) and excluding differential diagnoses. (6)

1.5.2 Electrocardiogram

The Electrocardiogram (ECG) is an important tool in the assessment of patients with suspected acute coronary syndrome (ACS) and should be performed as early as possible. (6) The ECG criteria of STEMI are discussed in the corresponding chapter. In patients with bundle branch block (BBB), the diagnosis of STEMI may be more difficult. However, if there are clinical signs of ischemia in these patients, the treatment should be the same as for patients with ST elevation. (6)

Considering that each ECG lead corresponds to specific anatomical regions of the heart, the affected vascular territory leading to myocardial infarction may be identified based on the distribution of ST segment changes in the ECG leads. (2)

Extensive anterior myocardial infarction presents as ST elevation in the leads V1–V6 and is usually caused by occlusion of the left anterior descending artery (LAD) or one of its branches. (57) Due to the extensive myocardial necrosis and associated higher complication and mortatlity rate, anterior myocardial infarction is considered to have the worst prognosis of all myocardial infarction locations. (58) Leads V1–V4 indicate an anteroseptal myocardial infarction (MI). An anterolateral myocardial infarction (MI) shows ST elevations in leads I, aVL, V5 and V6. An Inferior myocardial infarction (MI) presents on the ECG by ST elevations in leads II, III, and aVF, accompanied by reciprocal ST depressions in lead I, aVL, and VR.

ST depression in septal leads V1–V4 indicate posterior occlusion myocardial infarction with high specificity. Posterior leads (V7–V9) can be recorded for confirmation but may prove to have low amplitude and therefore a risk for false negative results.

Right-sided precordial leads V3R–V6R are required to detect rare isolated right ventricular infarctions. This type of myocardial infarction (MI) is common in hemodynamically unstable patients and frequently occurs in conjunction with an inferior myocardial infarction. (57,59)

1.5.3 Laboratory marker

Cardiac Troponin T (cTnT) and I (cTnI) are the most important biomarkers for the assessment of patients with suspected acute coronary syndrome (ACS), as they are released when myocardial cells undergo necrosis. (2) The recommended approach for using troponin assays in the diagnosis of acute coronary syndrome (ACS) is the “rule in or rule out” European Society of Cardiology (ESC) 0/1-hour algorithm, which recognizes dynamic changes of troponin levels. The high sensitivity of troponin assays makes them essential for the detection of NSTEMI and STEMI and for excluding differential diagnoses. (6) CTnT and cTnI are detectable in the blood within one hour after the onset of myocardial infarction symptoms and typically peak after approximately 20 hours.

However, there are other diseases besides myocardial infarction that can lead to increased troponin due to myocardial cell damage, such as myocarditis, pulmonary embolism, blood pressure derailment, or acute left-sided heart failure (HF), which indicates the strengh of high-sensitivity troponin (hs-troponin) in ruling out acute coronary syndrome. (2) Chronically elevated troponin levels may also be found in patients with chronic kidney disease (CKD) and end-stage kidney disease (ESKD). (60)

Nevertheless, the measurement of cardiac troponin (cTn) remains the gold standard for laboratory detection of acute coronary syndrome, while the determination of additional biomarkers is not recommended if a troponin assay is available. (6)

1.5.4 Non-invasive imaging

Imaging modalities can be used in addition to clinical diagnostics, ECG examinations, and laboratory evaluations in the diagnosis of acute coronary syndrome.

Echocardiography offers a valuable opportunity to rapidly obtain an overview of left and right ventricular function, which is particularly important in hemodynamically unstable patients. (7,8) Given that echocardiography is commonly available in emergency departments, it can be used as an additional diagnostic tool in patients with suspected acute coronary syndrome to detect early complications of

myocardial infarction (MI) and to rule out differential diagnoses. However, it should not delay coronary angiography. (6)

Conventional computed tomography (CT) is not considered valuable for the diagnosis of myocardial infarction. The potential utility of coronary CT angiography (CCTA) for the diagnosis of NSTE-ACS has been investigated in some studies, but it has not been shown to improve patient outcomes and is therefore not recommended. However, in cases where cardiac troponin (cTn) levels and ECG results are inconclusive, CCTA may provide additional diagnostic value due to its high negative predictive value (NPV) for ruling-out acute coronary syndrome (ACS). (6)

Cardiac magnetic resonance (CMR) can determine prognostically valuable parameters in patients with acute myocardial infarction, such as infarct size and is even able to detect small subendocardial myocardial infarctions. It is generally used after the acute treatment phase to asess wall motion abnormalities and infarct characteristics. (7,8)

1.6 Treatment of acute coronary syndrome

1.6.1 Emergency care and pharmacotherapy

Acute coronary syndrome management can be differentiated between pre-hospital and in-hospital care, which are described below. (2,8)

Any patient with suspected acute coronary syndrome (ACS) should undergo an ECG examination and symptom-oriented clinical assessment for risk evaluation at the time of first contact with healthcare professionals to distinguish between STEMI and NSTE-ACS, which is essential for further treatment. (6) As the current STEMI criteria associate total coronary occlusion with ST-segment elevation with limited sensitivity and specificity, resulting in many patients who would benefit from immediate reperfusion therapy being missed, some authors propose the implementation of a new classification system for diagnosing acute coronary syndrome. The OMI/NOMI concept contains more ECG signs besides ST-segment elevation that are more likely to detect occlusion myocardial infarction than the previous STEMI criteria and thus improving patient outcomes. (25)

An oxygen saturation of arterial blood (SaO2) below 90% indicates oxygen administration. Administration above this threshold is not recommende as it does not improve outcome in patients with acute coronary syndrome. (6,61,62) Intravenous (i.v.) administration of opioids serves as adequate pain relief in patients with suspected acute coronary syndrome and leads to a reduction in oxygen demand by suppressing the sympathetic nervous system. (8) Anticoagulation should be initiated with an i.v. bolus of unfractionated heparin (UFH) followed by an infusion; low molecular weight heparin can be used alternatively. (2,6)

For patients with acute coronary syndrome, dual antiplatelet therapy (DAPT) consisting of aspirin and a P2Y12-inhibitor is recommended. Recommended a P2Y12-inhibitors are the pharmaceutical agents prasugrel or ticagrelor, as they as they have shown superiority, regarding rates of reinfarction and mortality when compared to clopidogrel, which can be used alternatively in selected patients. (2,6,63,64) In patients with NSTE-ACS, in whom an early invasive strategy is planned a pretreatment with P2Y12-inhibitor should be avoided. It is recommended that treatment with aspirin is initiated at a dose of 150–300mg orally or 75–250mg intravenously, followed by a maintenance oral dose of 75–100mg alternatively. (6) Unless there are contraindications, dual antiplatelet therapy (DAPT) is recommended for the following 12 months for patients who had an acute coronary syndrome (ACS) and those which underwent PCI. (6)

Patients undergoing primary percutaneous coronary intervention (PPCI) who have systolic blood pressure above 120 mmHg and no evidence of acute heart failure (HF) or contraindications may receive a beta-blocker at first medical contact. (6) Metoprolol is the preferred beta-blocker in these patients, as studies have shown a reduction in infarct size, improved left ventricular (LV) function, and reduced hospitalization for heart failure. (6,66–68)

The use of nitrates may be considered as symptomatic treatment of angina symptoms in patients with a systolic blood pressure above 100 mmHg if right ventricular myocardial infarction is excluded. Otherwise, there is an elevated risk of hypotension and cardiac arrest. Nitrates do not improve the prognosis of

patients with acute coronary syndrome and are only used for symptomatic therapy. (2)

1.6.2 Reperfusion therapy in STEMI patients

A structured diagnostic evaluation allows to identify patients with acute coronary syndrome who would benefit from invasive reperfusion therapy and determines the urgency of the intervention. (6)

In patients with suspected acute coronary occlusion (ATO) based on ECG findings and with cardiac Troponin (cTn) dynamic, primary percutaneous intervention (PPCI) should be performed immediately. The time from diagnosis to PPCI should not exceed 120 minutes to rapidly reopen the occluded vessel and restore blood supply to the myocardium. (6,8)

Randomized controlled trials (RCT) have demonstrated the superiority of primary percutaneous coronary intervention over thrombolysis due to better survival, successful reopening of the occluded coronary artery in STEMI patients, frequency of reinfarction, and reduction in the stroke rate. (69,70) If primary percutaneous coronary intervention (PPCI) cannot be performed within 120 minutes, fibrinolysis offers an alternative therapy approach during the first 12 hours after symptom onset. The recommended time from STEMI diagnosis to fibrinolysis is 10 minutes. (6) Multiple trials have demonstraded that early and pre-hospital use of fibrinolytic agents within 2 hours of symptom onset compared to later in-hospital application reduces mortality in patients where PCI cannot be performed within this time frame. (71–73) If fibrinolysis is unsuccessful, symptoms of ischemia persist, or if hemodynamic complications occur, rescue PCI should be performed. A coronary angiography should also be performed in patients successfully treated with fibrinolysis within the first 24 hours (6).

1.6.3 Reperfusion therapy in NSTEMI patients

For NSTEMI patients, the recommended time from NSTE-ACS diagnosis to PCI depends primarily on the clinical presentation and risk profile. (8)

In very high-risk cases presenting with cardiogenic shock, dynamic ST-segment or T-wave changes, persisting symptoms, or sudden cardiac arrest, angiography and PCI should be performed immediately. Patients with cardiac Troponin (cTn)

elevation, dynamic ST-segment or T-wave changes, temporary ST-segment elevation or a GRACE risk score above 140 belong to the high-risk group and should be treated with an early invasive tratment strategy within 24 hours. Patients without very high- or high-risk features should be managed according to a selective invasive approach. These patients should primarily undergo non-invasive diagnostics, such as stress-echocardiography, stress-cardiac magnet resonance, ergometry or coronary computer tomography angiography (CCTA) to identify obstructive CAD.(6)

However, the fact that 25–30% of all NSTEMI patients have a total occlusion of a coronary artery, which is being missed by the current STEMI criteria demonstrates the underlying limitations of the current classification system. Notably, these patients usually receive delayed reperfusion and are at higher risk for major adverse cardiac events (MACE) and death. (10)

1.7 Artificial intelligence in medicine

1.7.1 Introduction

The development of artificial intelligence (AI) developement began in the 1950s due to technological advancements. This rising era was followed by a period of stagnation in the early 1990s. The progress then accelerated and benefited from increasing financial investments from various industries.

There is currently no universally accepted definition of artificial intelligence. In general, it describes computer systems that are capable of independently solving complex tasks that usually require human knowledge. (74)

The areas of application of artificial intelligence (AI) in medicine can be broadly categorized into two types: virtual and physical. The virtual part is based on informatics techniques and includes electronic health records, health management systems, and tools that assist physicians in making treatment decisions. The most prominent example on the physical side are surgical robots that assist surgeons during interventions. (75)

Today, artificial intelligence is already being used in most areas of medicine to improve, accelerate, and simplify the daily tasks of healthcare professionals. Whether it is enhancing skin cancer diagnostics, early detection of Alzheimer´s

disease, or the support of the evaluation of mammography images by machine-learning algorithms, to name just a few examples. (76–78)

1.7.2 Artificial intelligence in cardiology

Many decisions in cardiology are based on patient data. A strength of artificial intelligence is the processing of these increasing data sets; therefore, the implementation of artificial intelligence (AI) may provide a significant benefit. (79) This has the potential to improve the diagnosis and treatment of cardiovascular diseases and enhance the evaluation of personal cardiovascular risk profiles and cardiac imaging. (80)

As misdiagnosis in patiens with acute coronary syndrome (ACS) might end fatal, it is crucial to identify these patients accurately. Certain groups of patients with acute myocardial infarction, including women, racially and ethnically minoritized individuals, or those presenting to the emergency department with a normal ECG, are more likely to have an undiagnosed myocardial infarction (MI) and may not be hospitalized. (81) Therefore, artificial intelligence might help provide a solution to this issue. (82)

1.7.3 AI-powered diagnostic of acute coronary syndrome

Artificial intelligence has the potential to significantly improve ECG diagnostics by detecting pathologies such as arrhythmias or structural heart diseases and reducing artifacts to enhance quality of the ECG. AI may also record ECG signals from wearable devices, estimate individual risk for future cardiac events, suggest treatment strategies, and integrate ECG data with other diagnostic tools. (83) As ECG is crucial for the early detection of patients with suspected acute coronary syndrome and has a direct impact on further treatment and outcomes, the integration of machine learning (ML) can offer significant benefits. (84) Artificial intelligence can enhance the triage of patients with suspected acute coronary syndrome by improving the differentiation between unstable angina (UP), NSTEMI, and STEMI. (85) The sensitivity of identifying acute coronary syndrome might be improved by using an AI-powered ECG model compared to experienced clinicians, while maintaining a high negative predictive value (NPV). If AI is used in a prehospital setting, this allows earlier diagnosis or exclusion of acute coronary

syndrome, thereby reducing the time to reperfusion and improving patient outcomes. (86) It may also predict future cardiac events and complications in patients with acute coronary syndrome. The PRAISE study has demonstrated the benefits of using machine learning (ML) for predicting all-cause mortality, myocardial infarction and major bleeding in patients with acute coronary syndrome (ACS). (87)

Considering that 25–30% of all NSTEMI patients have an acute total occlusion of a coronary artery that is not recognzed by conventional STEMI criteria, and therefore these patients without very high-risk features are not immediately revascularized, the importance of identifying this group of patients becomes evident. To advance the paradigm shift from STEMI/NSTEMI to OMI/NOMI proposed by some authors, artificial intelligence can serve as a valuable tool by training it with datasets to recognize different ECG patterns with greater sensitivity for occlusion myocardial infarction than the current STEMI criteria in patients with acute total occlusion. (88) A retrospective study showed that using an AI-powered ECG model (Queen of Hearts, Powerful Medical) for detecting occlusion myocardial infarction (OMI) reduces the false-positive rates of OMI compared to clinicians and ECG software that is based on STEMI criteria. (89) Queen of Hearts outperformed the STEMI criteria in sensitivity by more than twice and was statistically comparable to ECG experts. (90)

1.8 Artificial intelligence (AI)-powered ECG model (Queen of Hearts, Powerful Medical)

Most patients with ACS do not present with typical ST-segment elevation. Approximately 25–30% of the patients diagnosed with NSTEMI have an OMI, resulting in poor outcomes because of delayed diagnosis and catheterization. (91)

To address this issue, Herman et al. (2024) developed an artificial intelligence (AI)-powered model to improve the accuracy of identifying angiographically confirmed acute coronary artery occlusion or obstruction from a single individual 12-lead ECG in patients with suspected ACS before coronary intervention, thereby exceeding the diagnostic performance of guideline-based ECG criteria. (91)

1.8.1 Occlusion myocardial infarction artificial intelligence ECG model development

The OMI AI model that we used in our analysis was created by Powerful Medical. They used a dataset of 18 616 ECGs collected from 10 543 patients suspected of having ACS from an international database featuring clinically validated results to develop the AI-ECG model.

ECG lead images obtained from various device manufacturers were transformed into digital waveforms applying CE-certified PMcardio ECG digitization technology (Powerful Medical, Samorin, Slovakia). ECGs recorded more than 24 hours before and after the coronary intervention and those with insufficient signal quality were excluded.

A 3 x 4 format was created using digital and digitized 12-lead ECG data with 2.5 seconds assigned to each lead. The first 2.5 seconds of limb leads, and the last 2.5 seconds of pre-cordial leads were used if the format was longer than 2.5 seconds. A deep convolutional neural network (CNN) architecture was used after the dataset was divided into a training and a validation subset. The two main sections are: feature extraction and classification. By examining each lead and incorporating the newly learned, the diagnostic approach of human experts was imitated. The validation set was used for hyperparameter tuning and threshold selection, with the optimal model threshold identified by augmenting Matthew´s correlation coefficient (MCC). A further threshold was chosen to fulfill the specificity of the STEMI criteria. (91)

To assess the accuracy of the AI model in detecting OMI, two OMI-ECG experts, blinded to all clinical parameters, interpreted the ECGs. Furthermore, blinded physician annotations of STEMI criteria were compared according to the fourth Universal Definition of Myocardial Infarction. (7,52,91)

1.8.2 OMI AI model benchmarking

The OMI AI model had a statistically significant higher sensitivity at 80.6% (95% CI: 76.8–84.0%) compared to the STEMI criteria, which showed a sensitivity of 32.5% (95% CI: 28.4–36.6%, $P < 0.001$) and was comparable to the ECG experts' sensitivity of 73.0% (95% CI: 68.7–77.0%) for detecting OMI. The STEMI criteria [97.7% (95% CI: 97.9–98.3%)] were superior to the OMI experts [95.7% (95% CI:

94.7–96.6%)] and the AI model [93.7% (95% CI: 92.6–94.8%)] in terms of specificity.

OMI experts and the OMI AI model have been significantly faster (2.3h and 2.9h) than the STEMI criteria (5.3h) to identify acute coronary occlusion based on ECG findings. (91)

1.9 Aim of the study

This study aims to determine the accuracy of Powerful Medical´s artificial intelligence (AI)- powered ECG model in detecting occlusion myocardial infarction (OMI) from a single individual 12-lead ECG in patients with non-ST elevation myocardial infarction (NSTEMI), compared to a diagnosis of acute coronary occlusion based on the angiography findings and levels of troponin. (52)

2 Materials and methods

2.1 Study design

This single-center retrospective study analyzes NSTEMI Patients who underwent coronary angiography at the Division of Cardiology at University Hospital of Graz.

Study population

300 consecutive Patients who received coronary angiography at the Division of Cardiology at the University Hospital of Graz, Austria, between January 2, 2022, and November 18, 2022, were included in the study.

Inclusion criteria

Adult patients who underwent coronary angiography at the University Hospital of Graz in 2022 with an admission diagnosis of NSTEMI. (6)

Exclusion criteria

Patients without an available ECG prior to angiography and those who did not undergo angiography were excluded from the analysis.

2.2 Clinical implications

The AI-powered ECG model is expected to detect acute coronary occlusions in NSTEMI patients with higher diagnostic accuracy, which could potentially facilitate faster reperfusion and hence might lead to improved outcomes.

2.3 Study setting

As part of the data collection process, the ECG with the shortest time interval prior to angiography was scanned using the AI-supported ECG app from Powerful Medical (PMcardio). The result from the AI-powered ECG app concerning detecting an occlusion myocardial infarction (OMI) and its confidence level were documented.

It was recorded whether the patient had a cardiac arrest before admission and the hospital to which they were initially admitted.

The following laboratory markers were essential for this study: type of troponin assay and upper limit, admission or first available troponin, highest pre-procedural

troponin, peak troponin, and always the first measurement available value for the value of the following markers: B-type natriuretic peptide (NT-pro-BNP), C-reactive troponin (CRP), creatinine, glomerular filtration rate (GFR), hemoglobin A1C (HbA1c), and low-density lipoprotein (LDL).

In case of multiple coronary angiographies during a single hospital stay only the first was included for the analysis. From the angiography report in Medocs, it was determined whether the culprit vessel was a bypass graft, determined the culprit/infarct-related artery (IRA) segment, recorded the visual degree of stenosis and the pre-procedural TIMI flow and examined whether a thrombectomy or PCI was performed, or a coronary artery bypass graft (CABG) was planned. Additionally, it was inspected how many vessels were affected, whether features of chronic occlusion were present, and the time of symptom onset.

Wall motion abnormalities in the infarct-related area were obtained from the first echocardiography report from Medocs, along with the left ventricular ejection fraction (LVEF) at discharge.

Patients' comorbidities, including hypertension, dyslipidemia, diabetes mellitus (DM), heart failure (HF), history of coronary artery disease (CAD), peripheral artery disease (PAD), atrial fibrillation (Afib), chronic kidney disease (CKD), and cerebral vascular disease, as well as the patients smoking status, were recorded from Medocs.

Baseline characteristics such as sex, age, height, weight, BMI, and with vital parameters such as heart rate and systolic and diastolic blood pressure were acquired.

The Killip classification system was used to assess the risk of myocardial infarction patients for developing heart failure (92).

Using Medocs, the following parameters were assessed for follow-up, ideally one-year post angiography: left ventricular ejection fraction (LVEF), reinfarction status, dead or alive status, and the date of last follow-up.

2.4 Sample size

To calculate the sample size, the sensitivity was estimated at 82% and the specificity at 95% based on the initial study of the AI-powered ECG model from Powerful Medical. A calculated sample size of 227 Patients was reached. (90) The sample size was then rounded to 300.

2.5 Data collection and management

The relevant parameters for the study were collected from the hospital information system Medocs and were documented separately from personally identifiable data in an Excel workbook.

2.5.1 Ethical issues

The ethics committee of the Medical University of Graz approved this study (vote number: 36–161 ex 23/24).

2.6 Outcomes

2.6.1 Primary outcome

The primary outcome was to determine the accuracy of detecting occlusion myocardial infarction (OMI) from a single 12-lead ECG in NSTEMI patients by Powerful Medical´s artificial intelligence (AI)- powered ECG model (Queen of Hearts) compared to the diagnosis of acute coronary occlusion based on the angiography findings and levels of troponin. The performance of the Queen of Hearts is based on sensitivity and specificity. In the coronary angiography, we defined acute coronary occlusion as TIMI flow 0 or 1 without evidence of a chronic total occlusion (CTO).

2.6.2 Secondary outcomes

The secondary outcomes include peak Troponin, Killip in patients with OMI and NOMI. In addition, it was investigated which coronary artery was the culprit vessel, whether a PCI was performed and the timing of revascularization.

2.7 Statistical analysis

Data analysis was performed using IBM SPSS 29. Baseline demographics and clinical characteristics were assessed using descriptive statistics. Continuous variables were presented as mean ± standard deviation (SD) or as median and categorical variables as absolute numbers and percentages.

The diagnostic performance of the AI-powered ECG model in detecting occlusion myocardial infarction (OMI) from a single individual 12-lead ECG in patients with non-ST elevation myocardial infarction (NSTEMI) was evaluated against two reference standards. The first reference standard is based on the comparison between the AI- predicted OMI and the angiographically confirmed OMI (Definition 1), defined as TIMI flow grade 0 or 1 without evidence of chronic occlusion. The second reference standard (Definition 2) defines occlusion myocardial infarction (OMI) angiographically (TIMI 0 or 1) or as significantly elevated hs-troponin levels (> 100 times the upper limit of normal) in patients who received immediate PCI.

The following statistical procedures were applied to both reference standards. The diagnostic accuracy of the OMI AI model was assessed using sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). A 2x2 crosstabulation between the predicted OMI status and the observed OMI status (Definition 1 and Definition 2) was performed. The statistical significance of the correlation between the model prediction (OMI_predicted) and the observed OMI status (OMI_observed_ACO or OMI_observed_PCI_Trop_ACO) was calculated using the Pearson chi square test. Additionally, the odds ratio (OR) with a 95% confidence interval was calculated, to quantify the association between predicted OMI by the AI-ECG model and the two reference standards. The diagnostic performance of the AI-ECG model was determined using receiver operating characteristics (ROC) analysis, from which the area under the curve (AUC) was derived. A two-sided p-value <0.05 was considered statistically significant.

3 Results

3.1 Baseline characteristics

A total of 300 patients diagnosed with NSTEMI who underwent coronary angiography at the University Hospital of Graz were analyzed.

The baseline characteristics are presented in Table 2. The average age was 69 years with a standard deviation (SD) of 12 years. Of the 300 patients, 194 (65%) were male and 106 (35%) females. The mean peak hs-troponin level was 2091 ng/L (± 6380 ng/L), correesponding to a 94-fold increase over the upper lmit of normal (ULN) with a standard deviation of 171. The median time from the last ECG before angiography to coronary angiography was 5.5 hours. In coronary angiography, 49 (18%) patients had no CAD, 74 (25%) patients had one-vessel CAD, 70 (23%) patients had two-vessel CAD, and 106 (35%) patients had 3-vessel CAD. The culprit vessel was the left main coronary artery (LM) in 4 (1%) patients, the left anterior descending artery (LAD) in 52 (17%) patients, the left circumflex artery (LCx) in 29 (10%) patients, the right coronary artery (RCA) in 38 (13%) patients, and in multiple vessels in 120 (40%) patients.

A total of 146 (49%) patients presented with wall motion abnormalities on initial echocardiography. Most of the patients, 238 (79%), were classified as Kilip class I, while 30 (10%) patients as Kilip class II, 13 (4%) patients as Kilip class III, and 7 (2%) patients as Kilip class IV.

The diagnostic performance of the AI-powered ECG model was assessed against two reference standards including one angiography-based definition of occlusion myocardial infarction (OMI) (OMI_observed_ACO) and a second definition grounded on angiography or the combination of significantly elevated hs-troponin and immediate PCI.

Table 2: Baseline characteristics of study population.

SD denotes standard deviation, ULN upper limit of normal, CAD coronary artery disease.

Characteristics	**Value**
Patients (n)	300
Male sex	194 (65%)
Female sex	106 (35%)
Age, years (mean ± SD)	69 ± 12
Wall motion abnormalities at initial echocardiography	146 (49%)
Killip Class	
1	238 (79%)
2	30 (10%)
3	13 (4%)
4	7 (2%)
Time from ECG to angiography $_{median}$	5h 30 min
Troponin	
Peak troponin $_{mean\ (SD)}$	2091 (±6380)
In relation to ULN $_{mean\ (SD)}$	94 (±171)
Angiography	
No CAD at angiography	49 (16%)
1 Vessel CAD	74 (25%)
2 Vessel CAD	70 (23%)
3 Vessel CAD	106 (35%)
Culprit Vessel	
Left main coronary artery (LM)	4 (1%)
Left anterior descending artery (LAD)	52 (17%)
Left circumflex artery (LCX)	29 (10%)
Right circumflex artery (RCA)	38 (13%)
Multi vessel	120 (40%)

3.2 Diagnostic performance of the AI-ECG model in detecting occlusion myocardial infarction compared to angiographically confirmed acute coronary occlusion (OMI_observed_ACO)

The angiographic-based reference standard defines occlusion myocardial infarction as total coronary occlusion with TIMI flow grade 0 and 1 on coronary angiography. A 2x2 crosstabulation of predicted OMI-cases of the AI-ECG-model compared to angiographically confirmed OMI is shown in Table 2.
Of the 300 patients, the AI-ECG model predicted occlusion myocardial infarction (OMI_predicted) in 99 patients (33%) and non-occlusion myocardial infarction (NOMI_predicted) in 201 patients (67%). Coronary angiography revealed occlusion myocardial infarction (OMI) with a TIMI flow grade 0 or 1 in 52 patients (17%) and non-occlusion myocardial infarction (NOMI) in 248 patients (83%). Of the 52 patients with angiographically confirmed OMI, 25 were correctly detected as OMI by the AI-ECG model, and 27 were falsely predicted as NOMI. Among the 248 patients who were angiographically classified as NOMI, 174 were correctly identified as NOMI by the AI-ECG model and 74 were assigned incorrectly as OMI.

Table 3: Crosstabulation of predicted and observed occlusion myocardial infarction (OMI). Comparison of AI-ECG model detected to angiographically confirmed OMI cases (OMI_observed_ACO).

OMI denotes occlusion myocardial infarction, NOMI non occlusion myocardial infarction

OMI predicted	True OMI	True NOMI	Total
OMI	25	74	99
NOMI	27	174	201
Total	52	248	300

The diagnostic performance of the AI-ECG model compared to the angiographically confirmed OMI (OMI_observed_ACO) is summarized in Table 4.

The sensitivity of the AI-ECG model in detecting OMI compared to the angiography reference standard was 48.1% (95% CI, 34.8–61.5). The specificity

was 70.2% (95% CI, 64.3–75.6). The positive predictive value (PPV) was 25.3% (95% CI, 17.4–34.4) and the negative predictive value (NPV) was 86.6% (95% CI, 81.4–90.8). Based on the first reference standard, the diagnostic accuracy of the AI-ECG model in detecting occlusion myocardial infarction (OMI) was 66.3% (60.1%–71.4%).

Table 4: Diagnostic performance of the AI-ECG model for detecting occlusion myocardial infarction (OMI) compared to angiographically confirmed acute coronary occlusion (OMI_observed_ACO).

Metric	**Value**	**95% Confidence Interval**
Sensitivity	48.1%	34.8%–61.5%
Specificity	70.2%	64.3%–75.6%
Positive Predictive Value (PPV)	25.3%	17.4%–34.4%
Negative Predictive Value (NPV)	86.6%	81.4%–90.8%
Diagnostic Accuracy	66.3%	60.1%–71.4%

The statistical association between the AI-ECG model and the angiography findings in the detection of OMI (OMI_observed_ACO) was analyzed using various statistical tests and are presentet in Table 5. The Pearson chi-square test showed a test statistic of 6.467 (df = 1, p = 0.011), with no expected cells count less than 5 and the minimum expected count is 17,16.

Table 5: Association between AI-predicted and observed occlusion myocardial infarction (OMI) cases (OMI_observed_ACO).

OMI denotes occlusion myocardial infarction.

Test	Value	df	p-value
Pearson Chi-Square	6.467	1	0.011
Number of valid cases	300	-	-

The odds ratio (OR) for detecting occlusion myocardial infarction (OMI) by the AI-ECG- model compared to angiographically confirmed acute coronary occlusion was 2.177 (95% CI, 1.19–4.00). The odds ratio (OR) of 2.177 indicates that using the AI-ECG model improved detection of occlusion myocardial infarction. The association is statistically significant with a p value of 0.012 and a confidence interval not including 1.0. Table 6 presents the odds ratios.

Table 6: Risk estimates for the prediction of occlusion myocardial infarction (OMI) by the AI-ECG model vs the angiographic reference standard (OMI_observed_ACO).

OMI denotes occlusion myocardial infarction, NOMI non occlusion myocardial infarction.

Comparison	Value	95% Condifence Interval
Odds Ratio (OR): OMI predicted (OMI/NOMI)	2.177	1.19–4.00
Odds Ratio (OR): True OMI	0.53	0.33–0.87
Odds Ratio (OR): True NOMI	1.16	1.02–1.32
Number of valid cases	300	-

A receiver operating characteristic (ROC) analysis was performed to further assess the AI-ECG model´s diagnostic discrimination between patients with angiographically confirmed OMI and NOMI. The area under the curve (AUC) was 0.591 (95% CI, 0.50–0.68) with a standard error of 0.045 and the p-value for the null hypothesis of AUC was 0.041. Figure 2 shows the ROC curve of the model.

Table 7: Area under the curve (AUC) analysis for the diagnostic performance of the AI-ECG compared to the angiographic reference standard. This tables shows the diagnostic power of the AI-ECG model to distinguish between patients with and without occlusion myocardial infarction according to angiographic reference standard (OMI_observed_ACO). OMI denotes occlusion myocardial infarction and ACO acute coronary occlusion.

Metric	Value	95% Confidence Interval	Standard Error
Area Under the Curve (AUC)	0.591	0.50–0.68	0.045

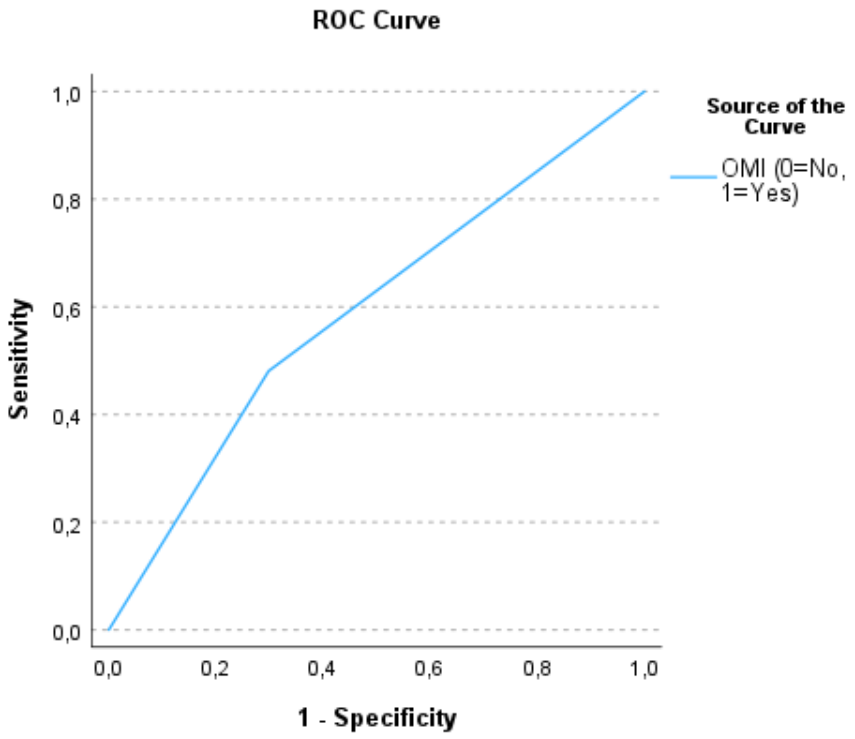

Figure 2: Receiver operating characteristic (ROC) curve of the AI-ECG model for the angiographic reference standard (OMI_observed_ACO). The curve presents the discriminatory ability of the AI-ECG model graphically.

ACO denotes acute coronary occlusion.

3.3 Diagnostic performance of the AI-ECG model in detecting occlusion myocardial infarction compared to angiographically and troponin confirmed acute coronary occlusion (OMI_observed_PCI_Trop)

The second reference standard (OMI_observed_PCI_Trop_ACO) was defined based on angiographically confirmed total occlusion (TIMI 0 or 1), or significantly elevated hs-troponin levels (> 100 times the upper limit of normal) in patients who received immediate PCI.

Table 8 presents a 2x2 crosstabulation of the AI-ECG model predictions (OMI_predicted) and the second reference standard (OMI_observed_PCI_Trop_ACO). Based on the second definition, 95 patients (32%) had an occlusion myocardial infarction (OMI), and 205 patients (68%) had a non-occlusion myocardial infarction (NOMI).

The AI-ECG model predicted in 99 patients (33.0%) an occlusion myocardial infarction (OMI) and a non-occlusion myocardial infarction (NOMI) in 201 patients (67.0%).

Of the 95 patients with confirmed OMI, the AI-ECG model correctly identified 44 cases as OMI and incorrectly recognized 51 patients as NOMI. Among the 205 patients with non occlusion myocardial infarction (NOMI), the AI-ECG model detected 150 correctly as NOMI and misclassified 51 as OMI.

Table 8: Comparison of predicted and confirmed OMI using the extended reference standard (OMI_observed_PCI_Trop_ACO).

OMI denotes occlusion myocardial infarction, PCI percutaneous coronary intervention, Trop troponin, ACO acute coronary occlusion and NOMI non occlusion myocardial infarction.

OMI predicted	**True OMI**	**True NOMI**	**Total**
OMI	44	55	99
NOMI	51	150	201
Total	95	205	300

The sensitivity of the AI-ECG model for detecting OMI compared to the second reference standard was 46.3% (95% CI, 36.5–56.3%). The specificity was 73.2% (95% CI, 66.8–78.9%). The positive predictive value (PPV) of the AI-ECG model in detecting OMI according to the second reference standard (OMI_observed_PCI_Trop_ACO) was 44.4% (95% CI, 34.9–54.3%) and the negative predictive value (NPV) was 74.6% (95% CI, 68.3–80.3%)

Table 9: Diagnostic performace of the AI-ECG model in detecting occlusion myocardial infarction (OMI) compared to the combined angiographic and troponin referenz standard. (OMI_observed_PCI_Trop_ACO)

OMI donates occlusion myocardial infarction, PCI percutaneous coronary intervention, Trop troponin, ACO acute coronary occlusion and NOMI non occlusion myocardial infarction.

Metric	**Value**	**95% Confidence Interval**
Sensitivity	46.3%	36.5%–56.3%
Specificity	73.2%	66.8%–78.9%
Positive Predictive Value (PPV)	44.4%	33.9%–54.3%
Negative Predictive Value (NPV)	74.6%	68.3%–80.3%
Diagnostic Accuracy	64.7%	59.1%–69.9%

The association between the AI-ECG model predictions and the second reference standard (OMI_observed_PCI_Trop_ACO) was analyzed using a chi-square test. The Pearson chi-square test showed a statistically significant association between the AI-ECG model prediction and the reference standard of 11.149 ($df = 1$, $p < 0.001$). No cells have an expected count less than 5 and the minimum expected count is 31.35. The diagnostic accuracy of the AI-ECG model in detecting occlusion myocardial infarction (OMI) was 64.7% (95% CI, 59.1%–69.9%)

Table 10: Association analysis between AI-ECG model predicted occlusion myocardial infarction (OMI) and the combined reference standard including angiography and troponin. (OMI_observed_PCI_Trop_ACO)

OMI donates occlusion myocardial infarction, PCI percutaneous coronary intervention, Trop troponin, ACO acute coronary occlusion and NOMI non occlusion myocardial infarction.

Test	Value	df	p-value
Pearson Chi-Square	11.149	1	<0.001
Number of valid cases	300	-	-

The odds ratio (OR) for detecting OMI with the AI-ECG model compared to the second reference standard (OMI_obserced_PCI_Trop_ACO) was 2.353 (95% CI, 1.42–3.91) indicating a statistically significant association.

Table 11: Risk estimates for the prediction of occlusion myocardial infarction (OMI) by the AI-ECG model compared the angiographic and tropoin reference standard (OMI_obserced_PCI_Trop_ACO).

OMI donates occlusion myocardial infarction, PCI primary cutaneous intervention, Trop troponin, ACO acute coronary occlusion and NOMI non occlusion myocardial infarction.

Comparison	Value	95% Confidence Interval
Odds Ratio (OR): OMI predicted (OMI/NOMI)	2.35	1.42–3.91
Odds Ratio (OR): True OMI	0.571	0.41–0.79
Odds Ratio (OR): True NOMI	1.34	1.11–1.63
Number of valid cases	300	-

To eveluate the discriminatice power of the AI-ECG model in detecting OMI according to the second reference standard (OMI_obserced_PCI_Trop_ACO), a receiver operating characteristic (ROC) was calculated. The area under the curve (AUC) was 0.597 (95% CI, 0.53–0.67), with a standard error of 0.036. The ROC curve is shown in Figure 3.

Table 12: Area under the curve (AUC) analysis for the diagnostic performance of the AI-ECG compared to the extended reference standard (OMI_obserced_PCI_Trop_ACO).

This table shows the discriminatory power of the AI-ECG model in differentiating between occlusion myocardial infarction (OMI) and non occlusion myocardial infarction (NOMI) bases on the combined angiographic and troponin reference standard. PCI donates percutaneous coronary intervention, ACO acute coronary occlusion.

Metric	Value	95% Confidence Interval	Standard Error
Area Under the Curve (AUC)	0.598	0.53–0.67	0.036

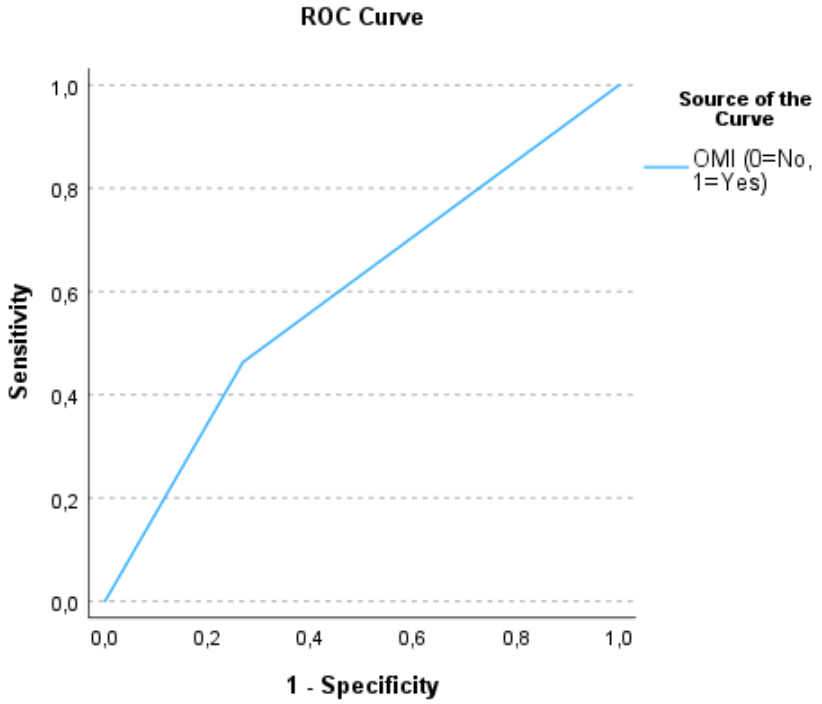

Figure 3: Receiver operating characteristic (ROC) curve of the AI-ECG model for the second reference standard (OMI_obserced_PCI_Trop_ACO). The curve shows the discriminatory power of the AI-ECG graphically. OMI donates occlusion myocardial infarction, PCI percutaneous coronary intervention, ACO acute coronary occlusion.

3.4 Comparison of AI-ECG model´s diagnostic performance between both reference standards

A direct comparison of the diagnostic performance of the two reference standards shows a higher sensitivity at 48.1% of the AI-ECG model in detecting OMI for the angiography-based definition (OMI_observed_ACO) compared to 46.3% for the extended reference standard (OMI_observed_PCI_Trop). However, specificity at 73.2% was higher for the extended reference standard (OMI_observed_PCI_Trop) compared to 70.2% for the angiography-based definition (OMI_observed_ACO). The positive predictive value of 44.4% was higher for the combined reference standard (OMI_observed_PCI_Trop) than for the angiography-based reference standard (OMI_observed_ACO) at 25.3%. Using the angiographic definition (OMI_observed_ACO) resulted in a higher negative predictive value (NPV) of 86.6%, compared to 74.6% for the extended reference standard (OMI_observed_PCI_Trop). The diagnostic accuracy of the AI-ECG model in detecting occlusion myocardial infarction in NSTEMI patients was 66.3% and 64.7%, using the first and second reference standards, respectively.

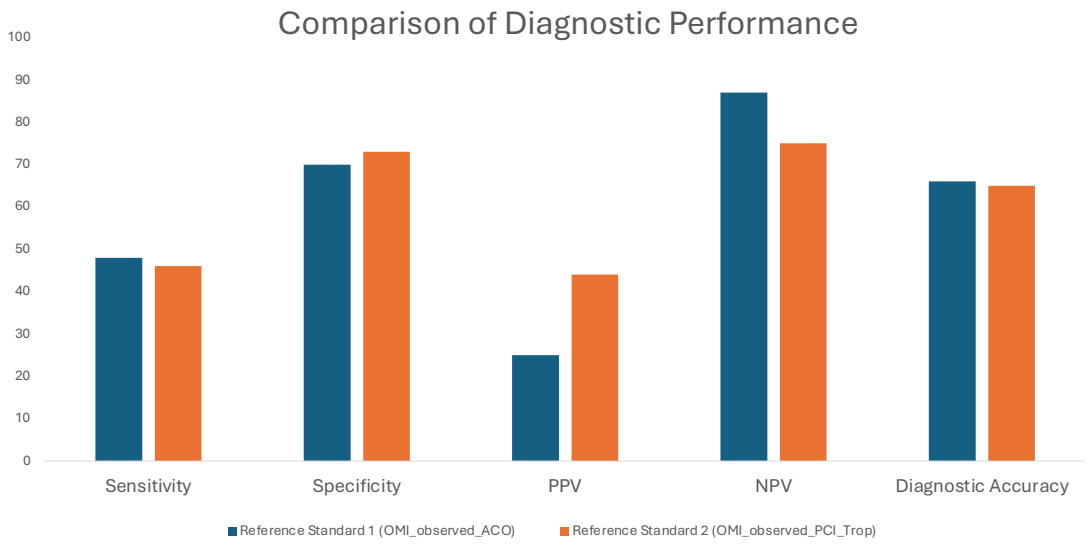

Figure 4: Comparison of diagnostic performance of AI-ECG model to both reference standards (OMI_observed_ACO vs OMI_observed_PCI_Trop). OMI denotes occlusion myocardial infarction, ACO acute coronary occlusion, PCI percutaneous coronary intervention, PPV positive predictive value, and NPV negative predictive value

4 Discussion

This retrospective analysis aimed to investigate the diagnostic performance of the AI-ECG model (PowerfulMedical) in detecting occlusion myocardial infarction (OMI) in patients with non-ST-elevation myocardial infarction (NSTEMI). The AI-model was compared to two reference standards, one defined angiographically on TIMI flow 0 or 1 (OMI_observed_ACO), and a second definition derived from coronary angiography (TIMI 0 and 1) or immediate PCI and troponin elevation (OMI_observed_PCI_Trop_ACO).

The Powerful Medical AI-ECG model we used in our analysis was trained on a large dataset of 18 616 ECGs from 10 543 patients with acute coronary syndrome to detect occlusion myocardial infarction and demonstrated strong diagnostic accuracy (90.9%), sensitivity (80.6%) and specificity (93.7%) with an AUC of 0.938. In our analysis, the AI-ECG model showed moderate specificity which varied between 70.2% and 73.2% depending on the applied definition and negative predictive value of 86.6% and 74.6% relative to both reference standards. However, low sensitivity of 48.1% and 46.3% and positive predictive value of 25.3% and 44.4% based on the chosen reference standard. The odds ratios (OR) of 2.177 (95% CI, 1.19–4.00) and 2.35 (95% CI, 1.42–3.91) were significant for both reference standards. Nevertheless, the area under the curve (AUC) of 0.591 and 0.597 indicate a low driscriminatory power of the AI-model. There are several possible factors that might have led to a lower diagnostic performance of the AI-ECG model in our analysis. One reason for the significantly lower diagnostic performance in our analysis could be the specific inclusion of only NSTEMI patients, whereas the AI-ECG model was trained on a mixed ACS population. The subgroup analysis by Herman et al. (2024) demonstrated a lower sensitivity of 67.6%, but a slightly higher specificity of 94.2% for NSTEMI patients compared to the overall ACS population (80.6% and 93.7%, respectively). A further difference can be seen regarding the definition of occlusion myocardial infarction. In the study by Herman et al. (2024), OMI was definded angiographically by either TIMI flow 0 and 1, as in our analysis, but also additionally by TIMI flow 2 and 3 in patient who received emergent PCI. We also defined OMI either on basis of angiographically determined TIMI flow 0 and 1, but furthermore also on the rise of

troponin above 100 times ULN in patients who have undergone immediate PCI. Therefore, the definition of occlusion myocardial infarction in the study by Herman et al. (2024) additionally includes TIMI flow 2 and 3 and, in contrast to our analysis. Additionally, the difference in study design should be taken into consideration to explain the lower diagnostic performance in our analysis. The AI-ECG model from Power Medical was tested on a large data set multicentrically and internationally, whereas our study was conducted in one center and with a smaller number of patients. Furthermore, only the ECG prior to angiography was used in our analysis, whereas in the study from Herman et. Al (2024) all available ECGs were analyzed. In addition, the time between ECG and angiography was longer in our analysis. (91)

A multi-site, prospective observational cohort study from Al-Zaiti et al. (2024) demonstrated that using a machine learning ECG model to detect occlusion myocardial infarction (OMI) in patients without ST-elevation outperformes practicing clinicians in terms of diagnostic performance. The considerably better overall diagnostic performance with sensitivity of 86%, specificity of 98% and area under the receiver operating characteristic curve (AUROC) of 0.87 of this study might be attributed to several methodological aspects including the prospective and multicenter approach. In contrast to our analysis in which we evaluated the last ECG before angiography, the study by Al-Zaiti et al. (2023) analyzed a pre-hospital ECG and thus closer to the potential onset of ischemia. In addition to TIMI flow 0 and 1, this study included also TIMI flow 2 as a diagnostic parameter for occlusion myocardial infarction in patients with a coronary stenosis of more than 70% in combination with a significantly elevated troponin (5–10 ng/ml). This extension of the reference standard may have contributed to an improved diagnostic performance. (93)

In large ongoing studies, such as the retrospective ASSIST study, AI-powered ECG models are being investigated to diagnose acute coronary occlusion (ACO) with and without ST-elevation corresponding to occlusion myocardial infarction (OMI) faster and more accurate and thereby shortening the time to revascularization and improving clinical outcomes. (94)

This shows the necessity of training AI-ECG models to detect occlusion myocardial infarction (OMI) specifically for NSTEMI to achieve a high diagnostic performance for this patient group.

The importance of a paradigm shift from the previous STEMI criteria, in which 25–30% of all NSTEMI patients have an acute coronary occlusion, is emphasized in a recent editorial by Dali et al. (2025). The authors point out that only about half of occlusion myocardial infarction are correctly identified when STEMI criteria are applied. Therefore, the use of AI in the detection of OMI, which can improve accuracy and lead to faster diagnosis and treatment, while reducing unnecessary interventions for false positive STEMI is proposed. (95)

Powerful Medical's AI-ECG model is currently being evaluated for the first time in a prospective multicenter study in which ECGs of ACS patients are analyzed at the time of angiography. This approach allows to evaluate the diagnostic performance of the AI-ECG model in actively occluded coronary arteries at the time of angiography and may identifiy ECG signs occuring during acute ischemia. (96)

In a prospective observational study by Díaz-Herrera et al. (2025) high sensitivity (100%), positive predictive value (84.6%), negative predictive value (100%) and moderate specificity (73.3%) of the AI-ECG model for detecting acute coronary occlusion myocardial infarction (ACOMI) in ACS patients compared to ECG interpretation by human experts was demonstrated. In the NSTEMI subgroup, the model achieved high sensitivity (100%) and moderate specificity (60%). The significant higher diagnostic power could be partly explained through selective enrichment of the study cohort with at least 50% of ACOMI cases to optimize the study aims. (97)

In this retrospective analysis, we evaluated the diagnostic performance of the AI-ECG model from Powerful Medical in detecting occlusion myocardial infarction (OMI) in NSTEMI patients. The results indicate lower diagnostic performance than in previous studies, that included NSTEMI using comparable AI-ECG models. These discrepancies might be attributed to different study poplations (STEMI and NSTEMI) and to models specifically trained to detect occlusion myocardial infarction (OMI) in patients without ST elevation.

Based on our results, the following implications for research and clinical practice emerge. The AI-ECG model showed positive results in the detection of occlusion myocardial infarction (OMI) in patients with acute coronary syndrome (ACS) in previous studies, although we were yet unable to replicate this in our monocentric analysis of a population comprised only of patients with NSTEMI. This higlights the relevance of the patient population in which the AI-ECG model is used.

4.1 Limitations

This analysis has several limitations. The retrospective study setting makes it difficult to prove causal relationships and the monocentric design limits generalizablitiy. A major limitation of our analysis leading to reduced diagnostic performance of the AI-ECG model compared to the initial study by Herman et al. (2023) evaluating the model of Powerful Medical, is the overly selective patient population containing only NSTEMI patients who underwent invasive coronary angiography. The AI-ECG model was trained to detect occlusion myocardial infarction in a heterogenous population of patients with acute coronary syndrome (ACS), including both STEMI and NSTEMI cases, which presumably led to higher diagnostic performance in their baseline study. (91) A direct comparison between the AI-ECG model and physicians in the detection of occlusion myocardial infarction in NSTEMI patients was not performed in our analysis but is planned. Thus, no assessment on the diagnostic superiority of the AI-model or physicians in this specific patient population can be drawn. The median time from the last ECG to coronary angiography of 5.5 hours is a further limitation of our study. During this time interval, significant changes in coronary status may occur and alterations of ischemia signs on the ECG may be missed. In our study, only the last ECG before coronary angiography was analyzed by the AI-ECG model, therefore signs of dynamic ECG changes seen in acute coronary syndrome (ACS) might be missed. Similarly to our definitions, the study by Herman et al. (2023) defines occlusion myocardial infarction (OMI) by angiographic stages of TIMI flow 0 to 3 in patients who underwent emergent coronary angiography. In our analyisis we used a second reference standard, which, in addition to angiographic evidence of occlusion, must exceed 100 times upper limit of normal (ULN) of hs-troponin. (91)

Furthermore, we found that the prolonged time between ECG and angiography (median 5.5 hours) as well as the selected definitions for the reference standards affect the diagnostic performance of the AI-ECG model. This analysis indicates that training AI-ECG models specifically to detect occlusion myocardial infarction (OMI) in NSTEMI patients may improve the diagnostic performance. The findings therefore provide important data for future prospective, multicenter studies and the use of a universal reference standard.

Although the AI-ECG model showed only moderate diagnostic performance in our analysis in detecting occlusion myocardial infarction (OMI) in NSTEMI patients, it is important to note that all OMI cases would have been missed based on the STEMI/NSTEMI paradigm. Thus, although the AI-ECG model did not perform excellently for the subgroup of NSTEMI, it was able to detect significantly higher rates of OMI compared to the current STEMI-ECG criteria. This indicates the possibility as a future tool for the detection of occlusion myocardial infarction (OMI) in NSTEMI patients, where previous criteria were considered insufficient. This would allow to identifiy NSTEMI patients with OMI more quickly, leading to faster reperfusion of the occluded vessel and thereby to an improved clinical outcome.

The modest diagnostic performance is mainly resulting from methodological limitations of the study design, including the selected patient population of only NSTEMI patients and the monocentric design, which is not representative for everyday clinical practice.

AI-ECG models could play an important role in clinical practice, especially in detecting and supporting decision-making in patients with suspected occlusion myocardial infarction (OMI). As AI-ECG models can detect occlusion myocardial infarction sooner than using current STEMI criteria, the time to revascularization in patients with a total occlusion can be decreased and therefore potentially improving the outcome (16). This observation could support the implementation of AI-ECG models as a triage tool in the emergency room to identify patients who would profit from immediate coronary angiography. Particularly, NSTEMI patients may substantially benefit from the implementation of an AI-ECG model specifically trained to detect occlusion myocardial infarction as a significant proportion of

whom have an acute total occlusion of a coronary artery that is missed using the current STEMI criteria.

Future studies should aim to investigate the feasibility of using the AI-ECG model in clinical settings in prospective and multicenter trials, focusing further on the performance of the AI-ECG model in detecting occlusion myocardial infarction (OMI) in NSTEMI patients. The effect of different time intervals between analysis of the ECG and angiography, as well as repeated ECG monitoring before angiography should be investigated. The application of a uniform reference standard may further be beneficial. However, how can we reliably determine which patients with suspected acute coronary syndrome (ACS) require coronary angiography? The definition of occlusion myocardial infarction (OMI) varies across studies. While some authors use solely angiographic findings for diagnosis, others also include biochemical markers as hs-troponin. It should be noted that a coronary artery may be completely occluded at the time of symptom onset but can be reperfused spontaneously or medically before angiography is performed. Therefore, a prolonged time interval between the first ECG or the assessment of hs-troponin and the performance of angiography could result in a false negative finding, although a total coronary occlusion was present at the beginning. This raises important questions: is TIMI flow and thus coronary angiography sufficient to confirme occlusion myocardial infarction, or are other surrogate parameters required for the diagnosis given frequent delays until angiography in NSTEMI patients? Can the level of hs-troponin point towards which patients had an initial total occlusion that improved by the time of angiography?

Regardless of which definition with a cut-off is applied, there will always be cases that are not correctly identified. For example, some patients with TIMI flow 2 and non-elevated troponin above 100 times ULN were classified as false positive. Although, in our opinion, they would have benefited from immediate coronary angiography, since they likely had an occlusion myocardial infarction. Similarly, some false negative OMI cases with TIMI flow 1 had only minimal troponin dynamic, raising the question of wheter they truly had an acute occlusion or rather a chronic stenosis was present that was not categorized correctly in the index angiography.

A clinical usability study examined the impact of an explainable AI which had been trained to recognize occlusion myocardial infarction (OMI) on ECG experts. Although the physicians considered the silency maps, which highlights the leads in the ECG that indicate signs of OMI, to be only of moderate relevance, a high level of confidence in the model predictions was achieved. The authors of the study attribute this to the fact that the AI-ECG model and the experts rated different ECG leads as relevant for the detection of occlusion myocardial infarction. Explainable AI could improve these discrepancies in the future by providing clinicians the knowledge of how such AI models predict occlusion myocardial infarction (OMI). (98)

In addition, further studies to assess the impact of using the AI-ECG model on clinically relevant endpoints including mortality, infarct size and development of heart failure are indicated. Furthermore, additional research is warranted to evaluate the feasibility of AI-ECG models in clinical practice and to determine the potential cost-effectiveness that can be achieved by reducing the number of not-indicated angiographies.

4.2 Conclusion

In conclusion, based on the results of our retrospective analysis, despite the potential of the AI-ECG model to improve the detection of occlusion myocardial infarction (OMI) in NSTEMI patients, the highly favorable results of previous studies could not be replicated in our NSTEMI cohort. Further investigations are planned to evaluate the clinical applicability in this patient group. We highlighted the limitations of the current definitions for acute coronary occlusion, for future studies we propose a blinded adjudication by interventional cardiologists based on all available data.

References

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. J Am Coll Cardiol [Internet]. 2020;76(25):2982–3021. Available from: https://www.sciencedirect.com/science/article/pii/S0735109720377755
2. Lüscher T, Landmesser U. Herz-Kreislauf. 3. Lüscher TF, Landmesser U, editors. Berlin, Heidelberg: Springer Berlin Heidelberg; 2024. 93–126 p.
3. Salari N, Morddarvanjoghi F, Abdolmaleki A, Rasoulpoor S, Khaleghi AA, Hezarkhani LA, et al. The global prevalence of myocardial infarction: a systematic review and meta-analysis. BMC Cardiovasc Disord [Internet]. 2023;23(1):206. Available from: https://doi.org/10.1186/s12872-023-03231-w
4. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). Eur Heart J [Internet]. 2021 Sep 7;42(34):3227–337. Available from: https://doi.org/10.1093/eurheartj/ehab484
5. Fuster V, Kovacic JC. Acute coronary syndromes: Pathology, diagnosis, genetics, prevention, and treatment. Circ Res [Internet]. 2014 Jun 19 [cited 2024 Oct 8];114(12):1847–51. Available from: https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.114.302806
6. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). Eur Heart J [Internet]. 2023 Oct 7;44(38):3720–826. Available from: https://doi.org/10.1093/eurheartj/ehad191
7. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Eur Heart J. 2019;40(3).
8. Reihe D, editor. Innere Medizin. Stuttgart: Georg Thieme Verlag; 2018. 83–98 p.
9. Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. The Lancet [Internet]. 2017;389(10065):197–210. Available from: https://www.sciencedirect.com/science/article/pii/S0140673616306778
10. Khan AR, Golwala H, Tripathi A, Bin Abdulhak AA, Bavishi C, Riaz H, et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: A systematic review and meta-Analysis. Eur Heart J. 2017;38(41).
11. Yusuf PS, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet [Internet]. 2004 Sep 11 [cited 2024 Oct 13];364(9438):937–52. Available from: https://pubmed.ncbi.nlm.nih.gov/15364185/

12. Mitsis A, Gragnano F. Myocardial Infarction with and without ST-segment Elevation: a Contemporary Reappraisal of Similarities and Differences. Curr Cardiol Rev. 2020;17(4).
13. Lu L, Liu M, Sun R, Zheng Y, Zhang P. Myocardial Infarction: Symptoms and Treatments. Cell Biochem Biophys [Internet]. 2015;72(3):865–7. Available from: https://doi.org/10.1007/s12013-015-0553-4
14. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and Treatment of Acute Coronary Syndromes: A Review. JAMA [Internet]. 2022 Feb 15;327(7):662–75. Available from: https://doi.org/10.1001/jama.2022.0358
15. Kapur NK, Kanwar M, Sinha SS, Thayer KL, Garan AR, Hernandez-Montfort J, et al. Criteria for Defining Stages of Cardiogenic Shock Severity. J Am Coll Cardiol. 2022 Jul;80(3):185–98.
16. Christ Julia. Kardiologie Basic. 6th edition. 2022.
17. Schulte KJ, Mayrovitz HN. Myocardial Infarction Signs and Symptoms: Females vs. Males. Cureus. 2023 Apr 13;
18. Schmitz T, Wein B, Raake P, Heier M, Peters A, Linseisen J, et al. Do patients with diabetes with new onset acute myocardial infarction present with different symptoms than non-diabetic patients? Front Cardiovasc Med. 2024 Jan 15;11.
19. Kumar A, Sanghera A, Sanghera B, Mohamed T, Midgen A, Pattison S, et al. Chest pain symptoms during myocardial infarction in patients with and without diabetes: a systematic review and meta-analysis. Heart. 2023 Oct;109(20):1516–24.
20. Dzikowicz DJ, Carey MG. Secondary electrocardiographic stratification of NSTEMI to identify an acutely occluded culprit artery. Physiol Meas [Internet]. 2023 Jul 1;44(7):07TR01. Available from: https://iopscience.iop.org/article/10.1088/1361-6579/acddc8
21. D'Souza M, Sarkisian L, Saaby L, Poulsen TS, Gerke O, Larsen TB, et al. Diagnosis of unstable angina pectoris has declined markedly with the advent of more sensitive troponin assays. Am J Med [Internet]. 2015 Aug 1 [cited 2024 Oct 8];128(8):852–60. Available from: https://pubmed.ncbi.nlm.nih.gov/25820165/
22. Pegg TJ, Maunsell Z, Karamitsos TD, Taylor RP, James T, Francis JM, et al. Utility of cardiac biomarkers for the diagnosis of type V myocardial infarction after coronary artery bypass grafting: insights from serial cardiac MRI. Heart [Internet]. 2011 May [cited 2024 Oct 9];97(10):810–6. Available from: https://pubmed.ncbi.nlm.nih.gov/21378388/
23. Jrgensen PH, Nybo M, Jensen MK, Mortensen PE, Poulsen TS, Pyndt Diederichsen AC, et al. Optimal cut-off value for cardiac troponin I in ruling out Type 5 myocardial infarction. Interact Cardiovasc Thorac Surg [Internet]. 2014 [cited 2024 Oct 9];18(5):544–50. Available from: https://pubmed.ncbi.nlm.nih.gov/24468543/
24. Avdikos G, Michas G, Smith SW. From Q/Non-Q Myocardial Infarction to STEMI/NSTEMI: Why It's Time to Consider Another Simplified Dichotomy; a Narrative Literature Review. Vol. 10, Archives of Academic Emergency Medicine. 2022.
25. Aslanger EK, Meyers PH, Smith SW. Time for a new paradigm shift in myocardial infarction. Anatol J Cardiol. 2021;25(3).

26. Al-Zaiti S, Macleod R, Dam P Van, Smith SW, Birnbaum Y. Emerging ECG methods for acute coronary syndrome detection: Recommendations & future opportunities. J Electrocardiol. 2022;74.
27. Sankardas MA, Ramakumar V, Farooqui FA. Of Occlusions, Inclusions, and Exclusions: Time to Reclassify Infarctions? Circulation. 2021;144(5).
28. Aslanger EK. Beyond the ST-segment in Occlusion Myocardial Infarction (OMI): Diagnosing the OMI-nous. Vol. 23, Turkish Journal of Emergency Medicine. 2023.
29. Group FTT (FTT) C. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. The Lancet [Internet]. 1994 Feb 5;343(8893):311–22. Available from: https://doi.org/10.1016/S0140-6736(94)91161-4
30. Herman R, Smith S, Meyers H, Bertolone D, Leone A, Bermpeis K, et al. Poor prognosis of total culprit artery occlusion in patients presenting with NSTEMI. Eur Heart J. 2023 Oct;44.
31. Meyers HP, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, et al. Comparison of the ST-Elevation Myocardial Infarction (STEMI) vs. NSTEMI and Occlusion MI (OMI) vs. NOMI Paradigms of Acute MI. J Emerg Med [Internet]. 2021;60(3):273–84. Available from: https://www.sciencedirect.com/science/article/pii/S0736467920310702
32. de Alencar Neto JN, Scheffer MK, Correia BP, Franchini KG, Felicioni SP, De Marchi MFN. Systematic review and meta-analysis of diagnostic test accuracy of ST-segment elevation for acute coronary occlusion. Int J Cardiol [Internet]. 2024 May 1 [cited 2024 Oct 12];402. Available from: https://pubmed.ncbi.nlm.nih.gov/38382857/
33. McLaren JTT, El-Baba M, Sivashanmugathas V, Meyers HP, Smith SW, Chartier LB. Missing occlusions: Quality gaps for ED patients with occlusion MI. Am J Emerg Med [Internet]. 2023 Nov 1 [cited 2024 Oct 18];73:47–54. Available from: https://pubmed.ncbi.nlm.nih.gov/37611526/
34. McCabe JM, Armstrong EJ, Kulkarni A, Hoffmayer KS, Bhave PD, Garg S, et al. Prevalence and Factors Associated With False-Positive ST-Segment Elevation Myocardial Infarction Diagnoses at Primary Percutaneous Coronary Intervention–Capable Centers: A Report From the Activate-SF Registry. Arch Intern Med [Internet]. 2012 Jun 11;172(11):864–71. Available from: https://doi.org/10.1001/archinternmed.2012.945
35. Larson DM, Menssen KM, Sharkey SW, Duval S, Schwartz RS, Harris J, et al. “False-Positive” Cardiac Catheterization Laboratory Activation Among Patients With Suspected ST-Segment Elevation Myocardial Infarction. JAMA [Internet]. 2007 Dec 19;298(23):2754–60. Available from: https://doi.org/10.1001/jama.298.23.2754
36. Degheim G, Berry A, Zughaib M. False activation of the cardiac catheterization laboratory: The price to pay for shorter treatment delay. JRSM Cardiovasc Dis [Internet]. 2019 Jan [cited 2024 Oct 11];8:204800401983636. Available from: /pmc/articles/PMC6456844/
37. Meyers HP, Smith SW. Prospective, real-world evidence showing the gap between ST elevation myocardial infarction (STEMI) and occlusion MI (OMI). Vol. 293, International Journal of Cardiology. 2019.

38. Miranda DF, Lobo AS, Walsh B, Sandoval Y, Smith SW. New Insights Into the Use of the 12-Lead Electrocardiogram for Diagnosing Acute Myocardial Infarction in the Emergency Department. Canadian Journal of Cardiology [Internet]. 2018 Feb 1;34(2):132–45. Available from: https://doi.org/10.1016/j.cjca.2017.11.011
39. Kim MC, Ahn Y, Rhew SH, Jeong MH, Kim JH, Hong YJ, et al. Impact of total occlusion of an infarct-related artery on long-term mortality in acute non-ST-elevation myocardial infarction patients who underwent early percutaneous coronary intervention. Int Heart J. 2012;53(3).
40. Morawska I, Niemiec R, Stec M, Wrona K, Bańka P, Swinarew A, et al. Total Occlusion of the Infarct-Related Artery in Non-ST-Elevation Myocardial Infarction (NSTEMI)—How Can We Identify These Patients? Medicina (B Aires) [Internet]. 2021 Nov 3 [cited 2024 Oct 2];57(11):1196. Available from: https://www.mdpi.com/1648-9144/57/11/1196
41. Yildirim U, Balaban F. Laboratory markers at admission to predict the presence of totally occluded culprit artery in NSTEMI. Medicine [Internet]. 2022;101(45). Available from: https://journals.lww.com/md-journal/fulltext/2022/11110/laboratory_markers_at_admission_to_predict_the.16.aspx
42. Grenne B, Eek C, Sjøli B, Dahlslett T, Uchto M, Hol PK, et al. Acute coronary occlusion in non-ST-elevation acute coronary syndrome: outcome and early identification by strain echocardiography. Heart [Internet]. 2010 Oct 1;96(19):1550. Available from: http://heart.bmj.com/content/96/19/1550.abstract
43. Kontos MC, de Lemos JA, Deitelzweig SB, Diercks DB, Gore MO, Hess EP, et al. 2022 ACC Expert Consensus Decision Pathway on the Evaluation and Disposition of Acute Chest Pain in the Emergency Department: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol [Internet]. 2022;80(20):1925–60. Available from: https://www.sciencedirect.com/science/article/pii/S0735109722066189
44. Aslanger EK, Meyers HP, Smith SW. Recognizing electrocardiographically subtle occlusion myocardial infarction and differentiating it from mimics: Ten steps to or away from cath lab. Turk Kardiyol Dern Ars [Internet]. 2021;49(6):488–500. Available from: https://dx.doi.org/10.5543/tkda.2021.21026
45. Miranda DF, Lobo AS, Walsh B, Sandoval Y, Smith SW. New Insights Into the Use of the 12-Lead Electrocardiogram for Diagnosing Acute Myocardial Infarction in the Emergency Department. Canadian Journal of Cardiology. 2018 Feb 1;34(2):132–45.
46. Pendell Meyers H, Limkakeng AT, Jaffa EJ, Patel A, Theiling BJ, Rezaie SR, et al. Validation of the modified Sgarbossa criteria for acute coronary occlusion in the setting of left bundle branch block: A retrospective case-control study. Am Heart J [Internet]. 2015 Dec 1 [cited 2024 Oct 10];170(6):1255–64. Available from: https://pubmed.ncbi.nlm.nih.gov/26678648/
47. Dodd KW, Zvosec DL, Hart MA, Glass G, Bannister LE, Body RM, et al. Electrocardiographic Diagnosis of Acute Coronary Occlusion Myocardial Infarction in Ventricular Paced Rhythm Using the Modified Sgarbossa Criteria. Ann Emerg Med [Internet]. 2021 Oct 1 [cited 2024 Oct

10];78(4):517–29. Available from: https://pubmed.ncbi.nlm.nih.gov/34172301/
48. Lee DH, Walsh B, Smith SW. Terminal QRS distortion is present in anterior myocardial infarction but absent in early repolarization. Am J Emerg Med [Internet]. 2016 Nov 1 [cited 2024 Oct 10];34(11):2182–5. Available from: https://pubmed.ncbi.nlm.nih.gov/27658331/
49. Smith SW, Khalil A, Henry TD, Rosas M, Chang RJ, Heller K, et al. Electrocardiographic differentiation of early repolarization from subtle anterior ST-segment elevation myocardial infarction. Ann Emerg Med [Internet]. 2012 [cited 2024 Oct 10];60(1):45-56.e2. Available from: https://pubmed.ncbi.nlm.nih.gov/22520989/
50. Klein LR, Shroff GR, Beeman W, Smith SW. Electrocardiographic criteria to differentiate acute anterior ST-elevation myocardial infarction from left ventricular aneurysm. Am J Emerg Med [Internet]. 2015 Jun 1 [cited 2024 Oct 10];33(6):786–90. Available from: https://pubmed.ncbi.nlm.nih.gov/25862248/
51. Bischof JE, Worrall C, Thompson P, Marti D, Smith SW. ST depression in lead aVL differentiates inferior ST-elevation myocardial infarction from pericarditis. Am J Emerg Med [Internet]. 2016 Feb 1 [cited 2024 Oct 10];34(2):149–54. Available from: https://pubmed.ncbi.nlm.nih.gov/26542793/
52. Pendell Meyers H, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, et al. Accuracy of OMI ECG findings versus STEMI criteria for diagnosis of acute coronary occlusion myocardial infarction. IJC Heart & Vasculature [Internet]. 2021;33:100767. Available from: https://www.sciencedirect.com/science/article/pii/S2352906721000555
53. Bildik B, Aker M, Çekmen B, Tabak BO, Atiş ŞE. Role of Laboratory Parameters in the Diagnosis of OMI/NOMI. Eurasian Journal of Emergency Medicine. 2024 Jul 19;
54. McLaren J, de Alencar JN, Aslanger EK, Meyers HP, Smith SW. From ST-Segment Elevation MI to Occlusion MI: The New Paradigm Shift in Acute Myocardial Infarction. JACC: Advances. 2024 Nov 1;3(11):101314.
55. Erhardt L, Herlitz J, Bossaert L, Halinen M, Keltai M, Koster R, et al. Task force on the management of chest pain. Eur Heart J [Internet]. 2002 Aug 1;23(15):1153–76. Available from: https://doi.org/10.1053/euhj.2002.3194
56. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and Treatment of Acute Coronary Syndromes: A Review. JAMA [Internet]. 2022 Feb 15 [cited 2024 Oct 8];327(7):662–75. Available from: https://jamanetwork.com/journals/jama/fullarticle/2789023
57. Trappe HJ, Schuster HP. EKG-Kurs für Isabel. Trappe HJ, Schuster HP, editors. Stuttgart: Georg Thieme Verlag; 2020. 82–89 p.
58. Ferrante G, Barbieri L, Sponzilli C, Lucreziotti S, Uriarte DS, Centola M, et al. Predictors of Mortality and Long-Term Outcome in Patients with Anterior STEMI: Results from a Single Center Study. J Clin Med [Internet]. 2021 Dec 1 [cited 2024 Oct 9];10(23). Available from: /pmc/articles/PMC8658372/
59. Pendell Meyers H, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, et al. Ischemic st-segment depression maximal in v1–v4 (Versus v5–v6) of any amplitude is specific for occlusion myocardial infarction (versus nonocclusive ischemia). J Am Heart Assoc. 2021;10(23).

60. Banerjee D, Perrett C, Banerjee A. Troponins, Acute Coronary Syndrome and Renal Disease: From Acute Kidney Injury Through End-stage Kidney Disease. European Cardiology Review [Internet]. 2019 Dec 1 [cited 2024 Oct 9];14(3):187. Available from: /pmc/articles/PMC6950405/
61. Stub D, Smith K, Bernard S, Nehme Z, Stephenson M, Bray JE, et al. Air versus oxygen in ST-segment-elevation myocardial infarction. Circulation [Internet]. 2015 Jun 16 [cited 2024 Oct 6];131(24):2143–50. Available from: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.114.014494
62. Hofmann R, James SK, Jernberg T, Lindahl B, Erlinge D, Witt N, et al. Oxygen Therapy in Suspected Acute Myocardial Infarction. New England Journal of Medicine [Internet]. 2017 Sep 28 [cited 2024 Oct 6];377(13):1240–9. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1706222
63. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes. New England Journal of Medicine [Internet]. 2009 Sep 10 [cited 2024 Oct 6];361(11):1045–57. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa0904327
64. Wiviott SD, Braunwald E, Mccabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al. Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes. New England Journal of Medicine [Internet]. 2007 Nov 15 [cited 2024 Oct 6];357(20):2001–15. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa0706482
65. Schüpke S, Neumann FJ, Menichelli M, Mayer K, Bernlochner I, Wöhrle J, et al. Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes. New England Journal of Medicine [Internet]. 2019 Oct 17 [cited 2024 Oct 6];381(16):1524–34. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1908973
66. Ibanez B, MacAya C, Sánchez-Brunete V, Pizarro G, Fernández-Friera L, Mateos A, et al. Effect of early metoprolol on infarct size in ST-segment-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: the Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction (METOCARD-CNIC) trial. Circulation [Internet]. 2013 Oct 1 [cited 2024 Oct 6];128(14):1495–503. Available from: https://pubmed.ncbi.nlm.nih.gov/24002794/
67. Pizarro G, Fernández-Friera L, Fuster V, Fernández-Jiménez R, García-Ruiz JM, García-Álvarez A, et al. Long-term benefit of early pre-reperfusion metoprolol administration in patients with acute myocardial infarction: results from the METOCARD-CNIC trial (Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction). J Am Coll Cardiol [Internet]. 2014 Jun 10 [cited 2024 Oct 6];63(22):2356–62. Available from: https://pubmed.ncbi.nlm.nih.gov/24694530/
68. García-Ruiz JM, Fernández-Jiménez R, García-Alvarez A, Pizarro G, Galán-Arriola C, Fernández-Friera L, et al. Impact of the Timing of Metoprolol Administration During STEMI on Infarct Size and Ventricular Function. J Am Coll Cardiol [Internet]. 2016 May 10 [cited 2024 Oct 6];67(18):2093–104. Available from: https://pubmed.ncbi.nlm.nih.gov/27052688/
69. Huynh T, Perron S, O'Loughlin J, Joseph L, Labrecque M, Tu J V., et al. Comparison of Primary Percutaneous Coronary Intervention and Fibrinolytic

Therapy in ST-Segment-Elevation Myocardial Infarction. Circulation. 2009;119(24).
70. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review of 23 randomised trials. Lancet. 2003;361(9351).
71. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky B V., Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction. A meta-analysis. Vol. 283, JAMA. 2000.
72. Boersma E, Maas ACP, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. Lancet. 1996;348(9030).
73. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al. Impact of Time to Treatment on Mortality after Prehospital Fibrinolysis or Primary Angioplasty: Data from the CAPTIM Randomized Clinical Trial. Circulation. 2003;108(23).
74. Iqbal JD, Vinay R. Are we ready for Artificial Intelligence in Medicine? Swiss Med Wkly [Internet]. 2022 May 9 [cited 2024 Oct 7];152(19–20). Available from: https://pubmed.ncbi.nlm.nih.gov/35758341/
75. Hamet P, Tremblay J. Artificial intelligence in medicine. Metabolism [Internet]. 2017 Apr 1 [cited 2024 Oct 7];69S:S36–40. Available from: https://pubmed.ncbi.nlm.nih.gov/28126242/
76. Tschandl P, Codella N, Akay BN, Argenziano G, Braun RP, Cabo H, et al. Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study. Lancet Oncol [Internet]. 2019 Jul 1 [cited 2024 Oct 7];20(7):938–47. Available from: https://pubmed.ncbi.nlm.nih.gov/31201137/
77. Ding Y, Sohn JH, Kawczynski MG, Trivedi H, Harnish R, Jenkins NW, et al. A Deep Learning Model to Predict a Diagnosis of Alzheimer Disease by Using 18F-FDG PET of the Brain. Radiology [Internet]. 2019 Mar 1 [cited 2024 Oct 7];290(2):456–64. Available from: https://pubmed.ncbi.nlm.nih.gov/30398430/
78. Batchu S, Liu F, Amireh A, Waller J, Umair M. A Review of Applications of Machine Learning in Mammography and Future Challenges. Oncology [Internet]. 2021 Jul 1 [cited 2024 Oct 7];99(8):483–90. Available from: https://pubmed.ncbi.nlm.nih.gov/34023831/
79. Johnson KW, Torres Soto J, Glicksberg BS, Shameer K, Miotto R, Ali M, et al. Artificial Intelligence in Cardiology. J Am Coll Cardiol. 2018 Jun 12;71(23):2668–79.
80. Wang H, Zu Q, Chen J, Yang Z, Ahmed MA. Application of Artificial Intelligence in Acute Coronary Syndrome: A Brief Literature Review. Adv Ther [Internet]. 2021 Oct 1 [cited 2024 Oct 7];38(10):5078–86. Available from: https://pubmed.ncbi.nlm.nih.gov/34528221/
81. Ector JH, Ope P, Om T, Ufderheide PA, Obin R, Uthazer R, et al. Missed Diagnoses of Acute Cardiac Ischemia in the Emergency Department. New England Journal of Medicine [Internet]. 2000 Apr 20 [cited 2024 Oct 7];342(16):1163–70. Available from: https://www.nejm.org/doi/full/10.1056/NEJM200004203421603

82. Chan PZ, Ramli MAI Bin, Chew HSJ. Diagnostic Test Accuracy of artificial intelligence-assisted detection of acute coronary syndrome: A systematic review and meta-analysis. Comput Biol Med. 2023 Dec 1;167:107636.
83. Martínez-Sellés M, Marina-Breysse M. Current and Future Use of Artificial Intelligence in Electrocardiography. J Cardiovasc Dev Dis [Internet]. 2023 Apr 1 [cited 2024 Oct 7];10(4). Available from: https://pubmed.ncbi.nlm.nih.gov/37103054/
84. Panjiyar BK, Davydov G, Nashat H, Ghali S, Afifi S, Suryadevara V, et al. A Systematic Review: Do the Use of Machine Learning, Deep Learning, and Artificial Intelligence Improve Patient Outcomes in Acute Myocardial Ischemia Compared to Clinician-Only Approaches? Cureus [Internet]. 2023 Aug 6 [cited 2024 Oct 7];15(8). Available from: https://pubmed.ncbi.nlm.nih.gov/37674942/
85. Salari N, Shohaimi S, Najafi F, Nallappan M, Karishnarajah I. Application of pattern recognition tools for classifying acute coronary syndrome: An integrated medical modeling. Theor Biol Med Model [Internet]. 2013 Sep 18 [cited 2024 Oct 8];10(1):1–17. Available from: https://tbiomed.biomedcentral.com/articles/10.1186/1742-4682-10-57
86. Al-Zaiti S, Besomi L, Bouzid Z, Faramand Z, Frisch S, Martin-Gill C, et al. Machine learning-based prediction of acute coronary syndrome using only the pre-hospital 12-lead electrocardiogram. Nat Commun [Internet]. 2020 Dec 1 [cited 2024 Oct 7];11(1). Available from: https://pubmed.ncbi.nlm.nih.gov/32769990/
87. D'Ascenzo F, De Filippo O, Gallone G, Mittone G, Deriu MA, Iannaccone M, et al. Machine learning-based prediction of adverse events following an acute coronary syndrome (PRAISE): a modelling study of pooled datasets. Lancet [Internet]. 2021 Jan 16 [cited 2024 Oct 7];397(10270):199–207. Available from: https://pubmed.ncbi.nlm.nih.gov/33453782/
88. McLaren JTT, Meyers HP, Smith SW. Kenichi Harumi Plenary Address at Annual Meeting of the International Society of Computers in Electrocardiology: "What Should ECG Deep Learning Focus on? The diagnosis of acute coronary occlusion!" J Electrocardiol. 2023 Jan 1;76:39–44.
89. Baker PO, Karim SR, Smith SW, Meyers HP, Robinson AE, Ibtida I, et al. Artificial Intelligence Driven Prehospital ECG Interpretation for the Reduction of False Positive Emergent Cardiac Catheterization Lab Activations: A Retrospective Cohort Study. Prehospital Emergency Care [Internet]. 2024 [cited 2024 Oct 8]; Available from: https://www.tandfonline.com/doi/abs/10.1080/10903127.2024.2399218
90. Herman R, Meyers HP, Smith SW, Demolder A, Bertolone DT, Leone A, et al. ECG-based deep learning for detecting epicardial coronary occlusion in acute myocardial infarction. Eur Heart J [Internet]. 2023 Nov 9 [cited 2024 Oct 8];44(Supplement_2). Available from: https://dx.doi.org/10.1093/eurheartj/ehad655.2930
91. Herman R, Meyers HP, Smith SW, Bertolone DT, Leone A, Bermpeis K, et al. International evaluation of an artificial intelligence–powered electrocardiogram model detecting acute coronary occlusion myocardial infarction. European Heart Journal - Digital Health [Internet]. 2024 Mar 1;5(2):123–33. Available from: https://doi.org/10.1093/ehjdh/ztad074

92. Hashmi KA, Adnan F, Ahmed O, Yaqeen SR, Ali J, Irfan M, et al. Risk Assessment of Patients After ST-Segment Elevation Myocardial Infarction by Killip Classification: An Institutional Experience. Cureus [Internet]. 2020 Dec 22 [cited 2024 Oct 8];12(12). Available from: /pmc/articles/PMC7815264/
93. Al-Zaiti SS, Martin-Gill C, Zègre-Hemsey JK, Bouzid Z, Faramand Z, Alrawashdeh MO, et al. Machine learning for ECG diagnosis and risk stratification of occlusion myocardial infarction. Nat Med [Internet]. 2023 Jul 1 [cited 2024 Oct 7];29(7):1804–13. Available from: https://pubmed.ncbi.nlm.nih.gov/37386246/
94. Domingo-Gardeta T, Montero-Cabezas JM, Jurado-Román A, Sabaté M, Aboal J, Baranchuk A, et al. Rationale and design of the artificial intelligence scalable solution for acute myocardial infarction (ASSIST) study. J Electrocardiol. 2024 Sep;86:153768.
95. Dali M, Bogle CME, Bogle RG. The Evolving Paradigm of Myocardial Infarction in the Era of Artificial Intelligence. Br J Hosp Med. 2025 Feb 25;86(2):1–7.
96. Herman R, Kisova T, Belmonte M, Wilgenhof A, Toth G, Demolder A, et al. Artificial Intelligence–Powered Electrocardiogram Detecting Culprit Vessel Blood Flow Abnormality: AI-ECG TIMI Study Design and Rationale. Journal of the Society for Cardiovascular Angiography & Interventions. 2025 Mar;4(3):102494.
97. Díaz-Herrera BA, Roman-Rangel E, Castro-García CA, Sierra-Lara Martinez D, Gopar-Nieto R, Velez-Talavera KG, et al. Derivación de un modelo electrocardiográfico basado en inteligencia artificial para la detección de infarto agudo del miocardio por oclusión trombótica. Arch Cardiol Mex. 2025 May 5;95(2).
98. Riek NT, Gokhale TA, Martin-Gill C, Kraevsky-Philips K, Zègre-Hemsey JK, Saba S, et al. Clinical usability of deep learning-based saliency maps for occlusion myocardial infarction identification from the prehospital 12-Lead electrocardiogram. J Electrocardiol. 2024 Nov;87:153792.

Appendix

The following AI-supported tools were used solely for language optimization between November 2024 to July 2025, in accordance with the applicable standards for good scientific practice of the Medical University of Graz:

1. DeepL Translator (various versions, most recently 25.5.12046922)
    - Publisher/Provider: DeepL SE
    - URL: https://www.deepl.com/de/translator
2. Grammarly Premium (various web versions)
    - Publisher/Provider: Grammarly, Inc.
    - URL: https://www.grammarly.com
3. ChatGPT (GPT-3.5, GPT-4.0)
    - Publisher/Provider: Open AI
    - URL: https://chatgpt.com