Rationale and design of the artificial intelligence scalable solution for acute myocardial infarction (ASSIST) study

Domingo-Gardeta, T.; Montero Cabezas, J.M.; Jurado-Román, A.; Sabaté, M.; Aboal, J.; Baranchuk, A.; ... ; Martínez-Sellés, M.

Journal of Electrocardiology 86 (2024) 153768

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

Rationale and design of the artificial intelligence scalable solution for acute myocardial infarction (ASSIST) study

Tomás Domingo-Gardeta [a,b,c], José M. Montero-Cabezas [d], Alfonso Jurado-Román [e], Manel Sabaté [b,f,g], Jaime Aboal [h], Adrián Baranchuk [i], Xavier Carrillo [j], Sebastián García-Zamora [k], Hélder Dores [l,m,n], Viktor van der Valk [d], Roderick W.C. Scherptong [d], Joan F. Andrés-Cordón [j], Pablo Vidal [f], Daniel Moreno-Martínez [j,o], Raquel Toribio-Fernández [p], José María Lillo-Castellano [p,q], Roberto Cruz [p], François De Guio [p], Manuel Marina-Breysse [b,p,q], Manuel Martínez-Sellés [a,b,c,r,*]

[a] Department of Cardiology, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain
[b] Centro de Investigación Biomédica en Red. Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain
[c] Facultad de Medicina, Universidad Complutense, 28040 Madrid, Spain
[d] Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands.
[e] Cardiology Department, La Paz University Hospital, Fundación de Investigación Hospital La Paz, IdiPaz Madrid, Spain.
[f] Institut Clínic Cardiovascular, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain
[g] Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[h] Servicio de Cardiología, Hospital Universitario Josep Trueta, Girona, Spain
[i] Division of Cardiology, Kingston Health Science Center, Queen's University, Kingston, Ontario, Canada
[j] Hospital Germans Trias i Pujol, Badalona, Spain
[k] Department of Cardiology, Sanatorio Delta, Rosario, Argentina
[l] Luz Hospital Lisbon, Lisbon, Portugal
[m] NOVA Medical School, Lisbon, Portugal
[n] CHRC, NOVA Medical School, Lisbon, Portugal
[o] Research group on innovation, health economics and digital transformation, Germans Trias i Pujol Research Institute
[p] Idoven Research, Madrid, Spain
[q] Centro Nacional de Investigaciones Cardiovasculares (CNIC), Myocardial Pathophysiology Area, Madrid, Spain
[r] Facultad de Ciencias de la Salud, Universidad Europea, Villaviciosa de Odón, 28670 Madrid, Spain

ARTICLE INFO

Keywords:
Acute coronary syndrome
Myocardial infarction
Electrocardiogram
Artificial intelligence

ABSTRACT

Background: Acute coronary syndrome (ACS), specifically ST-segment elevation myocardial infarction is a major cause of morbidity and mortality throughout Europe. Diagnosis in the acute setting is mainly based on clinical symptoms and physician's interpretation of an electrocardiogram (ECG), which may be subject to errors. ST-segment elevation is the leading criteria to activate urgent reperfusion therapy, but a clear ST-elevation pattern might not be present in patients with coronary occlusion and ST-segment elevation might be seen in patients with normal coronary arteries.

Methods: The ASSIST project is a retrospective observational study aiming to improve the ECG-assisted assessment of ACS patients in the acute setting by incorporating an artificial intelligence platform, Willem™ to analyze 12-lead ECGs. Our aim is to improve diagnostic accuracy and reduce treatment delays. ECG and clinical data collected during this study will enable the optimization and validation of Willem™. A retrospective multicenter study will collect ECG, clinical, and coronary angiography data from 10,309 patients. The primary outcome is the performance of this tool in the correct identification of acute myocardial infarction with coronary artery occlusion. Model performance will be evaluated internally with patients recruited in this retrospective study while external validation will be performed in a second stage.

* Corresponding author.
E-mail address: mmselles@secardiologia.es (M. Martínez-Sellés).

https://doi.org/10.1016/j.jelectrocard.2024.153768

Available online 5 August 2024

Conclusion: ASSIST will provide key data to optimize Willem™ platform to detect myocardial infarction based on ECG-assessment alone. Our hypothesis is that such a diagnostic approach may reduce time delays, enhance diagnostic accuracy, and improve clinical outcomes.

Introduction

Ischemic heart disease is the leading single cause of death in Europe [1]. A large percentage of patients are managed in the emergency care setting, where a correct and rapid interpretation of the electrocardiogram (ECG) is essential to avoid treatment delays, especially when emergent reperfusion therapy is indicated [2]. To date, the presence of ST-segment elevation is the leading criteria to activate primary percutaneous intervention or to use fibrinolytics. Usually this elevation implies acute occlusion of an epicardial coronary artery, which is associated with adverse outcomes. However, ECG interpretation can be challenging. Patients may not exhibit a clear ST-elevation pattern on the ECG but can still have a high-risk coronary lesion (occlusive or subocclusive in a clinically important vessel). In fact, increasing evidence suggests that the ST-segment elevation dogma fails to accurately classify patients who will benefit from invasive treatment [3] and the paradigm is shifting towards the identification of occlusion myocardial infarction (OMI) based on angiographic evidence of culprit vessels [4]. In addition, 10–28% patients who present with ST-segment elevation and are referred for emergent revascularization do not have significant coronary artery stenosis (Fig. 1) [5–10]. This inappropriate diagnosis might have important clinical and economic implications, as coronary angiography is an expensive invasive procedure with potential complications [11,12]. On the other hand, revascularization delays, due to either the absence of clear ECG abnormalities or ECG misinterpretation, have negative impact on left ventricular function preservation, in-hospital complications, and 30-day mortality [13,14].

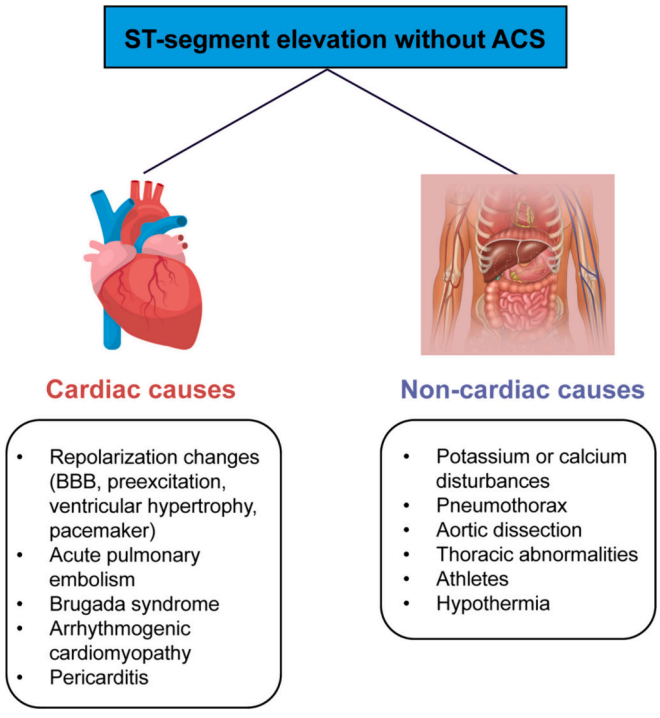

Fig. 1. ***Causes of ST-segment elevation not related with acute coronary syndromes (ACS).*** The figure classifies the possible causes responsible for ST-segment elevation not related with ACS into cardiac (repolarization changes, acute pulmonary embolism, Brugada syndrome, arrhythmogenic cardiomyopathy, and pericarditis) and non-cardiac (potassium or calcium disturbances, pneumothorax, aortic dissection, thoracic abnormalities, athletes, and hypothermia) causes.

In recent years, different tools based on artificial intelligence [AI] have been developed for ECG analysis [15,16]. In patients with suspected acute coronary syndrome (ACS), correct ECG interpretation is essential, and the use of AI tools in this clinical context is of particular interest. The ASSIST study aims to improve diagnostic accuracy and consequently reduce treatment delays in patients with ACS. These improvements are expected to reduce in-hospital mortality, closely associated with reducing revascularization delays [17,18].

Our aim is to optimize and validate the Willem™ Platform as a medical device (Idoven, Madrid, Spain), previously used for triage of ECG data from insertable cardiac monitors [19,20]. An ECG-analysis tool based on AI will be optimized for improving ACS triage. Our results could lead to a reduction in false positives (blank coronary angiographies) and improve diagnostic times.

Methods

Design

The ASSIST study includes retrospective and prospective phases but this manuscript is focused in the retrospective phase (Table 1). The prospective study intended to validate the Willem™ Platform within the current clinical setting will be detailed in a second step, once it has been optimized and validated in a subset of the retrospective cohort.

The retrospective study is a multicenter study for optimizing and validating a deep learning based 12-lead ECG analysis algorithm, Willem™, to classify OMI versus non-OMI patients. Its multicenter design will enable heterogeneity in the collection of ECG and clinical data, which is needed to ensure that the deep learning model can be generalized in different international hospitals and geographies, with different types of ECG machines, patient baseline characteristics, and clinical workflows.

Study population

We estimate that 10,309 patient records and ECGs with suspected ACS referred for emergent invasive coronary angiography will be collected from the following health areas:

- Leiden University Medical Center (Leiden, the Netherlands).
- Servicio Madrileño de Salud (Madrid, Spain).
- Institut Catalá de Salut (Catalonia, Spain).
- Latin America, through the Interamerican Society of Cardiology.

Data collection

Patient data will be pseudo-anonymized, all personal information will be removed or replaced by a unique code within the electronic case report form.

Retrospective inclusion will use two methods: 1) manual entry in the electronic Case Report Form (eCRF) of all relevant data obtained from medical records; 2) technical integration between the electronic medical record systems (EMRs) at each center and Idoven's platform. This integration allows data from the EMRs to be exported and transferred to the Willem™ platform.

All data will be stored and processed in Idoven's cloud platform in accordance with the regulations described in ISO 27001 and the Spanish National Security Framework. This ensures the application of best practices in information security management, guaranteeing the

confidentiality, integrity, and availability of data at all times. In addition, procedures complying with ISO 27017 for cloud security, ISO 27018 for personal data protection in the cloud, and ISO 27701 for privacy information management will be enforced, guaranteeing comprehensive data security and privacy protection.

To ensure proper correlation between ECGs and clinical data, each center will include a dedicated directory labeled with a unique patient identifier. All the data included will be regularly assessed to check for inconsistencies, ensuring the accuracy, quality, and reliability of all collected information.

ECG data

A 12-lead,10-s raw ECG data will be collected where possible. Other ECG formats might be included after checking technical feasibility.

ECG-derived data will be also collected such as device type and brand, version of the software, format, time of acquisition.

Clinical data and labels

In addition to ECG data, clinical data will be also collected. Clinical variables are needed for several reasons: to extract the labels needed for supervised learning, to define the population of interest in which the model has been developed and validated, to assess the performance of the model with regards to different subgroups of interest.

The following variables will be systematically collected: baseline characteristics including age, sex, height, weight, hypertension, diabetes, dyslipidemia, smoking, obesity, type of infarction, culprit coronary artery, number of coronary vessels with significant coronary stenosis, lab results such as hemoglobin, glucose, creatinine, and cardiac troponin; and follow-up clinical outcomes such as death or myocardial infarction.

If available, additional variables may be collected such as baseline information on previous ischemic heart disease, previous coronary revascularization, time of onset of chest pain, time of hospital arrival, door-to-balloon time; and outcomes during follow up such as medication at discharge, repeated coronary intervention, and major adverse cardiovascular events defined as the composite of first occurrence of stroke, myocardial infarction, heart failure, or all-cause mortality.

Angiographic reports will be used to extract the following relevant information to optimize the model, in particular: coronary dominance, culprit coronary vessel information, total coronary occlusion status, cardiac troponin level, creatinine level, and percutaneous coronary intervention.

The first level of classification will be OMI versus non-OMI patients. To do that, evidence of OMI will be extracted from the angiographic report. OMI will be defined as proof of percutaneous coronary intervention or evidence of occluded coronary vessel (TIMI flow 0–1). This data will be obtained from string search in angiographic reports. Differentiation between acute and chronic occlusion will be done locally based on information of troponin levels, symptoms, angiographic information, and ECG changes.

A second level of classification will be to classify OMI patients according to the presence of ST-segment elevation. A model to determine the culprit vessel will also be developed and tested in a second step.

Willem™ platform development for acute myocardial infarction

In order to develop and evaluate a machine learning model for the classification of OMI based on ECG data, we plan to use the last ECG recording available before coronary angiography. Next, we will apply inclusion and exclusion criteria to the dataset, considering factors such as ECG data quality, to ensure that only relevant and reliable data are included in the analysis. The dataset will then be split into training, validation, and test sets, with appropriate clinical variables being considered in order to minimize biases and ensure that the model is generalizable to a diverse patient population. Also, we will be evaluating scenarios where the entire database of a hospital is contained in only one of the sets whenever possible.

ECG data will be preprocessed and analyzed using Willem™ software, which extracts cardiac patterns from the raw ECG signal. The Willem™ Platform will then be optimized using the training and validation datasets to classify OMI vs. non-OMI patients based on ECG data alone. Further model development will also be performed, according to the presence of ST-segment elevation and the identification of occlusion areas if possible.

Model performance will be evaluated using both internal and external validation to ensure an independent assessment that mitigates the risk of overfitting and erroneous conclusions. Patient recruitment regarding the retrospective study described in the Study Population Section will feed the training and internal validation datasets. External validation will be carried out in a second stage with new and independent datasets.

For internal validation, the retrospective database will be divided by center into two random distinct sets: (1) a training set, which will contain a high percentage of the data (typically >70%) and will be used to train the model and fine-tuning its parameters; and (2) a test set, which will include the remaining data and will be used for validation. Furthermore, this process will be iterated multiple times (runs) to more accurately estimate the variability of the model's performance. Each iteration will involve: (1) a random selection of the samples included in each training and test set to ensure diverse training and validation scenarios; and (2) a training model and fine-tune of parameters.

For external validation, the model's performance will be assessed using entirely separate new databases that were not included in the internal validation phase. This validation will be conducted for each model iteration obtained from the internal validation runs, allowing for the evaluation of result variability. Additionally, this phase will incorporate new data from ongoing patient recruitment, further testing the model's robustness and applicability to new patient populations.

Sample size

The sample size of this study was calculated according to the preliminary performance that has been obtained from a previous multicenter study (*La Elevación del ST Observada no Necesita Necrosis Aguda Cardíaca* -LESTONNAC) [5]. Considering a 95% confidence interval, 95% power and assuming, respectively 16% and 14% of STEMI

Table 1
Inclusion and exclusion criteria of ASSIST retrospective study.

Inclusion criteria
Age ≥ 18 years.
Available digitally stored 12-lead ECG tracing prior to emergent invasive coronary angiography.
Available angiographic and clinical data.
Exclusion criteria
ECGs with poor signal quality.
Lack of digitally stored 12-lead ECG tracing prior to coronary angiography.
Non-available clinical or angiographic data.

inadequate activation without and with Willem [21] then at least 8278 patients would be needed to demonstrate a significant difference. Accounting for nearly 25% of patients with inappropriate ECG data as observed in ongoing Willem trial (NCT05890716), 10,309 individuals suitable for analysis must be included to demonstrate the performance of the Willem™ tool. This sample size is in accordance with the dataset size from previously reported and ongoing clinical studies [22,23] applying the Willem™ Platform as a Clinical Decision Support System in different environments with different intended uses. In addition, the proposed sample size is adjusted to a 50% confidence level for the total number of committed patients to be included in the study by the collaborating centers.

Study outcomes and statistical analysis

The primary outcome is the evaluation of the Willem™ platform performance to detect OMI. Accuracy of OMI diagnosis through ECG analysis will be compared with OMI clinical label as defined earlier (evidence of PCI or total coronary occlusion from angiography reports). Accuracy, positive predictive value, negative predictive value, sensitivity, specificity, F1-score, and the area under the curve ROC will be obtained as figures of merit for performance evaluation.

The same metrics will be also computed according to the presence of ST-segment elevation and coronary vessel area classification.

Sensitivity and specificity analysis will be performed according to different subgroups such as age categories, sex, presence/absence of different risk factors, lab measurements, extracted ECG cardiac patterns.

Patients with pacemaker rhythms will be analyzed in a separate subanalysis to assess whether these devices could affect diagnosis accuracy.

Ethics

This study protocol has been approved by the ethics committee of the Hospital General Universitario Gregorio Marañón, Madrid, Spain and is in accordance with the Helsinki Declaration. In the first retrospective phase, no informed consent will be registered. In the second prospective phase, the principal investigator at each participating center will be responsible for the on-site obtainment and storage of informed consents according to current European law.

Discussion

The results of the ASSIST study will provide information about the performance of an AI-based ECG-platform that helps to identify high-risk patients within the (suspected) ACS population. In recent years, we have been witnessing an acceleration in the development and use of digital technologies in medicine, some of these are based on AI software with increasingly complex functionalities. The expanding use of AI in cardiology is related with the key role of the ECG, a simple and readily available test. ECG databases can be used to train deep learning algorithms, but the clinical and angiographic information is frequently not available. AI applications have been developed in various cardiology fields [24,25], mainly in arrhythmias [26], heart failure, cardiac imaging, and ischemic heart disease [27–31]. For instance, the atrial fibrillation screening rate increased significantly when an ECG monitor equipped with ECG interpretation software was used [32]. However, automated arrhythmia detection is fundamentally different from detecting myocardial ischemia. While single-lead ECG is adequate for detecting arrhythmias, for the assessment of acute ischemia, a 12-lead ECG is needed.

The possibility of enabling physicians to make a prompt and accurate diagnosis, and therefore possibly improve clinical outcomes, is of particular interest in the context of suspected myocardial ischemia. This is specifically the case in patients with ECG signs suggestive of transmural myocardial infarction where several time frames, such as door-to-balloon time, have been improved over the last decades, with subsequent reduction of major adverse cardiovascular events [33]. This improvement in time frames was not as clearly observed in the time from symptom onset to diagnosis however [34]. Fast, correct and ECG interpretation is essential in patients with suspected ACS. Potentially, an AI ECG-platform can make such analyses available, additionally in prehospital settings where ECG analysis by specialists is not available. In order to do so, such an AI-platform should first be able to perform automated detection of ECG-patterns that are known to be associated with unfavorable coronary anatomy and patient outcome, such as the presence of ST-segment elevation. For example, Yifan Zhao et al. developed an algorithm for detecting ST-segment elevation myocardial infarction using a dataset of 667 ECGs with ST-segment elevation and 7571 control ECGs, demonstrating a good performance (an area-under-curve = 0.99 with 96% sensitivity and 99% specificity) [35]. However, the control group in this study had no ST-segment elevation. Outside of this, in the study, AI's response time to the emergency medical care in an ambulance has been shown to be shorter than the online physician's response, with an area-under-curve of 0.997 [36]. Secondly, the AI-platform should be able to detect other, more subtle ECG-patterns that may not be clear to all healthcare workers but are associated with a high-risk coronary anatomy. In these cases, currently referred to as OMI, an emergent revascularization strategy could favor positive patient outcomes. Additionally, the AI-platform should also be of assistance in patients where ECG-patterns are suggestive of OMI, but subsequent catheterization does not show an occluded or nearly occluded vessel, thus leading to the unnecessary or premature activation of the catheterization laboratory. Different registries have evaluated the range of false-positive cardiac catheterization laboratory activations. Depending on the definitions used, percentages vary from as low as approximately 5% to as high as approximately 40%. On average, around 25% of patients do not present with a culprit lesion in the coronary arteries [22,37].

This study comes with some limitations. First, ECG records will have to be in a good quality format, which may limit the applicability of the derived model to be used with ECGs in paper format, for example. Second, estimate of the myocardial infarction status will be determined based on ECG information at the time of the ECG, while the label will be based on the angiography occurring later. The algorithm will not consider a potential effect of medication until the angiography or any dynamic conditions. Such variability may be estimated in patients with several ECGs prior to angiography. Third, cases not managed with emergent coronary angiography will not be included. About a fifth of the patients who present with ST-segment elevation and are referred for emergent revascularization do not have significant coronary artery stenosis and our results could help to improve the positive predictive value, reducing this high rate of false positives ECGs. However, as we will only include cases for immediate angiography, the rate of patients with OMI not referred to urgent revascularization (false negatives) will not be improved. Finally, although the criteria for emergent coronary angiographies are clear, variations among centers might exist, particularly in patients without ST-segment elevation.

Conclusions

ASSIST will evaluate whether AI-based algorithms from the Willem™ platform can improve diagnostic accuracy and decrease time delays in patients with ACS. These findings might open a door to prognosis improvement in one of the main causes of death.

Funding

The ASSIST study has been funded by the European Institute of Innovation and Technology (EIT) within the call Start-up driven Projects (SUD) (2023-SUD-1831) and the flagship "Harnessing the full potential of health data for Innovation."

CRediT authorship contribution statement

Tomás Domingo-Gardeta: Writing – review & editing, Writing – original draft, Conceptualization. **José M. Montero-Cabezas:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Alfonso Jurado-Román:** Writing – review & editing, Methodology, Conceptualization. **Manel Sabaté:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Conceptualization. **Jaime Aboal:** Writing – review & editing, Conceptualization. **Adrián Baranchuk:** Writing – review & editing, Validation, Conceptualization. **Xavier Carrillo:** Writing – review & editing, Methodology. **Sebastián García-Zamora:** Writing – review & editing, Methodology, Investigation. **Hélder Dores:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Conceptualization. **Viktor van der Valk:** Writing – review & editing, Methodology, Data curation. **Roderick W.C. Scherptong:** Writing – review & editing, Methodology, Data curation. **Joan F. Andrés-Cordón:** Writing – review & editing, Methodology, Data curation. **Pablo Vidal:** Writing – review & editing, Methodology, Data curation. **Daniel Moreno-Martínez:** Writing – review & editing, Methodology, Data curation. **Raquel Toribio-Fernández:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **José María Lillo-Castellano:** Writing – review & editing, Validation, Supervision, Software, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Roberto Cruz:** Writing – review & editing, Validation, Supervision, Methodology, Data curation. **François De Guio:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Conceptualization. **Manuel Marina-Breysse:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Conceptualization. **Manuel Martínez-Sellés:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Conceptualization.

Acknowledgements

The authors acknowledge Cassandra Christian for the English grammar review and text edition.

References

[1] Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P, Leal J, Luengo-Fernandez R, et al. European cardiovascular disease statistics 2017. Brussels: European Heart Network; 2017.
[2] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur. Heart J. 2018;39(2):119–77.
[3] Aslanger EK. Beyond the ST-segment in occlusion myocardial infarction [OMI]: diagnosing the OMI-nous. Turkish Journal of Emergency Medicine 2023;23(1):1–4.
[4] 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. Int J Cardiol Heart Vasc 2021;33:100767.
[5] Martínez-Sellés M, Juárez M, Marina-Breyse M, Lillo-Castellano J, Ariza A. Rational and design of ST-segment elevation not associated with acute cardiac necrosis [LESTONNAC]. A prospective registry for validation of a deep learning system assisted by artificial intelligence. J. Electrocardiol. 2021;69:140–4.
[6] Larson DM, Menssen KM, Sharkey SW, et al. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocar- dial infarction. JAMA 2007;298:2754–60.
[7] Garvey JL, Monk L, Granger CB, et al. Rates of cardiac catheterization cancelation for ST-segment elevation myocardial infarction after activation by emergency medical services or emergency physicians: results from the North Carolina catheterization laboratory activation registry. Circulation 2012;125:308–13.
[8] Mixon TA, Suhr E, Caldwell G, Greenberg RD, Colato F, Blackwell J, et al. Retrospective description and analysis of consecutive catheterization laboratory ST-segment elevation myocardial infarction activations with proposal, rationale, and use of a new classification scheme. Circ Cardiovasc Qual Outcomes 2012;5:62–9.
[9] Tolles J, Bosson N, Kaji AH, Henry TD, French WJ, Gausche-Hill M, et al. The effect of implementation of the American Heart Association Mission lifeline PreAct algorithm for prehospital cardiac catheterization laboratory activation on the rate of "false positive" activations. Prehosp Disaster Med 2020;35:388–96.
[10] Tanguay A, Brassard E, Lebon J, Bégin F, Hébert D, Paradis JM. Effectiveness of a prehospital wireless 12-lead electrocardiogram and cardiac catheterization laboratory activation for ST-elevation myocardial infarction. Am. J. Cardiol. 2017;119:553–9.
[11] Lange DC, Rokos IC, Garvey JL, Larson DM, Henry TD. False activations for ST-segment elevation myocardial infarction. Interv Cardiol Clin 2016;5:451–69.
[12] Regueiro A, Bosch J, Martín-Yuste V, Rosas A, Faixedas MT, Gómez-Hospital JA, et al. Cost-effectiveness of a European ST- segment elevation myocardial infarction network: results from the Catalan Codi Infart network. BMJ Open 2015;5:e009148.
[13] Zahler D, Rozenfeld K, Pasternak Y, Itach T. Relation of pain-to-balloon time and mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Am. J. Cardiol. 2022;15(163):38–42.
[14] Park J, Choi KH, Lee JM, Kim HK, Hwang D, Rhee TM, et al. Prognostic implications of door-to-balloon time and onset-to-door time on mortality in patients with ST -segment-elevation myocardial infarction treated with primary percutaneous coronary intervention. J. Am. Heart Assoc. 2019;9:e012188.
[15] Siontis KC, Noseworthy PA, Attia ZI, Friedman PA. Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. Nat. Rev. Cardiol. 2021;18:1–14.
[16] Cho Y, Kwon JM, Kim KH, Medina-Inojosa JR, Jeon KH, Cho S, et al. Artificial intelligence algorithm for detecting myocardial infarction using six-lead electrocardiography. Sci. Rep. 2020;10:20495.
[17] Rodríguez-Leor O, Cid-Álvarez AB, Pérez de Prado A, Rosselló X, Ojeda S, Serrador A, et al. Analysis of the management of ST-segment elevation myocardial infarction in Spain. Results from the ACI-SEC infarction code registry. Rev. Esp. Cardiol. 2022;75(8):669–80.
[18] Nallamothu BK, Normand SLT, Wang Y, Hofer TP, Brush JE, Messenger JC, et al. Relation between door-to-balloon times and mortality after primary percutaneous coronary intervention over time: a retrospective study. Lancet 2015;385(9973):1114–22.
[19] Quartieri F, Marina-Breysse M, Toribio-Fernandez R, Lizcano C, Pollastrelli A, Paini I, et al. Artificial intelligence cloud platform improves arrhythmia detection from insertable cardiac monitors to 25 cardiac rhythm patterns through multi-label classification. J. Electrocardiol. 2023;81:4–12.
[20] Quartieri F, Marina-Breysse M, Pollastrelli A, Paini I, Lizcano C, Lillo-Castellano JM, et al. Artificial intelligence augments detection accuracy of cardiac insertable cardiac monitors: results from a pilot prospective observational study. Cardiovasc Digit Health J 2022;3(5):201–11.
[21] Degheim G, Berry A, Zughaib M. False activation of the cardiac catheterization laboratory: the price to pay for shorter treatment delay. JRSM Cardiovasc. Dis. 2019;8. 204800401983636.
[22] Gustafsson S, Gedon D, Lampa E, Ribeiro AH, Holzmann MJ, Schön TB, et al. Development and validation of deep learning ECG-based prediction of myocardial infarction in emergency department patients. Sci. Rep. 2022;12(1):19615.
[23] Su HY, Tsai JL, Hsu YC, Lee KH, Chang CS, Sun CK, et al. A modified cardiac triage strategy reduces door to ECG time in patients with ST elevation myocardial infarction. Sci. Rep. 2021;11(1):6358. Mar 18.
[24] Dorado-Díaz I, Sampedro-Gómez J, Vicente-Palacios V, Sánchez P. Applications of artificial intelligence in cardiology. The future is already Here. Rev. Esp. Cardiol. 2019;72:1065–75.
[25] Martínez-Sellés M, Marina-Breysse M. Current and future use of artificial intelligence in electrocardiography. J Cardiovasc Dev Dis 2023;10:175.
[26] Lillo-Castellano JM, GonzÁlez-Ferrer JJ, Marina-Breysse M, et al. Personalized monitoring of electrical remodelling during atrial fibrillation progression via remote transmissions from implantable devices. Europace 2020;22:704–15.
[27] Johnson KW, Torres Soto J, Glicksberg BS, Shameer K, Miotto R, Ali M, et al. Artificial Intelligence in Cardiology. J. Am. Coll. Cardiol. 2018;71(23):2668–79.
[28] Dilsizian SE, Siegel EL. Artificial intelligence in medicine and cardiac imaging: harnessing big data and advanced computing to provide personalized medical diagnosis and treatment. Curr. Cardiol. Rep. 2014;16(1):441.
[29] 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. Eur Heart J Digit Health 2023;5(2):123–33.
[30] Al'Aref SJ, Anchouche K, Singh G, Slomka PJ, Kolli KK, Kumar A, et al. Clinical applications of machine learning in cardiovascular disease and its relevance to cardiac imaging. Eur. Heart J. 2019;40(24):1975–86.
[31] Ahmad T, Lund LH, Rao P, Ghosh R, Warier P, Vaccaro B, et al. Machine learning methods improve prognostication, identify clinically distinct phenotypes, and detect heterogeneity in response to therapy in a large cohort of heart failure patients. J. Am. Heart Assoc. 2018;7(8):e008081.
[32] Halcox JPJ, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, et al. Assessment of remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. Circulation 2017;136(19):1784–94.
[33] Kurmi P, Tripathi VD, Tripathi SK. Impact of Total ischemic time on clinical outcomes in patients with ST-elevation myocardial infarction: lost time is never found again. Cureus 2022;14(3):e23143.
[34] Mixon TA, Suhr E, Caldwell G, Greenberg RD, Colato F, Blackwell J, et al. Retrospective description and analysis of consecutive catheterization laboratory ST-segment elevation myocardial infarction activations with proposal, rationale, and use of a new classification scheme. Circulation 2012;5:62–9.

[35] Zhao Y, Xiong J, Hou Y, Zhu M, Lu Y, Xu Y, et al. Early detection of ST-segment elevated myocardial infarction by artificial intelligence with 12-lead electrocardiogram. Int. J. Cardiol. 2020;317:223–30.
[36] Chen KW, Wang YC, Liu MH, Tsai BY, Wu MY, Hsieh PH, et al. Artificial intelligence-assisted remote detection of ST-elevation myocardial infarction using a mini-12-lead electrocardiogram device in prehospital ambulance care. Front Cardiovasc Med 2022;9:1001982.
[37] Nfor T, Kostopoulos L, Hashim H, Jan MF, Gupta A, Bajwa T, et al. Identifying false-positive ST-elevation myocardial infarction in emergency department patients. J Emerg Med 2012;43(4):561–7.