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**Perspective**

# The Next Clinical Decision Frontier: How to Efficiently and Safely Combine Machine Learning and Human Expertise

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The accurate identification of patients with myocardial infarction (MI) is essential to initiate appropriate treatment and reduce morbidity and mortality (1). The context of shortage of healthcare resources and overcrowded emergency departments (ED) can pose challenges in providing timely and accurate triage for patients with potential cardiac diseases. In recent years, emerging technologies such as new generations of troponin assays and highly sensitive point-of-care testing assays, for example, have greatly facilitated the diagnosis of MI using biochemical tests.

It is also clear that the field of healthcare and laboratory medicine is witnessing a rapid transformation with the advent of machine learning and artificial intelligence (AI) technologies (2). These technologies have the potential to revolutionize clinical decision-making processes and significantly impact patient outcomes. Concrete applications are coming with the example of diagnosis of cardiac diseases such as MI—recently, Doudedis and coworkers reported a significant milestone in the field of machine learning for MI diagnosis with the development of the CoDE-ACS score (1).

Previous studies have already evaluated the use of machine learning to improve the diagnosis of MI. Than and coworkers developed an algorithm called the myocardial-ischemic-injury-index (MI3) for patients with suspected MI (3). MI3 incorporates age, sex, and paired high-sensitivity cardiac troponin I concentrations to assess an individual's likelihood of a type 1 MI diagnosis. MI3's performance surpassed that of the European Society of Cardiology's 0/3-hour pathway and the 99th percentile approach, making it a valuable tool for risk assessment in patients with suspected MI. In another study, De Capretz and coworkers used data from 9519 consecutive patients with ED chest pain to create machine learning models based on logistic regression or artificial neural networks. The models incorporated patient information such as sex, age, ECG, and blood test results (high-sensitivity TnT, glucose, creatinine, and hemoglobin) (4). The best model, a convolutional neural network, successfully identified 55% of patients for safe early rule-out and 5.3% for rule-in while maintaining required sensitivity and specificity levels.

The CoDE-ACS score developed by Doudedis and coworkers integrates cardiac troponin concentrations, clinical features, and machine learning algorithms to calculate an individual's probability of MI. The CoDE-ACS score was trained on a large dataset of 10 038 patients and externally validated on 10 286 patients from various cohorts. The results showed excellent discrimination for MI, outperforming traditional fixed cardiac troponin thresholds. The CoDE-ACS score also identified more patients as having a low probability of MI at presentation, leading to a reduced rate of cardiac death compared to those with intermediate or high probability. Compared to existing guideline-recommended pathways, CoDE-ACS identified more low-probability acute myocardial infarction (AMI) cases with a similar negative predictive value and fewer high-probability cases with an improved positive predictive value. The system's performance remained consistent across various patient subgroups, including those based on gender, age, and renal function. CoDE-ACS offers flexibility in applying diagnostic parameters to optimize patient flow in different healthcare settings. It enables early rule-out of AMI with a single troponin test, reducing unnecessary hospital admissions and improving AMI recognition and treatment. The clinical decision support system's integration with machine learning allows for more personalized care based on individual patient data. While CoDE-ACS shows promising results, its implementation requires validation and consideration of clinical judgment and pretest probability. The system could significantly enhance patient care, reduce emergency department waiting times, and benefit both patients and healthcare providers.

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Overall, the use of machine learning models in healthcare, particularly in the diagnosis of MI, holds great promise for improving accuracy and patient outcomes. However, it is essential to consider several dimensions when implementing such models.

The first dimension is human oversight and responsibility, emphasizing that machine learning models should be utilized as decision support tools rather than replacing healthcare professionals. Clinicians must exercise professional judgment and consider patient-specific factors that may not be captured by the models. Critical clinical decisions will continue to rely on highly qualified and continuously updated human expertise, because:

1. Human experts can understand the unique needs and concerns of individuals and engage in meaningful and empathetic conversations.
2. Human experts possess the ability to better adapt to new or rare cases. When AI encounters data outside its training set, it may struggle to make appropriate and informed judgments.

The recent “AI Act” supported by the European Parliament fully acknowledges the principle of human oversight for AI providers (article 14) and deployers (article 29) of AI systems (article 4). Noncompliance with human oversight for “high-risk” AI systems, posing risks to health, safety, or fundamental rights, will result in penalties in a similar way to global data protection regulations. Human oversight is required for the conformity assessment and CE marking of high-risk AI systems entering European markets. It is also essential in the fundamental rights impact assessment before deploying high-risk AI systems. The AI Act is set for full implementation in 2025.

Ethical implications form the second dimension. The development, validation, and implementation of machine learning models should adhere to ethical principles, ensuring transparency, fairness, accountability, and privacy. Models should be trained on diverse datasets, addressing biases or limitations, and patients should be informed about their use, benefits, and potential risks. The richness of team-based decisions and multiexpert advice should be preserved and even enhanced by the use of clinical decision support systems relying on machine learning.

Liability and legal considerations represent the third dimension. Implementing machine learning models introduces potential liabilities, as errors or misinterpretations could have serious consequences. Clear guidelines and protocols must be established to determine the responsibility of healthcare providers. Collaboration between developers and healthcare organizations is crucial to address issues related to model accuracy, data integrity, and legal implications. The optimal care of each patient is the crucial focus of this issue: if human-only clinical decision-making results in more diagnostic errors, healthcare providers should be required to use models provided by machine learning in support of clinical practice if that improves quality of care either in terms of outcomes or safety.

AI and machine learning technologies have transformative potential beyond diagnosis and decision support (2, 4). The impact of these technologies on triage, clinical performance, and cost-effectiveness has the potential to revolutionize ED and primary care settings. Cloud infrastructures and high-performance computing are instrumental in harnessing the power of machine learning algorithms, enabling efficient and accurate predictions. Machine learning approaches, including generative AI, have the potential to augment the capabilities of healthcare professionals, automating certain activities and enhancing decision support systems. These approaches can significantly impact productivity and efficiency in healthcare, leading to improved patient care and outcomes. Multimodal approaches combining different modalities such as biological data and textual foundation models should be explored not only for their accuracy but also for their explainability (5).

The impact of AI-driven technologies extends beyond the healthcare sector, creating new opportunities and landscapes across industries. Businesses and companies can leverage machine learning and AI to develop new products and services, leading to economic growth and innovation. Challenges in the adoption of AI-driven technologies include regulation, complexities in deployment, and the consequences of workforce transformation. Regulation must keep pace with technological advancements to ensure patient safety and ethical use of AI. The deployment of AI-driven technologies requires collaboration between domain experts, computer scientists, and statisticians. Workforce transformation and retraining are vital to embrace the potential of AI while ensuring patient safety, job security, and skills development.

In conclusion, the integration of machine learning models, such as the CoDE-ACS score, into clinical practice for the diagnosis of MI holds significant potential for improving patient outcomes. However, responsible, and ethical implementation is crucial. Balancing technological advancements with human expertise is necessary to harness the full potential of machine learning models while safeguarding patient well-being and the integrity of healthcare systems. Addressing the dimensions of human oversight, ethics, and liability, along with the challenges and opportunities presented by AI-driven technologies, will pave the way for a future where machine learning transforms clinical decision-making and healthcare delivery.

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