A cloud-based platform for clinical decision support in acute coronary syndrome patients: Study methodology

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INTRODUCTION

Cardiovascular disease is the leading cause of death globally, with 18 million deaths annually. Almost 50% of patients presenting with ST-segment elevation myocardial infarction (STEMI) have more than one vessel disease. The re-vascularization of culprit and non-culprit lesions in a staged manner reduces the risk of death. The present short communication briefly describes the protocol of a study whose main aim is to build a cloud-based tool to assist physicians in making decisions about revascularization of non-culprit lesions during the index hospitalization for acute coronary syndrome (ACS), based on the estimation of long-term outcomes, comprehensively evaluated by multi-modalities (Figure 1), along with the development of a specific risk score for non-culprit lesions in ACS.

METHODS

The study whose protocol is presented in this article is a single-center study taking place at Emergency Clinical Hospital, Bucharest, after approval from the Institutional Review Board no. 9013/28.09.2018. The enrollment started in 2020 and ended in December 2021. The study comprised one main and two secondary surveys. Based on the main and the first secondary survey, a cloud-based platform will be built to assist physicians in making decisions about non-culprit lesions. The integration of data for the cloud platform will be accomplished by Transylvania University, Brasov, and Polytechnic University, Bucharest in collaboration with the Norwegian University of Science and Technology. Finally, the usability and clinical integration capability of the cloud-based platform will be tested in a small-scale study (the second secondary sub-study).

Main clinical study

The main clinical study will be collecting prospectively a large variety of data from 120 ACS subjects with at least one culprit coronary lesion, using various medical imaging techniques (e.g., X-ray angiography [XA], optical coherence tomography [OCT], coronary computed tomography angiography [CCTA]) and non-imaging techniques (genetic analysis, miRNAs, markers of inflammation, fractional flow reserve [FFR], etc.). The examinations will be performed at baseline, six months — M6, and one year — M12) (Supplementary material, *Table S1)*. Patients will be included only after signing informed consent. Once a patient with ACS is referred to the study, their eligibility will be checked against a set of inclusion and exclusion criteria. The inclusion criteria are as follows: acute coronary syndromes [1] in the first 7 days after the acute event with at least one lesion with visually estimated diameter stenosis ≥40% on XA and with the technical possibility to perform FFR, OCT in all remaining lesions, in subjects with a life expectancy of at least one year. The exclusion criteria were

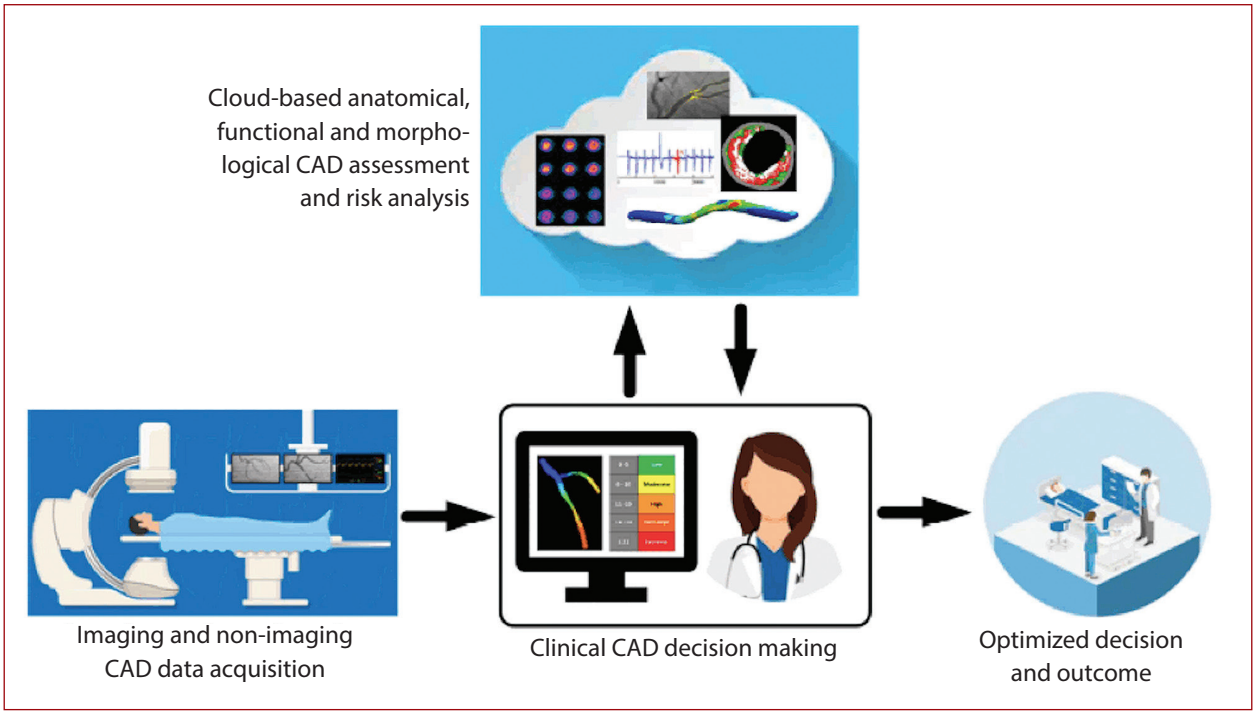

Figure 1. The schematic presentation of the study concept
Abbreviation: CAD, coronary artery disease

glomerular filtration rate <30 ml/min/1.73 m^2, surgical revascularization indication, diseases known to alter the inflammatory status, infection with hepatitis virus B, C, or human immunodeficiency virus, ACS with onset more than 7 days earlier or another ACS during the last 6 months, large surgery interventions in the last 3 months.

The baseline evaluation at enrolment will include:

- coronary angiography with Quantitative Coronary Analysis (QCA) calculation, OCT, FFR, and PCI (if deemed required) for the non-culprit lesions;
- genetic analysis: a panel of 79 genes (Supplementary material, *Table S2*);
- microRNAs: miR-296-3p, miR-296-5p [2, 3];
- inflammatory tests: C-reactive protein, resistin, and interleukin 1 receptor antagonist (IL-1ra).

A CCTA exam will be performed at M6 and M12 to inspect the coronary lesions and plaque evolution. Therapeutic adherence (the Morisky medication adherence scale) will be checked thoroughly at each follow-up along with endpoints focusing mainly on major adverse cardiovascular events (MACE).

Secondary clinical study 1

This will be a retrospective observational study of 500 ACS patients who were examined with XA during the past three years. A follow-up interview will be conducted for endpoint registration and previously acquired data will be registered, including demographic characteristics, medical history, clinical examination, standard blood tests, and XA. The comprehensive data from the main and the first secondary study will be used to design a risk score for non-culprit lesions in ACS and the cloud-based platform.

Secondary clinical study 2

This will be a prospective study enrolling 20 patients with the same baseline examinations (Supplementary material, *Table S1*). The main goal of this study is to determine the performance of the developed cloud-based solution in clinical workflows and its capacity to improve clinical decision-making for ACS.

Coronary lesion-specific risk score development

Risk prediction models that typically use several predictors based on patient characteristics to predict health outcomes are a cornerstone of modern medicine. Given the envisaged sample size in the clinical study and the two-year follow-up period, we expect overall 24–48 events (MACE), according to an event rate derived from the COMPARE-ACUTE study [4]. A pioneering lesion-specific risk stratification model will be implemented that leverages computer vision/image processing, computational modeling, and machine/deep learning. A multitude of risk scores will be developed, to be applied at different stages of patient care. Since no external validation dataset will be available during the project, bootstrap validation will be performed. Penalized regression, ridge regression, lasso regression, and deep learning-based approaches will be considered for risk score development.

Cloud-based platform

The cloud-based platform will address user management, data handling, fast data processing- components that need to react as soon as data becomes available, zero-footprint apps that allow data visualization and data insight (available on PC, tablet, and phone), and fault-tolerant services. Since many of the advanced analytic tools are run on massively parallel processors (graphics cards), we will develop a methodology for graphics processing unit (GPU) instance orchestration on the cloud.

Anatomical assessment of coronary lesions based on XA

Despite the introduction of functional indices, anatomical coronary lesion assessment remains an important cornerstone in the clinical decision-making process. Herein, we propose the use of deep learning-based techniques for fully automated anatomical assessment. Moreover, deep learning-based solutions will be integrated for the following tasks: optimal frame detection (determine the best frame for performing the anatomical/functional assessment of coronary lesions), automated view classification, and automated panning detection (detect and exclude automatically coronary angiographies displaying the table movement). Outputs to be used for the risk score computation include percent of diameter stenosis, stenosis entry/exit/total length, proximal/distal stenosis radius, stenosis/upstream/downstream ischemic contribution score, ischemic weight, type of branch.

Non-invasive functional assessment of coronary lesions based on XA and OCT data

A three-dimensional rigid-wall multiscale model developed in the past projects will be used herein for a non-invasive functional assessment. The main input is represented by a three-dimensional anatomical model of the coronary lumen of interest reconstructed from the segmentations performed on end-diastolic frames of two angiographic acquisitions at least 30° apart. The 3D anatomical model is then updated by performing a co-registration between the XA and OCT images, using a previously developed tool [5]. To compute patient-specific hemodynamics, the parameters of the model are personalized through a parameter estimation framework consisting of two sequential steps: outputs to be used for risk score computation are FFR and flow rate/velocity.

Anatomical and functional assessment of coronary plaque from OCT and CCTA

Different levels of vulnerability are associated with different types of coronary plaques. Specifically, calcified plaques will be annotated on OCT data, and next, deep learning-based methods will be employed to develop algorithms for automatic detection of the calcified plaques on OCT. Since intrinsic and extrinsic factors are linked to plaque vulnerability, we will perform a detailed hemodynamic analysis based on 3D anatomical models reconstructed from any of the envisaged medical imaging modalities. From the hemodynamic results, various quantities relevant for plaque analysis will be extracted. Outputs to be used for risk score computation: plaque composition (lipid, calcified, necrotic, fibrous, etc.), presence of high-risk features (napkin-ring shape, spotty calcification, thin cap, positive remodeling), wall shear stress (e.g. proximal/distal to the stenosis, oscillatory shear index).

Statistical analysis

All analyses will be conducted using SPSS version 23. Continuous variables will be presented as mean (standard deviation [SD]) for Gaussian distribution and as median (interquartile range [IQR]) for non-Gaussian variables, while for categorical variables, like numbers and percentages. For numerical, unpaired, and normally distributed variables, differences between two groups will be compared with Student's t-test, while for categorical data the chi-square or Fisher's exact test will be used; numerical, non-parametric data from two unpaired groups will be analyzed with the Mann-Whitney U test, while two paired groups with Wilcoxon pairs signed-rank test. *P*-values will be two-tailed and a cut-off of less than 0.05 considered statistically significant.

DISCUSSION

Current guidelines recommend complete revascularization of STEMI patients with non-culprit lesions as trials like COMPARE-ACUTE [4] showed its benefit. Despite this indication, the exact timing and optimal modalities to evaluate the significance of non-culprit lesions are because of a lack of data from randomized trials. Moreover, it is mentioned that CCTA and OCT [6] have limitations in the morphological characterization of coronary plaques, which may confound risk score calculation for non-culprit lesions in ACS.

The present short communication reports the protocol of a study that attempts to combine a multitude of medical imaging and non-imaging technologies to improve the clinical decision-making process for non-culprit lesions in ACS. The study aims to improve the way non-culprit lesions in ACS are assessed and treated, starting from an initial risk assessment to personalized treatment through digitization of the clinical data by a cloud-based platform.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

Conflict of interest: None declared.

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