A cloud-based platform for clinical decision support in acute coronary syndrome patients-a study methodology

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A cloud-based platform for clinical decision support in acute coronary syndrome patients—a 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-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 solution to assist physicians in deciding the need to revascularize non-culprit lesions during the index hospitalization for ACS, based on the estimation of long-term outcome, 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 below is monocentric taking place at Emergency Clinical Hospital, Bucharest, after approval from Institutional Review Board no. 9013/28.09.2018, starting enrollment in 2020 with end of inclusion in December 2021. The study is constituted by one main and two secondary surveys; based on the main and first secondary study a cloud-based platform will be built assisting the physician in the decision regarding non-culprit lesions. The integration of data for the cloud-platform will be accomplished by Transilvania University, Brasov and Polytechnic University, Bucharest in collaboration with 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 (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, one year — M12) (Supplementary material, Table S1). Patients will be included only after signing an informed consent. Once a patient with ACS is referred to the study, a set of inclusion criteria and exclusion criteria are checked. 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 life expectancy of at least one year. The exclusion criteria were: glomerular filtration rate <30 ml/min/1.73 m², 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 ago 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 IL-1F3II-1 beta antagonist receptor.

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

**Secondary clinical study 1**

This will be a retrospective observational study of 500 ACS patients investigated with XA during the past three years. A follow-up interview will be conducted for end-point registration and previously acquired data will be registered, including: demographic characteristics, medical history, clinical examination, standard blood tests, XA. The comprehensive data from the main and the secondary study 1 will be used to design the 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, for which 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 the integration of the clinical workflow to improve clinical decision making for ACS.
Coronary lesion-specific risk score development
Risk prediction models that typically use a number of 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 a 24–48 events (MACE), according to an event rate derived from 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 the 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-foot print apps that allow data visualization and data insight (available on PC, tablet and phone), fault tolerant services. Since many of the advanced analytics tools are run on massively parallel processors (graphics cards) we will develop a methodology for 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 detector (determine 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 table movement). Outputs to be used for the risk score computation: % 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 past projects will be used herein for
the 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, 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 automatically detecting 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, as number and percentage. 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 exact test were
used; numerical, non-parametric data from two unpaired groups will be analyzed with Mann-
Whitney U, 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.

RESULTS AND DISCUSSIONS
Current guidelines recommend complete revascularization of STEMI patients with non-culprit lesions as trials like COMPARE-ACUTE [4] proved its benefit. Despite this indication, the exact timing and optimal modalities to evaluate the significance of non-culprit lesions are debatable lacking randomized data. Moreover, it is to mention that CCTA and OCT [6] have limitations in the morphological characterization of coronary plaques that may intervene in the performance of the risk score calculator for non-culprit lesions in ACS.

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

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

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REFERENCES


Figure 1. The schematic representation of the study concept