Assessment of the prognostic value of pulse wave velocity in the acute phase of myocardial infarction – PROVOPe_FLA

J. Mesquita Bastos[1,2], V. Ribau[2], P. Damião[3], C. Leitão[4], R. Vitorino[1]

1- Department of Medical Sciences, Institute of Biomedicine – iBiMED, University of Aveiro, Aveiro, PORTUGAL
2 - Cardiology Department, Hospital Infante D.Pedro, Centro Hospitalar do Baixo Vouga, Aveiro, PORTUGAL
3- ARS Centro, ACeS Baixo Vouga, USF Aveiro/Aradas, Aveiro, PORTUGAL
4 - i3N, Physics Department, University of Aveiro, Aveiro, PORTUGAL

universidade de aveiro | ibimed institute of biomedicine

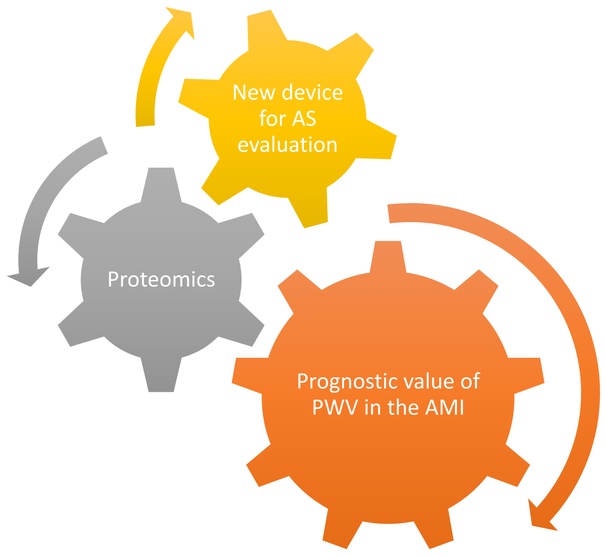
encontro CIÊNCIA '21 | ENCONTRO COM A CIÊNCIA E TECNOLOGIA EM PORTUGAL 28 a 30 JUNHO 2021 #ciencia2021PT | i3N INSTITUTE FOR NANOSTRUCTURES, NANOMODELLING AND NANOFABRICATION RESEARCH, INNOVATION AND ENGINEERING APPLICATIONS

Overview

Cardiovascular (CV) disease, namely acute myocardial infarct (AMI) and cerebrovascular diseases, are the leading cause of morbidity and mortality globally. In this project, an integrative analysis of AMI through its hemodynamic, metabolic and inflammatory determinants, will be performed. We aim to explore the impact of metabolic and inflammatory pathways on arteries; to create new evidence on the role of new hemodynamic parameters, as pulse wave velocity (PWV), central blood pressure, subclinical left ventricle (LV) systolic dysfunction (echocardiogram strain); and to develop new tools for a more accurate AMI outcome prediction. A greater knowledge of the disease and a more efficient prediction of its progression will permit a modulated, customized treatment to every patient, improving prognosis and diminishing AMI morbimortality.

Arterial stiffness (AS) reflects the aortic wall damage caused by several cardiovascular risk factors (CVRF), over time, signalling patients in which arterial risk factors translate to real risk. Aortic PWV, AS measurement gold standard, can be used as a marker of target organ damage, CV risk and mortality. Increased aortic AS has been shown to be an independent predictor of composite endpoint of major adverse cardiac and cerebrovascular events after acute ST-elevation myocardial infarction (STEMI) but its usefulness on non-ST elevation myocardial infarction (NSTEMI) remains unclear.

Atherosclerosis is a maladaptive, non-resolving, chronic inflammatory disease predisposing plaque development. AMI complex physiological, biochemical, and neurohumoral alterations are still incompletely understood. High-sensitivity C-reactive (hsCRP), a well-known inflammatory marker, is an independent risk factor for CV diseases, plaque burden and its assessment can help prevent a new event in intermediate risk patients. However, its prognostic value in AMI acute phase is yet to prove. Galectin 3 (G3) has a pivotal role in inflammation and fibrosis. Although validated as an independent prognostic biomarker, in both acute and chronic heart failure (HF) its precise role in AMI is not fully clarified.



Main objective:
To determine arterial stiffness, measured by PWV, prognostic value in AMI and its correlation with inflammation markers.

Secondary objectives:
1. Studying central hemodynamics during AMI and the following 12 months;
2. Characterize the evolution of inflammatory markers during AMI events;
3. Define the proteomic fingerprint of acute coronary syndromes;
4. Developing new devices to evaluate arterial stiffness;
4. Assessing the relationship between central hemodynamics, novel biologic biomarkers, proteomics and study´s primary and secondary endpoints.

Study Protocol

This cross-sectional study includes patients from Centro Hospitalar do Baixo Vouga (CHBV, Aveiro).
The study protocol will be performed accordingly with Table 1. The study is approved by the CHBV Ethics Committee and all the study procedures will be done in agreement with the Helsinki Declaration and good clinical practice guidelines.

Study population: 160 patients with a first episode of STEMI or NSTEMI.

Inclusion criteria: a) age between 19 and 85 years; b) first ACS event

Exclusion criteria: a) medical conditions precluding a life expectancy <1 year (eg: cancer, severe chronic obstructive pulmonary disease; b) inability to travel to CHBV for examinations; c) refusal to sign informed consent; d) end stage renal failure (glomerular filtration rate <30%); e) chronic inflammatory diseases; f) previous coronary event.

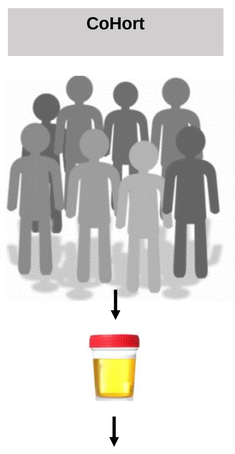
Study endpoints: Primary endpoint will be defined as a composite endpoint of major adverse cardiac and cerebrovascular events (MACCE) comprising death (defined as all-cause mortality), nonfatal myocardial reinfarction (European Society of Cardiology (ESC)/American College of Cardiology (ACC) criteria), newly diagnosed congestive heart failure (a first episode of cardiac decompensation requiring intravenous diuretic therapy), stroke (ischemic or hemorrhagic stroke with an episode of neurological dysfunction due to focal cerebral infarction according to the updated stroke criteria) and arterial peripheral disease (when justifying surgery). Secondary endpoints were defined as each individual endpoint of MAACE. When more than one MACCE endpoint occurs during follow-up, the most severe one will be selected for primary endpoint analysis (death >congestive heart failure > stroke > myocardial reinfarction).

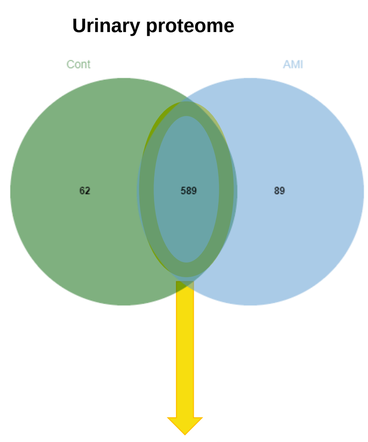
Table 1. Exams and variables evaluated with respective calendarization.

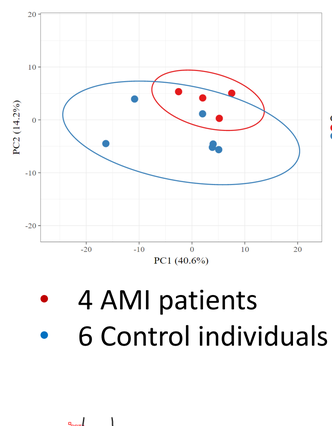
Exams/Variables	Admission	Discharge	1 month	6 months	12 months
Clinical History	X				
Cardiac frequency	X		X	X	X
Peripheral casual blood pressure	X		X	X	X
Central systolic pressure	X	X	X	X	X
Pulse wave velocity	X	X	X	X	X
Carotid Pulse wave morphology*	X	X	X	X	X
Inflamation biomarkers	X			X	X
NT-proBNP	X			X	X
Blood samples	X			X	X
Urine proteomics**	X		X	X	X
ECG	X		X	X	X
Ecocardiogram	X				X
Holter (if f_{ej} < 35%)			X		

*Evaluated by Complior Analyze and new optical fiber sensor for validation and machine learning studies.

Preliminary Results - Proteomics



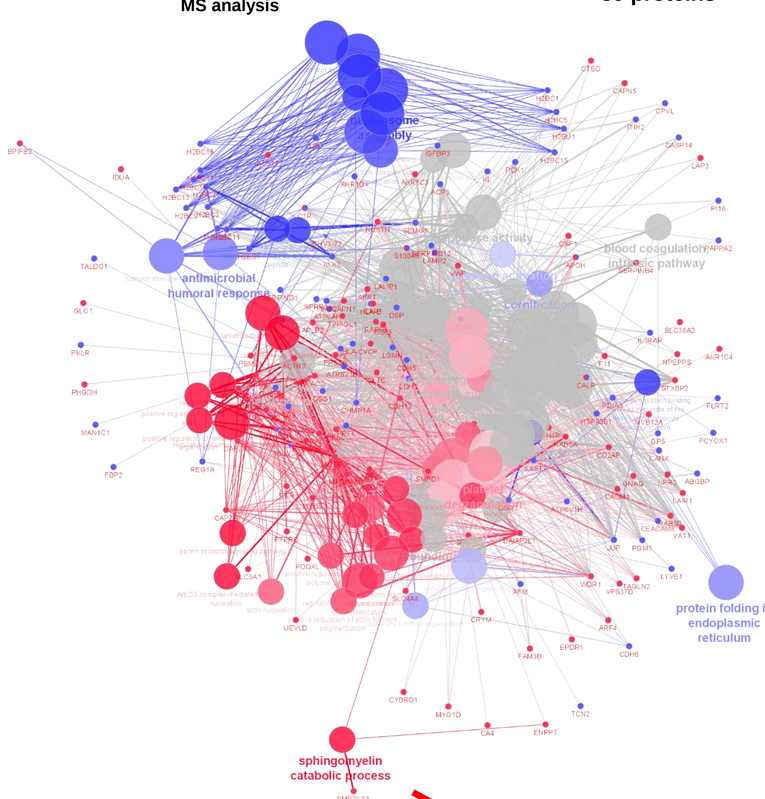


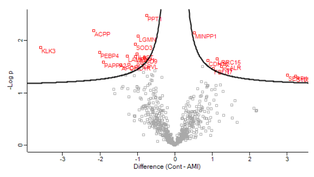


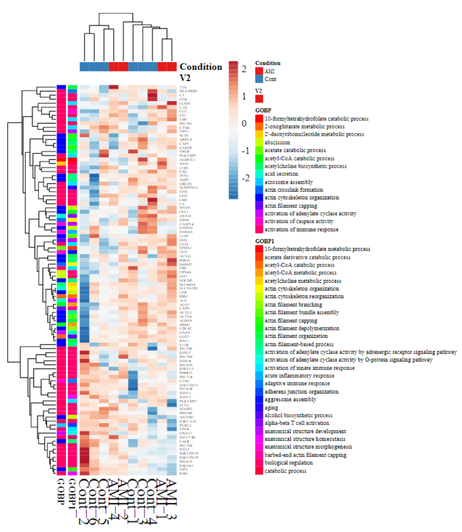
- 4 AMI patients
- 6 Control individuals

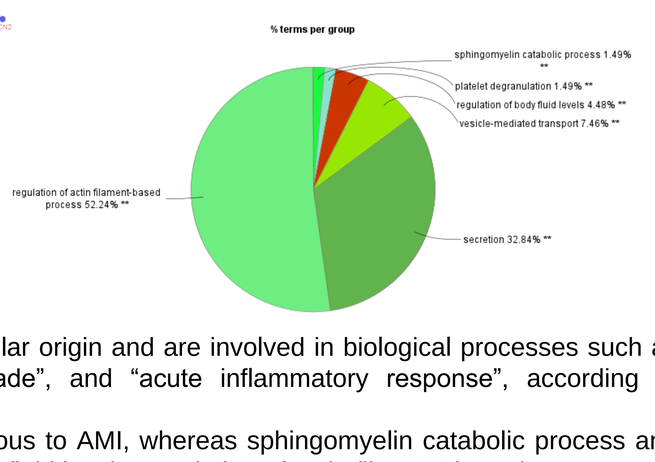
MS analysis

89 proteins









- Most of these proteins had an extracellular origin and are involved in biological processes such as “coagulation”, “protein activation cascade”, and “acute inflammatory response”, according to ClueGO analysis.
- A different protein fingerprint was notorious to AMI, whereas sphingomyelin catabolic process and platelet degranulation, regulation of body fluid levels, regulation of actin filament-based process.
- Sphingolipids have been implicated in the pathophysiology of cardiovascular disease, as they regulate numerous cellular processes that occur in primary and secondary cardiomyopathies.
- Biomarkers for AMI are associated to regulation of actin filament-based process, that include such as cardiac troponin and the natriuretic peptides.

Conclusions

- The identification of biomarkers that allow to characterize AMI.
- The identification of biomarkers that will help in the definition of clinical strategies for AMI management.
- GeLC-MS/MS profiling of urine proteome followed by bioinformatics analysis of data allow the identification of the biological processes modulated by AMI and, eventually, the definition of putative biomarkers to be included in multimarker strategies of diagnosis.

Acknowledgments

The authors thank the Portuguese Foundation for Science and Technology (FCT), European Union, QREN, FEDER and COMPETE for funding UnIC - Unidade de Investigação Cardiovascular (UIDB/00051/2020 and UIDP/00051/2020), iBiMED (UIDB/04501/2020, POCI-01-0145-FEDER-007628), FCT LAQV/REQUIMTE (UIDB/50006/2020) and i3N (UIDB/50025/2020 & UIDP/50025/2020) research units. C. Leitão also thanks FCT for the CEECIND/00154/2020 project.

IF INVESTIGADOR FCT | MEDISIS Sharing Knowledge | FCT Fundação para a Ciência e a Tecnologia | CENTRO HOSPITALAR BAIXO VOUGA Mais Saúde, Mais Vida!

Cofinanciado por: CENTRO 2020 | PORTUGAL 2020 | UNIÃO EUROPEIA Fundo Europeu de Desenvolvimento Regional