ITACARE-P ITalian Alliance for CArdiovascular REhabilitation and Prevention

SEcondary preVention and Extreme cardiovascular Risk Evaluation (SEVERE-1), focus on prevalence and associated risk factors: the study protocol.

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INTRODUCTION

Despite significant improvement in secondary CardioVascular (CV) preventive strategies, some Acute and Chronic Coronary Sindrome (ACS and CCS) patients will suffer recurrent events. Such patients are now recognized as being part of a "new" group: patients at extremely high CV disease risk. However, the definition of who belongs to such niche is still under refinement, as well as, its link to some newly discovered aspects and risk factors (UA, LpA, inflammatory markers) known to be associated to an increase in CV risk..

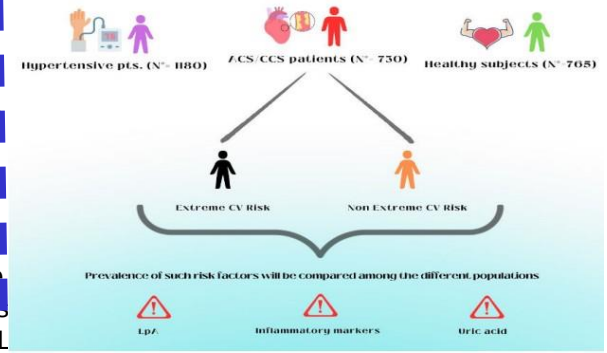
PURPOSE

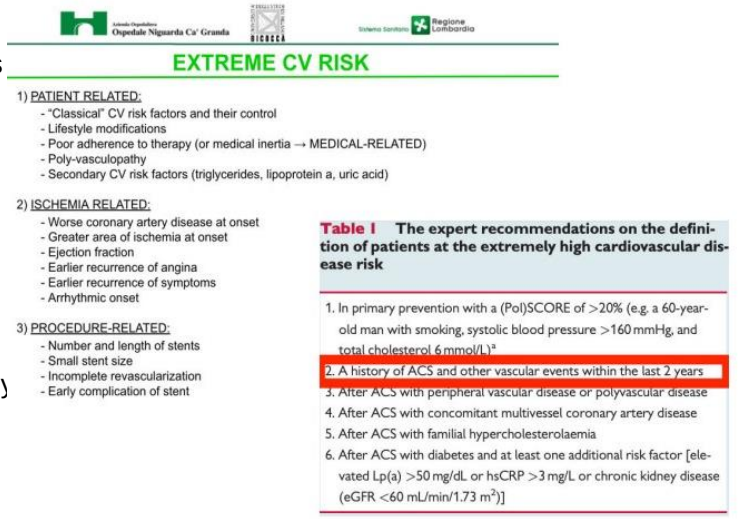
The SEcondary preVention and Extreme cardiovascular Risk Evaluation (SEVERE- 1) study will accurately characterize extreme CV risk patients enrolled in Cardiac Rehabilitation (CR) programs after a hospitalization due to ACS or CCS. Our aims will be to describe the prevalence of extreme CV risk in such setting while better defining the boundaries of such category and its association with newly described CV risk factors.

By being successful in our aims we will help physicians to identify patients at extreme CV risk. Identifying this group of subjects is crucial. In fact, if these subjects are correctly and readily identified they will be the ones that will be treated more intensively and will benefit more of newer approaches such as lipoprotein(a) treatment, triglycerides reduction, further LDL reduction, new diabetic agents or new antiaggregant approach.

METHODS

The protocol will consist in a prospective analysis on a population of 730 patients enrolled on the first day of their cardiac rehabilitation program after an ACS/CCS hospitalization. Inclusion criteria will be: (1) recent (< 12 months) hospitalization for an ACS (ST elevated myocardial infarction, non-ST elevated myocardial infarction and unstable angina) or a CCS leading to coronary revascularization; (2) being recruited in a CR program (both inpatients or outpatients); (3) being enrolled at least two weeks after the ACS; (4) signed informed consent. Three Italian Hospital will be involved in patients' enrolment: Niguarda Hospital (Milan, Outpatients Cardiac Rehabilitation Unit, Cardiology 4), Federico II University Hospital (Naples, Inpatients Cardiac Rehabilitation Unit) and S. Anna e S. Sebastiano Hospital (Caserta, Outpatients Cardiac Rehabilitation Unit, Cardiology Unit). Extreme CV risk will be defined as the presence of a previous (within 2 years) CV events in the patients' clinical history.





EXTREME CV RISK

1) PATIENT RELATED:
- "Classical" CV risk factors and their control
- Lifestyle modifications
- Poor adherence to therapy (or medical inertia → MEDICAL-RELATED)
- Poly-vasculopathy
- Secondary CV risk factors (triglycerides, lipoprotein a, uric acid)

2) ISCHEMIA RELATED:
- Worse coronary artery disease at onset
- Greater area of ischemia at onset
- Ejection fraction
- Earlier recurrence of angina
- Earlier recurrence of symptoms
- Arrhythmic onset

3) PROCEDURE-RELATED:
- Number and length of stents
- Small stent size
- Incomplete revascularization
- Early complication of stent

Table I The expert recommendations on the definition of patients at the extremely high cardiovascular disease risk

1. In primary prevention with a (Pol)SCORE of >20% (e.g. a 60-year-old man with smoking, systolic blood pressure >160 mmHg, and total cholesterol 6 mmol/L)[a]
2. A history of ACS and other vascular events within the last 2 years
3. After ACS with peripheral vascular disease or polyvascular disease
4. After ACS with concomitant multivessel coronary artery disease
5. After ACS with familial hypercholesterolaemia
6. After ACS with diabetes and at least one additional risk factor [elevated Lp(a) >50 mg/dL or hsCRP >3 mg/L or chronic kidney disease (eGFR <60 mL/min/1.73 m^2)]

Then, we will assess the association between newly described CV risk factors and extreme CV risk with multivariable model and, for biomarkers still significant, we will create two scoring system for an accurate identification of extreme CV risk patients. The first one will use only clinical variables while the second one will introduce the biochemical markers evaluated. The AUC analysis will show us the increase in diagnostic accuracy. Finally, by exome sequencing we will both evaluate polygenic risk score ability to predict recurrent events and perform mendelian randomization analysis on CV biomarkers.

CONCLUSIONS

Our study proposal was funded by the European Union - NextGenerationEU - M6C2 Investment 1.2 / PNRR - CUP H43C21000140006. Identification of the extreme CV risk patients is an important unmet clinical need in the field of secondary CV prevention and, generally, for the cardiology field. With this study we will give definitive data on extreme CV risk prevalence (probably higher than what is believed), will better describe its characteristics and its association to new CV RFs, and will contribute to the early identification (also with our scoring system) of extreme CV risk patients. The successful outcome of our study will permit early and tailored implementation of CV therapies leading to a lower rate of CV events and an improvement in money saving for the health system.