



## EXTREME CARDIOVASCULAR RISK IN CARDIOLOGICAL REHABILITATION: PREVALENCE AND IMPACT ON PATIENT'S FUNCTIONAL IMPROVEMENT.

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### INTRODUCTION

Among patients at very high cardiovascular risk, some are more likely to experience recurrent cardiovascular events. In May 2022, an article was published in the European Heart Journal proposing different definitions of patients at extreme cardiovascular risk. However, the process of defining such patient is still ongoing and more data on its prevalence are needed.

**Table 1** 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)<sup>a</sup>
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<sup>2</sup>)]

### OBJECTIVES AND METHODS

Our aims consisted in assessing the prevalence of patients at extreme cardiovascular risk in cardiological rehabilitation and in evaluating the clinical features of such patients.

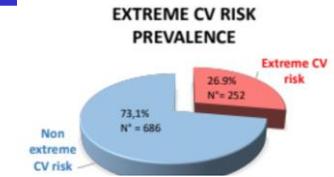
Furthermore, we wanted to establish how the extreme cardiovascular risk condition correlates with the functional improvement obtained during cardiac rehabilitation. The study included 938 patients suffering from atherosclerosis who attended the cardiological rehabilitation of Niguarda Hospital in Milan. In this study, patients meeting the criteria proposed in definitions 2, 3 or 4 were identified as being at extreme cardiovascular risk. Definition 1 was not considered because it refers to primary prevention, whereas definitions 5 and 6 were not considered because the required data were not available. Patients classified as at extreme cardiovascular risk were compared with the remaining patients and a multivariate linear regression was performed with absolute functional improvement (calculated as delta in meters between the 6MWT performed at the time of entry to cardiological rehabilitation and the 6MWT performed at the end of the rehabilitation program) as the dependent variable.

DEPENDENT VARIABLE: absolute functional improvement		
INDEPENDENT VARIABLES	Standardized β	p-value
Age	-0,128	0,083
Female sex	<b>-0,136</b>	<b>0,035</b>
Dyslipidemia	-0,027	0,671
Diabetes mellitus	-0,114	0,121
Arterial hypertension	0,047	0,509
GFR - MDRD	-0,016	0,808
Systolic blood pressure	-0,004	0,952
LVEF	-0,052	0,418
Glycaemia	-0,022	0,763
Smoking	-0,028	0,656
Overweight-obesity	-0,105	0,109
Atrial fibrillation	-0,070	0,280
Extreme cardiovascular risk	<b>-0,137</b>	<b>0,035</b>

### RESULTS

Among 938 patients, 26.9% belong to the category of extreme cardiovascular risk. Patients at extreme cardiovascular risk showed a higher average age ( $67.8 \pm 10.4$  vs  $64.1 \pm 11.1$  years;  $p \leq 0.001$ ), a higher prevalence of significant comorbidities (peripheral arterial disease, cerebrovascular disease, dyslipidemia, diabetes, chronic kidney disease, hypertension) and a lower functional improvement during cardiac rehabilitation ( $102.9 \pm 68.6$  vs  $138.1 \pm 86.5$  m;  $p \leq 0.001$ ).

At multivariate analysis extreme cardiovascular risk remains a significant determinant of the absolute functional improvement at Six-Minute Walking Test obtained during cardiac rehabilitation with  $b = -0.137$  and  $p = 0.035$ , together with female sex ( $b = -0.136$ ;  $p = 0.035$ ).



FACTOR	EXTREME CARDIOVASCULAR RISK		P-value
	NO (686 patients)	YES (252 patients)	
Age (years)	64,1±11,1	67,8±10,4	≤0,001
Males (%)	80	87	0,010
BMI (kg/m <sup>2</sup> )	26,7±3,9	26,9±3,3	0,889
Overweight-obesity (%)	53	54	0,941
Current smokers (%)	33	25	0,026
Peripheral artery disease (%)	2	25	≤0,001
Cerebrovascular disease (%)	0,3	32	≤0,001
Number of cardiovascular events	1,2±0,7	2,2±1,6	≤0,001
Recurrent ACS (%)	7	31	≤0,001
Prior coronary revascularization (%)	20	49	≤0,001
Myocardial infarction before 45 years old (%)	5	8	0,209
GFR (ml/min/1,73 m <sup>2</sup> ) - MDRD	80,5±20,2	75,9±22,7	0,009
Chronic kidney disease (GFR < 60 ml/min/1,73 m <sup>2</sup> ) (%)	15	25	0,007
LDL-C (mg/dl)	108,1±38,4	92,5±39,0	≤0,001
Dyslipidemia (%)	67	79	≤0,001
Glycaemia (mg/dl)	103,6±27,6	111,4±35,5	0,022
Diabetes mellitus (%)	17	32	≤0,001
Systolic blood pressure (mmHg)	122,3±14,9	127,1±16,7	≤0,001
Arterial hypertension (%)	62	77	≤0,001
Heart rate (bpm)	63,2±8,7	63,8±8,6	0,432
Atrial fibrillation (%)	2	2	0,626
LVEF (%)	54,2±8,0	52,8±8,6	0,041
6MWT-1 (m)	465,4±99,0	443,8±112,3	0,005
6MWT-2 (m)	599,7±106,7	545,7±118,1	≤0,001
Absolute functional improvement (m)	138,1±86,5	102,9±68,6	≤0,001

### CONCLUSIONS

Extreme cardiovascular risk is a widespread condition among patients with ischaemic heart disease and adversely affects the patient's functional improvement during cardiac rehabilitation. The ability to identify patients at extreme cardiovascular risk would allow an intensification of secondary prevention strategies. At present, the ESC guidelines recommend, for patients at extreme risk, a target of LDL cholesterol of less than 40 mg/dl and consider the administration of colchicine at low doses if the other risk factors are not adequately controlled. In addition, cardiological rehabilitation is recommended. Further studies are needed to determine the usefulness of other secondary prevention strategies