Molecular profile of Cardiovascular Risk in young population: a promising tool for early prevention

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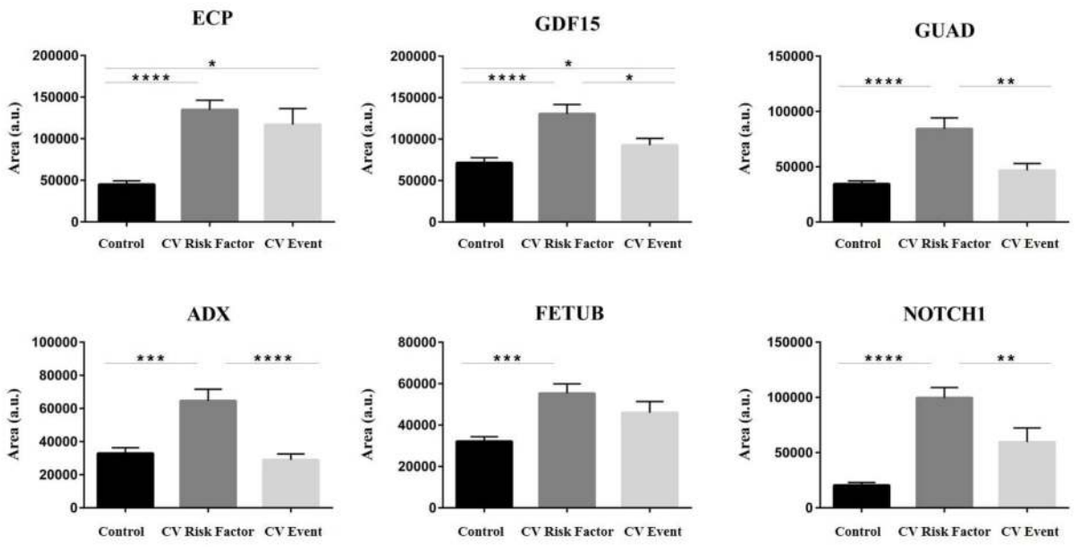
INTRODUCTION: The predictive value of traditional cardiovascular (CV) risk estimators is limited. As age is one of the most contributing variables used, CV risk is particularly underestimated in young population.

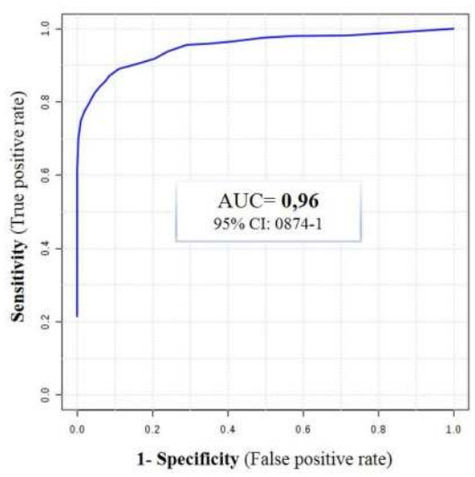
OBJETIVES: We first aimed to identify novel molecular markers of CV risk in subjects aged 30-50 years (young). Knowing that the relative contribution of traditional risk factors is changing through lifetime, we then investigated a potential modulation by age of identified patterns of CV risk in older populations: middle-age (50-70 years) and the elderly (>70 years).

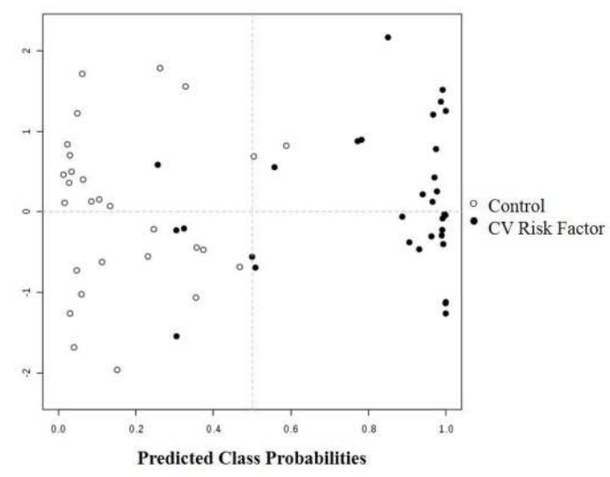
METHODS: Urine samples were collected from 234 subjects grouped in young, middle-age and elderly. Each cohort was classified in three groups from low to high CV risk: control (C); individuals with CV risk factors (F); and those who had suffered a previous CV event (E). A first discovery phase was carried out by isobaric labeling Mass Spectrometry (MS) (proteins) and Nuclear Magnetic Resonance (metabolites). Confirmation was performed by target MS and ELISA.

	Young			Middle-age			Elderly		
	C	F	E	C	F	E	C	F	E
n	33	25	25	28	23	25	25	25	25
eGFR (mL/min/1.73m^2)	93±10	89±15	98±21	81±10	75±20	77±18	75±13	40±9	66±19
DM %	0	12	8	4	44	28	40	32	40
Age (years)	43±5	44±5	45±4	60±5	62±5	61±5	83±5	86±5	83±6
Sex (male) %	49	72	80	75	91	68	52	48	48
Cholesterol (mg/dL)	193±37	210±37	147±40	180±21	171±24	157±37	144±29	145±35	145±26
Triglycerides (mg/dL)	82±38	190±99	143±158	109±39	131±65	126±56	110	88±37	103±43
HdL (mg/dL)	71±17	45±14	41±10	54±14	51±16	52±18	44±15	45±14	41±11
LdL (mg/dL)	105±32	135±33	81±38	105±22	95±21	80±35	79±23	70±20	78±22
Glycemia (mg/dL)	80±8	97±31	107±43	102±13	123±24	118±40	104±25	110±44	113±44
Creatinine (mg/dL)	0.81±0.12	0.90±0.12	0.90±0.18	0.9±0.2	1.1±0.3	1.0±0.3	0.8±0.2	1.4±0.3	1.0±0.4
Uric acid (mg/dL)	4.6±1.2	6.3±1.7	5.8±1.4	6.2±1.4	6.4±1.7	6.1±1.4	4.9±1.2	8±2	5.7±1.9
PAS	113±9	135±12	122±19	136±11	141±14	143±16	140±23	131±21	150±27
PAD	71±8	88±9	76±12	80±8	81±9	84 ±11	76±15	71±15	77±14
LTR QRISK	23±6	42±10	_						

Six proteins compose a urinary fingerprint associated with CV risk in the youngest
(all them positively correlate with Lifetime Risk)







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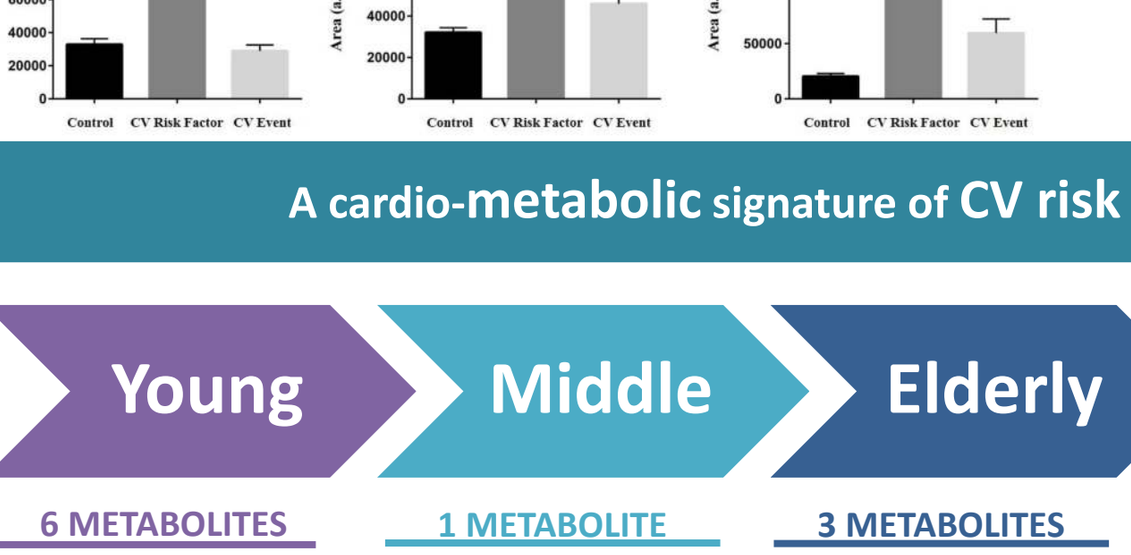
A cardio-metabolic signature of CV risk exists in urine and it is modulated by age

Young → **Middle** → **Elderly**

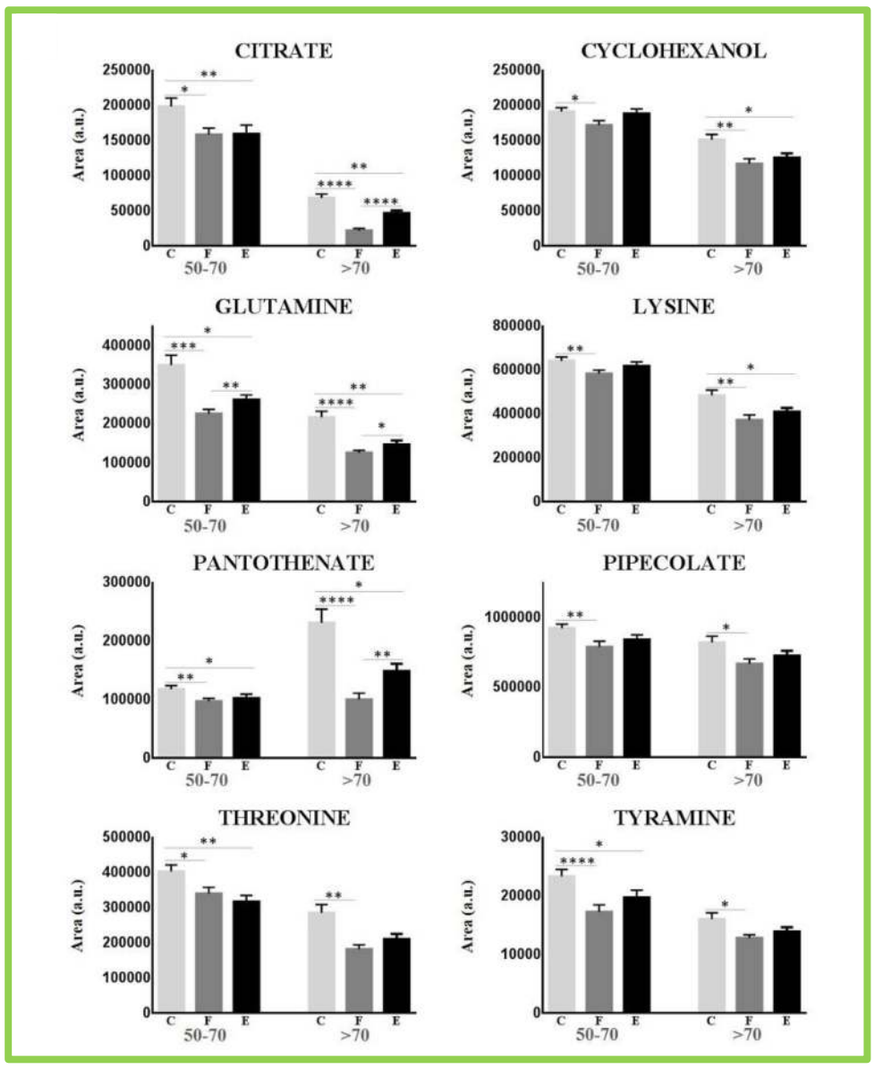
6 METABOLITES



YOUNG signature: ROC curve with AUC = 0.89

1 METABOLITE

8 METABOLITES



Common signature in MIDDLE and ELDERLY: ROC curve with AUC = 0.88 and 0.97, respectively

3 METABOLITES

2 METABOLITES

CONCLUSIONS: The urinary metabolome contains a cardiometabolic signature modulated by age in what refers to CV risk. Identified proteins and metabolites show potential to complement existing algorithms and thus improve accuracy of available CV risk estimators. Their biological role points to oxidative stress, cardiomyocytes apoptosis and inflammatory response are main physiopathological processes.

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