NMR plasma metabolomics and lipidomics can anticipate cardiac ischemic risk

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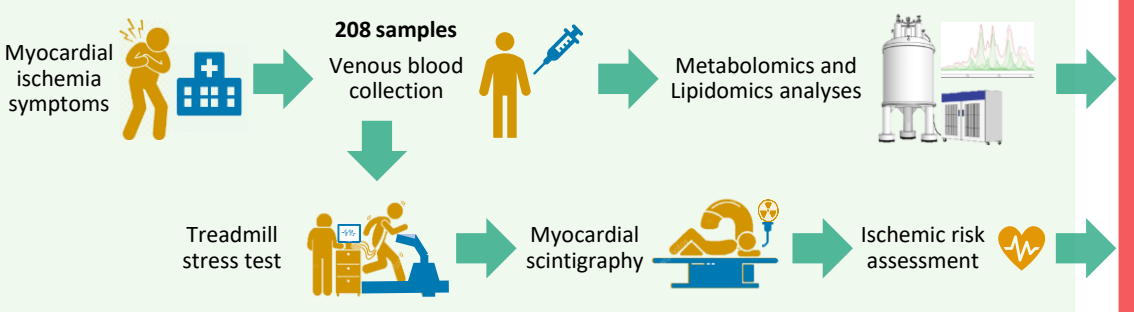
Background:

Myocardial ischemia[1]:
reduced oxygen flow to the heart

Traditional tests[2,3]:
Heart response at rest vs after physical exercise

- Treadmill test: low sensitivity and specificity
- Myocardial scintigraphy: high radiation doses
- Coronary angiography: highly invasive

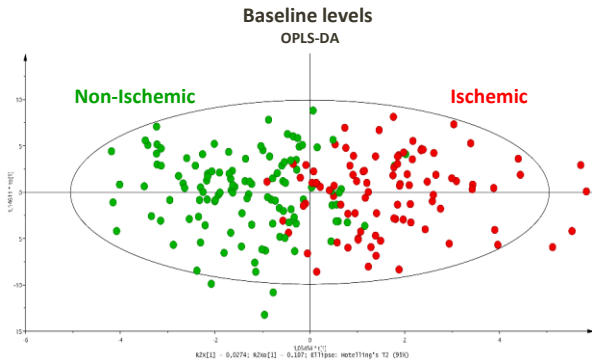
Method:



Aim:

Can metabolic profile help in increasing sensitivity and specificity for ischemic risk assessment?

BASELINE METABOLIC PROFILE PREDICTS ISCHEMIC RISK



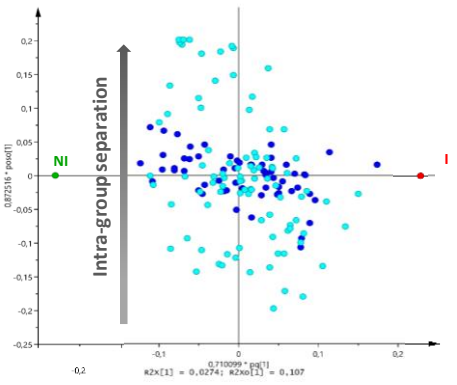
A=1+2+0; $R^2X(cum)=0.200$; $R^2Y(cum)=0.584$; $Q^2(cum)=0.320$; CV anova<<0.001

Myocardial scintigraphy scores correlate with metabolic profile

True positive rate= 92%
True negative rate= 87%

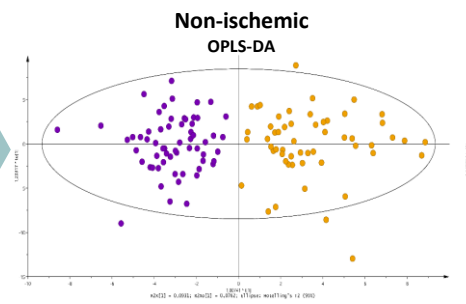
Polar metabolites:
- discriminant between **NI** and **I**

Lipids:
- discriminant between **NI** and **I**
- responsible for **intra-group separation**

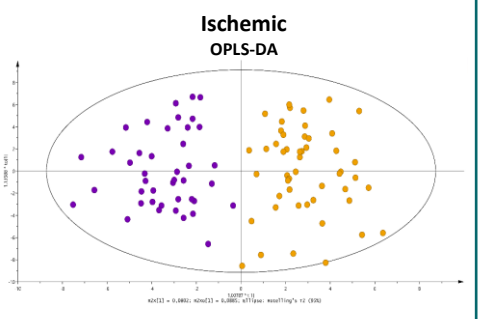


TWO LIPID PROFILES

Two lipid subgroups are identified inside each class



A=1+1+0; N=116; $R^2X(cum)=0.174$; $R^2Y(cum)=0.770$; $Q^2(cum)=0.656$; CV anova<0.001



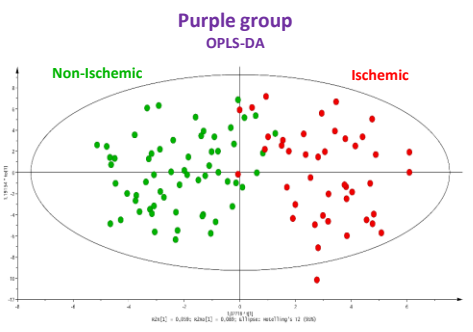
A=1+1+0; N=92; $R^2X(cum)=0.183$; $R^2Y(cum)=0.819$; $Q^2(cum)=0.717$; CV anova<0.001

Purple and orange groups share the same lipid composition

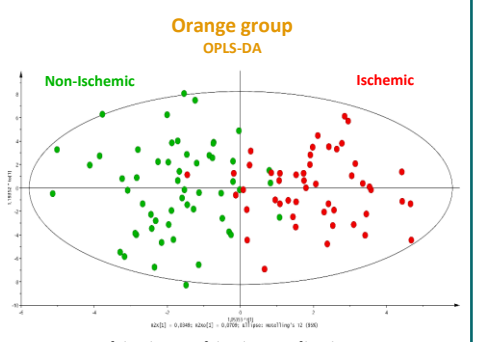
- Esterified cholesterol
- Free cholesterol
- 18:2 linoleic acid

- PUFAs
- 20:4 arachidonic acid
- Phospholipids
- 22:6 docosahexaenoic acid

LIPID STRATIFICATION PROVIDES BETTER CLASSIFICATION



A=1+1+0; N=106; $R^2X(cum)=0.163$; $R^2Y(cum)=0.699$; $Q^2(cum)=0.514$; CV anova<0.001



A=1+1+0; N=102; $R^2X(cum)=0.130$; $R^2Y(cum)=0.677$; $Q^2(cum)=0.419$; CV anova<0.001

True positive rate= 95%
True negative rate= 88%

True positive rate= 96%
True negative rate= 94%

Considering both models:
True positive rate= 96%
True negative rate= 91%

DIFFERENT LIPID PROFILE LEADS TO DIFFERENT ISCHEMIC FINGERPRINT

Only metabolites with calculated sample size minor or equal to the sample size of the study are considered[4]

Purple group

- 18:2 linoleic acid
- Triglycerides
- UFAs
- Creatinine
- Myo-inositol

- 2-Oxoglutarate
- Creatine
- Methionine
- Threonine
- Tyrosine

Orange group

- Phosphatidylcholines
- Sphingolipids

- Glycerol

FURTHER DEVELOPMENTS

- Model validation using an independent cohort
- Biochemical interpretation of the results

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