

New Advances in CE-based Metabolomics for Biomarker Discovery: Serum Metabolic Signatures of Peripheral Artery Disease

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Gold statement

- Learn about multiplexed CE-MS separations for rapid profiling of polar metabolites and ionic lipids
- Appreciate accelerated data workflows for biomarker discovery with stringent quality control
- Discover new serum biomarkers for differentiating two major subtypes of peripheral artery disease

Introduction

Peripheral artery disease (PAD) is characterized by atherosclerotic narrowing of lower limb vessels leading to ischemic muscle pain in older persons. Some patients experience progression to advanced chronic limb-threatening ischemia (CLTI) with poor long-term survivorship.

Body

Herein, we performed serum metabolomics to reveal the mechanisms of PAD pathophysiology that may improve its diagnosis and prognosis to CLTI complementary to ankle-brachial index (ABI) and clinical presentations [1]. Non-targeted metabolite profiling of serum was performed by multisegment injection-capillary electrophoresis-mass spectrometry (MSI-CE-MS) from age and sex-matched, non-diabetic PAD participants who were recruited and clinically stratified based on the Rutherford classification into CLTI (n=18) and intermittent claudication (IC, n=20). An accelerated data workflow based on multiplexed separations is used to authenticate both polar metabolites and ionic lipids from serum using three different MSI-CE-MS configurations [2,3]. Compared to non-PAD controls (n=20), PAD patients had lower serum concentrations of creatine, histidine, lysine, oxoproline, monomethylarginine, as well as higher circulating phenylacetylglutamine ($p < 0.05$). Importantly, CLTI cases exhibited higher serum concentrations of carnitine, creatinine, cystine and trimethylamine-N-oxide along with lower circulating fatty acids relative to well-matched IC patients. Most serum metabolites associated with PAD progression were also correlated with ABI ($r = \pm 0.24-0.59$, $p < 0.05$), whereas the ratio of stearic acid to carnitine, and arginine to propionylcarnitine differentiated CLTI from IC with good accuracy (AUC = 0.87, $p = 4.0 \times 10^{-5}$).

Conclusion

This work provides new biochemical insights into PAD progression for early detection and surveillance of high-risk patients who may require peripheral vascular intervention to prevent amputation and premature death.

References

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