Exploring cardiac disfunction expressed in chemotherapy treaded children using a sophisticated metabolomics workflow.

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Cardiac disfunction (CD) is a common adverse effect of chemotherapy, expressed even in pediatric oncology patients. The condition impacts the growth and the quality of life of childhood cancer survivors and thus, it is a challenge for the physicians. The CD onset has been already associated with genetic polymorphisms, however, there is no metabolomics research for the investigation of CD predisposition so far. Therefore, to explore potential pre-existing CD trends expressed in metabolome, a cohort of pediatric oncology patients was examined. Blood samples of 89 pediatric oncology patients were collected before their submission to chemotherapy. According to the latter diagnosis of CD-events at the period of chemotherapy, the patients were grouped into CD (26) and Control (63) classes. A plasma-based untargeted UPLC-QTOFMS metabolomics analysis was developed and supported by a sophisticated workflow for variables selection and DIA data interpretation. Semi-supervised KODAMA was employed as intermediated step between un-supervised PCA and semi-supervised OPLS-DA. BORUTA variables selection algorithm, and univariate t-test were also included in variables prioritization procedure. Finally, statistically driven identification was based on a consistent workflow, suitable for DIA, designed to increase the identification confidence.

The study succeeded the early classification of children that finally expressed CD, by their metabolic profiles. Furthermore, determined several important metabolites, i.e., 4-hydroxynenal and indoleacrylic acid, that enlighten the underlying pathway of CD onset. The research findings implied early dysregulation of amino acids and lipids metabolism, observations already linked to oxidative stress conditions and cardiovascular dysfunction states.