Enteric microbiome markers as early predictors of clinical outcomes in liver transplant: results of an ongoing prospective study

Melania Maccario1*, Virginia Amato1, Roberto Ferrarese2, Paola Carrai3, Mauro Pistello3, Fabrizio Maggi3, Rossana Cavallo4, Renato Romagnoli4, Nicola Clementi1, Roberto Burioni1, Massimo Clementi1, Nicasio Mancini1

* m.maccario@studenti.unisr.it
1 Laboratory of Microbiology and Virology, "Università Vita-Salute" San Raffaele, Italy
2 Laboratory of Microbiology and Virology, Ospedale San Raffaele, Italy
3 Azienda Ospedaliera Pisana, Pisa, Italy
4 Ospedale Le Molinette, Torino, Italy

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Background
Early hepatic complications, including early graft dysfunction and infections, still represent major, not easily predictable complications in liver transplant. It is now well established that altered gut bacterial composition is associated with the pathogenesis of many inflammatory diseases and there is increasing evidence of gut dysbiosis being a significant factor in the development of the main chronic liver diseases. Currently the MELD (model of end-stage liver disease) score is an accurate predictor of short-term survival after the liver transplantation, but it is only partially influencing the risk stratification of outcomes in the long term. The main objective of this study is to identify possible early microbiome-based markers useful in pretransplant risk stratification in order to upgrade the current scores.

Methods
Stool and plasma samples were collected at the beginning of the pretransplant conditioning regimen (T0) and at 7 (T1) and 90 (T2) days following transplant. The patients were enrolled from the two main Italian liver transplantation centers (“Ospedale Le Molinette” and “Azienda Ospedaliera Pisana”). The identified microbiome markers were used in univariate and then in multivariate regression analyses, together with other significant clinical variables for liver-related risk stratification.

Results
The transplant procedures impacted the enteric microbiome, with a decrease in bacterial α-diversity (Shannon index) particularly between T0 and T1. A significant increase was observed in the phylum Proteobacteria, almost completely represented by the Enterobacteriaceae. Furthermore, the preponderance of Enterobacteriaceae at T0 was a significant marker for the risk of early graft dysfunctions and infectious complications, especially when it was considered together with the MELD score, with a statistical significant increase of relative risk even in the short term.

Conclusions
Early microbiome-based biomarkers could be useful in the pre-transplant risk stratification of liver recipient, especially when combined with other known scores for risk assessment (MELD Score). The long term complications are currently being evaluated in order to create a comprehensive clinical and microbiomical model for the prediction of clinical outcomes and possibly define the potentially most effective and patient-tailored flora-modulating strategies.