

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

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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 statistically 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 microbiological model for the prediction of clinical outcomes and possibly define the potentially most effective and patient-tailored flora-modulating strategies.