

## Challenges in Liver Transplantation

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Transplantation medicine is still regarded as one of the most challenging areas in medicine. On the one hand, patients in need of a donor organ are seriously ill in most cases, while on the other hand, physicians and researchers need to be at the highest level of medical excellence. Liver transplantation has evolved from an experimental therapeutic approach in the 20th century to a standard therapy in today's high-care medicine. In the realm of liver transplantation, there are still many highly relevant aspects in the field of translation of knowledge from basics to clinics not only in the pre-transplantation scenario but also during the evaluation process, indication, and intra- and postoperative management, especially given that the number of donors does not comply with the demand of organs needed, which results in long waiting times. However, not all recipients survive until an organ becomes available and the mortality among patients on the waiting list remains high. Beside the need for recent and ongoing research focusing on the improvement of transplantation procedures, a lot of additional general issues related to transplantation problems have been the focus of debate, including clinical implications, regulations and limitations, and even gender mainstreaming.

Therefore, the articles of this special issue focus on different aspects associated with liver transplantation, describing current standards as well as the latest developments.

Canbay et al. [1] deal with the tremendously rising prevalence of non-alcoholic fatty liver disease (NAFLD), becoming the number one indication for liver transplantation in developed countries by 2020. However, NAFLD is a challenging and multifactorial disease with a high socio-economic impact. In the near future, non-alcoholic steatohepatitis cirrhosis complicated by hepatocellular carcinoma (HCC) will be the leading clinical problem regarding the indication for liver transplantation.

Meanwhile, Saner and Kirchner [2] focus on end-stage liver disease which is assumed to come with a high bleeding risk in association with a poor outcome. According to the authors, hepatic coagulopathy should be managed with coagulation factors rather

than with fresh frozen plasma as these are more affected and have fewer side effects in terms of potential infection and patient volume overload.

Hoyer and Minor [3] highlight current advances concerning the future of liver preservation and emphasize liver reconditioning methods. First comparative studies are currently emerging and will provide further clarification of optimal reconditioning preservation. Hypothermic oxygenated perfusion as an ischemic reconditioning method was recently compared to continuous normothermic machine perfusion in a clinically relevant donation after circulatory death rodent model. However, the combination of different preservation methods might provide the best preservation conditions in the future.

Strategies for hepatitis C virus (HCV) eradication before and after liver transplantation due to HCV-associated liver diseases are described by Herzer and Gerken [4]. The recently introduced combinations of direct-acting antivirals are now effective and safe for treating any HCV genotype and stage of the disease, including acute fibrosing cholestasis as well as liver cirrhosis. Nevertheless, the primary aim might be to achieve HCV eradication before transplantation. Certainly, for patients who are decompensated and for those on the waiting list, treatment of HCV before transplantation has to be carefully evaluated. Progressed and decompensated cirrhosis together with portal hypertension seem to severely reduce treatment efficacy. Therefore, it might be preferable to start HCV treatment after liver transplantation, considering that there will be the antiviral regimens which, in the meantime, allow safe treatment of HCV recurrence after liver transplantation in any case.

Indeed, HCC represents the most increasing health burden worldwide and a challenging disease both in diagnosis and treatment, including the indication for liver transplantation. Currently, the Milan criteria are the best evaluation decision tool for liver transplantation but many issues such as downstaging, favorable biological behavior during treatment, expansion of the morpho-

logical classification, molecular predictors, and individualized approaches are not yet satisfactorily addressed. Liver transplantation can be considered as the only true curative approach and meanwhile represents an established standard treatment option for HCC. Although general practice shows that HCC outside of the Milan criteria are transplanted in up to 50% according to regional and center-specific protocols, the Milan criteria are still the most robust allocation criteria and the benchmark for survival benefit assessed in HCC. In the past, patients who had been beyond the Milan criteria once never qualified for standard exception priority again. A new feature of the revision is the opportunity to regress an external audit when a positive prognosis is likely although the allocation criteria for standard exception priority are not met. Thus, the new revision has contributed to the clarification of diagnostic modalities, emphasizing the indication for liver transplantation in single HCC nodules >2 cm and defining HCC nodules more than 25 months after successful local therapy as new HCC with respect to standard evaluation eligibility, and includes standardized reporting and managing requirements.

Thus, Strassburg [5] clearly describes the continuous process of developing allocation rules in view of the continuing advances in the management of HCC.

In addition, Kocabayoglu et al. [6] report on their first experiences with morbidity and mortality conferences, especially in the field of liver transplantation. Altogether, these represent a new tool and an adequate platform on which surgical procedures, workflow arrangements, and outcome measures can be presented, discussed, and approved with every individual involved in the clinical case. Conducting morbidity and mortality conferences properly holds the potential to combine all aspects, i.e. educational values as well

as increasing patient safety and quality of care. Especially in the light of transplantation surgery, a critical assessment of approving patient safety in combination with the advancement of medical educational needs to be performed. Thus, there is an urgent need for a structured approach to identify system defects and establish follow-up recommendations.

New implications in the face of donor shortage during the liver allocation process are being focused on by Lauerer et al. [7]. However, various factors can reduce the demand or increase the supply of donor organs. Due to a lack of consensus or a lack of medical technical feasibility, most of these implications cannot be implemented readily. The main reasons for refusals to donate organs are the ancient fear of abuse and organ trafficking, unfair allocation of organs, as well as not being decisive. In sum, external controls need to be carried out in order to strengthen confidence, while transparency should be established to make the general public understand allocation criteria, i.e. change of success, urgency, quality, and safety of donation.

Last but not least, Teegen et al. [8] address the problem of gender mainstreaming and transplantation surgery. Gender differences in medicine are gaining importance. In transplantation surgery, not only the patient's gender but also the donor's gender plays an important role concerning the outcome of transplantation due to social, cultural, and genetic factors. Further investigations are necessary to detect the probably underlying mechanisms, especially on immunological and tumor levels, in order to understand the complex relationships of gender medicine.

In summary, the interesting, highly focused articles in this special issue of *VISCERAL MEDICINE* present today's standards as well as the latest developments in liver transplantation medicine.

## References

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