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INVITED COMMENTARY

Equitable distribution in rare indications for liver transplantation: the dilemma of the too small tablecloth continues!

Andreas A. Schnitzbauer & Wolf O. Bechstein

Clinic for General and Visceral Surgery, Frankfurt University Hospital, Goethe-University Frankfurt, Frankfurt/Main, Germany

Correspondence
Andreas A. Schnitzbauer, MD, FACS, FEBS, Clinic for General and Visceral Surgery, Frankfurt University Hospital, Goethe University Frankfurt, Theodor-Stern-Kai 7, 60590 Frankfurt/Main, Germany.
Tel.: +49-69-6301-5253;
fax: +49-69-6301-84028;
e-mail: andreas.schnitzbauer@kgu.de

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Primary biliary cholangitis (formerly known as primary biliary cirrhosis) has been a classic indication for liver transplantation for more than thirty years [1]. Due to the changing epidemiology of liver diseases combined with the universal lack of postmortal grafts, the question of prioritizing allocation amongst sick patients competing for these rare grafts on the waiting list remains an unresolved challenge. In their UNOS database analysis, Ashwani Singal and co-workers focus on wait-list mortality for a nowadays rare indication for liver transplantation: primary biliary cholangitis (PBC) [2]. Recently, the terminology of PBC has been changed to primary biliary cholangitis as this term better depicts the inflammatory character of the disease and is recommended to be used to remove stigmatization from the association of alcohol abuse and cirrhosis [3]. In their analysis of UNOS data spanning the period from 2002 to 2013, Singal *et al.* showed that PBC has a significantly higher wait-list mortality (almost twofold in general and after 3 months on the list) compared to most other indications. Based on these results, the group strongly recommends that exceptional points should be given to patients with PBC to reduce wait-list mortality [2].

The work impressively unveils a general dilemma in the equitable distribution of scarce medical interventions and opens an ethical and medical discussion in organ allocation [4]. Besides the highly complex ethical issues, stakeholders should consider basic medical aspects, when creating and fixing rules for the allocation of organs. First, the mortality for PBC patients on the waiting list is obviously in a crass disparity to other indications listed for liver transplantation. In a publication by Genda and co-workers from a Japanese multicenter study, waiting-list mortality for PBC was 79% higher than for patients with hepatitis C [5]. Second, the number of patients on the wait list and the indication for transplantation is approximately 5-10%, and comparable to other indications such as primary sclerosing cholangitis, hepatocellular carcinoma, hepatitis B or congenital biliary disease [2,5,6]. Third, the survival after liver transplantation for patients with PBC is

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considered to be more favourable (approximately 5% higher at 1, 3 and 5 years after transplantation) than for other indications and independent from the type of transplantation (living or deceased donor) [6,7].

On the other hand, there is also good evidence that patients responding to medical treatment with ursodeoxycholic acid (UDCA) most likely will have a normal life expectancy compared to the general population [8]. However, 40% of patients do not respond to therapy with UDCA and require additional medical treatment to avoid listing for liver transplantation which should be considered when patients reach a bilirubin level of 6 mg/dl, the Mayo risk score is over 7.8 and the MELD score is over 12 in accordance with the EASL (European Association for the Study of the Liver) guidelines for cholestatic disease [9]. Other drugs like budesonide and fibrates can significantly improve the cholestatic course of the disease [8]. A new kid on the block is obeticholic acid (OCA) which has been shown to have the potential to reduce cholestatic parameters in nonresponders to UDCA [10].

All these aspects create a foggy picture of the relevance of liver transplantation for PBC. It is a disease representing one of the indications with the best survival data and an indication for liver transplantation with one of the highest mortalities on the waiting list. Is it ignorance, a lack of lobbyism in the medical, surgical and transplant societies for one minor indication or simply limited knowledge of the urgency of the disease once it comes to decompensating liver function with adverse outcomes (death on the waiting list)? The call for exceptional points on waiting lists is more than justified taking all these arguments and data from literature together and should be urgently discussed in advisory boards for organ allocation. However, as a consequence, other indications for liver transplantation would suffer from an amended and improved organ distribution shifting towards PBC. In the end, it all comes down to organ shortage and the simple lack of enough donors for patients on the waiting list, which requires tough decisions. In numbers, this means that by the end of 2015, there were still more than 1.800 patients waiting for a liver allograft in the Eurotransplant area, compared to the 1.700 that received an organ in the same year [11]. This shows that there is still a considerable high discrepancy between available organs and patients requiring an organ. Thus, tearing at one side of the tablecloth gains space for one indication, but leads to a drop of indications on the floor on the other side due to a too small number of organs available.

In conclusion, the wait-list mortality for PBC is currently too high. Exceptional points should urgently be discussed and considered due to the fact of excellent outcomes after liver transplantation. Fortunately, conservative medical treatment of PBC after UDCA failure seems to be improved by combination therapy and new agents. Real-time knowledge of indication-specific dynamics on the wait list and after liver transplantation (e.g. in the form of a scientifically attended registry in the hands of clinicians) would more easily allow for an ad hoc adjustment of reasonable allocation rules in the future. It is worth a try for better outcome in our patients.

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