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INVITED COMMENTARY

The introduction of MELD-based organ allocation impacts 3-month survival after liver transplantation by influencing pretransplant patient characteristics

Invited Commentary on Weissmüller et al.

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As there are insufficient organs to transplant everyone who might benefit from the procedure, rationing has to occur and the processes which will, in effect, result in the denial of a life-saving procedure for many individuals, need to be explicit, objective, just, equitable, transparent and retain public trust and confidence. Therefore, robust processes both for selection (determining who gets on to the transplant list) and allocation (who gets a donated liver) need to be developed and implemented. The principles of selection and allocation policies should be (and usually are) developed after full public consultation so that the various and often competing demands of equity, fairness, utility and benefit can be met as far as possible but the delivery of the principles will need to be implemented by clinicians.

It is, of course, essential to define the purpose of the selection and allocation systems adopted and then audit the outcomes to ensure that the goals have been fulfilled, and identify any unintended consequences. In the UK, as in many other countries, for liver allograft recipients we have adopted what is primarily a utilitarian approach, listing when the survival probability is greater with transplant and there is a greater than 50% probability that the patient will be alive (with an acceptable quality of life) at 5 years [1]. Allocation is based on a national priority for super-urgent cases (such as those with fulminant liver failure) and thereafter allocated to the centre: we, as are some others, are exploring moving to an allocation system based on benefit.

The USA has adopted an alternative approach, which has been widely used throughout the world [2]. After extensive research, discussion and consultation, in 2002 an allocation system was introduced with the primary aim of reducing the mortality of those on the transplant list. Within the defined geographical area, a donor organ is offered for an individual, in an order determined by the MELD score. There are literally hundreds of publications on the use of the MELD system and both its strengths and deficiencies are well recognized. The model has been well validated in many diseases and different health care systems: it is objective and not too susceptible to manipulation. However, technical, pharmacological, physiological and pathological factors may all affect the MELD score to give an inappropriate (high or low) survival probability and it may underestimate survival of those with hyponatraemia and ascites and, although there

are mechanisms in place to deal with variant syndromes, it seems not to serve well those with relatively good liver function but symptoms such as encephalopathy or intractable pruritus [3]. There is a relatively poor correlation between MELD and outcome [4]. Furthermore, the formula for MELD is being constantly reviewed and revised, as more data are generated; it is not clear whether the German model uses the latest version nor whether the model is validated in a German population of patients awaiting liver transplantation.

There have been several studies looking at the impact of the introduction of the MELD-based system of allocation. While most of these have been single-centre, retrospective analyses, often with short-term outcomes, the overall message is relatively clear: the system is effective in reducing the mortality on the transplant list, probably has not affected overall survival after transplantation but probably has increased resource utilization [2,5]. This clearly will impact on overall costs of transplantation [6] but further evaluation will be needed to assess cost-benefit. It is counter-intuitive that the degree of sickness of the recipient will not affect outcome: the explanation is more likely to reflect the skill of the surgeon in matching donor organ and recipient and the importance of the impact of the quality of the graft in determining the outcome (as confirmed by the various risk models for outcome), rather than the state of health of the recipient not affecting survival post-transplant. Current data from the USA suggests that over 40% of grafts are not implanted in the first patient in the offering system.

Other countries and health care systems have adopted the principles of MELD-based allocation system with varying enthusiasm and varying outcomes, as shown by the report from Hannover [7], suggesting that, for that unit at least, a MELD-based system is associated with a worse outcome than the previous model. This is in keeping with their recent observation that 1-year survival was greater in those with a MELD score less than 16 [8].

Does this mean that MELD does not deliver as well as its proponents suggest? There are several possible reasons. MELD may not travel: in the UK we have found that MELD does not predict survival as accurately as a model derived from data of UK patients awaiting transplantation [1]; (MELD was derived from USA patients at the Mayo Clinic undergoing shunt insertion). It is, to many clinicians, counter-intuitive that one model can accurately predict outcome, irrespective of aetiology and one model using serological variables can predict survival outcome irrespective for both parenchymal and cholestatic disease; however, the MELD does perform well in the context of patients with end-stage cirrhosis awaiting transplantation [4]. The allocation system is not proscriptive: it is the responsibility of the surgeon to decide whether to accept the liver for the given patient: this is clearly a difficult decision as the possible recipient will be ill and may not afford the luxury of waiting for the next offer. Although the characterization of an extended donor criteria graft is becoming easier and there are now mathematical models for helping the clinician decide the best donor-recipient match, the matching remains a difficult one, relying on inadequate data and many unquantifiable factors: yet the Hannover clinicians are all experienced so a lack of ability to match donor and recipient is unlikely to be the explanation for the worse outcomes at 3 months they have noted. One consequence of the MELD-based allocation system is that clinicians have tended to pair high-risk grafts (as shown by the Donor Risk Index) with less sick patients (lower MELD score) and those least in need of a graft will receive the higher-risk grafts [9]: because of the importance of the graft in its impact on outcome, this will result in the failure to maximize survival; indeed, modelling suggests that high risk organs are most effectively used in sicker patients [10]. Of course, worsening outcomes at 3 months may not necessarily imply worse outcomes at 1 year: those factors that predict short-term survival are not identical to those that predict long-term survival. Thus, in an analysis of the UNOS data base, Waki [11] found that those with a pretransplant serum bilirubin greater than 7 mg/dl who survived more than 1 year actually had a better survival than others. The worsening outcomes may reflect the increasing poor quality of the donors and be unrelated to the change in allocation system: the increasing age of donors, the increasing obesity rates with more steatotic grafts, the use of splitting livers which will turn high-quality grafts into extended criteria grafts and the increasing use of donors who have suffered intra-cerebral catastrophes may all adversely impact patient and graft survival. The use of a national allocation system, rather than a centre-based system, may be associated with an increase in the travel times and so with a longer cold ischemia time, especially with a steatotic graft, may lead to a worse outcome.

The outcome of even well planned changes may not always be as expected. A review of the USA system, based on retrospective analysis of data held by UNOS suggested that the introduction of the MELD-based allocation system was associated with a reduction in the racial inequality but an increase in gender inequality [12]. Thus the outcomes of the Hannover group need to be taken seriously but, in themselves, do not imply that the MELD-based system is responsible for deteriorating risk-adjusted outcomes. Furthermore, deterioration in post-transplant outcome may well be more than counter-balanced by a benefit in the reduction in pretransplant mortality so

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there remains an overall benefit from the newer system. Review of the aims of the allocation system, on-going audit and analysis are needed to show that the allocation system adopted is fit for the purpose – if not, it needs to be changed. Transparency in the allocation system is important but may be too high a price to pay for increased patient mortality and decreased benefit from a donor pool that is far too small.

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