Editorial

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Allocation of deceased-donor livers – Is there a most appropriate method?

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Organs donated by deceased donors are a bequest to those awaiting transplantation, therefore, their allocation must be transparent and according to agreed principles. These principles must not only be compatible with all legal requirements, but also meet agreed and transparent ethical criteria. These principles include the need for equity and justice. The American Medical Association (AMA) identified acceptable and unacceptable criteria for allocation of donated organs.[1] Allocation policies should be based on criteria relating to medical need (including urgency), likelihood and anticipated duration of benefit, and change in quality of life. In some circumstances, the AMA opined it may be appropriate to take into consideration the amount of resources required for successful treatment. It is not appropriate to base allocation policies on social worth, perceived obstacles to treatment, patient contribution to illness, past use of resources, or other non-medical characteristics. The AMA suggested that first priority should be given to those patients for whom transplantation will avoid premature death or extremely poor outcomes, then to patients who will experience the greatest change in quality of life. Within these principles, there are several approaches to organ allocation:

- Urgency or sickest first: the organ is allocated to the candidate in greatest need or most likely to die first
- Utility: the organ is allocated to the candidate who will have greatest survival after transplantation with that organ
- Benefit: organ is allocated to the candidate who will derive greatest benefit
- First come, first served: organ is allocated in the order of listing

All, with the possible exception of the last approach, which has few if any reasons to recommend it, have their advantages and disadvantages.

In the accompanying manuscript by Tschuor and colleagues published in the current issue,[2] the authors describe the approaches taken in countries around the world and conclude that a system based on the sickest first is the ‘most reasonable’ approach. To conclude one approach as the most reasonable requires that the goal or goals of organ allocation are clearly defined and in alignment with the goals of various stakeholders – potential candidates, donors and donor families, health care professionals and (perhaps controversially) their respective medical centres, ethicists and the public. Different constituencies hold a variety of views, and what is most reasonable to one constituency may not be fully aligned with the goals of another constituency. Different jurisdictions, with different levels of need and availability of organs, will wish to adopt their own goals.

The responsibility for defining the aims of allocation vary: in the US, the goals are defined by law whereas in the UK, defining the goals of allocation is delegated to statutory bodies. Having a legal basis provides a clear accountability and a legitimate democratic basis although making modifications, similar to changing other types of laws, is often a lengthy process and gaining consensus requires a commitment to collaboration and compromise from the transplant community that if lost, risks the delegation of policy development solely to the legal realm.

Certainly, the sickest first has many advantages and practice has clearly shown that the introduction of a sickest first policy is associated with a major reduction in mortality of those on the wait list;[3] In the US, deaths on the liver transplant waiting list fell from 15.5% in 2018 to 9%.[4] However, not all countries have seen this effect.[5]

The underlying principles are simple: survival in the absence of transplantation is estimated using a validated model and the liver is offered to eligible candidates in order. Estimation of survival is usually done using the model for end-stage liver disease (MELD) score. This score is well validated, uses commonly measured laboratory parameters and avoids subjective and semi-quantifiable variables (such as ascites or encephalopathy). However, there are many well-documented concerns with its use, such as the significant variation between laboratories in the measurement of serum analytes (such as serum bilirubin or creatinine), the impact of non-hepatic diseases on MELD variables (such as haemolysis and serum bilirubin).[6] Although the score is widely used throughout the world and this has led many jurisdictions to use modified MELD models.[7] Despite early concerns, introduction of the sickest first principle was

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generally not associated with a decrease in post-transplant survival,[8] high MELD patients (>30) have only a slightly inferior survival but do have a longer stay in intensive care unit and attract greater post-transplant costs, (though overall cost of care may actually be reduced due to reduced costs of pre-transplant care).[9] Indeed, since the implementation of Share 35 which allows for broader sharing for MELD 35 and higher, transplanting high MELD patients more quickly actually reduces overall costs because the cost of pre-transplant care is reduced.[10] It should be noted that one recent study suggested that a simple sickest first policy may not accurately reflect the views of the US population.[11]

Of the other options for allocating organs, a benefit model ranks candidates according to benefit which combines both urgency and utility. The period of time over which the benefit is measured will affect allocation ranking:[12] a longer period will benefit younger candidates at the expense of older ones and benefit those with indications that are associated with a better long-term prognosis (such as primary biliary cholangitis) at the expense of those with a poorer log-term prognosis (such as primary liver cell cancer). A key challenge for widespread adoption of a benefit-based liver allocation model are the large number of factors that impact post-transplant survival, which limit the predictability of the model. Adoption of a benefit-based model was strongly considered in the United States a decade ago but ultimately not adopted because of concerns about the complexity and reliability of the model and the recognition that the most predictive and thus heavily weighted variables were actually those on the pre-transplant side of the equation, similar to an urgency-based model. A recent study also suggested that the MELD-based approach also improves benefit.[13]

Both the sickest first and benefit models rely on the use of robust and validated models to predict survival with and without transplantation. Predicted outcomes from these models have fairly wide confidence intervals and thus the numerical outcome of application of these models are treated as though they have a greater precision than is merited. Nonetheless, modelling in the UK has suggested that the predicted wait list mortality/removal rates would be similar for an urgency-based system and a benefit-based system, the patient years gained by a benefit approach were slightly greater.[14] Neither approach defines futility: it is both ethically and clinically acceptable not to allocate scarce organs to those with very little chance of benefit. Ideally, criteria for de-listing for futility need to be developed, validated, agreed and implemented but the challenges may preclude this goal.

Application of either model means some candidates are disadvantaged: the MELD score may disadvantage women and those from some ethnic groups as equivalent serum creatinine levels, a major determinant of the MELD score, have slightly different implications in these groups.[15] Models are derived from data registries that may not capture clinically relevant data: these data may be difficult to quantify objectively (such as frailty scores).[16] Furthermore, repeated use of a static model to a dynamic situation may not be appropriate.[17] Some of the candidates whose survival is not well captured by the MELD score, because their probability of liver-related death is not determined by tests of parenchymal function, can be accommodated by adjusting their MELD score: models are well developed for some indications such as primary liver cell cancer but for others, such as those with hepatopulmonary syndrome for example, a reliable estimate of survival is difficult. To overcome the challenge of estimation of survival in those where robust, validated models are either non-existent or insufficiently precise, Appeals Panels have been set up. These do work reasonably well, although it is difficult to ensure equity and reliability between and within panels.[18] Having to rely on clinical judgement, because there is no suitable alternative measure of survival, is not only difficult but also moves away from the many benefits of using objective methodology.

Another group of patients who are disadvantaged by both models is those whose short- and medium-term survival is good but whose quality of life is intolerable: such patients include those with intractable severe pruritus, intractable encephalopathy or polycystic liver disease. While such patients represent a small proportion of those who are eligible for a transplant, their options are to find a living donor, accept an organ that has been declined for use by all other suitable candidates or get assigned an additional number of MELD points, an option which thwarts the sickest first principle. Finally, these systems do not readily account for those who are awaiting a re-graft, or how splitting of livers can be accommodated.

The inevitable outcome of the need to serve a wide variety of candidates who may benefit from transplant means that the rules are complex and rigorously applied. Like any system, this allows for gaming or manipulation of data, and requires rigorous oversight with meaningful consequences for policy violation. Of greater concern is that, we believe, any allocation system should be flexible enough to respond to previously undefined needs and also to support appropriately approved research, and development of novel techniques. Ensuring flexibility and fostering innovation while fulfilling regulations is often a difficult challenge.

Overall, it is unlikely that a single, fixed international standard model of organ allocation will ever be identified or agreed: and the most appropriate is the one that best meets with the priorities for that jurisdiction and is able to be modified over time as new knowledge is gained. The key issue is to ensure the aims of the allocation process are defined, transparent and meet legal and ethical goals. They should also be able to be revised to account for changes in availability of organs and needs of the patients. Comparisons between different approaches can provide very useful insight, but they should recognise that there are differences in the populations, and the health care systems, not to mention differences in topography and infrastructure that may impact any organ allocation systems. In striving to develop and implement the optimal model, attention should not be averted from the oversight of the other essential components of organ allocation.

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

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