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Meeting Report

A Multistep, Consensus-Based Approach to Organ Allocation in Liver Transplantation: Toward a ''Blended Principle Model''

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Since Italian liver allocation policy was last revised (in 2012), relevant critical issues and conceptual advances have emerged, calling for significant improvements. We report the results of a national consensus conference process, promoted by the Italian College of Liver Transplant Surgeons (for the Italian Society for Organ Transplantation) and the Italian Association for the Study of the Liver, to review the best indicators for orienting organ allocation policies based on principles of urgency, utility, and transplant benefit in the light of current scientific evidence. MELD exceptions and hepatocellular carcinoma were analyzed to construct a transplantation priority algorithm, given the inequity of a purely MELD-based system for governing organ allocation. Working groups of transplant surgeons and hepatologists prepared a list of statements for each topic, scoring their quality of evidence and strength of recommendation using the Centers for Disease Control grading system. A jury of Italian transplant surgeons, hepatologists, intensivists, infectious disease specialists, epidemiologists, representatives of patients' associations and organ-sharing organizations, transplant coordinators, and ethicists voted on and validated the proposed statements. After carefully reviewing the statements, a critical proposal for revising Italy's current liver allocation policy was prepared jointly by transplant surgeons and hepatologists.

Abbreviations: AISF, Italian Association for the Study of the Liver; HCC, hepatocellular carcinoma; LT, liver transplantation; MELD, model for end-stage liver disease; NTC, National Transplantation Center; OPTN, Organ Procurement and Transplantation Network; SITO, Italian Society for Organ Transplantation; T_{NT}, nontransplantable; TT, transplantable; UNOS, United Network for Organ Sharing

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Introduction

Allocation systems relying mainly on the principle of urgency, like those prioritizing patients with higher MELD scores, have several inherent weaknesses because MELD score measures severity of disease, but often fails to predict outcome after liver transplantation (LT) (1). MELD scores also cannot gauge the severity of several diseases currently considered ''MELD exceptions,'' or of hepatocellular carcinoma (HCC) in patients with compensated cirrhosis (2). In a recent prospective Italian series of LT, MELD was unable to describe the disease's severity in almost 50% of the cases (3).

Assessments designed to assure equitable access to LT should therefore distinguish between patients with decompensated cirrhosis (when the urgency principle based on MELD score is applicable) and patients with MELD exceptions or HCC and compensated cirrhosis. The latter can be considered prototypic MELD exceptions because a MELD-based system fails to capture their risk of dropout due to tumor progression or liver-related complications with no bearing on MELD score (4). The appropriate selection of candidates with or without HCC for LT, and their priority on the waiting list, therefore cannot be achieved with models based on urgency alone (Appendix 1). The principles of urgency and utility must be balanced and integrated with transplant benefit (5).

Several proposed models focusing on urgency, utility or benefit principles, or combinations thereof, involve adjusting scores, matching donors and recipients, and other optimizations, assuming that access to LT is not the only goal; delisting criteria, long-term transplantation outcomes, and organ availability must be considered, as well as the expected results of alternative therapies (6–12). The issue's complexity, the number of variables and different medical, social and political figures involved, and the huge differences in local and regional scenarios have all contributed to hindering the development of a consensual allocation/priority system that considers all the above elements.

Italy's organ transplantation network is governed by the National Transplantation Center (CNT). It has 21 LT centers in 13 regions, grouped into 2 macro areas (central-northern and central-southern Italy). Since the CNT's inception, its liver allocation policies have seen several modifications. The current policy stems from a revision in 2012 designed to expand macro area and nationwide organ sharing according to urgency principles. Organs are shared: nationwide for the most severely ill candidates classifiable as UNOS Status 1 (super-urgent); by macro area for patients with MELD $\geq$30; and regionally for patients with MELD $\leq$29 (the minimum score for listing a patient for LT is 15) (10). The arbitrary cutoff at 30 was chosen because patients with MELD $>$30 at transplantation represented the highest decile (10%) of patients transplanted in Italy in the previous year (2011). With this allocation system, policies at local level may be heterogeneous, with a potential imbalance among different liver disease etiologies.

Given these areas of contention, a national consensus conference process was arranged with the contribution of all interested parties to enable a broad discussion of these important aspects of Italy's liver allocation policies. The aims of the multistep consensus conference were to

- identify the best urgency, utility, and benefit indicators to consider for organ allocation purposes (first step);
- identify MELD exceptions, and choose the best indicators to consider for organ allocation in such cases (second step); and
- prepare a working proposal for revising the current allocation system (third step).

A further consensus conference on the ethical issues of LT was held within the same time frame (the results of which will be presented elsewhere).

Liver allocation to pediatric patients was not considered because they are the object of a separate national list and different policy.

The present report outlines the group discussions, and the resulting working proposal for revising Italy's current allocation policy for LT. The consensus conference method and results could serve as a model and stimulate the debate for future improvements to liver allocation systems adopted in Italy and elsewhere.

Methods

The consensus conference was promoted by the Italian College of Liver Transplant Surgeons (for the Italian Society for Organ Transplantation [SITO]) and the Italian Association for the Study of the Liver (AISF). The promoters appointed a Scientific Board of Experts with two coordinators from SITO and AISF, two liver transplant surgeons, and two transplant hepatologists, all recognized as leading experts in their field.

The topics of the first and second steps were discussed at separate consensus conferences in 2012 and 2013. For each topic, the promoters and Scientific Board identified working groups of surgeons and hepatologists chosen for their expertise and publications on liver disease and transplantation. The working groups independently conducted systematic literature reviews, then met for morning background presentations and afternoon discussions, drafting definitions and statements graded according to the CDC system (13). Appendix 2 contains a flowchart summarizing the key steps in this preparatory phase.

The statements were put to the vote of a jury of transplant surgeons, hepatologists, intensivists, infectious disease specialists, epidemiologists, representatives of patients' associations, representatives of organ-sharing organizations, transplant coordinators, and ethicists. None of the jury members had been involved in choosing the topics or preparing the statements. Each working group's chairman presented their statements in a format that involved first asking a question, then giving one or more answers based on a statement's CDC-graded quality of evidence and strength of recommendation. A general discussion was held to refine and revise the statements, then each statement was voted on, taking the jury's votes as valid and the audience's votes for reference.

After further careful review of the approved statements, a group of expert liver transplant surgeons and transplant hepatologists prepared the operative scheme described here, which will be presented to all parties involved in LT at a meeting scheduled for mid-2015.

Consensus Conference Outcomes

The statements approved at the conference on the definition of the principles of utility, urgency, and benefit, and their prognosticators (first step) are listed in Appendix 3. Given their relevance to the discussion, the statements concerning transplant benefit are also listed in Table 1. Each statement is associated with a measure of the quality of the evidence and the strength of the recommendation, as appropriate.

MELD exceptions were identified analytically, constructing a priority for transplantation algorithm based on currently-available scientific evidence. Four priority categories (P1–4) were identified for MELD exceptions, defined as follows:

- P1: Very high priority: warrants organ sharing by macro area (central-northern or central-southern Italy, each serving a population of 20–25 million) as for patients with MELD $\geq$30;

Table 1: Statements on transplant benefit. Quality of evidence and strength of recommendation are provided, when appropriate, according to the CDC grade score (mettere voce bibliografica)

	Quality of evidence	Strength of recommendation
BENEFIT STATEMENTS		
Benefit		
1. Transplant benefit of at least 5 years after transplantation is the best available indicator for maximizing the life-saving potential of procured livers.	E2	R2
2. Transplant benefit should be regulated according to minimal acceptable posttransplant results (UTILITY), and take into account the risk of dropout from the waiting list (URGENCY).	E2	R2
3. When measuring transplant benefit, the gain in life years is equivalent to the difference in the mortality ratio of patients with or without LT. The measure of gain in life expectancy is more understandable than the difference in mortality ratio with or without transplant.	E2	
4. Most studies on transplant benefit calculation are based on waiting list populations.	E2	
5. However, the implementation of a national registry to sample prospective cohorts of cirrhotic patients potentially eligible for LT based on the ITT principle is strongly recommended.		R1
6. Quality-adjusted life years (QALYs) should be included in the transplant benefit estimation as a relevant endpoint. Cost effectiveness should also be evaluated, though neither evidence nor data are available in the transplant benefit estimation.	E3	R3
7. Evaluation of potential harm to individuals and waiting-list populations should be included in the transplant benefit estimation.	E2	R2
Benefit predictors		
8. The predictors of transplant benefit in the cirrhotic patients are, at minimum, the following: MELD and its variables, albumin, donor age, recipient age, previous liver transplant, diagnosis of HCV, and portal vein thrombosis. Studies assessing predictors of transplant benefit are warranted.	E2	
9. Liver function is a predictor of transplant benefit in HCC patients. Indeed, in patients within criteria for transplantation according to tumor features, BCLC stages seem to predict the magnitude of transplant benefit.	E2	R2
10. Applicability of therapies as alternatives to transplantation is a predictor of transplant benefit in HCC patients.	E2	
11. Studies on transplant benefit, including hepatic function parameters and tumor characteristics, are warranted.	E2	R2
Minimum threshold of benefit		
12. A MELD score of 15 corresponds to a 5-year transplant benefit of 12 months of life gain. This should be the minimal acceptable benefit. Excluding exceptions, the minimum listing criteria in Italy for patients with end-stage liver disease is MELD 15.	E2	R2

BCLC, Barcelona Clinic Liver Cancer; CDC, Centers for Disease Control and Prevention; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ITT, intention-to-treat; LT, liver transplantation; MELD, model for end-stage liver disease.
No strength of recommendation is given for cases where the content of the statements is accepted as evidence-based but does not prompt any recommendations.

- P2: High priority: organs to be shared within each region (serving populations of 1–6 million, 4 regions have more than one LT center), priority increasing with time on the waiting list (extra points for time, capping at 29);
- P3: Intermediate priority: organ sharing by region, priority increasing with time on the waiting list (extra points for time, capping at 29);
- P4: Low priority, organ sharing by region, priority increasing with time on the waiting list (extra points for time, capping at 29);
- P Multidisciplinary: Patients with particular indications (see list in Table 2) must be attributed a P1–4 category by a center's multidisciplinary team (hepatologist, LT surgeon, intensivologist) given the substantial lack of scientific evidence for generally deciding priority. Such multidisciplinary decisions will be submitted to the CNT.

Table 2 and Appendix 4 contain the proposed detailed list of MELD exceptions relating to individual priorities. Appendix 5 provides a detailed list of statements referring to the prioritization indicators for patients with MELD exceptions. A list of pertinent comments explaining the content of each statement in more detail, with related references, is also provided (Appendix 5A).

A new classification (Table 3) and prioritization policy (Table 4) were agreed for HCC patients. First, patients were defined as transplantable (TT) or nontransplantable (T_{NT}). Since a common nationwide criterion for HCC patient selection has yet to be agreed, HCC patients were defined as TT if they satisfy a minimal posttransplant utility requirement (50% 5-year patient survival). Centers have to clearly and publicly state their chosen criteria, and select HCC patients with at least a 50% chance of surviving

Table 2: Agreed priority strata for MELD exceptions and corresponding organ-sharing areas

Priority and sharing	LT indication
P1 (Macro area sharing after serving those with MELD>30)*	Rendu–Osler–Weber
	Hepatoblastoma (young adult)
	Hemangioma (if Kasabach Merritt syndrome)
	Acute late ReLT
	FAP (if domino)
P2 (Sharing at regional level)	Hepato-pulmonary syndrome
	PPH
	Refractory hydrothorax
	Chronic late ReLT
	Hepato-renal syndrome (if not automatically equated to MELD)
	Previous severe infections
P3 (Sharing at regional level)	Refractory ascites
	FAP
	Wilson's (with compensated cirrhosis and initial neurological symptoms)
	NET metastases
	Hemangioendotheliomas
P4 (Sharing at regional level)	PSC or PBC with intractable pruritus
	Polycystic disease
	Complicated adenoma
	Hemangiomas
P Multidisciplinary (Center-based)	Hepatic encephalopathy
	Fibrolamellar HCC
	Liver adenomatosis (not complicated)
	Hilar cholangiocarcinoma
	CRC metastases

CRC, colorectal cancer; FAP, familial amyloidotic polyneuropathy; HCC, hepatocellular carcinoma; LT, liver transplantation; MELD, model for end-stage liver disease; NET, neuroendocrine tumours; PBC, primary biliary cirrhosis; PPH, portopulmonary hypertension; PSC, primary sclerosing cholangitis.

5 years posttransplant. Either conventional (Milan criteria) or extended criteria (e.g., up to 7, total tumor volume, UCSF, α fetoprotein model) (9,14–16) may therefore be used to characterize a tumor as TT (9,14,17). Patients thus defined as TT were then classified using more dynamic categories (Table 3): first presentation, early or late recurrence, type of response to bridging therapy, successful downstaging.

Then HCC patients were grouped into 3 priority strata, based mainly on transplant benefit, but the risk of dropout (urgency) and patients' and/or physicians' expectations were also considered (18) (Table 3).

Patients' position within each priority stratum would be based on the only currently-available benefit prognosticator (''HCC-MELD'') (19), and an agreed definition of disease progression (Table 4).

Table 4 summarizes the whole prioritization process, including super-urgent cases, MELD patients, MELD exceptions, and HCC patients, all prioritized according to the same incremental numerical scoring system.

The MELD 30 cutoff (based on the decile of the most severe patients transplanted in 2011) for distinguishing between macro area and regional allocations remained unchanged for the sake of simplicity, but will be revised in future, based on the decile of the most severe patients transplanted in 2015.

Capping extra points for P2–4 and HCC at 29 aimed to avoid any influence of MELD exceptions and low MELD HCC on urgent patients. P1 and MELD >30 patients deserve the highest possible priority (after super-urgent cases) by macro area due to their inherent high risk of death. In future, this capping will be reevaluated and potentially down-modulated if it will reveal a priority unbalance favoring MELD exceptions and/or low MELD HCCs at the expense of biochemical MELD patients.

There is also a plan to adapt the system from MELD to MELD-Na in the future.

Discussion

Organ allocation for LT is evolving in various parts of the world (20–24). For instance, European transplant organizations basing their liver allocation criteria on blood group, recipient size, clinical urgency, and time on the waiting list reportedly revised their rules 13 times between 2006 and 2013 (20). The OPTN/UNOS is currently considering a new liver distribution format in the US to reduce variability in access to LT, that would divide the country geographically into 4 or 8 districts (21). The latest UK policy changes were

Table 3: Staging and prioritization of HCC patients for LT: Proposed new patient stratification

Category of transplantable (T) HCC	Priority according to HCC dropout models	Priority according to transplant benefit principle	Priority based on patient's/physician's expectations
$T0_C$ No residual tumor after curative treatment of a T-HCC	Very low Very low risk of dropout in cured HCC	Low Transplant benefit depending on lab-MELD only	Low Patients with no tumor should not be transplanted
$T0_L$ No residual tumor after loco-regional embolo-therapies for a TT-HCC	Low-intermediate Low risk of dropout in cured HCC	Low Transplant benefit depending on HCC-MELD	Intermediate The patient was transplantable but can now be put on hold because the tumor seems to be cured.
$T0_{NT}$** No residual tumor after treatment of an NT (nontransplantable) HCC	Not applicable NT HCC should not be listed, as in cases of no HCC in low MELD patients	Low Transplant benefit depending on lab-MELD only	Low The patient was not transplantable and has now been cured by other means.
T1 Single HCC $\leq$2cm (very early HCC)	Low Low risk of dropout in very early HCC	Low Low benefit in presence of alternative nontransplant treatments	Low No need to transplant someone who can be treated by other means
TT_{FR}* Any transplantable TT-HCC at presentation or recurrent HCC >2 years after curative treatment for a T-HCC (late recurrence)	Intermediate Demonstrated increase of dropout risk over time and across T2-HCC substages	Intermediate Benefit depending on true feasibility of alternative nontransplant treatments	High This is the patient with the best posttransplant survival (utility)
TT_{PR} Partial response to bridge therapy (cycle of multimodal therapy)	Intermediate-high Risk of selection of biologically aggressive clones with increased proliferative activity	High Failure of a bridge therapy with no residual therapeutic alternative	High Patients still with good posttransplant expected utility and high need for OLT
TT_{DR} TT-HCC after downstaging or recurrent HCC <2 years after curative treatment of any HCC (early recurrence)	Intermediate-high High dropout risk over time and across HCC substages	High Benefit depending on absence of feasible alternatives among nontransplant treatments	High Transplant is a chance to be offered before it is too late.

HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease.

*TT-HCC: any HCC meeting transplantability criteria (either conventional or expanded criteria, after donor rate and dynamics of waiting list considerations, in agreement with regional/national allocation rules).

**NT-HCC: Nontransplantable HCC: any other conditions not within the T-HCC definitions and/or any conditions of extrahepatic tumor spread and/or macrovascular invasion. Early or late recurrence: Recurrence within or beyond 24 months after previous complete treatment. Type of response to bridging therapy: Complete or partial response, stable or progressive disease according to the mRECIST.

Table 4: Proposed and agreed national waiting list prioritization policies and geographical distribution of organ allocation for patients with or without HCC and those considered MELD exceptions.

Priority	PTS Category	Points	Allocation area
Super-Urgent	FHF, early reLT	(first come, first served)	Nationwide
Urgent	MELD >30	Biochemical MELD	Macro area
Urgent	EXCEPTIONS P1	30	Macro area
Standard	EXCEPTIONS P2	25 + 1/month	Region
Standard	Bioch MELD 15–29	Biochemical MELD	Region
Standard HCC Stratum 1	HCC: TT_{DR}-TT_{PR} (downstaged patients or partial responders to bridge therapies)	HCC-MELD[19] + extra points for time or MELD 22 at entry + extra points for time (at regional board's discretion)§ Cap at 29	Region
Standard HCC Stratum 2	HCC: TT_{FR} (first presentation or late recurrence)	HCC-MELD[19] Criteria for awarding extra points for longer waits and priority class migration on disease progression will be set regionally (regional board approval)#	Region
Standard HCC Stratum 3	HCC: $T0_C$–T1-$T0_L$ (complete responders or T1 tumors)	Biochemical MELD	Region
Standard	EXCEPTIONS P3	20 + 1 every 2 months	Region
Standard	EXCEPTIONS P4	15 + 1 every 2 months	Region

FAP, familial amyloidotic polyneuropathy; FHF, fulminant hepatic failure; HCC, hepatocellular carcinoma; LT, liver transplantation; MELD, model for end-stage liver disease; NET, neuroendocrine tumours; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.
§Choice between ''HCC MELD + extra points for longer waits'' or ''22 points at entry + extra points for longer waits'' will be decided on a regional basis.
#Points for disease progression while on the waiting list can be discussed and adjusted (fast vs. slow pace) according to pattern of response or progression within the transplantability criteria. Progression has to be assessed after optimal treatments within defined protocols.
P1 = Rendu–Osler–Weber, young adult hepatoblastoma, Kasabach–Merritt, late ''acute'' retransplant.
P2 = Hepato-pulmonary syndrome, porto-pulmonary hypertension, late ''chronic'' retransplant, refractory hydrothorax, hepatorenal syndrome, previous severe infections.
P3 = Refractory ascites, FAP, Wilson's with initial neurological symptoms and well-compensated cirrhosis, NET metastases, hemangioendothelioma.
P4 = Complicated adenomatosis, polycystic disease, PSC or PBC with intractable pruritus.

approved by the Transplant Policy Review Committee in March 2014 (22). Many other countries, mainly in Asia, with relatively recent experience of cadaveric organ donation are now faced with the complexity of organ allocation, and are developing *de novo* algorithms for this purpose.

The methods used to establish organ allocation policies vary, but usually involve an organ-specific advisory board (e.g., the Liver Advisory Group for the NHSBT in the UK, or EUROTX in continental Europe). In some national transplant experiences (e.g., OPTN/UNOS in the USA), major changes to organ allocation policy are first circulated as ''concept documents'' to receive valuable input from all interested parties. Resulting proposals are then submitted to the public for further comment before final decisions are made (23).

The consensus conferences described here made it clear that Italy's existing allocation policy needed adapting to the diversity of patients on the waiting list with similar MELD scores, because there was evidence of some subgroups being at a disadvantage, and of regional inequities.

Our consensus conference process began with a critical review of the scientific evidence, with contributions from all players in the system. This generated a shared awareness and understanding of the problems, available solutions, and their pros and cons. Careful attention was paid to the outcome measures to consider in the LT setting in the light of recent evidence and experience (first step).

The introduction of the MELD score in 2002 (25) vastly improved the objectivity, transparency, and efficiency of organ allocation and patient prioritization for LT, but a far from negligible number of patients—including HCC patients with compensated cirrhosis, and MELD exceptions—are still prioritized using arbitrary national or regional approaches. The equity and efficiency of many international allocation models have been questioned, particularly concerning their endpoints (urgency vs. utility). Imbalances in the likelihood of patients with different etiologies on the same waiting list receiving a transplant have emerged and prompted policy adjustments.

In our discussions on outcome measures (first step) emerged that separately applying utility and urgency principles without an integrated approach to allocation and prioritization policy has several drawbacks. A broader ''blended principle model'' including the transplant benefit concept might strike a better balance between urgency and

posttransplant utility in the LT setting (10,12). In fact, transplant benefit—adjusted for a minimal accepted posttransplant utility—resulted from our national debate as an outcome measure well worth testing with a view to improving equity for different etiologies, and the LT system's efficiency at both individual and population level (1,26–28) (Table 1).

The consensus reached at our final meeting (in February 2015, third step) was consequently that—while awaiting more robust transplant benefit prognosticators—our organ allocation system should reflect an appropriate combination of the three principles (urgency, utility, and benefit) consistent with the fundamental statement from Persad et al. (29): ''To achieve a just allocation of scarce medical interventions, society must embrace the challenge of implementing a coherent multiprinciple framework rather than relying on simple principles or retreating to the status quo.''

A ''pure urgency'' endpoint was identified for patients at high risk of death in the short term (super-urgent cases, MELD $\geq$30 and P1 exceptions) who should access a broad geographical organ allocation area (nationwide or macro area). P2 patients should also be granted extra points because of their high risk of death.

The other two endpoints, ''benefit'' and ''pure posttransplant utility,'' could be better managed with a regional allocation procedure, offering the advantages of easier donor-recipient matching and greater flexibility.

Under the unifying ''blended principle concept,'' and in the areas of benefit and posttransplant utility, other MELD exceptions—including complications of cirrhosis, rare liver diseases or unusual presentations, and liver tumors—were discussed at our second consensus conference (second step). It was proposed an arbitrary approach to prioritizing MELD exceptions that met with broad approval: the aim was to focus more on a benefit principle, whenever possible and appropriate, whereas priority had been regulated by urgency or utility in many other cases.

The equation between MELD cases and exceptions was also arbitrary, dividing scores from 15 to 30 into quartiles, and equating each P category to the lowest MELD score for the corresponding quartile (e.g., P4 = MELD 15) (30). Extra points for time on the waiting list were calculated according to the mean waiting time for patients stratified by disease in 2014. Patients with the same score would be served in order of their time on the waiting list.

For HCC patients, the difference between expected survival after transplantation versus any alternative therapies is crucial. Accurate benefit prognosticators are lacking, so the feasibility of other treatments, response to therapy, and successful downstaging were considered as surrogates (17,31,32). It was agreed that the benefit for patients with very early HCC in compensated cirrhosis, or HCC patients with other radical therapeutic options (such as liver resection) is intrinsically too low to warrant their prioritization for transplantation, whereas impaired liver function in HCC patients substantially increases the potential transplant benefit because it limits the alternative treatment options (5). Avenues for successfully prioritizing downstaged HCC patients can follow a similar logic, providing the benefit achievable with LT is ''capped'' by a minimal accepted posttransplant utility (predicted long-term survival after transplantation of at least 50% at 5 years (see statement 6, Appendix 3). These considerations led to HCC patients being grouped into three strata, as shown in Table 4.

Despite numerous important limitations, the HCC–MELD system (19) was used to prioritize patients within the same HCC stratum because it is the only published score that strikes a balance between HCC and non-HCC patients, and considers benefit as an endpoint. The score gives considerable weight to the severity of liver function impairment as an indication of the inapplicability of alternative therapies, and reflects the negative impact of α-fetoprotein on posttransplant prognosis. The system still needs prospective validation, however (7,26,27).

Due to an intrinsically greater benefit of LT, patients in HCC stratum 1 (TT_{DR}, TT_{PR}) could be given higher priority by adding more extra points to their HCC MELD score than in the other HCC strata (TT_{FR}).

Our open debate clearly revealed, however, that considering transplant benefit as a major outcome measure has important drawbacks. Prognostic benefit models are still relatively inaccurate, and little is known about benefit predictors in certain numerically relevant indications for LT, such as HCC and MELD exceptions.

An allocation policy focusing exclusively on transplant benefit might also intrinsically favor patients with underlying diseases associated with a better posttransplant prognosis (e.g., PBC), and younger patients (1,12). Such equity imbalances could be partially adjusted by choosing an appropriate time horizon for transplant benefit (e.g., 10 years after LT). Ethical issues will play a relevant part in any such adjustments.

As a final step, our group tested the weight of the main organ allocation principles on the nationwide distribution of liver resources in 2014 (see Figure 1). This somewhat general and arbitrary graphic representation can serve as a benchmark in future national or international comparisons for optimizing the balance between the different principles, and guiding future resource investments. It was agreed, for instance, that transplant centers should adopt a ''pure posttransplant utility'' policy to allocate no more than 40% of their next year's overall donor resources and this proportion should be adjusted annually in the light of epidemiological studies and waiting list dropout data.

It was also agreed that up to 5% of the country's liver resources be used in innovative, multicenter studies and a crucial commitment was made to conduct prospective studies on benefit prognosticators (particularly for HCC patients) for validating benefit-oriented allocation models.

This report has a contribution to offer the transplant community partly because it comes 9 years after the International Consensus on MELD Exception was published in *Liver Transplantation* in 2006 (3). Another interesting consensus conference report dedicated specifically to HCC was published a few years ago (33) and was widely appreciated, the outcome becoming a reference for most LT centers around the world. No other equally thorough and detailed consensus conference reports on LT have been published since.

In conclusion, our multistep consensus-based procedure is a potentially effective solution for dealing with the complex issue of liver allocation, with its conflicting principles, diverging endpoints, and different clinical disease presentations. It generated a ''blended principle model'' in which a weighted, dynamic, and verifiable balance of different organ allocation principles was judged the best solution.

We hope our Italian experience will stimulate further discussion in the international transplant community, both in countries where LT is already well established, and in those where the deceased donor transplant process is still being developed.

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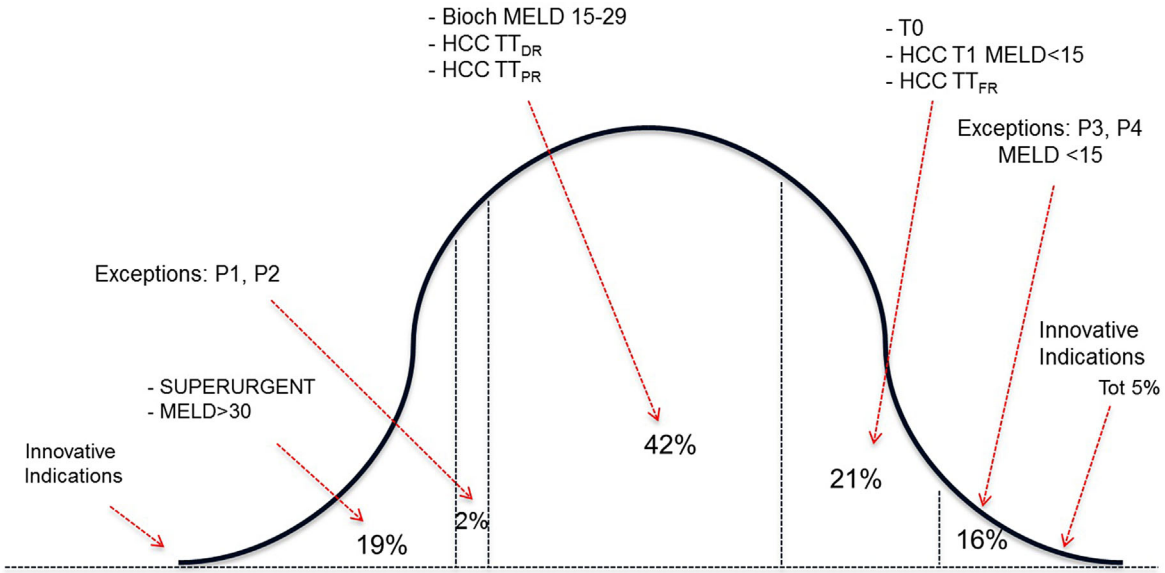

PRINCIPLE	FUTURE BENEFIT	Pure URGENCY HIGH BENEFIT	Low ALTERNATIVES HIGH BENEFIT	Post OLT UTILITY LOW BENEFIT	FUTURE BENEFIT
PRIORITY	Multidisc	Sickest first	Greater benefit	Waitlist time	Multidisc
PREDICTOR	-----	MELD/time bonus	MELD, HCC-MELD	MELD + time bonus	-----
PREVAL 2014	-----	21%	42%	37%	------
FUTURE AIM	Up to2.5%	To be reduced	To be increased	Not greater than 40%	Up to2.5%

Figure 1: Ideogram of donor resource distribution among the main liver allocation principles in Italy. Location of the different diseases in the urgency, benefit, or utility principles is for guidance only, intended to reflect the dominant principle, with a marked potential for overlaps. Multidisc: arbitrary multidisciplinary decision on priority for unconventional indications. PREVAL 2014: prevalence of national guidelines for transplantation in 2014 stratified by main allocation principle. FUTURE AIM: nationwide agreement on resource distribution goals for the next 3 years. HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease.

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Details of the members of the working parties and jury are provided in Appendix 6.

Disclosure

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Supporting Information

Additional supporting information may be found in the online version of this article.

Appendix 1: Differences in the criteria adopted for selecting cirrhotic patients with or without HCC for liver transplantation.

Appendix 2: Flowchart showing the structure and methods used to prepare the consensus conferences.

Appendix 3: Final recommendations and statements approved at the consensus conferences. The statements are divided into three sections: Section A refers to utility, Section B to urgency, and Section C to benefit. The quality of evidence (E) and strength of recommendation (R) based on the CDC grading system are provided for each statement, as appropriate.

Appendix 4: Prioritization for liver transplantation of patients with MELD exceptions. Priorities are divided into those predicted and those not predicted by the MELD score, and a coefficient of priority (P) is indicated for the latter.

Appendix 5: List of statements referring to MELD exceptions considered for liver transplantation and proposed tools for their prioritization. MELD exceptions are divided into two sections: Section D refers to MELD exceptions that are not tumor-related; Section E refers to tumor-related MELD exceptions. The quality of evidence (E) and strength of recommendation (R) based on the CDC grading system are provided for each statement, as appropriate.

Appendix 5A: List of comments on the statements concerning MELD exceptions (Appendix 5).

Appendix 6: Detailed list of participants involved in the multi-step Italian Consensus Conference process on organ allocation for liver transplantation.