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SPECIAL ARTICLE

Report of a National Conference on Liver Allocation in Patients with Hepatocellular Carcinoma in the United States

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A national conference was held to better characterize the long-term outcomes of liver transplantation (LT) for patients with hepatocellular carcinoma (HCC) and to assess whether it is justified to continue the policy of assigning increased priority for candidates with early-stage HCC on the transplant waiting list in the United States. The objectives of the conference were to address specific HCC issues as they relate to liver allocation, develop a standardized pathology report form for the assessment of the explanted liver, develop more specific imaging criteria for HCC designed to qualify LT candidates for automatic Model for End-Stage Liver Disease (MELD) exception points without the need for biopsy, and develop a standardized pretransplant imaging report form for the assessment of patients with liver lesions. At the completion of the meeting, there was agreement that the allocation policy should result in similar risks of removal from the waiting list and similar transplant rates for HCC and non-HCC candidates. In addition, the allocation policy should select HCC candidates so that there are similar posttransplant outcomes for HCC and non-HCC recipients. There was a general consensus for the development of a calculated continuous HCC priority score for ranking HCC candidates on the list that would incorporate the calculated MELD score, alpha-fetoprotein, tumor size, and rate of tumor growth. Only candidates with at least stage T2 tumors would receive additional HCC priority points. ***Liver Transpl 16:262-278, 2010.*** © **2009 AASLD.**

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Additional Supporting Information may be found in the online version of this article.

Abbreviations: 3D, 3-dimensional; AFP, alpha-fetoprotein; CT, computed tomography; DEB, drug-eluting bead; FAT SAT, fat saturation; HCC, hepatocellular carcinoma; HR, hazard ratio; LRT, locoregional therapy; LT, liver transplantation; MC, Milan criteria; MDCT, multidetector computerized tomography; MELD, Model for End-Stage Liver Disease; MRI, magnetic resonance imaging; NS, not significant; OPTN, Organ Procurement and Transplantation Network; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; UCSF, University of California San Francisco; UNOS, United Network for Organ Sharing; Y-90, yttrium-90.

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A US national conference of transplant physicians, surgeons, and other medical specialists was convened under the auspices of the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS), American Society of Transplant Surgeons, American Society of Transplantation, and International Liver Transplantation Society to address liver transplantation (LT) for hepatocellular carcinoma (HCC). The conference participants included more than 180 leaders in LT, including representation from 50 of the most active LT programs in the United States and participants with expertise in hepatic pathology, radiology, and oncology.

Six work groups were assembled to fulfill the conference objectives:

1. To identify relevant elements of data collection in order to develop a standardized pathology report form for the assessment of the explanted liver in patients transplanted with a diagnosis of HCC.
2. To develop more specific imaging criteria for HCC designed to qualify LT candidates for automatic Model for End-Stage Liver Disease (MELD) exception points without the need for biopsy and to develop a standardized pretransplant imaging report form for the assessment of patients with liver lesions.
3. To consider whether the current data support an incremental expansion of the Milan criteria (MC) without increased risk of tumor recurrence to justify an increased priority score on the LT waiting list.
4. To discuss the use of locoregional therapy (LRT) to prevent waitlist dropout, improve posttransplant survival, and down-stage advanced disease in patients with HCC awaiting LT.
5. To explore the concept of down-staging tumors exceeding the MC and to define criteria for eligibility and successful treatment.
6. To review the current liver allocation system for patients with HCC in order to determine whether additional priority on the waiting list remains justified and whether underlying liver disease and/or tumor characteristics should be incorporated into the MELD/HCC score.

The leaders of each working group reported their findings in a plenary presentation to all participants at the conference and were charged with providing a summary of the discussion and evidence-based recommendations pertaining to the specific questions addressed.

WORK GROUP 1: PATHOLOGY (MICHAEL NALESNIK AND DAVID DOUGLAS, GROUP LEADERS)

Currently, reporting HCC pathology components in LT patients to UNOS is inconsistent and heavily dependent on clinical circumstances. For example, if a MELD exception is being requested for a patient with HCC, the center must report the original number of tumors along with the tumor size and the dates of imaging studies. After LT, the center's explant pathology report is forwarded to UNOS for confirmation, but not in a standardized format.

These inconsistencies severely limit the usefulness of these data. Thus, the members of the pathology work group unanimously recommended that uniform and complete reporting of HCC be required for all patients undergoing LT, regardless of the clinical circumstance. The participants weighed the desirability of such information against the burden of data collection and strove to minimize the number of individual data points while maximizing the presumed value of the resulting database.

In addition to defining the data to be gathered and formulating a Web-based questionnaire to carry out this process (Table 1), the work group also recommended that a pathology resource document be published to encourage standardization in the pathological assessment and reporting of these lesions.

Recommendations for the evaluation of liver tumor specimens were put forth by the Association of Directors of Surgical Pathology in 2004.[1] The pathology work group recommended that measurements of the greatest dimension be taken of the largest tumors to a maximum of 5 lesions. Tumor localization is reported simply as right or left lobe. Satellite lesions, defined as tumor nodules <4 cm in diameter, <2 cm from the primary tumor, and $<50\%$ of the primary tumor's diameter, are noted in a yes/no format. Vascular invasion is characterized as either macroscopic or microscopic. Macroscopic vascular invasion is used to imply any involvement of large vessels noted on gross pathological inspection. Vascular invasion seen only under microscopic inspection is identified as microvascular and is synonymous with angiolymphatic or lymphovascular invasion. Metastatic spread of HCC is reported in a yes/no format individually for both lymph node involvement and any other evidence of extrahepatic spread.

The degree of differentiation of HCC has been shown to have prognostic significance in terms of both tumor recurrence and survival following LT.[2] The classic 4-grade approach of Edmondson and Steiner[3] is used in some centers, whereas in others, this has been simplified into 3 grades. The prognostic significance appears to lie in the separation of well and poorly differentiated neoplasms, and for reporting purposes, the working group recommends a simple 3-stage system of well, moderately, and poorly differentiated neoplasms. In this approach, grades 1 and 2 of Edmondson and Steiner's approach are combined to form the well-differentiated category. Only the worst grade of differentiation mentioned in a pathology report should be recorded. The working group is in the process of preparing a resource document that will provide multiple examples of different grades of differentiation in an effort to provide additional standardization for this process.

TABLE 1. Recommended Data Elements for Standardized Organ Procurement and Transplantation Network Explant Pathology

Item	Report	Comment
Evidence of HCC present in explant?	Yes/no	Include in all reports; if yes, complete other items.
Pretransplant treatment for HCC?	Yes/no	Includes any form of bridge therapy
Number of tumors	0, 1, 2, 3, 4, 5, or infiltrative	For reporting purposes, only the largest tumors (up to 5 in number) are considered.
Satellite lesions?	Yes/no	Defined as a tumor nodule <4 cm in diameter, <2 cm from the primary tumor, and <50% of the primary tumor diameter (may or may not be included in the 5 measured lesions)
Size	cm	Size for each of the 5 largest lesions
Location	Right/left lobes	For reporting, it is not necessary to distinguish further.
Tumor necrosis	None/incomplete/complete	The committee consensus was that further distinction would be burdensome and unreliable.
Tumor differentiation	Well/moderate/poor	Single entry for worst recorded histological differentiation level
Vascular invasion	None/microvascular/ macrovascular	Does not include bland thrombus
Lymph node involvement	Yes/no	
Other extrahepatic spread	Yes/no	Separate from nodal involvement

There are a number of histological variants of HCC, including sarcomatoid HCC, clear cell HCC, sclerosing subtypes, fibrolamellar HCC, and mixed HCC/cholangiocarcinoma. For registry purposes, it was concluded that the reporting of these data would be onerous and of questionable reliability, and likely would provide minimal additional insight. All of these variants, except for the fibrolamellar type, can be considered moderately or poorly differentiated HCC, and it was felt that characterization as HCC currently suffices for registry purposes. Similarly, immunophenotypic and molecular studies of HCC are often important components of the diagnostic evaluation and may provide significant prognostic information. Indeed, molecular analysis may supersede our present approach to pathological diagnosis in the not too distant future.[4] It appears too early at this time to mandate a specific subset of these assays for routine reporting purposes, and the subcommittee does not include any immunophenotypic or molecular data points in the proposed report form.

Patients with HCC who are on the waiting list for LT may undergo tumor LRT in order to stabilize or downstage the tumor until a liver becomes available. Necrosis can be evaluated with routine histology or with more sophisticated methods that evaluate the extent of apoptosis. The differences in these approaches and the difficulties in assessing whether necrotic areas indeed represent previous tumor sites or cirrhotic nodules were discussed. It was agreed that assessment may be less than definitive in individual cases because of differences in techniques as well as interobserver variability. Nevertheless, it is important to gather these data to the best extent possible. For this reason, it was recommended that ablated tumors be sampled entirely through their largest diameter if the tumor/nodule size is 2 cm or less. For every additional centimeter, an additional section (approximately 1 cm^2) should be submitted for evaluation. For reporting purposes, it was felt that a simple 3-tier system of no, incomplete, or complete necrosis for each reported tumor nodule, up to a maximum of 5, would provide reasonable stratification while minimizing variability. Bland portal vein thrombosis may also have negative prognostic implications in patients with HCC. However, this information is independently gathered at the time of transplant on the Transplant Recipient Registration Form and need not be submitted via the pathology report. Similarly, the presence of a transjugular intrahepatic portosystemic shunt is also collected on the recipient registration form and need not be reported in duplicate.

In order to accurately report the pathological status of HCCs in LT patients, it is necessary for the recommended reportable information to be readily available. The work group recognizes that the role of

pathologists as clinical consultants naturally supports this requirement, and it encourages pathologists who work in these specialized centers to review their report construction to ensure that it provides this information in a clear, unambiguous, and readily accessible form.

Recommendations

1. Use the synoptic report template previously proposed by the Association of Directors of Surgical Pathology and provide any necessary translations or modifications to allow recovery of the specific data points relevant to HCCs in LT patients.
2. Provide an extensive visual reference of HCCs of various degrees of differentiation as assessed by a panel of hepatopathologists.
3. Provide direction in the reporting of HCC variants for subsequent OPTN registry purposes.
4. Provide a central reference for the processing of tumor-bearing liver explants and the approach to processing previously ablated tumors. The work group participants anticipate working with pathology societies to establish such a document.

WORK GROUP 2: IMAGING (CHRISTOPH WALD AND MARK RUSSO, GROUP LEADERS)

The current OPTN policy for LT in the United States specifically allows a pretransplant diagnosis of HCC based solely on imaging criteria; it states that "a prelisting biopsy is not mandatory but assessment of the candidate should include ultrasound of the candidate's liver, a computerized tomography (CT) or magnetic resonance imaging (MRI) scan of the abdomen that documents the tumors and a CT of the chest that rules out metastatic disease." The imaging characteristic that is required by the current policy for the diagnosis of HCC on CT or MRI is "a vascular blush corresponding to the area of suspicion seen on the above imaging studies" (policy 3.6.4.4, published September 18, 2007 and available at http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_8.pdf).

There is considerable concern that the limited imaging criteria in the current policy may be inadequate and lead to inappropriate organ allocation. To this end, the imaging work group participants, which included radiologists, transplant surgeons, and hepatologists, sought to establish new imaging criteria meeting the following goals: (1) reducing the false-positive rate resulting from the current policy, (2) developing recommendations for minimum technical requirements for scanner hardware and scan protocols, and (3) standardizing the reporting of imaging findings while recognizing that robust and high-quality liver imaging is dependent on careful execution of imaging examinations performed on appropriate equipment.

An online survey tool with follow-up conference calls was used by the group leaders prior to the conference to ascertain current practice standards in accredited and recognized transplant centers. The survey focused on all ramifications of the use of contrast-enhanced dynamic CT and MRI in this context as well as associated radiologist reporting. Results of the survey were discussed at the conference, and there was agreement that the current imaging criteria used to qualify patients with HCC for increased priority were inadequate. The working group reached a consensus on minimal hardware requirements and image acquisition protocols for liver lesions assessed with MRI (Table 2) or CT (Table 3). A new classification system for focal liver lesions observed on these examinations was created (Table 4), and it was recommended that incomplete or technically inadequate examinations be explicitly classified as such and repeated prior to potential priority point allocation consideration.

Largely on the basis of expert consensus and a review of published evidence, specific imaging characteristics were defined that need to be met under this draft policy in order to make the diagnosis of HCC in a patient with chronic liver disease on the basis of imaging alone (Table 5). Essential imaging characteristics of HCC included increased contrast enhancement in comparison with the background liver parenchyma on late arterial phase images, portal venous phase washout (ie, decreased contrast enhancement in comparison with the background liver), late (pseudo) capsule enhancement, and documented interval growth on serial imaging. The choice of late arterial phase images for this purpose reflects the practice pattern of the expert group. It is known that optimal detection of nodules with a predominantly arterial vascular supply (such as HCC) on cross-sectional imaging (CT or MRI) requires careful timing of image acquisition to take place during the late arterial phase of contrast enhancement. At that point in time, there is maximal signal-to-background contrast between capillary enhancement in the lesion and surrounding hepatic parenchyma. Early arterial images do not achieve this enhancement.[5,6]

Patients with focal lesions $\geq$2 cm in maximum diameter meeting these criteria (Table 4, class 5B lesions) would qualify for automatic MELD-based priority under this new policy. Criteria for smaller (T1 stage) HCC lesions (Table 5, class 5A) and for recurrent HCC after prior LRT were proposed (Table 5, class 5T). These latter criteria (classes 5A and 5T) would not automatically qualify patients for extra priority because they are not associated with increased waitlist dropout in comparison with standard MELD patients.

In an attempt to objectify and standardize the reporting of liver lesions in the context of liver allocation for transplant, reporting forms were developed for MRI (Supporting Appendix A), CT (Supporting

TABLE 2. Minimum Technical Specifications for Dynamic Contrast-Enhanced MRI of the Liver

Feature	Specification	Comment
Scanner type	1.5-T or greater main magnetic field strength	Low-field magnets not suitable
Coil type	Phased array multichannel torso coil	Unless patient-related factors precludes use (eg, body habitus)
Gradient type	Current-generation high-speed gradients (providing sufficient coverage)	
Injector	Dual-chamber power injector recommended	Bolus tracking desirable
Contrast injection rate	2-3 mL/second of gadolinium chelate	Preferably resulting in vendor-recommended total dose
Minimum sequences	Precontrast and dynamic post gadolinium T1-weighted gradient echo sequence (3D preferable), T2 (with and without FAT SAT), and T1w in- and out-of-phase imaging	
Mandatory dynamic phases on contrast-enhanced MRI (comments describe typical hallmark image features)	1. Late arterial phase	1. Artery fully enhanced, beginning contrast enhancement of portal vein
	2. Portal venous phase	2. Portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins
	3. Delayed phase	3. Variable appearance, >120 seconds after the initial injection of contrast
Dynamic phases (timing)	The use of a bolus tracking method for timing contrast arrival for late arterial phase imaging is preferable: portal venous phase (35-55 seconds after the initiation of a late arterial phase scan) and delayed phase (120-180 seconds after the initial contrast injection).	
Slice thickness	5 mm or less for dynamic series, 8 mm or less for other imaging	
Breath holding	Maximum length of series requiring breath hold should be about 20 seconds with a minimum matrix of 128 × 256.	Compliance with breath hold instructions is very important; technologists need to understand the importance of patient instruction before and during the scan.

Appendix B), and patient summaries (Supporting Appendix C). Under the new proposed policy, only those patients with class 5B lesions would be eligible for increased MELD-based priority. The transplant center would be responsible for submitting the appropriate imaging report form to UNOS prior to consideration of priority MELD point allocation. Although the use of the standardized reporting would be mandatory for patients with class 5 lesions, radiologists would be encouraged to also use standard reporting for lesions meeting the other classes, especially class 4 (typically representing dysplastic nodules).

The work group recognized several limitations of the aforementioned approach and the resulting proposed imaging criteria. Much of the proposed policy is based on broad expert consensus subject to potential bias resulting from prevailing practice patterns in the participating United States–based transplant centers. Qualitative HCC imaging characteristics, sensitivity, and specificity reported in the literature, which were also considered during this process, are mostly based on small single-center studies that compare the accuracy of imaging-based diagnosis of HCC with biopsy, explant pathology, or growth of lesions on serial imaging. HCCs with atypical imaging characteristics have not been well studied: hypovascular and isovascular HCCs may not be captured with the proposed criteria but may comprise a small but real number of HCCs.[3] The work group strongly recommended that consideration be given to performing biopsy of liver lesion(s) that do not meet all class 5 imaging criteria but are suspicious for HCC.

Imaging and descriptors of recurrent HCC after LRT deserve further study because quantification of tumor burden remains difficult and traditional diameter

TABLE 3. Minimum Technical Specifications for Dynamic Contrast-Enhanced Computerized Tomography of the Liver

Feature	Specification	Comment
Scanner type	Multidetector row scanner	
Detector type	Minimum of 8 detector rows	Need to be able to image the entire liver during the brief late arterial phase time window
Reconstructed slice thickness	Minimum reconstructed slice thickness of 5 mm	Thinner slices are preferable, especially if multiplanar reconstructions are performed.
Injector	Power injector, preferably a dual-chamber injector with a saline flush	Bolus tracking desirable
Contrast injection rate	No less than 3 mL/sec of contrast, 4-6 mL/sec better with at least 300 mg I/mL or a higher concentration for a dose of 1.5 mL/kg of body weight	
Mandatory dynamic phases on contrast-enhanced MDCT (comments describe typical hallmark image features)	1. Late arterial phase	1. Artery fully enhanced, beginning contrast enhancement of portal vein
	2. Portal venous phase	2. Portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins
	3. Delayed phase	3. Variable appearance, >120 seconds after the initial injection of contrast
Dynamic phases (timing)	Bolus tracking or timing bolus recommended for accurate timing	

TABLE 4. OPTN Classification System for Nodules on Imaging of Cirrhotic Livers

OPTN Class	Description	Comment
0	Incomplete or technically inadequate study	Repeat study is required for adequate assessment; automatic priority MELD points cannot be assigned on the basis of an OPTN class 0 classified imaging study.
1	No evidence of HCC on good-quality, appropriate surveillance examination	Typically, surveillance would continue according to the routine practice at the respective transplant center.
2	Benign lesion(s) or diffuse parenchymal abnormality with no dominant focal lesion	Typically, the need for any further imaging would be determined on a clinical basis according to the routine practice at the respective transplant center (MRI preferred over CT).
3	Abnormal scan, indeterminate focal lesion(s), not currently meeting radiological criteria for HCC	Typically, follow-up imaging would be performed in 6-12 months (MRI preferred over CT).
4	Abnormal scan, intermediate suspicion for HCC (meets some radiological criteria for HCC and could represent HCC)	Consider short-term follow-up in 3 (maximum diameter of lesions $\geq$ 2 cm) to 6 months (maximum diameter of lesions $<$ 2 cm), with MRI preferred over CT or biopsy. Imaging follow-up should be considered if biopsy is negative or not possible.
5	Meets radiological criteria for HCC	Patient may be eligible for automatic priority MELD points on the basis of this imaging study. Please refer to definitions for class 5 criteria.

TABLE 5. Proposed Imaging Criteria for OPTN Class 5 Lesions (Compatible with an Imaging Diagnosis of HCC)

OPTN Class	Lesion Size	Appearance	Comment
5A	Maximum diameter of lesion $\geq$ 1 cm and $<$ 2 cm, measured on late arterial or portal vein phase images	Increased contrast enhancement on late arterial phase (with respect to hepatic parenchyma) AND washout during later contrast phases AND peripheral rim enhancement (capsule/pseudocapsule) on delayed phase OR Increased contrast enhancement on late arterial phase (with respect to hepatic parenchyma) AND growth (maximum diameter increase) of 50% or more documented on serial MRI or CT obtained $\leq$6 months apart. Growth criteria do not apply to ablated lesions.	This category describes a T1 stage HCC that meets stringent qualitative imaging criteria diagnostic of HCC OR a rapidly growing T1 stage HCC with some qualitative imaging features diagnostic of HCC.
5B	Maximum diameter of lesion $\geq$ 2 cm, measured on late arterial or portal vein phase images	Increased contrast enhancement on late hepatic arterial images (with respect to hepatic parenchyma)* AND washout on portal venous/delayed phase and/or late capsule or pseudocapsule enhancement OR Increased contrast enhancement on late hepatic arterial images (with respect to hepatic parenchyma)* AND growth (maximum diameter increase) of 50% or more documented on serial MRI or CT obtained $\leq$6 months apart. Growth criteria do not apply to previously ablated lesions.	This category describes a T2 stage HCC that meets qualitative imaging criteria diagnostic of HCC OR a rapidly growing T2 stage HCC with some qualitative imaging features diagnostic of HCC. Class 5B lesions qualify for automatic HCC exception MELD points.
5T	Prior local regional treatment for HCC	Past local regional treatment for HCC (OPTN class 4 or biopsy-proven prior to ablation) AND evidence of persistent/recurrent HCC such as nodular or crescentic extrazonal or intrazonal enhancing tissue on late arterial imaging (with respect to hepatic parenchyma)	This category describes residual or recurrent HCC after previous local ablative therapy.

*Isovascular and hypovascular HCC may occur that does not exhibit this feature; consider biopsy if this is suspected.

measurements are often inaccurate after such treatment. The impact of the occurrence of peripheral cholangiocarcinoma in patients with chronic liver disease on the false-positive rate of the proposed imaging criteria is unknown. The work group recognized that other areas of the world use contrast-enhanced ultrasound with apparently good clinical results. However, given the lack of availability and experience with contrast-enhanced ultrasound in this country, proposed imaging criteria were limited to CT and MRI for this new draft policy, which is applicable to US patients only.

The American College of Radiology is sponsoring the development of the Liver Imaging Reporting and Data System, which will refine and expand imaging categorization of liver lesions and is expected to be released in 1 to 2 years. The Liver Imaging Reporting and Data System categorization will be based and expand on the UNOS system described in this document. The American College of Radiology Imaging Network will conduct a trial entitled "A Prospective Comparison of DCE-CT and DCE-MRI for the Diagnosis of Hepatocellular Carcinoma Prior to Liver Transplantation Allocation." It is expected to commence in the first quarter of 2010. Funding is provided by the National Cancer Institute. Liver imaging criteria in the trial protocol are modeled after the new proposed OPTN policy and will evaluate its impact on clinical practice. The trial protocol includes as a key component a one-to-one comparison of imaging diagnoses with explant pathology diagnosis.

Recommendations

1. A new OPTN liver imaging policy is proposed that requires

a. Minimum equipment specifications.
b. A standardized imaging protocol.
c. Structured reporting.

2. A new OPTN classification of liver nodules is proposed. The diagnosis of HCC will be based on the presence of specific, well-defined imaging findings on dynamic contrast-enhanced CT and/or MRI.

WORK GROUP 3: RATIONALE FOR EXPANSION OF THE MC (KENNETH WASHBURN AND JOHN ROBERTS, GROUP LEADERS)

The MC for LT for HCC, based on tumor size and number (1 nodule $\leq$ 5 cm or 2-3 nodules, each $<$3 cm), describe a population of patients in whom the recurrence rate of the tumor has been considered to be acceptable.[7] The basis of the risk of tumor recurrence after LT being related to the size and number of the tumors appears to be established. The concept of the "Metro ticket" has been used to demonstrate this point and the fact that expansion of these criteria can have a price; the further the criteria are pushed, the higher the price is in terms of the effect on survival.[8,9] What are not well established are the cutoffs for the size and number at which the risk of recurrence may be considered to be acceptable. A number of reports indicate that these criteria can be safely expanded without penalty with respect to patient death or recurrence of disease in comparison with the MC.[10-13] The University of California San Francisco (UCSF) criteria (1 nodule $\leq$ 6.5 cm or 2-3 nodules $\leq$ 4.5 cm and total tumor diameter $\leq$ 8 cm) have been independently validated.[14-16] These reports demonstrate that incremental changes can be made in the acceptable tumor size and number without a risk of recurrence that is significantly different from the risk with the MC. As with the original Milan report, these reports concern single-center experiences. Unfortunately, tumor recurrence is underreported in the OPTN database. Thus, there are no national tumor-free survival data with which the current criteria can be compared to expanded criteria beyond single-center reports.

If we accept the premise that recurrence is related to the size and number of tumors and that we do not have national data to suggest what the safe margins of these parameters are, the temptation is to remain conservative. The major reason for a conservative approach is that transplanting a patient with a tumor results in a patient without a tumor possibly missing a chance for LT. Volk et al.[17] examined the issue of what the acceptable outcome risk is for the transplantation of patients with HCC versus the use of the organ in a patient without HCC with a Markov model. The authors found that 5-year survival following LT for the expanded criteria patients had to exceed 61% before expansion of the MC resulted in an improvement in overall survival and did not harm patients without HCC.

Although a higher degree of survival has been demonstrated in patients with tumors who exceed the MC but are within the UCSF criteria, the authors showed a dramatic difference in the effect of a policy change on a regional basis. The regional variation arose from the dramatic difference in the risk of death for patients without HCC; that is, the MELD score of the non-HCC patients was quite low in some regions. Posttransplant survival in HCC patients ranged from 25% in regions with few non-HCC patients with high MELD scores to greater than 70% in regions in which there was a greater need for LT (higher MELD scores) in the non-HCC population. This wide variation in outcomes suggests that changes in national policies would have a variable effect depending on the region.

Another potentially confounding issue in expanding the MC is the extreme variability of the time to transplantation of patients with HCC in the country. Data from the OPTN (Fig. 1) show the percentage of HCC patients undergoing transplantation within the first cycle by region in 2007 (J.R., unpublished data, 2007). The wide variability in the time to LT suggests that the waitlist management strategies and outcomes may vary widely around the country. Concern has been raised that short times to LT may lead to an increase in posttransplant recurrence because the tumor biology has not had enough time to be exposed. The lack of national data on recurrence rates limits one's ability to study this national experiment of nature based on the divergent waiting times for transplantation for HCC.

Rather than expand the MC on a national level, we should give consideration to allowing expansion of the criteria beyond the MC but with down-staging and waiting for some predetermined period of time allowing the tumor biology to be exposed.[10,18] This expansion should be instituted on a regional basis with the requirement of center reporting and confirmation of the accuracy of reporting with audits. At present, it appears that allowing regions to develop agreements independent of national policy may allow local

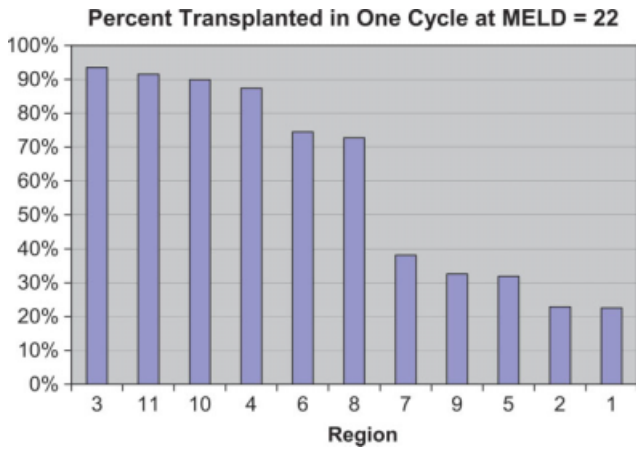

Figure 1. Patients with hepatocellular carcinoma undergoing transplantation by geographic region. In the United States, organ allocation occurs by geographic region. Fuller details may be found at http://www.unos.org.

application of expanded MC, but this must be coupled with the ability to collect longer term follow-up data.

Recommendations

1. There should be no change in current national policy regarding HCC criteria and exception priority scores.
2. Regional agreements to explore expanding the MC should be encouraged.
3. There should be enhanced reporting of tumor recurrence data.

WORK GROUP 4: THE ROLE OF LOCAL-REGIONAL THERAPY (LRT) IN THE TREATMENT OF HCC (DAVID J. REICH, LUIS MIELES, AND FRED T. LEE, GROUP LEADERS)

LRT for HCC, including various transarterial and ablative techniques, is increasingly used to prevent list dropout, improve posttransplant survival, and downstage advanced disease. There is compelling evidence that pretransplant LRT decreases wait list dropout, particularly for patients expected to wait longer than 3 to 6 months for LT and those with a focal HCC $>$ 3 cm in greatest diameter or multiple HCCs.[19-26] In the United States during the MELD era, patients with single, $<$3-cm HCC are at low risk of early dropout (0% at 12 months) and can be followed without immediate LRT if they are expected to have a short wait time ($<$3-6 months) and are watched closely. In 2006, more than half of the HCC patients on the OPTN waiting list received LRT; this ranged from 31% to 65% and depended on the allocation region.[27]

Evidence indicates that pretransplant LRT of HCC improves posttransplant survival in addition to preventing list dropout. Scientific Registry of Transplant Recipients data show that patient and graft survival rates at 3 years were better for HCC patients treated by LRT than for untreated patients (patient survival: 79% versus 75%, $P = 0.03$; graft survival: 76% versus 71%, $P = 0.03$).[27] Posttransplant survival rates of HCC patients treated with pretransplant LRT were equivalent to the survival rates of non-HCC patients in a University of California Los Angeles series.[25]

Patients with advanced HCC, especially beyond the MC, should typically undergo LRT followed by a surveillance wait period, even where there is a short waiting time or when a living donor is available. Such an approach may facilitate the identification of patients who have HCC with poor biological behavior that is more likely to recur post-transplant.[28]

There is a paucity of data comparing radiofrequency ablation (RFA) with transarterial therapies for the treatment of HCC prior to LT, and most single-center trials have a mixture of LRTs included in the study population. The examination of explant specimens demonstrates a high rate of complete necrosis for HCCs $<$ 3 cm in greatest diameter with RFA and a lower rate with transarterial chemoembolization (TACE).[29] As tumors increase in size, the likelihood of incomplete treatment with RFA increases. Early data suggested a high rate of tumor seeding with percutaneous RFA, but larger series in more experienced centers showed seeding to be a rare event.[30,31] For large tumors, the likelihood of complete treatment may increase with combination therapies, but this remains unproven.

The choices of approach for RFA include percutaneous, laparoscopic, and open techniques, each having benefits and disadvantages. The choice should be individualized to a particular patient and based on local expertise. Compared with laparotomy, the percutaneous and laparoscopic approaches are less invasive and painful, provide a shorter hospital stay, and are less prone to complicating future transplantation. However, laparoscopy may not be possible if the patient has had abdominal surgery and significant adhesions are present. In an early meta-analysis, ablation by laparoscopy or laparotomy resulted in superior local control independently of tumor size, and this led to questioning of the short-term benefits of the less invasive percutaneous route.[32] More recent data indicate that as experience with percutaneous RFA has increased, this therapy now provides excellent local control, especially for HCCs less than 2 to 3 cm.[33] Intra-arterial LRTs include bland embolization, different drug combinations and delivery systems, and radioembolization. TACE has been shown to improve survival in comparison with bland embolization.[34,35] Recently, the relatively new drug-eluting beads (DEBs) and yttrium-90 (Y-90) microspheres have gained interest. DEBs act as an embolic device and gradually release chemotherapeutic agents into the tumor; in this way, they increase the drug intratumor dwell time and minimize systemic drug absorption. Randomized controlled trial results comparing DEBs to conventional TACE are pending. Similarly, Y-90 microspheres deliver large doses of radiation while minimizing exposure to the surrounding nontumor tissue. TheraSphere glass microspheres (MDS Nordion, Mississauga, Canada) are Food and Drug Administration–approved for unresectable HCC. In retrospective trials, Y-90 has demonstrated a favorable toxicity profile and effectiveness as a tool to bridge/down-stage patients for LT,[36] but randomized controlled trials on the efficacy of radioembolization compared with other treatment modalities are lacking.

LRT should be viewed not as a single procedure but rather as a course of procedures using strict surveillance and repeat intervention as necessary. Because partial tumor necrosis after LRT may be a risk factor for posttransplant HCC recurrence,[37] it is critical to strive for complete necrosis, regardless of whether this requires repeating LRT. With respect to TACE, there is no evidence that repeat celiac/hepatic artery catheterization leads to adverse events or difficulties at the time of surgery. In general, technical success (defined as complete LRT based on imaging) can be achieved after the initial session for small, easily accessible tumors, but it is not uncommon to require 2 or occasionally more sessions. Serial high-quality imaging and subsequent interpretation are central to defining whether a residual tumor requiring additional LRT exists.

Despite imaging documentation of complete ablation, a viable tumor often remains in the LRT zone beyond the resolution of current imaging methods, particularly with HCCs > 3 cm, as shown by explant pathological correlation studies.[29] Furthermore, as many as 36% of Milan HCC pretransplant patients have synchronous HCC nodules not found on pretransplant and postablation imaging studies that are subsequently discovered at the time of explant pathology.[38] In an Italian series, new tumors developed elsewhere in the liver in 80% of patients by 5 years, despite LRT of the initial tumor.[39] LRT devices and image guidance techniques are constantly improving, and the true complete ablation rate will likely improve. With this in mind, LRT should currently be viewed as a bridge to rather than a replacement for LT.

Role of Resection

Resection is an alternative to LT for patients with a solitary HCC < 5 cm in the setting of Child A cirrhosis without portal hypertension, which is defined by no varices, a platelet count greater than 100,000 platelets/μL, and a wedged hepatic venous pressure gradient less than 10 mm Hg.[40] HCC patients who meet the criteria for resection have an alternative to LT that offers a survival rate that is marginally less than that of transplant candidates[19,41,42] and in many cases can be safely resected. This is the rationale for the current policy that affords priority only to HCC patients who are not resection candidates.

Results of salvage transplantation for recurrent HCC have been variable.[43] On the basis of the ability to use genomic data to clarify recurrences as either metastatic or de novo, it has been clearly shown that recurrence of HCC in the liver appearing more than 2 years after resection is nearly always de novo.[44] Therefore, patients who develop HCC that meets T2 criteria more than 2 years after resection could be considered eligible for priority if the HCC is not re-resectable, whether the original HCC was within T2 criteria or not. Patients who undergo resection for HCC meeting T2 criteria who have a recurrence within the first 2 years should qualify for priority if the recurrence meets T2 criteria.

In summary, LRT decreases list dropout and is associated with improved posttransplant survival rates. Several types of LRT are available, and the comparative risks and benefits of each will become more evident with improved and more detailed data collected in the OPTN database. Additional research and particularly multicenter, randomized controlled trials are needed in these areas.

Recommendations

1. Consideration should be given to priority for biopsy-proven T1 HCC.
2. The use of LRT should be strongly encouraged in HCC candidates awaiting LT.
3. Resection of HCC should be encouraged.
4. Recurrence more than 2 years after resection for HCC of any stage should be considered de novo, and if the lesion meets T2 criteria, the candidate should be eligible for an HCC priority score.
5. Recurrence less than 2 years after resection for a T2 lesion should be eligible for an HCC priority score if the recurrence meets T2 criteria.

WORK GROUP 5: THE ROLE OF DOWN-STAGING IN LT CANDIDATES WITH HCC (SANDER FLORMAN AND FRANCIS YAO, GROUP LEADERS)

Patients with tumors beyond the MC can potentially undergo transplantation after showing a response to LRT with long-term survival that is comparable to that of patients with tumors initially meeting the MC. This practice has been called down-staging. However, results of down-staging before LT are heterogeneous.[10,22,28,45-48] In the majority of these studies, there were no upper limits for the tumor size and number before down-staging treatments were applied.[22,28,45-48] Criteria for a response to down-staging also vary among these studies. Two groups have used the MC as the endpoint for down-staging before LT.[10,48] Three studies have applied the Response Evaluation Criteria in Solid Tumors to evaluate the response to treatment.[22,28,48]

Definition of Down-Staging

The working group proposed a practical definition of tumor down-staging as the application of LRT, including TACE and various ablation techniques, to decrease the size of liver lesions (that are consistent with HCC by imaging criteria) to meet currently "acceptable" criteria for LT. The group also decided that surgical resection of the tumor is not considered a down-staging treatment at this time.

An essential component of this definition is the adequacy of imaging techniques to assess the response after therapeutic interventions (see the section by the imaging work group). The panel had extensive discussions before making a proposal for standardized inclusion criteria for down-staging as well as criteria for a response to down-staging (Table 6).

Inclusion Criteria

Fundamentally, the premise that some patients can be successfully down-staged and then undergo transplantation with acceptable long-term survival depends on the establishment of inclusion criteria for down-staging. It is imperative that the proposed criteria have reasonably realistic expectations for success by an intention-to-treat principle. Currently, only regions 5 (California, Nevada, Arizona, New Mexico, and Utah) and 11 (Kentucky, North Caroline, South Carolina, and Virginia) have adopted a down-staging protocol for LT, whereas region 4 (Texas and Oklahoma) has approved a different set of expanded criteria for LT. In some regions, there is little or no consideration for

TABLE 6. Criteria for Transplantation After Down-Staging

Inclusion criteria for down-staging*
1. Single tumor > 5 cm and ≤ 8 cm in maximal diameter
2. Two to 3 tumors, each ≤ 5 cm in maximal diameter, with the sum of the maximal tumor diameters of all the tumors ≤ 8 cm
3. No evidence of vascular invasion on multiphase CT or MRI of the abdomen
Criteria for successful down-staging
1. Posttreatment imaging evaluation (multiphase CT or MRI) showing a residual tumor size and number meeting the MC (see the imaging standards)
2. For patients with AFP > 1000 ng/mL, successful down-staging requires a significant decrease in AFP to <500 ng/mL. All subsequent AFP levels must also be <500 ng/mL prior to liver transplantation.
Criteria for priority listing for liver transplantation after successful down-staging
1. There will be a minimum timeout or observation period of 3 months from the date that imaging is documented to meet the MC before eligibility for active priority listing.
2. A bone scan will show no metastatic focus within 3 months of listing.
3. Imaging requirements for priority listing and maintaining listing for liver transplantation will be the same as those for an initial tumor stage meeting the MC. These requirements include CT of the chest and either multiphase CT or MRI of the abdomen at baseline and every 3 months showing a tumor stage within the MC to maintain priority listing.

*Modified from the University of California San Francisco down-staging protocol.[7] Patients with 4 or 5 lesions are excluded in this proposal.

patients outside the MC, whereas in other regions, many patients do receive extra priority on a case-by-case basis but with little uniformity in the decision-making process.

Arguably, the best single-center experience to date on tumor down-staging comes from the UCSF group,[10,47] in which the inclusion criteria for down-staging and criteria for successful down-staging are well defined. The working group proposed that criteria determining eligibility for down-staging be modified from the UCSF study.[10,47] These include a single tumor ≤ 8 cm or 2 to 3 tumors, each ≤ 5 cm, with a total tumor diameter ≤ 8 cm and no vascular invasion by imaging criteria (Table 6). The working group also proposed excluding patients with 4 or 5 lesions for down-staging because of the very small number of these patients undergoing down-staging in the UCSF study.[10]

Similar to the MC, the UCSF criteria are somewhat arbitrary, but they are the currently accepted criteria and provide a reasonable starting point. Mandating an upper limit for tumor size is not totally reliable because of limited data, but the consensus was that having no upper limit is probably worse. Patients with initial tumors beyond the inclusion criteria may be eligible for down-staging and subsequent priority listing with MELD exception on a case-by-case basis upon approval by the regional review board.

Criteria for Successful Down-Staging

Criteria for successful down-staging after LRT are based on imaging studies with either multiphase CT or MRI to assess the residual tumor size and number of tumors meeting the MC.[49] The working group agreed on using the MC as the endpoint on the basis of results from published data[10,47,48] and because this approach provides a conservative starting point.

Multiphase CT and MRI are the only acceptable imaging modalities for the determination of a response to therapeutic intervention for the purpose of down-staging. Only residual tumor(s) and not the ablation focus or areas of retained lipiodol after TACE should be measured in the staging of the tumor after the initial treatment. Imaging should be performed 4 to 6 weeks after each treatment.

Once successful tumor down-staging to meet the MC has been achieved, updated data including imaging studies are required every 3 months. Imaging requirements for priority listing and maintaining listing for LT are the same as those for patients with an initial tumor stage meeting the MC. These requirements include CT of the chest and either multiphase CT or MRI of the abdomen at baseline and every 3 months showing a tumor stage within the MC to maintain priority listing.

An additional requirement for priority listing after tumor down-staging pertains to patients who initially present with an alpha-fetoprotein (AFP) level > 1000 ng/mL. Successful down-staging also requires a significant decrease in the AFP level to <500 ng/mL. In addition, subsequent AFP levels must be <500 ng/mL prior to LT. This requirement is based on multiple studies showing a preoperative AFP level > 1000 ng/mL to be a strong independent predictor of tumor recurrence after LT.[13,50]

Timeout or Observational Period

For patients undergoing tumor down-staging, the working group agreed that a minimum timeout or observational period of 3 months is required before the

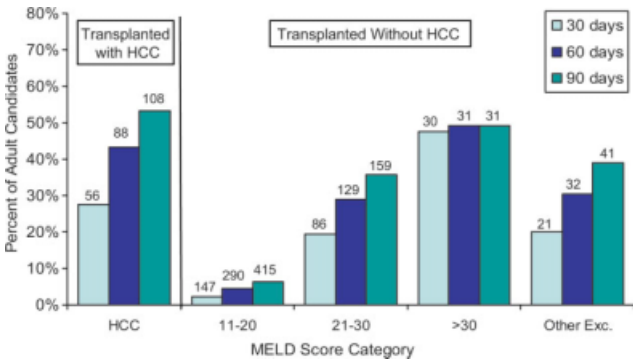

Figure 2. Organ Procurement and Transplantation Network data showing the percentages of waiting list candidates with and without HCC exceptions receiving liver transplants within 30, 60, and 90 days: Snapshot (January 1, 2006) by MELD. The source was a Scientific Registry of Transplant Recipients analysis (data as of May 2007).

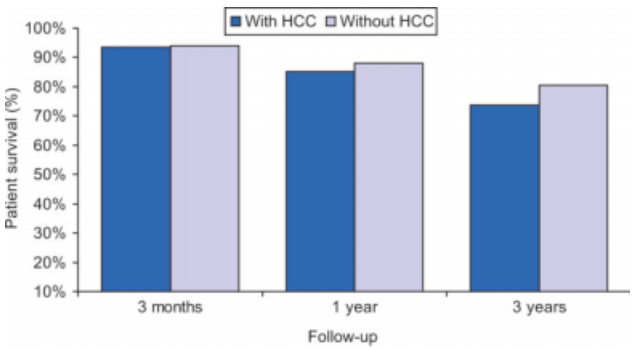

Figure 3. Organ Procurement and Transplantation Network data showing the adjusted patient survival of liver transplant recipients with and without HCC exceptions [3-month/1-year cohort: n = 10,179 (HCC = 2002, non-HCC = 8177); 3-year cohort: n = 19,034 (HCC = 3750, non-HCC = 15,284)]. The source was a Scientific Registry of Transplant Recipients analysis (data as of May 2007). The rates were adjusted to the means of the 3-month/1-year cohort for all liver transplants. The model includes the Model for End-Stage Liver Disease score at transplant.

patient is eligible for listing for LT. This timeout period starts from the date on which the imaging study shows the tumor size and number to be within the MC after down-staging treatments. The requirement for a time-out period was uniformly considered to be a critical part of down-staging in this meeting. This will help to identify tumors with unfavorable tumor biology that will continue to progress despite treatment. Tumors with more favorable biology will more likely have stable disease or a sustained response to down-staging treatments before LT.[10,22,28,47]

The 3-month observational period[10,47] has resulted in acceptable intention-to-treat survival and post-transplant survival. Three months was therefore felt to be the minimum acceptable time interval, although some advocated an even longer period of 6 months.

Data Collection and Outcome Analysis

If transplant centers wish to pursue LT after the down-staging of tumors initially exceeding the MC, then down-staging should be done in an organized fashion with support from their respective regional review board so that data can be collected prospectively with uniform criteria as proposed in this report. Ideally, this proposal would be supported by all regions.

An intention-to-treat principle should be used for data collection and outcome analysis. In other words, all patients treated with the intent of down-staging for LT should have data submitted. A standardized form for imaging reporting should be developed. Consideration should be given to implementing a separate review board for any patient with HCC initially beyond the MC. This group should also examine survival data collected from region 5, in which a down-staging protocol was accepted and incorporated into the regional policy in 2006.[47] This should include a reasonably large cohort of patients who received LT after successful tumor down-staging.

Recommendations

1. The inclusion criteria for downstaging should be a single tumor $\leq$ 8 cm or 2 to 3 tumors, each $\leq$ 5 cm, with a total tumor diameter $\leq$ 8 cm and no vascular invasion by imaging criteria.
2. The criteria for successful downstaging should be as follows: the tumor must meet the MC after the downstaging procedure(s), as assessed by imaging requirements for priority listing and maintaining listing for LT every 3 months. Successful down-staging also requires a significant decrease in the AFP level to <500 ng/mL for those patients with an initial AFP level > 1000 ng/mL.
3. There will be a minimum timeout or observation period of 3 months from the date on which imaging is documented to meet the MC before eligibility for active priority listing.

WORK GROUP 6: ORGAN ALLOCATION FOR LT CANDIDATES WITH HCC (RICHARD FREEMAN AND JACK LAKE, GROUP LEADERS)

The HCC allocation work group reviewed the available data on the OPTN waiting list and posttransplant outcomes for patients with HCC exceptions available in the 2007 annual report of the OPTN/Scientific Registry of Transplant Recipients.[27] These data suggest that HCC candidates have increased access to deceased donor livers in comparison with standard MELD candidates (Fig. 2). Adjusted 3-year survival data show that patients who undergo transplantation with HCC exceptions have inferior patient survival (Fig. 3). The survival data do not distinguish HCC recurrence–free survival from recurrent hepatitis C (HCV) or other causes of recipient mortality. There appears to be an advantage for HCC candidates, but there is also a reduction in system utility as a result

TABLE 7. Characteristics at HCC Exception Approval Associated with an Increased Risk of Waiting List Dropout for Candidates with HCC

	Cox		Competing Risks	
Factor	Coefficient	HR	Coefficient	HR
MELD	0.1142	1.12	0.0781	1.08
Log AFP	0.0424	1.06	0.0344	0.99
Log AFP^2	0.0146	1.06	0.02018	0.99
Maximum size	0.1658	1.18	0.0785	1.08
3+ tumors	0.2907	1.34	NS	NS

of this advantage. Three broad goals, listed in order of importance, should guide future allocation policy for candidates with HCC:

1. The policy should result in similar risks of removal from the waiting list for HCC and non-HCC candidates.
2. It should result in similar transplant rates for HCC and non-HCC candidates.
3. It should select HCC candidates so that there are similar posttransplant outcomes for HCC and non-HCC recipients.

Dropout data were analyzed with Cox models, and the results indicated that HCC candidate dropout from the waiting list is associated with 3 variables: the maximum tumor size, AFP level, and MELD score at the time of HCC exception approval. A competing risk approach was used for further evaluation of dropout because the censoring of HCC candidates at transplant artificially increases dropout rates in the Cox models for the HCC candidates who remain on the list. This analysis reaffirmed that HCC candidates have lower dropout rates than standard MELD patients and dropout rates similar to those of standard MELD candidates who have MELD scores less than 21. LRT did not influence dropout rates in this analysis, but again, the maximum tumor size, AFP level, and MELD score at HCC exception approval were all associated with the risk of dropout for the HCC candidates (Table 7). Tumor number was not associated with the dropout rate, and this finding is consistent with several reports in the literature indicating that the size of HCC lesions, not the number, is more often associated with vascular invasion and a more aggressive phenotype.

HCC patients appear to be advantaged in the current system, and the question was raised whether added priority is necessary. All participants agreed that some dispensation should be made for HCC patients meeting the MC, but there should be a method to limit priority for rapidly expanding or unresponsive lesions, conditions that the literature suggests have an unacceptably higher posttransplant HCC recurrence rate.[28] Some patients who are downstaged to within the MC may have acceptable outcomes, and it was felt that there should be some method to account for this possibility.[51]

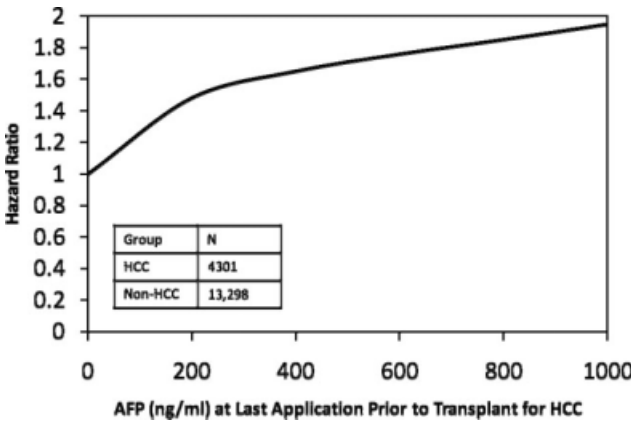

Figure 4. Effect of the AFP level on the risk of graft failure after liver transplantation in recipients with HCC versus recipients without HCC with adjustments for the Model for End-Stage Liver Disease score at the time of transplant, age, ethnicity, and gender of the recipient. This figure is based on deceased donor liver transplants from May 2003 to June 2007.

The current HCC policy does not adhere to the general principles for liver allocation adopted with the introduction of the MELD score. That is, the current HCC prioritization rules are categorical and based purely on the waiting time, are not based on any tumor biology variables, and do not take into account the degree of underlying liver disease. The development of a more dynamic score was highly endorsed.

There was general agreement that variation in HCC transplantation rates is a problem that is the result of the overall regional differences in donor availability and transplant center/waitlist density and that solving this problem for HCC patients requires tackling the entire issue of regional variation overall. The competing risk and Cox modeling of rising/elevated AFP showed this to be predictive of dropout. Yet, prioritizing the highest AFP level or the largest tumor may select HCC lesions at higher risk for recurrence. The AFP values could be capped analogously to capping MELD values to avoid prioritizing the maximum-risk candidates. The literature supports AFP as a good marker for recurrence risk and posttransplant graft survival (Fig. 4). Although there are other markers, AFP is universally available, widely studied, and reasonably objective. The group agreed that AFP should be included so that increasing AFP below 500 ng/mL would add additional priority on urgency grounds (individual justice) but that additional priority should not be allowed for AFP $>$ 500 ng/mL as this level has already been incorporated into past HCC allocation policy. There was agreement that AFP $>$ 500 ng/mL without imaging data to support the presence of a tumor should no longer be eligible for additional priority because in most cases either there is no actual cancer present or there is a diffuse, small, but highly aggressive malignancy with a poor prognosis.

In an effort to continue to balance justice and utility, participants discussed methods to select

candidates with "favorable biology" markers such as a response to LRT or slower tumor growth. One method for selecting these types of patients would be to incorporate a time-from-diagnosis variable to provide more weight for the slower, less aggressive, "good biology" tumors in balance with the urgency criteria. Region 5 has incorporated this into a policy that allows down-staged patients to get priority if they remain at their down-staged status for 3 months.[10] The work group suggested adding a variable defined as "time from when MC is met" as a component of a continuous score because this would allow candidates down-staged to within the MC to be eligible for increased priority, especially if they stayed within the MC for more than a few months.

Recommendations

1. Additional priority should be maintained for candidates with HCC who meet the MC. There is no regional adjustment in assigned priority for HCC candidates in this iteration.
2. A calculated continuous HCC priority score should be developed that incorporates the calculated MELD score, AFP level, tumor size, and rate of tumor growth. Only candidates with at least stage T2 tumors will receive additional HCC points.
   a. Candidates with T1 tumors or tumors outside the MC must be designated as having HCC on waitlist registrations and/or updates.
   b. A designation for HCC (yes/no) will be captured at registration for all candidates regardless of any requests for priority.
3. The candidate must be within the MC for a minimum of 3 months before additional points are assigned.
   a. The time is calculated from the date of the first imaging study indicating that the MC are met if the liver tumor meets class 5B imaging criteria.
4. Patients with a diagnosis of HCC within the MC and a calculated MELD score < 15 will start with a MELD/HCC priority score of 15 until they have had the HCC diagnosis for 3 months; then, they will receive the calculated MELD/HCC priority score.
5. Patients with a calculated MELD score > 15 will receive their calculated MELD score until the 3 months since the diagnosis of HCC within the MC have elapsed; then, they will receive their calculated MELD/HCC priority score.
6. The MELD/HCC priority score will be recalculated every 3 months and can increase or decrease according to changes in the tumor characteristics, underlying MELD score, and time within the MC.
7. Allocation points will be based on a candidate's calculated MELD score plus the following factors:
   a. AFP < 500 ng/mL.
   b. Tumor size within the MC.
   c. Time within the MC (this includes patients down-staged to within the MC).
8. No points will be added if the AFP level is greater than 500 ng/mL.
9. Patients with an elevated AFP level and no tumor by imaging will no longer receive additional MELD points.

The weighting of the various factors (MELD, AFP, tumor size, and time within the MC) will need to be worked out by the OPTN/UNOS Liver and Intestinal Committee as part of a formal policy proposal. The work group also noted that a similar system that incorporates MELD, tumor factors, and time within the MC is already in use in Italy.

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