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Early liver transplantation for severe alcoholic hepatitis: moving from controversy to consensus

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Abstract

Purpose of review—Alcohol-related liver disease is now the most common indication for liver transplant in the United States. Acute alcoholic hepatitis represents a subpopulation with short-term mortality approaching 70% in severe cases – these patients are not typically eligible for liver transplant, as most centers require a period of alcohol abstinence (typically 6 months) prior to transplant. Early liver transplant (prior to a requisite period of abstinence) is being increasingly offered in a minority of U.S. centers. The present review examines clinical and ethical considerations surrounding liver transplant for severe alcoholic hepatitis, key published studies and knowledge gaps, and future directions for clinical research to achieve optimal patient outcomes.

Recent findings—Since a European pilot study published in 2011, published U.S. original studies in early liver transplantation for severe alcoholic hepatitis are limited to 1 UNOS review, and 2 retrospective single-center studies. A preliminary report from the ACCELERATE-AH consortium show short-term outcomes are acceptable but that use of alcohol posttransplant occurs in 25% of patients. These studies confirm the survival benefit of early liver transplant for alcoholic hepatitis and report rates of alcohol use posttransplant similar to historic cohorts in alcohol-related cirrhosis.

Summary—Early liver transplantation for severe alcoholic hepatitis is lifesaving, with acceptable short to intermediate-term patient survival and rates of alcohol use posttransplant. Further study is needed to determine long-term outcomes, and how best to select and manage patients for this new indication for liver transplant.

Keywords

INTRODUCTION

Globally, alcohol-related liver disease (ALD) accounts for half of liver-related deaths [1]. In the United States, ALD recently surpassed hepatitis C as the most common indication for

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liver transplantation [2]. Alcoholic hepatitis represents a subset of ALD, and accounts for 10% of ALD deaths [3]. There are few effective medical therapies for alcoholic hepatitis [4,5], and despite wide acceptance for liver transplantation in ALD, liver transplantation as rescue therapy for severe alcoholic hepatitis remains controversial.

Traditionally, transplant centers require 6 months of abstinence prior to liver transplantation for ALD [3,6]. In severe alcoholic hepatitis, this requirement is largely unattainable – by definition, the patient has recently consumed alcohol and 75–90% of deaths occur within 2 months [7–9]. Given the high mortality and lack of effective therapies, early liver transplantation (i.e. before 6 months of sobriety) may improve survival.

The present review details the clinical and ethical considerations, key published studies, and future directions for this emerging liver transplantation indication.

DEFINING ALCOHOLIC HEPATITIS

Alcoholic hepatitis is defined by rapid onset of jaundice because of chronic, excessive alcohol intake [6]. Severe cases can result in hepatic decompensation with ascites, gastrointestinal hemorrhage, or encephalopathy – the majority have underlying cirrhosis, often previously undiagnosed [5,10]. Given the overlap in clinical presentation of severe alcoholic hepatitis and acute-on-chronic liver failure (ACLF) with recent alcohol consumption, the NIAAA Alcoholic Hepatitis Consortia recently recommended a standard definition for alcoholic hepatitis [11■■]: onset of jaundice within the last 8 weeks, ongoing heavy alcohol consumption for at least 6 months with less than 60 days abstinence prior to jaundice, AST more than 50 IU/l, AST/ALT ratio more than 1.5, and serum bilirubin more than 3.0 mg/dl [11■■]. With 'confounding factors' (e.g. sepsis, shock, or possible drug-induced liver disease) liver biopsy is recommended [11■■]. Histologic alcoholic steatohepatitis is defined as macrovesicular steatosis with at least one of the following: neutrophil infiltration, hepatocyte ballooning, or Mallory–Denk bodies [11■■]. As liver transplantation for severe alcoholic hepatitis grows in application, a standard definition for alcoholic hepatitis is timely and facilitates uniformity for liver transplantation selection and clinical studies.

PROGNOSTIC MODELS FOR SEVERE ALCOHOLIC HEPATITIS: IDENTIFYING PATIENTS WHO NEED EARLY LIVER TRANSPLANT

Early identification of patients with high likelihood of short-term mortality is necessary if liver transplantation is to be a viable option. Maddrey's discriminant function, model of end-stage liver disease (MELD), age-bilirubin-INR-creatinine (ABIC), Glasgow alcoholic hepatitis score (GAHS), and Lille model are all predictive (Table 1) [12,13]. No individual model has shown consistent prognostic superiority, although models generally show superior negative versus positive predictive value [12,13].

Maddrey's discriminant function was the first prognostic model developed in AH is still widely used [14]. Maddrey's discriminant function is the standard to guide initiation of corticosteroids, and identifies poor clinical prognosis. Limitations include inter-laboratory

variability of PT and studies have reported high short-term mortality (up to 30%) in those with a score less than 32, calling into question the model's sensitivity [12–14].

MELD is also predictive in alcoholic hepatitis [15]. The benefits of MELD compared to Maddrey's discriminant function include: INR compared to PT allows standardized measurement of coagulopathy and inclusion of renal function with serum creatinine, which is an independent predictor of mortality in alcoholic hepatitis [16]. MELD is predictive of 30- and 90-day mortality – one of the first studies specific to biopsy-proven AH found that MELD of 21 had 75% sensitivity and 75% specificity to predict 90-day mortality [15]. Studies have suggested other cut-offs to stratify poor prognosis and there is not yet consensus [14,17]. The ABIC score was developed by the Barcelona group from 103 prospectively enrolled patients with biopsy-proven AH – severe disease (75%) based on Maddrey's discriminant function was treated with corticosteroids [18]. ABIC stratifies into low (0%), intermediate (30%), and high (75%) risk of 90-day mortality, and also predicts 1-year survival [18]. The Glasgow alcoholic hepatitis score was developed from 241 patients from eight U.K. centers [16]. Notably, none received corticosteroids, and given that inclusion was based on clinical criteria, only a third had biopsy-proven alcoholic hepatitis [16]. With a cut-off of less than 9 versus at least 9 (scale 5–12), GAHS predicted 28-day (87 versus 46%) and 84-day (79 vs. 40%) survival [16]. There was no accuracy difference in biopsy-proven versus clinically diagnosed alcoholic hepatitis [16]. Within its validation cohort, GAHS was more accurate than Maddrey's discriminant function and MELD [16].

In 2007, the Lille model was developed, which differs in utilizing both baseline values and day 7 serum bilirubin [7]. The model was derived from 438 prospectively enrolled patients with biopsy-proven alcoholic hepatitis, severe disease with Maddrey's discriminant function at least 32, and all received corticosteroids [7]. With a cut-off of 0.45 or less versus more than 0.45, 6-month mortality was 25 versus 85% ($P < 0.0001$), and identified 75% of deaths [7]. In its validation cohort, the model was more accurate than MELD and GAHS [7]. The model is used to determine corticosteroid-response, and whether corticosteroids should be stopped early [14]. A recent study [19] concluded that Lille score at Day 4 was as predictive as Day 7. In the context of identifying potential candidates for liver transplantation, early identification of medically refractory disease is imperative.

Joint-effect modeling, which combines prognostic scores, appears to be most predictive [20]. A 2015 study included 538 patients with severe alcoholic hepatitis treated with corticosteroids, and compared three joint-effect models (Mad-drey + Lille, MELD + Lille, and ABIC + Lille) [20]. MELD + Lille was most accurate to predict 2-month and 6-month survival, and was validated in a cohort of 604 patients [20]. By Day 7 of medical treatment, a normogram provides deciles of mortality risk; for example, 6-month mortality is less than 10% with MELD less than 15 and Lille less than 0.25, whereas 6-month mortality exceeds 70% with MELD more than 35 and Lille more than 0.70 (Fig. 1) [20]. This appears to be the best means to identify patients with exceedingly high risk of early mortality and should be considered for early liver transplantation.

LACK OF EFFECTIVE MEDICAL THERAPIES FOR SEVERE ALCOHOLIC HEPATITIS AND RATIONALE FOR LIVER TRANSPLANT AS RESCUE THERAPY

Beyond alcohol abstinence and treatment of decompensated liver disease, international guidelines advocate corticosteroids [14]. Pentoxifylline can be considered if contraindications to corticosteroids exist [21]. The most recent meta-analysis found improved short-term (~1 month) survival with corticosteroids, no benefit with pentoxifylline, and neither therapy provided long-term survival benefit [22]. More recently, the STOPAH trial, the largest multicenter, prospective, double-blind, randomized trial of prednisolone and pentoxifylline in severe alcoholic hepatitis, reported results that largely echo this meta-analysis [4]. STOPAH found only a trend towards 28-day survival benefit with prednisolone (OR 0.72; $P = 0.06$), and no improvement in 90-day or 1-year survival compared to placebo [4]. Pentoxifylline had no benefit [4]. Prior to STOPAH, studies showing benefit of medical therapy versus placebo had largely been limited to very short-term survival (e.g. 28-day) as primary endpoint [22]. Notably, 28-day mortality in STOPAH was significantly lower than historic cohorts [23], but similar to more recent trials [21,24], which may reflect improvements in medical management, and highlights the need for randomized-controlled trials.

More recent clinical trials exploring other interventions have largely yielded negative results, but may warrant further study. In a Franco-Belgian trial of 136 patients with biopsy-proven severe alcoholic hepatitis receiving methylprednisolone, patients were randomized to intensive enteral nutrition by feeding tube versus standard of care [25]. In intention-to-treat analysis, there was no difference in 6-month mortality, but enteral feeding was withdrawn prematurely in almost half of patients. However, low (vs. high) daily caloric intake was associated with twofold increase in mortality, suggesting a nutritional intervention may still be important [25]. In a trial of extracorporeal liver therapy (ELAD) in severe alcoholic hepatitis, 203 patients from 40 sites were randomized to ELAD or standard of care [26]. In intention-to-treat analysis, there was no difference in 90-day survival; however, in a nonprespecified subgroup analysis of MELD less than 28 and younger age (<47), 90-day survival was higher with ELAD versus standard of care (100 vs. 73%, $P = 0.006$), and a new trial investigating this subgroup is ongoing [26].

The lack of effective medical therapies has led to interest in liver transplantation as rescue therapy for severe alcoholic hepatitis. Because most deaths occur within 28 days, liver transplantation must forego the '6-month abstinence requirement abstinence' used in many programs for ALD.

CLINICAL EXPERIENCE WITH LIVER TRANSPLANTATION FOR SEVERE ALCOHOLIC HEPATITIS

The European experience

In 2011, Mathurin *et al.* conducted a pilot study of early liver transplantation for severe alcoholic hepatitis (Table 2) [9]. Key inclusion criteria were severe alcoholic hepatitis as first

liver-decompensating event (i.e. no prior episode of alcoholic hepatitis or liver disease), nonresponse to medical therapy (i.e. Lille Score >0.45, or continuous increase in MELD), presence of close supportive family members, absence of severe comorbid disorders, agreement to adhere to lifelong abstinence from alcohol, and consensus about liver transplantation selection among a broad group of medical professionals [9]. Using these strict criteria, only 7.7% presenting with severe alcoholic hepatitis were eligible for liver transplantation [9]. A clear survival benefit was shown with 77% in the liver transplantation group versus 23% without liver transplantation alive at 6 months ($P < 0.001$) [9]. This survival benefit persisted with 2-year follow-up: 71 versus 23% [9]. Three of 26 (12%) had alcohol use post-liver transplantation, with time to first drink at 720–1140 days post-liver transplantation [9]. This study was the first to show that liver transplantation in highly selected patients with severe alcoholic hepatitis could provide survival benefit with low incidence of alcohol use post-liver transplantation [9].

The U.S. experience

In a study of United Network for Organ Sharing (UNOS) data from 2004 to 2010, liver transplantations for alcoholic hepatitis ranged 4–18 per year, without a clear temporal trend [27]. Five-year graft and patient survival were similar in patients transplanted for alcoholic hepatitis versus alcoholic cirrhosis, at 75 versus 73% and 80 versus 78%, respectively, and no cases of graft failures or death were alcohol-related [27]. Although this represented one of the largest reports of liver transplantation in alcoholic hepatitis, limitations inherent to UNOS data are present. Thus, two single-center retrospective studies provide important additional information on the U.S. landscape of liver transplantation for alcoholic hepatitis.

In 2016, Mount Sinai Hospital published their experience (Table 2) [28■■]. Their protocol for early liver transplantation in severe alcoholic hepatitis was initiated January 2012 [28■■]. Although inspired by the European protocol, key differences were: previously controlled or newly diagnosed depression or anxiety disorders were not excluded; recent infection and gastrointestinal bleeding were not excluded; one patient underwent liver transplantation with history of prior alcoholic hepatitis, and thus did not satisfy the criteria of severe alcoholic hepatitis as first liver-decompensating event; and liver biopsy to confirm alcoholic hepatitis was not required [28■■]. Of 111 patients presenting with severe alcoholic hepatitis, 9 (9.6%) underwent liver transplantation. Median interval of abstinence prior to presentation with alcoholic hepatitis among liver transplantation recipients was 30 days. Six-month survival with early liver transplantation versus matched controls without liver transplantation was 89 versus 11% [28■■]. With median follow-up of 2.0 years, survival was 89% and 2/9 (22%) had alcohol use post-LT. Median time to first drink was 132 days post-liver transplantation [28■■]. The one post-liver transplantation death was caused by sepsis secondary to necrotizing pancreatitis 16 weeks after initial presentation [28■■].

In 2017, Johns Hopkins Hospital published the second U.S. single-center study (Table 2) [29■]. Their pilot for early liver transplantation in severe alcoholic hepatitis was initiated October 2012 [29■]. Similar to Mount Sinai, patients with history of psychiatric disease, gastrointestinal bleeding, or recent infection, were not excluded [29■]. In contrast to Mount Sinai, all patients presented with severe alcoholic hepatitis as first liver-decompensating

event [29■]. Seventeen patients who underwent early liver transplantation were compared to 26 consecutive patients who underwent liver transplantation for alcoholic cirrhosis with at least 6 months abstinence [29■]. In those with alcoholic hepatitis, with median follow-up of 1.5 years, survival was 88% – identical (88%) to the overall survival in those with alcoholic cirrhosis. However, both post-liver transplantation deaths in alcoholic hepatitis were directly alcohol-related, whereas the three post-liver transplantation deaths in alcoholic cirrhosis were attributed to sepsis or hepatocellular carcinoma – this study was the first to report an alcohol-related post-liver transplantation death for this indication [29■]. Median time to first drink was 83 days post-liver transplantation. Alcohol use post-liver transplantation was similar in alcoholic hepatitis versus alcohol cirrhosis: 24 versus 29% ($P > 0.99$) [29■].

The two U.S. single-center experiences confirmed the survival benefit of early liver transplantation achieved in the European experience, but some differences are noteworthy: U.S. protocols were more inclusionary and did not exclude comorbid psychiatric disease, gastrointestinal bleeding, recent infection; less than half of patients in the U.S. studies received corticosteroids for alcoholic hepatitis; U.S. survival post-liver transplantation appears to be higher; U.S. incidence of alcohol use post-liver transplantation appears to be higher; and U.S. time to first alcohol use post-liver transplantation occurred at much shorter intervals. Of course, these observations are limited by small sample size and risk of center-specific bias.

A NEW U.S. MULTICENTER COHORT: THE ACCELERATE-ALCOHOLIC HEPATITIS CONSORTIUM

Most recently, preliminary data from the American Consortium of Early Liver Transplantation for Alcoholic Hepatitis (ACCELERATE-AH), which includes 12 U.S. centers from 8 UNOS regions studying early liver transplantation for severe alcoholic hepatitis, extends and suggests generalizability of the observations from the smaller pilot studies [30■]. This preliminary data included 147 highly selected patients who underwent early liver transplantation for severe alcoholic hepatitis between 2006 and 2017 with median MELD of 39 and Day 7 Lille score of 0.82. Short-term and intermediate-term survival were excellent at 94 and 84% at 1 year and 3 years post-liver transplantation [30■]. Probability of alcohol use post-liver transplantation was 25 and 34% at 1 year and 3 years post-liver transplantation – similar to historic cohorts in alcoholic cirrhosis [30■,31]. Corticosteroid use for alcoholic hepatitis was associated with early post-liver transplantation death, whereas the majority of deaths beyond 1-year post-liver transplantation were alcohol-related [30■]. These findings suggest that early liver transplantation for severe alcoholic hepatitis is feasible with acceptable intermediate-term outcomes, but that larger prospective multicenter studies are needed to better understand the risks and benefits of transplantation in this setting.

NEED TO RE-EVALUATE THE 6-MONTH ABSTINENCE RULE FOR LIVER TRANSPLANTATION CANDIDACY

A requirement of 6-months of alcohol abstinence for patients with ALD exists in many liver transplantation programs. There are two prime reasons cited to support the 6-month rule. First, it provides sufficient time to determine if liver function could improve and potentially avoid liver transplantation. However, in severe alcoholic hepatitis, prognostic models can predict those unlikely to survive 6-months and thus a 'wait and see' approach is not appropriate in this setting. Second, it selects patients who would presumably be at low risk for alcohol use post-liver transplantation. Indeed, some studies support that shorter duration of pre-liver transplantation abstinence may be associated with alcohol use post-liver transplantation [31,32]. In a French cohort of 712 liver transplantation recipients for ALD between 1990 and 2007, less than 6 months pre-liver transplantation abstinence and younger age were associated with alcohol relapse [32]. A meta-analysis of 54 studies (50 liver, 3 kidney, 1 heart) which examined alcohol use after solid organ transplantation in over 3600 patients found that less than 6 months preliver transplantation abstinence was modestly associated with alcohol use post-liver transplantation, as were poor social support, and family history of alcohol use disorder [31].

However, abstinence is never the only, nor necessarily the strongest, factor associated with absence of harmful drinking post-liver transplantation. Other risk factors identified include younger age [32–34], poor social support [31,34], incomplete acceptance of alcohol use disorder [35], family history of alcohol use disorder [31,36], other substance abuse [35,36], underage children [34], female sex [34], and past failed attempts at rehabilitation [35]. This suggests a more comprehensive approach to assess harmful drinking post-liver transplantation, rather than one factor (i.e. duration of abstinence) with veto priority above all others. Indeed, most transplant centers require a psychosocial evaluation encompassing all possible risk factors for alcohol use post-liver transplantation [14,37].

ALCOHOL USE AFTER LIVER TRANSPLANT: FOCUSING ON HARMFUL DRINKING

Although complete abstinence post-liver transplantation is desired, reported alcohol use ranges 8–22% and 30–40% at 1-year and 5-years post-liver transplantation, respectively, and exceeds 50% with longer term follow-up [35,36,38]. There is no standard definition for alcohol relapse either with quantity or frequency of alcohol use – data across studies are consequently challenging to interpret [36,39,40]. In 2010, University of Pittsburgh published a prospective single-center study describing trajectories of alcohol use post-liver transplantation [36]. In 208 liver transplantation recipients for ALD between 1998 and 2004 (median 20 years of heavy drinking and 107 drinks/week pre-liver transplantation), 54% had no evidence of alcohol use post-liver transplantation [36]. Among those with alcohol use post-liver transplantation (46%), the study found four 'trajectories': low amounts infrequently (58%); early onset moderate use (average of 3.5 drinks per week at peak amount) that diminished over time (14%); later onset moderate use that increased over time (16%); early onset, heavy (average of 4 drinks per day at peak amount), increasing pattern of

use (13%) [36]. All deaths from recurrent ALD (*n* = 5) were liver transplantation recipients with early onset moderate or heavy alcohol use post-liver transplantation [36]. Short length of pre-liver transplantation sobriety, family history of alcohol use disorder, and other substance abuse disorder were most predictive of alcohol use post-liver transplantation [36]. This study highlights the infrequency of clinically relevant alcohol use and the importance in distinguishing different patterns of drinking, both clinically and in research studies [36]. Despite these rates of alcohol use post-liver transplantation, 1-year and 5-year survival post-liver transplantation for ALD are similar to other indications and widely accepted as an appropriate indication for liver transplantation [14,39,42].

Among those transplanted for alcoholic cirrhosis, harmful alcohol use has been associated with rapid allograft fibrosis and patient death [32,33]. Similarly, early results of liver transplantation for severe alcoholic hepatitis report graft losses due to alcohol, although in only a minority of cases. Going forward, post-liver transplantation outcomes for alcoholic hepatitis are best compared to ALD, with the latter being an accepted indication with good long-term outcomes. In the realm of liver transplantation for severe alcoholic hepatitis, there may be a greater need for prospective studies focused on prognostication, prevention, and treatment of post-liver transplantation alcohol use. As we seek to appropriately expand liver transplantation for severe alcoholic hepatitis and ensure acceptable long-term outcomes, we anticipate that what is learned will also aid in the management of alcoholic cirrhosis.

OTHER ETHICAL CONSIDERATIONS

A central controversy remains whether a patient who has consumed alcohol to the limits of mortality, apparently by his/her own volition, can be entrusted with long-term stewardship of an allograft [43]. Some believe that priority should be given to those with liver disease caused by conditions independent of patient behavior (e.g. autoimmune hepatitis, primary sclerosing cholangitis) [37]. First, to limit access to healthcare based upon perceived patient responsibility is unethical – core to the MELD allocation system is to prioritize those who are most ill and would derive the greatest survival benefit. Second, responsible and ethical use of liver transplantation for recent 'self-injurious' behavior is not foreign: acetaminophen-induced liver failure by suicide attempt and NASH cirrhosis by obesity and its metabolic complications are widely accepted indications for liver transplantation.

Another consideration is the public perception of offering liver transplantation for patients with recent alcohol use and how this might affect future organ donation – Stroh *et al.* [44] addressed this issue in a recent study. Using a well known crowd-sourcing marketplace to reach a large diverse population, they surveyed 503 participants to assess general attitude towards liver transplantation, and then specifically early liver transplantation for alcoholic hepatitis [44]. A total of 341 (68%) intended to be organ donors [44]. The majority (82%) were at least neutral towards early liver transplantation for alcoholic hepatitis, and 74% indicated that early liver transplantation for severe alcoholic hepatitis would not make them hesitant to donate their organs [44]. Thus, negative public reaction for early liver transplantation in alcoholic hepatitis is likely overstated and while more studies are needed, there is insufficient evidence to limit liver transplantation for alcoholic hepatitis on this basis.

FUTURE DIRECTIONS AND CONCLUSIONS

Although published experience is modest, the survival benefit is so striking that greater use of liver transplantation for severe alcoholic hepatitis seems likely. Understandably, the indication comes with considerable cost and ethical implications surrounding a limited resource. Early results highlight the importance of careful selection and demonstrate that this potentially life-saving intervention will be applicable to only a minority of those affected by alcoholic hepatitis.

Thus, alternative therapies to treat severe alcoholic hepatitis are needed. The European and U.S. experiences all had close involvement of transplant psychologists and addiction specialists – resources that may not be available at all liver transplantation centers. Moreover, despite rigorous selection, some patients had poor outcomes related to harmful alcohol use post-liver transplantation, including graft failure from recurrent ALD. Future studies need to address how best to select patients who would derive greatest survival benefit, and at lowest risk for harmful alcohol use posttransplant, and what resources are required to achieve acceptable outcomes. We need to study interventions to prevent and treat alcohol use posttransplant. Presently, there is limited guidance as to how centers should proceed with pre-liver transplantation selection and post-liver transplantation care. Going forward, a concerted effort to address these knowledge gaps is essential. Finally, there is urgent need to develop a unified national policy on liver transplantation for this indication – to effectively and informatively move towards consensus among transplant centers.

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KEY POINTS

- Early liver transplantation for severe alcoholic hepatitis is feasible and lifesaving.

- Early liver transplantation should only be reserved for very select patients with medically refractory disease and psychosocial profiles at low risk for alcohol use posttransplant.

- Published data in this field are sparse, and long-term outcomes remain largely unknown.

- Future studies need to focus on how best to select patients suitable for early liver transplant.

- Alcohol use posttransplant remains of significant concern, and further study as how to prevent and treat alcohol use posttransplant is needed.
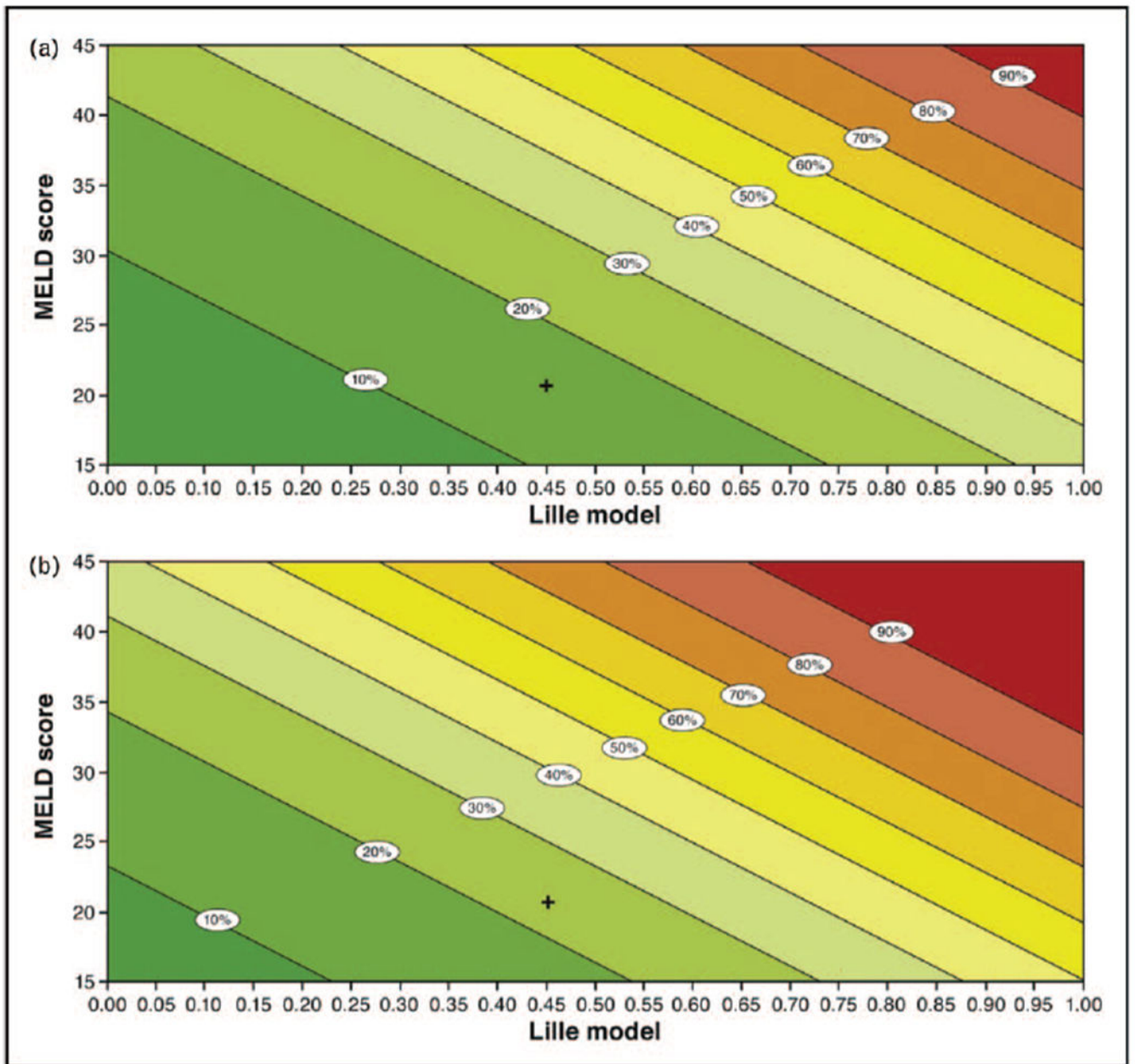
FIGURE 1.
Joint-effect model (MELD+Lille score) to predict 2-month and 6-month mortality in alcoholic hepatitis. Reproduced from Louvet and Labreuche *et al.* [20] with permission from Dr Philippe Mathurin and publisher. (a) Two-month mortality by joint-effect model combining Lille and MELD scores. (b) Six-month mortality by joint-effect model combining Lille and MELD scores.

Table 1.

Prognostic models for severe alcoholic hepatitis

| Prediction model | Lab components | | Cut-off score | 30-Day mortality[a] | | 90-Day mortality[a] | |
	Day of admission	Day 7 of treatment		PPV	NPV	PPV	NPV
Maddrey's mDF	Bilirubin, PT	–	32	0.20	1.00	0.29	1.00
MELD	Bilirubin, INR, creatinine	–	21	0.38	0.96	0.57	0.96
ABIC	Bilirubin, INR, creatinine, age	–	9	0.33	0.92	0.50	0.91
Glasgow AH	Bilirubin, PT, Age, WBC, BUN	–	9	0.27	0.94	0.38	0.97
Lille	Bilirubin, PT, creatinine, age, albumin	Bilirubin	0.45	0.44	0.91	0.56	0.86

ABIC, age/bilirubin/INR/creatinine score; AH, alcoholic hepatitis; mDF, modified discriminant function; MELD, model for end-stage liver disease.

[a]Positive predictive values (PPV) and negative predictive values (NPV) from results of U.K. study [12], which sought to validate prediction models in a cohort of 71 consecutive patients with biopsy-proven AH.

Table 2.

Key studies in early liver transplantation for severe alcoholic hepatitis

Study	Mathurin *et al.*	Im *et al.*	Lee *et al.*
N	26	9	17
Study design	Prospective	Retrospective	Retrospective
Comparison group	Historic, severe AH, no LT	Contemporaneous, severe AH, no LT	Contemporaneous, alcoholic cirrhosis with 6 months abstinence, underwent LT
Median follow-up	NR	2.0 years	1.5 years
Survival			
6-month	77%	89%	100%
2-year	71%	NR	NR
Alcohol use post-LT	12%	22%	24%
Median time to alcohol use post-LT	740 days	132 days	83 days

AH, alcoholic hepatitis; LT, liver transplantation; NR, not reported.