ORIGINAL ARTICLE

Characteristics of liver transplant candidates delisted following recompensation and predictors of such delisting in alcohol-related liver disease: a case–control study

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SUMMARY

Whether and when recovery beyond the need for transplant may occur in patients listed for decompensation remains unclear. This study aimed to investigate the characteristics of patients delisted following recompensation. Seventy-seven patients who were listed between 2005 and 2015 for decompensation, but later delisted following recompensation were included. Alcohol-related liver disease (ALD) was the underlying etiology in the majority (n = 47, 61%). Listing characteristics of these patients were compared with those of decompensated ALD patients who either underwent deceased donor liver transplantation or died on the waiting list. The model for end-stage liver disease (MELD) score <20 and serum albumin ≥32 g/l at listing were the only independent predictors of recompensation/delisting in ALD. The probability of recompensation was 70% when both factors were present at listing. Interestingly, about a tenth of decompensated ALD patients who died on the waiting list (median duration on waiting list 11 months) and a quarter of decompensated ALD patients who underwent living donor liver transplantation (median duration on waiting list 2 months) also had both factors at listing. In conclusion, ALD seems to be the most favorable etiology for recompensation beyond the need for transplantation. Both MELD and serum albumin at listing independently predict recompensation/delisting in ALD. It seems advisable to implement a period of observation for ALD patients with both favorable factors, before embarking on living donor liver transplantation.

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alcohol-related liver disease, delisting, model for end-stage liver disease score, recompensation, serum albumin

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Introduction

Development of hepatic decompensation, which marks the onset of end-stage liver disease, is an ominous milestone of chronic liver disease progression, irrespective of the etiology. It is defined as the manifestation of an index complication such as ascites, hepatic encephalopathy, variceal hemorrhage,

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or hepatocellular dysfunction in a patient with cirrhosis [1,2].

Decompensation impairs patient survival [3,4], and liver transplantation (LT) remains the only treatment option improving the dismal prognosis. Development of ascites is associated with a 1-year mortality of 15%, which increases to >60% when complicated by hyponatremia, hepatorenal syndrome, and/or superimposed spontaneous bacterial peritonitis [5,6]. Similarly, both hepatic encephalopathy [7] and variceal bleeding [8] are associated with poor prognosis. However, improvement in hepatic function and recompensation is occasionally seen in day-to-day clinical practice, even in patients listed for LT.

The availability of potent antiviral agents against hepatitis B and C has confirmed the potential for recompensation in selected patients, thus changing the paradigm of hepatic decompensation. The use of direct-acting antivirals in patients on transplant waiting list has shown significant clinical improvement leading to delisting [9–11]. However, literature on recompensation of liver disease from other etiologies is sparse.

This study aimed to determine the clinical characteristics of patients delisted following recompensation and to identify the clinical parameters at listing which were associated with recompensation on waiting list.

Materials and methods

Patient selection and data collection

This is a retrospective analysis of prospectively collected data from a single, high volume liver transplant center. All adult patients who were wait-listed in the Toronto liver transplant program between January 2005 and December 2015 for decompensated chronic liver disease, but later delisted following recompensation were eligible for inclusion into the study cohort. Etiology-matched patients who were listed during the same period for decompensation and either underwent deceased donor LT or died on waiting list were chosen as controls. Etiology-matched patients who were listed during the same period for decompensation and underwent living donor LT and therefore did not follow the 'natural' course on the waiting list served as a second control group.

The following patients were excluded from the study: (i) patients with associated hepatocellular carcinoma, (ii) patients listed for decompensation and later delisted for reasons other than recompensation, (iii) patients listed for reasons other than decompensation such as recurrent cholangitis in primary sclerosing cholangitis and intractable pruritus in primary biliary cholangitis, (iv) patients listed for acute liver failure, (v) patients listed for other reasons such as polycystic liver disease, amyloidosis, vascular liver disease (e.g. Budd-Chiari syndrome, sinusoidal obstruction syndrome), inborn errors of metabolism (e.g. glycogen storage diseases, Tyrosinemia, Citrullinemia, Maple Syrup Urine Disease, and Hyperoxaluria), and (vi) patients listed for re-transplantation or with a prior non-liver organ transplant including bone marrow transplantation.

Demographic and clinical data were retrospectively extracted from the prospectively collected electronic transplant database (OTTR: Transplant Care Platform 6, OTTR Chronic Care Solutions, Omaha, NE, USA). The original Model for End-stage Liver disease score ($MELD_{(O)}$) [12,13] and the recently updated, serum sodium incorporated Model for End-stage Liver Disease score (MELD; Organ Procurement and Transplantation Network Policy 9.1, January 2016) were calculated at listing. The study was approved by the Toronto University Health Network Research Ethics Board (16–5178–BE).

Listing criteria for decompensation and delisting criteria following recompensation

The listing criteria of the Toronto liver transplant program are that of Ontario province. Patients are only considered for listing when all other therapeutic options have been exhausted and expected 5-year survival (from non-liver-related comorbidity) is ≥50%. Listing for hepatic decompensation is considered in patients with ascites or complications thereof such as hepatic hydrothorax and spontaneous bacterial peritonitis (resolved), jaundice, hepatic encephalopathy, or portal hypertensive gastrointestinal bleed and a MELD score of ≥15. Patients with decompensation and MELD 11–14 are reviewed on a case-by-case basis and are listed only if the MELD score is deemed not reflective of their poor prognosis. Prior to the incorporation of MELD score in 2007, Child-Pugh B score ≥7 was used for listing of patients with decompensation. In addition, a minimum 6-month alcohol abstinence and specialist psychiatrist review to confirm the commitment to abstinence and to assess the risk of recidivism are mandatory for patients with alcohol-related liver disease (ALD).

Recompensation was a clinical diagnosis. The absence of ascites/hepatic hydrothorax/peripheral edema despite the discontinuation of diuretics and the absence of hepatic encephalopathy without the need for prophylactic treatment along with an improvement in the MELD score to <15 in a patient who was initially placed on the waiting list for such features of decompensation was considered as recompensation. All patients who

achieved recompensation were placed 'on hold' for at least 6 months to confirm the durability of recompensation and were reviewed by at least two hepatologists prior to delisting. Delisting is defined as the permanent removal of a patient from the LT waiting list.

Endpoint

The primary endpoint was to identify factors at listing, which were associated with delisting following recompensation.

Data analysis and statistics

An etiology-matched comparison was only undertaken if there were adequate numbers of patients in the study group. Data are shown as median (interquartile range) or number (percentage) unless otherwise stated. All statistical analyzes were performed using either GRAPHPAD PRISM 5 (San Diego, CA, USA) or SPSS for Windows v20 (IBM Corp, Armonk, NY, USA). A *P*-value of <0.05 was considered statistically significant. Clinical parameters at listing were analyzed for association with the outcome (delisting following recompensation versus transplantation or death on waiting list) using the Mann–Whitney *U*-test or one-way ANOVA (Kruskal–Wallis test) as appropriate. A multivariable logistic regression model incorporating variables with a *P* value of <0.10 on univariate testing was used to determine independent associations with delisting following recompensation.

Results

Clinical characteristics of all patients delisted following recompensation (all etiologies)

A total of 935 patients were listed for decompensation alone and underwent LT, died on the waiting list, or delisted following recompensation during the 10-year study period – ALD (n = 284, 30%), hepatitis C (n = 239, 26%), and non-alcohol-related fatty liver disease (n = 115, 12%) were the three most common etiologies, followed by primary sclerosing cholangitis (n = 71, 8%), hepatitis B (n = 55, 6%), primary biliary cholangitis (n = 47, 5%), cryptogenic cirrhosis (n = 45, 5%), autoimmune hepatitis (n = 38, 4%), and others (n = 41, 4%).

Of the 935 patients, 77 patients were delisted following recompensation and formed the study group (cases). The median age at listing was 54 years (IQR 47–59); the majority were males (n = 49, 64%), and the median Body Mass Index (BMI) at listing was 26.2 (IQR 24.5–29.3). The median $MELD_{(O)}$ and MELD scores were 14 (IQR 13–16) and 15 (IQR 13–19), respectively. The median duration on the waiting list was 18 months [12–29]. In the vast majority (n = 64, 83%), recompensation was spontaneous; in the rest, potential contributing factors for recompensation included insertion of a transjugular intrahepatic portosystemic shunt (n = 4, 5%) and initiation of specific treatment of the underlying etiology (n = 9, 12%).

Alcohol-related liver disease was the most common etiology (n = 47, 61%) in the study cohort; the rest of etiologies only accounted for a small number of patients. Etiology-specific clinical characteristics and potential reasons for recompensation are summarized in Table 1. All 77 patients had clinical manifestation of primary hepatocellular dysfunction in the form of ascites with/without hepatic hydrothorax and peripheral edema at listing. Over half these patients (n = 40, 52%) had at least one episode of overt hepatic encephalopathy, nearly a quarter of patients (n = 18, 23%) had a history of gastrointestinal bleeding attributed to portal hypertension, and 13% (n = 10) had a history of confirmed spontaneous bacterial peritonitis.

Only four (5%) patients (two with ALD, one with hepatitis C, and one with autoimmune hepatitis) were re-referred for LT evaluation after delisting, with a median interval of 4 years (IQR 3–6). Of the four patients, two were accepted for LT and are currently on the waiting list (one with hepatitis C and the other with autoimmune hepatitis); the other two, both with ALD and previous transjugular intrahepatic portosystemic shunt insertion, were felt not to have favorable risk/benefit balance for LT due to advanced age and medical comorbidities, and were not accepted on the waiting list.

Comparison of patients delisted following recompensation and those who underwent deceased donor LT/died on waiting list (only ALD)

Alcohol-related liver disease accounted for nearly two-thirds of patients who were delisted following recompensation; the rest of the etiologies were not adequately represented in number. Therefore, further analyzes were undertaken only in those who were listed for decompensated ALD.

A comparison between the patients who were delisted following recompensation (n = 47) and those who

Table 1. Summary of all patients delisted following improvement of liver function and recompensation following listing for liver transplantation (n = 77).

Etiology of liver disease	Number (%) of patients	Likely reason/s for recompensation	Laboratory characteristics at listing median (IQR)	Duration on waiting list (months)	Re-referrals
ALD	47 (61%)	TIPS insertion (n = 3) Spontaneous (n = 44)	Bilirubin 38 (24–56); INR 1.40 (1.30–1.56) Creatinine 86 (70–108); Sodium 136 (134–138) Albumin 34 (30–36); Platelets 125 (95–165)	19 (14–30)	2
HCV	12 (16%) [9 HCV RNA +ve]	Successful antiviral treatment (n = 4) TIPS insertion (n = 1) Spontaneous (n = 7)	Bilirubin 43 (33–51); INR 1.49 (1.38–1.56) Creatinine 76 (53–94); Sodium 137 (136–140) Albumin 29 (29–33); Platelets 86 (60–119)	20 (12–24)	1
ALD/HCV	4 (5%) [3 HCV RNA +ve]	Spontaneous (n = 4)	Bilirubin 37 (31–42); INR 1.50 (1.44–1.51) Creatinine 89 (81–93); Sodium 138 (135–141) Albumin 30 (28–32); Platelets 83 (69–118)	33 (24–37)	None
AIH	4 (5%)	Initiation of Azathioprine treatment (n = 2) Spontaneous (n = 2)	Bilirubin 46 (34–88); INR 1.46 (1.24–1.65) Creatinine 70 (66–77); Sodium 133 (129–136) Albumin 26 (26,27); Platelets 98 (71–130)	11 (9–25)	1
HBV	3 (4%)	Initiation of antiviral treatment (n = 3)	Bilirubin 58 (38–81); INR 1.35 (1.28–1.39) Creatinine 111 (92–114); Sodium 141 (139–142) Albumin 32 (28–37); Platelets 152 (98–172)	16 (15–17)	None
NASH	3 (4%)	Spontaneous (n = 3)	Bilirubin 28 (26–45); INR 1.46 (1.42–1.48) Creatinine 86 (74–100); Sodium 136 (135–138) Albumin 32 (32–33); Platelets 148 (106–185)	26 (18–39)	None
Sarcoidosis	2 (3%)	Spontaneous (n = 2)	Bilirubin 25*; INR 1.25* Creatinine 113*; Sodium 138* Albumin 35*; Platelets 86*	11*	None
PSC	1 (1%)	Spontaneous (n = 1)	Bilirubin 65†; INR 1.37†; Creatinine 62†; Sodium 137† Albumin 36†; Platelets 81†	16†	None
Cryptogenic	1 (1%)	Spontaneous (n = 1)	Bilirubin 10†; INR 1.32† Creatinine 74†; Sodium 123† Albumin 22†; Platelets 225†	40†	None

AIH, autoimmune liver disease; ALD, alcohol-related liver disease; HBV, hepatitis B-related liver disease; HCV, hepatitis C-related liver disease; INR, international normalized ratio; NASH, non-alcohol-related steatohepatitis; PSC, primary sclerosing cholangitis; TIPS, transjugular intrahepatic portosystemic shunt.

*Average.

†Actual values.

underwent deceased donor LT or died on waiting list (n = 194) is summarized in Table 2. Age, BMI, and duration of abstinence at listing were similar between the two groups. All laboratory parameters at listing except serum creatinine were significantly worse in those who underwent deceased donor LT or died on the waiting list.

On univariate analysis (Table 3) female sex, bilirubin, INR, creatinine, serum sodium, $MELD_{(O)}$, MELD, albumin, and platelets at listing were predictive of delisting following recompensation. Before proceeding with multivariate analysis, a receiver operating characteristic (ROC) curve analysis was performed to compare the predictability of MELD and its components (Fig. 1). MELD at listing was a better predictor (AUROC 0.853) of delisting following recompensation than $MELD_{(O)}$, bilirubin, INR, creatinine, and serum sodium. Therefore, only MELD along with sex, BMI, albumin, and platelets at listing were taken forward for multivariate analysis.

On multivariate analysis (Table 3), MELD and albumin at listing were the only independent predictors of delisting following recompensation. Using Youden-Index (J), MELD <20 at listing (sensitivity 79%,

Table 2. Comparison between patients delisted following recompensation (n = 47) and those who underwent deceased donor transplantation (DDLT) or died on the waiting list (n = 194) after being listed for decompensation of ALD.

	Recompensation (n = 47) Median (IQR)/number (%)	DDLT or Death (n = 194) median (IQR)/number (%)	P-value
Age at listing (years)	55 (50–59)	57 (51–61)	0.15
Male sex	30 (64%)	158 (81%)	**0.009**
BMI at listing (kg/m^2)	26.2 (24.5–28.2)	27.7 (23.8–31.0)	0.08
Duration on waiting list (months)	19 (14–30)	3 (1–9)	**<0.0001**
Duration of abstinence at listing (months)	12 (10–16)	12 (10–21)	0.22
Bilirubin at listing (μmol/l)	38 (24–56)	83 (58–196)	**<0.0001**
INR at listing	1.40 (1.30–1.56)	1.90 (1.58–2.71)	**<0.0001**
Creatinine at listing (μmol/l)	86 (70–108)	113 (71–164)	0.06
MELD$_{(O)}$ score at listing	14 (12–16)	23 (19–30)	**<0.0001**
Sodium at listing (mmol/l)	136 (134–138)	134 (130–137)	**0.0005**
MELD score at listing	15 (12–19)	24 (20–29)	**<0.0001**
Albumin at listing (g/l)	34 (30–36)	30 (26–34)	**<0.0001**
Platelets at listing (× 10^9/l)	125 (95–165)	75 (53–114)	**<0.0001**

BMI, body mass index; DDLT deceased donor liver transplantation; INR, international normalized ratio; MELD, model for end-stage liver disease.

Of the 194 patients, 122 patients underwent DDLT and 72 died on the waiting list. A P value <0.05 in indicated in bold.

Table 3. Predictors of recompensation – univariate and multivariate logistic regression.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age at listing	0.97 (0.93–1.01)	0.13		
Male sex*	0.40 (0.20–0.81)	0.01	0.43 (0.17–1.06)	0.07
BMI at listing*	0.94 (0.88–1.00)	0.07	1.01 (0.93–1.10)	0.81
Duration of abstinence at listing	0.99 (0.98–1.01)	0.29		
Bilirubin at listing	0.97 (0.96–0.99)	<0.001		
INR at listing	0.02 (0.00–0.10)	<0.001		
Creatinine at listing	0.99 (0.98–1.00)	0.02		
MELD$_{(O)}$ score at listing	0.74 (0.66–0.82)	<0.001		
Sodium at listing	1.11 (1.03–1.19)	0.004		
MELD score at listing*	0.78 (0.73–0.85)	<0.001	0.81 (0.74–0.88)	**<0.001**
Albumin at listing*	1.13 (1.06–1.21)	<0.001	1.11 (1.02–1.21)	**0.02**
Platelets at listing*	1.01 (1.01–1.02)	<0.001	1.00 (1.00–1.01)	0.20

BMI, body mass index; INR, international normalized ratio; MELD, model for end-stage liver disease.

A P value <0.05 in indicated in bold. MELD score and its components were included in the univariate analysis. Having shown that MELD is a better predictor of recompensation that its components (Fig. 1), only the MELD score was included in the multivariate analysis.

*Indicates the parameters which were included in the multivariate analysis.

specificity 76%) and albumin ≥32 g/l at listing (sensitivity 68%, specificity 67%) were found to be the optimal cutoffs in predicting delisting following recompensation in ALD.

The probability of being delisted following recompensation (positive predictive value, PPV) with MELD <20 at listing was 0.45 and with albumin ≥32 g/l at listing was 0.33. Combing both factors improved the PPV to 0.71. The cumulative incidence of being delisted following recompensation of patients with MELD <20 and albumin ≥32 g/l is shown in Fig. 2. On the other hand, the negative predictive values (NPV) for delisting following recompensation of MELD <20, albumin ≥32 g/l, and both combined were 0.94, 0.90, and 0.89, respectively.

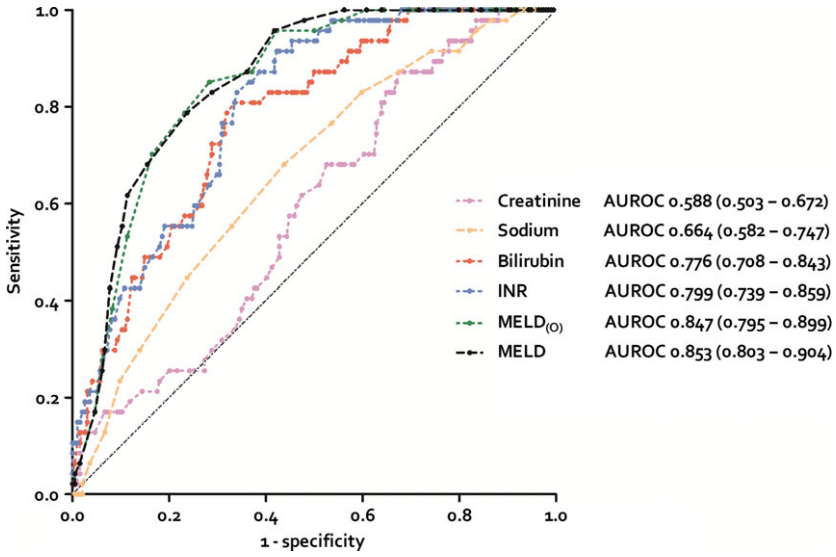

Figure 1 Receiver operating characteristic (ROC) curve analysis of model for end-stage liver disease scores and their individual components in predicting delisting of patients following recompensation. Abbreviations: $MELD_{(O)}$, original model for end-stage liver disease score; MELD, recently updated (January 2016) model for end-stage liver disease score, which incorporates serum sodium in the calculation; INR, international normalized ratio.

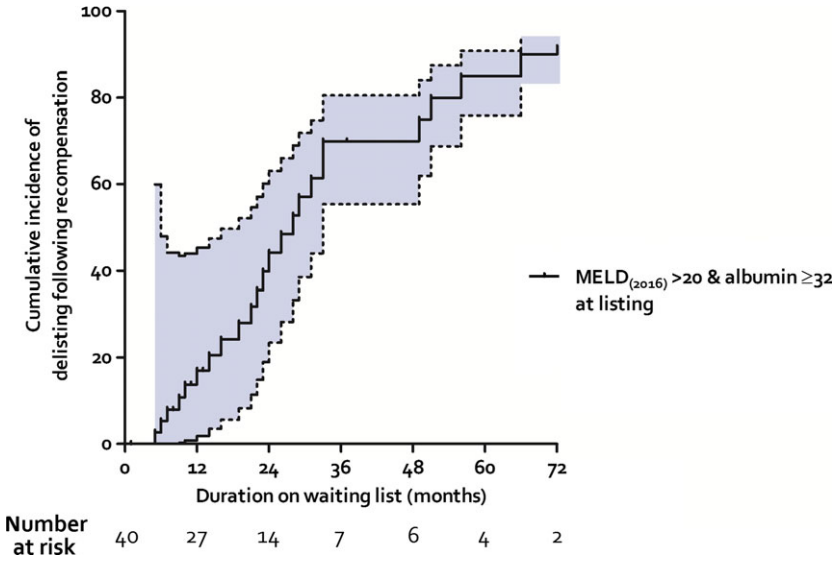

Figure 2 The cumulative incidence of being delisted following recompensation of patients with both MELD <20 and albumin ≥32 g/l at listing.

Interestingly, eight of the 72 (11%) patients who died on the waiting list had both MELD <20 and albumin ≥32 g/l at listing. These patients spent a median of 11 months (IQR 6–18) on the waiting list compared with 23 months (IQR 14–33) spent by those who were delisted following recompensation.

Comparison of patients delisted following recompensation and those who underwent living donor LT (only ALD)

A comparison between the patients with decompensated ALD who were delisted following recompensation ($n = 47$) and those who underwent living donor LT ($n = 43$) is summarized in Table 4. $MELD_{(O)}$, MELD, serum sodium at listing, and duration on waiting list were significantly different between the two groups. Difference in bilirubin ($P = 0.053$), INR ($P = 0.08$), creatinine ($P = 0.07$), and albumin ($P = 0.0503$) approached but did not reach statistical significance.

The difference in clinical parameters between the patients delisted following recompensation and those that underwent living donor LT (Table 4) were less marked compared with the difference between those delisted following recompensation and those that underwent deceased donor LT/died on waiting list (Table 2). Therefore, further analysis was undertaken to explore the possibility that at least some of the patients who underwent living donor LT may have had the chance to recompensate and be delisted, if the 'natural' course of

Table 4. Comparison between those who were listed for decompensation of ALD and later delisted following recompensation (n = 47) and those underwent living donor transplantation (n = 43).

	Recompensation (n = 47) Median (IQR)/number (%)	LDLT (n = 43) Median (IQR)/number (%)	P-value
Age at listing (years)	55 (50–59)	57 (50–61)	0.18
Male sex	30 (64%)	32 (74%)	0.28
BMI at listing (kg/m^2)	26.2 (24.5–28.2)	26.2 (22.9–29.6)	0.87
Duration on waiting list (months)	19 (14–30)	3 (2–5)	**<0.0001**
Duration of abstinence at listing (months)	12 (10–16)	12 (10–15)	0.80
Bilirubin at listing (μmol/l)	38 (24–56)	50 (27–68)	0.053
INR at listing	1.40 (1.30–1.56)	1.51 (1.36–1.73)	0.08
Creatinine at listing (μmol/l)	86 (70–108)	120 (90–150)	0.07
$MELD_{(O)}$ score at listing	14 (12–16)	19 (15–22)	**0.0008**
Sodium at listing (mmol/l)	136 (134–138)	131 (126–135)	**0.0009**
MELD score at listing	15 (12–19)	20 (17–24)	**<0.0001**
Albumin at listing (g/l)	34 (30–36)	31 (28–34)	0.0503
Platelets at listing (x 10^9/l)	125 (95–165)	93 (69–138)	0.35

BMI, body mass index; INR, international normalized ratio; LDLT, living donor liver transplantation; MELD, model for end-stage liver disease.

A P value <0.05 in indicated in bold.

the disease had not been intervened upon with living donor LT.

Eleven of the 43 (26%) patients who underwent living donor LT were found to have both MELD <20 and albumin ≥32 g/l at listing. These patients spent a median of 2 months (IQR 1–4) before undergoing LT.

Discussion

This retrospective, single-center study describes the listing characteristics of patients with decompensated chronic liver disease of all etiologies, who recompensated on the waiting list and were delisted as transplantation no longer carried a survival benefit. Potential predictors of delisting following recompensation were assessed only for ALD; other etiologies were present in too small numbers in the recompensation group to allow a meaningful statistical analysis. In patients with decompensated ALD, MELD <20, and serum albumin ≥32 g/l at listing were independently associated with being delisted following recompensation. The presence of both factors at listing improved the probability of recompensation and delisting to >70%.

Improvement in fibrosis and portal hypertension has been demonstrated in patients with hepatitis C compensated cirrhosis following successful antiviral treatment [14–16]. Disease regression has also been documented in patients with hepatitis B compensated cirrhosis following antiviral therapy [17,18] and nonalcoholic steatohepatitis compensated cirrhosis following bariatric surgery [19]. Studies from as early as a decade ago also demonstrated significant improvements in hepatic function and Child-Pugh scores in patients with decompensated hepatitis B cirrhosis following antiviral treatment [20–23]; thus accentuate the potential for reversibility in both compensated and decompensated cirrhosis, which were once thought to be irreversible. However, it was not until the availability of potent, direct-acting antivirals for hepatitis C that it became apparent that recompensation can occur to such a robust degree that patients no longer require transplantation. A recent multicenter European study showed recompensation with antiviral therapy leading to delisting of patients who were initially listed for decompensated hepatitis C [11]. In addition, both MELD (at listing and improvement with antiviral treatment) and serum albumin (improvement with antiviral treatment) were predictive of recompensation following successful antiviral therapy [11].

The role of MELD as a predictor of recompensation in patients on the transplant waiting list is strongly supported by both, the European [11] and the current study. While lower MELD scores at baseline/listing increase the probability of recompensation, higher MELD scores seem to have a strong negative predictive role in patients with decompensated hepatitis C cirrhosis undergoing antiviral treatment [11] and wait-listed patients with decompensated ALD. This seems to suggest that the reversibility of liver damage upon cessation of injury depends on the severity of the liver disease, i.e.

beyond a critical point, decompensation may no longer reverse to a clinically relevant degree even when the damaging insult no longer exists. Moreover, this 'point of no return' seems to be surprisingly similar for hepatitis C-related liver disease and ALD. Which factor/s determine this critical point of no return has yet to be identified, and is beyond the scope of this discussion.

Allocation of deceased donor grafts to patients depends on the regional waiting list and organ availability. In our transplant program, deceased donor grafts are only offered to patients with MELD of 25–30 or higher due to the scarce resource of donated organs. This prolongs waiting time during which patients' clinical condition deteriorates substantially with increased waiting list mortality. Therefore, living donor LT is offered to all patients at their initial encounter with the service, and this option is discussed and encouraged thereafter while they are on the waiting list. Living donor LT has a survival benefit comparable to that of deceased donor LT [24]; even in the very sick [25,26]. In addition, the patient survival is significantly better with living donor LT compared with deceased donor LT, when measured from the time of listing [27,28]. However, living donor LT is not without its risks and complications not only to the recipient but also to the donor, and therefore should not be taken lightly. One-quarter of patients who underwent living donor LT in our study fulfilled both criteria for potential recompensation (i.e. MELD <20 and albumin ≥32 g/l at listing), thus raising the question as to whether these patients were transplanted prematurely. Such a conclusion may be an oversimplification as 11% of patients who died on the waiting list also fulfilled these criteria at listing. Therefore, rather than deny the option of living donor LT to those who fulfill both criteria of potential recompensation, a reasonable approach might be to institute a 'period of observation' on the waiting list to determine whether or not the clinical condition improves. Based on the duration on the waiting list of those who died despite fulfilling the predictive criteria (median 11 months; IQR 6–18), we propose that this 'period of observation' should be not more than 6 months from listing irrespective of the duration of abstinence prior to listing.

As controversial as it may be, similar to most transplant centers, only those with at least 6 months of alcohol abstinence ('6-month abstinence rule') are considered for listing/transplantation. Interestingly and against expectations, alcohol abstinence beyond 6 months did not impact recompensation in this study. Whether this is because the beneficial effect of alcohol abstinence on recompensation is only evident within the first 6 months of abstinence or whether recompensation is dependent only on alcohol abstinence itself and not the duration of abstinence is not known.

Interestingly, improvement of hepatic function allowing delisting was also evident in a small number of patients with etiologies such as hepatitis C, non-alcohol-related fatty liver disease, and cryptogenic cirrhosis, which are not known to result in spontaneous recompensation. This raises the question as to whether there were additional etiologies in these patients that were not reported/identified. Deliberate underestimation of self-reported alcohol consumption is widespread and well documented [29,30]. Whether some of these patients underreported the amount of alcohol consumed and later stopped it upon listing which led to recompensation is not known. Further, due to the lack of literature on hepatic recompensation, it is not known whether true spontaneous recompensation does occur in a small number of patients in the above etiologies.

The study has several strengths and limitations. The use of listing characteristics in the analysis (as opposed to progressive/dynamic changes in clinical parameters) makes the findings reflect prospective decision making in a day-to-day clinical practice. On the other hand, this being a single-center study and having included limited numbers of patients in etiologies other than ALD prohibits further analysis for other causes of liver disease. Moreover, due to the retrospective design, the unavailability of data of factors which may have impacted recompensation such muscle mass/sarcopenia and alcohol-related characteristics such as lifetime total amount and type of alcoholic beverage, the duration of abuse and patterns of drinking could not be included in the analysis. Further, due to the '6-month abstinence rule' those who recompensated during the first 6 months of abstinence are not included in this analysis, potentially underestimating the actual proportion of recompensation.

In conclusion, ALD seems to have a greater potential for recompensation especially in those with early stage decompensation. The severity of liver disease (MELD <20 and serum albumin ≥32 g/l) at the time of listing remains the only relevant predictor of recompensation. Interestingly, the duration of alcohol abstinence (beyond 6 months) seems to have no impact on recompensation. It may be advisable to implement a period of observation on the waiting list for those with early decompensated ALD to determine the course of

progression before embarking on transplantation, especially in living donor LT candidates.

Authorship

ADA: conceived and designed the study, collected, analyzed and interpreted the data, and drafted the article. ASB: involved in statistical analysis. ACD: involved in statistical analysis and critical revision of the article. MT: involved in statistical analysis. GS, MSC, AG, IGM, PDG, MB, NS, DRG and LBL: involved in data provision and critical revision of the article. ELR: overall supervision of the study and involved in critical revision of the article.

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Conflict of interest

None to declare.

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