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MELD exception points provide an enourmous advantage for receiving a liver transplant in Brazil

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ABSTRACT – **Background** – Current policy for listing to liver transplant (LT) may place cirrhotic patients without MELD exception points (CIR) in a disadvantageous position if compared to patients enlisted with appealed MELD scores – patients with hepatocellular carcinoma (HCC) or special conditions other than hepatocellular carcinoma (SPE). Transplant rates, delisting, and waitlist mortality of CIR, HCC, and SPE candidates were compared. **Objective** – The aim of this study is to counterweight the listing rate and speed of listing of HCC, SPE, and CIR patients. To the best of our knowledge, this is the first study comparing the outcomes of patients enlisted for SPE to those of HCC and CIR. In several countries worldwide, SPE patients also receive appealed MELD scores in a similar way of HCC patients. **Methods** – Two cohorts of patients listed for LT in a single institution were evaluated. The first cohort (C1, n=180) included all patients enlisted on August 1st, 2008, and all additional patients listed from this date until July 31st, 2009. The second cohort (C2, n=109) included all patients present on the LT list on October 1st, 2012, and all additional patients listed from this date until May 2014. **Results** – In both cohorts, HCC patients had a higher chance of receiving a LT than CIR patients (C1HR =2.05, 95%CI=1.54–2.72, *P*<0.0001; C2HR =3.17, 95%CI =1.83–5.52, *P*<0.0001). For C1, 1-year waiting list mortality was 21.6% (30.0% for CIR vs 9.5% for HCC vs 7.1% for SPE) (*P*<0.001). For C2, 1-year waiting list mortality was 13.3% (25.7% for CIR, 8.3% for HCC, and 4.0% for SPE) (*P*<0.001). Post-transplant survival was similar among the three groups. **Conclusion** – Compared to CIR, SPE and HCC patients had lower wait list mortality. CIR patients had the highest waitlist mortality and the lowest odd of LT. Current LT allocation system does not allow equitable organ allocation.

HEADINGS – Liver transplant. Liver diseases. Hepatocellular carcinoma. Hepatic cirrhosis. Severity of illness index. Waiting lists.

INTRODUCTION

Liver transplant (LT) is the treatment of choice for a number of serious and life-threatening liver diseases. However, the small number of donors has been a major obstacle to performance of more procedures. Moreover, organ allocation policies are not always based on fair and objective parameters[1-7].

Brazil is the World's third leading country in annual number of LTs performed, and the Model for End-Stage Liver Disease (MELD) allocation system was introduced in Brazil in 2006. In several countries worldwide, exception points are given to patients with hepatocellular carcinoma (HCC) upon inclusion on the transplant waiting list. In Brazil, an appealed MELD score of 20 is granted to HCC patients, progressing to a score of 24 after a period of 3 months, and achieving an appealed score of 29 starting at 6 months after waitlist inclusion. In contrast, patients with decompensated cirrhosis (CIR) are transplanted based on their calculated MELD score. Exceptionally, a few cirrhotic patients suffer from special health conditions other than HCC (SPE), being listed for LT under appealed MELD scores that are similar to those attributed to patients with HCC under the Milan criteria. Those special conditions vary from country to country, but may involve refractory ascites, persistent encephalopathy with one or more grade 3 or 4 acute bouts, repeated episodes of cholangitis, and intractable pruritus[1-12]. In Brazil, such patients are evaluated by a committee of experts from the Ministry of Health. Specifically, the SPE patients need to fulfill specific criteria for receiving an appealed MELD score.

Liver graft allocation has been a matter of debate[1-5,8-10], even in countries with high donation rates. Navasa & Bruix[5] have addressed this topic, describing the waiting list pharmacokinetics, which is explained by Michaelis-Menten kinetics by theoretically discussing two populations of transplant candidates (MELD-served and non-MELD-served diseases) with regard to the rate of patients entering the system (or patients enlisted), rate of toxic clearance (or dropout), and product formation (or patients transplanted). They called the number of livers from donors "the enzyme concentration" that would drive the final product. We hypothesize that the current LT policy stated above may place CIR patients in a disadvantageous position compared to the non-MELD-served population of HCC and SPE patients. The aim of the present study was to compare evaluation time, rates of inclusion on the transplant waiting list, transplant rates, delisting, waiting list mortality, and survival of LT candidates divided into three populations: LT candidates with CIR, SPE, and HCC. Specifically, this is the first study to evaluate and compare the listing rate of HCC, SPE, and CIR patients.

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METHODS

This study was approved by the Ethical Committee of Research of *Hospital de Clínicas de Porto Alegre* (GPPG–HCPA / study number 14-0347) (CAAE: 27256914.0.0000.5327). The study is in accordance with Resolution 466/2012 of the National Health Council of the Ministry of Health (Brazil), which deals with the Code of Ethics for Human Research. Written informed consent was obtained from all individual participants included in the Second Cohort. The need for informed consent was waived for the patients in the First Cohort (analyzed retrospectively) by the IRB of HCPA.

A total of 347 patients with an indication for LT were included in this study. The patients were evaluated by the Adult Liver Transplant Program from *Hospital de Clínicas de Porto Alegre*, a university-affiliated tertiary care hospital in Southern Brazil. The first cohort (C1) consisted of patients who were present on the LT list on August 1st, 2008, and all additional patients listed from this date until July 31st, 2009. This cohort was analyzed retrospectively. The second cohort (C2) consisted of patients who were present on the LT list on October 1st, 2012, and all additional patients who were evaluated for LT from this date until May 2014. This cohort was analyzed prospectively. Both cohorts were followed until November 30th, 2015.

All enlisted patients aged >18 years with an indication for LT due to clinical complications of CIR, HCC, and SPE were eligible for inclusion. LT candidates due to acute liver failure and patients listed for a re-transplant were excluded.

The following variables were analyzed for all patients in both cohorts: age, sex, disease etiology, date of indication for LT, date of waiting list registration, evaluation time (time elapsed between indication and listing), length of time on the waiting list, dropout rates, waiting list mortality, date of the final event, date of LT, post-transplant death, and date of post-transplant death. In C2, the following variables were also analyzed: MELD score at indication for LT, MELD at the time of listing, calculated and appealed MELD prior to surgery, and MELD-sodium (MELD-Na).

In both cohorts, the participants were divided into three groups: patients with CIR, HCC, and SPE. SPE were defined as conditions in which, as in HCC, exception points are given to patients in addition to the MELD score, such as in persistent hepatic encephalopathy, refractory ascites, hepatic hydrothorax, intractable pruritus, and recurrent cholangitis, in accordance with current Brazilian legislation[12].

The data were tabulated in a Microsoft Excel spreadsheet and analyzed using SPSS, version 21.0. A *P*-value of <0.05 (two-tailed) was considered statistically significant. In the descriptive analysis, continuous variables with normal distribution were expressed as mean (SD) and those with skewed distribution were expressed as median and interquartile range. Categorical variables were expressed as absolute numbers and percentages. In the inferential analysis, the log-rank test was used to compare survival curves estimated using the Kaplan-Meier method. The Mann-Whitney and Kruskal-Wallis tests were used to compare the length of time from waiting list registration and indication until LT between groups and per blood type. Group effects on the probability of LT were assessed by hazard ratios (HR) and 95% confidence intervals (95%CI).

RESULTS

A total of 347 patients were included in this study (180 in C1 and 167 in C2). C1 was composed of patients present on the LT list on August 1st, 2008, and all additional patients listed from this date until July 31st, 2009. This cohort was composed only by patients enlisted to LT.

C2 was composed of 167 patients who were evaluated for LT. Of these, 58 patients were not enlisted due to several contraindications or refused to undergo LT. All patients who were present on the LT list on October 1st, 2012, and all additional patients listed from this date until May 2014 (n=109) were analyzed prospectively, being followed until November 30th, 2015. The rate of enlisted patients in C2 was 65.3% (109 of 167 patients). Therefore, a total of 289 enlisted patients (C1=180, C2=109) were analyzed in this study.

The general characteristics of all enlisted patients are shown in TABLE 1. There was no difference between the three groups (CIR, HCC, and SPE) in sex ratio in either cohort. Chronic hepatitis C virus (HCV) infection was the most common cause of LT in both cohorts. In both cohorts, the mean age of HCC patients was significantly higher than that of patients in the other two groups (CIR and SPE). HCC patients also had a higher rate of HCV infection than that of CIR and SPE patients.

In C1, out of the total of 180 patients, 108 (60.0%) had CIR, 58 (32.2%) had HCC, and 14 (7.8%) had SPE (FIGURE 1.A).

In C2, out of the total of 109 enlisted patients, 45 (47.9%) had CIR, 38 (34.9%) had HCC, and 26 (23.9%) had SPE. For the CIR group, 45 of the 94 patients evaluated (47.9%) were enlisted. For HCC, 38 of the 45 patients evaluated (84.4%) were enlisted. For SPE, 26 of the 28 patients evaluated (92.8%) were enlisted (*P*<0.001) (FIGURE 1.B).

TABLE 1. General features of all 289 enlisted patients included in this study.

	Total sample	CIR	HCC	SPE	*P*
First cohort	n=180	n=108	n=58	n=14	
Age, years – mean ±SD	53.7±12.1	51.3±12.8	58.7±8.0	49.8±14.7	<0.001
Male – n (%)	108 (60%)	65	39	8	0.934
HCV – n (%)	125 (69.4%)	65	53	7	<0.001
Second cohort[a, b]	n=109	n=45	n=38	n=26	
Age, years – mean ±SD	53.2±12.8	51.0±14.2	60.0±6.7	49.8±11.5	<0.001
Male – n (%)	63 (58.8%)	24	22	17	0.861
HCV – n (%)	62 (56.8%)	25	29	8	<0.001

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions; HCV: hepatitis C virus infection. [a] This cohort included all patients evaluated for liver transplant (n=167). [b] 109 of the total of 167 patients in this cohort were listed for liver transplant.

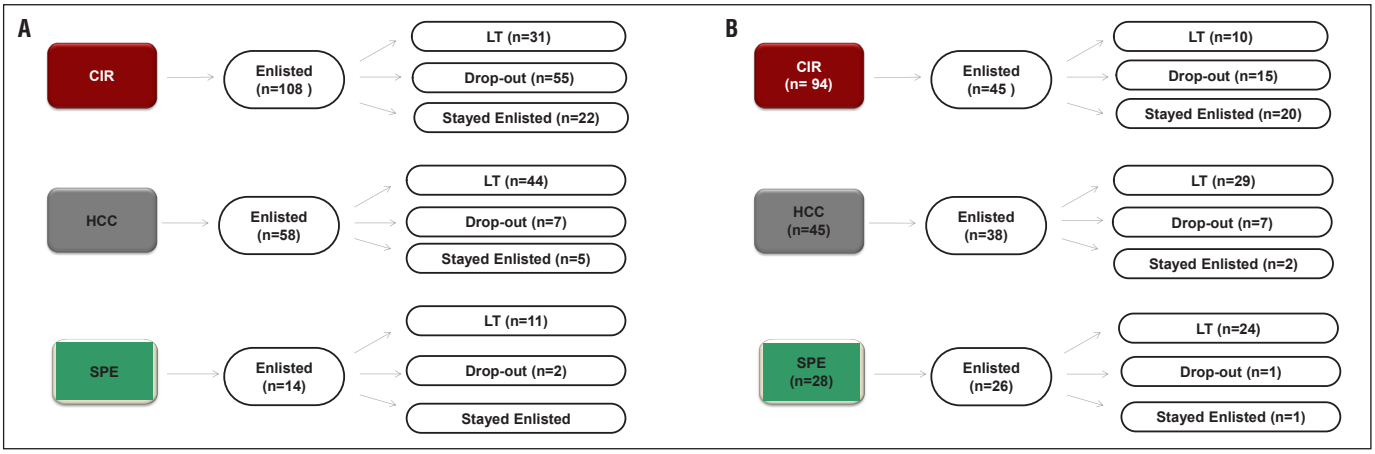

FIGURE 1. Dynamics of the transplant list. A) First cohort (n=180). B) Second cohort, including all patients evaluated (n=167). CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions.

In C2, the mean overall time (for all patients) from selection to enlisting was 246 days (95%CI, 167–330) (TABLE 2). For CIR, the mean time from selection to enlisting was 321 days (95%CI, 203–440) vs 66 days (95%CI, 43–89) for HCC vs 375 days (95%CI, 111–639) for SPE (P<0.001 for comparison among all three groups; P=0.012 for CIR vs HCC; P=0.894 for CIR vs SPE; P=0.011 for HCC vs SPE).

TABLE 3 shows the rate of patients who entered the waiting list per group in both cohorts. Three months after the pre-transplant evaluation, more than half of the patients with HCC (62.9% in C1 and 61.9% in C2) were enlisted, while only 28.2% and 17.1% of patients with CIR, respectively, were enlisted. Wait-listing rate was higher in the SPE group than in the CIR group in both cohorts (P<0.001).

In C2, MELD scores were evaluated at different time points (TABLE 4). Patients with CIR needed to achieve a calculated MELD score much higher than that of patients in the other two groups to be transplanted (MELD 25 for CIR vs 11 for HCC vs 13 for SPE). Before LT, the appealed MELD score was 24 in both the HCC and SPE groups.

TABLE 2. Time elapsed between transplant indication and listing. First cohort comparisons: CIR vs HCC, P<0.001; SPE vs CIR, P=0.188. SPE vs HCC, P<0.001. Second cohort comparisons: CIR vs HCC, P<0.001. SPE vs CIR, P<0.001; SPE vs HCC, P=0.047.

Variables	Fist cohort (n=189)			Second cohort (n=110), Overall mean = 246 days		
	CIR	HCC	SPE	CIR	HCC	SPE
Days – mean (95%CI)	194 (152–236)	36 (21–50)	98 (0–308)	321 (203–440)	66 (43–89)	375 (111–639)

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions.

TABLE 3. Rate of patients entering the waiting list (%).

	At 3 months	At 6 months	At 12 months	Median (95%CI), months
First cohort				
HCC	62.9%	74.2%	83.9%	1.20 (0.72–1.68)
SPE	42.9%	64.3%	78.6%	3.27 (0.00–10.3)
CIR	28.2%	47.3%	71.8%	6.47 (5.07–7.87)
Second cohort				
HCC	61.9%	81.0%	88.6%	1.73 (0.55–2.92)
SPE	45.7%	47.1%	73.5%	6.13 (0.63–11.6)
CIR	17.1%	24.2%	40.1%	26.1 (11.0–41.2)

HCC: hepatocellular carcinoma; SPE: special conditions; CIR: decompensated cirrhosis.

TABLE 4. Median (Md) calculated MELD scores at different time points: second cohort (n=109).

MELD	Groups			P*
	CIR Md (P25–P75)	HCC Md (P25–P75)	SPE Md (P25–P75)	
Atindication	15 (11–22)[c]	10 (8–11)[a]	12 (8–15)[b]	<0.001
Atlisting	18.5 (12–24)[c]	9 (7–12)[a]	13 (7.8–16.5)[b]	<0.001
Transplant date*	25 (23.8–31.3)[c]	11 (9–13)[a]	13 (10.3–16)[b]	<0.001
MELD-Na on Transplant date**	25 (23.8–32.8)[c]	11 (9.5–13)[a]	13.5 (10.3–18.8)[b]	<0.001
MELD-appealed on transplant date	–	24 (24–29)	24 (24–29)	–

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions. [a,b,c] Values with different superscript letters are significantly different at the 5% significance level determined by the Mann-Whitney test. *Kruskal-Wallis test. **MELD scores and MELD-Na scores at the date of transplant were collected only for the 63 patients who underwent LT in this cohort).

TABLE 5 shows the time from LT indication to LT and also the time from enlisting to LT in C2. Regarding length of time from indication to LT, CIR patients in C2 had the shortest waiting time among the three groups (*P*=0.036). The median waiting time from enlisting to LT was 54 days for CIR, 160 days for HCC, and 238 days for SPE (*P*<0.001) (TABLE 5).

TABLE 5. Length of time on the waiting list: second cohort.

Time elapsed (days)	Groups			*P***
	CIR (n=10) Md (P25–P75)	HCC (n=29) Md (P25–P75)	SPE (n=24) Md (P25–P75)	
Indication to transplant	205 (80–677)	235 (164–322)*	472 (212–634)*	0.036
LT Wait list inclusion	54 (31–103)*	160 (127–213)*	238 (137–391)*	0.001

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions; Md: median; LT: liver transplant. *Values with different superscript letters are significantly different at the 5% significance level determined by the Mann-Whitney test. **Kruskal-Wallis test.

The overall LT rate in C1 was 47.8% (86/180). LT rates in this cohort were 28.7% (31/108) for CIR patients, 75.9% (44/58) for HCC patients, and 88.6% (11/14) for SPE patients (*P*<0.001).

In C2, the overall LT rate was 57.8% (63/109). For CIR, LT rate was 22.2% (10/45). For HCC, LT rate was 76.4% (29/38). For SPE, LT rate was 92.3% (24/26). In both cohorts, patients with HCC had a higher chance of receiving a LT.

In C1, the LT HR for HCC vs CIR was 2.05 (95%CI, 1.54–2.72; *P*<0.0001). In the same cohort, SPE patients had a higher chance of receiving a LT than did CIR patients (HR=1.30; 95%CI, 1.083–1.569; *P*<0.0001). SPE and HCC patients had a similar chance of receiving a LT (HR=1.03; 95%CI, 0.796–1.331; *P*<0.83).

In C2, the LT HR for HCC vs CIR was 3.17 (95%CI, 1.83–5.52; *P*<0.0001). Likewise, SPE patients also had a much higher chance of receiving a LT than did CIR patients (HR=3.216; 95%CI, 1.900–1.544; *P*<0.0001). SPE and HCC patients had a similar chance of receiving a LT (HR=1.462; 95%CI, 0.985–2.170; *P*<0.136).

Overall post-transplant survival rates were similar among the three groups in both cohorts (*P*=0.26 for C1; *P*=0.384 for C2). FIGURE 2.A and TABLE 6.A show the survival rates for the three groups of patients in C1. In this cohort, 1-year survival was 74.2% for CIR, 79.5% for HCC, and 90.9% for SPE (*P*=0.401 for CIR vs HCC; *P*=0.124 for CIR vs SPE; *P*=0.220 for HCC vs SPE) (TABLE 6.A).

FIGURE 2.B and TABLE 6.B show the survival rates for the 3 groups of patients in C2. One-year survival was 80.0% for CIR, 85.9% for HCC, and 72.4% for SPE (*P*=0.886 for CIR vs HCC; *P*=0.374 for CIR vs SPE; *P*=0.192 for HCC vs SPE) (TABLE 6.B).

Intention-to-treat survival was similar among the three groups in both cohorts. In C1, 1-year survival was 53.5% for CIR, 50.5% for HCC, and 75.0% for SPE (*P*=0.9). In C2, 1-year survival was 72.5% for CIR, 84.2% for HCC, and 88.0% for SPE (*P*=0.5).

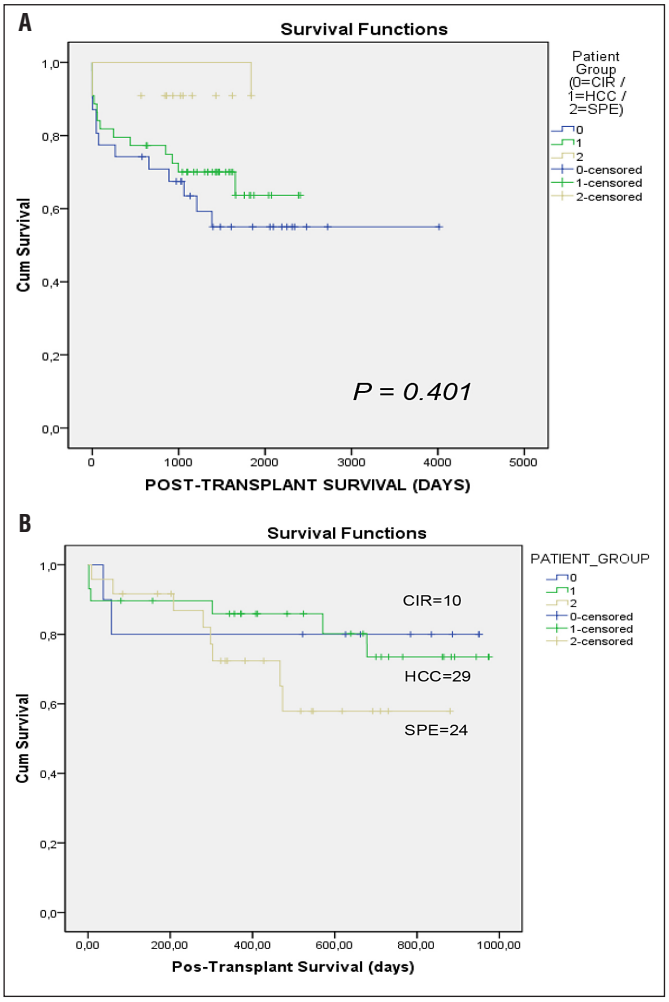

FIGURE 2. Survival rates after liver transplant. A) First cohort. B) Second cohort.
CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions.

TABLE 6.A. Survival rates after liver transplant: first cohort.

Groups*	Post-transplant survival (%)		
	1 year	2 years	3 years
CIR	74.2%	70.8%	63.5%
HCC	79.5%	77.3%	70.0%
SPE	90.9%	90.9%	90.9%
Overall	79.1%	76.7%	70.1%

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions. *CIR vs HCC: *P*=0.401. CIR vs SPE: *P*=0.124. SPE vs HCC: *P*=0.220.

TABLE 6.B. Survival rates after liver transplant: second cohort.

Groups*	Post-transplant survival (%)		
	1 year	2 years	3 years
CIR	80.0%	80.0%	80.0%
HCC	85.9%	73.5%	73.5%
SPE	72.4%	57.9%	57.9%
Overall	80.2%	69.3%	69.3%

CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions. *CIR vs HCC: *P*=0.886. CIR vs SPE: *P*=0.374. SPE vs HCC: *P*=0.192.

In C1, the overall waiting list mortality rate, as estimated using the Kaplan-Meier method (first year in-list mortality), was 22.2% (FIGURE 3.A). One-year waiting list mortality was 30.9% for CIR, 9.5% for HCC, and 7.1% for SPE (P<0.001 for comparison among all three groups; P<0.001 for comparisons between CIR and each of the two other groups; P=0.878 for comparison between HCC and SPE) (FIGURE 3.B). During a mean follow-up period of 2372 days, 64 out of the total of 180 patients (35.6%) were delisted either due to death (n=62) or to disease progression (n=2) (FIGURE 1.A). Per group, dropout rates were 55/108 (50.9%) for patients with CIR, 7/58 (12.1%) for patients with HCC, and 2/14 (14.3%) for patients with SPE (P<0.001 for 3-group analysis).

In C2, the overall waiting list mortality rate, as estimated using the Kaplan-Meier method (first year in-list mortality), was 13.3% (FIGURE 4.A). One-year waiting list mortality was 25.7% for CIR, 8.3% for HCC, and 4.0% for SPE (P<0.001 for comparison among all three groups; P<0.001 for comparisons between CIR and each of the two other groups; P=0.878 for comparison between HCC and SPE) (FIGURE 4.B). Sixteen out of the total of 109 patients died while on the LT list (14.7%). During a mean follow-up period of 973 days, waiting list mortality was 26.7% (12/45) for CIR, 7.9% (3/38) for HCC, and 3.8% (1/26) for SPE (P<0.001). During the entire follow-up period, the dropout rate for this cohort was 29.4% (32/109). Dropout rates were 33.3% (15/46) for CIR, 18.4% (7/38) for HCC, and 3.84% (1/26) for SPE (P<0.001 for 3-group analysis).

DISCUSSION

The present study evaluated two cohorts of patients with liver disease mainly related to HCV infection in a large referral tertiary university hospital located in the south of Brazil, a country that is the World's third country in number of LTs performed annually. This study has shown that CIR patients were less likely than HCC and SPE patients to be listed for LT. CIR patients also waited longer to be listed than patients prioritized by the MELD exception points (HCC and SPE). The transplant rate of CIR patients also was much lower than those of the other two groups of patients. The mortality of CIR patients also was substantially higher than that of HCC and SPE patients.

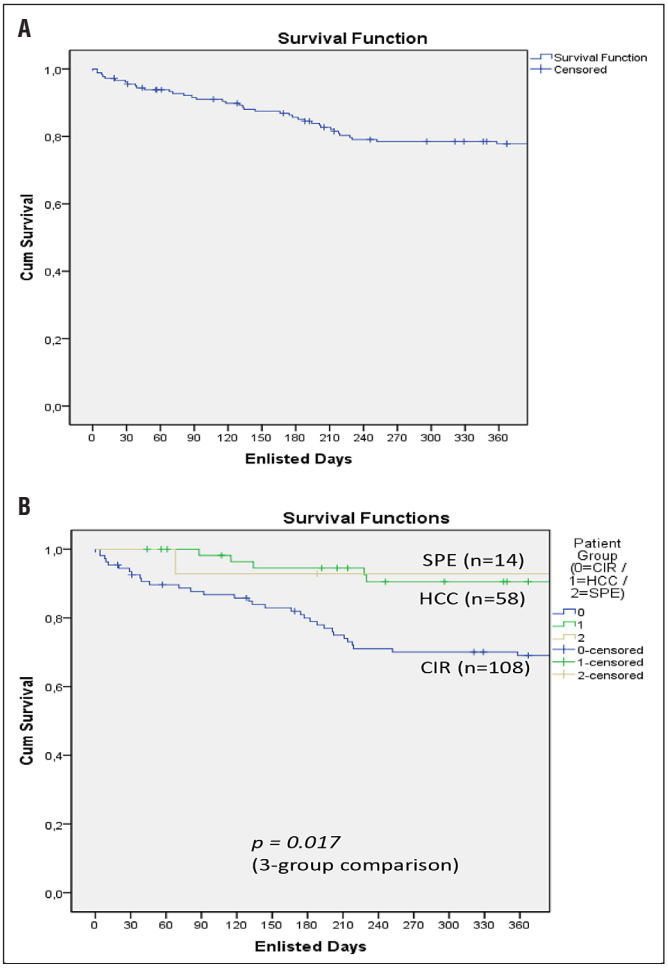

FIGURE 3. One-year survival rates after being listed for liver transplant. A) Entire first cohort. B) First cohort stratified by patient group. Patients who underwent a liver transplant during the 1-year follow-up were censored. CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions.

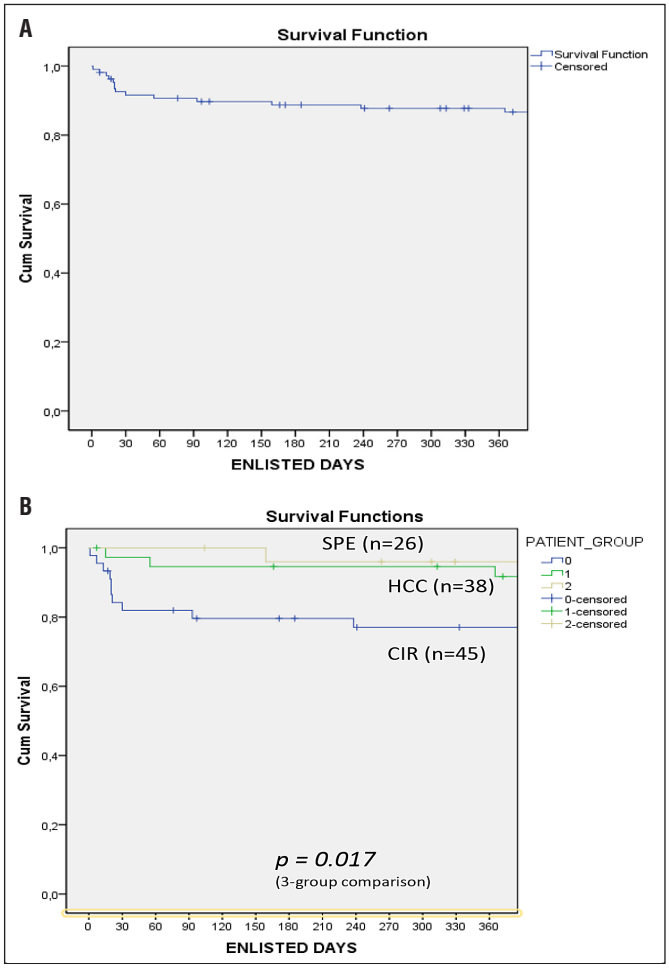

FIGURE 4. One-year survival rates after being listed for liver transplant. A) Entire second cohort. B) Second cohort stratified by patient group. Patients who underwent a liver transplant during the 1-year follow-up were censored. CIR: decompensated cirrhosis; HCC: hepatocellular carcinoma; SPE: special conditions.

To the best of our knowledge, no prior studies have compared the listing rate and the speed of listing and the of CIR as compared to that HCC and SPE patients. Thus, this is the first study to evaluate and compare both the enlisting speed and rates of CIR, HCC and SPE patients. Another peculiar aspect of the present study was the evaluation of the dynamics in the waiting list of SPE patients in comparison to other two populations of patients (CIR and HCC) listed for LT.

In the present study, CIR patients were less likely than HCC and SPE patients to be listed for LT. In C2, less than half of all patients with CIR evaluated for LT were enlisted (47.9%), as compared to 84.4% in the HCC group and 92% in the SPE group.

From selection to inclusion on the transplant waiting list, CIR patients waited longer than did HCC patients. In C1, the mean waiting time from indication to enlisting was 158 days longer for CIR patients than for HCC patients. In C2, this period was 255 days longer. In C1, CIR patients also had a longer waiting time to LT than that of SPE patients (mean of 96 days longer). Interestingly, SPE patients had a longer waiting time than that of CIR patients in C2. In C2, the mean time from selection to enlisting was almost five times longer for CIR patients than for HCC patients (321 vs 66 days). Three months after the pre-transplant evaluation, more than half of HCC patients (62.9% in C1 and 61.9% in C2) were enlisted, while only 28.2% and 17.1% of CIR patients, respectively, were enlisted.

Prior studies have shown that introduction of the introduction of the MELD score on liver allocation was associated to an increased patient survival[13]. Even if MELD score cannot reflect the risk of dropout due to tumor progression, patients with HCC appear to benefit from the current policy of exception point allocation[7,14]. In the present study, patients with MELD exception points (HCC and SPE) also had a much higher chance of receiving a LT than did CIR patients. In C1, the odds of LT of HCC vs CIR patients were nearly twice. In the same cohort, enlisted patients with SPE had a 30% higher chance of receiving a LT than those with CIR. In C2, both HCC and SPE patients had over a three times higher chance of receiving a LT than CIR patients. Likewise, previous studies comparing the LT chances of waitlisted HCC patients to those of non-prioritized patients have reported a significantly higher likelihood of transplant in the HCC group vs the non-prioritized group[15,16].

In the present study, the calculated MELD score was higher in the CIR group at all time points evaluated: at indication for LT, at the time of listing, and before LT. In C2, patients with CIR needed to achieve a calculated MELD score much higher than that of patients in the other two groups to be transplanted (MELD 25 for CIR vs 11 for HCC vs 13 for SPE). Before LT, the appealed MELD score was 24 in both the HCC and SPE groups. This means that patients with CIR represent more severe cases based not only on the clinical point of view but also on MELD score. In addition, for these patients, dropout was nearly equivalent to death. Patients with HCC and SPE benefited from the exception points and were often transplanted with an appealed MELD score of 24 before 6 months on the waiting list. Considering that the goal of prioritization is to allow different populations to have an equal access to LT[5], it becomes clear that the organ allocation policy has been detrimental to CIR patients.

The advantage of patients with MELD exception points has driven a recent change in the liver allocation rules in the United States. Since October 2015, HCC candidates must wait 6 months after initial application to obtain exception points. Historically, HCC candidates have experienced a substantial advantage in deceased donor liver allocation with lower waiting list mortality/dropout within 1 year of listing than have non-HCC candidates (11.5% vs 17.7%). However, after the 2015 liver allocation policy change, this 6-month waiting period has attenuated the LT advantage of HCC patients over the non-prioritized patients[17,18].

CIR patients also had higher dropout and mortality rates. The present study revealed that the chance of being delisted was three times higher for CIR patients than for HCC patients. In spite of a substantial decrease in 1-year waiting list mortality from C1 to C2 (22.2% to 13.3%), waiting list mortality among CIR patients did not show any decrease. Indeed, Mehta et al. reported that patients with HCC are less likely to die on the waiting list than are other patients[19]. An additional study found that the rate of waitlist removal for death or clinical deterioration was significantly higher in non-HCC candidates, which suggests that the current practice of granting exception points to patients with HCC should be reassessed[14]. In 2003, the Bologna Transplantation Center proposed a MELD adjustment based on native MELD scores or laboratory tests that added 1 point to the score for every month on the list plus the tumor stage score, which remains a matter of debate. This illustrates the continuing concern of the transplant community regarding this topic.

The present study also revealed that the post-transplant survival for CIR patients was comparable to those of HCC and SPE patients in both cohorts. This finding contributes to the concept that CIR patients underwent an unfair liver allocation for LT.

This is a single-center analysis that may be subject to local or institutional issues, which may have some influence on the external validity of the study. A Brazilian single center analysis revealed that the prevalence of HCC among patients undergoing LT was higher in the post-MELD era as compared to the pre-MELD era[20]. However, a recent study evaluating on the outcomes of enlisted patients from the other liver transplant center from Porto Alegre also revealed that HCC patients confirmed that that HCC patients were transplanted fasted and at a higher rate than CIR patients[21]. Unfortunately, except from few studies performed in the USA, multicenter studies evaluating the dynamics of the LT waiting list are lacking[22-24]. Thus, single center analysis such as the one performed herein currently may be the only source to document the outcomes of national LT allocation policies. In addition to that, single center studies are less subject to selection biases than analyses of large multicenter database. A potential bias of the present study is that this study population was largely composed of HCV recipients (70%). However, HCV is still the leading indication for LT in the United States (33% of all LTs) and in several Western countries[25,26]. Therefore, evaluating patients undergoing LT for HCV still is of utmost importance. A recent study has evaluated a cohort of patients waitlisted for LT in Brazil. Although the cohort was composed of a much lower percentage of HCV patients (26.8%) than that of the present study, the study also reported that prioritized patients (HCC and SPE) have a much higher transplant rate (56.7% vs 19.1%) and a lower waiting list mortality (18.4% vs 19.5%) than non-prioritized patients[27].

In conclusion, this study revealed that cirrhotic patients with an appealed MELD score (HCC and SPE) have a two times higher chance of being listed for LT than non-prioritized candidates. Enlisted patients with HCC also waited much shorter to receive a LT than did all other enlisted patients. Additionally, HCC and SPE patients had a 2- to 3-fold greater chance of receiving a LT than the non-prioritized candidates. SPE patients had the lowest waiting list mortality. Conversely, CIR patients had the highest waiting list

mortality. Conversely, post-transplant mortality of CIR patients was not higher to those of HCC and SPE points. This finding corroborates that a policy change that would increase the transplant rate of CIR patients likely would not deteriorate the post-transplant results. These finding suggest that the current LT allocation system does not allow equitable organ allocation in Brazil. Therefore, the current organ allocation policy in Brazil and in several countries worldwide should be reassessed to ensure an equitable process for all LT candidates. Adoption of the 6-month waiting period before granting HCC patients MELD exception points would potentially lead to a more equitable process. Another potential modification would be to reduce the maximum MELD exception points to 24. This would make CIR patients more competitive for deceased donor liver grafts than they are nowadays. We believe that similar adjustments should be applied to SPE recipients. As these patients tend to wait longer than HCC patients to be listed for LT, perhaps a shorter waiting period (e.g., 3 months) could be applied before those patients are granted MELD exception points.

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Authors' contribution

Study conception and design: Arruda S, Álvares-da-Silva MR. Acquisition of data: Arruda S, Chedid MF, Jacinto MM. Analysis and interpretation of data: Arruda S, Chedid MF, Jacinto MM, Álvares-da-Silva MR. Drafting of manuscript: Arruda S, Chedid MF, Álvares-da-Silva MR. Critical revision of manuscript: Chedid MF, Alvares-da-Silva MR.

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Arruda S, Chedid MF, Jacinto MM, Álvares-da-Silva MR. Os critérios especiais de pontuação MELD proporcionam uma enorme vantagem a pacientes listados para transplante de fígado no Brasil. Arq Gastroenterol. 2020;57(3):254-61.

RESUMO – **Contexto** – É possível que política atual de inclusão no transplante de fígado (LT) esteja colocando os pacientes cirróticos sem pontos de exceção MELD (CIR) em uma posição desvantajosa se comparados aos pacientes listados com escores de critério especial MELD – pacientes com carcinoma hepatocelular (HCC) ou outras condições especiais (SPE). As taxas de transplante, exclusão e mortalidade de lista de espera de candidatos com CIR, HCC e SPE foram comparadas. **Objetivo** – O objetivo deste estudo é comparar a taxa de listagem e também a velocidade de listagem de pacientes listados pelas três possíveis categorias de listagem no Brasil (HCC, SPE e CIR). Há muito poucos estudos prévios comparando os desfechos de pacientes listados por SPE ao desfecho de pacientes com HCC e também ao desfecho de pacientes não priorizados (CIR). Em muitos países, pacientes listados para transplante de fígado com SPE são priorizados para transplante em um modo similar ao que ocorre com pacientes com HCC. **Métodos** – Foram avaliadas duas coortes de pacientes listados para LT em uma única instituição. A primeira coorte (C1, n=180) incluiu todos os pacientes listados em 1º de agosto de 2008 e todos os pacientes adicionais listados dessa data até 31 de julho de 2009. A segunda coorte (C2, n=109) incluiu todos os pacientes presentes na LT em 1º de outubro de 2012 e todos os pacientes listados dessa data até maio de 2014. **Resultados** – Em ambas as coortes, os pacientes com CHC tiveram uma chance maior de receber uma LT do que os pacientes com CIR (C1HR =2,05, CI95% =1,54–2,72, *P*<0,0001; C2HR =3,17, CI95% =1,83–5,52, *P*<0,0001). Para C1, a mortalidade na lista de espera em um ano foi de 21,6% (30,0% para CIR vs 9,5% para HCC vs 7,1% para SPE) (*P*<0,001). Para C2, a mortalidade na lista de espera em um ano foi de 13,3% (25,7% para CIR, 8,3% para HCC e 4,0% para SPE) (*P*<0,001). A sobrevida pós-transplante foi semelhante entre os três grupos. **Conclusão** – Comparados aos pacientes CIR, os pacientes SPE e HCC, apresentaram menor mortalidade na lista de espera. Os pacientes com CIR tiveram a maior mortalidade na lista de espera e a menor probabilidade de LT. O atual sistema de alocação de LT não permite alocação equitativa de órgãos.

DESCRITORES – Transplante de fígado. Hepatopatias. Carcinoma hepatocelular. Cirrose hepática. Índice de gravidade de doença. Listas de espera.

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