DOI:10.1111/j.1477-2574.2010.00199.x

HPB

ORIGINAL ARTICLE

Model for end-stage liver disease-based allocation system for liver transplantation in Argentina: does it work outside the United States?

L. McCormack[1], A. Gadano[2], J. Lendoire[3], O. Imventarza[4], O. Andriani[5], O. Gil[6], L. Toselli[7], L. Bisigniano[8] & E. de Santibañes[2]

[1]Liver Transplant Unit, Hospital Alemán of Buenos Aires, [2]Liver Transplant Unit, Hospital Italiano of Buenos Aires, [3]Liver Transplant Unit, Sanatorio Trinidad Mitre, [4]Liver Transplant Unit, Hospital Argerich, Buenos Aires, [5]Liver Transplant Unit, Hospital Austral University, Pilar, [6]Liver Transplant Unit, Sanatorio Allende of Córdoba, Córdoba, [7]Liver Transplant Unit, CRAI Norte, and [8]Scientific and Technical Section, INCUCAI, Buenos Aires, Argentina

Abstract

Background: In July 2005, Argentina was the first country after the United States to adopt the MELD system. The purpose of the present study was to analyse the impact of this new system on the adult liver waiting list (WL).

Methods: Between 2005 and 2009, 1773 adult patients were listed for liver transplantation: 150 emergencies and 1623 electives. Elective patients were categorized using the MELD system. A prospective database was used to analyse mortality and probability to be transplanted (PTBT) on the WL.

Results: The waiting time increased inversely with the MELD score and PTBT positively correlated with MELD score. With scores ≥ 18 the PTBT remained over 50%. However, the largest MELD subgroup with <10 points ($n = 433$) had the lower PTBT (3%). In contrast, patients with T_2 hepatocellular carcinoma benefited excessively with the highest PTBT (84.2%) and the lowest mortality rate (5.4%). The WL mortality increased after MELD adoption (10% vs. 14.8% vs. $P < 0.01$). Patients with <10 MELD points had >fourfold probability of dying on the WL than PTBT (14.3% vs. 3%; $P < 0.0001$).

Conclusions: After MELD implementation, WL mortality increased and most patients who died had a low MELD score. A comprehensive revision of the MELD system must be performed to include cultural and socio-economical variables that could affect each country individually.

Keywords

transplant, indications < transplant, ethical < transplant

Received 21 March 2010; accepted 8 June 2010

Correspondence

Lucas McCormack, Liver Transplantation, Hospital Alemán of Buenos Aires. Argentina, Av. Pueyrredón 1640, CP: 1118. Ciudad Autónoma de Buenos Aires. Argentina. Tel: +54 11 4727 7000; Fax: +54 11 4727 7014; E-mail: lmccormack@hospitalaleman.com

Introduction

At present, there is consensus that a liver allocation policy should use objective medical criteria to prioritize waiting candidates based on the severity of liver disease. Since February 2002, the allocation of grafts for liver transplantation (LT) from cadaveric donors in the US has been based on medical urgency, which is estimated according to the model for end-stage liver disease (MELD) score.[1] MELD is an objective score based on pre-transplantation laboratory data, including serum creatinine level, total bilirubin level and international normalized ratio (INR). The MELD-based allocation policy was designed prospectively using validated predictive models and employing a continuous scale in contrast to the previous subjective system.[2–4]

In the US, the change in the allocation system from a waiting time-based system to a risk-based system using the MELD score has lowered pre-transplant mortality, without adversely impacting post-transplant survival despite increased severity of illness at

This paper was presented at the International Hepato-Pancreato-Biliary Association Meeting, 18–22 April 2010, Buenos Aires, Argentina.

the time of transplantation.[1] Clearly, the new allocation system has been scrutinized more closely and rigorously than any other method for liver allocation.[5] Although this interest has been widespread throughout the world, few countries have adopted the system. To date, the MELD-based allocation system created and initiated in the US lacks international validation.

In Argentina, the first LT was performed in 1988. Initially, as in most countries, liver allocation policy was based on patient's location of care and time on the waiting list. Before 2005, two categories existed: emergency and non-emergency patients. Among the non-emergency patients, those requiring continuous intensive care received first priority (i.e. Urgency A), organ allocation was prioritized next to patients requiring continuous hospitalization (i.e. Urgency B), and finally to patients who were cared for at home (i.e. Electives). Among each category, as the waiting list continued to grow, waiting time became a major factor in determining who received a donor organ. In July 2005, Argentina was the first country that followed the US in adopting the MELD-based allocation system for patients requiring LT. Although more than two decades of LT history have passed, only case reports or a few partial single-centre experiences have been reported in the English literature from Argentina.[6–14]

With the intention to validate internationally the new allocation system using a large cohort of LT candidates, we analysed a consecutive series of patients listed for LT in Argentina for almost 4 years under the MELD system. This is the first report in the literature using a large national cohort of patients from a prospectively collected official database from the INCUCAI (Instituto Nacional Central Unico Coordinador de Ablacion e Implante) that represents the National Institute for organ allocation in Argentina.

Materials and methods

In July 2005, all liver transplant candidates listed in Argentina were re-categorized under the MELD-based allocation system. With the aim to assess the impact of the new allocation system on the waiting list of LT candidates, data referred to a cohort of consecutive adult patients (i.e. ≥18 years) listed between July 2005 and April 2009 who were analysed using a prospective collected national database.

All patients were grouped in two categories: emergency and non-emergency or elective. Emergency status included fulminant liver failure, primary non-failure of the graft or vascular complication after LT leading to the need of re-transplantation in the first 7 postoperative days. In the pre-MELD era, the elective category included all patients listed under the status Urgency A, Urgency B or Electives. After the MELD system implementation, each non-emergency patient was stratified according to the MELD score calculation and defined as elective. For patients in whom the MELD score was thought to estimate inaccurately their need of LT, each centre could make a request to an Experts Committee. for priority points A specific regulation including three entities for upgrading of the MELD score including familial amyloidotic polyneuropathy (16 points), hepatopulmonary syndrome (20 points) and T_2 hepatocellular carcinoma (HCC) defined as 1 tumour 2–5 cm or 2 or 3 tumors < 3 cm in diameter according to pre-operative imaging (22 points).[15] Similar to US practice, patients with a MELD score of 22 as a result of the pre-transplant diagnosis of T_2 HCC received an additional point for every 3 months on the waiting list.

For other conditions for which the need for LT was not defined accurately by the MELD score, each centre could also request additional points. Each non-established category in the regulation was considered individually by the Experts Committee to determine the appropriateness of the requested increase in priority on the basis of medical evidence from the literature or expert opinions.

During the MELD era, several adult candidates variables were analysed including age, gender, aetiology of liver disease, MELD score (i.e. score registered at the time of LT, drop-out, death or the most recent), waiting list time, status on the waiting list (emergency or non-emergency) and reasons for removal of the waiting list. For the global analysis of the cohort of patients, the MELD score calculation included additional points given as MELD exceptions.

Elective candidates were grouped according to the MELD points on the list as follows: <10, 10–13, 14–17, 18–21, 22–25, 26–29, 30–33, 34–37 and >37, to analyse intergroup variation of studied variables. To properly assess accessibility to cadaveric donor LT and mortality rate on the waiting list for each subgroup of MELD points regardless of the decision of the Experts Committee, all patients with additional priority MELD points were excluded and analysed separately.

To analyse the impact of the MELD system adoption on mortality rate on the waiting list for LT, many variables related to organ donation and transplantation activity were revised using the official registry at the INCUCAI. Since 2004 (i.e. first year before MELD adoption) analysis included: number of live and cadaveric donor LT, status on the waiting list (emergency or non-emergency), annual total and multi-organic donation rate, deaths and number of patients on the waiting list. Using the official national registry, the number of centres performing adult LT and its activity was also revised.[16]

Statistical analysis

Summary data are presented as median (range) or interquartile range. Differences between groups were tested using the χ^2-test for categorical and Mann–Whitney *U*-test for continuous variables. All tests were performed two-tailed. Statistical significance was indicated by *P*-values of less than 0.05. Calculations were undertaken with SPSS statistical software package (version 13.0; SPSS Inc., Chicago, IL, USA).

Results

Donation rate, waiting list and transplantation activity in Argentina

The national overall donation rate [from 10.5 donors per million in population (PMP) to 13.1] and the multi-organic donation rate

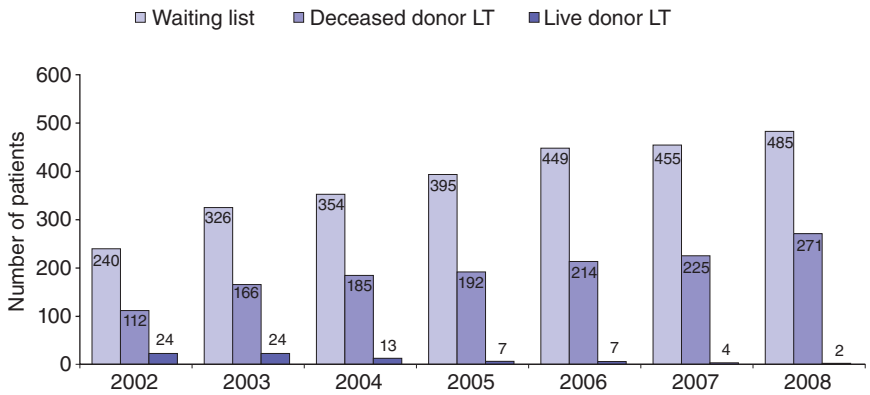


Figure 1 Number of adult patients included in the national waiting list and number of cadaveric and live donor liver transplantations performed in the last years in Argentina

(5.4 to 7.6 donors PMP) had a continuous increment from 2004 to 2008. However, a great variation in the national overall donation rate was documented among 24 regions or provinces in our country ranging from as high as 34.5 PMP in Corrientes to as low as zero in Santiago del Estero and San Luis.

During the study period, a cohort of 1773 adult patients was listed for LT in Argentina. The total number of patients on the waiting list and the number of LT had a continuous increment reaching 485 patients on the national waiting list and 271 cadaveric donor LT, respectively, during 2008 (Fig. 1). To assess the magnitude of the gap between the number of patients on the waiting list and the number of deceased donor LT, the ratio of deceased donor LT/number of patients on the waiting list was used. This ratio increased constantly with time from 0.46 in 2002, 0.48 in 2004 and peak of 0.55 in 2008 demonstrating that the increment was higher in the number of transplants compared with the number of patients included on the waiting list. Inversely, the number of live donor LT continuously decreased in the same period which is unusual in the last years. The overall access of elective adult candidates to cadaveric LT was 41% and less than 1% to live donor LT.

A total of 760 adult LT (rate per year: 202) were performed in this 45-month period: 665 in elective and 95 in emergency candidates. The number of accredited centres to perform LT at the end of 2008 was 18. However, when the number of LT was analysed individually in each centre during 2008, dissimilar activity was observed: 2 centres with no transplant activity, 9 centres with <10 transplants, 4 with 10–20 and only 5 centres performed > 20 transplants in 2008.

Characteristics of elective adult patients listed for LT

In the study period, among all adult candidates included in the national liver waiting list, 150 (28%) were under emergency and 1623 (72%) under elective status (Table 1). Patients listed under elective status were older and more frequently male when compared with emergency candidates. The most frequent underlying liver disorder in elective candidates was hepatitis C infection-related cirrhosis (25.4%) followed by alcoholic cirrhosis (18.7%), cryptogenic cirrhosis (13.1%), autoimmune hepatitis (9.9%), primary biliary cirrhosis (7.5%) and metabolic cirrhosis (3.2%).

The median MELD score of elective patients was 33 (range: 6–48). In this cohort, it was observed that 141/1623 (8.6%) patients had upgraded MELD scores as a result of extra-points provided according to the following entities: 2 familial amyloidotic polyneuropathy, 6 hepatopulmonary syndrome, 111 T_2 HCC and 22 other reasons not included in the official national regulation.

When stratified in subgroups according to the MELD scores, the number of cadaveric LT for elective candidates was mainly centralized in the subgroup with 22–25 MELD points (Fig. 2). Cadaveric LT for patients with MELD score < 18 were performed exceptionally during the study period.

Impact of MELD-based allocation system on probability to be transplanted

Adult elective patients had a median waiting list time of 155 days with an overall accessibility to decease donor LT of 41% (Table 1). As expected, the median waiting time increased inversely with the MELD score reaching a median time of 440 days for the group with <10 points (Fig. 3).

To assess the impact of the 'real MELD score' on waiting list mortality and on probability to be transplanted, 141 patients were excluded who had awarded points by the MELD exception Experts Committee. The probability of receiving a cadaveric LT positively correlated with the calculated MELD score with higher chances to be transplanted in the highest MELD score subgroups (Fig. 4). With scores ≥ 18′ the probability of receiving a liver remained greater than 50%. The largest MELD subgroup with <10 points ($n = 433$) had the lower probability of being transplanted with a decease donor LT (3%) among all subgroups of elective patients. Surprisingly, the subgroup of patients with extra-points because of T_2 HCC had the highest probability to be transplanted (94/111,

Table 1 Characteristics and reasons for removal from the waiting list grouped by category of the cohort of adult LT candidates in Argentina during the study period ($n = 1773$)

	Elective status	Emergency status	Total
Number of cases (%)	1623 (72)	150 (28)	1773 (100)
Age (years)	53.7 (18–74)[a]	44.1 (18–70)[a]	53.1 (18–74)
Gender (M/F)	926/697[a]	54/96[a]	980/793
Waiting list time (days)[b]	155 (40–519)	4.5 (3–8.2)	125 (25–477)
Cadaveric donor LT (%)	665 (41)	95 (63.3)	760 (42.9)
Live donor LT (%)	15 (0.9)	1 (0.7)	16 (0.9)
Deaths (%)	240 (14.8)	37 (24.7)	277 (15.6)
Drop-out from the list[c] (%)	46 (2.8)	4 (2.6)	51 (2.8)
Improved of clinical situation (%)	19 (1.2)	10 (6.7)	29 (1.6)

Data expressed as median and range or interquartile range (IQR) when indicated.
[a]$P < 0.001$.
[b]Median and interquartile range.
[c]Drop-out from the waiting list because of infection, poor overall status, neurological disorders or tumour progression.

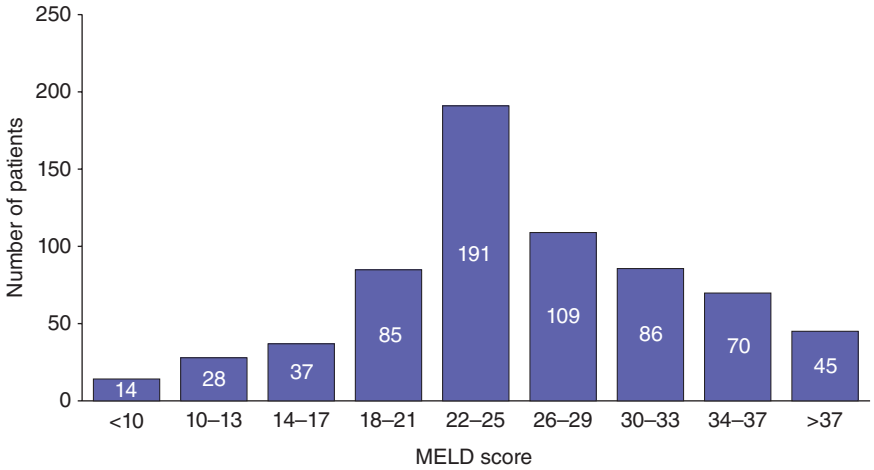


Figure 2 Distribution of the number of cadaveric donor liver transplantations performed according to each model of end-stage liver disease (MELD) subgroup in a cohort of 1623 adult elective candidates in Argentina

84.6%) compared with all others subgroups of MELD score categories, and even higher compared with other patients without cancer but stratified in the same subgroup with a MELD score 22–25 (72.9%, $P < 0.03$).

The number of adult live donor LT performed during the MELD era was extremely low representing only 15/680 (2.2%) of LT performed for elective candidates. Adult live LT was only performed electively in patients with low MELD scores (median 8, range 6–15).

Impact of the MELD-based allocation system on waiting list mortality

For elective candidates, the overall mortality rate during the MELD era was higher compared with the pre-MELD period (Table 2). While the mortality in patients under the emergency status remained equal over both periods, the mortality rate in elective candidates increased significantly from 10.4% in the pre-MELD to 14.8% in the MELD era. As expected, the mortality rate during the MELD era in emergency patients was significantly higher compared with elective patients (24.7% vs. 14.8%, $P < 0.002$).

When elective patients stratified by 'real MELD score' ($n = 1482$) were grouped by MELD score, patient deaths were more frequent in those subgroups with MELD < 18 points. The highest number of deaths was present in the subgroup with MELD < 10 points (Fig. 5). In this cohort of elective patients, the absolute number of deaths in each subgroup of MELD score was mainly equal on the early phase after listed (i.e. within the first 3 months) but this number increased within the first year for patients with a MELD score below 18 (Fig. 6).

When the probability of being transplanted was compared with the probability of dying waiting for a liver, the subgroups with

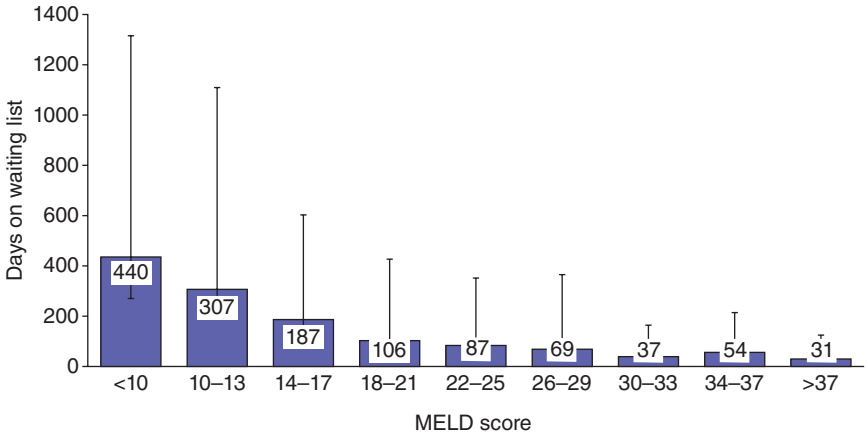
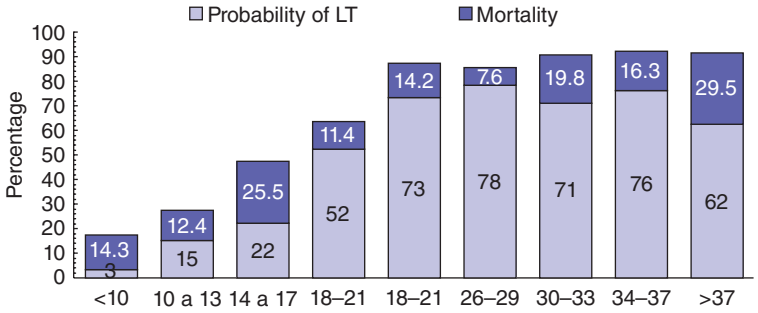


Figure 3 The median waiting time in days (interquartile range) in a cohort of 1623 adult elective candidates distributed according to each model of end-stage liver disease (MELD) subgroup in Argentina



										Total
Exposed to risk	433	185	168	148	133	131	121	92	71	1482
Deceased LTs	14	28	37	77	97	103	86	92	44	564
Deaths	62	23	43	17	19	10	24	15	21	234

Figure 4 Probability to be transplanted with a cadaveric donor and mortality rate in the waiting list for elective adult candidates (=1482) according to each model of end-stage liver disease (MELD) score subgroup (excluding candidates benefited with MELD exceptions points)

Table 2 Deaths and mortality rate (%) on the waiting list of adult patients listed for liver transplantation in Argentina in two periods: pre-MELD ($n = 659$) and MELD era ($n = 1773$)

Period	Pre- MELD era (2004)	MELD era (2005–2009)	*P* value
Global (%)	78/659 (12)	277/1773 (15.6)	<0.02
Emergency status (%)	18/77 (23.3)	37/150 (24.7)	<0.95
Elective status (%)	61/582 (10)	240/1623 (14.8)	<0.01

≥18 points were more likely to be transplanted (Fig. 4). In contrast, patients with <18 points had a higher probability of dying waiting for the liver compared with the probability to be transplanted with a cadaveric liver donor (16.2% vs. 10%; $P < 0.01$). Patients with <10 MELD points had more than a fourfold probability of dying on the waiting list than of being transplanted (14.3% vs. 3%; $P < 0.0001$). Among the subgroup with a MELD score 22–25, the mortality was lower in patients with extra-points as a result of early stage HCC (6/111, 5.4%) compared with other patients without cancer (19/131, 11.5%) but not significantly.

'Real MELD score' patients (=1482) were stratified based on aetiology of the liver disease and those patients with extra-MELD points as a result T_2 HCC (=111) were analysed as an independent subgroup without considering the aetiology of the underlying liver disease (Fig. 7). Mortality was significantly lower in the subgroup with T_2 HCC compared with all other elective patients

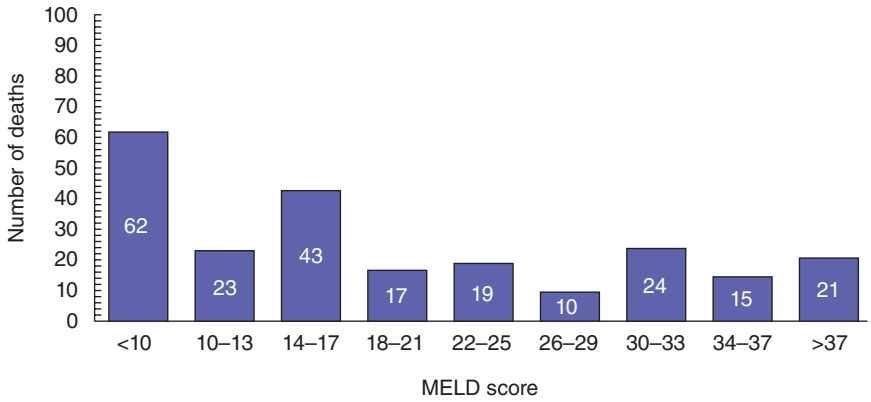


Figure 5 Distribution of the number of deaths ($n = 234$) on the waiting list in a cohort of adult elective candidates ($n = 1482$) for liver transplantation in Argentina according to subgroups of 'real model of end-stage liver disease (MELD) score'

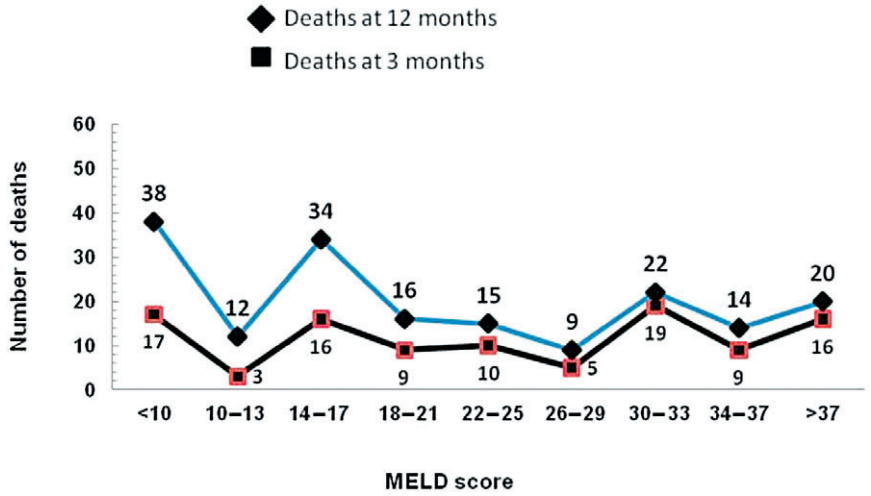


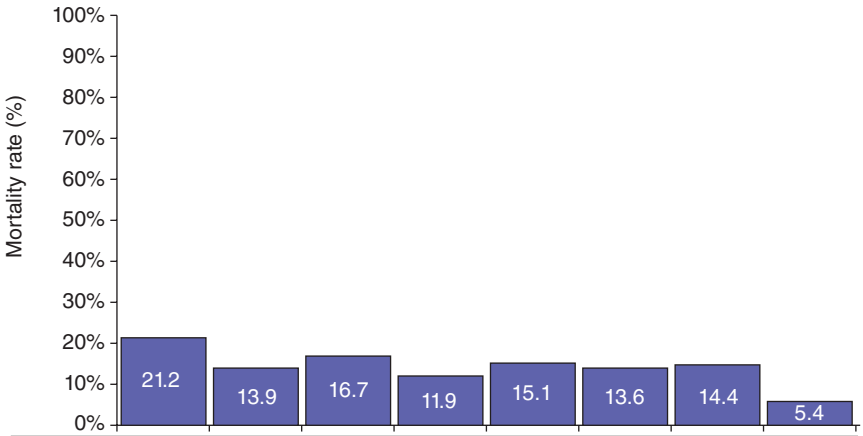
Figure 6 Distribution of the number of deaths at 3 and 12 months after inclusion on the liver waiting list in each 'real model of end-stage liver disease (MELD)' score subgroup in a cohort of adult elective candidates ($n = 1482$) in Argentina

without cancer (5.4% *vs.* 15.8%, $P < 0.05$) and compared with several subgroups of patients having specific underlying benign disorders such as hepatitis C virus infection ($P < 0.01$), cholestatic liver disease ($P < 0.02$), cryptogenic cirrhosis ($P < 0.02$), alcoholic abuse ($P < 0.02$) or autoimmune hepatitis ($P < 0.01$).

Discussion

The MELD-based allocation policy was adopted with the primary goal of achieving a significant reduction in waiting list mortality. In contrast with the reported experience in US, the implementation of this new allocation system in Argentina led to a significant increment on waiting list mortality compared with the pre-MELD era.[1,17] As expected, the new 'sickest first' policy resulted in most cadaveric donor LT being performed in patients with a high MELD score. In contrast with the North American experience, patient deaths on the waiting list occurred more frequently in low MELD candidates (i.e. <10 MELD points) who had the lowest probability to be transplanted and more than a fourfold risk of dying waiting for a liver. The subgroup of patients with T_2 HCC benefited most with the lower mortality rate and the highest probability of being transplanted using a cadaveric donor organ. Therefore, an intense review process is urgently needed to maintain equity and justice of access to the limited donor pool of cadaveric liver organs available.

The implementation of the MELD-based allocation policy by the US has triggered continuous re-examination of its efficiency for measuring severity of liver disease and its utility for prioritizing candidates for LT. However, to the best of our knowledge, this is the first analysis of patients listed for LT under the MELD system that is not based on the United National Organ Sharing database. Therefore, the major strength from our study is that a large national cohort of patients was used for a period of almost 4 years with the intention of validating this new model outside US.



	Cholest.	Alcohol	Autoim.	PSC	HCV	HBV	Crypto	HCC
Exposed to risk	165	288	156	42	365	44	194	111
Deaths	35	40	26	5	55	6	28	6

Figure 7 Mortality rate in 'real model of end-stage liver disease (MELD) score' patients (n = 1482) stratified according to the aetiology of the liver disease. Autoim., autoimmune hepatitis; Cholest, aholestasic diseases including primary biliary cirrhosis, secondary biliary cirrhosis; Crypto, aryptogenic cirrhosis; HBV, hepatitis B virus infection; HCC, T_2 stage hepatocellular carcinoma; HCV, hepatitis C virus infection; PSC, primary sclerosing cholangitis

Although our experience was not in line with the previously reported experience from North America, we have to accept that the MELD system dramatically improved organ allocation in comparison with the previous subjective system that emphasized time on the waiting list as the main variable for liver allocation. Particularly in Argentina, many reasons motivated that we consider the implementation of the MELD policy as an important 'step forward' in organ allocation. First, the INCUCAI was forced to create a modern centralized electronic database for collecting data from each patient listed in the national waiting list. Second, as the MELD score is based on the results of three readily available, objective and easily reproducible laboratory tests, logistics in each LT centre were facilitated. Third, the MELD system provided transparency in the allocation system and this fact will permit a continuous reviewing process to ensure equity and justice in organ allocation.

Our national centralized database has many limitations that could jeopardize the quality of our study. First, the use of a national database poses recognized limitations. Changes in the database, recording systems and/or personnel during the study period may affect data quality.[18] Missing data and erroneously recorded data could also affect the validity of the results. Second, it analyses the patient's MELD score at a given point in time (i.e. at the time of allocation, drop-out, death or the most recent) without considering the initial MELD score at the time of listing. Therefore, an analysis of the accuracy of variation in MELD score for predicting mortality in the waiting list cannot be performed. Third, as donor variables were not matched for each patient in the central database, further studies investigating allocation of marginal organs in high or low MELD patients cannot be performed.[19,20] Finally, post-operative outcome and long-term survival are not prospectively recorded by the INCUCAI so far and, unfortunately, the survival benefit of the MELD-base allocation policy is unpredictable in Argentina. Consequently, after this first comprehensive analysis of this new national database, donor characteristics must be recorded as well as each patient outcome after transplantation. Continuous analyses using other national databases are urgently needed to better evaluate and continuously validate the MELD-based allocation system in each country individually to guaranty transplantation utility and equity worldwide.

Many variables could eventually increase LT waiting list mortality including a low donation rate, a low number of cadaveric and live donor LT, a growing gap between the number of patients listed and the number of transplants and finally, an inadequate allocation system directing liver grafts to candidates in good clinical conditions. For example, the implementation of the MELD-based policy in the US was associated with an overall decline in waiting list mortality and time to transplantation.[1,18] However, the 2005 Organ Procurement and Transplantation Network annual report reveals that the mortality has been declining since 1995 and in fact remained relatively flat after 2002.[21] This steady decline in death rate despite an increase in the number of patients on the waiting list was attributed to a 34% increase in the number of transplantations performed since 1999, independent of any impact that the MELD implementation had.[21] The experience in Argentina revealed that even in the presence of encouraging sta-

tistics including a higher overall and multi-organic donation rate, an increment in the number of LT and a decreasing gap between the number of patients on the waiting list and number of deceased donor LT; the adoption of the MELD allocation system resulted in a higher mortality rate on the waiting list but only for elective candidates. Mortality on the waiting list for patients listed under emergency conditions who are not influenced by this new policy remained stable after MELD system adoption. As the variable 'cause of death' is not included in our prospective national database, we failed to provide this information in the present study. However, we can state that the absolute number of deaths increased considerably within the first year for patients with a MELD score below 18 probably because of the fact that they had a very low accessibility to LT in contrast with an easy access of 'sickest' candidates with MELD score $\geq$ 22 points. Perhaps we can speculate that socio-economical factors and differences in the US and the Argentinean health systems (e.g. regional vs. national allocation system, lack of homogeneous distribution of LT centres among the country, larger geographical distances from patient location to LT center, etc.) are the surrogate factors impairing patient survival on the waiting list in Argentina. Further investigation focused on causes rather than number of deaths on the waiting list in both countries will help to clarify these contradictory experiences.

We should acknowledge the constant efforts reflected in many studies in developing a better prognostic scoring system for cirrhotic patients to improve equity and utility of LT. However, several criticisms could be raised against the MELD allocation system. Some subjective clinical situations such as patients with intractable pruritus, encephalopathy, refractory ascites or recurrent bacterial cholangitis should better qualify for LT regardless of a low MELD score.[22] Other authors suggested that serum sodium values that are deteriorating in patients with refractory ascites or hepatorenal syndrome should be added to the MELD score to better assess transplant need.[23,24] Moreover, variability between laboratory methods in determination of the INR and those patients requiring anticoagulants could falsely increase the MELD score overestimating the overall severity of the liver disease.[25] Finally, although the MELD score proved to be a robust marker of early mortality across a wide spectrum of causes of cirrhosis, patients with cholestatic diseases such as primary and secondary biliary cirrhosis are still underestimated. In our cohort of adult elective patients, those having cholestatic cirrhosis had the highest mortality rate compared with other aetiologies. Perhaps, to overcome this problem, the weight of the bilirubin level in the mathematical formula of MELD score could be increased to compensate this undesirable situation.

An important finding of our study is that patients with presumed T_2 stage HCC benefit excessively from the MELD exception resolution. This subgroup benefited from the greater access to cadaveric donor LT, a depreciable drop-out rate for tumour progression and the lowest mortality rate compared with other subgroups of patients stratified according to their MELD scores on the waiting list. Moreover, patients with presumed T_2 stage HCC regardless of the underlying liver disease had the lowest mortality rate on the waiting list compared with other patients without cancer. In this scenario, the best notice for a cirrhotic patient listed for LT is that a new nodule that fulfills the non-invasive criteria for diagnosis of T_2 stage HCC was detected. Surprisingly, patients with T_2 HCC had the highest probability to be transplanted compared with other MELD score subgroups, and even among patients with a MELD score of 22–25 but without cancer. Surgeons may prefer to transplant patients with HCC rather than patients with benign disorders. Clearly, this 'fast track LT' with a short waiting time for patients with T_2 HCC motivated a significant reduction on adult live donor LT application in Argentina as compared with the pre-MELD era. During the MELD era, only a few adult live donor LTs were performed and none in patients with T_2 HCC. To provide equity in the allocation system, these data raise the question as to whether the priority points of patients with T_2 HCC should be reduced. Further multidisciplinary discussion is urgently needed to discuss how to allocate fairly, cadaveric donor livers without compromising patient survival of patients without early stage liver cancer who were listed for LT in Argentina.

Finally, the survival benefit of the MELD-based allocation system has been validated only in US.[1] A negative survival benefit has been demonstrated for candidates with MELD scores below 15.[17] Current controversy is whether the national liver allocation policy in the US should disallow LT for those patients listed with low MELD scores.[26] Clearly, the North American experience cannot be extrapolated to other countries such as Argentina where most patients are dying with a low MELD score but requiring a LT. Probably, the most important conclusion that arises from this study relies on the fact that the MELD-based allocation system is not a 'copy and paste' policy that should be automatically adopted for all countries worldwide. Perhaps many financial, logistic and structural limitations existing in developing countries that motivated validation of the reported experience in North America was not feasible in our country. Probably, some modifications to the MELD system are required and maximum efforts should be done to properly adapt this novel and promising policy to the local situation of each country.

Conclusions

The new MELD-based allocation system has been successfully adopted in Argentina. However, after its implementation, the mortality rate of elective patients on the waiting list increased and most patients are dying with a low MELD score. Patients with T_2 HCC are excessively benefiting from additional points of MELD jeopardizing the principle of justice and equity in allocation of cadaveric donor liver grafts. A comprehensive revision of the impact of the MELD-based allocation system on the waiting list must be performed in each new country adopting this novel strategy. The re-estimation of the risk of dying contrasted to the prob-

ability to be transplanted must be performed individually in every country for every patient listed for LT according to their MELD score. Further investigations focused on the strict analysis of specific variables including cultural, logistic and socio-economical factors inherent to developing and developed countries would help in optimizing the principles of justice and equity in each country individually.

Conflicts of interest

None declared.

References

1. Freeman RB, Wiesner RH, Edwards E, Harper A, Merion R, Wolfe R. (2004) Results of the first year of the new liver allocation plan. *Liver Transpl* 10:7–15.
2. Cholongitas E, Marelli L, Shusang V, Senzolo M, Rolles K, Patch D *et al*. (2006) A systematic review of the performance of the model for end-stage liver disease (MELD) in the setting of liver transplantation. *Liver Transpl* 12:1049–1061.
3. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. (2000) A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology* 31:864–871.
4. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL *et al*. (2001) A model to predict survival in patients with end-stage liver disease. *Hepatology* 33:464–470.
5. Freeman RB Jr. (2004) MELD and liver allocation: continuous quality improvement. *Hepatology* 40:787–789.
6. de Santibanes E, Pekolj J, McCormack L, Nefa J, Mattera J, Sivori J *et al*. (2002) Liver transplantation for the sequelae of intra-operative bile duct injury. *HPB (Oxford)* 4:111–115.
7. de Santibanes E, Ardiles V, Gadano A, Palavecino M, Pekolj J, Ciardullo M. (2008) Liver transplantation: the last measure in the treatment of bile duct injuries. *World J Surg* 32:1714–1721.
8. Villamil F, Levy G, Grazi GL, Mies S, Samuel D, Sanjuan F *et al*. (2006) Long-term outcomes in liver transplant patients with hepatic C infection receiving tacrolimus or cyclosporine. *Transplant Proc* 38:2964–2967.
9. Yantorno SE, Varela EB, Raffa SR, Descalzi VI, Gomez Carretero ML, Pirola DA *et al*. (2005) How common is delayed cyclosporine absorption following liver transplantation? *Liver Transpl* 11:167–173.
10. Yantorno SE, Kremers WK, Ruf AE, Trentadue JJ, Podesta LG, Villamil FG. (2007) MELD is superior to King's college and Clichy's criteria to assess prognosis in fulminant hepatic failure. *Liver Transpl* 13:822–828.
11. Lendoire J, Raffin G, Cejas N, Duek F, Barros Schelotto P, Trigo P *et al*. (2007) Liver transplantation in adult patients with portal vein thrombosis: risk factors, management and outcome. *HPB (Oxford)* 9:352–356.
12. Cueto G, Trigo P, Arata A, Rodriguez D, Brana E, Braslavsky G *et al*. (1999) Evaluation of prognostic factors for early infection in liver transplantation. *Transplant Proc* 31:3061–3062.
13. de Santibanes E, McCormack L, Mattera J, Pekolj J, Sivori J, Beskow A *et al*. (2000) Partial left lateral segment transplant from a living donor. *Liver Transpl* 6:108–112.
14. McCormack L, Quinonez EG, Capitanich P, Chao S, Serafini V, Goldaracena N *et al*. (2009) Acute liver failure due to concomitant arterial, portal and biliary injury during laparoscopic cholecystectomy: is transplantation a valid life-saving strategy? A case report. *Patient Saf Surg* 3:22.
15. Bruix J, Sherman M, Llovet JM, Beaugrand M, Lencioni R, Burroughs AK *et al*. (2001) Clinical management of hepatocellular carcinoma. Conclusions of the Barcelona-2000 EASL conference. European Association for the Study of the Liver. *J Hepatol* 35:421–430.
16. INCUCAI: Instituto Nacional Central Unico Coordinador de Ablacion e Implante. Argentina. http://www.incucai.gov.ar [accessed 26 July 2009].
17. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. (2005) The survival benefit of liver transplantation. *Am J Transplant* 5:307–313.
18. Austin MT, Poulose BK, Ray WA, Arbogast PG, Feurer ID, Pinson CW. (2007) Model for end-stage liver disease: did the new liver allocation policy affect waiting list mortality? *Arch Surg* 142:1079–1085.
19. Halldorson JB, Bakthavatsalam R, Fix O, Reyes JD, Perkins JD. (2009) D-MELD, a simple predictor of post liver transplant mortality for optimization of donor/recipient matching. *Am J Transplant* 9:318–326.
20. Bonney GK, Aldersley MA, Asthana S, Toogood GJ, Pollard SG, Lodge JP *et al*. (2009) Donor risk index and MELD interactions in predicting long-term graft survival: a single-centre experience. *Transplantation* 87:1858–1863.
21. Philosophe B, Barlett ST. (2007) Model for end-stage liver disease: did the new liver allocation policy affect waiting list mortality? Invited critique. *Arch Surg* 142:1086.
22. Wiesner RH. (2005) Patient selection in an era of donor liver shortage: current US policy. *Nat Clin Pract Gastroenterol Hepatol* 2:24–30.
23. Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. (2005) Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. *Liver Transpl* 11:336–343.
24. Samuel D. (2009) MELD-Na as a prognostic score for cirrhotic patients: hyponatremia and ascites are back in the game. *J Hepatol* 50:836–838.
25. Trotter JF, Olson J, Lefkowitz J, Smith AD, Arjal R, Kenison J. (2007) Changes in international normalized ratio (INR) and model for endstage liver disease (MELD) based on selection of clinical laboratory. *Am J Transplant* 7:1624–1628.
26. Perkins JD, Halldorson JB, Bakthavatsalam R, Fix OK, Carithers RL Jr, Reyes JD. (2009) Should liver transplantation in patients with model for end-stage liver disease scores < or =14 be avoided? A decision analysis approach. *Liver Transpl* 15:242–254.