

DOES THE PATIENT SELECTION WITH MELD SCORE IMPROVE SHORT-TERM SURVIVAL IN LIVER TRANSPLANTATION?

A seleção de pacientes utilizando-se o critério MELD melhora a sobrevida a curto prazo dos pacientes submetidos ao transplante de fígado?

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ABSTRACT – Introduction: The Model for End-Stage Liver Disease (MELD) score introduced in 2002 has come to improve selection of patients dying in the liver transplantation waiting list. **Objective:** To evaluate the short-term survival in liver transplantation around the world when MELD score was applied as selection criteria. **Methods** - A review has been done at the online database PubMed/ Medline/Scielo. The expressions applied for the search were “liver transplantation and/or MELD and/or survival analysis” from 2002 to 2009. Among the 124 analyzed articles, 94 were excluded due to irrelevance of the subject and lack of information. Were considered L1, L2A and MELD \geq 20 the sickest patient; L2B, L3 and MELD \leq 20 the healthiest. Was compiled the data of transplanted patients, their one-year survival rate related to MELD score and compare it with pre-MELD era. **Results:** MELD score has been applied, mainly in America and Europe patients, range from 8.4 to 30. One-year survival ranged from 66.5 to 92%. Analysis of patient survival rate significance between the pre-MELD and post-MELD era showed: Group I (L1 and L2A) x Group III (MELD \geq 20), significant ($p < 0,0001$); Group II (L2B and L3) x Group IV (MELD \leq 20), not significant. Also, comparative one-year survival by country in the MELD era was search. **Conclusion:** The MELD score have significantly improved short-term survival for the sickest patient on the waiting list for liver transplantation; additionally, it does not have any significant impact in survival for the healthiest patient.

HEADINGS - Liver transplantation. Survival analysis.

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DESCRITORES - Transplante de fígado. Análise de sobrevida.

RESUMO – Introdução: O escore para modelo de doença terminal do fígado (MELD) introduzido em 2002 foi criado para melhorar a seleção de pacientes que estavam morrendo na lista de espera para o transplante de fígado. **Objetivo:** Avaliar a sobrevida precoce dos pacientes submetidos ao transplante de fígado quando o MELD é aplicado como critério de seleção. **Métodos:** Foi realizada revisão “online” na base de dados PubMed/Medline/Scielo. Os termos utilizados foram transplante de fígado e/ou MELD e/ou análise de sobrevida no período de 2002 a 2009. Entre 124 artigos analisados, 94 foram excluídos devido a irrelevância do assunto e a falta de dados. Foram considerados L1, L2A e MELD \geq 20 os pacientes mais afetados; L2B; L3 e MELD \leq 20 os mais saudáveis. Foram compilados os dados dos pacientes transplantados, sobrevida de um ano, correlacionando-se os achados com MELD e as sobrevidas da era pré-MELD. **Resultados:** O MELD foi aplicado principalmente em pacientes dos Estados Unidos e Europa com escore variando de 8,4 a 30. A sobrevida de um ano variou de 66,5 a 92%. A sobrevida de um ano antes e depois da era MELD mostrou: Grupo I (L1 e L2A) x Grupo III (MELD \geq 20) com significância ($p < 0,0001$); Grupo II (L2B e L3) x Grupo IV (MELD \leq 20) não significante. Também foi comparada a sobrevida média dos pacientes em um ano por países na era MELD. **Conclusão:** O escore MELD melhorou significativamente a sobrevida dos pacientes a curto prazo, principalmente naqueles considerados mais doentes na lista de espera para o transplante de fígado. Por outro lado não houve impacto naqueles considerados mais saudáveis da lista de espera.

INTRODUCTION

One of the most controversial and significant problems in the liver transplantation area is the high mortality rates on the waiting list³. Recently the United Network for Organ Sharing (UNOS) implemented a new policy using the Model for End-Stage Liver Disease (MELD)¹¹. The MELD score, based on serum creatinine and bilirubin levels as well as prothrombin^{2,10} was designed to prioritize orthotopic liver transplantation for patients with the most severe liver disease rather than time spent on the waiting list⁸. Subsequent studies proved that MELD score was really effective to decrease the mortality rate on the waiting list. The number of patients who either died on the waiting list or were removed as too sick for transplant decreased from 1220 in 2001 to 1113 in 2002. When adjusted for changes in the waiting list size, this represents a 23% decrease in deaths⁷.

The aim of this review was to examine and discuss several aspects of the new allocation system, including short-term patient survival rate according to the MELD score comparing it with pre-MELD era.

METHODS

Was performed a structured literature review at the online database PubMed/ Medline/Scielo using both the English and non-English literature and also the terms of "liver transplantation and/ or MELD score and/or survival rate" from 2002 to 2009. Was performed a retrospective cohort study using data from the UNOS Scientific Registry and European Liver Transplant Statistic. In countries within the alliance of Eurotransplant, the MELD score for prioritization of patients awaiting for liver transplantation was initiated in November 2006 and at present little information is available concerning the prognostic ability of this allocation system compared to the previous one, which was based on Child-Turcotte-Pugh (CTP) score and waiting time.

Were found 678 articles. Exclusion criteria included: 1) irrelevance of the subject; 2) lack of information; 3) non-significant number of transplantation (fewer than 100); 4) patients who were transplanted previously were excluded for the purposes of this analysis because of the variability in the methods used for determining prothrombin time. Were also excluded those who underwent combination transplant procedures (eg, combined liver-renal procedure) or a prior liver transplant. By the end, 30 articles have been reviewed. Was analyzed one-year patient survival rate related to MELD score in those papers. The data of pre-MELD era was collected from UNOS and European Liver

Transplant Statistic. As far as to assess the short-term survival, patients with hepatocellular carcinoma were not given a priority MELD score.

Liver failure patient in pre-MELD era in USA was ranked as: liver status 3, 2B, 2A and 1 according to their liver function meaning that the worst patient was liver status 1. MELD score with higher standard deviation was excluded from statistic analysis. Were considered L1; L2A and MELD \geq 20, the sickest patient; L2B, L3 and MELD \leq 20, the healthiest patient. Was summarized patient survival rate from pre-MELD era and compare it with currently patient survival rate in MELD era. The X² test was applied for comparing both groups. Statistic significance was considered for p<0.05.

RESULTS

Analysis of patient survival rate significance between the pre-MELD (1996-2001) and post-MELD era (2003-2009) (Data collected from Organ Procurement and Transplantation Network (USA) and European Liver Transplant Statistic), are shown in Table 1.

TABLE 1 – Analysis of patient survival rate significance between the pre-MELD (1996-2001) and post-MELD era (2003-2009) (Data collected from Organ Procurement and Transplantation Network (USA) and European Liver Transplant Statistic)

Group	Gravity Status	América		Europe		
		PSR (%)	N Alive	PSR (%)	N Alive	
Pre-MELD Era	I*	E1	79,6	1.153	---	---
		E2A	82,0	192	---	---
	II	E2B	89,1	352	---	---
		E3	93,3	96	---	---
Pos-MELD Era	III*	≥ 20	88,3	5.914	66,5	114
	IV	≤ 20	87,4	10.333	84,4	912

*Group I (L1 e L2A) x Group III (MELD \geq 20) – significant (p< 0,0001); Group II (L2B e L3) x Group IV (MELD \leq 20) – not significant; L1; L2A and MELD \geq 20 – the sickest patient; L2B; L3 and MELD \leq 20 – the healthiest patient. (–) Data not available. N – Number of patients. PSR - Patient survival rate. MELD - Model for End-stage Liver Disease. L – Liver status

DISCUSSION

Increased mortality of patients on the waiting list for liver transplantation and shortage of donors organ gave rise to efforts to improve allocation criteria for liver transplantation candidates. The MELD was developed to predict short-term mortality in patients with cirrhosis. The model's accuracy to predict short-term mortality among patients with end-stage liver disease has been largely established⁶. It has since become the standard tool to prioritize patients for liver transplantation.

Since the implementation of MELD on liver allocation in the United States, new registrations on the waiting list have been reduced and transplantation rates have improved without increasing mortality rates of waiting candidates or changing early transplant rates⁵. Some authors showed no correlation between MELD and short-term post-transplant survival. However, other reports suggested that pre-transplant MELD predicted post-transplant survival¹.

The authors, in a retrospective study, evaluated the capacity of the MELD score, at the time of liver transplantation, to predict post-transplant survival and found that MELD score had significantly better prediction in the outcome of liver transplantation in sickest patient (MELD \geq 20) when compared with healthiest patient (MELD \leq 20). Were analyzed not only patients survival rate but also death on the waiting list and well removal from the waiting list due to poor condition; additionally was extended to the patient observation time over a period of one year. Our data do not argue against the use of MELD concerning prioritization of patients during initial period on the waiting list. But in patients with a longer time on waiting list other methods of gravity evaluation (such as CTP) may be used for assessment of patient prognosis. Was also identified some parameters that are not used to calculate the MELD score: retransplantation and the need for mechanical ventilation. The impact of including patient need for pre-transplant mechanical ventilation into MELD-based allocation is unknown. Intuitively, it is expected that patients requiring ventilator support are likely to have an increased risk of death without rapid transplantation. Similarly, whether the patient is awaiting a primary graft or a retransplant was not considered in the development of the MELD scoring system. Numerous studies identify retransplantation procedures to have significantly worse outcome than primary transplantations⁴. Whether patients awaiting a retransplant also have reduced survival compared with patients waiting for a first transplant, remains to be determined. It is even unclear whether the MELD score has comparable predictive capacity in this unique and difficult subgroup of patients. Inclusion of either of these variables into MELD may improve allocation to patients most in need; however, the efficient use of cadaver livers may be decreased because each also portends inferior outcome post-transplant.

Recent reports have shown that patients with higher MELD scores have poorer post-transplant survival, but the correlation between MELD and post-transplant patient survival was only marginally better than that for graft survival; the MELD score seems less predictive than the specific disease⁹. Although this is not surprising, the MELD score was designed to predict pre-transplant survival. The

characteristics that are predictive of survival while awaiting transplantation are not identical to those that substantially contribute to success of a liver transplant and predict post-transplant survival (age, specific disease, surgical times, immunosuppressive therapy, etc). However, these differences indicate that our understanding of the predictors of transplant success and failure remains dynamic and that the reevaluation of risk factors and survival predictors is an important ongoing activity⁵. Using a combination of MELD with other pre or post-transplant factors may be a better alternative.

In countries within the alliance of Eurotransplant, the MELD score for prioritization of patients awaiting liver transplantation was initiated in November 2006 and at present little information is available concerning the prognostic ability of this allocation system compared to the previous system which was based on CTP score and waiting time, that's why there is a gap on Table 1 in data of pre MELD era in Europe.

The increasing numbers of standard exceptions for MELD scores, for example cholestatic diseases, reflect the clinical need to improve this allocation system. Although the authors study does not argue against the use of the MELD score for short term allocation of organs and prioritization of recipients, the long-term prediction of mortality or removal from waiting list in patients awaiting liver transplantation might be better assessed by CTP score than the MELD.

Although overall outcomes of patients whose MELD scores were high at the time of liver transplantation were inferior to those of patients whose MELD scores were lower; there was no significant difference for specific thresholds of MELD above which liver transplantation was discouraged and a patient should be removed from the waiting list.

CONCLUSION

The MELD score have significantly improved short-term patient survival rate for the sickest patient on the waiting list for liver transplantation; additionally, it does not have any significant impact in patient survival rate for the healthiest patient. It is fair to say that the impact of pre-transplant MELD is maximal during the first year post-transplant; however, better predictive models are needed to assess the survival benefit with liver transplantation.

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