

Donor Risk Index and MELD Score Interactions in Graft Survival Prediction after Liver Transplantation. An Analysis of the OPTN-UNOS Database

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Abstract: Donor Risk Index (DRI) has been introduced to predict post-transplant graft survival (GS) using donor data. The MELD score, which is the gold-standard in scoring liver disease in liver transplant candidates, has a low prognostic significance. The present analysis is aimed to assess the role of DRI and of MELD score in predicting the outcome after liver transplantation, in short (180 days) and medium term (1460 days). The Organ Procurement Transplantation Network (OPTN) database relevant to 23.392 consecutive cases in the MELD era was used. Cases were stratified in classes according to DRI (4 classes), MELD (6 classes), and DRI-MELD match (24 classes). GS was assessed by Kaplan Meier method at 0-1460 days. Differences were tested by Log-rank test.

All three parameters allow an effective stratification. Using the DRI, the gaps between the highest and lowest GS were 7.8% and 14.9%, at 180 and 1460 days, respectively. Using the MELD score, the gaps were 10.2% and 9.5%, respectively. Using DRI-MELD, the gaps were 25.5% and 35.4%, respectively. Both the DRI and the MELD can predict the outcome, although the predictive power of the DRI is the highest of the two, and the predictive power of the donor-recipient match, is even higher.

The combination of DRI and MELD represents the best prognostic index in both short and medium-term observation period. On the basis of our results we believe that, in order to increase GS without refusing donors with high DRI, we should not allocate these organs to patients with a high MELD score.

Keywords: Donor-recipient match, DRI, donor risk index, MELD, liver transplantation, liver allocation, graft survival.

INTRODUCTION

Several attempts to identify the risk factors and to quantify their predictive power have been performed in liver transplantation [1-5]. Both donor and recipient factors have been proposed as predictive of early and long-term survival. The Donor Risk Index (DRI) has been introduced as an index calculated from 8 variables of the donor able to predict the post-transplant outcome [6]. However, the DRI has been developed on using a database with 20.023 cases, almost all of which performed before the adoption of the MELD and, as far as now, it is the index that better characterized and quantified donor quality. Since the Model for End-stage Liver Disease (MELD) score has been recognized as the best method to score liver disease in liver transplant candidates [7], and since its implementation in the American wait-list ranking, its prognostic significance has also been used for the prediction of post-transplant graft survival (GS) at least in the short and medium term [5, 8]. Up to the present, an

extensive analysis of GS in the MELD era has not been performed on a large database.

The present analysis is aimed to assess the role of the DRI and of the MELD score in predicting the outcome after liver transplantation in the short (180 days) and medium term (1460 days) period.

PATIENTS AND METHODS

The Organ Procurement Transplantation Network (OPTN) database relevant to 23.392 consecutive cases in the MELD era was used for this study. For the purpose of this analysis, we included only patients transplanted from February 28, 2002 to April 25, 2007. In order to avoid possible biases, the patients aged below 16 y.o., and the retransplants were not included. The DRI and the MELD score were calculated according to the original formulas [6,7]. The final database used for the study consisted of 18.998 cases.

The cases were divided in sextiles according to the DRI and stratified into 4 classes, as follows: class A includes the first sextile, class B includes the second and the third sextile,

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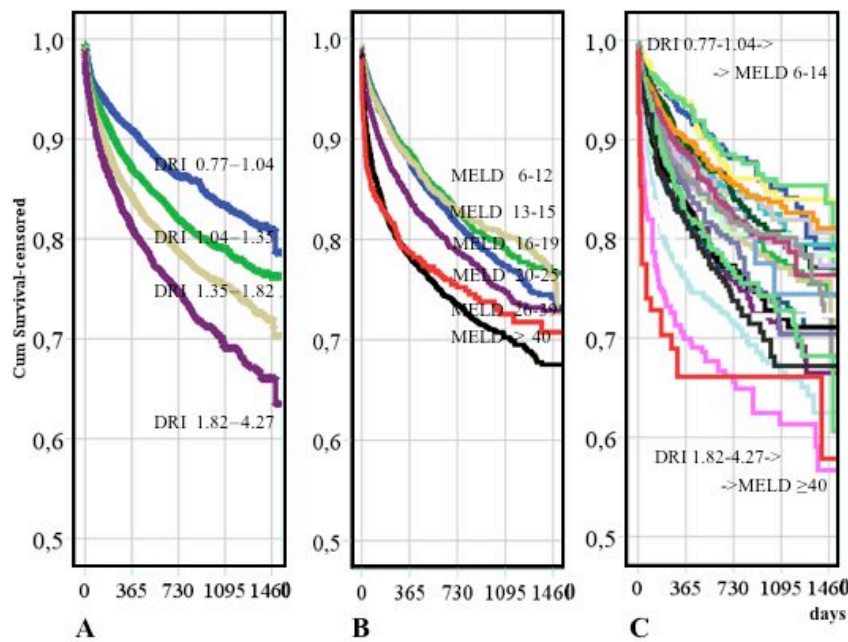


Fig. (1). A, DRI stratification in 4 classes ($p < 0.001$). B, MELD stratification in 6 classes (see Table 1 for p values). C, DRI-MELD stratification in 24 classes (see Table 3 for p values).

class C includes the fourth and the fifth sextile, class D includes the sixth sextile. Class A refers to cases with a DRI between 0.77 and 1.04 ($N=3167$, 16.7%), class B refers to cases with a DRI between 1.05 and 1.35 ($N=6322$, 33.3%), class C refers to cases with a DRI between 1.36 and 1.82 ($N=6331$, 33.4%), class D refers to cases with a DRI between 1.83 and 4.27 ($N=3158$, 16.6%).

The cases were also stratified in classes according to the MELD score in order to remain consistent with the previous studies. There were 6 MELD classes, as follows. MELD class 6-12 ($N=4720$, 25.1%), MELD class 13-15 ($N=3199$, 17.0%), MELD class 16-19 ($N=3709$, 19.7%), MELD class 20-25 ($N=3321$, 17.7%), MELD class 26-39 ($N=3278$, 17.4%), MELD class 40 and above ($N=571$, 3.0%).

GS was assessed by Kaplan Meier method at 365, 730, 1095 and 1460 days. Differences between curves were tested by Log-rank test. A p value ≤ 0.05 was considered statistically significant.

The statistical analysis was performed using the SPSS statistical package (ver 15.0, SPSS Inc, Chicago, Ill, USA).

RESULTS

Short- and medium-term graft survival figures as predicted by the DRI and by the MELD score are shown in Fig. 1 (A, B).

DRI Stratification of Graft Survival

At 180 days, the highest GS was achieved in the 0.77-1.04 class ($93.5\% \pm 0.5\%$), while the lowest GS was achieved in the 1.83-4.27 class ($85.7\% \pm 0.6\%$).

Also at 1460 days, the highest GS was achieved in the 0.77-1.04 class ($80.9\% \pm 1.2\%$), while the lowest was achieved in the 1.83-4.27 class ($66.0\% \pm 1.5\%$). The remaining two classes achieved an intermediate GS, both at 180 and 1460

days. Differences between the 4 classes were significant ($p < 0.001$).

The gap between the highest and the lowest GS was 7.8% at 180 days, and 14.9% at 1460 days.

MELD Stratification of Graft Survival

At 180 days, the highest GS was achieved in the 6-12 MELD class ($92.3\% \pm 0.4\%$), while the lowest GS was achieved in the 40 or above MELD class (82.7%). However, the 6-12 MELD class, the 13-15 MELD class and the 16-19 MELD class achieved comparable short-term GSs. In a similar way, also the 26-39 MELD class and the 40 or above MELD class achieved comparable short-term GSs.

At 1460 days, a better stratification was obtained. The highest GS was achieved in the 13-15 MELD class ($77.7\% \pm 1.1\%$), while the lowest GS was achieved in the 26-39 MELD class ($67.5\% \pm 1.2\%$). Differences between the 6 MELD classes were significant, as expressed in Table 1. The gap between the highest and lowest GS was 10.2% at 180 days, and 9.5% at 1460 days.

Table 1. Pairwise Comparisons among the 6 MELD Classes (Log-rank)

| MELD class | 6-12 | 13-15 | 16-19 | 20-25 | 26-39 | ≥ 40 |
|------------|-----------|-----------|-----------|-----------|-----------|-----------|
| | p value | p value | p value | p value | p value | p value |
| 6-12 | - | 0.171 | 0.164 | 0.000 | 0.000 | 0.000 |
| 13-15 | 0.171 | - | 0.989 | 0.000 | 0.000 | 0.000 |
| 16-19 | 0.164 | 0.989 | - | 0.000 | 0.000 | 0.000 |
| 20-25 | 0.000 | 0.000 | 0.000 | - | 0.000 | 0.002 |
| 26-39 | 0.000 | 0.000 | 0.000 | 0.000 | - | 0.649 |
| ≥ 40 | 0.000 | 0.000 | 0.000 | 0.002 | 0.649 | - |

Donor-Recipient Stratification of Graft Survival

Using the donor-recipient match a better stratification was obtained (Fig. 1C). Twenty-four paired matches were analyzed.

At 180 days the highest GS was achieved when organs in the 0.77-1.04 DRI class were transplanted in patients belonging to the MELD class 16-19 (95.8%±0.8%). Similar GS were also achieved when the same organs were transplanted in patients belonging to the MELD class 13-15 (95.4%±0.1%) or in patients belonging to the MELD class 6-12 (95.1%±0.8%). The lowest survival was achieved when organs in the 1.83-4.27 DRI class were transplanted in patients belonging to the MELD class 40 or above (70.3%±0.3%).

At 1460 days the highest GS was achieved when organs in the 1.36-1.82 DRI class were transplanted in patients belonging to the MELD class 13-15 (92.1%±0.9%). The lowest GS was achieved when organs in the 1,83-4,27 DRI class were transplanted in patients belonging to the MELD class 26-39 (56.7%±4.3%) or in patients belonging to the MELD class 40 or above (57.8%±0.9%). The gap between

the highest and lowest GS was 25.5% at 180 days, and 35.4% at 1460 days.

A detailed analysis of GS for each donor-recipient match is reported in Table 2. The differences between the 24 paired matches are reported in Table 3.

DISCUSSION

The prediction of liver transplant outcome with adequate accuracy represents the dream of every doctor involved in the care of liver transplant candidates. All potential factors have been investigated during the last 10 years, although most studies rely on small, single-center, experiences.

The introduction of indices that quantify the donor quality allowed the opportunity of stratifying the postoperative outcome in relation to the donor data [1-5]. The DRI has been developed and tested on the OPTN database relevant to the 1998-2002 period [6]. The index was calculated using 8 donor parameters (age, race, cause of death, type of death, height, partial or total hepatectomy, national or regional share, Cold Ischemia Time) and was aimed to predict the GS

Table 2. Short and Medium-Term Graft Survival in Relation to the Donor-Recipient Match. Graft Survivals (± Standard Error) were Stratified in Decreasing Order According to the 24 DRI-MELD Classes

| Donor-Recipient Match | N | % | 180-day %GS | Donor-Recipient Match | N | % | 1460-day %GS |
|---------------------------|------|-----|---------------|---------------------------|------|-----|---------------|
| DRI 0.77-1.04->MELD 16-19 | 652 | 3.4 | 0.958 ± 0.008 | DRI 1.36-1.82->MELD 13-15 | 1070 | 5.6 | 0.921 ± 0.009 |
| DRI 0.77-1.04->MELD 13-15 | 494 | 2.6 | 0.954 ± 0.010 | DRI 0.77-1.04->MELD 13-15 | 494 | 2.6 | 0.840 ± 0.023 |
| DRI 0.77-1.04->MELD 6-12 | 710 | 3.7 | 0.951 ± 0.008 | DRI 0.77-1.04->MELD 16-19 | 652 | 3.4 | 0.840 ± 0.026 |
| DRI 1.05-1.35->MELD 13-15 | 1046 | 5.5 | 0.938 ± 0.008 | DRI 1.05-1.35->MELD 16-19 | 1230 | 6.5 | 0.811 ± 0.019 |
| DRI 1.05-1.35->MELD 6-12 | 1425 | 7.5 | 0.931 ± 0.007 | DRI 0.77-1.04->MELD 26-39 | 564 | 3.0 | 0.806 ± 0.024 |
| DRI 1.05-1.35->MELD 16-19 | 1230 | 6.5 | 0.929 ± 0.007 | DRI 0.77-1.04->MELD 20-25 | 618 | 3.3 | 0.794 ± 0.026 |
| DRI 1.36-1.82->MELD 6-12 | 1624 | 8.5 | 0.922 ± 0.007 | DRI 0.77-1.04->MELD 6-12 | 710 | 3.7 | 0.791 ± 0.031 |
| DRI 1.36-1.82->MELD 13-15 | 1070 | 5.6 | 0.921 ± 0.009 | DRI 1.05-1.35->MELD ≥40 | 286 | 1.5 | 0.784 ± 0.033 |
| DRI 0.77-1.04->MELD 20-25 | 618 | 3.3 | 0.915 ± 0.012 | DRI 1.05-1.35->MELD 20-25 | 1147 | 6.0 | 0.773 ± 0.020 |
| DRI 1.05-1.35->MELD 20-25 | 1147 | 6.0 | 0.912 ± 0.009 | DRI 1.05-1.35->MELD 13-15 | 1046 | 5.5 | 0.771 ± 0.024 |
| DRI 1.36-1.82->MELD 16-19 | 1241 | 6.5 | 0.911 ± 0.008 | DRI 1.36-1.82->MELD 6-12 | 1624 | 8.5 | 0.758 ± 0.017 |
| DRI 1.83-4.27->MELD 6-12 | 961 | 5.1 | 0.903 ± 0.010 | DRI 0.77-1.04->MELD ≥40 | 129 | 0.7 | 0.744 ± 0.058 |
| DRI 0.77-1.04->MELD ≥40 | 129 | 0.7 | 0.902 ± 0.027 | DRI 1.05-1.35->MELD 6-12 | 1425 | 7.5 | 0.743 ± 0.022 |
| DRI 0.77-1.04->MELD 26-39 | 564 | 3.0 | 0.899 ± 0.013 | DRI 1.36-1.82->MELD ≥40 | 239 | 1.3 | 0.723 ± 0.035 |
| DRI 1.83-4.27->MELD 16-19 | 606 | 3.2 | 0.894 ± 0.013 | DRI 1.36-1.82->MELD 16-19 | 1241 | 6.5 | 0.722 ± 0.030 |
| DRI 1.83-4.27->MELD 13-15 | 589 | 3.1 | 0.893 ± 0.013 | DRI 1.05-1.35->MELD 26-39 | 1208 | 6.4 | 0.711 ± 0.020 |
| DRI 1.05-1.35->MELD ≥40 | 286 | 1.5 | 0.886 ± 0.019 | DRI 1.36-1.82->MELD 20-25 | 1065 | 5.6 | 0.711 ± 0.021 |
| DRI 1.36-1.82->MELD 20-25 | 1065 | 5.6 | 0.875 ± 0.010 | DRI 1.83-4.27->MELD 13-15 | 589 | 3.1 | 0.704 ± 0.028 |
| DRI 1.83-4.27->MELD 20-25 | 491 | 2.6 | 0.866 ± 0.016 | DRI 1.83-4.27->MELD 16-19 | 606 | 3.2 | 0.682 ± 0.035 |
| DRI 1.05-1.35->MELD 26-39 | 1208 | 6.4 | 0.863 ± 0.010 | DRI 1.83-4.27->MELD 20-25 | 491 | 2.6 | 0.672 ± 0.031 |
| DRI 1.36-1.82->MELD ≥40 | 239 | 1.3 | 0.807 ± 0.027 | DRI 1.83-4.27->MELD 6-12 | 961 | 5.1 | 0.665 ± 0.032 |
| DRI 1.36-1.82->MELD 26-39 | 1092 | 5.7 | 0.805 ± 0.012 | DRI 1.36-1.82->MELD 26-39 | 1092 | 5.7 | 0.624 ± 0.026 |
| DRI 1.83-4.27->MELD 26-39 | 414 | 2.2 | 0.747 ± 0.022 | DRI 1.83-4.27->MELD ≥40 | 97 | 0.5 | 0.578 ± 0.089 |
| DRI 1.83-4.27->MELD ≥40 | 97 | 5.7 | 0.703 ± 0.048 | DRI 1.83-4.27->MELD 26-39 | 414 | 2.2 | 0.567 ± 0.043 |

Table 3. Pairwise Comparisons among the 24 Donor-Recipient Classes (Log-Rank p Values). N.S. Not Significant

| | | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | p | |
|--------------------------------|---|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | A | B | C | D | E | F | G | H | I | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z |
| DRI 0.77-1.04 -> MELD 6-12 | A | | 0.00 | 0.00 | 0.00 | N.S. | N.S. | N.S. | 0.05 | 0.03 | N.S. | N.S. | 0.00 | 0.00 | 0.01 | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 1.05-1.35 -> MELD 6-12 | B | 0.00 | | N.S. | 0.00 | 0.01 | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.04 | N.S. | 0.00 | N.S. | N.S. | N.S. | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 1.36-1.82 -> MELD 6-12 | C | 0.00 | N.S. | | 0.00 | 0.00 | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.01 | N.S. | 0.00 | N.S. | N.S. | N.S. | 0.00 | 0.00 | 0.00 | 0.08 | 0.02 | 0.00 | 0.00 | 0.00 |
| DRI 1.83-4.27 -> MELD 6-12 | D | 0.00 | 0.00 | 0.00 | | 0.00 | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.01 | N.S. | N.S. | 0.00 | 0.01 | N.S. | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.00 | 0.00 |
| DRI 0.77-1.04 -> MELD 13-15 | E | N.S. | 0.01 | 0.00 | 0.00 | | N.S. | N.S. | N.S. | 0.04 | N.S. | N.S. | 0.01 | 0.00 | 0.01 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 0.77-1.04 -> MELD 16-19 | F | N.S. | 0.00 | 0.00 | 0.00 | N.S. | | 0.02 | 0.01 | 0.01 | 0.02 | N.S. | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 0.77-1.04 -> MELD 20-25 | G | N.S. | N.S. | N.S. | 0.00 | N.S. | 0.02 | | N.S. | N.S. | N.S. | N.S. | 0.00 | N.S. | N.S. | N.S. | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 0.77-1.04 -> MELD 26-39 | H | 0.05 | N.S. | N.S. | 0.00 | N.S. | 0.01 | N.S. | | N.S. | N.S. | N.S. | 0.00 | N.S. | N.S. | N.S. | 0.01 | 0.00 | 0.00 | 0.04 | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 0.77-1.04 -> MELD ≥40 | I | 0.03 | N.S. | N.S. | N.S. | 0.04 | 0.01 | N.S. | N.S. | | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | 0.02 | N.S. | N.S. | N.S. | N.S. | 0.00 | 0.00 | 0.00 |
| DRI 1.05-1.35 -> MELD 13-15 | L | N.S. | N.S. | N.S. | 0.00 | N.S. | 0.02 | N.S. | N.S. | N.S. | | N.S. | N.S. | 0.00 | N.S. | N.S. | 0.07 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 1.05-1.35 -> MELD 16-19 | M | N.S. | 0.04 | 0.01 | 0.00 | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | | 0.02 | 0.00 | 0.02 | N.S. | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 1.05-1.35 -> MELD 20-25 | N | 0.00 | N.S. | N.S. | 0.01 | 0.01 | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.02 | | 0.00 | N.S. | N.S. | N.S. | 0.00 | 0.00 | 0.00 | N.S. | 0.02 | 0.00 | 0.00 | 0.00 |
| DRI 1.05-1.35 -> MELD 26-39 | O | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | | N.S. | 0.00 | 0.00 | N.S. | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.00 | 0.00 |
| DRI 1.05-1.35 MELD ≥40 | P | 0.01 | N.S. | N.S. | N.S. | 0.01 | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.02 | N.S. | N.S. | | N.S. | N.S. | N.S. | 0.00 | 0.05 | N.S. | N.S. | N.S. | 0.00 | 0.00 |
| DRI 1.36-1.82 -> MELD 13-15 | Q | 0.01 | N.S. | N.S. | 0.00 | 0.02 | 0.00 | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | 0.00 | N.S. | | N.S. | 0.00 | 0.00 | 0.00 | 0.03 | 0.00 | 0.00 | 0.00 | 0.00 |
| DRI 1.36-1.82 -> MELD 16-19 | R | 0.00 | N.S. | N.S. | 0.01 | 0.00 | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.01 | N.S. | 0.00 | N.S. | N.S. | | 0.01 | 0.00 | 0.00 | N.S. | 0.03 | 0.00 | 0.00 | 0.00 |
| DRI 1.36-1.82 -> MELD 20-25 | S | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | 0.01 | N.S. | 0.00 | 0.00 | 0.00 | N.S. | N.S. | 0.00 | 0.01 | | 0.00 | N.S. | N.S. | N.S. | N.S. | 0.00 | 0.00 |
| DRI 1.36-1.82 -> MELD 26-39 | T | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | | N.S. | 0.00 | 0.00 | N.S. | 0.03 | N.S. |
| DRI 1.36-1.82 -> MELD ≥40 | U | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | N.S. | 0.05 | 0.00 | 0.00 | 0.12 | N.S. | | N.S. | N.S. | N.S. | 0.04 | 0.05 |
| DRI 1.83-4.27 -> MELD 13-15 | V | 0.00 | 0.02 | N.S. | N.S. | 0.00 | 0.00 | 0.02 | 0.04 | N.S. | 0.00 | 0.00 | N.S. | N.S. | N.S. | 0.03 | N.S. | N.S. | 0.00 | N.S. | | N.S. | N.S. | 0.00 | 0.00 |
| DRI 1.83-4.27 -> MELD 16-19 | W | 0.00 | 0.00 | 0.02 | N.S. | 0.00 | 0.00 | 0.00 | 0.01 | N.S. | 0.00 | 0.00 | 0.02 | N.S. | N.S. | 0.00 | 0.03 | N.S. | 0.00 | N.S. | N.S. | | N.S. | 0.00 | 0.00 |
| DRI 1.83-4.27 -> MELD 20-25 | X | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | 0.00 | N.S. | 0.00 | 0.00 | 0.00 | N.S. | N.S. | 0.00 | 0.00 | N.S. | N.S. | N.S. | N.S. | N.S. | | 0.00 | 0.01 |
| DRI 1.83-4.27 -> MELD 26-39 | Y | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.03 | 0.04 | 0.00 | 0.00 | 0.00 | | N.S. |
| DRI 1.83-4.27 -> MELD ≥40 | Z | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | N.S. | 0.05 | 0.00 | 0.00 | 0.01 | N.S. | |

using only donor data. Adopting coefficients derived from the multivariate analysis, the index was conceived in order to

stratify GS in a continuous way. However, in the original report by Feng *et al.*, the DRI allowed a stratification of

cases in classes with a difference in the survival rate equal to 11% at 3 months, and to 21% at 3 years. Although the DRI is a continuous variable, for practical purposes the 1.7 cut-off has been later identified and proposed by other Authors to identify Extended Criteria Donor grafts (ECDg) [9]. Donors with $DRI \geq 1.7$ can be classified as ECDg, while, donors with $DRI < 1.7$ cannot.

The introduction of the MELD score, as the main prioritization criterion in the waiting-list, allowed to perform a detailed analysis of GS by using the large database already filled with MELD values at the listing. In addition, today, the great variability in the spectrum of both donor quality and recipient decompensation recorded over the last 5 years leads to a more complex dynamic alchemy, in which donor and recipient factors are matched together. Paradoxically, the large variability which today exists in both donor and recipient data, facilitates the development of tailor-fit algorithms, able to stratify the risk. To our knowledge, an exhaustive analysis of donor risk factors and recipient risk factors has never been performed in the MELD era using the large OPTN database.

After the elimination of the possible biases due to pediatric cases and re-transplants, we stratified the 18998 OPTN cases and obtained 4 different DRI classes, with a difference in GS ranging from 7.8% at 6 months to 14.9% at 4 years. In the same way, the database was also stratified in 6 MELD classes, with a difference in GS ranging from 10.2% to 9.5%. Interestingly, using a model based on 24 paired donor-recipient match classes, we obtained a better stratification of outcomes, with a difference in GS ranging from 25.5% at 6 months to 35.4% at 4 years. In other words, donor quality, as synthesized in the DRI, is a more powerful predictive factor than the degree of liver decompensation, as represented by the MELD. However, the donor-recipient match is even more predictive.

Several efforts have been made to draw algorithms in order to ideally match donors and recipients. Some authors suggest that the negative effect of ECDg can be cancelled by choosing a well-defined class of low-risk recipients [9-12]. Moreover, a large survey, recently published, shows that in grafts from donation after cardiac death (probably, the category with the worse prognosis), with cold ischemia time below 10 hours and with warm ischemia time below 30 minutes, when transplanted in low-risk patients, GS at 1 and 3 years is not different from GS recorded using standard donors [13].

Organ shortage represents the major limitation to the growth of transplantation. The introduction in the current practice of ECDg is today the strongest answer to the organ shortage problem. Although there is no direct relation between ECDg organs and organs with a high DRI (between 1.83 and 4.27), being the former defined on a qualitative approach and the latter on a quantitative computation, we can assume an analogy. On these grounds, we believe that sufficient evidence has been provided for suggesting to avoid the allocation of ECDg to patients who are in the 2 upper MELD classes. Nevertheless, such organs should indeed be transplanted, preferentially in less decompensated patients.

Data from our center, published in the 2005-2006 period, and a subsequent survey performed on data from all Italian

liver transplant centers, indicate that non-standard donors transplanted in patients with a high MELD class face the worst outcome; conversely, more satisfactory results can be obtained by using the mismatch choice [10-12]. The recent study performed by Ioannou reached similar conclusions in both HCV and non-HCV recipients [14]. However, the number of transplants performed by using ECDg has been growing exponentially in the last 5 years all over the world, and particularly in Italy. Today, in several Italian programs, ECDs represents almost 50% of all deceased donors [1, 2], and the prevalence of ECDg is growing higher worldwide. Probably, in the near future, the number of donors will double. At that time, the so-called difference in quality of organs should be considered, not yet as a limitation, but only as an indication for different options of treatment.

In conclusion, our analysis of prognostic factors performed on the OPTN database indicates that both the DRI and the MELD score can predict the outcome, although the predictive power of the DRI is the highest of the two, and the predictive power of the donor-recipient match is even higher. All three parameters acts in a continuous way and can be easily stratified in classes. However, we should underline that the combination of the DRI and the MELD score represents the best prognostic index with great outcome stratification, at both short and medium term. Being the stratification almost continuous, it is difficult to draw a dichotomus algorithm. However, taking into account the different possibilities of matching donor and recipient, we believe that sufficient data have been collected to conclude that in order to increase GS without refusing donors with a high DRI, we should not allocate those organs to patients with high MELD score.

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