

# Prioritization and Organ Distribution for Liver Transplantation

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THE CURRENT policies for cadaver kidney distribution were recently discussed in *THE JOURNAL*.<sup>1</sup> Questions about liver allocation are even more important, because there is not the option of artificial organ support.<sup>2</sup> Two principles of liver deployment have been advocated: efficiency of organ use and urgency of need.

## THE EFFICIENCY PRINCIPLE

### Single Disease Studies

**Primary Biliary Cirrhosis.**—Patients with this disease have been stratified retrospectively into low-, medium-, and high-risk categories, and their actual survival after liver transplantation has been compared with the outcome expected without such intervention.<sup>3</sup> This comparison depended on a Mayo hazard prediction model of the natural history of primary biliary cirrhosis (Table 1).<sup>4</sup> Before the National Institutes of Health Consensus Development Conference of 1983,<sup>5</sup> we reserved liver transplantation candidacy for patients with chronic disease whose life expectancy was a few months.<sup>6</sup> The effect of this restrictive policy could be seen in liver recipients treated for primary biliary cirrhosis between March 1980 and June 1987. Even in the low-risk group, the bilirubin level averaged 205  $\mu\text{mol/L}$  (12 mg/dL), and in the high-risk group, it averaged 480  $\mu\text{mol/L}$  (28 mg/dL). All three cohorts had hypoalbuminemia (Table 1).

The 75% 1-year patient survival rate after transplantation was a 30 percentage point gain over the 45% rate predicted with medical treatment.<sup>3</sup> Because 1-year survival rates were 83%, 75%, and 58% in the low-, medium-, and high-risk categories, respectively, the results have been used to demonstrate the inefficient use of organs when they are transplanted to high-risk recipients. Viewed from a different perspective, the gain of survival in the first postoperative year relative to projected outcome without transplantation was actually highest (58 percentage points) in the high-risk patients, next highest (55 percentage points) in the medium-risk group, and lowest (only 14 percentage points) in the low-risk group, whose 1-year survival rate without intervention would have been 69% (Fig 1). The life survival slope and degree of rehabilitation after 1 year were the same in all groups.<sup>5</sup>

**Sclerosing Cholangitis.**—Similar but more pronounced trends were seen with sclerosing cholangitis<sup>7</sup> using a second Mayo hazard prediction model that factored in age, bilirubin level, splenomegaly, and histopathologic stage.<sup>8</sup> The gain in 1-year survival rate with transplantation vs the predicted outcome without this procedure was only 7 percentage points in low-risk cases, a gain relative to the surrogate control that did not increase in the succeeding 7 years (Fig 2). In the medium-risk patients, the 1-year survival dividend from transplantation was zero, but this steadily increased thereafter. In contrast, the high-risk group achieved a stunning 40 percentage point life survival gain by 12 months, an improvement that had grown to nearly 80 percentage points at 7 years, by which time all patients without transplantation were long since projected dead. By 7 years, the best absolute sur-

vival rate belonged to the patients who originally had been the most ill (Fig 2).

## Heterogeneous Diseases: Risk Factors and Cost

At the New England Medical Center, Boston, Mass, 124 adults and children who had a full spectrum of diagnoses and medical urgency were given 142 livers between 1984 and 1992. These cases illustrated the relationship between the severity of pretransplant illness, patient survival, and cost of treatment.<sup>9</sup> Urgency of need was determined with the 5-tier scale (called the United Network for Organ Sharing [UNOS] score) that was used nationally through 1990 (see legend of Fig 3). UNOS 1 and 2 candidates (the least ill) had the highest rates of posttransplant survival (Fig 3). The poorest results were with the UNOS 4 and 5 recipients. However, the rescue of the majority of these patients whose expected survival was essentially zero without transplantation was at least as noteworthy as the fact that the survival curve was degraded by their admission into candidacy. The cost of caring for the UNOS 4 and 5 recipients was high, reaching nearly \$250 000 and \$190 000 per case, respectively, including the expenditures before transplantation, which can exceed the expenses afterward.

Poorer and more expensive results also were evident when the high-risk patients were identified using the criteria of the Blue Cross/Blue Shield consortium or using the APACHE II (Acute Physiology and Chronic Health Evaluation) score, which expresses pretransplantation need for intensive care.<sup>9</sup> No matter how sick the patients were before transplantation or how high the risk, however, those who lived (the majority in every subgroup) and were tested 1 year later had the same degree of rehabilitation, as determined by Karnof-

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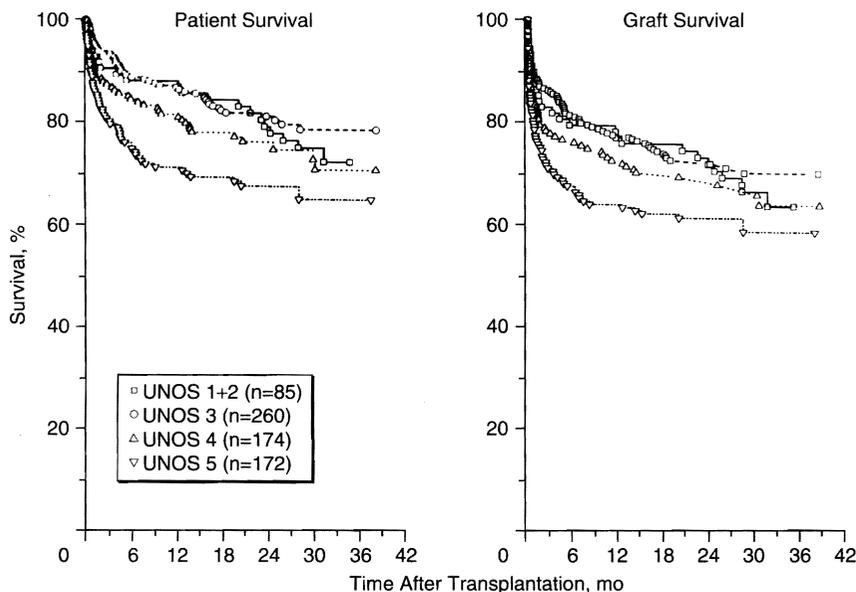


Fig 5.—Patient and graft survival following primary orthotopic liver transplantation in adults, stratified by pre-1991 United Network for Organ Sharing (UNOS) risk categories. The difference between patient and graft survival is accounted for by successful retransplantation.

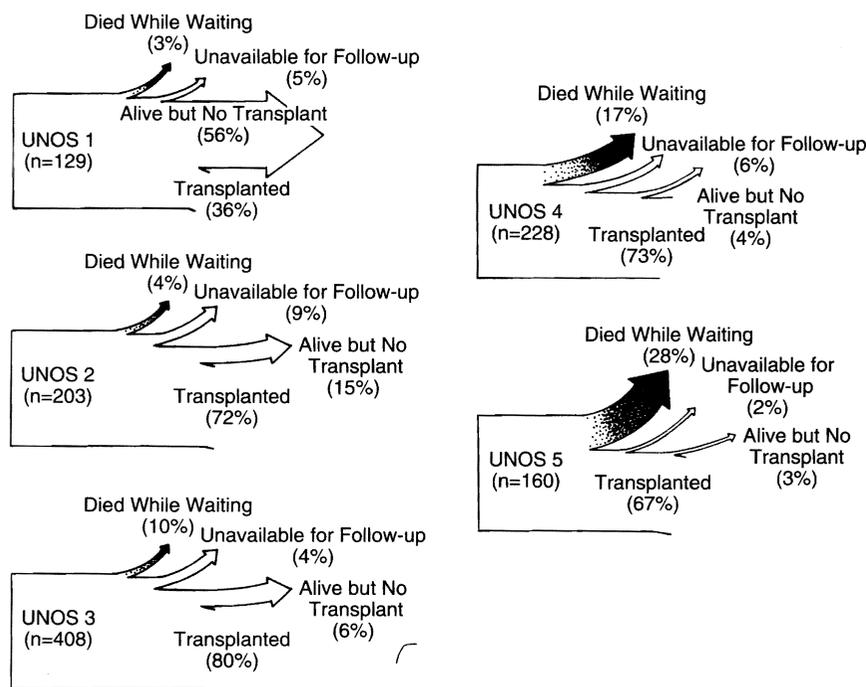


Fig 6.—Increasing incidence of death while waiting with each increase of the United Network for Organ Sharing (UNOS) entry score of liver transplant candidates. The percentage of patients alive who had not received transplants decreased with increasing UNOS score.

of the immunosuppressive drug, FK 506, which could be used for either primary or rescue treatment.<sup>15</sup>

As expected, the best results were in the low-risk recipients. Few in number (n=12 [1.7%]), those in UNOS class 1

survived for 1 year at a rate of 91%; those in combined classes 1 and 2 at 88%; those in class 5 (UNOSStat [a life expectancy of only a few days without transplantation, often because of fulminant hepatic failure]) at 71%; and those

in classes 3 and 4 at rates in between (Fig 5, left). The incidence of retransplantation was approximately the same in all cohorts, although it was less frequently successful in the sickest patients, as reflected in the graft survival curve (Fig 5, right). The crucial observation was that the gap in results with different urgency classes had narrowed to the point of nonsignificance except for the UNOSStat group, which trailed the low-risk groups by 17%. Still, 71% of even this highest-risk cohort was alive at 1 year. After 1 year, the decline in survival rates was the same in all groups.

#### Candidate Stability by UNOS Score

The case flow after evaluation is summarized in Fig 6. At the end of the first year, more than half (56%) of the patients who had entered as UNOS 1 candidates remained at this status, while 3% had died. As the risk level at entry increased from UNOS 1 to UNOS 3, the population of patients who had transplantations increased, frequently precipitated by worsening status and reclassification. The death rate while waiting was 10% for UNOS 3 patients and escalated to 17% for UNOS 4 patients and 28% for UNOS 5 patients (Fig 6). Of interest, 27 (3.4%) of the 796 patients in UNOS categories 3 through 5 improved enough with medical management to leave the hospital. These recoveries were dominated by patients with the entry diagnosis of fulminant hepatic failure.

#### Termination of Trial

These recipients, including those who were gravely ill at entry or whose condition deteriorated while waiting, could be treated efficiently because of the emphasis on urgency of patient need and the national donor reservoir designed to meet this need. This was changed when a directive from UNOS, effective January 1, 1991, created a functional confederacy in the United States of 11 regions from which the free national movement of organs was discouraged in favor of elective regional use. Urgency of need at a national level was removed as the most pervasive internal principle of the American organ allocation framework.

### CONSEQUENCES OF THE UNOS RULES CHANGE

#### Loss of Patient Choice

Factors that preclude candidacy at any given center, such as age, technical or medical complexity, or advanced illness, frequently are not contraindications in other centers to which rejected candidates can go for a second opinion. Under the new system, such patients no longer have easy access to a national