ACADEMIC DEBATE

AMERICAN LIVER FOUNDATION
NOVEMBER 30, 2006

The Mission of Transplant Professionals

To save lives and enhance the quality of life of patients with end stage organ failure.

To identify patients that will benefit from organ transplantation

To maximize the utilization of organs to benefit the maximum people

Should we use marginal donors for otherwise good risk patients with HCC beyond Milan criteria

Is the Milan criteria imperfect?

Should we transplant patients who have less optimal prognoses?

Can we transplant patients without affecting current organ allocation and utilization?

Milan criteria

Based on preoperative staging liver transplantation for HCC should be limited to patients with solitary tumors <5 cm in diameter or no more than 3 nodules, each 3 cm or less in diameter

Radiologic imaging accurate only 60% of the time

Most studies show that number of tumors do not matter

Achkar JP, Araya V, Baron RL, Marsh JW, Dvorchik I, Rakela J. Undetected hepatocellular carcinoma: Clinical features and outcome after liver transplantation. Liver Transpl Surg 1998;4(6):477–482.

Liver Transplantation for Hepatocellular Carcinoma in Cirrhosis: Is Clinical Tumor Classification before Transplantation Realistic?

RAPID COMMUNICATION

Liver Transplantation Outcomes for Early-Stage Hepatocellular Carcinoma: Results of a Multicenter Study

Valls C, Figueras J, Jaurrieta E, Sancho C, Domínguez J, Benasco C, et al. Hepatocellular carcinoma: Iodized-oil CT TNM classification. AJR Am J Roentgenol 1996;167:477–481.

Liver Transplantation for Hepatocellular Carcinoma: Expansion of the Tumor Size Limits Does Not Adversely Impact Survival

Expanding Special Priority to Include Stage III Disease

Liver Transplantation for Hepatocellular Carcinoma: A Registry Report of the Impact of Tumor Characteristics on Outcome

Influence of Tumor Characteristics on the Outcome of Liver Transplantation Among Patients With Liver Cirrhosis and Hepatocellular Carcinoma

Size may not matter

Several studies using multivariate analysis suggest that many other factors may be more predictive to disease-free and overall survival

Studies that challenge the Milan Criteria

Author	year	allograft	patients	Milan criteria		Extended Milan criteria	
				total survival	free survival	total survival	free survival
Todo	2004	LDLT	316	82	79.4	74.5	60
Kneteman	2004	OLT	40	94	81	90.5	76.8
Yao	2001	OLT	70	91.5	72.4	82.4	74.1

Is the Milan criteria imperfect? YES

Should we transplant patients who have less optimal prognoses?

Can we transplant patients without affecting current organ allocation and utilization?

Prognosis beyond Milan Criteria is not as good

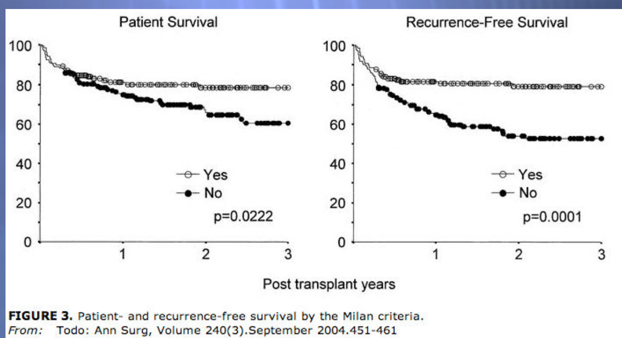

FIGURE 3. Patient- and recurrence-free survival by the Milan criteria.
From: Todo: Ann Surg, Volume 240(3).September 2004.451-461

Prognosis for HCC is grave without liver transplantation

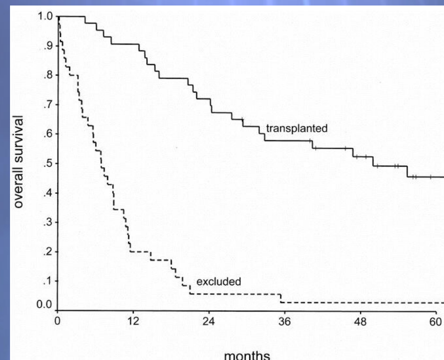

Figure 1. Overall survival of patients entered into the protocol based on eventual transplant or removal from protocol ($P < .0001$).
From: Roayaie: Ann Surg, Volume 235(4).April 2002.533-539

Outcomes for Bone Marrow Transplant

Survival (% of patients)
100
80
60
40
20
0
0 2 4 6 8 10 12 14 16 18 20 22
Years after Transplantation

HCC is the best place to start with Marginal Donors

Transplant procedure is less complicated since patients are usually not ravaged by their liver disease

Low incidence of extrahepatic manifestations of liver failure such as hepato-renal syndrome

Is the Milan criteria imperfect? YES

Should we transplant patients who have less optimal prognoses? YES

Can we transplant patients without affecting current organ allocation and utilization?

How do we transplant patients beyond the Milan Criteria without affecting current allocation?

Utilize Organs Currently Being discarded

2005
- 6120 liver transplants from cadaveric donors
- **570** hepatic allografts were procured and not utilized

2006 – (Jan-July)
- 3771 liver transplants from cadaveric donors
- **351** hepatic allografts were procured and not utilized

(projection: 600 discarded hepatic allografts for 2006)

www.unos.org (October 16, 2006)

Marginal donors

- Age (>55 years old)
- Hypotension prior to donation
  - Use of vasoactive drugs, dopamine
- Laboratory:
  - Serum sodium> 150 mEq/L
  - Bilirubin > 2mg/dL
  - ALT > 150 UI/L
- Viral infections: HCV+, HBV+, HIV+
- History of drug or alcohol abuse
- Micro or macro-steatosis

Will These Discarded Organs Work? YES

- Allografts from HCV+
  - Excellent results when both donor and recipient are HCV+
  - Excellent results with de novo HCV+ infection
- Allografts from HBSAg+
  - Preferentially allocated to anti-HBs+ or HBSag+ patients
  - De novo HBV infection appears benign and new anti-virals are extremely promising
- Allografts from HIV positive donors-HIV infection after LTX can be controlled
- Marginal grafts (by age, lab criteria, or clinical course prior to donation) with careful selection have been shown to work as well as "ideal" grafts

Will These Discarded Allograft Work

- Assume 600 hepatic allografts will be discarded this year
- If a minimum of 10% are utilized then 60 patients can be transplanted a year (300/5 years) from discarded allografts alone

- Is the Milan criteria imperfect? YES
- Should we transplant patients who have less optimal prognoses? YES
- Can we transplant patients without affecting current organ allocation and utilization? YES

Proposed Scheme for Allocation of Discarded Hepatic Allografts

- Five-year multi-center trial
- Patients breach the Milan criteria
- Evaluate
  - Patient survival
  - Graft survival
  - Various types of neo-adjuvant chemotherapy

He is the best physician who is the most ingenious inspirer of hope.

Samuel Taylor Coleridge