Choosing the Right Liver; Organ Allocation and Matching

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Matching

- Choice of Liver
- 1. Standard DBD
- 2. Partial liver
- 3. DCD
- 4. HCV +ve donor
- 5. "Aggressive offer"

- Recipient factors
- 1. Body size and ascites
- 2. Portal hypertension
- 3. Surgical risk (PVT, Re-LT)
- 4. HCV vs. other
- 5. "Hot list"

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Patients with low MELD but is symptomatic or has HCC beyond Milan criteria, thus willing to accept marginal grafts.

Gap between supply and demand

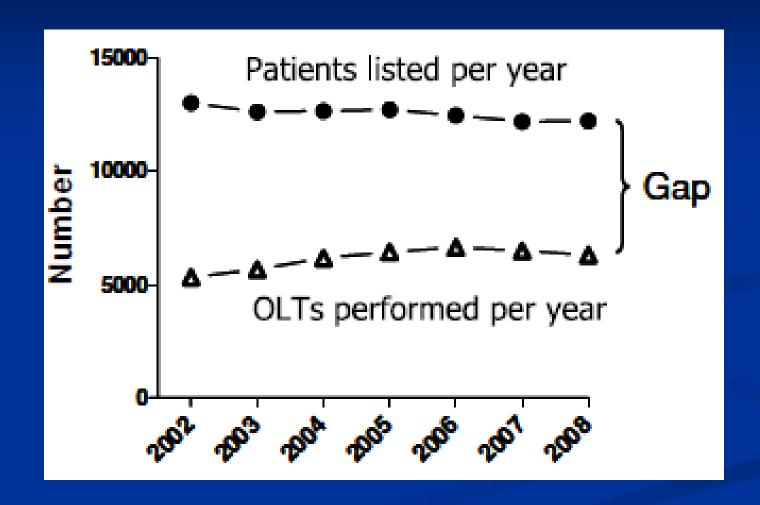
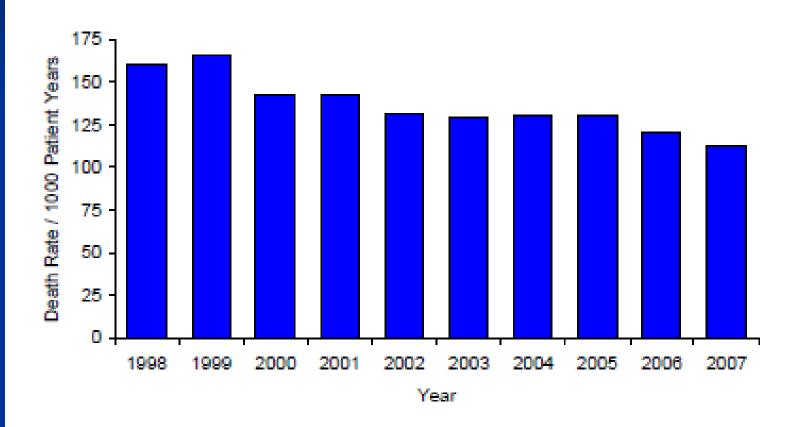
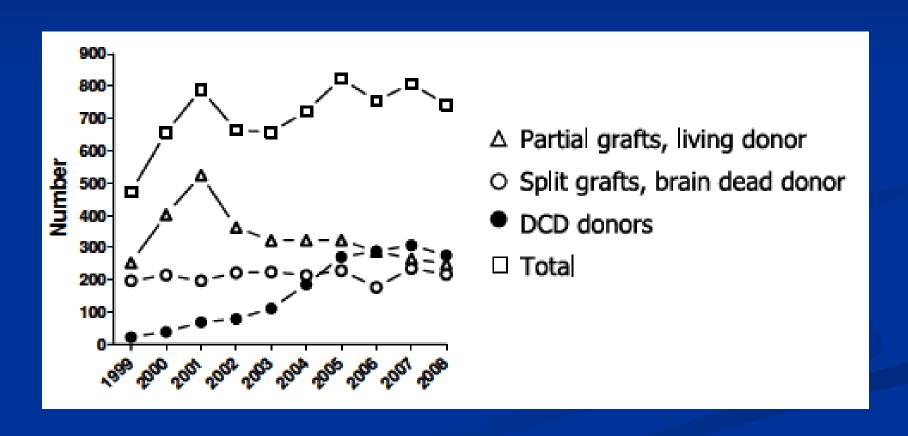


Figure IV-4. Unadjusted Death Rates per 1,000 Patient-Years at Risk, 1998-2007, Liver Waiting List



Source: 2008 OPTN/SRTR Annual Report, Table 9.3.

Alternative liver grafts in US 1999-2008



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Split Transplantation in US

- Survey for split liver transplant, 4/00-3/01
 - 207 LLS, 152 RTS, 15 left lobe, and 13 right lobe grafts

 Ann Surg, Renz, 2004
- 1260 Pediatric LT for <12 yo recipient, 2/02-12/04</p>
 - 52% received whole liver transplantation
 - 33% SLT
 - 15% LDLT

Liver Transplant, Becker, 2008

LDLT vs. cadaveric graft: Advantages and Disadvantages

Advantages

- Assures a healthy organ with minimal preservation damage
- Independence from long cadaveric waiting list
- Optimizes the timing of transplantation
- Helps alleviate the severe shortage of cadaveric livers and death on the waiting list

Disadvantages

- Finite risk of donor morbidity and mortality
- Both operation are technically complex
- The program is extremely laborintensive
- Reputational risk

Split vs. whole liver graft: Advantages and Disadvantages

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- The program is extremely laborintensive
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Ideal Candidates for LDLT

- 1. Patients who has live donors
- 2. Pediatric patients (Anonymous donor)
- 3. Patients with lower MELD who need to wait long but are suffering from symptoms
 - Refractory ascites
 - Encephalopathy
- Exclusion in Cleveland Clinic
- 1. Re-LT
- 2. Kidney failure

Right vs. Left Lobe in LDLT

Depends on graft size and severity of portal hypertension







Cut1, Right Lobe Graft without MHV

Cut1, Right Lobe Graft without MHV (Volumes)

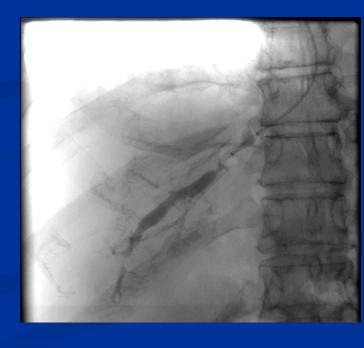
Territory	Volume	Relative (%)
Cutting Plane	10 ml	< 1.0
Graft	698 ml	57.8
Remnant	498 ml	41.2
Total	1206 ml	100.0

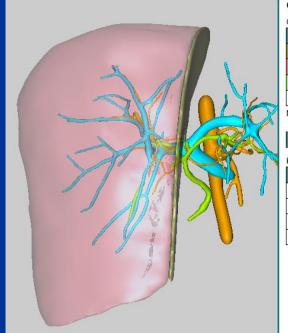
Minimal deviations can be caused by rounding errors.

The estimated graft weight is about 635 g.

Kay figures

Ratio	Based On	Value
Graft Recipient Body Weight Ratio	Estimated Graft Weight	0.87
Graft Recipient Body Weight Ratio	Graft Volume	0.96
Graft to SLV Ratio	Estimated Graft Weight	0.49
Graft to SLV Ratio	Graft Volume	0.54





Splittable Donor

- 1. Donor age less than 40 years
- 2. Stable systemic hemodynamics
- 3. Normal gross appearance of the liver during organ procurement.
 - Liver biopsy as needed.
 - Macrosteatosis < 20%</p>

Ideal Candidates for Split - 1st half of hemi-liver

- 1. Got an offer of good donor, but big
- 2. Recipient with standard surgical risk
 - Avoid re-LT, or extensive PVT



Ideal Candidates for Split - 2nd half of hemi-liver

- 1.Smaller patients
 - > <70%, <100% of donor BW for L, and R lobe
- 2. Recipient with standard surgical risk
- 3. Not much portal hypertension
- 4.(With good portosystemic shunt)

Other consideration

- 1.Man power (Young Attendings in town?)
- 2. Patients who don't have live donors

Ideal Candidates for Right Trisegment Split

1. Anybody who needs liver transplant

Question -1

32 year-old male. 180cm,120kg (5'10", 264 lbs), BMI 37.

Drinker 5 beer/day. COD Trauma. Brain dead 2 days after admission. Platelet at admission was 150 K, and now 70K.

Normal LFTs. Had transfusions but now hemodynamically stable.

Here is your center's allocation list. What would you do?

#1	MELD 28	56 yo F, PBC, minimal Portal HTN	160cm, 56 kg (5' 3", 123 lbs)
#2	Other center	******	*****
#3	MELD 26	65 y/o M, PCS, minimal PHT	180cm, 120kg (5' 10", 264 lbs)

doi: 10.1111/ajt.12791

Split Liver Transplantation Using Hemiliver Graft in the MELD Era: A Single Center Experience in the United States

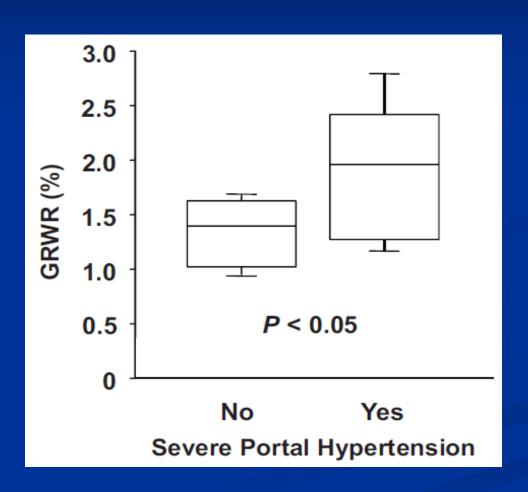
K. Hashimoto*, C. Quintini, F. N. Aucejo, M. Fujiki, T. Diago, M. J. Watson, D. M. Kelly, C. G. Winans, B. Eghtesad, J. J. Fung and C. M. Miller

Department of General Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH *Corresponding author: Koji Hashimoto, hashimk@ccf.org

Split Donor Demographics

Table 2: Donor de	Table 2: Donor demographics				
	Hemiliver	Whole liver			
	(n = 16)	(n = 121)	p-Value		
Age (years) ¹	22 (11–39)	27 (10–40)	0.14		
Gender (male)	16 (100.0%)	85 (70.2%)	< 0.01		
Height (cm) ¹	180 (170-193)	175 (120-203)	0.02		
Weight (kg)1	89 (38-115)	77 (24-143)	0.11		
BMI (kg/m ²) ¹	27.0 (13.1–33.5)	24.6 (17.2-48.8)	0.69		
Vasopressor use	12 (75.0%)	67 (55.4%)	0.18		
Cause of death			0.97		
Trauma	13 (81.3%)	95 (78.5%)			
Cerebrovascular	2 (12.5%)	18 (14.9%)			
Anoxia	1 (6.3%)	8 (6.6%)			
Serum sodium ¹	152 (139-172)	147 (125-167)	0.02		
ALT ¹	36 (17-442)	37 (3-1357)	0.51		
Total bilirubin ¹	1.0 (0.4–2.0)	0.8 (0.2–5.3)	0.25		

Good matching to get an appropriate GRWR



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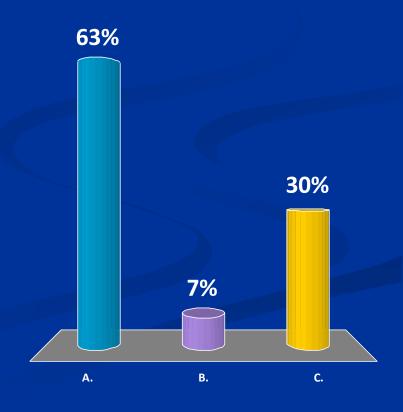
#1	MELD 28	56 yo F, PBC, some PHTN	160cm, 56 kg (5' 3", 123 lbs)
#2	Other center	******	*******
#3	MELD 26	65 yo M, HCV, severe PHTN	180cm, 120kg (5' 10", 264 lbs)

- 1. Decline for #1. Liver would be fatty. Also I don't think #2 in the other center is such big.
- 2. Accept for #1 for left lobe, and admit #3 for right lobe.
- 3. Accept for #1 for left lobe, and admit #3 for back up.

What would you do?

#1	MELD 28	56 yo F, PBC, minimal Portal HTN	160cm, 56 kg (5' 3", 123 lbs)
#2	Other center	******	******
#3	MELD 26	65 y/o M, PCS, minimal PHT	180cm, 120kg (5' 10", 264 lbs)

- A. Decline for #1. Liver will be fatty. Also I don't think #2 in the other center is so big; therefore we will get it for #3.
- B. Accept for #1 for left lobe, and admit #3 for right lobe.
- c. Accept for #1 for left lobe, and admit #3 for back up if liver is marginal and #2 declines.



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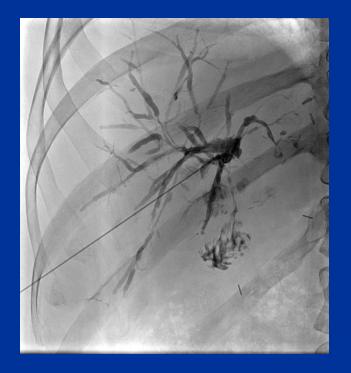
Over the last decade, controlled DCD liver transplantation has been a fast growing source of liver grafts in Europe and the US

Table 1. The classification of DCD donors as originally described by the First International Workshop on NHB donors that was organised in Maastricht in 1995. The term 'controlled' and 'uncontrolled' were not used at the workshop but added later. (Reproduced from Talbot and D'Alessandro [45,85], and Kootstra [3,4] by Permission of Oxford University Press, Inc.).

Categorie of non-heart beating donors				
Category	Alternative categorization	Status of potential donor	Hospital department	Process
I	Uncontrolled	Dead upon arrival	Accident and emergency	Viability testing
ا _	Uncontrolled	Resuscitation attempted without success	Accident and emergency	Viability testing
_	Controlled	Awaiting cardiac arrest	Intensive care	Transplantation
IV	Controlled	Cardiac arrest while brain dead	Intensive care	Transplantation

DCD grafts are associated with increased incidence of PNF, HAT or ischemic cholangiopathy.

If in a DBD the organ make a single step from warm oxygenated and metabolically active to cold, hypoxic and metabolically inactive the DCD organ at the time of X-clamp has already suffered from a period of hypotension/hypoxia followed by the cardiac arrest



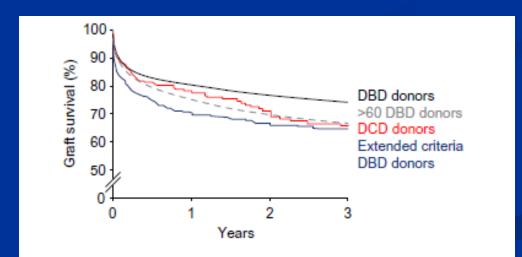


Fig. 1. Graft survival at 1, 2, and 3 years after liver transplantation using standard criteria DBD donors (black line), extended criteria DBD donors (blue line), >60 DBD donors (grey dotted line), and DCD donors (red line). Data from the Collaborative Transplant Study (CTS).

How to improve the outcome? Limit the donor warm ischemia time (DWIT)

- 1. Huddle with the local hospital personnel (where patient will be extubated; assess men power to move the donor from ICU during the "no touch time"; surgical prep and drape during the "no touch" time)
- 2. Experienced surgeon to perform the "super-rapid technique"
- 3. Discard livers with *in situ* WIT > 30min

The "super rapid technique"

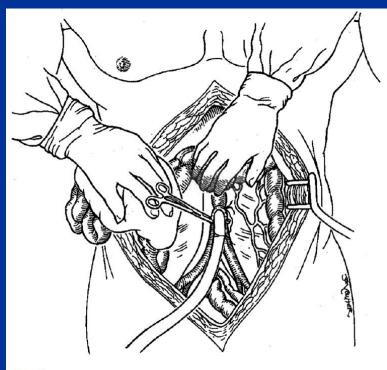


Figure 1. The super-rapid technique. Midline abdominal incision and aortic cannulation for immediate perfusion of cold preservation solution.

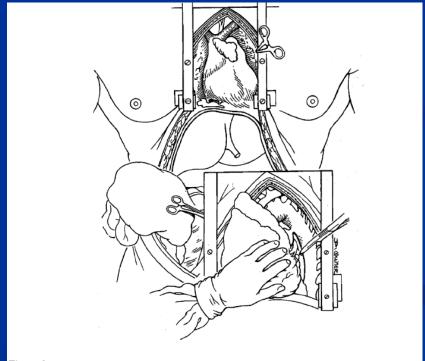


Figure 2.Sternal-splitting, thoracic aorta cross-clamping and intrapericardial inferior vena cava venting.

Transplantation. 1995 January 27; 59(2): 197-203.

Each minute increase in the asystole-to-cross clamp duration is associated with a 16.1% increase in the odds for the development of ischemic cholangiopathy or hepatic necrosis

The goal of the rapid procurement technique is to clear the blood from the peribiliary arterioles in a rapid manner

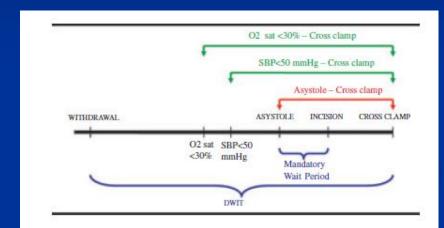


Figure 1 Different time points during procurement.

	No ITBS	ITBS	P
DCD WIT	24.31 ± 8.70 (18, 24, 30)	24.41 ± 7.67 (19, 24, 30)	0.756
Withdrawal-asystole	15.36 ± 8.55 (10, 14, 19)	14.42 ± 6.07 (9.75, 13, 19)	0.819
Asystole-cross clamp	8.81 ± 3.27 (7, 8, 11)	10.65 ± 3.96 (8, 10, 12.25)	0.048
Hypotensive WIT			
Withdrawal-SBP < 50	10.24 ± 8.42 (5, 9, 14)	10.39 ± 56.8 (6, 10, 15)	0.405
SBP < 50-Asystole	5.2 ± 5.09 (1, 3, 8)	$3.35 \pm 4.59 (1, 3,5)$	0.176
SBP<50-cross clamp	14.13 ± 5.84 (10, 13, 17)	14.26 ± 4.84 (11, 13, 17)	0.839
Hypoxic WIT			
Withdrawal-O2 Sat < 30	8.19 ± 7.03 (4, 6,11)	8.76 ± 5.71 (4, 7, 12.5)	0.483
O2 Sat < 30-asystole	7.51 ± 6.12 (3, 7, 11)	5.67 ± 4.28 (2, 4, 9.5)	0.305
O2 Sat < 30-cross clamp	16.52 ± 6.75 (11, 16, 21)	16.52 ± 5.29 (12, 16, 19.5)	0.998

Table 3. Comparison of procurement time points in DCD liver grafts with diagnosis of ITBS versus no ITBS (seven patients who had HAT and five patients who had PNFs were excluded from analysis).

Values in minutes, presented as mean \pm SD (25th, 50th, 75th percentile). Bold values indicates significant at P < 0.05.

How to improve the outcome? Best donor-recipient match

- 1. Cut off of the DCD donor age?
- 2. Avoid "redo" or recipient on life support at the time of transplant

TABLE 2.	Multivariate Cox proportional ha	zards model of risk fa	actors for graft loss and DCD risk index	
	Risk factors	Coefficient	95% confidence interval	P value
Recipient				
Previous tr	ransplant			
No		Reference		
Yes		0.692	1.997 (1.318-3.027)	0.001
Life suppo	rt at transplantation			
No				Reference
Yes		0.632	1.882 (1.241-2.854)	0.003
Donor				
Age (years)			
≤45				Reference
45-60		0.314	1.369 (1.027-1.825)	0.032
>60		0.569	1.766 (1.076-2.900)	0.025
Donor war	rm ischemic time (minutes)			
≤15				Reference
15-30		0.315	1.370 (1.037-1.809)	0.027
>30		0.576	1.780 (1.137-2.785)	0.012
Cold ische	mic time (hours)			
≤10				Reference
>10		0.284	1.329 (1.001-1.763)	0.049
DCD rtsk	index-exp[(0.692 if previous transplant	(TX) htstory)+(0.632 tf	on life support)+(0.314 if 45 <donor age≤60)+(<="" td=""><td>0.569 If donor</td></donor>	0.569 If donor

DCD risk index—exp[(0.692 if previous transplant (TX) history)+(0.632 if on life support)+(0.314 if 45<donor age≤60)+(0.569 if donor age>60)+(0.315 if 15<DWIT≤30)+(0.576 if DWIT>30]+)0.284 if CIT>10)].

How to improve the outcome? Minimize the cold ischemia time (CIT)

- 1. Select recipient with standard technical difficulty
 - No previous liver surgery or transplant
 - Avoid the case with concern in portal inflow
- 2.Start the recipient sooner



How to improve the outcome? Consider improved liver preservation (TPA etc..)

Journal of Hepatology 2012 vol. 56 | 474-485

Table 5. Strategies to optimize the outcome of DCD liver transplantation along the time line of the different steps during the course of organ donation, preservation and transplantation and their status (clinically applied vs. preclinical status).

Time period	Principle	Solution	Status
Donor			Ethically difficult
	Donor pretreatment		
	Avoid extended warm ischaemia time	Discard livers with in situ warm ischaemia >30 minutes	Clinically applied
Flush-out			
	Improve complete flush-out of the microcirculation	Warm prefibrinolytic pre-flush	Clinically applied
		Inital flush with low viscosity preservation solution	Clinically applied
		Final flush-out with UW (high viscosity-gold standard preservation solution)	Clinically applied
Preservation			
	Limit cold ischaemia	Allocation of the liver to the procuring transplant center	Clinically applied
		Transplant livers as soon as possible Select a recipient in whom the hepatectomy is expected to be of short duration	Clinically applied
	Alternative cold perfusion solutions	Cytoprotective additives to the perfusion solution	Preclinical status
	Ex vivo preservation by machine perfusion	Oxygenated hypothermic machine perfusion preservation	Preclinical status but clinically applied in a safety and feasibility trial for normal livers
		Hypothermic oxygenated machine perfusion preservation	Preclinical status
		ex vivo normothermic liver perfusion	Preclinical status
	In vivo normothermic recirculation	in vivo normothermic liver perfusion using ECMO	Clinically applied
Recipient			
		Select a recipient who may tolerate dysfunction	Clinically applied
	Reducing the ischaemia reperfusion injury	Multi-factorial biological modulation strategy	Preclinical status

Question -2

20 year-old male, football player, BMI 29 in ICU with ALF due to acetaminophen intoxication.

Intubated and sedated, clinical condition rapidly deteriorating, small pressors requirement, INR 6, Bil 10, sCr 1.5 MELD 39.

PMH negative

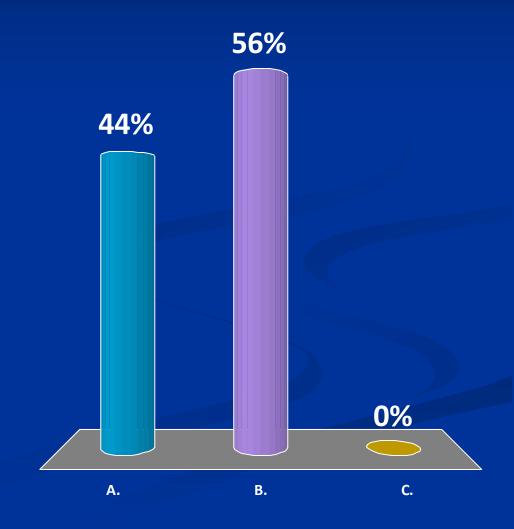
You have been offered, simultaneously:

- #1. 25 yo DCD, car accident, no PMH, LFTs WNL, BMI 25
- #2. 62 yo DBD, trauma, mild transaminitis, BMI 32, Type 2 DM and hypertension

Considering that size is not an issue, which would you choose? Unfortunately, you cannot accept both at this time.

Which would you choose?

- A. Accept #1
- B. Accept #2
- c. Decline both



Answer

Accept #2 because the risk of PNF is lower as well as the risk of a bad IR related intraoperative coagulopathy. Moreover 1 might not expire!

Remember, the best DCD is a defacto extended criteria donor and, considering the concept of donor risk index, DCD liver are associated with a greater risk of graft failure when compared to 60-70 donor age.

Our recipient is rapidly deteriorating therefore waiting is not an option.

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Hepatitis C and Liver Transplant

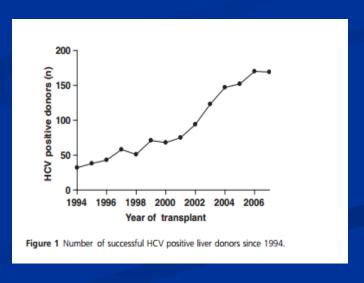
- HCV among the most common causes of liver disease worldwide
- HCV prevalence in USA: 1.6 % of population
- HCV infection causes 20 % of acute and 70% of chronic hepatitis.
- The most common indication for OLT for now, but not in near future.
- Patient and graft survival rates comparable with other indication for OLT.

Recurrence of Hepatitis C post-OLT

- Almost universal
- Progression is variable:
 - > 70% develop mild fibrosis
 - > 25% progress to cirrhosis within 5 years of LT
 - > 5% develop fibrosing cholestatic hepatitis (FCH)
 - Grafts from older donors (>50 years old) associated with lower patient and graft survival
 - HCV recurrence lowers graft and patient survival rates.

Liver allografts from HCV positive donors

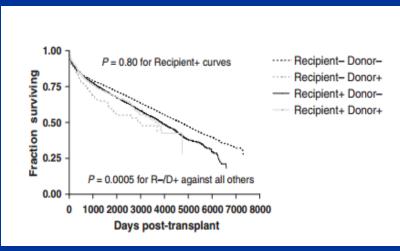
- With background of donor shortage, HCV +ve donor has become one of the important ECDs: up to 1.7 % of all successful OLTs
- Recipients of HCV +ve grafts: slightly older (age 51.8 years), have higher prevalence of pre-transplant HCC (8.9% vs 6.6 %)
- HCV + donors: older (41.4 vs 37 yo), CVA and anoxia were most common cause of death.
- HCV + organs: more likely to exported to other UNOS regions (20.1 vs 7.5 %)

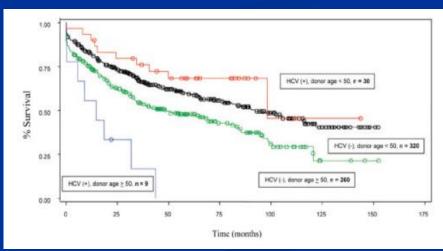


Impact of donor age on survival and fibrosis progression in patients with hepatitis C undergoing liver transplantation using HCV + allografts Liver Transpl. 2006 12: 1496-1503

Liver allografts from HCV positive donors

- No statistical difference in 5 year survival in HCV recipients using HCV + or HCV – allografts.
- Recipients of HCV + grafts from older donors (>50 yo) have higher rates of death and graft failure, and develop more extensive fibrosis.
- Donor HCV status is not an independent predictor of mortality after liver transplantation.





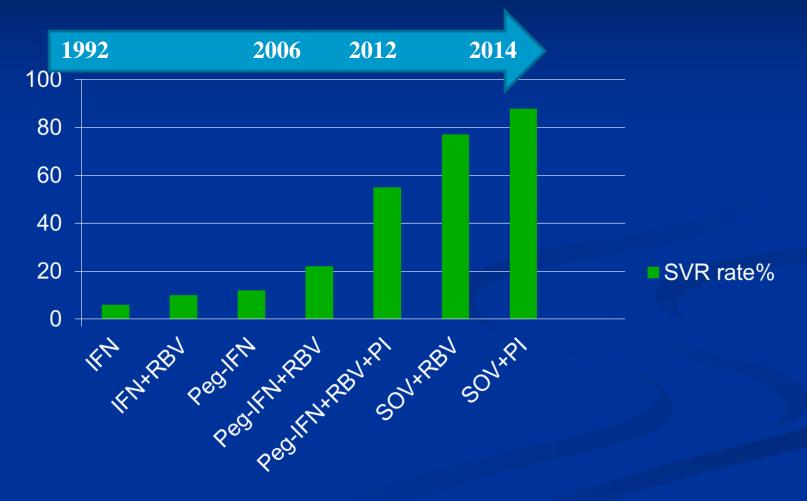
Liver allogtafrs from Hepatitis C positive donors can offer good outcomes in hepatitis C positive recepiebts: a US national transplant registry analysis: Northup P. Pruett T, et al: Transp Inter 2010: 23; 1038-1044

Dramatic Advance in the Treatment for Recurrent HCV

"There are decades where nothing happens; and there are weeks where decades happen"

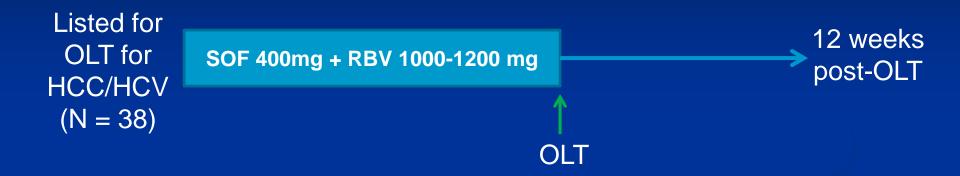
Vladimir Ilyich Lenin

Treatment of HCV Post-OLT



PI = Protease Inhibitor (talepravir, bocepravir or now lepdepasvir)

SOF + RBV to Prevent Recurrence of HCV post-OLT



- Recurrence of HCV post-OLT in 10/38 (26%)
- No recurrence in 24/25 (96%) of patients who maintained negative HCV RNA >4 weeks prior to OLT

Question -3

Donor offer of 55 year old female HCV Ab +ve DBD. Liver Bx showed mild inflammation with periportal fibrosis.

Mild elevation of transaminase but normal bili. Platelet count at admission was 140 K.

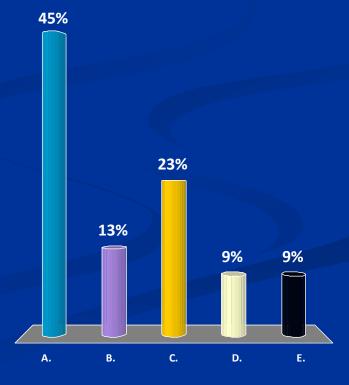
Which HCV RNA +ve recipient(s) is/are suitable for the donor?

		MELD	genotype	Treatment
Α	44 yo M	35	1a	IFN failure, HCV RNA+ve
В	54 yo M	18	1b	SOF-RBV started 2 months ago with significant reduction in viral load
С	56 yo F	26	3	IFN failure, HCV RNA+ve

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- A. A
- B. B
- c. A and B
- D. B and C
- E. None



Answer

1. A

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Re-OLTX



It is already complicated.
Select non-complicated donor.

Volumetry of recipient liver is useful to determine the acceptable size of donors.

A small patient with splenomegaly awaiting 3rd re-do. Liver volume is 1300 mL

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"Aggressive offer"

- Marginal donors who are likely to be turned down by many centers
 - > Aged DBD (>75 y.o.) with extensive cardiovascular history
 - > Aged DCD (>55 y.o.), DCD with high BMI (>40)
 - Concern of transmittable disease (meningitis, infection, brain tumor)
 - > Offer from donor OR
 - > Before or after X clamp
- Often from other OPO
- Many cases become "open offer"
 - Because all other center turned down, you can use the liver for anybody you want.

Who should receive "aggressive offer"?

- If the risk is acceptable for regular patients, accept for them.
- Great opportunity for patients on "hot list"
- Offer from donor OR
 - Try to delay X clamp if it is not done
 - Find a suitable recipient who;
 - 1. lives close to the hospital,
 - 2. has a standard surgical risk, and
 - doesn't have blood antibody



Question

64 YO M, HCV, Blood type B with MELD 17. Six admissions (2 in ICU) in the last year for encephalopathy due to large splenorenal shunt. Now admitted in your hospital. Waiting LT for 2 years, now on "hot list".

170 cm, 67 kg (5'7", 147 lbs). No PVT or previous surgery. Needs 4 hrs to get blood ready.

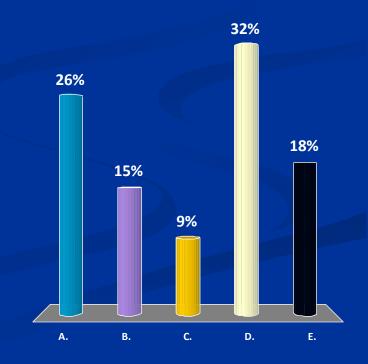
Which donors are suitable for him with 10 patients being on the waiting list above him?

Α	Left-lobe split	34 yo M, 165 cm, 70 kg (5'5", 154 lbs) (Est. L-lobe 620 g)
В	DCD	58 yo M, 165 cm, 65 kg (5'5", 143 lbs), BMI 24
С	DCD	35 yo M, 160 cm, 103 kg (5'3", 227 lbs), BMI 40
D	DBD, 3hrs after X clamp	57 yo, liver 2.6 kg, macrosteatosis 30-40%, Standard HA anatomy. Liver at the hospital across the road

Which donors do you think are suitable for him with 10 patients being on the waiting list above him?

А	Left-lobe split	34 yo M, 165 cm, 70 kg (5'5", 154 lbs) (Est. L-lobe 620 g)
В	DCD	58 yo M, 165 cm, 65 kg (5'5", 143 lbs), BMI 24
С	DCD	35 yo M, 160 cm, 103 kg (5'3", 227 lbs), BMI 40
D	DBD, 3hrs after X clamp	57 yo, liver 2.6 kg, macrosteatosis 30-40%, Standard HA anatomy. Liver at the hospital across the road

- A. A
- B. A and B
- c. A,B and C
- D. B and C
- E. All



Answer

А	L-lobe split	34 yo M, 165 cm, 70 kg, (Est. L-lobe 620 g)
В	DCD	58 yo M, 165 cm, 65 kg, BMI 24
С	DCD	35 yo M, 160 cm, 103 kg, BMI 40
D	DBD, 3hrs after X clamp	57 yo, liver 2.6 kg, macrosteatosis 30-40%, Standard HA anatomy. Liver at the hospital across the road

- A) Good match. GRWR of 0.92 is acceptable with a large shunt.
- B) Controversial. Depends on program. May be a good chance for him.
- C) When liver is not fatty, good enough for regular patients above him on the list.
- D) Seems to be very high risk of PNF and too big liver for him. Big fatty liver with prolonged CIT and possibly poor inflow are bad combinations.

My answer is 2) A and B.

Conclusions

- In the background of high mortality rate on the waiting list of LT, it is crucial to use aggressively the alternative organ pool including partial liver, DCD, and "high risk donor".
- Partial liver transplant can be done with favorable outcome by good donor-recipient pairing.
- DCD LT reportedly has inferior graft outcome, but can be improved with careful donor and recipient selection in addition to fundamental efforts including shortening canulation time in donor, and total CIT.

Conclusions

 The recent advance in HCV treatment has potential to rewrite the strategy of LT for HCV. The fear of graft failure from recurrent HCV is significantly decreased. There will be much less HCV +ve recipients in near future.

 It is imperative to maximize the effort to provide the chance of transplant to low MELD patients who have significant complications.



 Table 4: Recipient demographics

Creatinine (mg/dL)¹

 INR^1

	Hemiliver (n = 25)	Whole liver (n = 121)	p-Va
Age (years) ¹	56 (13–75)	55 (18–77)	0.8
Gender (female)	20 (80.0%)	33 (27.3%)	< 0.0
Height (cm) ¹	158 (114–180)	173 (145–203)	< 0.0
Weight (kg) ¹	58 (25-101)	88 (41–160)	< 0.0
BMI (kg/m ²) ¹	24.2 (16.3–39.5)	29.1 (17.6-49.4)	0.0
Underlying liver disease			< 0.0
Viral hepatitis	4 (16.0%)	92 (76.0%)	
Alcoholic	3 (12.0%)	6 (5.0%)	
Cryptogenic/NASH	3 (12.0%)	13 (10.7%)	
PBC/PSC/AIH	7 (28.0%)	5 (4.1%)	
Fulminant hepatic failure	1 (4.0%)	1 (0.8%)	
Metabolic disorder	3 (12.0%)	0 (0.0%)	
Others	4 (16.0%)	4 (3.3%)	
Donor risk index ¹	1.60 (1.31-2.02)	1.10 (0.87-1.65)	< 0.0
Cold ischemia time (min) ¹	390 (248-592)	421 (150-840)	0.3
Chemical MELD score ¹	17 (7–26)	18 (6–43)	0.1
Listing MELD score ¹	22 (14–28)	21 (10-40)	0.8
Platelet count (×10 ³ /μL) ¹	98 (30-651)	73 (13-422)	0.0
Albumin (g/dL) ¹	3.2 (2.0-4.5)	3.0 (1.5-4.9)	0.2
Total bilirubin (mg/dL) ¹	3.2 (0.2–27.7)	3.2 (0.2–32.6)	0.4
Serum sodium (mEq/L) ¹	137 (124–147)	137 (119–148)	0.9

0.64 (0.35-11.01)

1.3 (0.6-2.1)

< 0.0

0.5

1.00 (0.41-11.21)

1.3 (0.9-3.7)