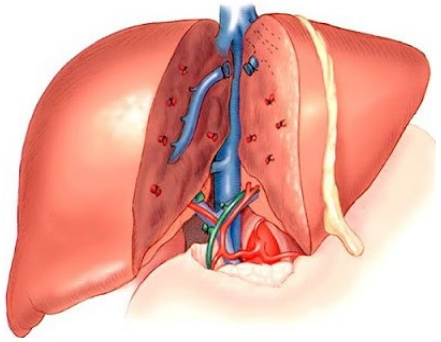

Innovations in Living Donor Liver Transplant

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Outline

- Ethics of LDLT
- LDLT Trends
- Donor-Recipient Incompatibility
- High and Low MELD Recipients
- Older Donors
- Steatotic Donors
- LDLT in Transplant Oncology
- Advances in Surgical Techniques

Equipoise

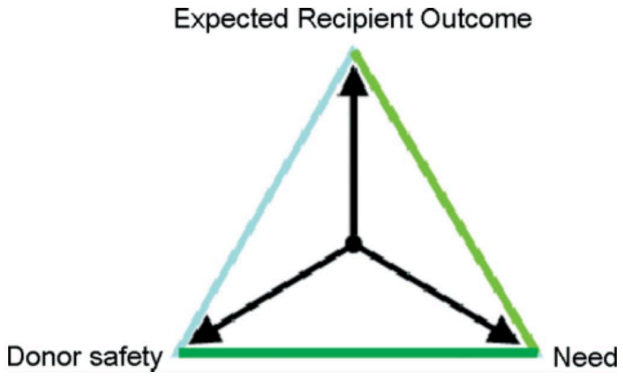
-Foundational ethical principles to justify living organ donation:

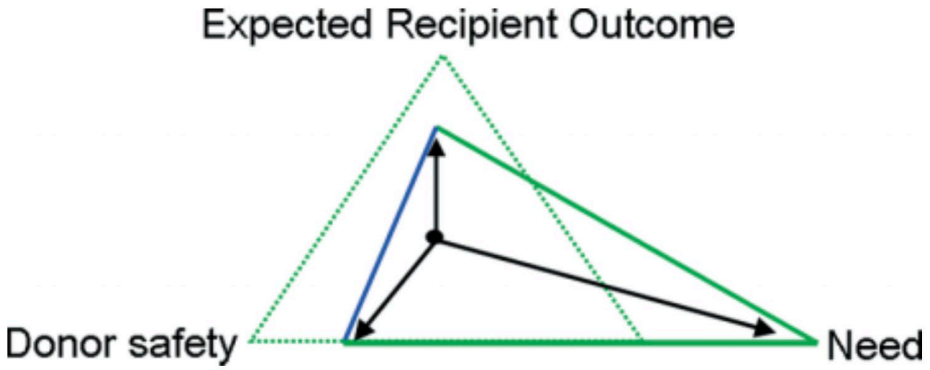
- Autonomy
- Beneficence
- Nonmaleficence *
- Distributive justice (more significant role in deceased donor organ allocation)

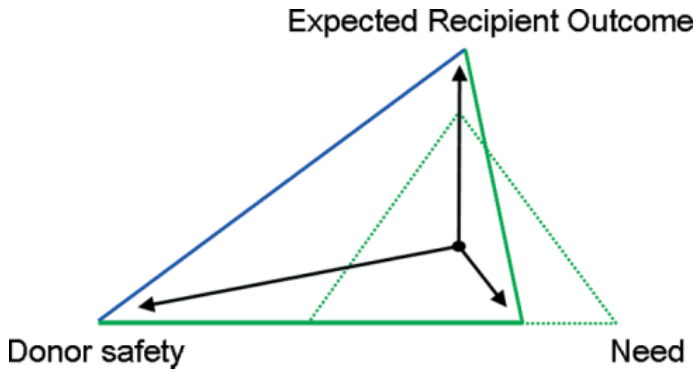
- Assessing and optimizing donor safety, evaluating expected recipient outcomes, and considering individual and societal needs

- Equipoise in living donor: risk to donor, balanced by benefit to recipient

Equipoise







Miller CM, et al. Mount Sinai Journal of Medicine 2012

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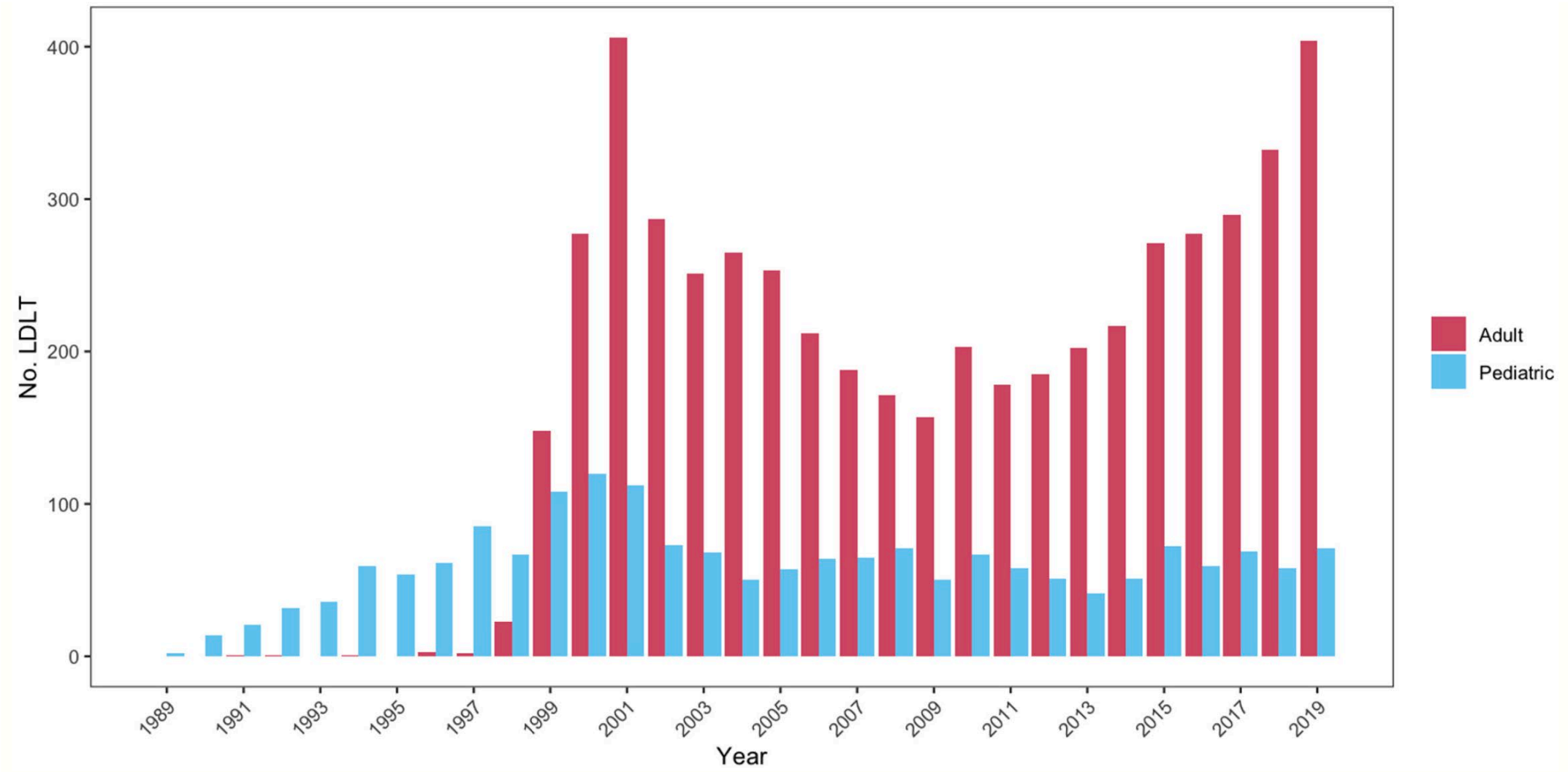
U.S. LDLT Trends



Fox A, et al. Hepatology 2022

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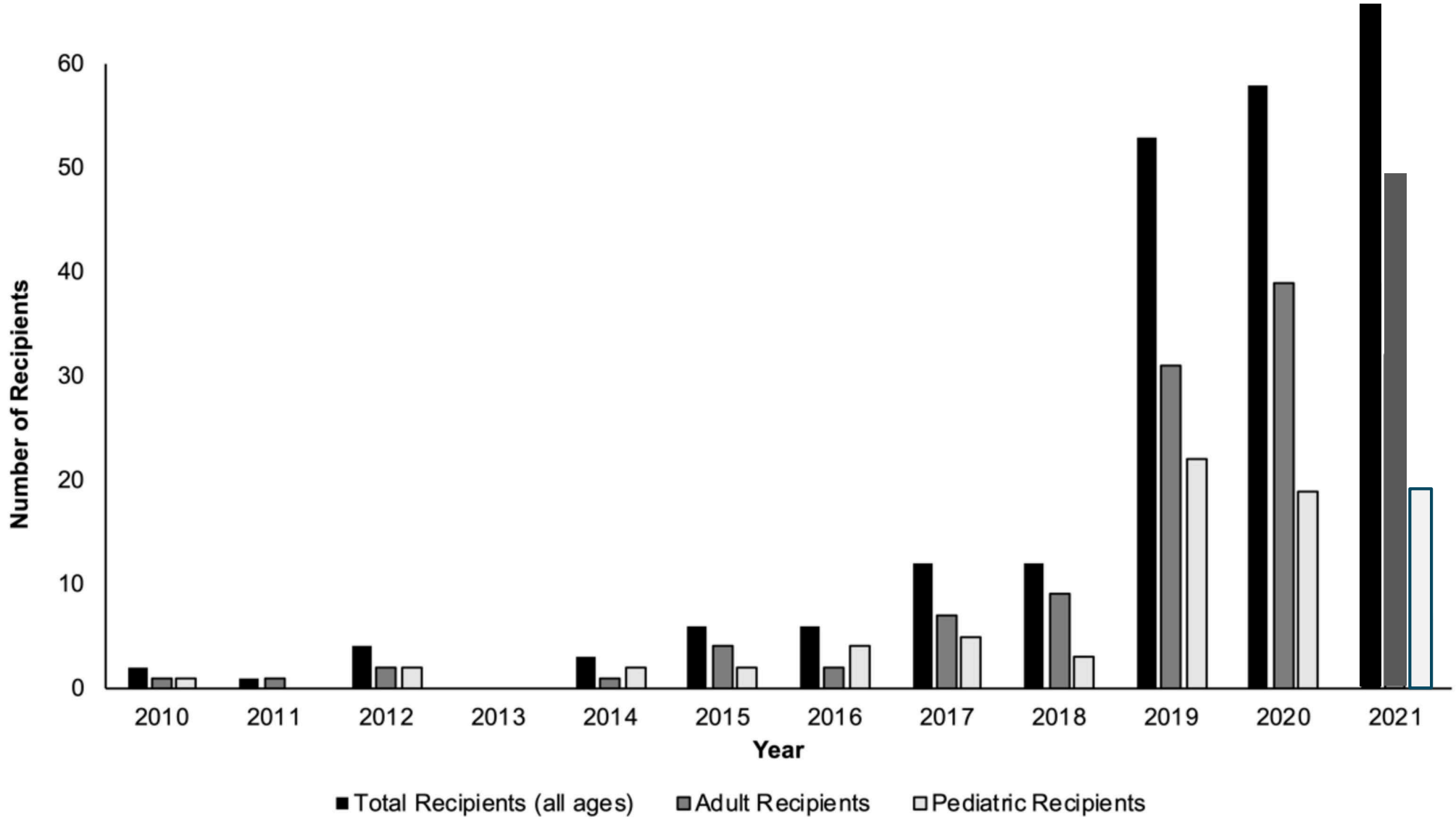
U.S. Non-Directed Donor LDLT Trends



Bambha K, Biggins SW, et al. Frontiers in Immunol 2023

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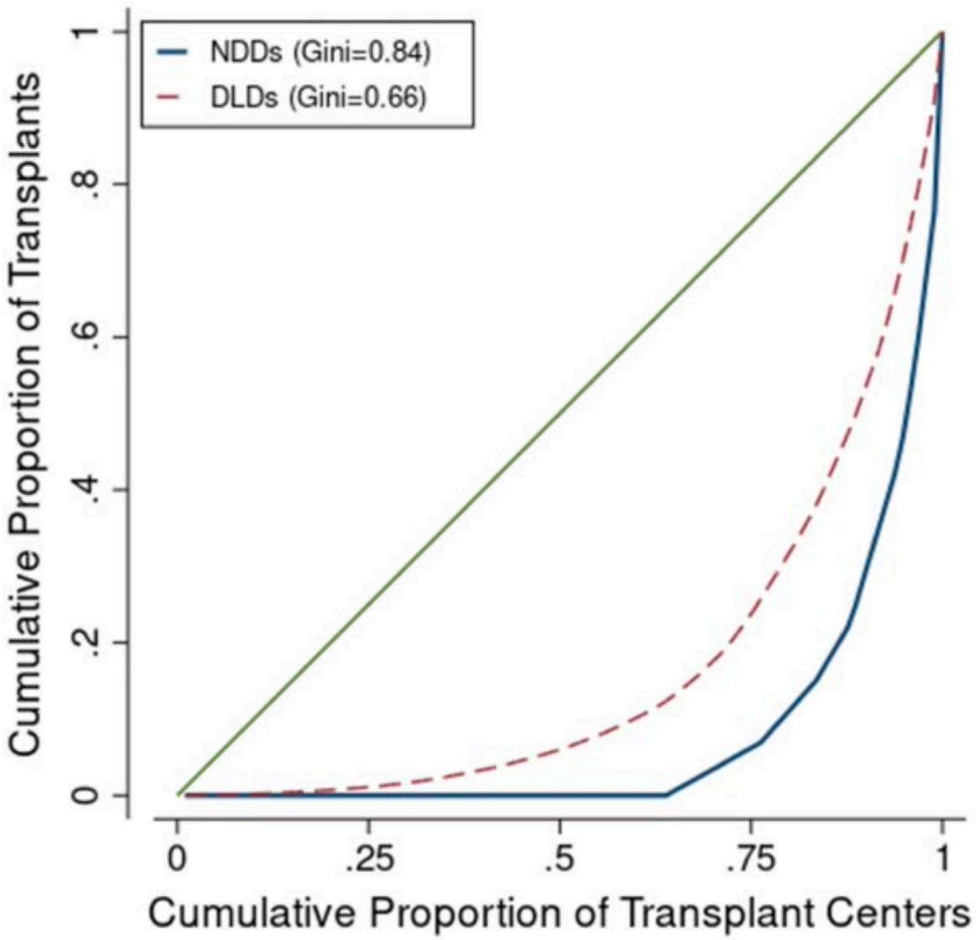
Non-Directed Living Liver Donors



Herbst et al. Transplantation 2022

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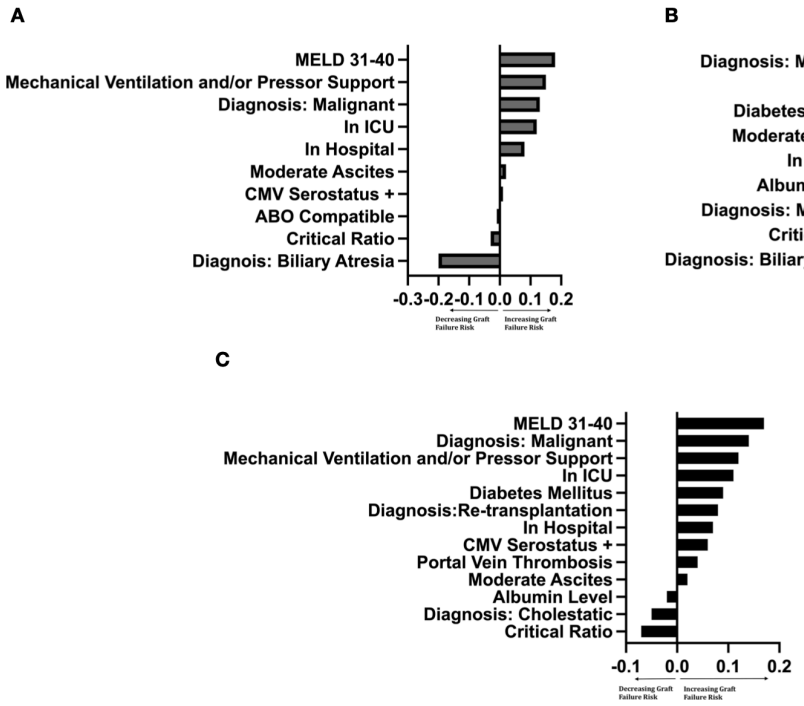
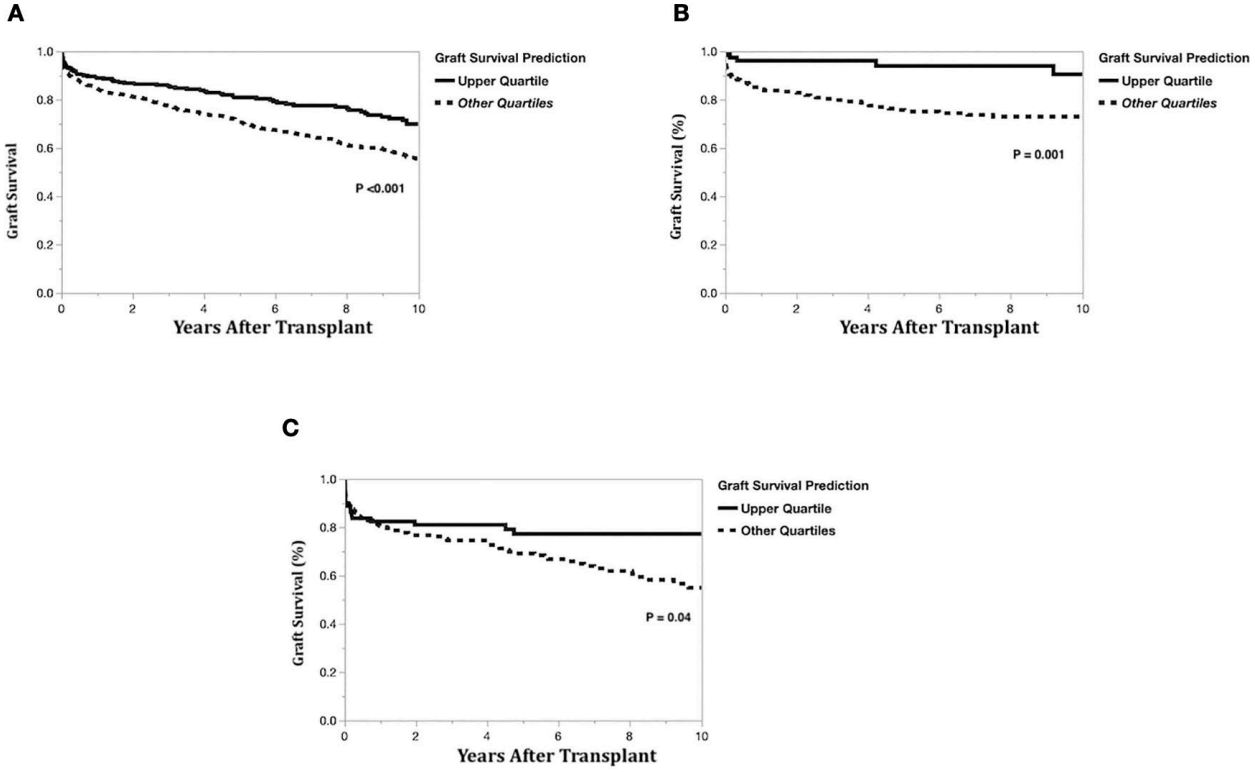
Maximizing Utility of Nondirected LLD Grafts Using Machine Learning





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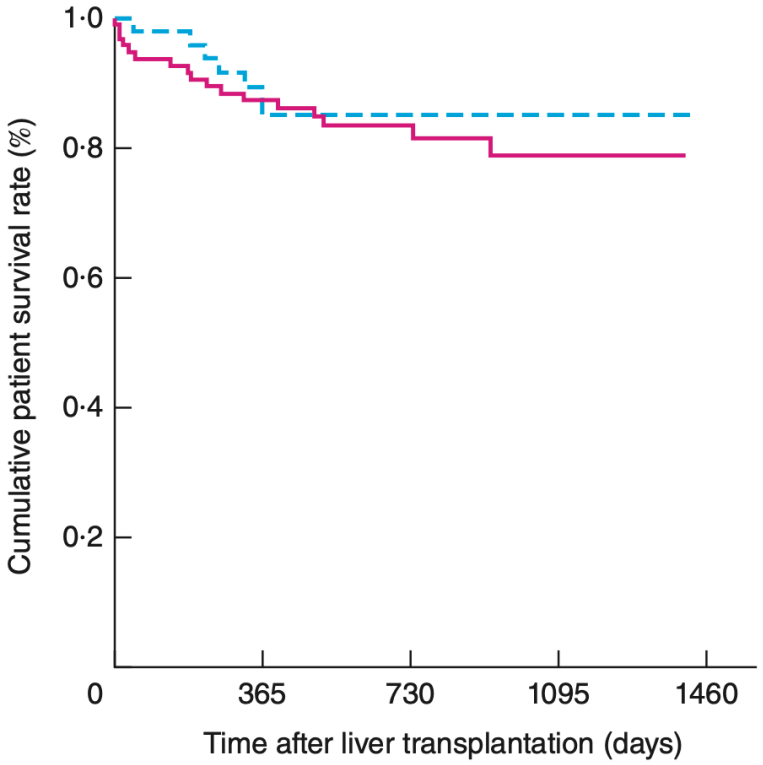
Donor-Recipient Incompatibility

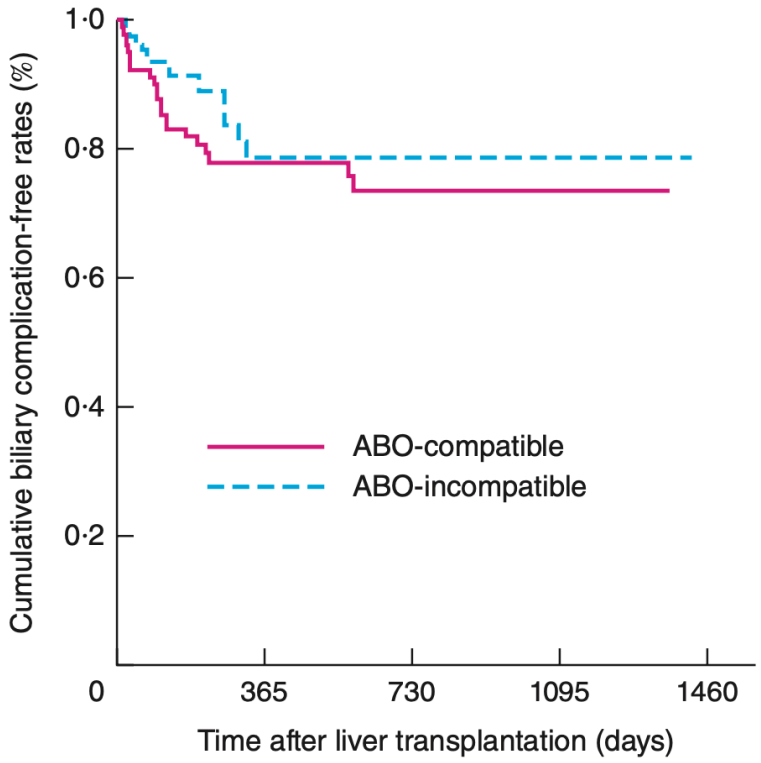
- LDLT accounts for about 6% of all liver transplantations in the US

- Most common reasons for donor-recipient incompatibility
  - ABO incompatibility between the donor and the recipient
  - Donor liver graft size is too small for the recipient
  - Potential remnant liver volume is too small for the donor

ABOi LDLT



No. at risk					
ABO-compatible	94	78	43	21	0
ABO-incompatible	47	40	24	9	1



No. at risk					
ABO-compatible	94	51	23	12	0
ABO-incompatible	47	29	14	5	1

Kim JM, et al. BJS 2016

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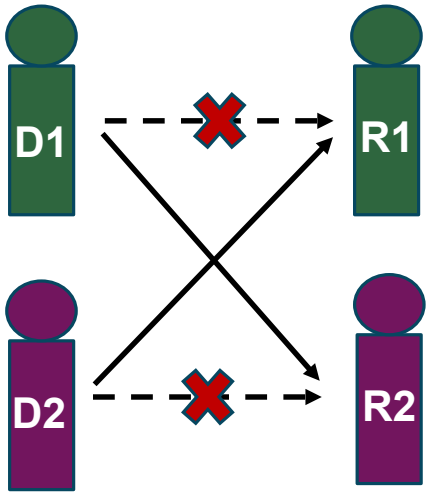
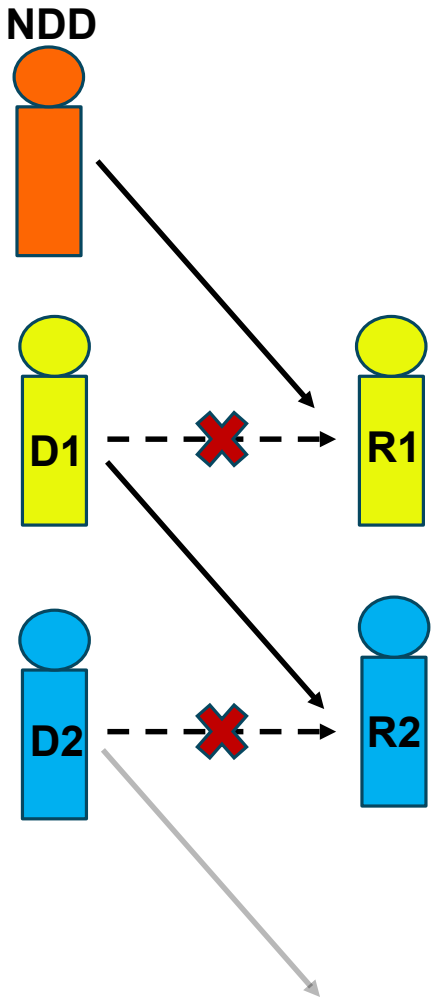
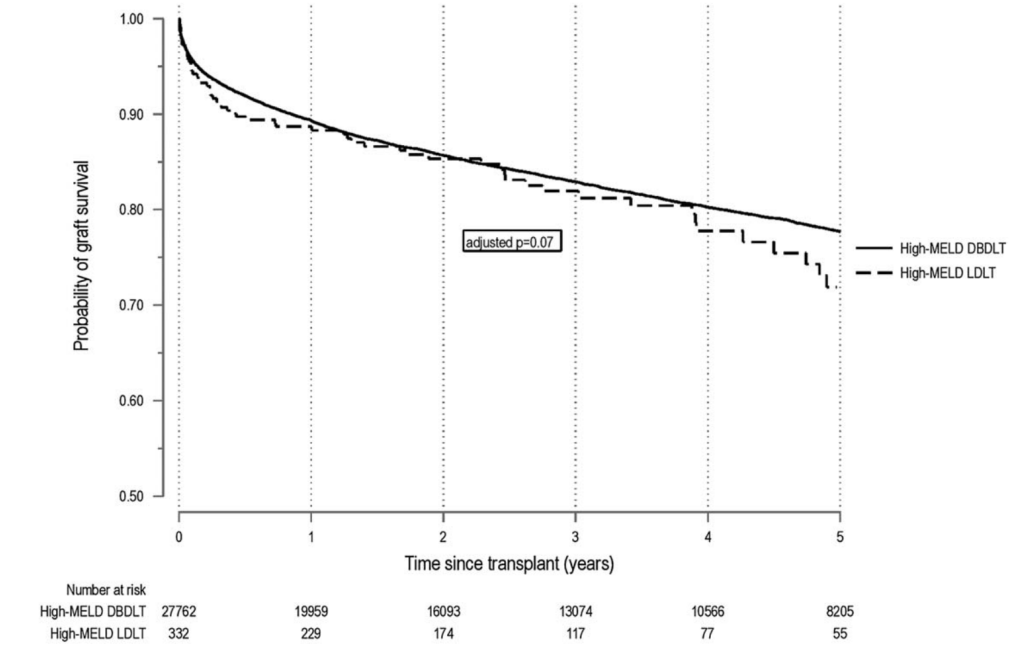
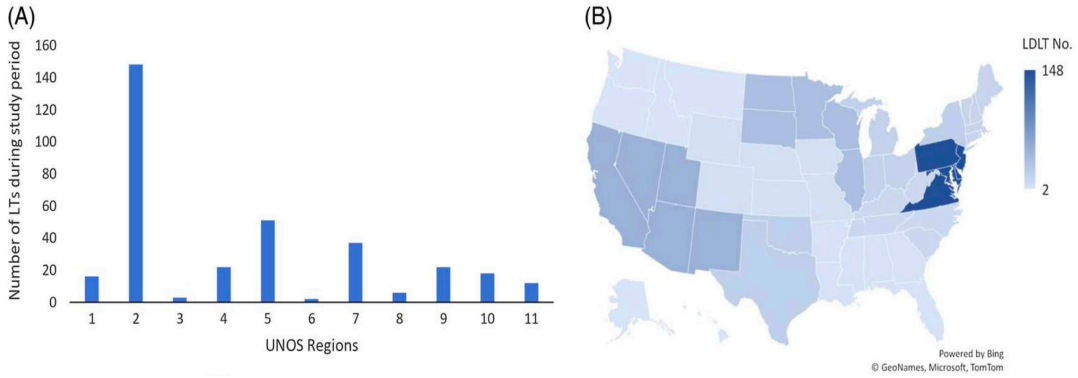
Liver Paired Exchange/Donor Chains





LDLT in High MELD Recipients

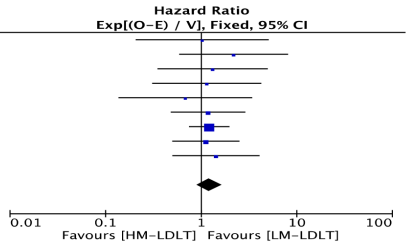




(A)

Study or Subgroup	HM-LDLT Events	HM-LDLT Total	LM-LDLT Events	LM-LDLT Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
Chok, 2013	4	75	2	68	0.037	1.496	3.8%	1.03 [0.21, 5.09]
Dabbous, 2016	6	33	5	38	1.74	2.23	5.6%	2.18 [0.59, 8.11]
Jiang, 2013	4	29	5	41	0.598	2.18	5.5%	1.32 [0.35, 4.96]
Li, 2013	4	16	15	102	0.2984	2.226	5.6%	1.14 [0.31, 4.25]
Poon, 2012	10	120	1	23	-0.57	1.48	3.7%	0.68 [0.14, 3.41]
Selzner, 2010	18	227	1	23	0.785	4.76	12.0%	1.18 [0.48, 2.90]
Yadav, 2017	24	151	101	849	3.11	16.15	40.5%	1.21 [0.74, 1.97]
Yi, 2008	10	52	14	105	0.652	5.83	14.6%	1.12 [0.50, 2.52]
Yoshizumi, 2007	7	25	13	94	1.24	3.48	8.7%	1.43 [0.50, 4.08]
Total (95% CI)		**728**		**1343**			**100.0%**	**1.22 [0.89, 1.66]**
Total events	87		157					

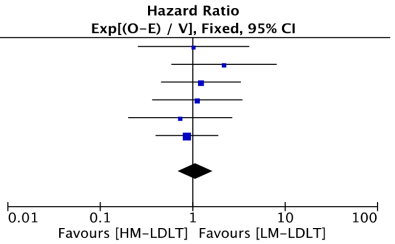
Heterogeneity: Chi² = 1.46, df = 8 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)



(B)

Study or Subgroup	HM-LDLT Events	HM-LDLT Total	LM-LDLT Events	LM-LDLT Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
Chok, 2013	5	75	3	68	0.0423	1.995	10.1%	1.02 [0.26, 4.09]
Dabbous, 2016	6	33	2	38	1.74	2.23	11.3%	2.18 [0.59, 8.11]
Jiang, 2013	9	29	7	41	0.798	3.88	19.7%	1.23 [0.45, 3.32]
Li, 2013	4	16	22	102	0.349	3.04	15.4%	1.12 [0.36, 3.45]
Poon, 2012	1	23	16	120	-0.711	2.29	11.6%	0.73 [0.20, 2.68]
Selzner, 2010	7	44	39	227	-0.9	6.256	31.8%	0.87 [0.40, 1.90]
Total (95% CI)		**220**		**596**			**100.0%**	**1.07 [0.69, 1.66]**
Total events	32		89					

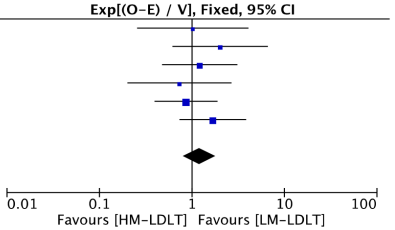
Heterogeneity: Chi² = 1.82, df = 5 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.30 (P = 0.77)



(C)

Study or Subgroup	HM-LDLT Events	HM-LDLT Total	LM-LDLT Events	LM-LDLT Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
Chok, 2013	5	75	3	68	0.0423	1.995	8.6%	1.02 [0.26, 4.09]
Dabbous, 2016	8	33	3	38	1.92	2.73	11.8%	2.02 [0.62, 6.62]
Jiang, 2013	9	29	7	41	0.842	4.36	18.8%	1.21 [0.47, 3.10]
Poon, 2012	1	23	16	120	-0.711	2.29	9.9%	0.73 [0.20, 2.68]
Selzner, 2010	7	44	41	227	-0.92	6.258	27.0%	0.86 [0.39, 1.89]
Yoshizumi, 2007	10	25	23	94	2.9	5.58	24.0%	1.68 [0.73, 3.86]
Total (95% CI)		**229**		**588**			**100.0%**	**1.19 [0.79, 1.79]**
Total events	40		93					

Heterogeneity: Chi² = 2.66, df = 5 (P = 0.75); I² = 0%
Test for overall effect: Z = 0.85 (P = 0.40)



Anouti et al. Liver Transplantation 2024; Jayant et al. J Clin Med 2023

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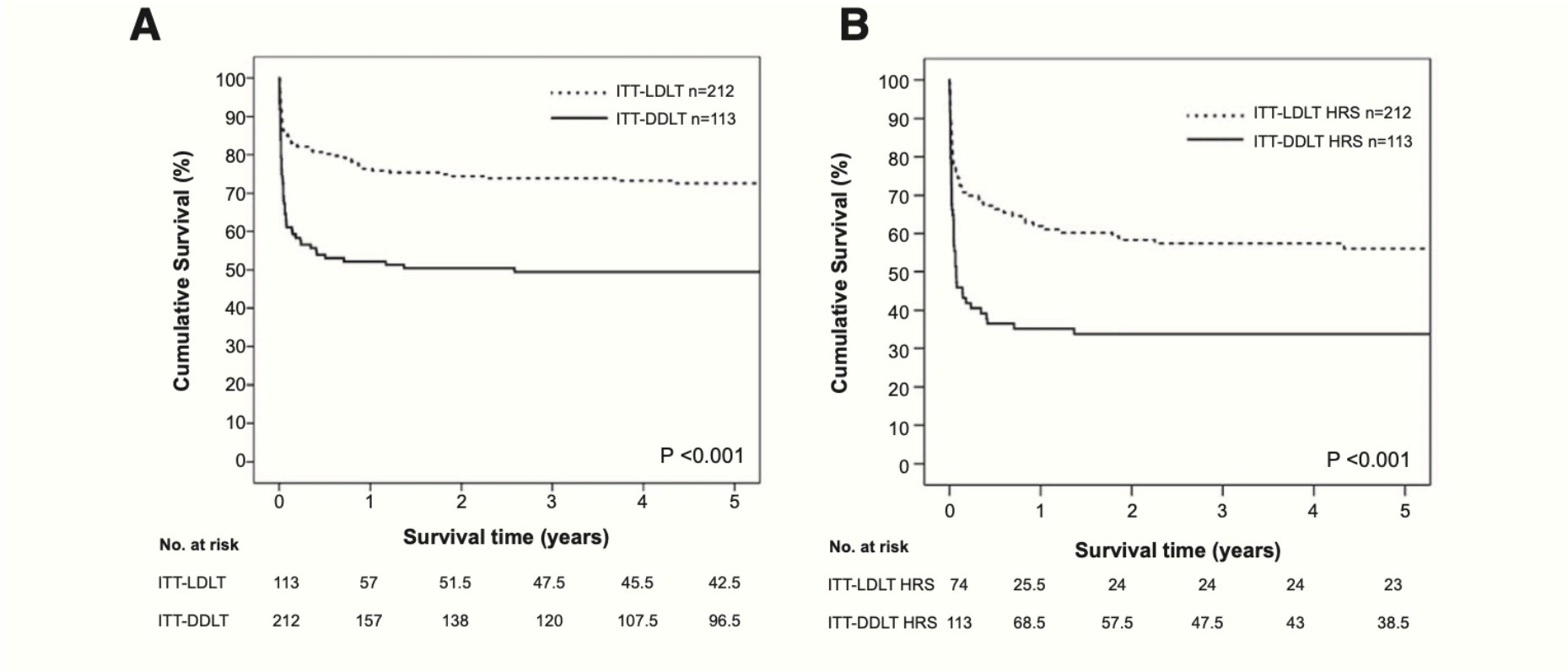
LDLT in High MELD and Hepatorenal Syndrome



Wong et al. Hepatology 2021

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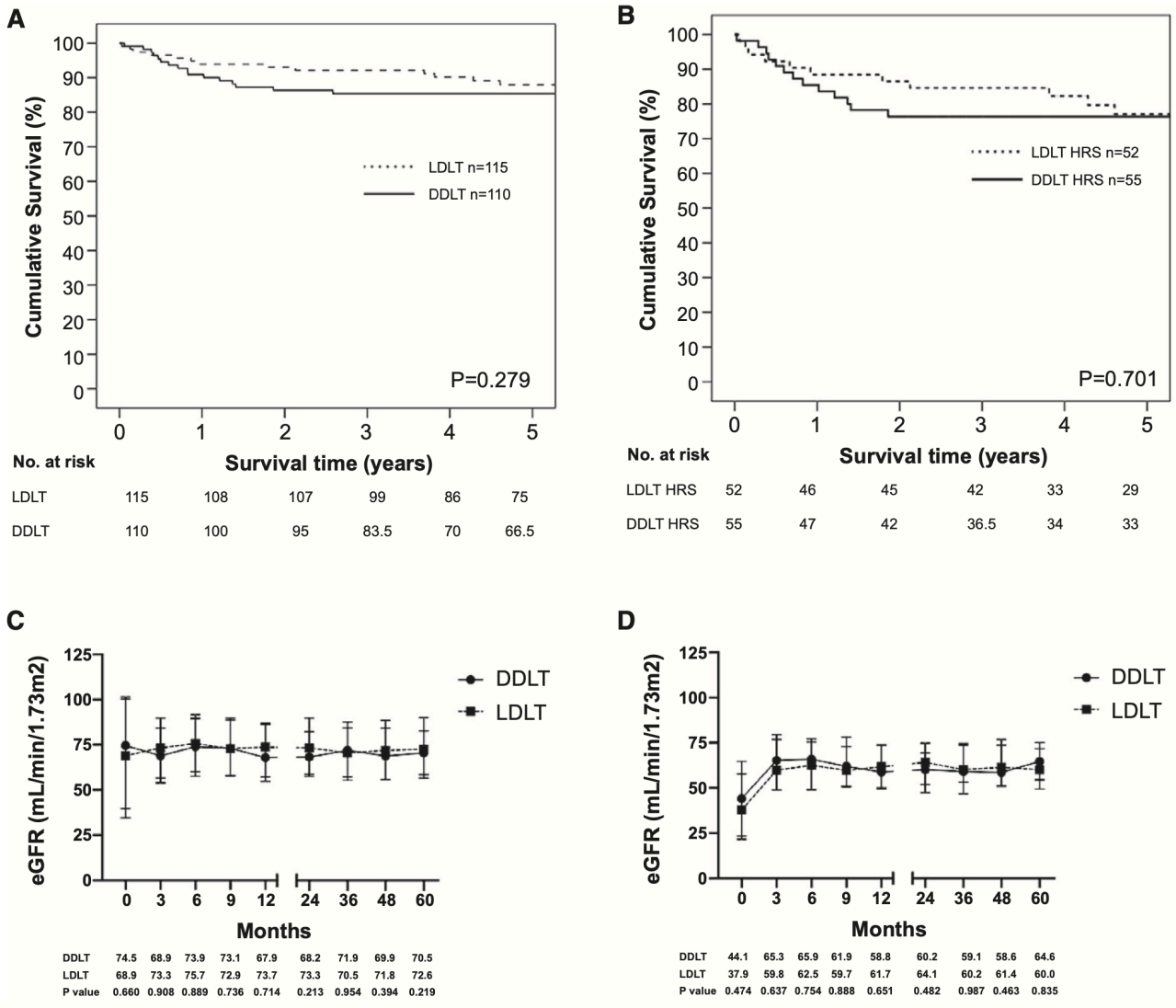
LDLT in High MELD and Hepatorenal Syndrome



Wong et al. Hepatology 2021

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LDLT in Low MELD Recipients

Figure 1. One-Year Mortality Risk Across Model for End-stage Liver Disease Incorporating Sodium Levels (MELD-Na) Score Categories for Patients Receiving a Living-Donor Liver Transplant vs Remaining on the Wait List, 2011-2021

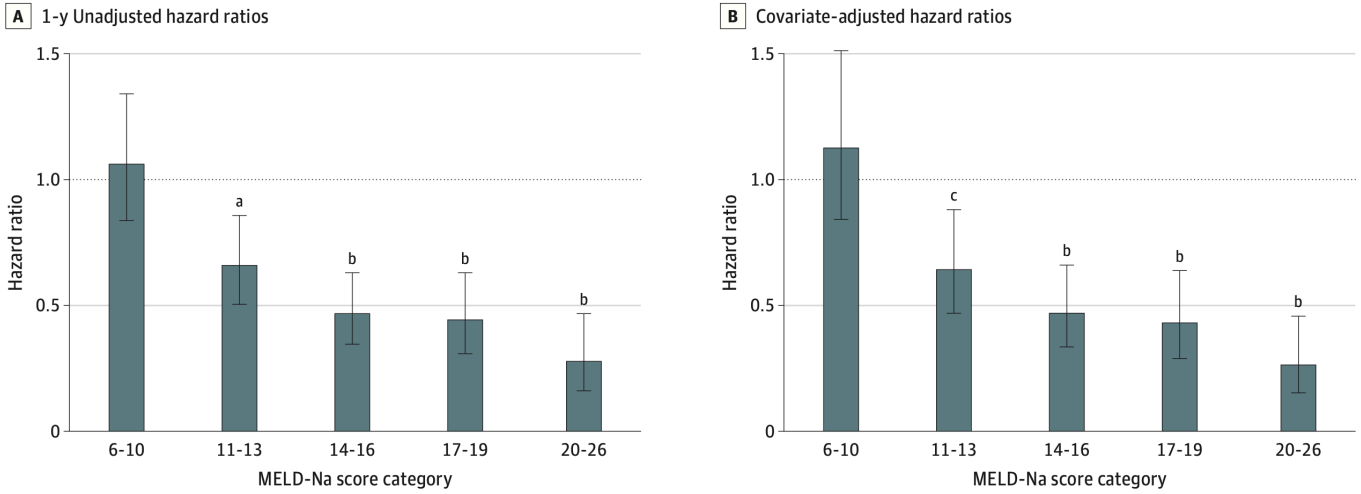
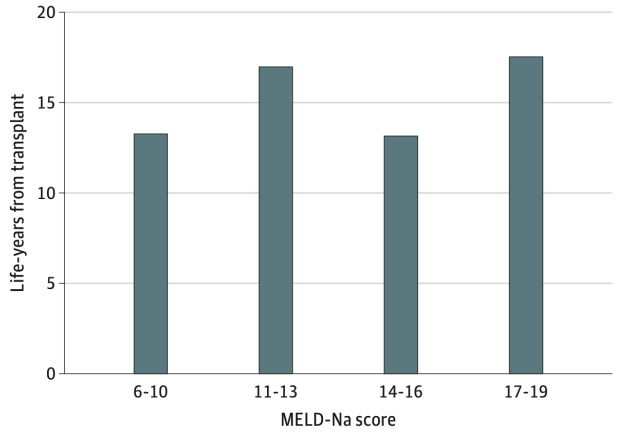


Figure 3. Life-Years Saved After Living-Donor Liver Transplant



Life-years from transplant (LYFT) were calculated for Model for End-stage Liver Disease incorporating sodium levels (MELD-Na) groups with scores below 20 using parametric survival regression and extrapolated to 10 000 days, or 27.38 years. The MELD-Na score category of 20 to 26 was excluded from this analysis because this group was underpowered. The overall projected survival benefit, or life-years saved, was calculated by subtracting the median number of days on the wait list from life-years from transplant. The median life-years saved ranged from 13.2 to 17.6 years.

Jackson et al. JAMA Surgery 2022

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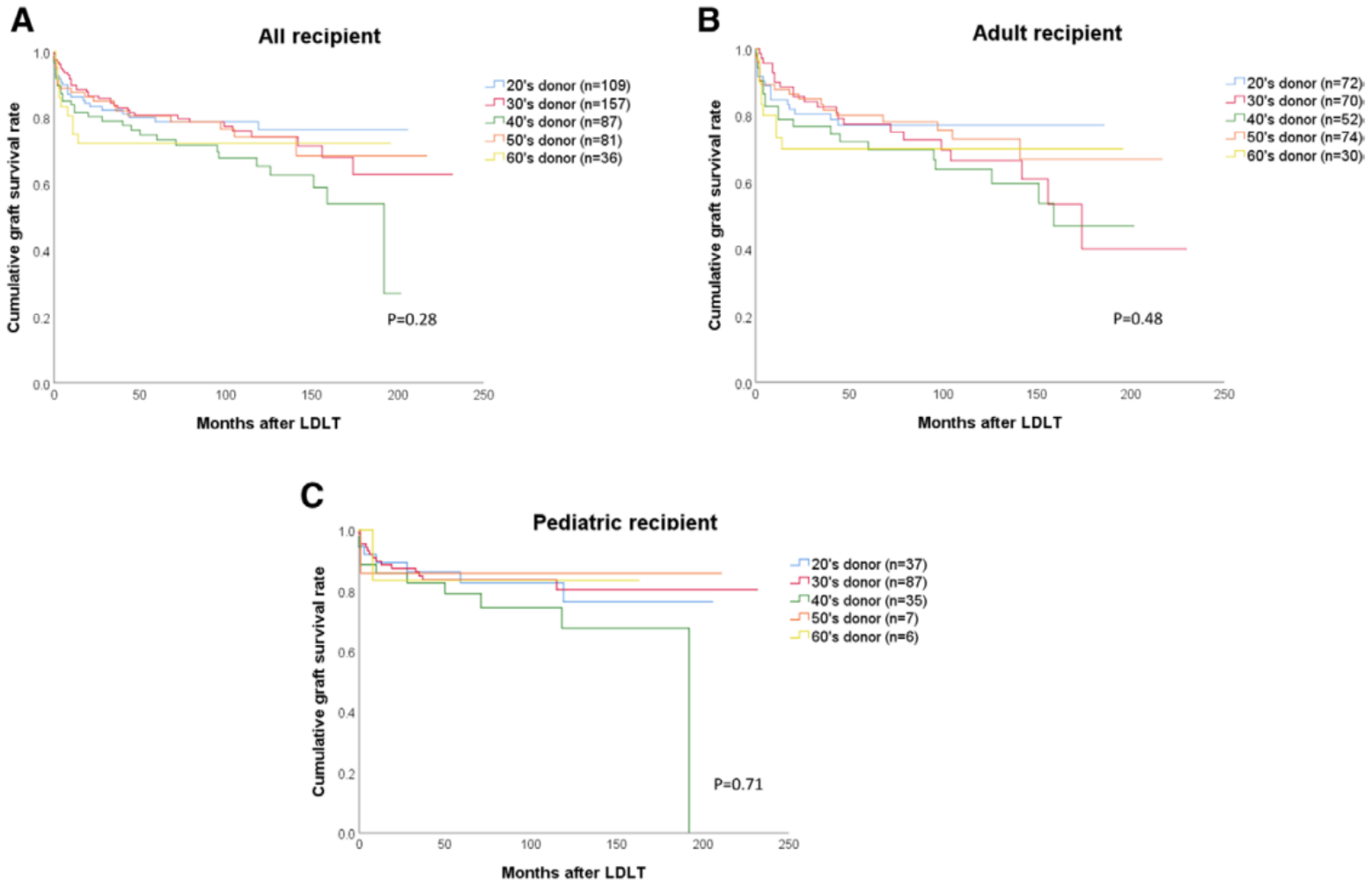
Older Donors



Kadohisa M et al. Transplantation 2021

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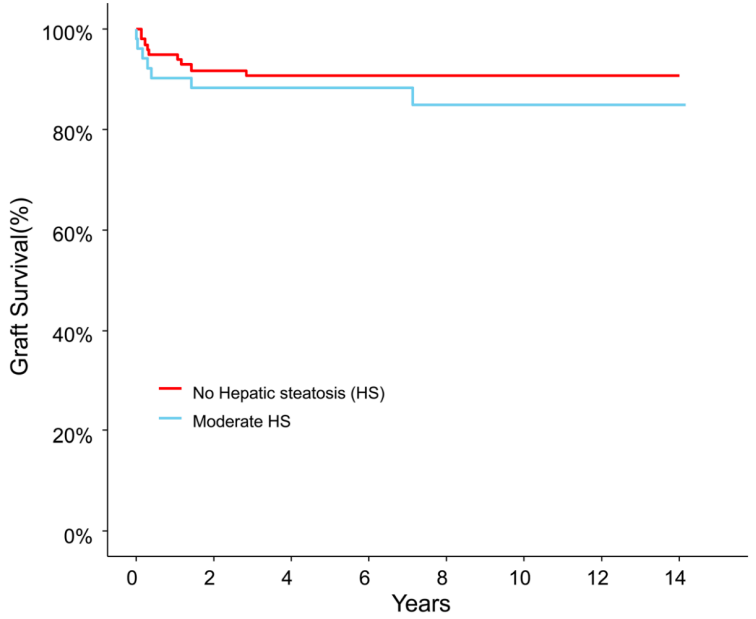
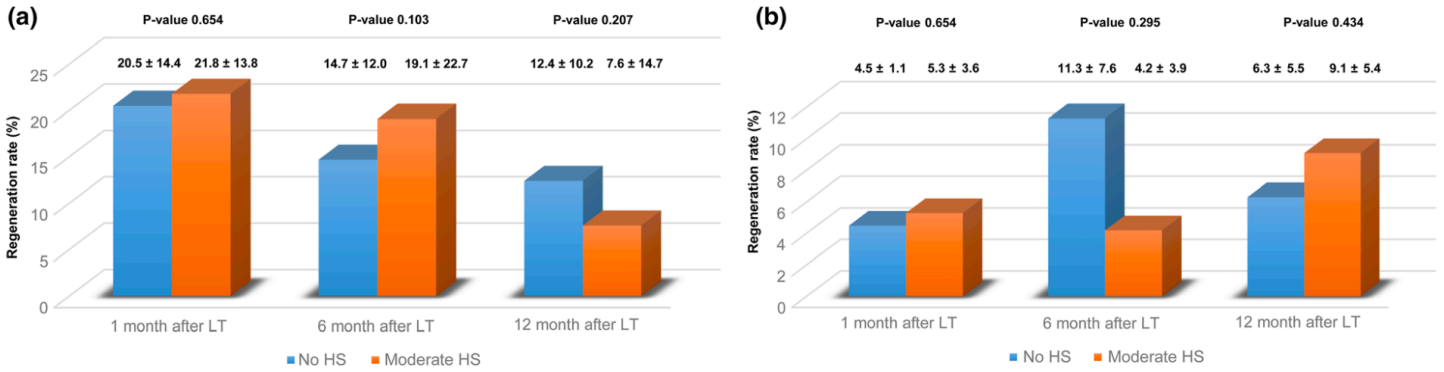
Steatotic Donor Livers





Yoon et al. Transplant International 2021

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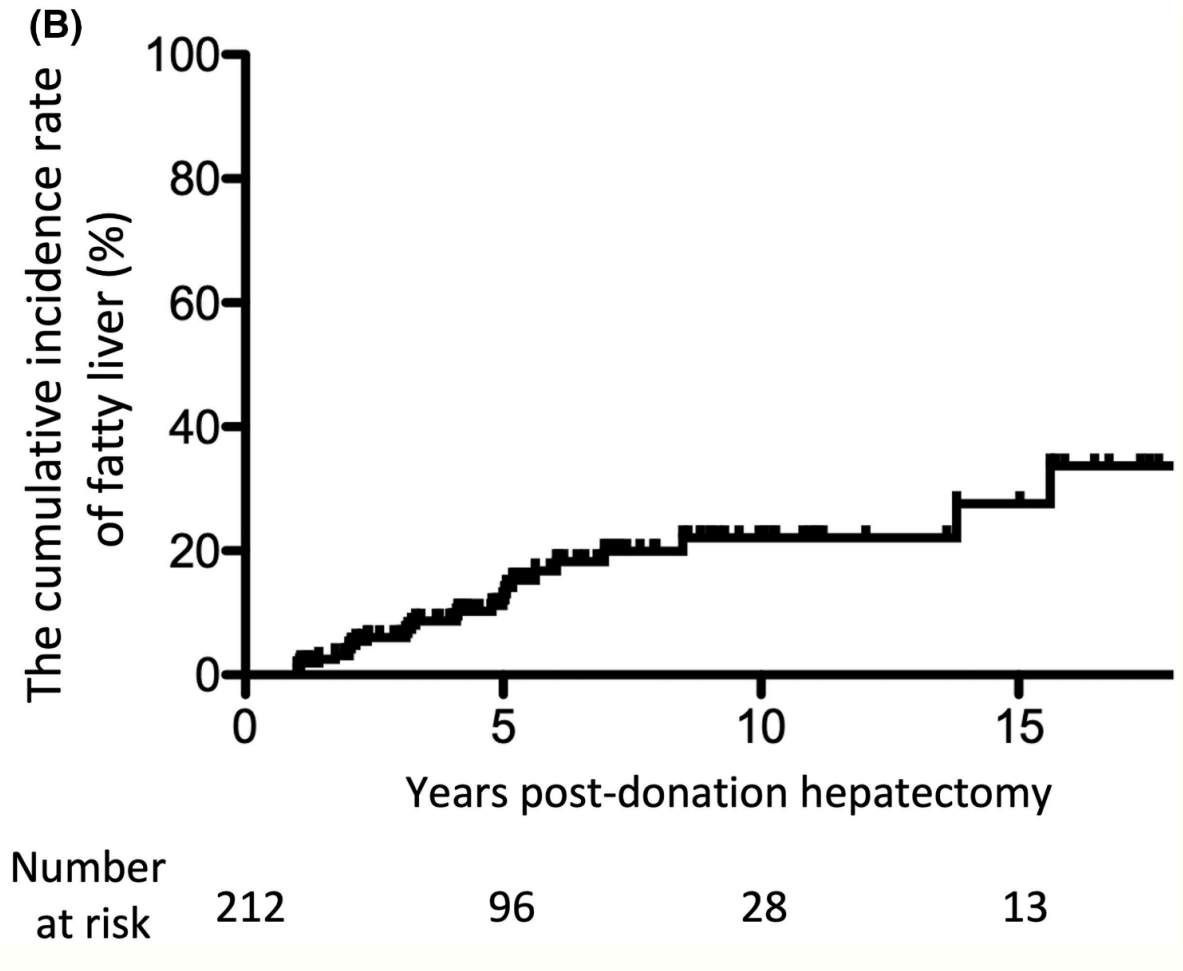
Donors with Steatosis - Post Donation



Intrahepatic Cholangiocarcinoma (iCCA)

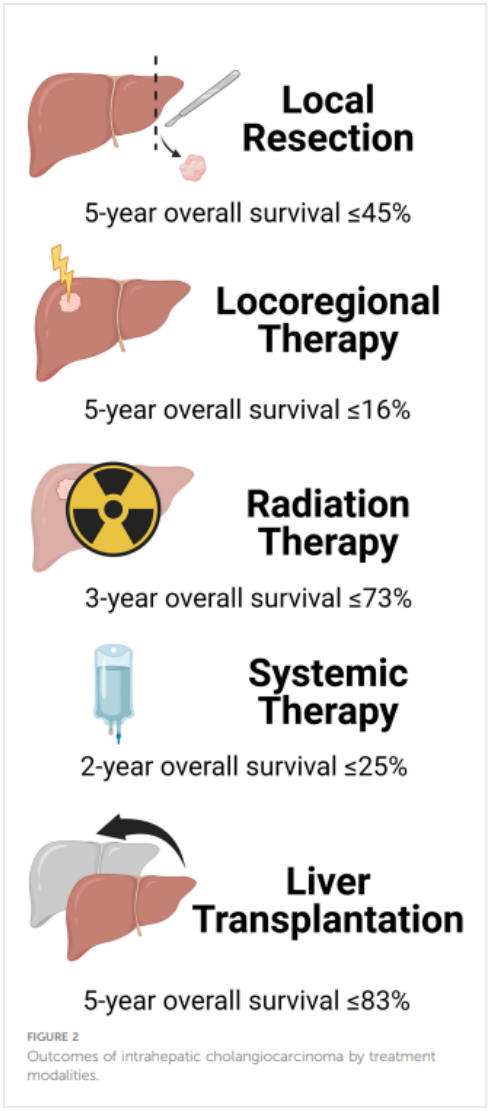
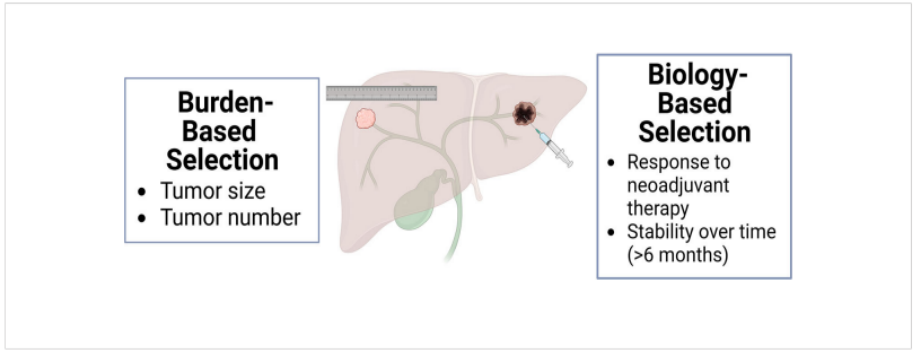
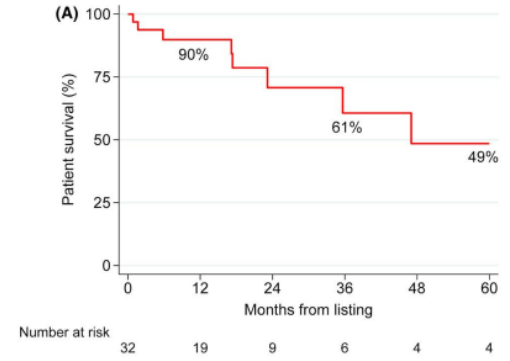
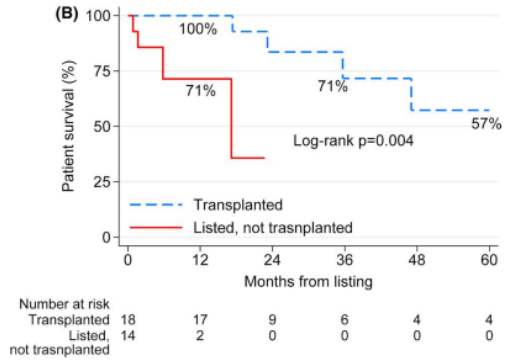
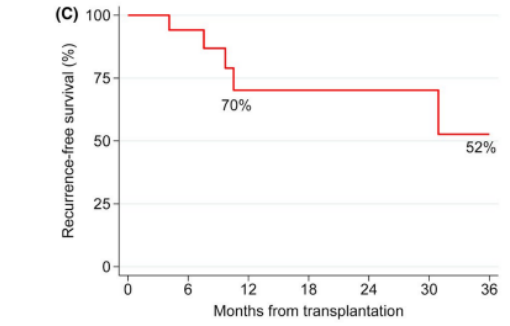


FIGURE 2
Outcomes of intrahepatic cholangiocarcinoma by treatment modalities.









Eletta, et al. Surg Clin N Am 2024; Connor et al Front in Onc 2022; McMillan et al AJT 2021

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Colorectal Cancer Metastases to the Liver

Table 2. Oncologic Treatment Characteristics of Patients Who Underwent Total Hepatectomy and Living-Donor LT

Patient	Timing of CRLM	Systemic treatment	Prior resection	Local therapy	Time from diagnosis of CRLM to LT, y
1	Synchronous metastases	FOLFOX, FOLFIRI, targeted agent	None	None	1.6
2	Synchronous metastases	FOLFOX, FOLFIRI, targeted agent	None	None	5.5
3	Synchronous metastases	FOLFOX, FOLFIRI, targeted agent	Wedge resection, aborted ALPPS	None	1.6
4	Synchronous metastases	FOLFOX, FOLFIRI, targeted agent	None	None	1.4
5	Synchronous metastases	FOLFOX, targeted agent	Right hemihepatectomy	Ablation	1.1
6	Synchronous metastases	FOLFOXIRI, targeted agent	Bisegmentectomy	Hepatic artery infusion	1.4
7	Synchronous metastases	FOLFOX, FOLFIRI, targeted agent	None	Ablation	2.3
8	Metachronous metastases	FOLFIRI, targeted agent	Right posterior sectionectomy, wedge resection	Ablation, hepatic artery infusion	7.8
9	Synchronous metastases	FOLFIRI, targeted agent	None	None	1.7
10	Synchronous metastases	FOLFIRI, targeted agent	None	Hepatic artery infusion	2.0

Figure. Kaplan-Meier Estimates of Overall and Recurrence-Free Survival in Patients Who Underwent Total Hepatectomy and Living-Donor Liver Transplant

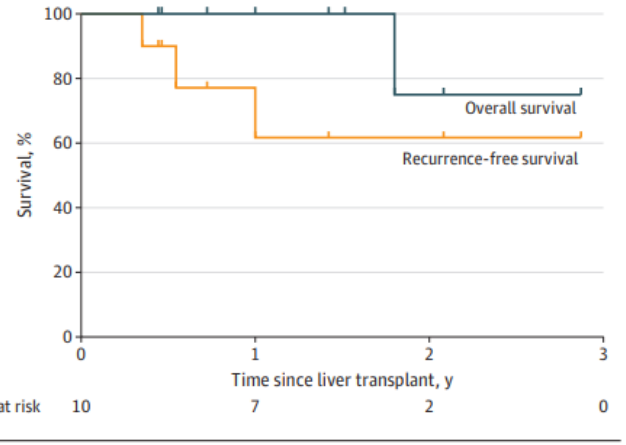

Table 4. Liver Explant Pathology and Postoperative Complications of Patients With Unresectable CRLMs Who Underwent Total Hepatectomy and Living-Donor Liver Transplant

Pathologic and postoperative outcome	Patients, No. (%) (N = 10)
Viable tumor	
Yes	9 (90)
No	1 (10)
Underlying liver histology	
Normal parenchyma	5 (50)
Cirrhosis	3 (30)
Steatosis	1 (10)
Scarring, necrosis, and vascular changes	1 (10)
Portal nodal involvement	
Negative	9 (90)
Positive	1 (10)
CD complications	
None	3 (30)
II	3 (30)
IIIA	2 (20)
IIIB	2 (20)

Abbreviations: CD, Clavien-Dindo; CRLMs, colorectal liver metastases.

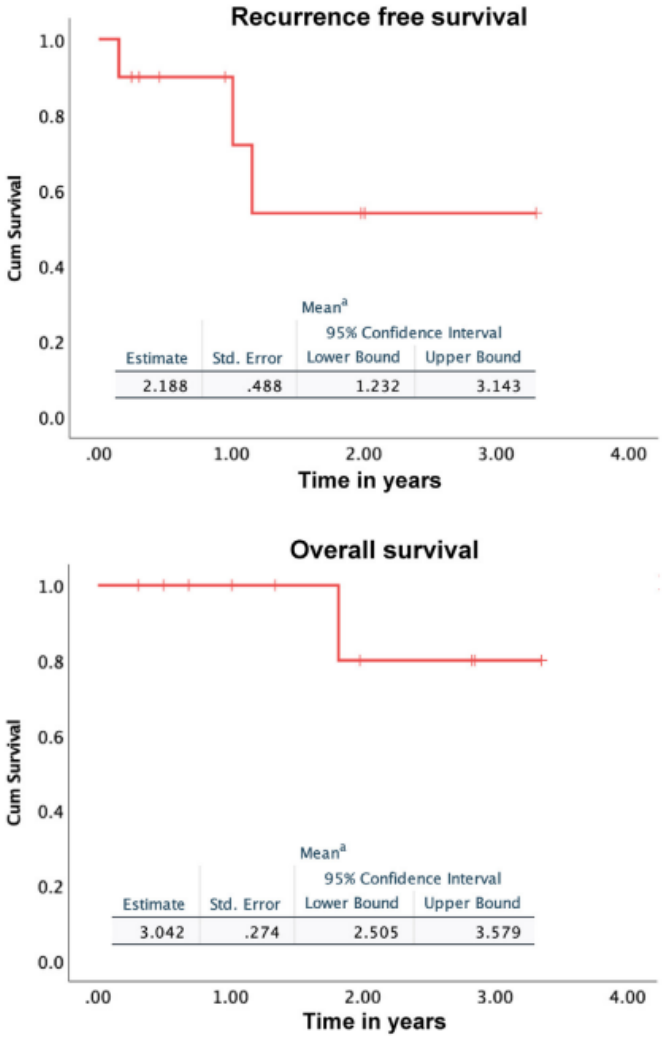

Figure. 1. Recurrence and overall survival of the study population.

Hernandez-Alejandro et al. JAMA Surgery 2022

Kaltenmeier et al. AJT 2023

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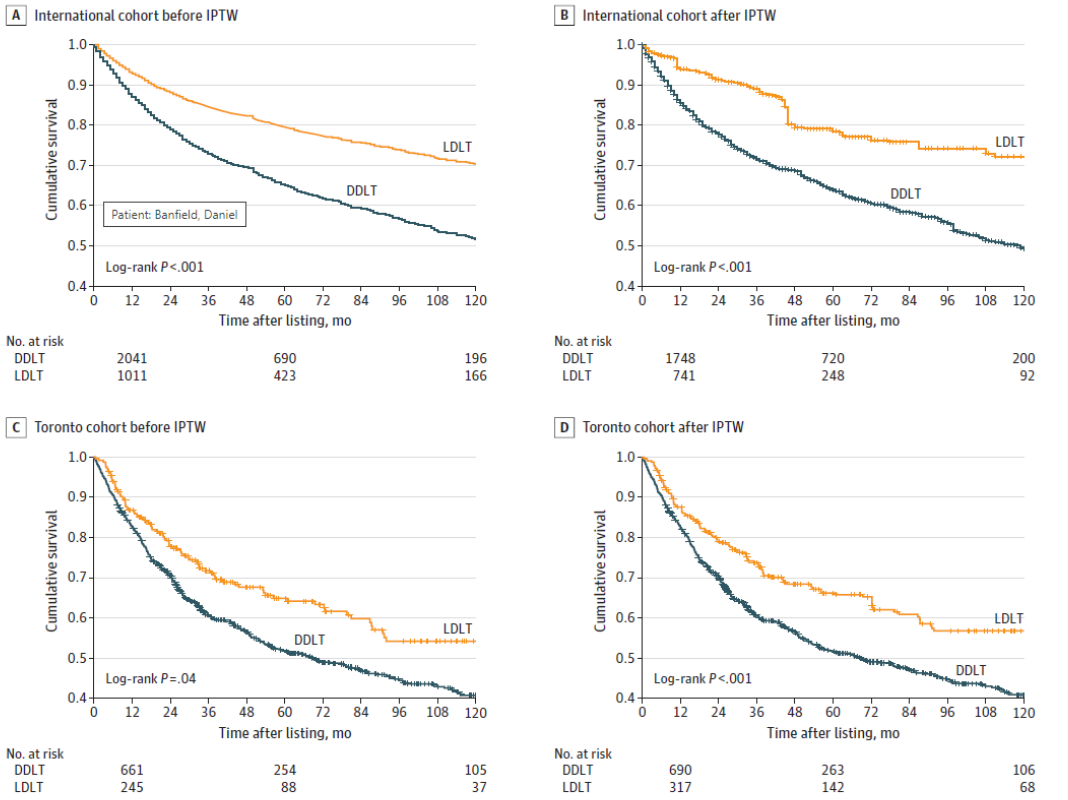
HCC and LDLT

Figure 2. Intention-to-Treat Patient Survival Rates Before and After Inverse Probability of Treatment Weighting (IPTW) in the International Cohort (A and B) and Toronto Cohort (C and D)



DDLT indicates deceased-donor liver transplant; LDLT, living-donor liver transplant.

Table 1. Characteristics of Patients in the International and Toronto Cohorts

Variable	No. (%) International cohort Total	DDLT	LDLT	Toronto cohort Total	DDLT	LDLT
No. (%)	3052 (100.0)	2041 (66.9)	1011 (33.1)	906 (100.0)	661 (73.0)	245 (27.0)
Center volume >70 LT cases/y	2227 (73.0)	1587 (77.8)	640 (63.3)	NA	NA	NA
LT performed before 2010	1458 (47.8)	1102 (54.0)	356 (35.2)	487 (53.8)	366 (55.4)	121 (49.4)
Age at first referral, median (IQR), y	58 (53-63)	59 (54-63)	57 (52-62)	59 (53-63)	59 (53-63)	59 (54-63)
Male sex	2447 (80.2)	1707 (83.6)	740 (73.2)	743 (82.0)	544 (82.3)	199 (81.2)
Female sex	605 (19.8)	334 (16.4)	271 (26.8)	163 (18.0)	117 (17.7)	46 (18.8)
Underlying liver disease						
HCV	1383 (45.3)	889 (43.6)	494 (48.9)	471 (52.0)	335 (50.7)	136 (55.5)
HBV	880 (28.8)	493 (24.2)	387 (38.3)	194 (21.4)	169 (25.6)	25 (10.2)
Alcohol-related cirrhosis	630 (20.6)	539 (26.4)	91 (9.0)	121 (13.4)	85 (12.9)	36 (14.7)
NASH	204 (6.7)	140 (6.9)	64 (6.3)	78 (8.6)	49 (7.4)	29 (11.8)
Other	156 (5.1)	129 (6.3)	27 (2.7)	45 (5.0)	26 (3.9)	19 (7.8)
Waiting time duration, me	(1-10)	6 (3-13)	1 (0-2)	6 (3-11)	6 (3-12)	5 (3-8)
MELD score at first referral, median (IQR)	12 (9-16)	12 (9-16)	12 (9-15)	10 (8-14)	10 (8-14)	11 (8-14)
Tumor characteristics at first referral						
Diameter of the major lesion, median (IQR), cm	2.5 (1.8-3.7)	2.5 (1.8-3.8)	2.5 (1.7-3.6)	2.7 (1.9-3.9)	2.7 (1.9-3.7)	2.9 (1.7-4.4)
No. of lesions, median (IQR)	2 (1-3)	1 (1-3)	2 (1-3)	1 (1-2)	1 (1-2)	1 (1-2)
Outside of MC	959 (31.4)	601 (29.4)	358 (35.4)	267 (29.5)	185 (28.9)	82 (33.5)
Tumor characteristics at LT or dropout						
Diameter of the major lesion, median (IQR), cm	2.2 (1.4-3.3)	2.1 (1.2-3.0)	2.5 (1.7-3.5)	2.0 (0.0-3.6)	2.0 (0.0-3.5)	2.2 (0.0-3.9)
No. of lesions, median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	1 (0-3)	1 (0-3)	1 (0-2)
Outside of MC	912 (29.9)	553 (27.1)	359 (35.5)	269 (29.7)	201 (30.4)	68 (27.8)
AFP level, median (IQR), ng/mL						
At first referral	14 (5-60)	11 (5-43)	22 (7-114)	11 (5-42)	12 (5-43)	10 (5-41)
At LT or dropout	11 (4-56)	10 (4-47)	14 (4-77)	11 (5-62)	12 (5-62)	10 (5-60)
LRT	2369 (77.6)	1819 (89.1)	550 (54.4)	623 (68.8)	474 (71.7)	149 (60.8)
Type of LRT						
TACE	1857 (60.8)	1451 (71.1)	406 (40.2)	146 (16.1)	104 (15.7)	42 (17.1)
PEI	486 (15.9)	402 (19.7)	84 (8.3)	22 (2.4)	18 (2.7)	4 (1.6)
RFA	743 (24.3)	506 (24.8)	237 (23.4)	423 (46.7)	329 (49.8)	94 (38.4)
Hepatic resection	266 (8.7)	218 (10.7)	48 (4.7)	14 (1.5)	14 (2.1)	0
Other	251 (8.2)	229 (11.2)	22 (2.2)	25 (2.8)	14 (2.1)	11 (4.5)
Dropout	295 (7.8)	295 (14.5)	0	247 (27.3)	213 (32.2)	34 (13.9)
Death during waiting time	159 (5.2)	159 (7.8)	0	70 (7.7)	59 (8.9)	11 (4.5)
Tumor progression	80 (2.6)	80 (3.9)	0	129 (14.3)	109 (16.5)	20 (8.2)
Posttransplant recurrence	360 (11.8)	223 (12.9)	137 (13.6)	116 (17.6)	88 (19.7)	28 (13.3)

Age/Gender: 52 year old / M

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HCC Beyond Milan

TABLE 2. Demographic, Clinicopathologic, Tumor, and Recurrence Data for Patients

	Overall (N = 360); n (%)
Preoperatively available data	
Patient demographic characteristics	
Sex	
Male	264 (73)
Female	96 (27)
Age (yr); mean (SD)	57 (8.4)
Laboratory MELD at transplantation; median (IQR)	14 (9–18)
Waiting time (mo); median (IQR)	4.1 (2.3–7.9)
Time from diagnosis to listing (mo); median (IQR)	4.8 (3.0–9.7)
Diagnosis	
HCV	234 (65)
HBV	29 (8)
Alcohol-related liver disease	42 (12)
Cryptogenic/NASH	36 (10)
Other (PBC, PSC, AIH, hemochromatosis)	27 (8)
Tumor characteristics at transplantation	
Size of largest tumor (cm); mean (SD)	2.5 (2.5)
Tumor size (largest mass) >3 cm	79 (22)
Multifocal HCC	124 (34)
T1 category tumors at diagnosis	61 (17)
AFP level at diagnosis (ng/mL); median (IQR)	15 (6–46)
Maximum AFP level (ng/mL); median (IQR)	30 (10–126)
Final AFP level (ng/mL); median (IQR)	11 (5–46)
Not meeting MC at diagnosis	106 (30)
Not meeting UCSF at diagnosis	61 (17)
Not meeting MC at transplantation	73 (21)
Not meeting UCSF at transplantation	38 (11)
Not meeting MC at pathology	155 (44)
Not meeting UCSF at pathology	141 (40)
French-AFP score >2	37 (11)
Receiving LRT	246 (72)
NYCA score,	
Low (0–2)	193 (63)
Acceptable (3–6)	96 (31)
High (≥ 7)	17 (6)
Recurrence/survival data	
Recurrence rates	58 (16)
RFS (yr); %	
1	94.4
3	87.9
5	83.7
OS (yr); %	
1	91.1
3	81.6
5	75.6
Time from recurrence to death (mo); median (IQR)	14.0 (6.6–29.9)

AIH indicates Autoimmune hepatitis; HBV, hepatitis B virus; HCV, hepatitis C virus; LRT, Locoregional therapy; MELD, Model for End-stage liver disease; NASH, nonalcoholic steatohepatitis; PBC, Primary biliary cholangitis; PSC, Primary sclerosing cholangitis.

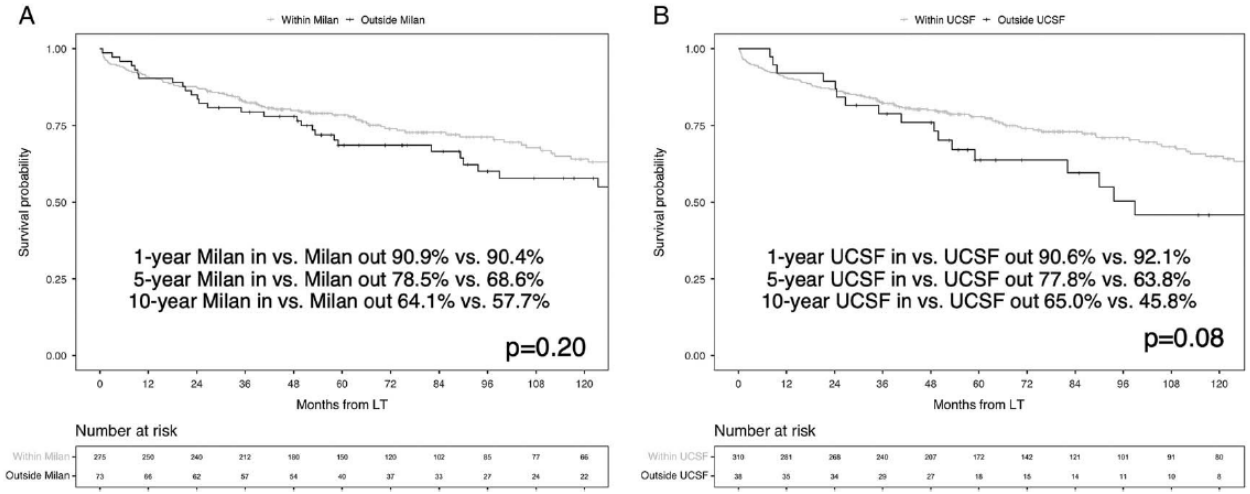

FIG. 1. Post-LDLT survival for patients (A) within MC versus outside MC at transplantation and (B) within UCSF versus outside UCSF at transplantation.

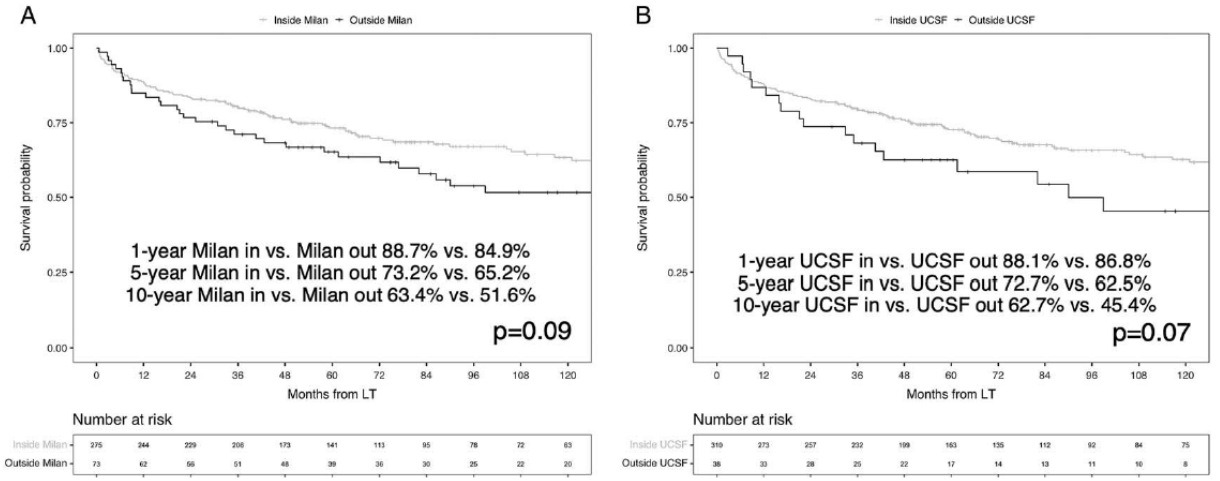

FIG. 2. Post-LDLT RFS for patients within (A) MC versus outside MC at transplantation and (B) within UCSF versus outside UCSF at transplantation.

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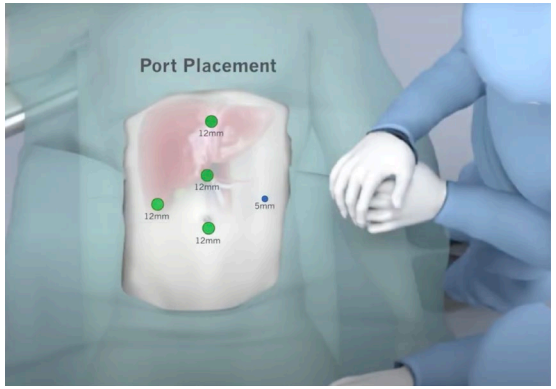
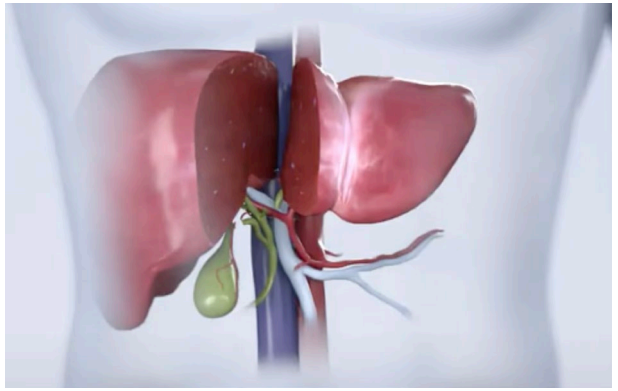
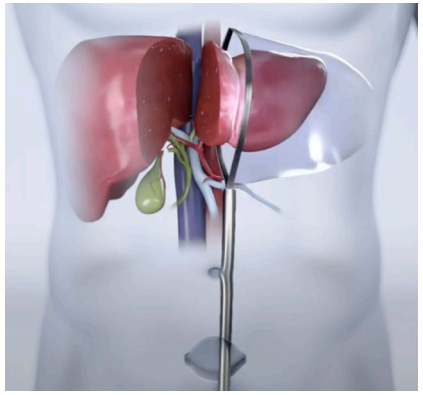
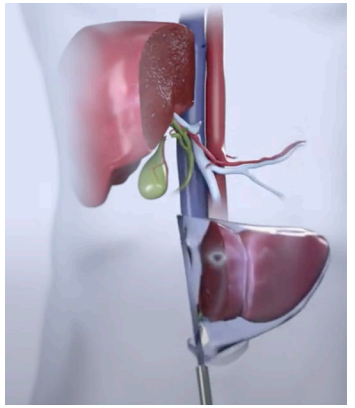
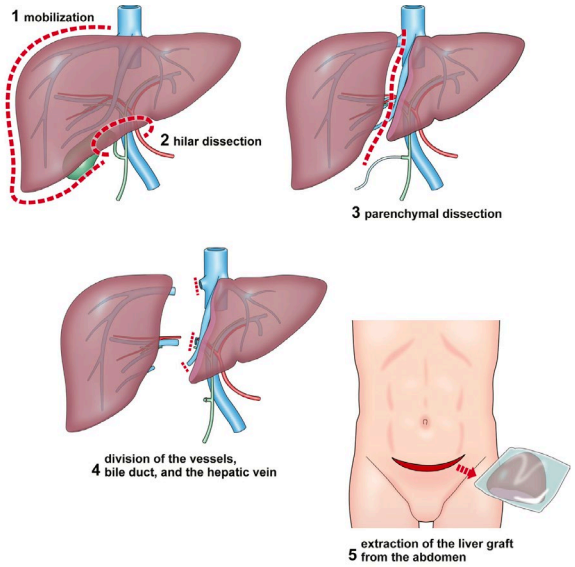
Laparoscopic LDLT

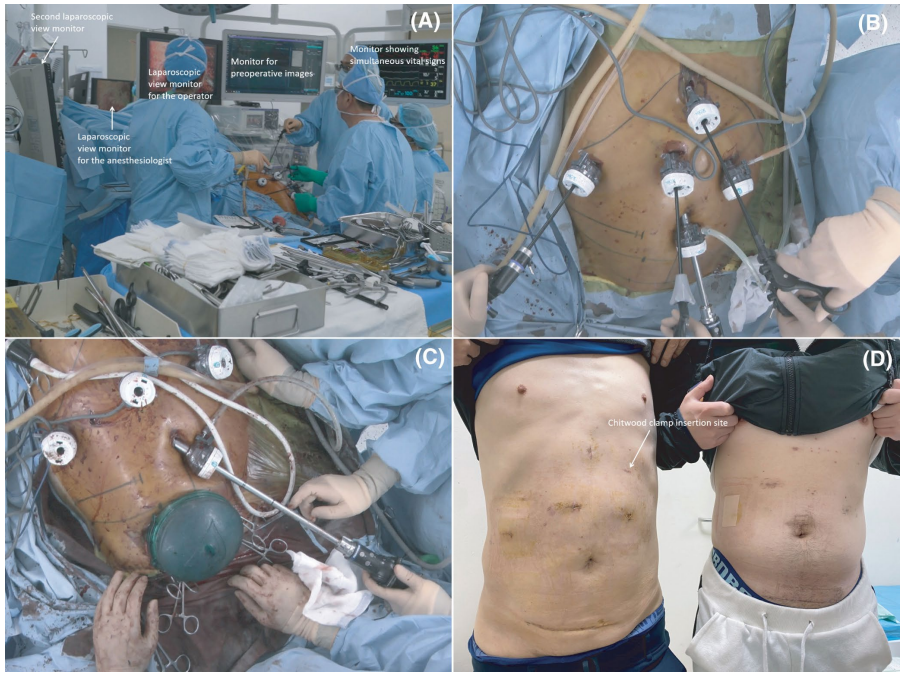






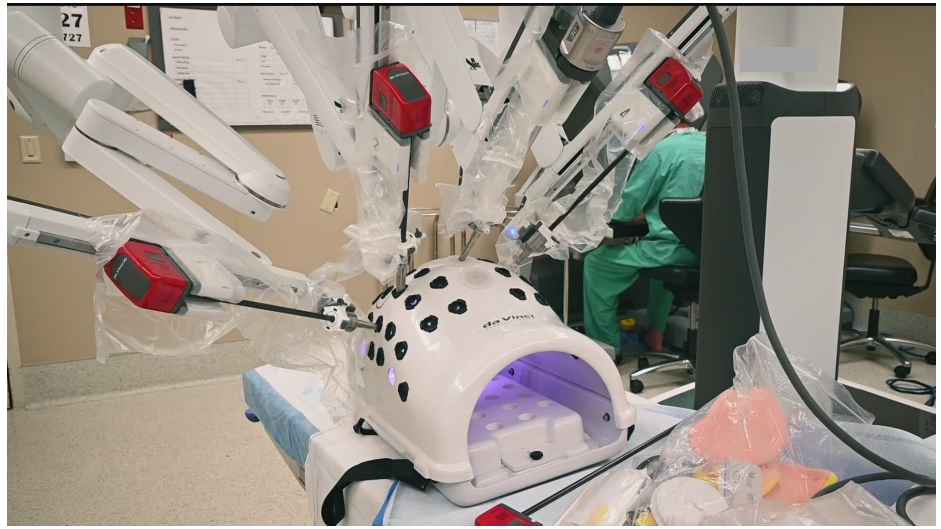


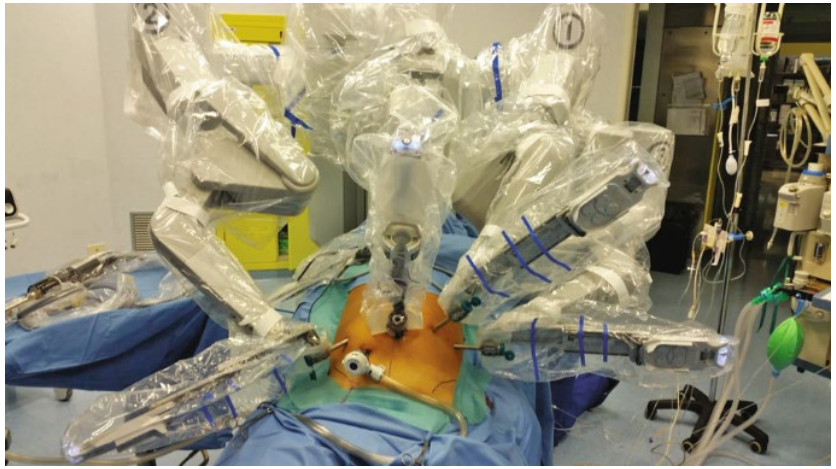




Marubashi and Nagano. Ann of Gastroenterological Surgery 2021; ccf.org

Robotic Living Donor Hepatectomy





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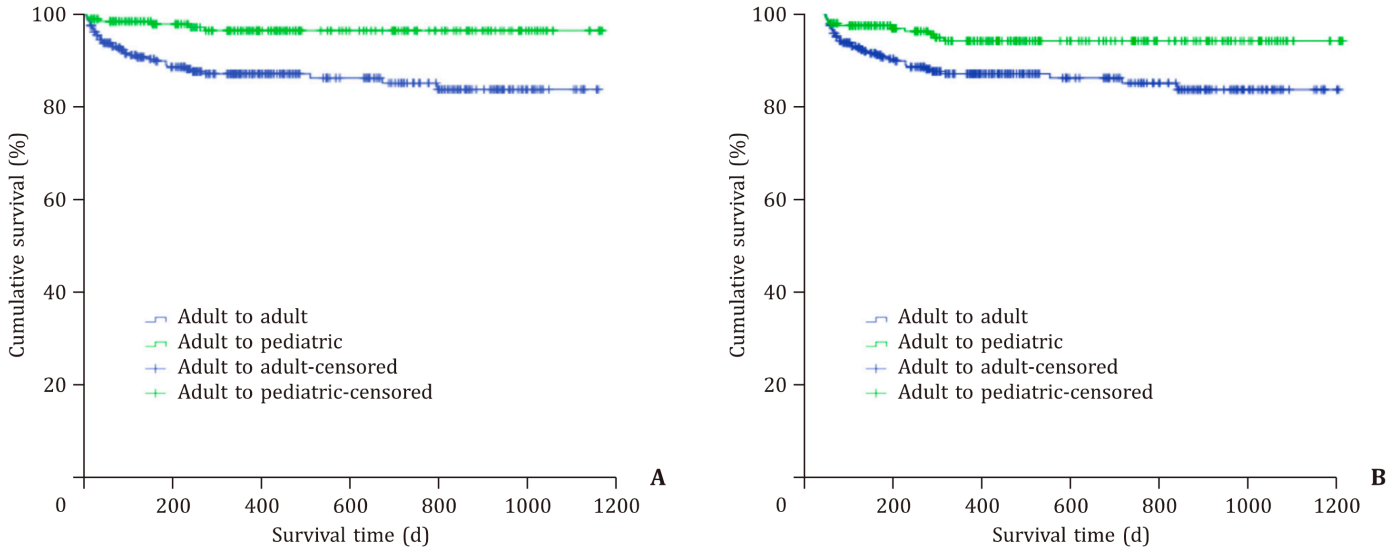
Robotic Living Donor Hepatectomy
Series of 501 cases in Saudi Arabia



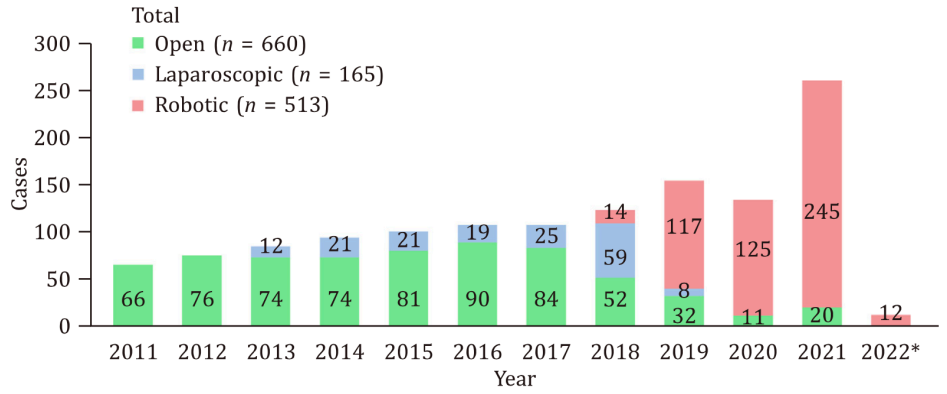


Fig. 1. Evolution of donor hepatectomy techniques during the period of 2011-2022*.

Schulze et al. Hepatobiliary & Pancreatic Diseases International 2022

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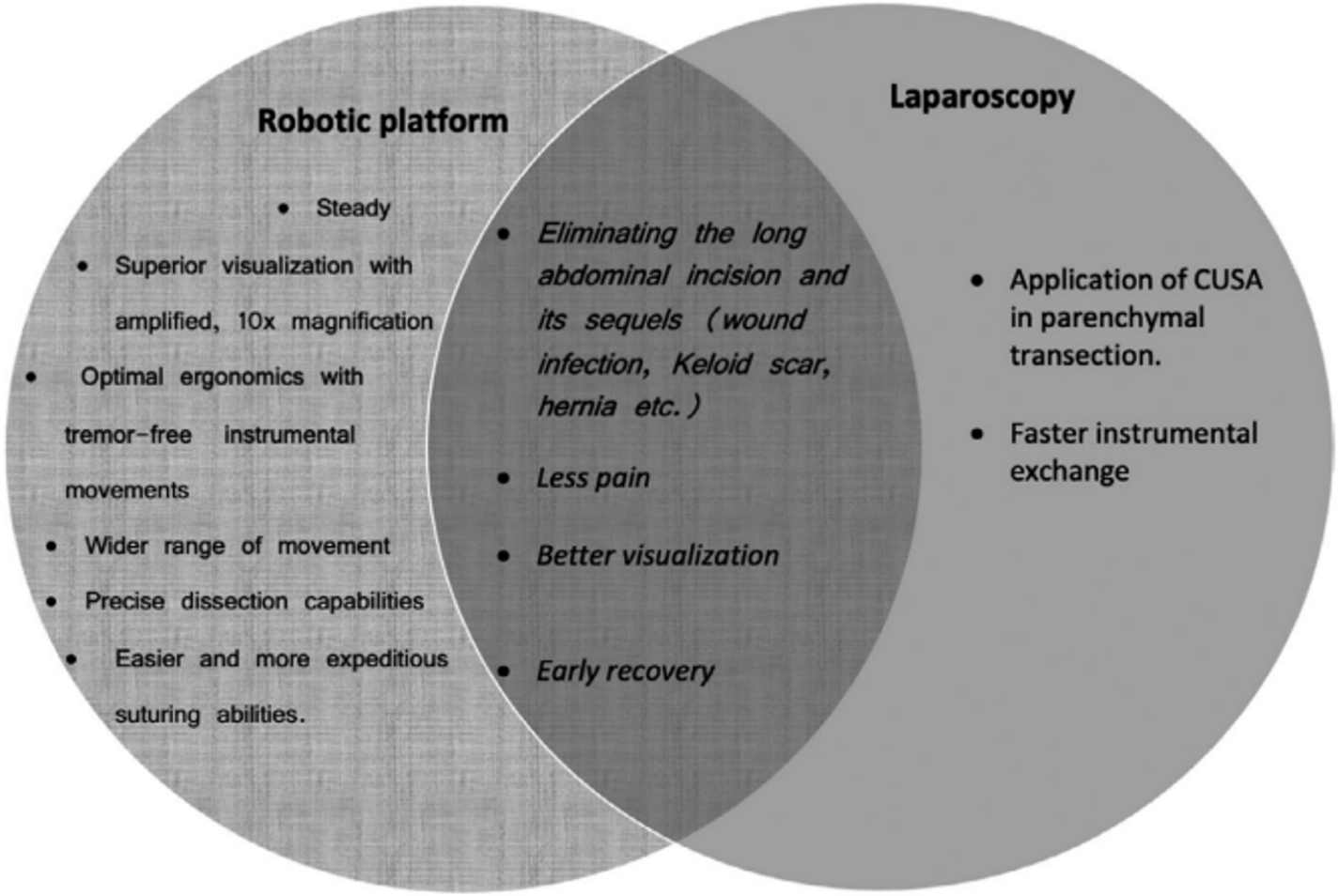
Robotic vs Laparoscopic LDLT



Broering, Sturdevant, Zidan. AJT 2022

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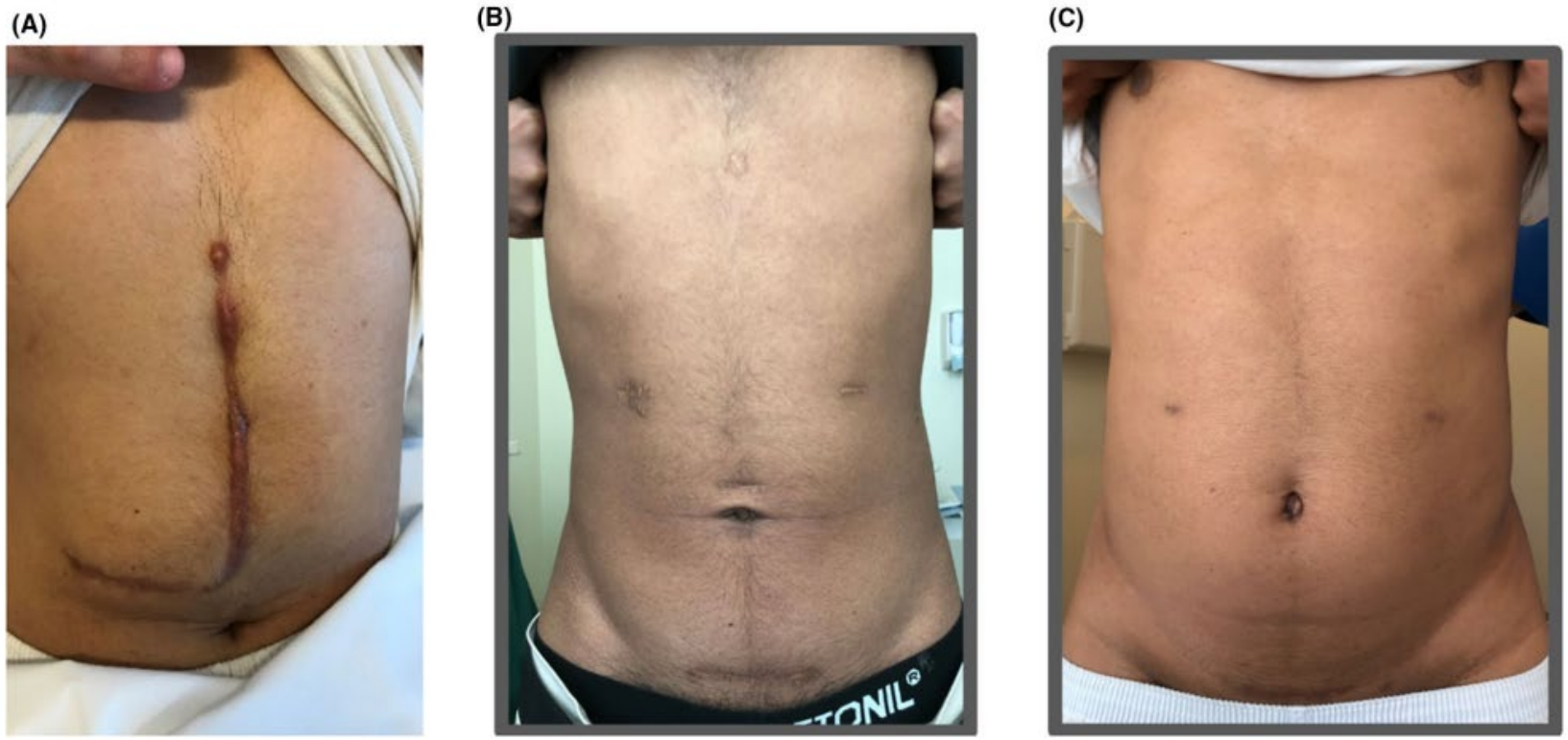
Surgical Approaches in LDLT



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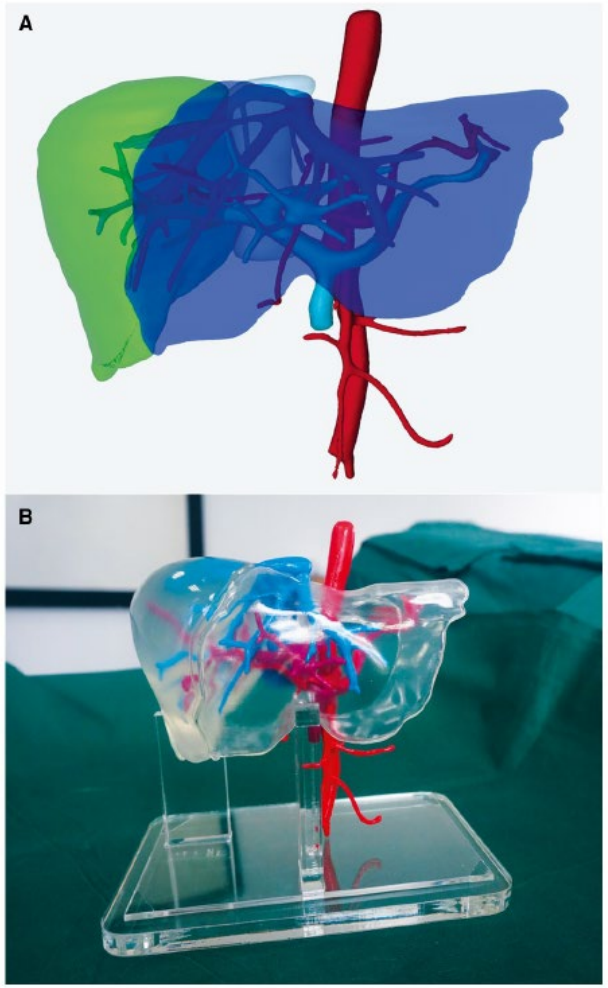
3-D Liver Printing



Wang et al. Liver Transplantation 2019

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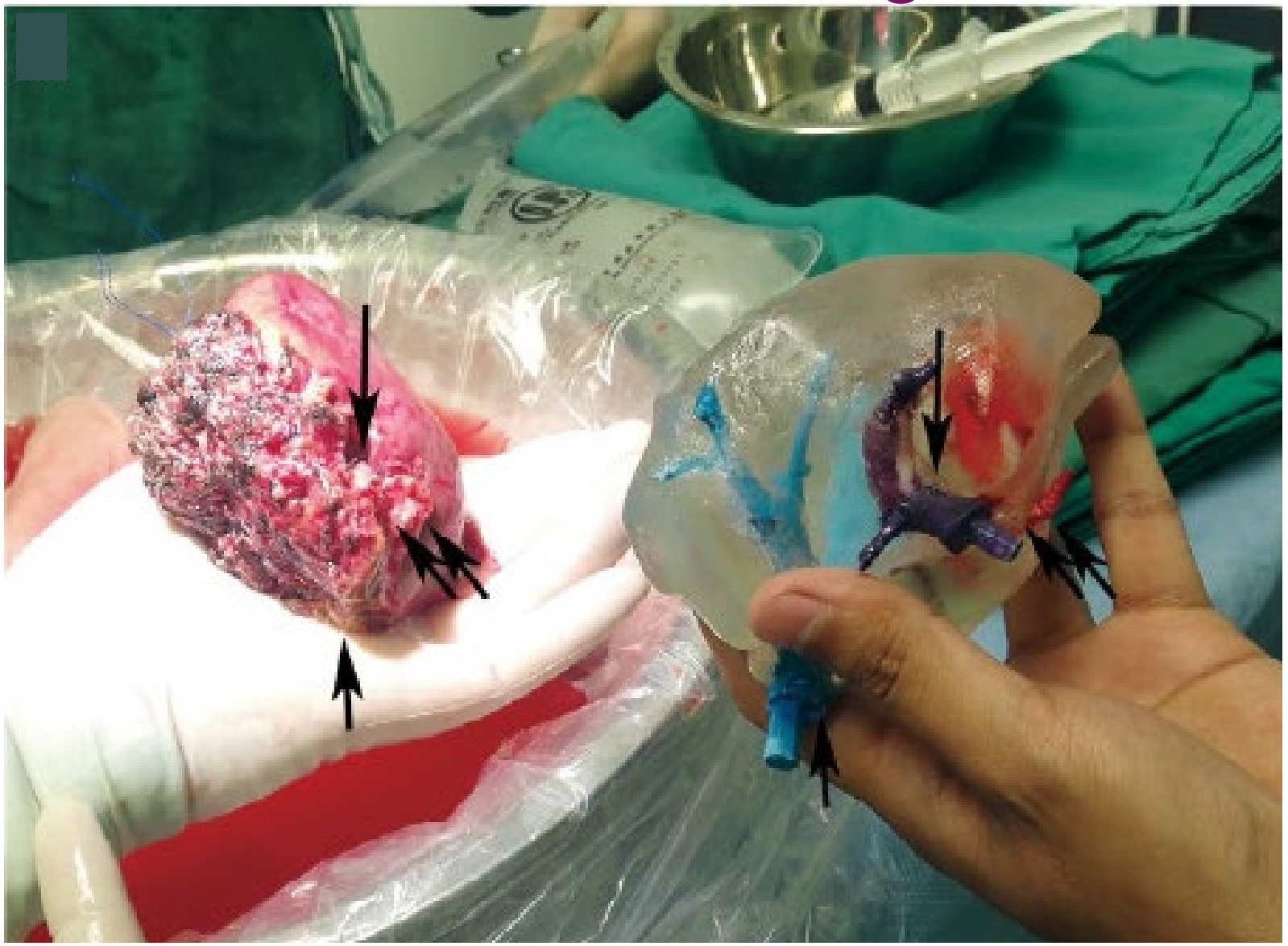
3-D Liver Printing



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