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Liver Transplantation Abstracts Review American Association for the Study of Liver Diseases 2023

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Disclosures

- Consultant: Gilead, Madrigal
- Speaker Bureau: AbbVie, Gilead, Intercept, Takeda, Salix, Eisai

Themes

- Hepatocellular carcinoma
- Access to care
- Impact of co-morbidities

Temporal Trends in Clinical Patterns and Outcomes of Patients With Hepatocellular Carcinoma

El Dahan KS¹, Daher D¹, Anouti A¹, Rich NE¹, Cano A¹, Gonzalez M¹, Verschleisser S¹, Ransom C¹, Juarez Farfan E¹, Carranza O¹, Quirk L¹, Morgan T¹, VanWagner LB¹, Lieber SR¹, Cotter TG¹, Louissaint J¹, Hoshida Y¹, Patel M¹, Purva Gopal P¹, Yopp AC¹, Parikh ND² Singal AG¹

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Temporal Trends in Clinical Patterns and Outcomes of Patients With Hepatocellular Carcinoma

Aim

- Characterize temporal trends of clinical outcomes in a large cohort of patients with HCC.

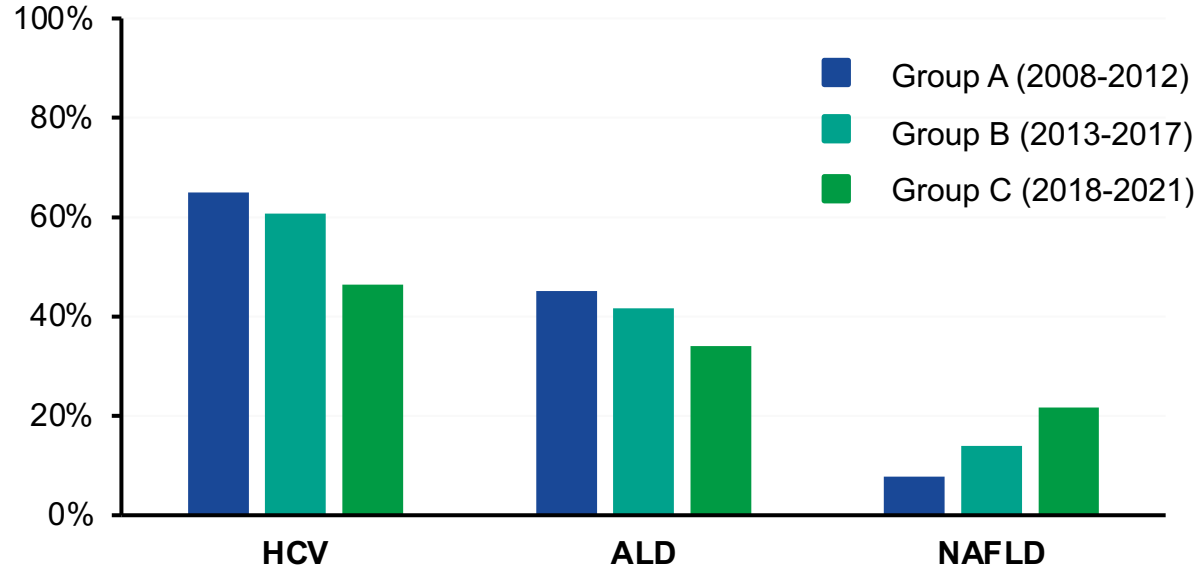
Methods

- Retrospective cohort study at two large health systems of patients diagnosed with HCC between January 2008 and December 2021.
- Three subgroups based on HCC diagnosis date: Group 1 (2008–2012), Group 2 (2013-2017), and Group 3 (2018-2021).
- Multivariable analysis

Temporal Trends in Clinical Patterns and Outcomes of Patients With Hepatocellular Carcinoma

Results

Temporal Trends in Hepatocellular Carcinoma



Temporal Trends in Clinical Patterns and Outcomes of Patients With Hepatocellular Carcinoma

Results

Outcomes in Hepatocellular Carcinoma

Group	Proportion of patients with BCLC Stage 0/A	Median Patient Survival
Group A (2008-2012)	39%	9.8 months
Group B (2013-2017)	45%	19 months
Group C (2018-2021)	56%	24 months

- Compared to group 1, patients in group 2 (OR 2.27, 95%CI 1.61-3.23) and group 3 (OR 1.88, 95%CI 1.28-2.77) had increased curative treatment.
- Median survival for groups 1, 2, and 3 were 9.8 (95%CI, 8.1-12), 19 (95%CI, 16-22), and 24 (95%CI 20-30) months, respectively.
- Group 2 (HR 0.83, 95%CI 0.72-0.95) and group 3 (HR 0.68, 95%CI 0.58-0.80) had significantly reduced mortality versus group 1.

Temporal Trends in Clinical Patterns and Outcomes of Patients With Hepatocellular Carcinoma

Conclusion

- Significant improvements in early HCC detection, curative treatment receipt, and overall survival among patients with HCC.
- Over one-third of HCC are detected beyond an early stage and median survival remains below 3 years, highlighting a need for improvements in surveillance.

Significant Reduction in Post-transplant Hepatocellular Carcinoma Recurrence in the Post-Six-Month Waiting Policy Era

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Significant Reduction in Post-transplant Hepatocellular Carcinoma Recurrence in the Post-Six-Month Waiting Policy Era

Aim

- Analyze the impact of policy and associated practice patterns on post-LT HCC recurrence.

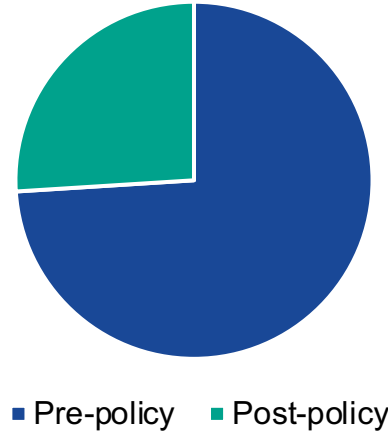
Methods

- Retrospective cohort study of UNOS registry patients HCC who underwent LT from 1/2010-5/ 2019.
- Compare outcomes pre/policy ~ six-month waiting period before MELD exception points are granted to liver transplant (LT) candidates with hepatocellular carcinoma.
- Kaplan-Meier analysis and Cox regression models used.

Significant Reduction in Post-transplant Hepatocellular Carcinoma Recurrence in the Post-Six-Month Waiting Policy Era

Results

- Total 7,940 patients were included
 - Pre-policy ~ 5,879
 - Post-policy ~ 2,061

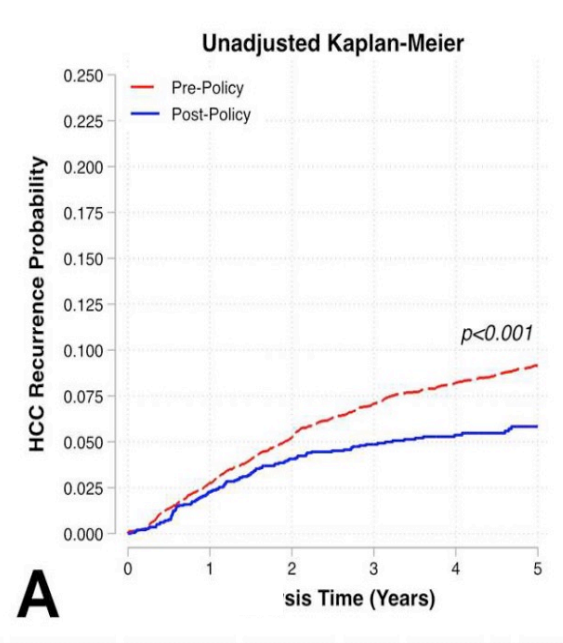


- Post-policy patients were older, more likely to have non-alcoholic fatty liver disease, received more LRT, and had lower AFP levels and smaller tumor sizes at transplant

Significant Reduction in Post-transplant Hepatocellular Carcinoma Recurrence in the Post-six-Month Waiting Policy Era

Results (continued)

- Post-policy era associated with an unadjusted 35% reduction in risk of post-LT HCC recurrence (HR 0.65, 95% CI 0.52-0.80, $p < 0.001$).
- Association remained after adjusting for tumor characteristics at listing (SHR 0.69, 95% CI 0.55-0.86, $p = 0.001$).
- No association after adjusting for LRT episodes and RETREAT score (SHR 0.77, 95% CI 0.59-1.00, $p = 0.054$).
- Significant reduction in mortality associated with post-policy era in unadjusted analysis (HR 0.81, 95% CI 0.72-0.92, $p = 0.001$)



Significant Reduction in Post-transplant Hepatocellular Carcinoma Recurrence in the Post-Six-Month Waiting Policy Era

Conclusion

- Significant reduction in post-LT HCC recurrence and mortality after policy implementation.
- Sequential analyses demonstrate that this difference is likely mediated through waitlist selection of relatively healthier patients, increased opportunity for LRT use, and potential selection of favorable tumor biology.

Nonalcoholic Steatohepatitis (NASH) Has Become the Most Common Indication for Liver Transplantation Among Candidates With Hepatocellular Carcinoma in the US

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Nonalcoholic Steatohepatitis (NASH) Has Become the Most Common Indication for Liver Transplantation Among Candidates With Hepatocellular Carcinoma in the US

Aim

- Assess the most recent trends in patients with chronic liver disease (CLD) listed for liver transplantation (LT) in the U.S. using a national registry.

Methods

- Assess the recent trends in patients with chronic liver disease (CLD) listed for liver transplantation (LT) in the U.S. using a national registry.
- The Scientific Registry of Transplant Recipients (SRTR) was used to select adult (≥ 18 y at listing) LT candidates included between 2013-2022.
- Primary and secondary listing etiologies were used to identify patients with the most common etiologies of CLD

Nonalcoholic Steatohepatitis (NASH) Has Become the Most Common Indication for Liver Transplantation Among Candidates With Hepatocellular Carcinoma in the US

Results

- 116,292 LT candidates with a known etiology of CLD.
- 21%(n = 24,657) of LT candidates had HCC.

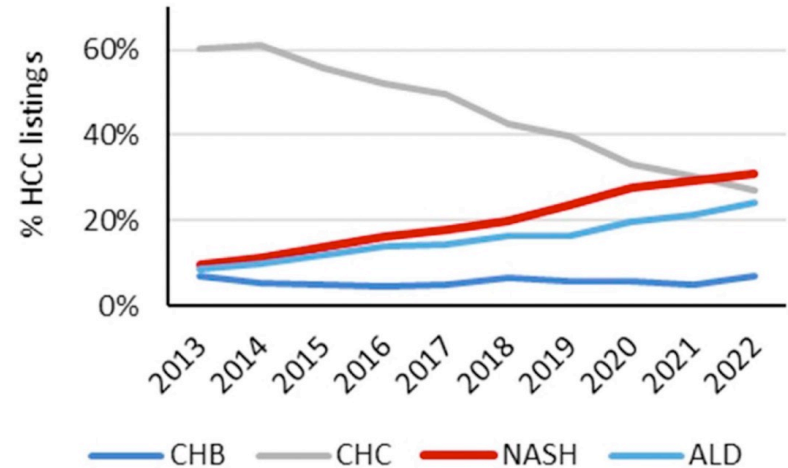
Temporal Changes in Indications for Transplant

Group	HCV		NASH		ALD	
	2013	2022	2013	2022	2013	2022
Year	2013	2022	2013	2022	2013	2022
HCC negative	28%	4%	19%	27%	23%	48%
HCC positive	60%	27%	10%	31%	9%	24%

Nonalcoholic Steatohepatitis (NASH) Has Become the Most Common Indication for Liver Transplantation Among Candidates With Hepatocellular Carcinoma in the US

Results (continued)

Among candidates with HCC, the rapid increase in the proportion of NASH continued during the most recent study years: 20% (2018) to 28% (2020) to 31% (2022)



Nonalcoholic Steatohepatitis (NASH) Has Become the Most Common Indication for Liver Transplantation Among Candidates With Hepatocellular Carcinoma in the US

Conclusion

The impact of different etiologies of CLD to LT burden in the U.S. has been changing over the last decade.

ALD and NASH remain the two most common indications for non-HCC-LT, while NASH is currently the most common indication for HCC-LT.

Disparities in Access to Liver Transplantation for Metabolic Dysfunction-Associated Steatohepatitis – Associated Hepatocellular Carcinoma

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Disparities in Access to Liver Transplantation for Metabolic Dysfunction-Associated Steatohepatitis – Associated Hepatocellular Carcinoma

Aims

- Assess whether racial and ethnic minorities are waitlisted and transplanted for MASH-HCC at lower-than-expected rates

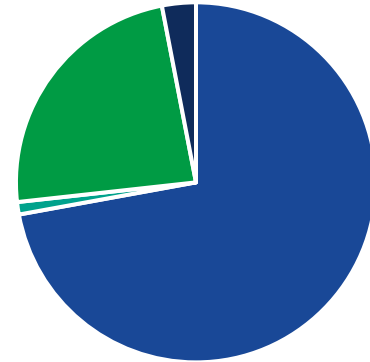
Methods

- Adults with HCC waitlisted for LT between 1/2015 and 12/2021 were identified in the US Scientific Registry of Transplant Recipients standard analysis file.
- Patients were included if they (1) had a MASH diagnosis, or (2) had a diagnosis of cryptogenic/idiopathic cirrhosis and body mass index > 30 kg/m².
- Differences between groups were compared using Chi-square, Fisher's exact, or Kruskal Wallis tests as appropriate. Cox regression modeling was also used.

Disparities in Access to Liver Transplantation for Metabolic Dysfunction-Associated Steatohepatitis – Associated Hepatocellular Carcinoma

Results

- 3810 LT candidates
 - NH White (n=2713, 71.2%)
 - Black (n=49, 1.1%)
 - Hispanic (n=891, 23.4%)
 - Asian (n=115, 3.0%)

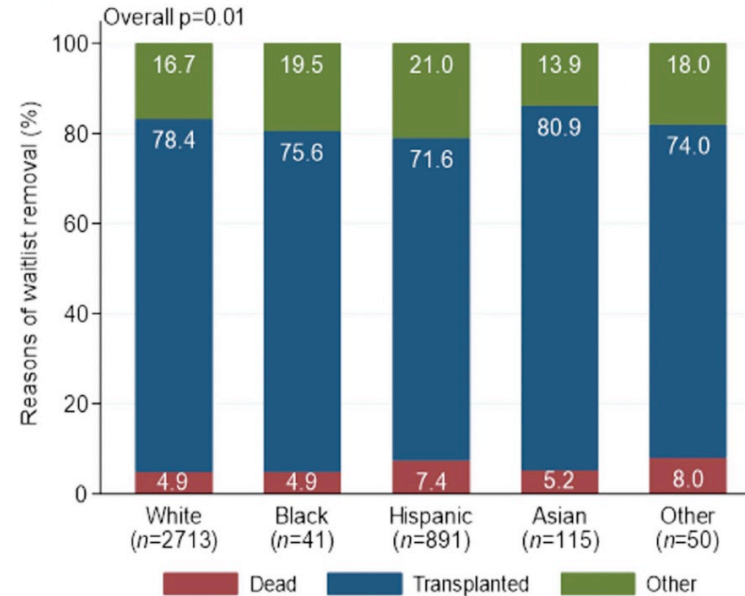


■ NH White ■ Black ■ Hispanic ■ Asian

Disparities in Access to Liver Transplantation for Metabolic Dysfunction-Associated Steatohepatitis – Associated Hepatocellular Carcinoma

Results (continued)

- Proportions of patients receiving LT different ($p=0.01$). Hispanics underwent LT at significantly lower rates than NH whites ($p < 0.001$).
- Waitlist mortality rates not different among races/ethnicities ($p = 0.06$).
- Hispanic (HR, 0.85; 95% CI, 0.77-0.95; $p = 0.002$) and Asian (HR, 0.79; 95% CI, 0.63-0.98; $p = 0.04$) patients were less likely to receive LT than NH white patients.



Disparities in Access to Liver Transplantation for Metabolic Dysfunction-Associated Steatohepatitis – Associated Hepatocellular Carcinoma

Conclusion

- Hispanics and Asians less likely to receive LT for MASH-HCC than other races/ethnicities.
- A significantly greater proportion of Hispanic patients had LT in the post-MMAT era, likely reflecting efforts across the country to mitigate access disparities.
- The proportion of Black patients waitlisted for LT was low.

Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

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Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Aims

- Review local experience with LT and concurrent sleeve gastrectomy (LTSG) with aims to determine long-term safety, efficacy, and impact on progression of Metabolic Syndrome (MS) and liver disease after transplantation.

Methods

- A multi-center retrospective analysis of patients undergoing LTSG with a single protocol (n = 73).
- Outcomes assessed included morbidity and mortality, graft loss, BMI, evolution of MS, and development of allograft steatosis on ultra-sound and fibrosis on MRE.
- A comparison cohort included all 185 patients with BMI > 30 who underwent LT-only for NASH transplanted during the same time period

Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Results

- Follow-up duration was 4 to 153 months.
- No significant difference in all-cause mortality or graft loss between LT and LTSG patients.
- At last follow up:

Outcome	LT	LTSG	P-value
Steatosis	40.2%	20.3%	0.01
Fibrosis	37.3%	23.4%	0.12

Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Results (continued)

Efficacy

Metabolic	LT	LTSG
Diabetes	No significant change	Decreased significantly
HTN	No significant change	Decreased significantly
hyperlipidemia	No significant change	No significant change
BMI	No significant change	Decreased significantly

Complications

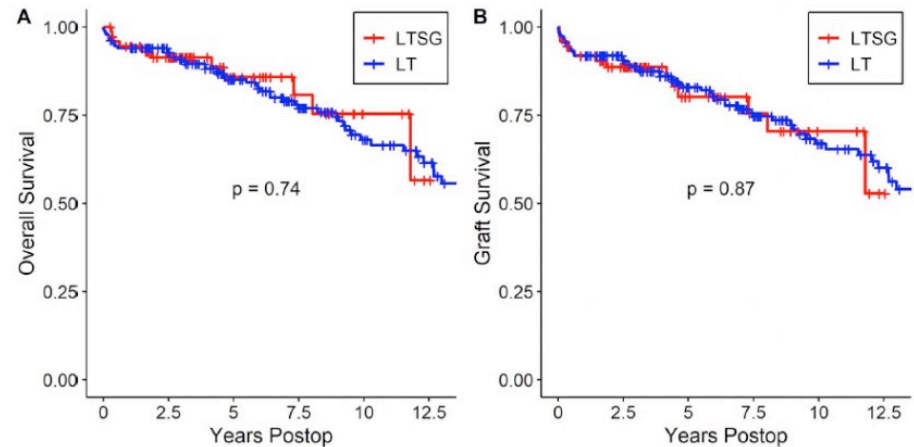
One LTSG patient with gastric sleeve leak

One LTSH patient required hiatal hernia repair
Severe gastric reflux in 11.1% LTSG patients

Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Results (continued)

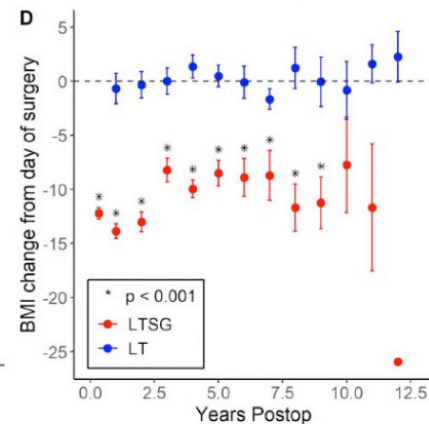
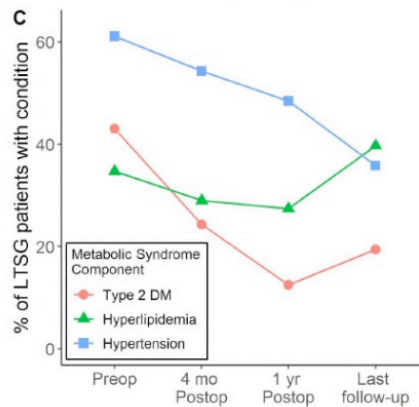
No significant difference in all-cause mortality or graft loss between LT and LTSG patients



Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Results (continued)

- Prevalence of hypertension in LTSG patients decreased ($p < 0.01$) and hyperlipidemia was not significantly changed (Figure C).
- LTSG patients, starting with an average BMI of 45.5, had significantly reduced BMI for at least 9 years following surgery (all $p < 0.001$). LT-only patients, with an average BMI of 34.0, had no significant change in BMI (Figure D)



Simultaneous Liver Transplant and Sleeve Gastrectomy Is a Safe Surgical Option That Improves Metabolic Syndrome and Reduces Allograft Steatosis

Conclusion

- LTSG is an excellent option for those with BMI > 40
- Confers no increase in mortality or graft loss even when compared to a less obese cohort.
- LTSG reduces recurrence of steatosis and trends toward less fibrosis when compared to LT alone, and leads to sustained weight loss and resolution of diabetes and hypertension.

Early Graft Failure After Living Donor Liver Transplant

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Early Graft Failure After Living Donor Liver Transplant

Aim

- Perform contemporary analysis of short-term outcomes to better understand risk factors and opportunities for improvement in living donor liver transplantation (LDLT).

Methods

- Adult (≥ 18 y) LDLT recipients from January 2004 to December 2021 were analyzed from the United States Scientific Registry of Transplant Recipients.
- Graft status at 30 days assessed (graft failure defined as retransplantation or death).
- Bivariate analysis of continuous and categorical variables was performed, and a multi-variable logistic regression was used to identify risk factors of early graft failure.

Early Graft Failure After Living Donor Liver Transplant

Results

- 4,544 LDLTs were performed with a graft failure rate of 3.4% (155/4544) at 30 days.
- Asian recipient race (vs. White; aOR: 3.37, CI: 1.98-7.07, $p < 0.001$) and history of recipient PVT (aOR: 2.7, CI: 1.52-4.77, $p = 0.001$) were associated with inferior outcomes.
- LDLTs performed during the most recent 2016-2021 period (compared to 2004-2009 and 2010-2015) resulted in superior outcomes (aOR: 0.45, $p < 0.001$, CI: 0.23-0.69) .

Early Graft Failure After Living Donor Liver Transplant

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aOR: Adjusted Odds Ratio; PVT: Portal Vein Thrombosis.
AASLD 2023. Abstract 228. Oral.

Variables	aOR	CI	Multivariable P-Value
Donor Characteristics			
Male Sex	0.633	0.45-0.89	0.009
Recipient Characteristics			
Age (years)	0.99	0.97-0.99	0.015
Race (ref: white)			
• African American	0.73	0.7-2.03	0.55
• Asian	3.73	1.97-7.07	<0.001
• Other	0	0	0.998
PVT	2.7	1.52-4.77	0.001
Encephalopathy	0.73	0.57-0.93	0.001
OR Characteristics			
Right lobe	0.41	0.27-0.62	<0.001
Transplant Period (ref: 2004 – 2009)			
• 2010-2015	0.95	0.63-1.45	0.823
• 2016-2021	0.45	0.29-0.69	<0.001

Early Graft Failure After Living Donor Liver Transplant

Conclusion:

- Short-term adult LDLT graft failure is uncommon
- Opportunities for optimizing outcomes by prioritizing right lobe donation, improving candidate nutritional status, and careful pretransplant risk assessment of candidates with known PVT.
- Period effect exists whereby increased LDLT experience in the most recent era correlated with improved outcomes

Conclusion

- Fatty liver has emerged as an important risk factor for liver cancer
 - Survival has improved and OLT may not be necessary
 - Barriers to access to care exist, and need to be corrected
- Bariatric surgery safe and effective in liver transplant recipients, and may be considered during transplant in select cases
- Portal vein thrombosis may impact graft survival after living donor liver transplant