Liver Transplantation For Alcoholic Hepatitis

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Changing Terminology…

- The term ‘alcoholic’ is stigmatizing
  - Undermines patient dignity and self-esteem

Previous	Suggested	Abbreviation
Alcoholic	Alcohol use disorder	AUD
Alcoholic liver disease	Alcohol-related liver disease	ALD
Alcoholic steatohepatitis	Alcohol-related steatohepatitis	ASH
Alcoholic cirrhosis	Alcohol-related cirrhosis	AC
Alcoholic hepatitis	Alcohol-related hepatitis	AH
Recidivism	Relapse	

EASL CPG ALD. J Hepatol 2018;69:154–81.
Crabb et al. AASLD Practice Guideline 2019.
Asrani et al. Liver Transpl. Nov 2019.

Liver Transplantation For Alcoholic Hepatitis

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Liver Transplantation For Alcohol-Related Hepatitis

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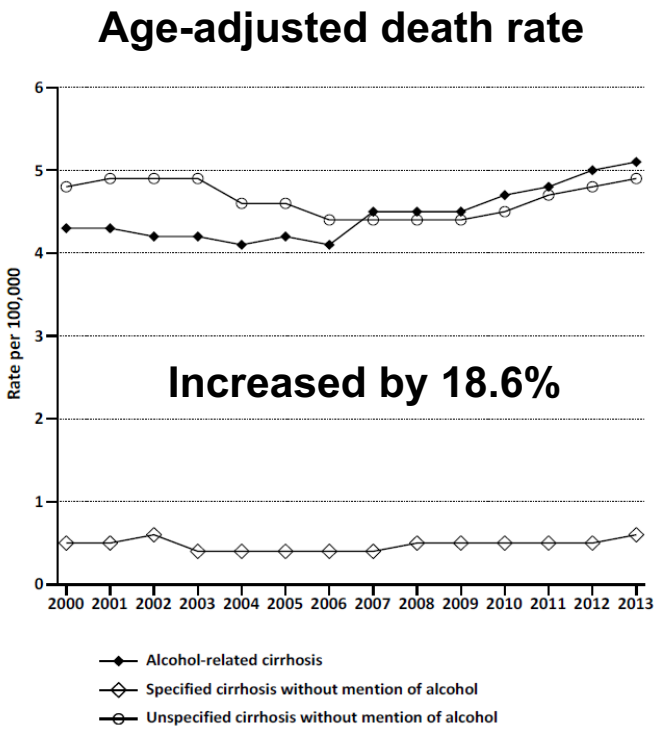
Overview

- Epidemiology and Trends in ALD
- Review of AH Diagnosis and Management
- Liver Transplant (LT) for AH
  - Candidate Evaluation and Selection
  - Post-LT Outcomes
  - Post-LT Management

Trends in ALD

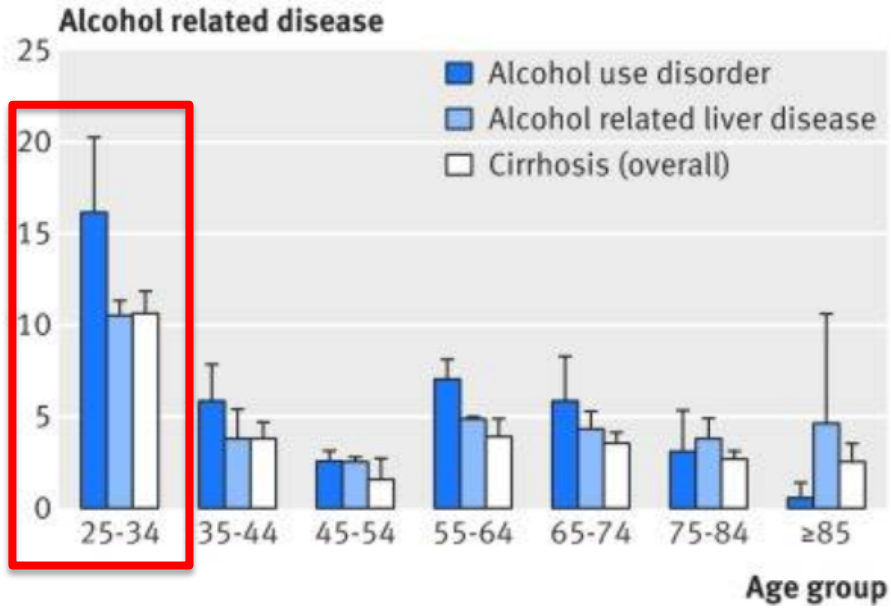
- ALD rates & mortality increasing in US
- Alcohol projected to be single most common cause of cirrhosis in US in next decade



Godfrey et al. Clin Liv Dis. 2019.
Yoon and Chen. NIAAA Surveillance Report. 2016.

Trends in ALD

- AC prevalence may be increasing at faster rate in **women** than men
  - Mirrors rise in alcohol use in women in US
- Increased AC mortality in **young adults** (25-34yo)
  - Highest average annual %increase in cirrhosis-related, ALD, AUD mortality
- Incidence of AH difficult to estimate due to coding
  - In US, admissions for AH increased to 0.8% of all admissions in 2010

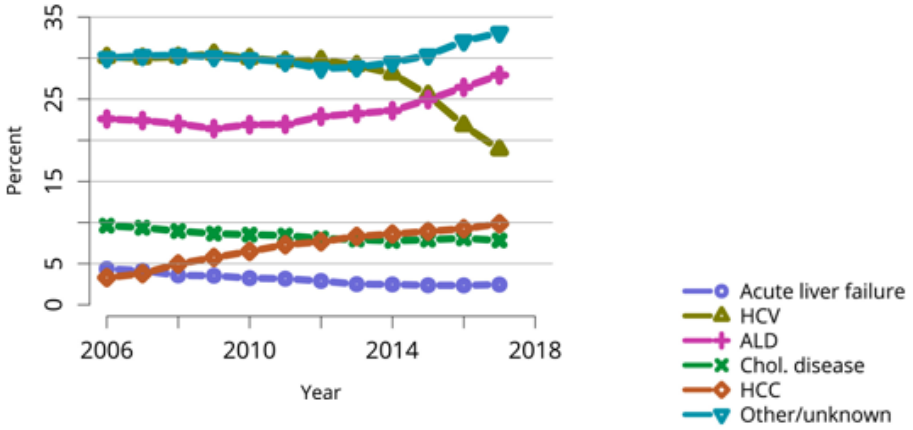


Crabb et al. AASLD Practice Guidelines. 2019.
Tapper and Parikh. BMJ. 2018.
Chirapongsathorn et al. Hep Comm. 2018.

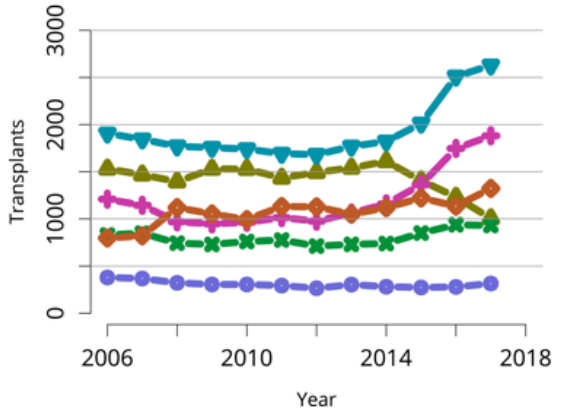
Trends in ALD and LT

- By 2017, ALD had become the most common liver disease indication for LT in US

- Increasing proportion of adults with ALD waiting for LT



- Increasing number of LT recipients with ALD



Kim et al. OPTN/SRTR 2017 Annual Data Report: Liver. AJT. 2019.

Alcohol-related Hepatitis (AH)

- Defining AH…

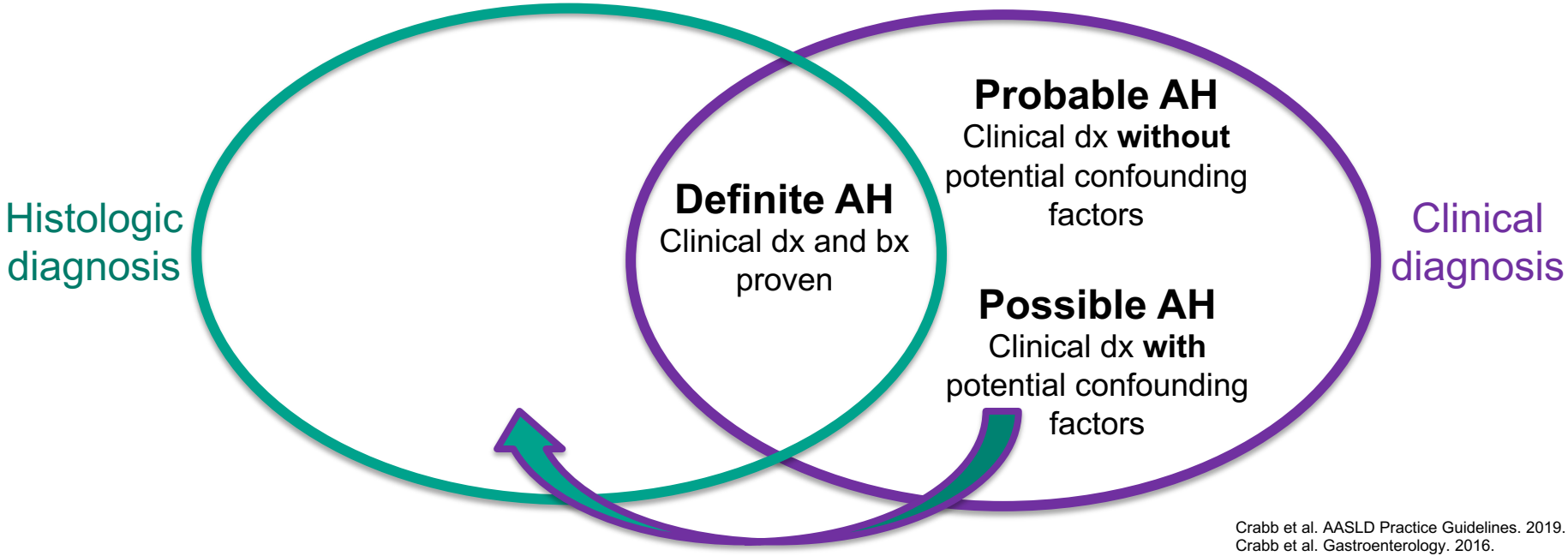
Clinical Diagnosis of AH
Onset of jaundice within prior 8 weeks
Ongoing consumption of >40g (F) or 60g (M) alcohol/day for ≥6 months, with <60d of abstinence before onset of jaundice
AST >50 AST/ALT >1.5 Both AST and ALT <400 IU/L
Total Bilirubin >3 mg/dL

Potential Confounding Factors
Possible ischemic hepatitis (severe UGIB, hypotension, recent cocaine)
Metabolic liver disease (Wilson, a1AT def)
Possible DILI
Uncertain alcohol use (pt denies excess use)
Atypical lab tests AST <50 or >400 AST/ALT <1.5 ANA >1:160 or SMA >1:80

Crabb et al. AASLD Practice Guidelines. 2019.
Crabb et al. Gastroenterology. 2016.

Alcohol-related Hepatitis (AH)

- 2016 consensus statement regarding clinical diagnosis of AH and when to consider bx for confirmation of ASH



Crabb et al. AASLD Practice Guidelines. 2019.
Crabb et al. Gastroenterology. 2016.

Assessing AH Prognosis

- Lab-based prognostic scores assess severity and short-term prognosis in AH
  - Common variables shared between scores, including combinations of:
    - Total bilirubin
    - PT/INR
    - BUN/creatinine
    - Age
    - Albumin
    - WBC
- Extra-hepatic complications, most notably acute kidney injury and serious infection, profoundly impact outcomes
- In the long term, **abstinence from alcohol** is the main driver of outcome in severe AH patients surviving >6 months

Assessing AH Prognosis

Score & Components	Stratification	Clinical Application	Pros	Cons
Maddrey Discriminant Function - TB, PT	Severe ≥32 Predicts high risk of short-term mortality	Start steroids if severe	Extensive experience in AH Inclusion criteria for most AH clinical trials	False positive → excess steroid use

- MDF derived from results of early clinical trial comparing steroids to placebo and later modified to identify AH patients with high risk of short-term mortality when DF ≥32 → 30-50% at 28days
- Score <32 indicates a low but not zero risk of mortality with supportive care

Crabb et al. AASLD Practice Guidelines. 2019.
Maddrey et al. Gastroenterology. 1978.

Assessing AH Prognosis

Score & Components	Stratification	Clinical Application	Pros	Cons
MELD - TB, INR, Cr	Severe ≥21	Prognosis	Extensive experience ΔMELD over time may add additional prognostic info	Unclear threshold to start steroids, MELD >20 proposed

- MELD can be calculated at different time points and may have improved accuracy in intermediate and long term prognostication
- Δ MELD, while not specifically studied in AH, can reflect progression of liver disease over time → rising MELD indicating greater risk of death and declining MELD indicating improving risk of death

Crabb et al. AASLD Practice Guidelines. 2019.

Assessing AH Prognosis

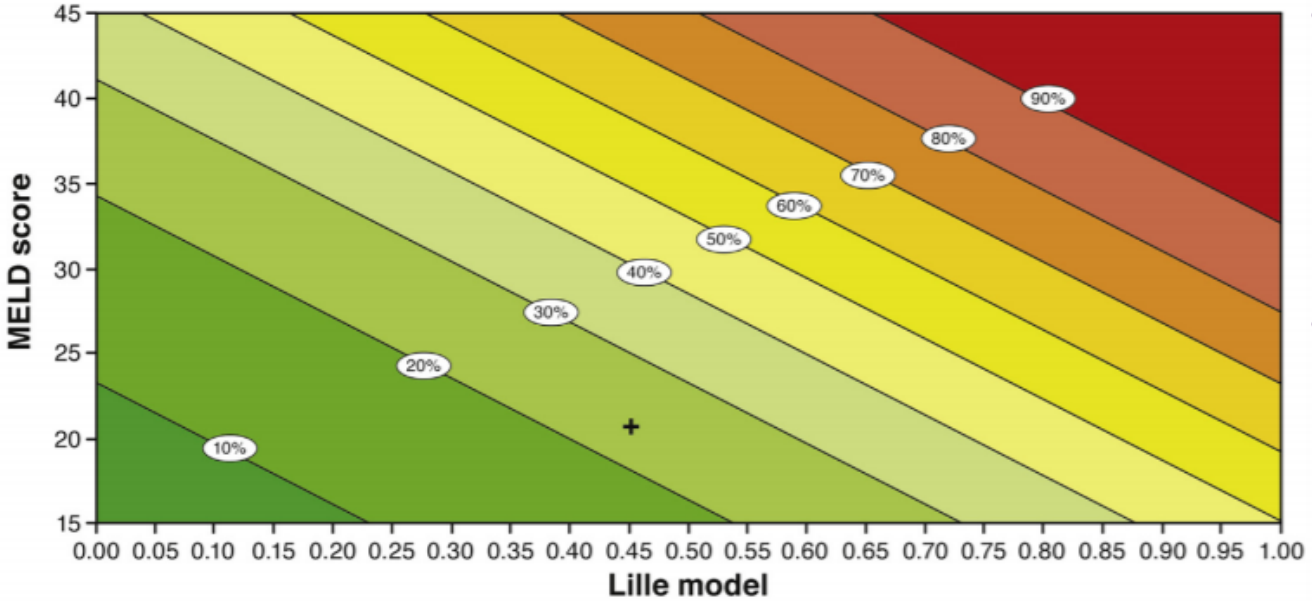
Score & Components	Stratification	Clinical Application	Pros	Cons
Lille - TB, INR, Cr, age, albumin	≥0.45: nonresponse, poor prognosis <0.45: response	Assess response to steroids at D7, determine continuation vs cessation *D4 score shown to have similar accuracy, needs additional validation	Guides early cessation of steroids	Unclear decision-making if partial response (Lille 0.46-0.56)

- Dynamic score that incorporates the change in bilirubin at 7 days after starting steroids to assess early treatment response and utility of continuation for 28 days
- Lille score at day 4 has been shown to have similar accuracy, potentially reducing unnecessary steroid exposure, though needs validation

Crabb et al. AASLD Practice Guidelines. 2019.
Louvet et al. Hepatology. 2007.
Garcia-Saenz-de-Sicilia et al. AJG. 2017.

Assessing AH Prognosis

- Combining static (MELD) and dynamic (Lille) models can enhance outcome prediction in AH



- Estimated mortality at 6 months by joint effect model of MELD plus Lille
- MELD 21, Lille 0.45 ~24% 6mo mortality rate

Louvet et al. Gastroenterology. 2015.

AH Treatment

Proven Benefit

Alcohol Abstinence

Likely Benefit

Corticosteroids

Nutrition

Potential Benefit

N-Acetylcysteine

G-CSF

Unlikely Benefit

Pentoxifylline

TNF-α inhibitors

Extracorporeal cellular tx

Vitamin E

Crabb et al. AASLD Practice Guidelines. 2019.

AH Treatment – **Abstinence**

- **Alcohol abstinence** is critical
- All patients with ALD should be advised to **completely abstain** from alcohol
- Continued alcohol use leads to:
  - Increased rates of variceal bleeding, HE, ascites
  - Increased risk of HCC and death

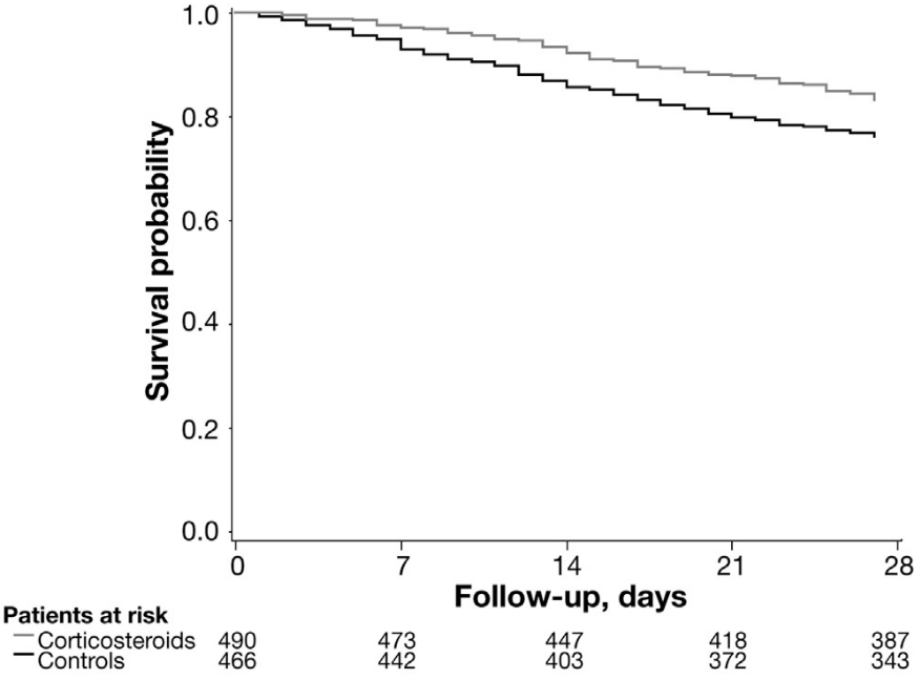
AH Treatment – Corticosteroids

- **STOPAH** – Steroids or Pentoxifylline for AH
  - Largest RCT in severe AH → multicenter, randomized, double-blind, 2x2 factorial design enrolled 1103 pts with clinically severe AH in UK
  - No significant survival benefit with prednisolone vs placebo at 28d (OR 0.72; 95% CI 0.52-1.01)
  - *Post hoc* multivariable analysis → steroids associated with improved 28d survival (OR 0.61, p=0.02), but not 90d or 1y
  - Pentoxifylline did not improve survival
  - Serious infections occurred in 13% tx with steroids vs 7% who did not receive steroids (p=0.002)

Thursz et al. NEJM. 2015.

AH Treatment – Corticosteroids

- Meta-analysis of individual pt data from 11 RCTs (2111 pts) comparing steroids, pentoxifylline or combo in severe AH
  - Steroids significantly reduced 28d mortality vs placebo (36% risk reduction) or pentoxifylline
  - No significant differences in 6 month mortality with any tx or controls



Louvet et al. Gastroenterology. 2018.

AH Treatment – Corticosteroids

- These studies offer **modest support for prednisolone 40mg/day to improve 28d mortality in severe AH (MDF ≥32)**

- No MDF or MELD cutoff above which steroids should be avoided
  - Meta-analysis showed most severely ill with MDF ≥68 had similar responses to steroids vs those with lower MDF
  - Very high scores (MDF >90, MELD >30) = very severe disease, need to evaluate for occult infection and other contraindications to steroids

- Lille score should be used to reassess prognosis, identify nonresponders, guide treatment after 7d of steroids

Crabb et al. AASLD Practice Guidelines. 2019.
Louvet et al. Gastroenterology. 2018.

AH Treatment – Corticosteroids

- Assessing Contraindications to Steroids

	Considerations
Uncontrolled infection	- Need thorough evaluation and time to r/o infection prior to starting steroids - If infection found, need prompt abx initiation - Unknown if empiric abx improve outcomes
Acute kidney injury Cr > 2.5	- AKI excluded in major AH trials so data lacking - If AKI resolves, then steroids can be considered
GI bleeding	- GIB excluded from many trials - After control of GIB, can consider steroids
Other: multisystem organ failure, shock, active HBV, active TB	

Crabb et al. AASLD Practice Guidelines. 2019.

AH Treatment – Nutritional Therapy

- Meta-analyses of nutritional support for AH have suggested **improvement in HE** and **fewer infections**

- RCT in severe AH tx with steroids
  - Intensive enteral nutrition via FT showed no additional survival benefit vs conventional nutrition
  - Lower daily caloric intake (<21.5 kcal/kg/d) associated with increased infections and 6 month mortality vs higher caloric intake

- Adequate nutritional intake should be a major goal
  - 1.2-1.5g/kg protein and 35Kcal/kg daily goals
  - Enteral route preferred

Moreno et al. Gastroenterology. 2016.
Singal et al. Am J Gastroenterol. 2018.
Fialla et al. Liver Int. 2015.
Antar et al. Can J Gastroenterol. 2012.

AH Treatment – **N-acetylcysteine**

- RCT (France) showed IV NAC plus steroids reduced some early complications (infection, HRS) vs steroids alone
  - Steroids + NAC improved 1 mo mortality vs steroids alone (8% vs 24%, p=0.006)
    - Benefit not seen at 3 or 6 months

- Network meta-analysis of 22 RCT (>2600 pts) also supported addition of NAC providing survival benefit beyond steroids alone

- **Addition of IV NAC to prednisolone 40mg/d may improve 30d survival in severe AH**

Nguyen-Khac et al. NEJM. 2011.
Singh et al. Gastroenterology. 2015.
Crabb et al. AASLD Practice Guidelines. 2019.

AH Treatment – Pentoxifylline

- Pentoxifylline use was supported by RCT showing improved short-term survival with pentoxifylline vs placebo
- Subsequent studies have failed to confirm survival benefit though have shown reduced development of HRS with pentoxifylline
- STOPAH and meta-analysis of individual pt data have failed to demonstrate any benefit of pentoxifylline
- **Existing evidence does not support use of pentoxifylline for severe AH**

Thursz et al. NEJM. 2015.
Louvet et al. Gastroenterology. 2018.
Crabb et al. AASLD Practice Guidelines. 2019.

AH Treatment – Relapse Prevention

- As abstinence is key to long-term survival, **relapse prevention strategies** should be implemented to promote complete abstinence

- Integrated multidisciplinary care = best option for management of AUD and ALD
  - Referral to AUD treatment professional is recommended
  - Care may include combination psychotherapy with CBT, motivational enhancement therapy, 12-step programs
  - Few data to show that one treatment modality superior to another

Crabb et al. AASLD Practice Guidelines. 2019.
Khan et al. Clin Gastro Hep. 2016.

AH Treatment – Relapse Prevention

- Pharmacotherapy for AUD
  - 3 FDA approved = disulfiram, naltrexone, acamprosate
    - Disulfiram, naltrexone undergo hepatic metabolism
    - **Acamprosate** does not undergo hepatic metabolism
      - Number needed to treat to prevent return to any drinking ~12 for acamprosate
  - Non-FDA approved include gabapentin, baclofen, topiramate, varenicline
    - **Baclofen is only agent tested in RCT in cirrhotics with AUD**
      - RCT included compensated and decompensated cirrhotics (exclude HE)
      - 12 wk of baclofen shown to decrease relapse and improve abstinence vs placebo
  - **Acamprosate or baclofen can be considered for AUD tx in ALD**

Crabb et al. AASLD Practice Guidelines. 2019.
Addolorato et al. Lancet. 2007.

AH Treatment – Relapse Monitoring

- Biomarkers of alcohol use aid in dx and support recovery
- Important to disclose biomarker use prior to testing to maintain therapeutic alliance and improve alcohol use disclosure
- Direct markers (alcohol metabolites) → ethyl glucuronide (EtG), ethyl sulfate (EtS), phosphatidylethanol (PEth)
  - Higher specificity than indirect markers (GGT, AST, ALT, MCV)
  - Longer detection window vs blood ethanol or exhaled air (4-12 hours)
  - **EtG, EtS and PEth not affected by liver disease → preferred for ALD pts**

Crabb et al. AASLD Practice Guidelines. 2019.
EASL. CPG ALD. J Hepatol. 2018.

AH Treatment – Biomarkers

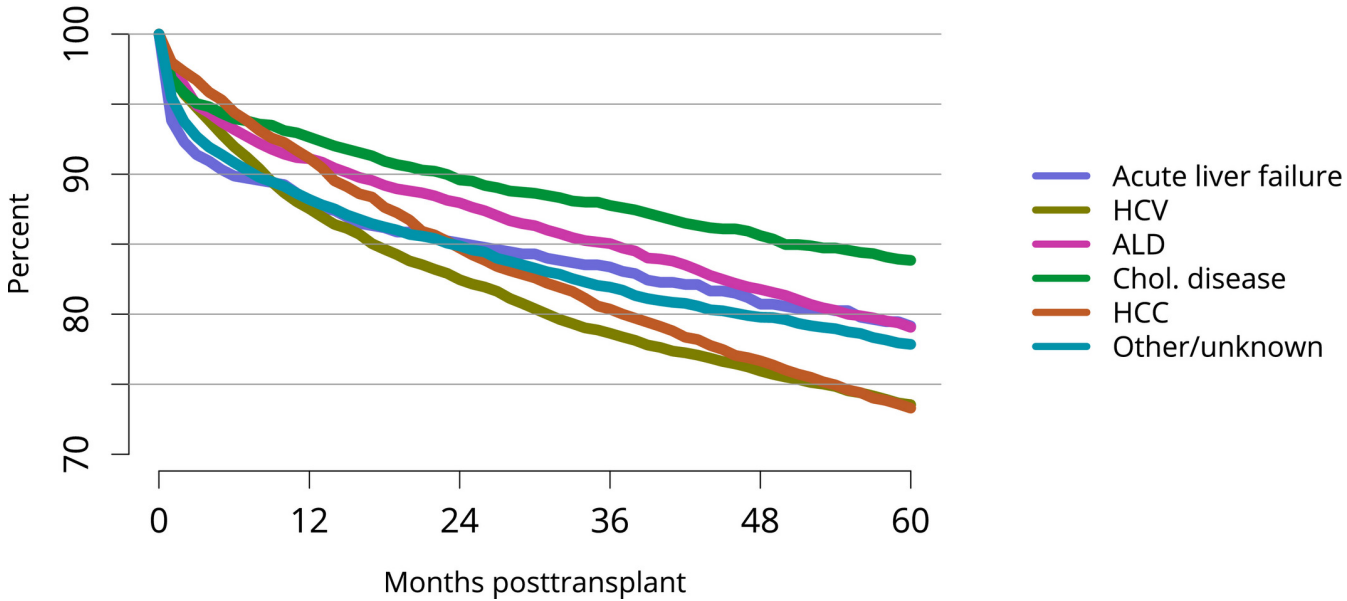
Biomarker, source	Detection window	Cutoff value	Sensitivity	Specificity	Considerations
EtG*, urine	Up to 80hr	500ng/mL	76-89%	93-99%	- Longer detection with higher intake and renal failure - False (+): alc-containing mouthwash or hand sanitizer, nonalc beer/wine - EtS often used to confirm +EtG
EtS, urine	Up to 80hr	75ng/mL	82%	86%	
PEth, blood	2-3 weeks	20 ng/mL	97-100%	66-96%	- More expensive than urine EtG - Longer detection with more chronic repeated alc use

*EtG can be detected after consuming as little as 5g → In the US, 1 "standard" drink ~14g of pure alcohol (12oz regular beer, 5oz wine, 1.5oz distilled spirits

Crabb et al. AASLD Practice Guidelines. 2019.
EASL. CPG ALD. J Hepatol. 2018.

Liver Transplant for ALD

Patient Survival Post-LT 2010-2012 by Diagnosis



Kim et al. Am J Transplant. 2019.

Post-LT Relapse in Chronic ALD

- Rate of relapse post-LT highly variable in literature

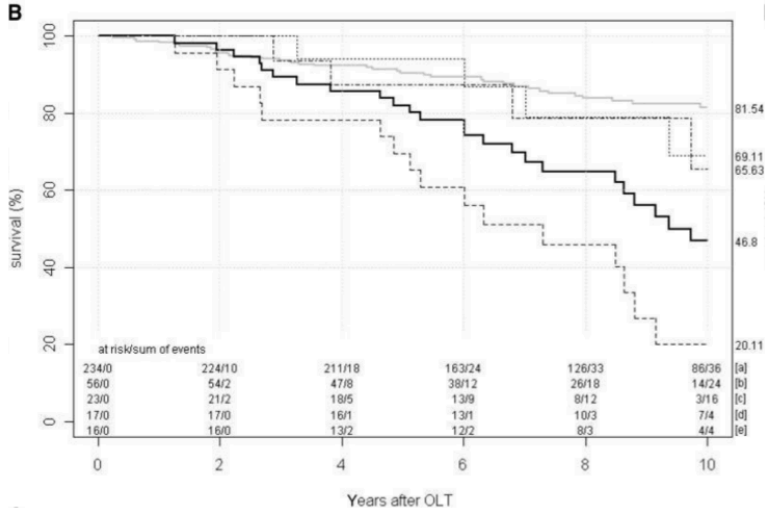
- Studies have described relapse rates 18-50% for recipients transplanted for ALD
  - Varied definitions of relapse makes this difficult to assess
  - Relapse often defined as any alcohol use without distinction in amount, duration, nature of relapse (slip vs sustained use)
  - Likely underreported

- Relapse rate to harmful drinking ~20%

Rice et al. Liver Transplantation. 2013..
Godfrey et al. Clin Liv Dis. 2019.

Post-LT Relapse in Chronic ALD

- In relapsing pts, 10y survival is significantly lower (45-71%) vs abstainers or those with only occasional slips (75-93%)
- 300 ALD pts transplanted 1989-2002, similar overall survival for ALD vs non-ALD but significant differences if relapse post-LT



← **Abstinent**

"Slipped" or severity unknown

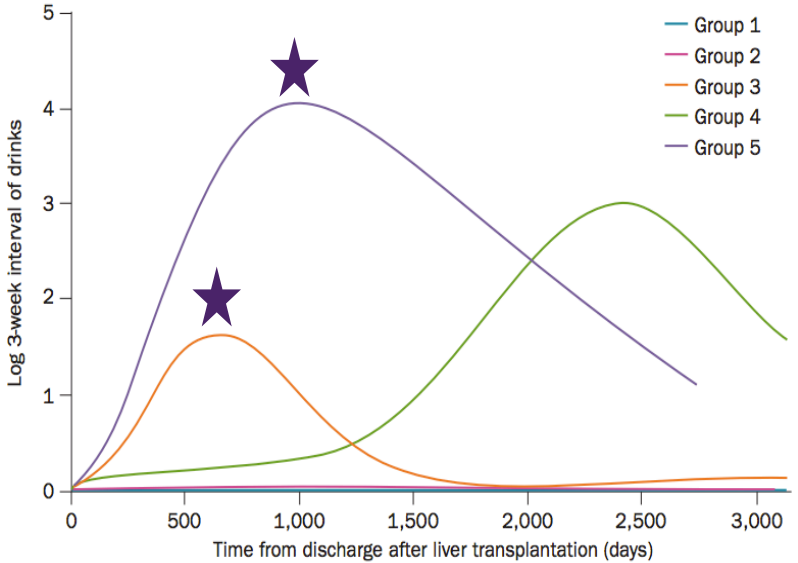
← **All pts who resumed alcohol**

← Resumed abusive drinking

Rice et al. Liver Transplantation. 2013.
DiMartini et al. Am J Transplant. 2010.

Liver Transplant for ALD

- Univ Pittsburg study identified 4 trajectories of alcohol use post-LT
  - When comparing pts with early onset moderate to heavy use (stars) post-LT to all other patterns and abstainers:
    - More frequently had steatohepatitis on bx
    - More frequently had ACR on bx
    - More likely to have graft failure
    - All pts who died from recurrent ALD demonstrated these patterns of use



DiMartini et al. Am J Transplant. 2010.

Liver Transplant for AH

- Severe AH not responding to medical therapy has very poor prognosis, up to 70% at 6 months
- Until recently, >85% of LT programs and 43% of 3rd party payors in US required 6 months of abstinence pre-LT → excludes AH pts
- "6 month rule" → 1997 consensus conference with 2 goals:
  - Allow time for recovery from acute effects of alcohol-toxicity to the liver without undergoing unnecessary LT
  - Evaluate commitment to sobriety while implementing preventative strategies against future relapse

Leong and Im. Clin Liver Dis. 2012.
Louvet et al. Hepatology. 2007.

Liver Transplant for AH

- "6-month rule" became a surrogate for prediction of future drinking by ALD candidates for LT
  - While pre-LT abstinence < 6mo has been associated with post-LT relapse, studies have shown post-LT relapse still occurs with >6mo sobriety
  - Some studies have suggested that abstinence might not be secure until after **5 years of abstinence**

- Multiple series for early LT for severe AH have demonstrated relapse rates comparable with or lower than ALD cohorts with pre-LT abstinence periods

DiMartini et al. Liver Transplantation.2006.
Gallegos-Orozco and Charlton. Clin Liv Dis. 2016.
Pfitzmann et al. Liver Transplantation. 2007
Dew et al. Liver Transplantation. 2008.
Godfrey et al. Clin Liv Dis. 2019.

Liver Transplant for AH

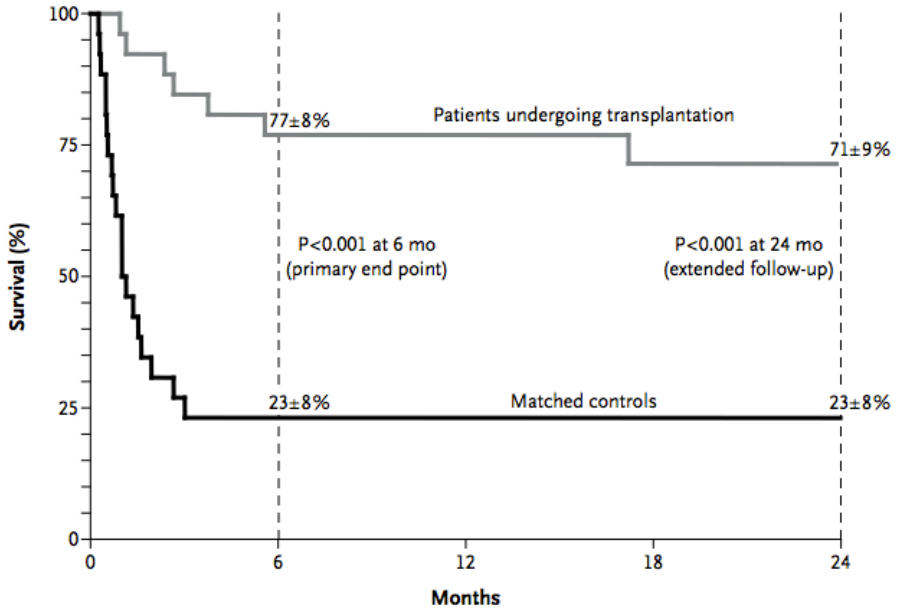
- Early LT for severe AH has questioned the value of a fixed interval of pre-LT abstinence

- Landmark French-Belgian multicenter prospective trial
  - Rigorous evaluation of severe AH pts not responding to medical tx
  - Key inclusion criteria = severe AH as **first liver decompensating event**
    - Nonresponse to medical tx, close supportive family, no severe psych comorbidities, agreement by pt (with strong family support) to lifelong abstinence
  - ~90% excluded from LT due to poor psychosocial profiles
  - <2% of pts admitted for severe AH were eligible for LT

Mathurin et al. NEJM. 2011.

Liver Transplant for AH

- 26 underwent early LT with improved 6mo and 24mo survival
- Low impact on available organs ~2.9% of available grafts used for AH
- 3/26 later resumed alcohol



No. at Risk					
Patients undergoing transplantation	26	20	15	14	13
Matched controls	26	6	6	5	4

Mathurin et al. NEJM. 2011.

Liver Transplant for AH

- The impact of French-Belgian trial was immediate
  - Online survey of providers at 17 of 18 French LT centers with 38% response rate reported:
    - 88% changed their practice re: AH since 2011
    - 97% considered AH as a potential indication for LT
    - 71% of centers performing LT for AH
    - Prior to 2011, 75% applied 6 month rule → fell to 29% at time of survey and 65% reported reducing to a 3 month rule

- US response more hesitant with only a handful of single center pilot studies initiated followed by large observational multicenter study

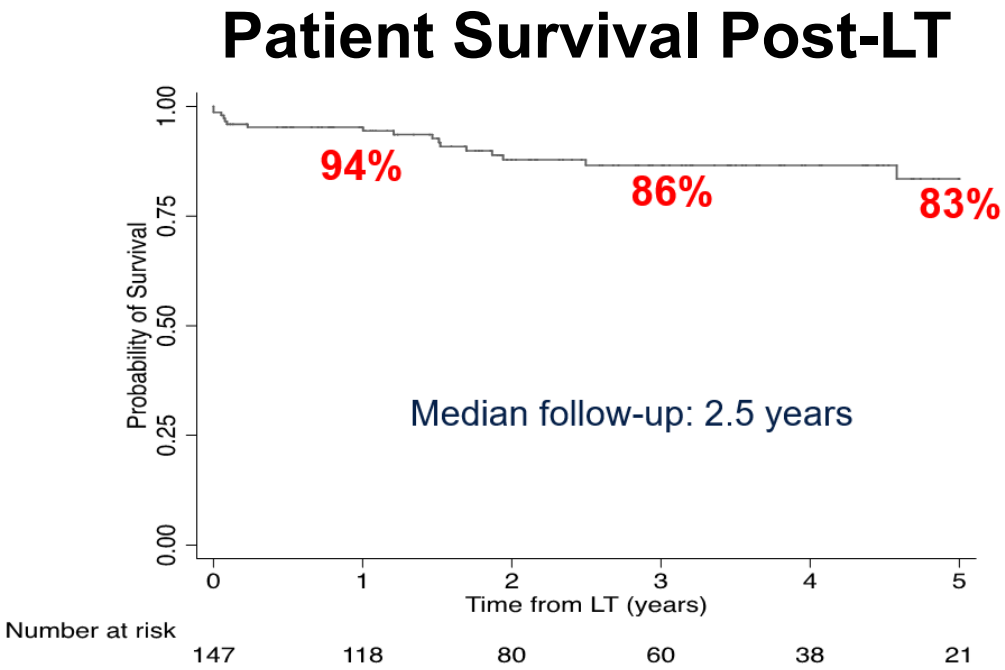
Im et al. J Hepatology. 2019.
Antonini et al. Liver Transpl. 2018.

Liver Transplant for AH

- ACCELERATE-AH: American Consortium of Early Liver Transplantation for Alcoholic Hepatitis
  - 12 centers in 8 UNOS regions
  - 147 **highly selected pts** with severe AH, no prior dx of liver disease, no prior episodes of AH
  - All had strong social support, did not have severe comorbid medical disorders, were expected to adhere to lifelong alcohol abstinence
  - No mandated or prescribed period of abstinence pre-LT
  - Exclusion criteria: other co-existing liver disease, HIV, severe comorbid medical conditions, standard contraindications to LT
  - Median days from last drink to LT 54 (IQR 36-91)
  - Median MELD-Na 39 (36-40)

Lee et al. Gastroenterology. 2018.

Liver Transplant for AH



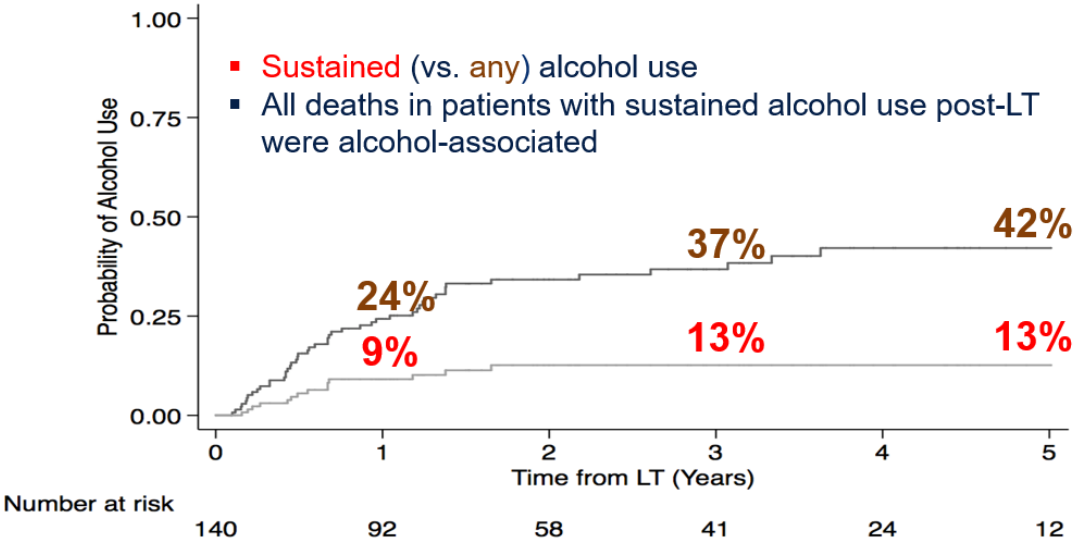
Causes of death:

- Early (within 90d of LT):
  - Majority due to sepsis
- Late (>1y post-LT):
  - Majority were alcohol-associated

Lee et al. Gastroenterology. 2018.

Liver Transplant for AH

Sustained Alcohol Use Post-LT

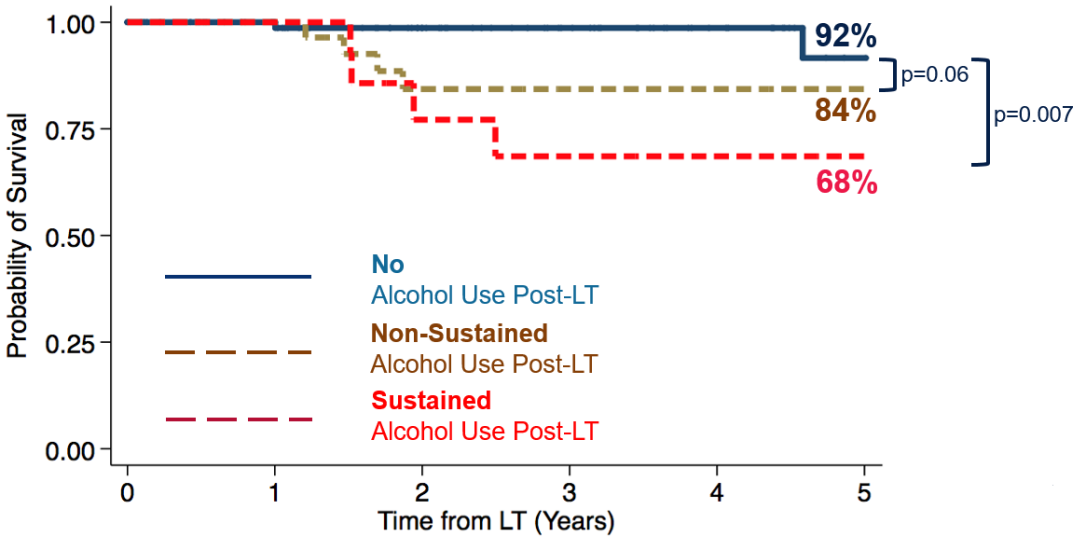


- Length of pre-LT abstinence was **not** associated with any or sustained alcohol use post-LT
- Median return to sustained drinking was ~6 months post-LT
- Younger age associated with alcohol post-LT

Lee et al. Gastroenterology. 2018.

Liver Transplant for AH

Alcohol Use Post-LT Affects Late Survival



- Sustained alcohol post-LT strongest predictor of post-LT death
- Non-sustained alcohol use post-LT not predictive of overall post-LT death
- Length of pre-LT abstinence not associated with post-LT death

Lee et al. Gastroenterology. 2018.

Liver Transplant for AH

- Retrospective review of ACCELERATE-AH data, 4 distinct longitudinal patterns of post-LT alcohol use identified
  - Abstinence/early (<1y) slip 11%
  - Abstinence/late (>1y) slip 69%
  - Early fluctuating harmful (binge, frequent) 10%
  - Early sustained harmful 10%

- Compared to abstinence/late slip, early sustained harmful use (HR 12.4, $p<0.001$) and early fluctuating harmful use (HR 5/7, $p<0.001$) associated with increased risk of death
  - Overt HE and h/o alcohol-related legal issues associated with early sustained
  - H/o multiple relapse attempts associated with early fluctuating use

Im et al. AASLD Oral Abstract 5. 2019

Tool	Nature of Tool	Elements Assessed
University of Michigan Alcoholism Prognosis Score	Specific to LT in ALD	Isolation Previous treatment Insight Psychological health
Alcohol Relapse Risk Assessment (ARRA)	Based on retrospective review of ALD LT outcomes, single center	Absence of HCC Tobacco dependence Continued alcohol despite liver disease dx Low motivation for alcohol treatment Poor stress management skills No rehab relationship Limited social support Lack of nonmedical consequences Continued activities with alcohol present
High-Risk Alcoholism Relapse (HRAR)	Predicts harmful drinking, based on study in male vets	Duration of heavy drinking Usual number of drinks/d # prior alcoholism inpt treatment experiences
Stanford Integrated Psychological Assessment for Transplantation (SIPAT)	Developed for all solid organ transplantation, not only LT	Very comprehensive evaluation with complex administration

Im et al. J Hepatol. 2019

Tool	Nature of Tool	Elements Assessed
University of Michigan Alcoholism Prognosis Scor		Isolation Previous treatment ght logical health
Alcohol Relapse Ris Assessment (ARR		of HCC pendence lcohol despite liver disease dx on for alcohol treatment anagement skills tionship l support nedical consequences ctivities with alcohol present
High-Risk Alcoholism (HRAR)		of heavy drinking number of drinks/d or alcoholism inpt treatment experiences
Stanford Integrated Psychological Assessment for Transplantation (SIPAT)	tran	Very comprehensive evaluation with comprehensive evaluation

No single tool reliably predicts alcohol relapse after LT

Im et al. J Hepatol. 2019

Liver Transplant for AH

- To succeed in LT for AH, must improve candidate selection with easily measured pre-LT variables that accurately predict post-LT relapse

- Dallas Consensus Conference 2019 suggested criteria for listing:

Criteria Related to AH
1st presentation of decompensated ALD
Absence of severe uncontrolled medical or psych comorbidities
Non-response to medical tx

Criteria Related to AUD	
Establish acceptable risk of relapse by multidisciplinary assessment (SW, addiction med)	Accepts ALD dx with insight
Coherent pt (not intubated or HE)	Pt commitment to lifelong abstinence
No repeated failed rehab attempts	Sober support
Lacks current other SUD	Close family, caregivers

Asrani et al. Liver Transpl. 2019.

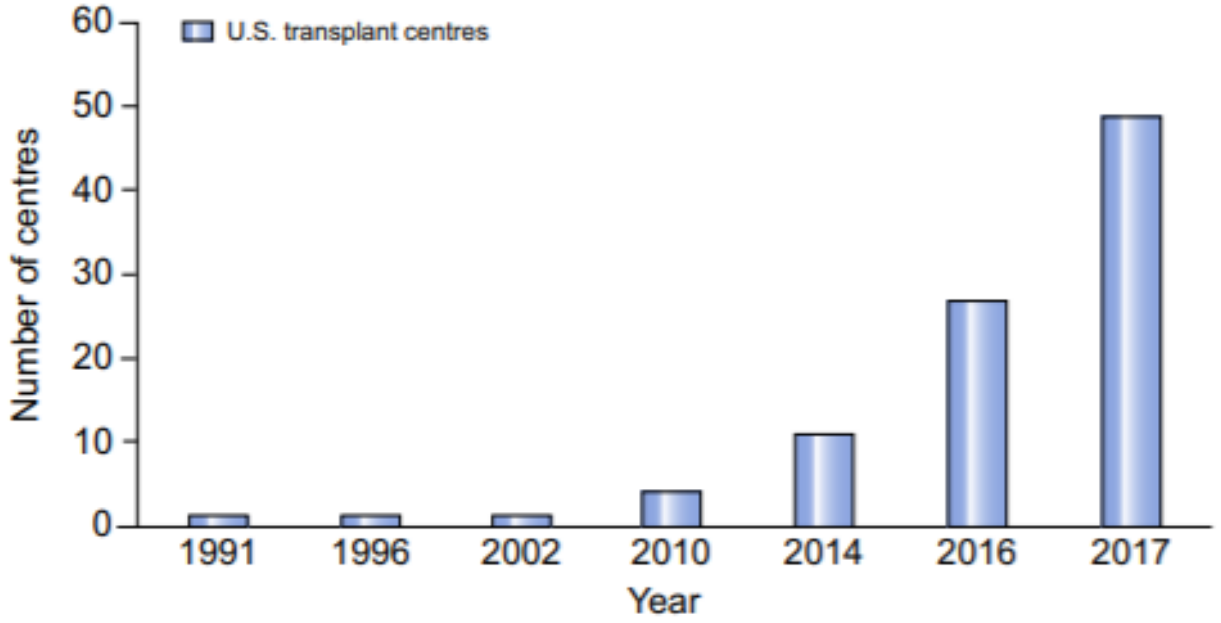
Liver Transplant for AH

- Post-LT AUD management is critical
  - Need pre-LT confirmation of a plan for AUD treatment after LT
  - Start AUD treatment as soon as medically feasible post-LT
  - Need integration of addiction medicine and psychosocial professionals in pre and post-LT management
  - Need robust monitoring for alcohol slips or relapse
    - Should include direct interviewing of pt and caregivers re: alcohol use
    - Routine monitoring of alcohol use with biomarkers (EtG, EtS, PEth)

Asrani et al. Liver Transpl. 2019.

Liver Transplant for AH

Rising # US Centers Having Performed LT for AH



Im et al. J Hepatol. 2019

Goals of LT for AH

- Avoid LT in patients who will recover without LT
- Avoid futility and achieve acceptable short and long-term outcomes comparable to other LT indications
- Avoid creating further disparity in LT by indication, geography, sex, race, insurance status, other socioeconomic factors
- Identify LT candidates likely to have long-term abstinence
- Incorporate treatment of AUD into pre and post LT care

Asrani et al. Liver Transpl. 2019.

Responsibilities of LT Centers

- Demonstrate transparency in candidate selection practices
- Ensure adequate oversight of program components:
  - Presence of adequate addiction medicine and psychosocial providers. LT evaluation for AH is resource-intensive.
  - Monitor pre and post-LT outcomes
  - Monitor for post-LT relapse with ongoing support of abstinence via integrated management with addiction/mental health providers
  - Structured collection of objective data to assess outcomes
- Consideration of national or regional oversight of program adherence to listing practices and outcomes

Asrani et al. Liver Transpl. 2019.

Liver Transplant for AH - **Challenges**

- Challenges in evaluation of severe AH candidates for LT:
  - Severity of illness requires expedited evaluation and decision making so assessment and selection occurs in limited time frame
  - AUD may be inadequately assessed
    - In life-threatening illness, difficult to expect pt or family to contemplate hypothetical scenarios → willingness to attend rehab, lifelong abstinence, adherence to LT management plans
  - No opportunity to reassess pt response after AUD treatment initiation
  - Payer limitations in coverage
    - Insurance coverage for LT may be limited by enforcement of 6 mo rule
    - Post-LT AUD treatment may not be covered

Liver Transplant for AH – **Ethical Considerations**

- Can pts who drank to the limits of mortality be entrusted with stewardship of allograft?
  - Some believe pts with liver disease independent of pt behavior should be prioritized (AIH, PSC, PBC)
  - Cannot limit access based on perceived pt responsibility → NASH widely accepted indication for LT

- Will public perception affect organ donation rates?
  - 500 surveyed re: LT for AH with 68% intending to be organ donors, 82% at least neutral towards early LT for AH, 74% did not feel early LT for AH would lead to hesitation to donate

Stoh et al. Am J Transpl. 2015.
Lee and Terrault. Curr Opin Organ Transp. 2019.

Liver Transplant for AH – **LDLT?**

- AH pts listed for DDLT can be considered for LDLT however, there are additional considerations:
  - Potential increased psychological risks to donors related to recipient risks of relapse and graft loss
  - Program must ensure that the urgency of need does not interfere with information disclosure, processing or ultimate decision making of the donor
  - Potential donors may be victims of unwarranted persuasion as they are asked to decide in time pressured manner to help recipient at imminent risk of death
- If LDLT is to be considered, then independent living donor advocate and the transplant team must ensure that donor decision meets standards of voluntariness

Asrani et al. Liver Transpl. 2019.

Liver Transplant for AH

- While pre-LT duration of alcohol abstinence is an important predictor of post-LT relapse, a fixed 6 month interval may exclude otherwise excellent candidates with low risk of relapse

- Studies of LT for AH demonstrate acceptable post-LT outcomes in **highly selected patients**
  - Need improved candidate selection via easily measurable pre-LT variables that accurately predict post-LT relapse

- Integrated post-LT AUD management, monitoring for relapse is critical


Thank You!