

Alkoholihepatiitti maksansiirron aiheena

Johanna Savikko, dosentti, erikoislääkäri
Elinsiirto- ja maksakirurgia, HUS Vatsakeskus

**SHOULD WE OFFER TRANSPLANTATION TO
PATIENTS NOT RESPONDING TO STEROIDS?**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Liver Transplantation for Severe Alcoholic Hepatitis

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Georges-Philippe Pageaux, M.D., Ph.D., Vincent Leroy, M.D., Ph.D.,
Sébastien Dharancy, M.D., Ph.D., Alexandre Louvet, M.D., Ph.D.,
Emmanuel Boleslawski, M.D., Ph.D., Valerio Lucidi, M.D., Thierry Gustot, M.D., Ph.D.,
Claire Francoz, M.D., Christian Letoublon, M.D., Denis Castaing, M.D.,
Jacques Belghiti, M.D., Vincent Donckier, M.D., Ph.D.,
François-René Pruvot, M.D., and Jean-Charles Duclos-Vallée, M.D., Ph.D.

N ENGL J MED 365;19 NEJM.ORG NOVEMBER 10, 2011

Potilaat

26 potilasta, 7 keskusta, 8/06-6/10

ei vastetta konservatiiviselle hoidolle

median MELD score 34 Tx päätöksen yhteydessä

Tx päätös median 13 vrk lääkeshoidon jälkeen

Tx median 9 vrk

Vaatimukset



EI AIEMPIA VIITTEITÄ
ALKOSAIRAUKSISTA



NOPEA MAKSAN
HUONONEMINEN
LÄÄKEHOIDOSTA
HUOLIMATTA



LÄHIOMAISTEN TUKI



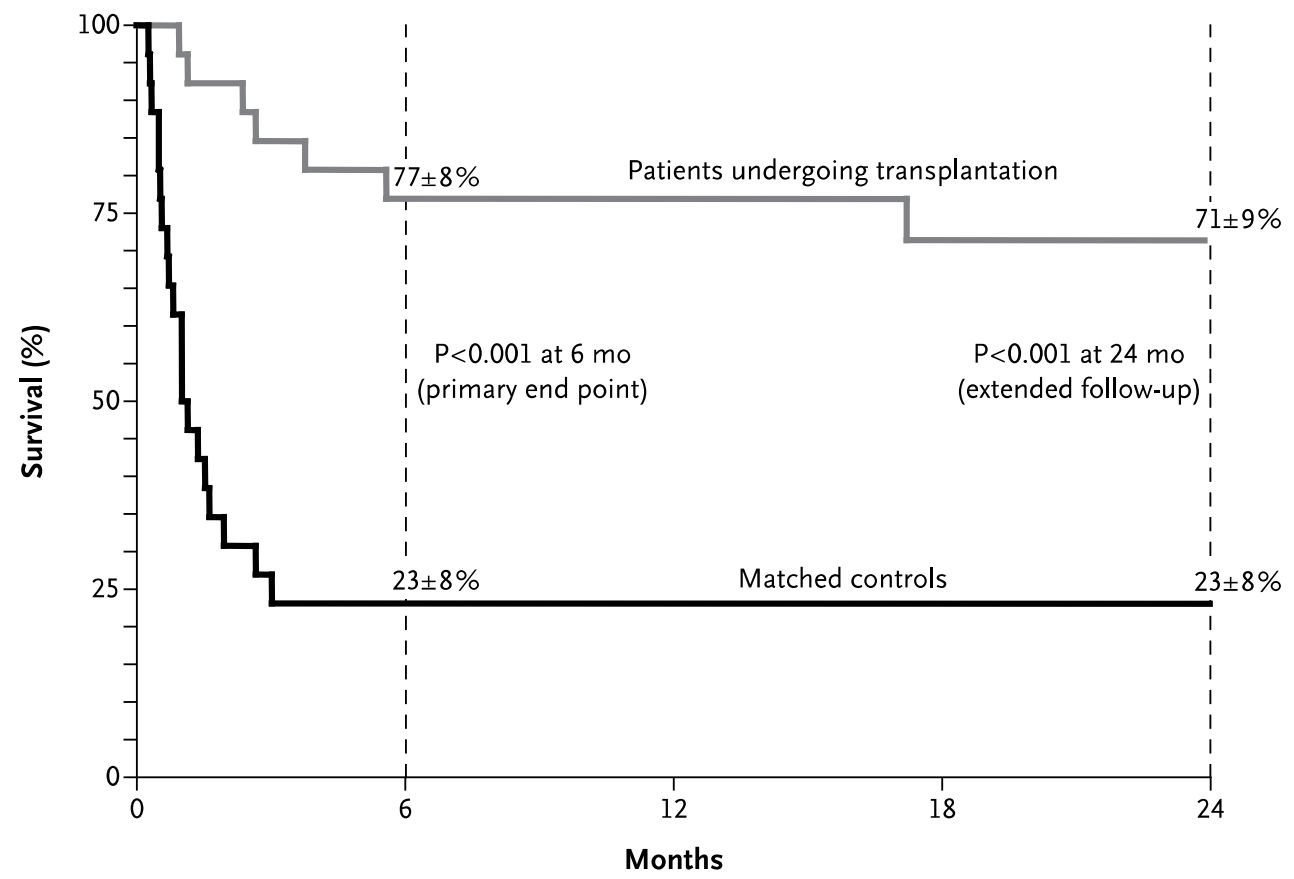
EI MUITA
SAIRAUKSIA



ABSTINENSSI-
LUPAUS

6 kuukauden eloonjäänti

- $77 \pm 8\%$ vs. $23 \pm 8\%$ controls, $p < 0.001$
- 90% kontrollien kuolemista tapahtui 2kk sisällä konservatiivisen hoidon epäonnistumisesta
- tx-kuolemat pääasiassa infektiopohjalta (5/6), invasiivinen aspergillus 4/6 potilaalla



No. at Risk		0	6	12	18	24
Patients undergoing transplantation	26	20	15	14	13	
Matched controls	26	6	6	5	4	

Figure 1. Kaplan–Meier Estimates of Survival in the 26 Study Patients and the 26 Best-Fit Matched Controls.

Alkon käyttö

- ei alkorelapseja 6kk seurannassa
- 3 myöhempää retkahdusta: 720d, 740d, 1140d
- 2 jatkoi päivittäistä käyttöä, 1 satunnainen käyttäjä
- retkahtaneilla ei seurannassa merkkejä siirteen huononemisesta (??)

CONCLUSIONS

Early liver transplantation can improve survival in patients with a first episode of severe alcoholic hepatitis not responding to medical therapy. (Funded by Société Nationale Française de Gastroentérologie.)

Transplantation for Alcoholic Hepatitis — Time to Rethink the 6-Month “Rule”

Robert S. Brown, Jr., M.D., M.P.H.

N ENGL J MED 365;19 NEJM.ORG NOVEMBER 10, 2011

Table 1. Prospective and retrospective studies of liver transplantation for alcoholic hepatitis

Study first author	Year published	Study design	Number with AH	Relapsers	Survival
Mathurin <i>et al.</i> [11]	2011	Prospective, multisite, AH with vs. without transplant	26	3/26 (11.5%)	6 month: 77 ± 8%
Singal <i>et al.</i> [12]	2012	Retrospective, multisite, AH vs. AC	46	Unknown	5 year: 75%
Im <i>et al.</i> [13 [■]]	2016	Prospective, single site, AH with vs. without transplant	9	1/8 (12.5%)	6 month: 89%
Cholankeril <i>et al.</i> [14 [■]]	2016	Retrospective, multisite, AH vs. other acute liver failure	97	Unknown	1 year: 82.5%
Lee <i>et al.</i> [15 [■]]	2017	Prospective, single site, AH vs. AC	17	4/17 (23.5%)	6 month: 100%

AC, alcoholic cirrhosis; AH, alcoholic hepatitis.

Schneekloth *et al.* *Curr Opin Organ Transpl* 2017

Table 2. Inclusion and exclusion criteria comparison in three prospective studies of liver transplantation for alcoholic hepatitis

Criteria	Mathurin <i>et al.</i> [11]	Im <i>et al.</i> [13 ²²]	Lee <i>et al.</i> [14 ²³]
Condition	AH with nonresponse to medical therapy	AH with nonresponse to medical therapy	AH with nonresponse to medical therapy
Coexisting disorders	Absence of severe coexisting or psychiatric disorders	Recent infection or GI bleeding did not preclude consideration	Free of severe comorbid disease; recent infection or GI bleed did not preclude consideration
Duration of liver disease	First liver-decompensating event	First liver-decompensating event	First liver decompensation
Support system	Presence of close supportive family members	Presence of good social support	Strong familial social support
Abstinence motivation	Agreement to lifelong total alcohol abstinence	Signed agreement to lifelong alcohol abstinence	Able to commit to lifelong alcohol abstinence
Relapse risk	Interviewers included a specialist in addictions	Favorable psychosocial profile suggesting a low risk of alcohol relapse	Rigorous assessment of risk factors for relapse by specialist
Levels of review	Four medical team circles of review: complete consensus	Consensus of institutional selection committee	Full consensus agreement by transplant committee
Percentage of patients with AH selected for transplant	Less than 2%	9.6%	2.3%

AH, alcoholic hepatitis; GI, gastrointestinal.

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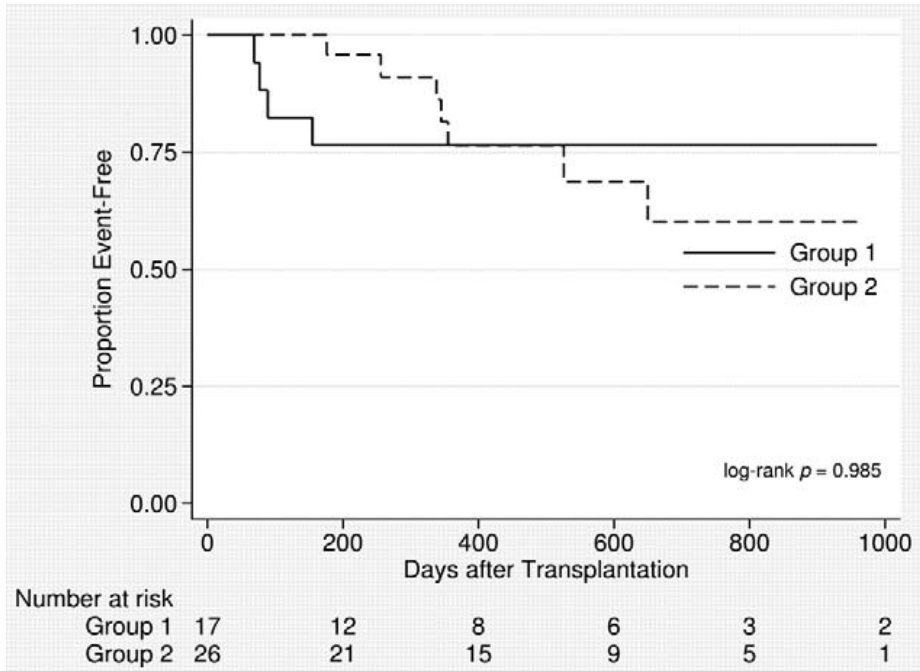
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Three-year Results of a Pilot Program in Early Liver Transplantation for Severe Alcoholic Hepatitis

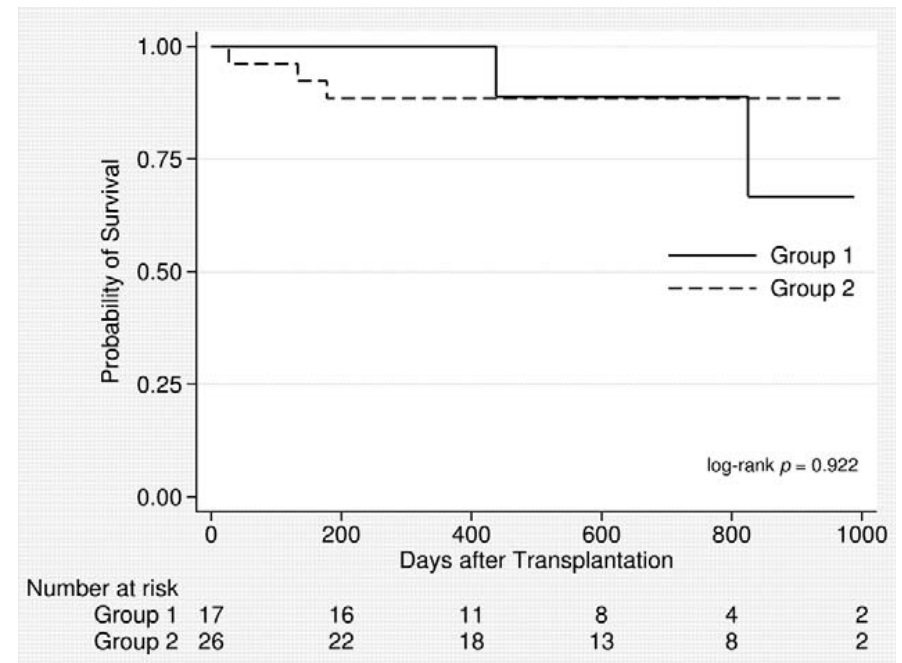
Brian P. Lee, MD, Po-Hung Chen, MD,* Christine Haugen, MD,† Ruben Hernaez, MD, PhD,*
Ahmet Gurakar, MD,* Benjamin Philosophe, MD, PhD,†
Nabil Dagher, MD,† Samantha A. Moore, BA,† Zhiping Li, MD,* and
Andrew M. Cameron, MD, PhD†*

Annals of Surgery • Volume 265, Number 1, January 2017

Group 1. Ac alc hep Group 2. Alci > 6mo abstinence



Abstinence



Survival

TABLE 4. Patient Outcomes

	Acute Alcoholic Hepatitis Group 1 (n = 17)	Alcoholic Cirrhosis, ≥6 Month Abstinence Group 2 (n = 26)	<i>P</i>
Follow-up –median (SD)	1.5 (0.86)	1.6 (0.86)	0.89
Posttransplant hospital stay – days – median (min-max)	18 (7–51)	12.5 (4–133)	0.38
6-Month survival – no. (%)	17 (100)	23 (88.5)	0.27
Any alcohol relapse – no. (%)	4 (23.5)	7 (29.2)*	>0.99
Alcohol relapse with harmful patterns – no. (%) [†]	4 (23.5)	3 (11.5)*	0.42

*Excluding two patients who died during the immediate postoperative period.

[†]Harmful patterns defined as presence of alcohol relapse with binge (6 units of alcohol for men, 4 units for women in a single day) or frequent patterns (any alcohol consumption on 4 days in 1 week).

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Conclusions: In this pilot with carefully selected patients, early liver transplant provided excellent short-term survival, and similar rates of alcohol relapse compared with patients with 6 months of abstinence. Harmful patterns of relapse remain challenging in this population, highlighting the need for validated models to predict alcohol relapse, and need for extreme caution in selecting patients for this exceptional indication. Larger prospective studies and longer follow up are necessary.

Outcomes of Early Liver Transplantation for Patients With Severe Alcoholic Hepatitis

Brian P. Lee¹, Neil Mehta¹, Laura Platt², Ahmet Gurakar², John P. Rice³, Michael R. Lucey³, Gene Y. Im⁴, George Therapondos⁵, Hyosun Han⁶, David W. Victor⁷, Oren K. Fix⁸, Lisanne Dinges⁸, Deepti Dronamraju⁹, Christine Hsu¹⁰, Michael D. Voigt¹¹, Mary E. Rinella¹², Haripriya Maddur¹², Sheila Eswaran¹³, Jessica Hause¹³, David Foley³, R. Mark Ghobrial⁷, Jennifer L. Dodge¹, Zhiping Li², and Norah A. Terrault¹

Published in final edited form as:

Gastroenterology. 2018 August ; 155(2): 422–430.e1.

American Consortium of Early Liver Transplantation for Alcoholic Hepatitis: ACCELERATE-AH

12 centers in 8 UNOS regions

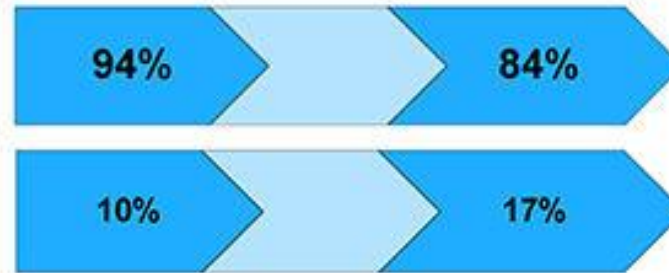
Early Transplant
= no specific sobriety
period (n=147)

Mortality without
transplant up to
70% at 6 months

→ Survival

→ Sustained
Alcohol Use
After
Transplant

Post-Transplant Outcomes
1 Year 3 Year



Gastroenterology

Gastroenterology. Author manuscript; available in PMC 2019 April 12.

Analytic Review

The Role of Liver Transplantation in Alcoholic Hepatitis

Michelle Ma, MD¹, Katie Falloon, MD², Po-Hung Chen, MD¹, Behnam Saberi, MD¹, Aliaksei Pustavoitau, MD³, Elif Ozdogan¹, Zhiping Li, MD¹, Benjamin Philosophe, MD⁴, Andrew M. Cameron, MD⁴, and Ahmet Gurakar, MD¹

Journal of Intensive Care Medicine
2019, Vol. 34(4) 277-291

^a The Author(s) 2018

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DOI: 10.1177/0885066618780339

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Table 2. Risk Factors and Protective Factors for Alcohol Relapse After Liver Transplantation in Patients With Alcoholic Liver Disease.^{35,129-132}

Risk Factors for Alcohol Relapse	Protective Factors Against Alcohol Relapse
Shorter pretransplant abstinence Younger age at time of LT Lack of social support Family history of alcohol abuse Comorbid psychiatric condition Prior nonadherence to treatment Tobacco use	Longer pretransplant abstinence Older age at time of LT Presence of cohabitating partner or marriage

strategies for severe AH. The limited supply of available organs necessitates a need for careful selection of candidates, but the exact optimal criteria have yet to be fully elucidated. Alcohol relapse also remains a major challenge; therefore, resources dedicated to early detection and intervention are critical in the posttransplant follow-up period.

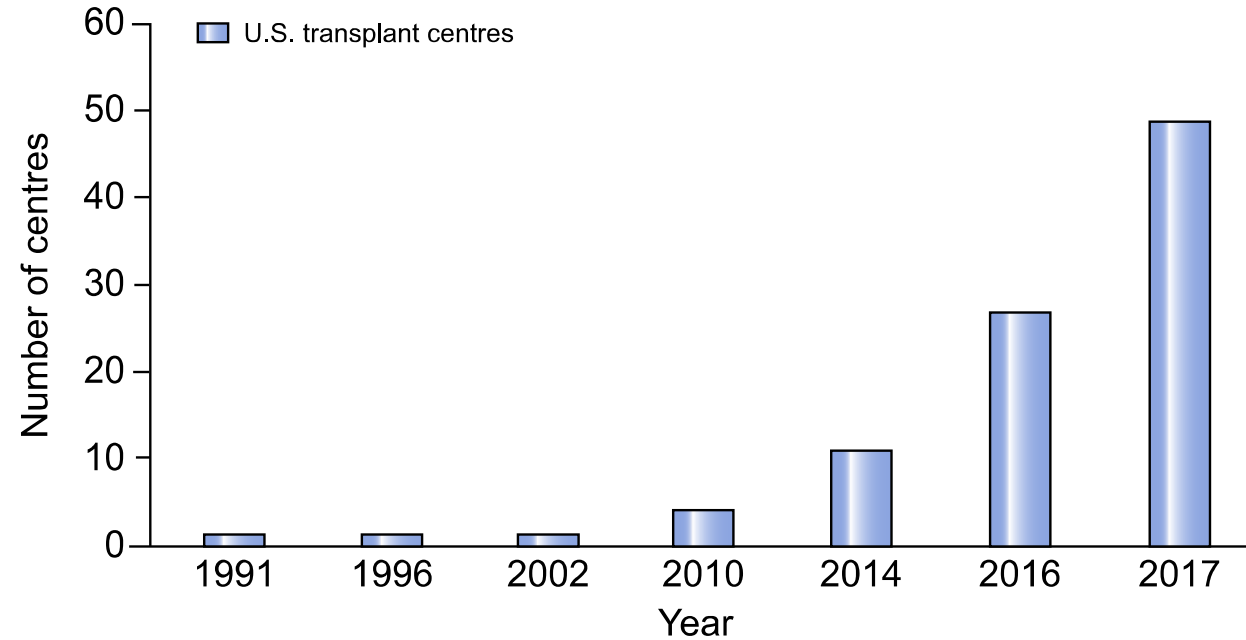


Fig. 1. Centres having performed liver transplantation for alcoholic hepatitis in the United States over time. Data based on references^{2,14-15,26-28,48} and unpublished data.

Impact of a First Study of Early Transplantation in Acute Alcoholic Hepatitis: Results of a Nationwide Survey in French Liver Transplantation Programs

ANTONINI ET AL. LIVER TRANSPLANTATION, June 2018

TABLE 1. Survey Items and Results

	Yes	No
Regarding AAH, were there any changes to its management after 2011?	88%	12%
Since 2011, have you considered AAH to be a potential indication for LT?	97%	3%
Regarding AAH, have there been any changes to the management of LT for alcoholic cirrhosis since 2011?	88%	12%
Did you perform LT for AAH in your center before 2011?	35%	65%
Have you performed LT for AAH in your center since 2011?	71%	29%
Are alcoholic patients with cirrhosis systematically evaluated by an addiction specialist during the pretransplant workup (before and after 2011)?	76%/100%	24%/0%

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	Yes	No
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Did you perform LT for AAH in your center before 2011?	35%	65%
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Are alcoholic patients with cirrhosis systematically evaluated by an addiction specialist during the pretransplant workup (before and after 2011)?	76%/100%	24%/0%

*Pitäisikö hoitokäytäntöjä
muuttaa Suomessa???*