Alcol e Trapianto

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UO Alcologia e Patologie Correlate

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per la Ricerca sul Cancro, Genova

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

Direzione centrale salute e protezione sociale

Le Regioni e le Provincie Autonome si interrogano sui Problemi Alcol Correlati Trieste, Ottobre 2012

Alcol e Trapianto

OBIETTIVI

Necessita' in tutte le Regioni di UO di Alcologia territoriali (autonome?) nell'ambito dell'attivita' multidisciplinare trapiantologica (raggiungimento astensione-sobrieta' e follow-up dell'astensione)

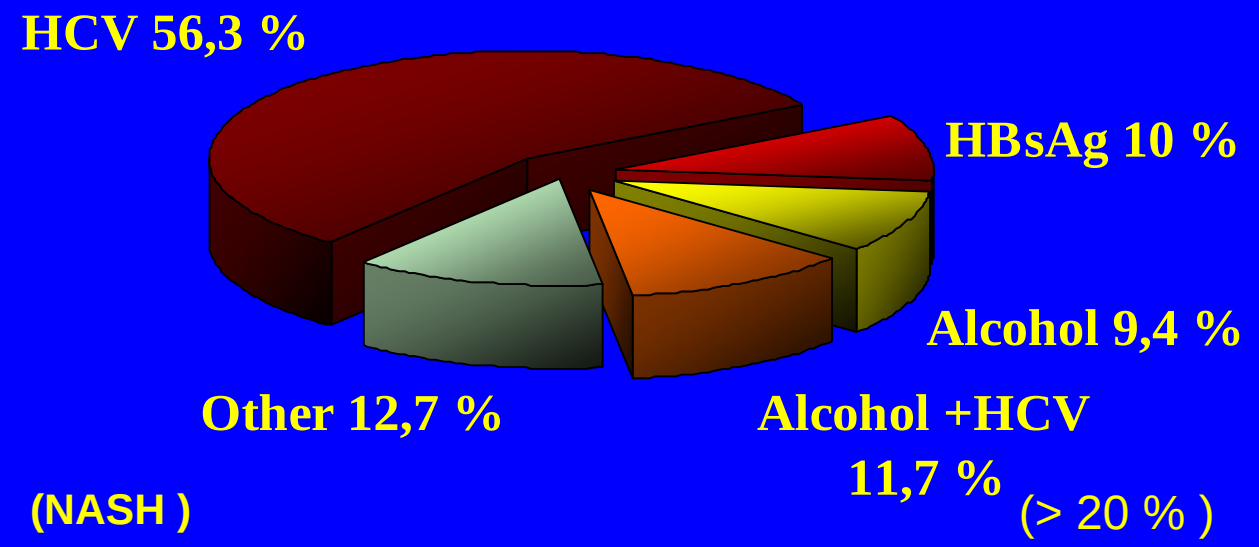
Necessita' a livello Ospedaliero di una UO Alcologia (regionale) per le competenze epato-alcologiche (per ragioni epidemiologiche necessaria la figura dell'epato-alcologo)

Inserimento nel percorso assistenziale delle Associazioni di Auto-Mutuo Aiuto

Attivita' Interdisciplinare ospedale-territorio con pieno coinvolgimento della famiglia, della comunita' di appartenenza e delle Associazioni di auto-mutuo-aiuto (pre-post),

Rivalutazione del timing trapiantologico e rivalutazione dei fattori di rischio di «ricaduta» post-trapianto

CHRONIC LIVER DISEASE



Sagnelli E. et al. J Med Virol 2005

Epatopatia Alcol Correlata

44% di tutti i decessi per cirrosi e' alcol correlata

O'Shea et al,Hepatology 2010; 51:308-328

Associazione Alcol/HCV nel 30% dei casi (Testino G et al, 2008)

RAPPORTO 2013 ISS – Osservatorio Nazionale Alcol-CNESPS
RELAZIONE MINISTRO DELLA SALUTE AL PARLAMENTO – Dicembre 2012

113 ricoveri ogni 100000 ab. (50% epatopatia, 39% cirrosi)

Mortalita' per cirrosi epatica importante indicatore di danno alcol correlato

Attribuibili all'uso dannoso di alcol il 59.3% dei decessi per cirrosi tra i maschi e il 48.7% tra le donne
Valore massimo fra i 45-64 anni di entrambi i sessi

APPROPRIATEZZA DELLA DIAGNOSI DI DIPENDENZA ALCOLICA

25% : consumo rischioso-dannoso, presenza di cofattori!!!!!!!!

Lucey, Merion, Beresford 1994

P. Burra, 2007; XX Congresso Societa' Italiana di Alcologia

gr/die ⟶

12-20 women, 25-80 men

O'Shea, 2010

Daily Alcohol Intake > 30 g/day

Odds of developing cirrhosis or lesser degrees of liver disease

cirrhosis: 13.7; lesser degrees: 23.6

Bellentani et al, 1997

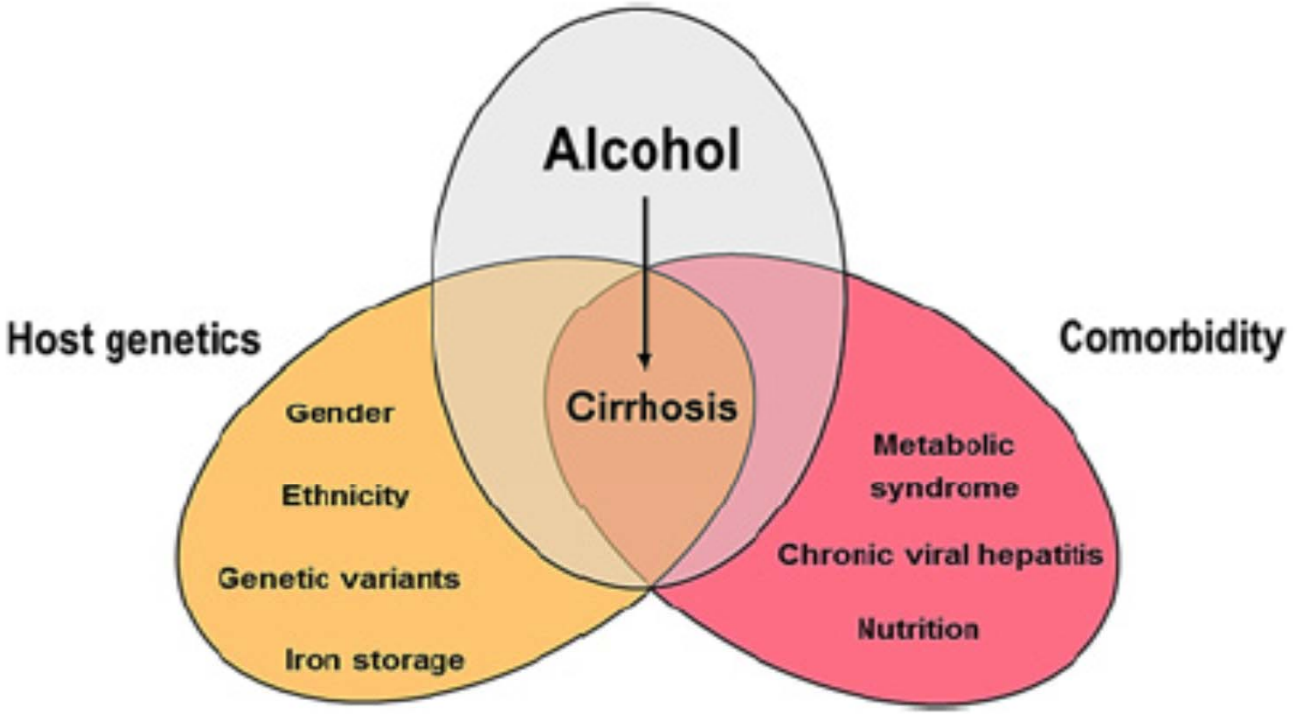


Figure 1 Schematic account of factors of progression in alcoholic liver disease showing the multifactorial pathogenesis of the disease.

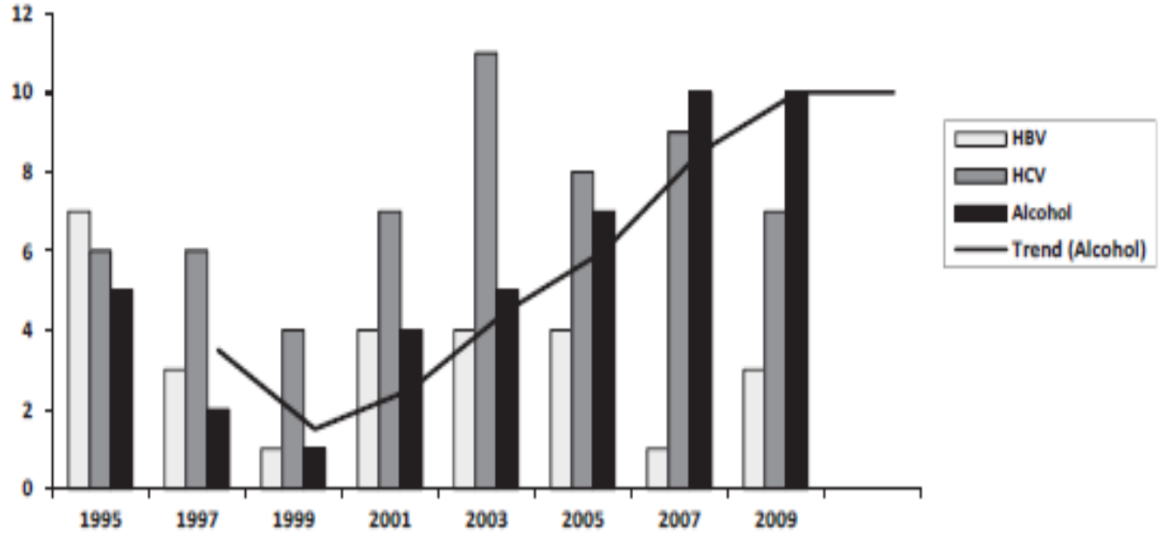
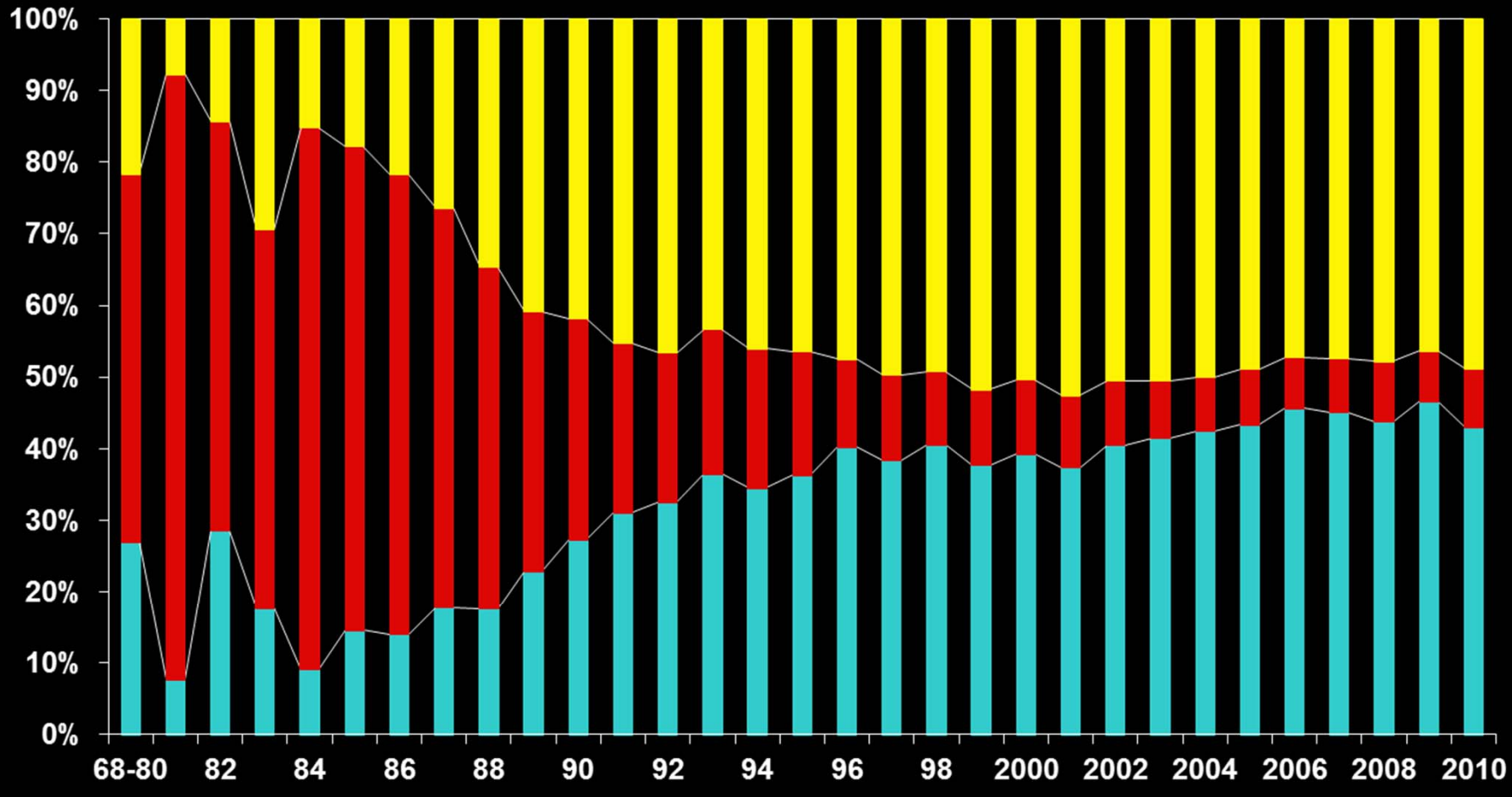
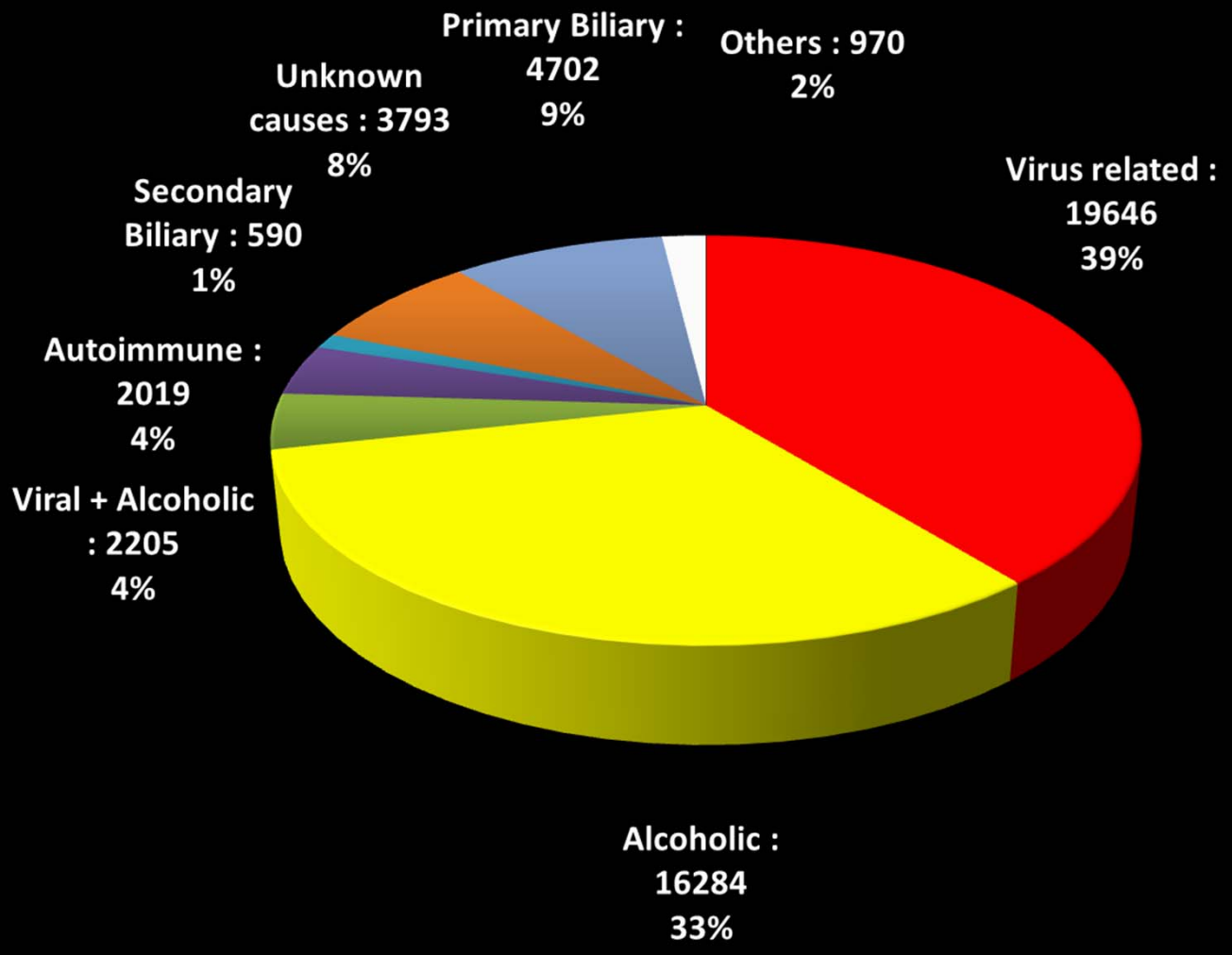


Fig. 1. Number of patients, divided by etiologies, who underwent liver transplantation between 1995 and 2009. Trend of transplantation for alcoholic cirrhosis. HBV, hepatitis B virus; HCV, hepatitis C virus.

Evolution of Indications for Cirrhosis in Europe



Liver Transplantation in Europe
Indications of Cirrhosis
01/1988 - 12/2010



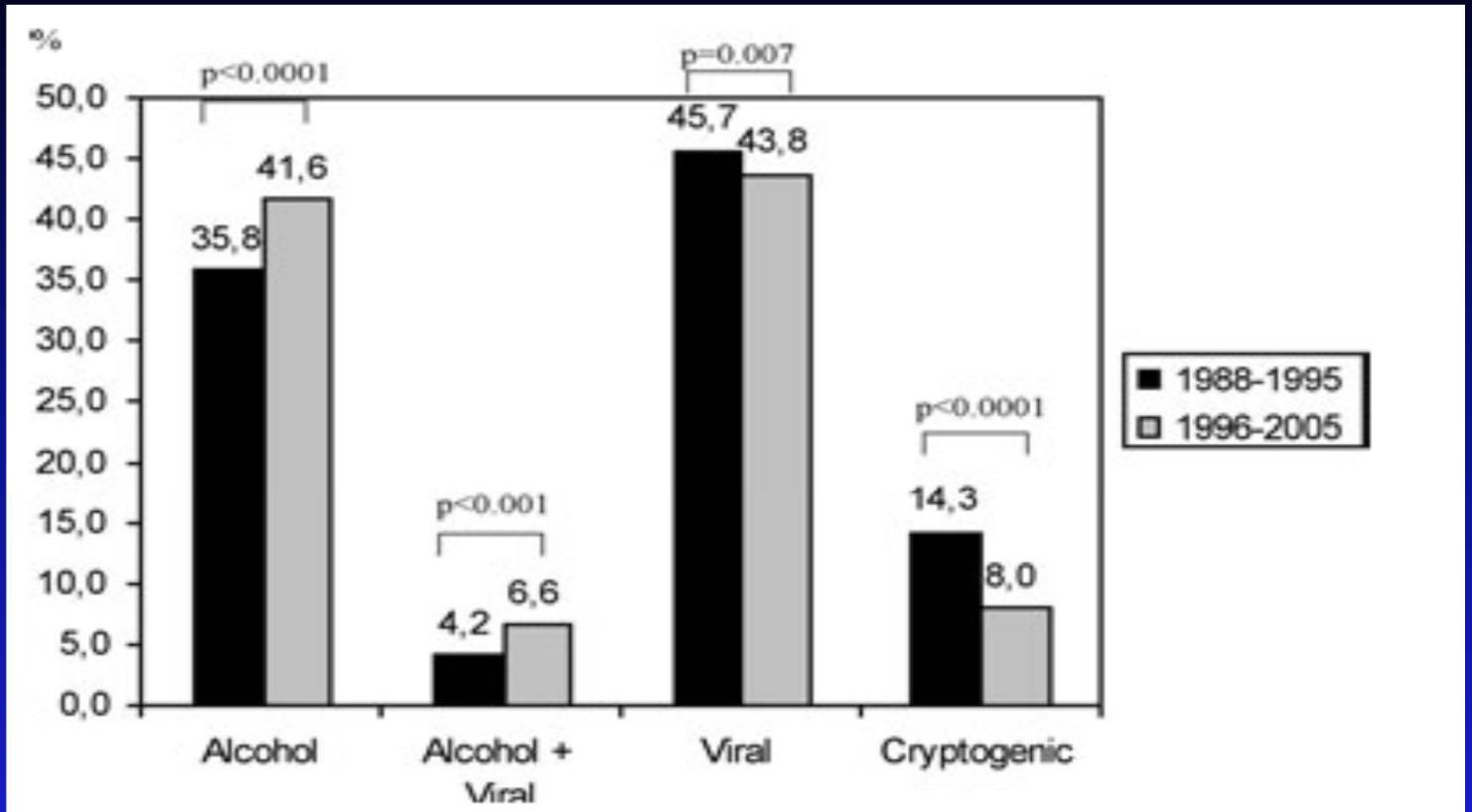


Figure 1: ELTR Indication to liver transplantation in periods 1988–1995 and 1996–2005.

Burra P et al, Am J Transpl 2010

TRAPIANTO DI FEGATO PER EPATOPATIA ALCOL-CORRELATA

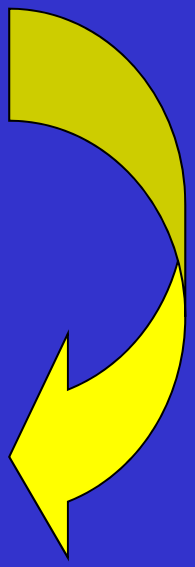
Fattori di rischio rispetto ad epatopatie ad altra eziologia

- Comorbidità (neoplasie, cardiopatia, neuropatia, nefropatia, pancreatite, …)
- Astinenza (regola dei 6 mesi)

P. Burra, XX Congresso Societa' Italiana di Alcologia; 2007

PROBLEMI ETICI
TRAPIANTO DI FEGATO e ALCOL

- **Patologia “auto-inflitta”**
- **Opinione pubblica**
- **Difficoltà nel definire criteri predittivi di recidiva**
  - **» Rischio di scarsa “compliance”**



CARENZA DI DONATORI D’ORGANO

STUDIO HONG KONG

281 intervistati sulla utilità del Trapianto di Fegato

75%

per chi affetto da **malattia naturale**

ma non per chi presenta **malattia epatica autoinflitta**

Chang, Hong Kong Medical Journal 2006

Assessing priorities for allocation of donor liver grafts: survey of public and clinicians

,

Opinione:

- Il 17% di 1.000 persone intervistate tra la popolazione generale
- Il 40% di 200 medici di Medicina Generale
- Il 33% di 100 medici Specialisti in Gastroenterologia

riteneva che

"Il paziente con malattia epatica alcol correlata
e' il candidato meno meritevole per il trapianto di fegato"

Neuberger J Br Med J 1998

Liver Transplant : HCV + vs HCV -

Table 4. Patient Survival of HCV-Positive vs. Subgroups of HCV-Negative Recipients

Group	1 year (95% CI)	3 year (95% CI)	5 year (95% CI)
HCV+	86.4% (85.3–87.5)	77.8% (76.3–79.2)	69.9% (67.3–72.3)
HCV−	87.5% (86.7–88.3)	81.8% (80.7–92.8)	76.6% (74.9–78.2)
Cholestatic[a,b]	91.5% (89.3–93.2)	88.6% (86.0–90.7)	86.1% (82.6–88.9)
Metabolic[a]	86.5% (82.3–89.8)	83.3% (78.5–87.1)	82.4% (77.1–86.5)
HBV	87.4% (83.8–90.2)	79.5% (74.7–83.5)	78.6% (73.5–82.9)
AIH	84.7% (81.2–87.7)	82.2% (78.4–85.5)	76.8% (70.5–81.9)
Cryptogenic	86.3% (84.1–88.2)	80.9% (78.3–83.3)	73.0% (68.2–77.1)
ETOH	86.7% (84.8–88.3)	78.1% (75.6–80.4)	72.0% (68.1–75.5)
HCV+	86.4% (85.3–87.5)	77.8% (76.3–79.2)	69.9% (67.3–72.3)
Malignancy[a]	82.5% (75.9–87.5)	64.1% (54.7–72.0)	51.8% (34.6–66.5)

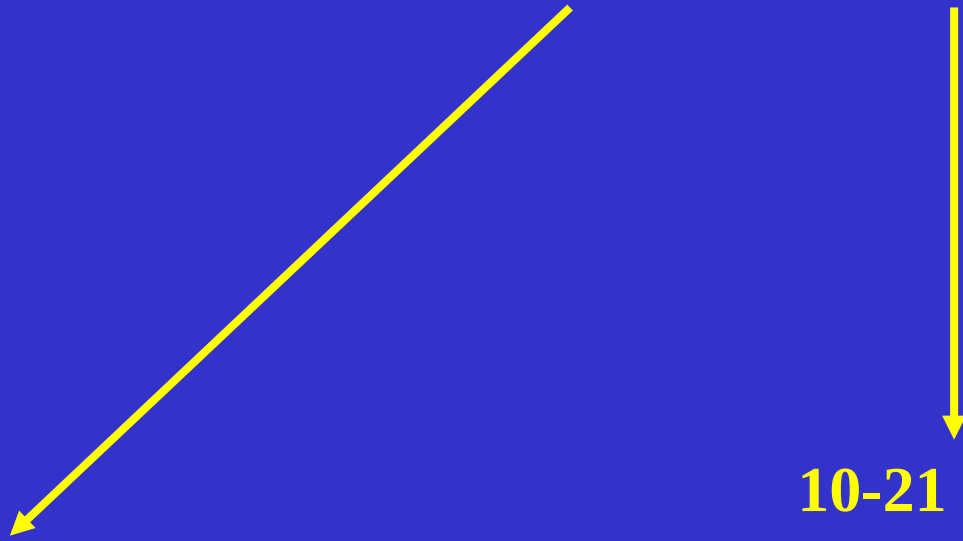
CI, confidence interval; HBV, hepatitis B virus; AIH, autoimmune hepatitis.

[a]$p < 0.05$. This is based on a proportional-hazards model, using all available follow-up time, comparing each of the subgroups to the HCV-positive group.

[b]Cholestatics refers to patients with either primary sclerosing cholangitis or primary biliary cirrhosis.

L Forman Gastroentererology 2002

HCV induced allograft hepatitis and fibrosis/cirrhosis



10-21 % a 5 years dal tx

75-80 % a 5 years tx

L Forman Gastroentererology 2002

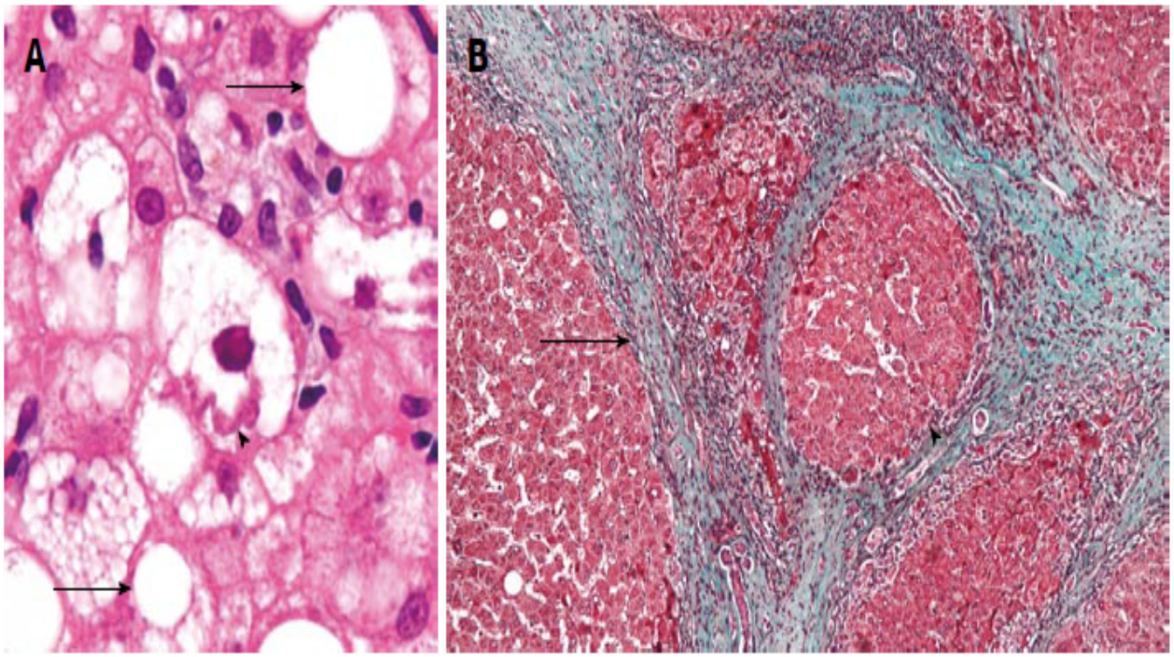


Figure 1 Photomicrograph. A: Photomicrograph showing a Mallory body (arrowhead), with twisted rope-like appearance, and fat vacuoles (arrows) as seen in alcoholic steatohepatitis (image from http://en.wikipedia.org/wiki/Alcoholic_hepatitis, licensed under Creative Commons Attribution-Share Alike 3.0 Unported); B: Photomicrograph showing a regenerating nodule (arrowhead) and bridging fibrosis (arrow) as seen in alcoholic cirrhosis (image from http://en.wikipedia.org/wiki/Alcoholic_cirrhosis, licensed under Creative Commons Attribution-Share Alike 3.0 Unported).

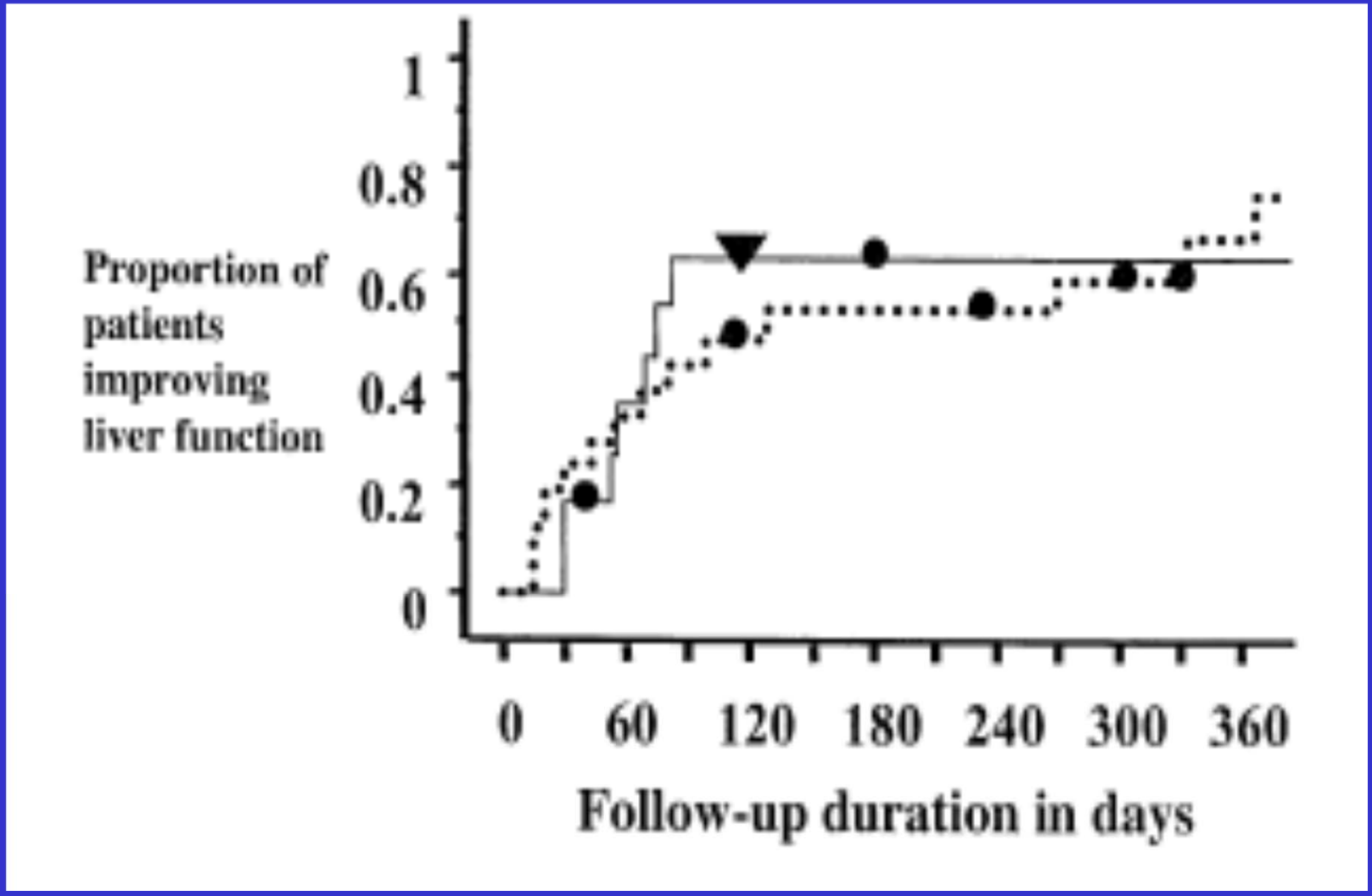
Jaurigue et al, WJG 2014

COMPLICATIONS OF CIRRHOSIS

- ASCITES
- DILUTIONAL HYPONATREMIA
- HEPATORENAL SYNDROME
- BACTERIAL INFECTION
- SPONTANEOUS BACTERIAL PERITONITIS
- HEPATIC ENCEPHALOPATY
- VARICEAL BLEEDING
- PORTOPULMONARY HYPERTENSION
- HEPATOPULMONARY SYNDROME
- HEPATOCELLULAR CARCINOMA

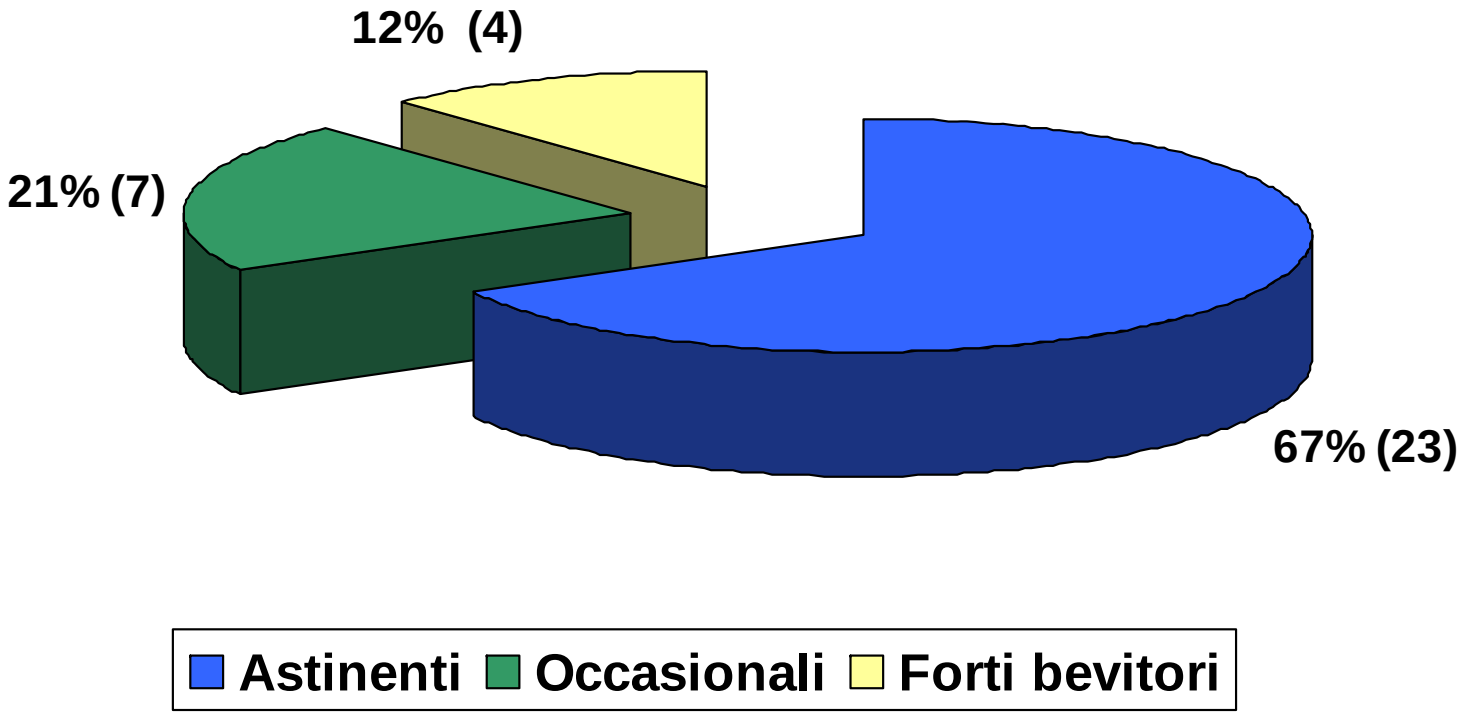
Testino G, 2008

Improving liver function



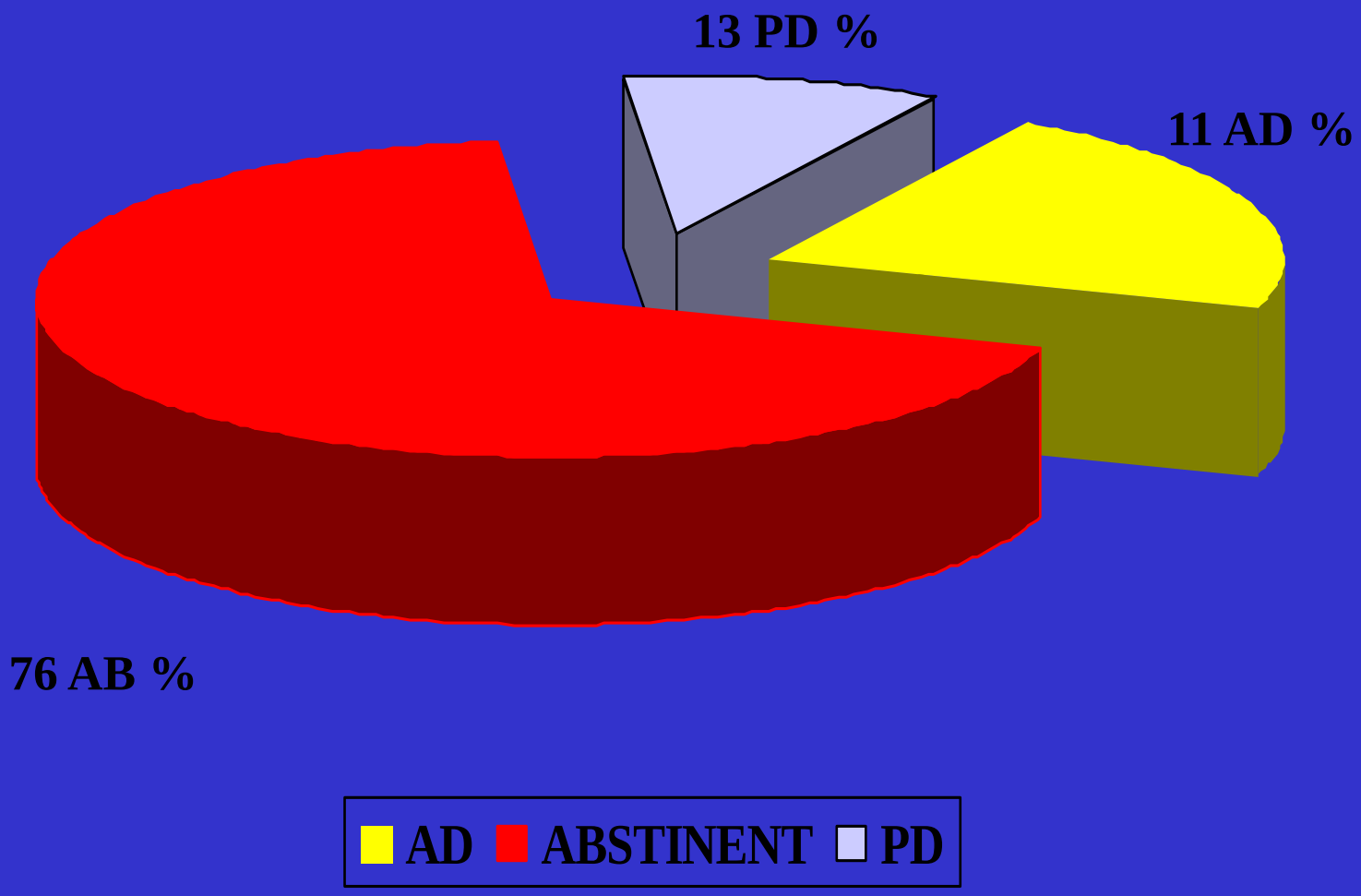
B. J. Veldt. Journal of Hepatology 2002

RECIDIVA DI CONSUMO ALCOLICO DOPO TRAPIANTO DI FEGATO



Burra Transpl Int 2000; 13(1): 174-178

RECIDIVA CONSUMO ALCOLICO

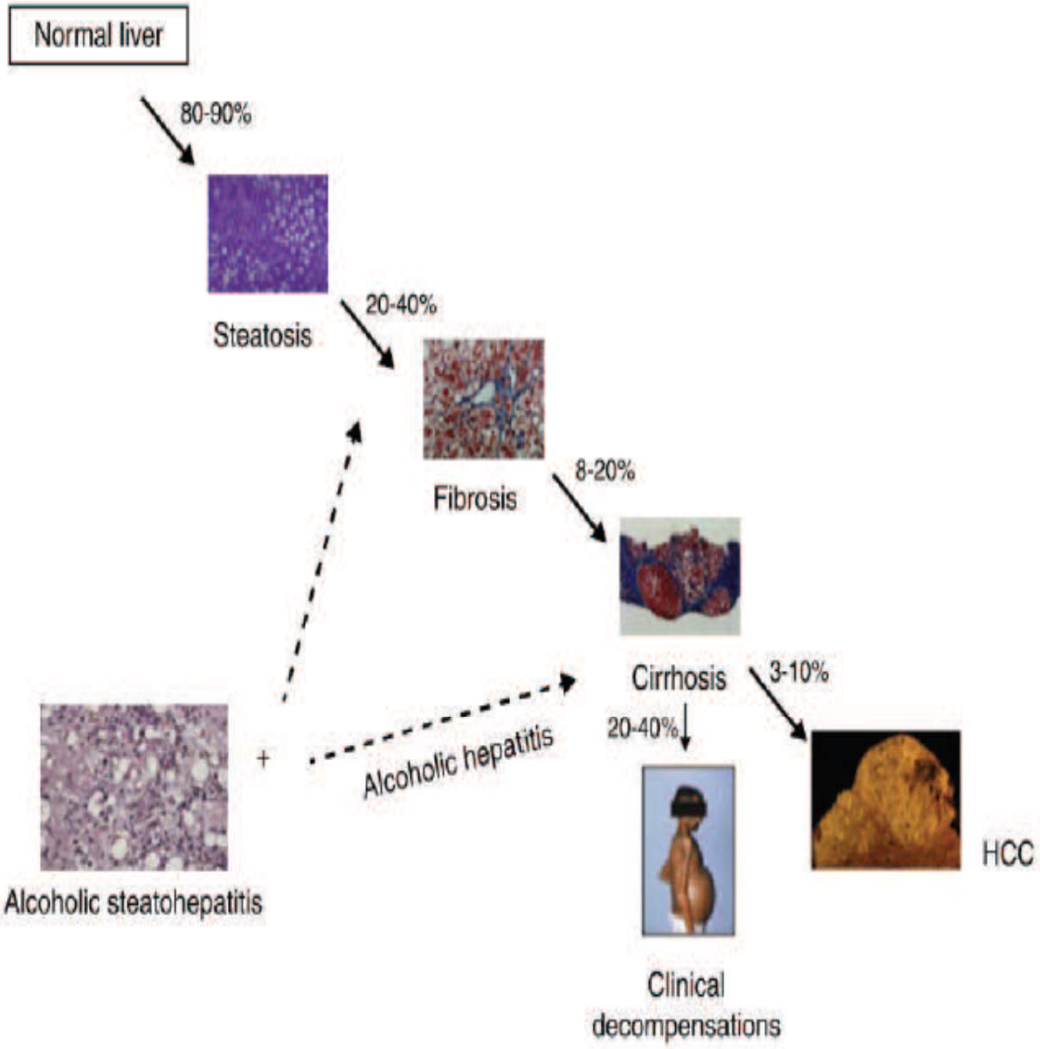


Tandon P. Am J Gastroent 2009

Analisi fattori predittivi di recidiva di consumo alcolico dopo trapianto di fegato per patologia epatica alcol-correlata

Authors	Type of study	Patients (N)	Duration of study	Relapse rate	Factors associated with relapse
Berlakovich et al. [9]	retrospective	58	33 months	31%	none
Osario et al. [10]	retrospective	43	21 months	19%	Abstinence < 6 months
Lucey et al. [11]	retrospective	59	63 months	34%	None
Foster et al. [12]	retrospective	63	49.3 months	21%	Associated drug use, drunken driving, club member, life insurance policy, number of alcohoic sisters
Tang et al. [13]	retrospective	56	24 months	48%	None
Pageaux et al. [14]	retrospective	53	42 months	32%	Abstinence < 6 months, age
Conjeevaram et al. [15]	retrospective	68	42 months	—	Histological signs of alcoholic hepatitis on explant
Platz et al. [16]	retrospective	167	ND	26%	Abstinence < 6 months, female, unstable personality, unfavorable environment
Burra et al. [17]	prospective	51	40 months	33%	Patient and/or family awareness of alcoholism
Pereira et al. [18]	retrospective	47	ND	50%	Age at onset of regular consumption, age at onset of excessive intake, duration of abstinence before transplantation
Gisch et al. [19]	prospective	61	62.5 months	20%	Personality disorder, lack of compliance
Bellamy et al. [20]	retrospective	123	7 years	13%	Duration x quantity of alcohol

Miguet, Gastroenterol Clin Biol 2004



Casanova and Bataller; Gastroenterol Hepatol 2014

EPATITE ALCOLICA ACUTA

La manifestazione clinica copre un largo spettro di segni e sintomi che vanno dall'ittero asintomatico a forme piu' severe caratterizzate dalla combinazione di encefalopatia, febbre, astenia, coagulopatia, leucocitosi

Wells JT, Liver Transplantation 2007

Mortalita' a 30 giorni: 35-40% dei casi; a 6 mesi: 70% dei casi

Day CP, Liver Transplantation 2007; Burroughs AK, Int Hepatol 2012

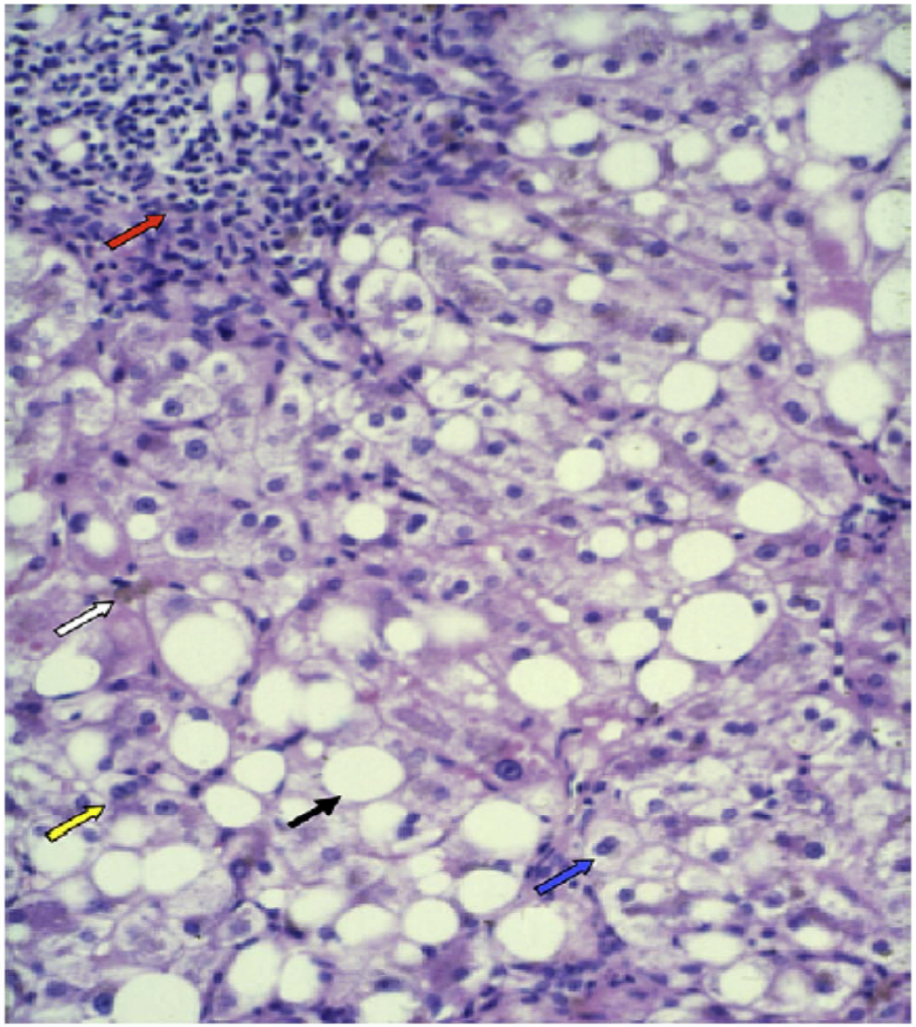


Fig. 1. Histology of ASH (magnification 40×). Typical features include steatosis (black arrow), cholestasis (white arrow), periportal, lymphocytic infiltrates (red arrow), ballooned hepatocytes, and neutrophilic infiltrates (yellow arrow). Although not mandatory for definite diagnosis, histology may help to confirm suspected ASH, and excluded other etiologies.

Stickel and Seitz, Best Practice Research Clinical Gastroenterology 2010

COMPLICATIONS OF CIRRHOSIS

- ASCITES
- DILUTIONAL HYPONATREMIA
- HEPATORENAL SYNDROME
- BACTERIAL INFECTION
- SPONTANEOUS BACTERIAL PERITONITIS
- HEPATIC ENCEPHALOPATY
- VARICEAL BLEEDING
- PORTOPULMONARY HYPERTENSION
- HEPATOPULMONARY SYNDROME
- HEPATOCELLULAR CARCINOMA

Testino G, 2008

COMPONENTS OF SCORING SYSTEMS USED TO ASSES PROGNOSIS IN ALCOHOLIC HEPATITIS

	Poor Prognosis
Maddrey ' s Discriminant Function	> 32
MELD SCORE (Model for End Stage Liver Disease)	> 18
GLASGOW SCORE	> 8
LILLE SCORE	> 0.45

MR Lucey et al,N Engl J Med 2009

AASLD , Hepatology 2010

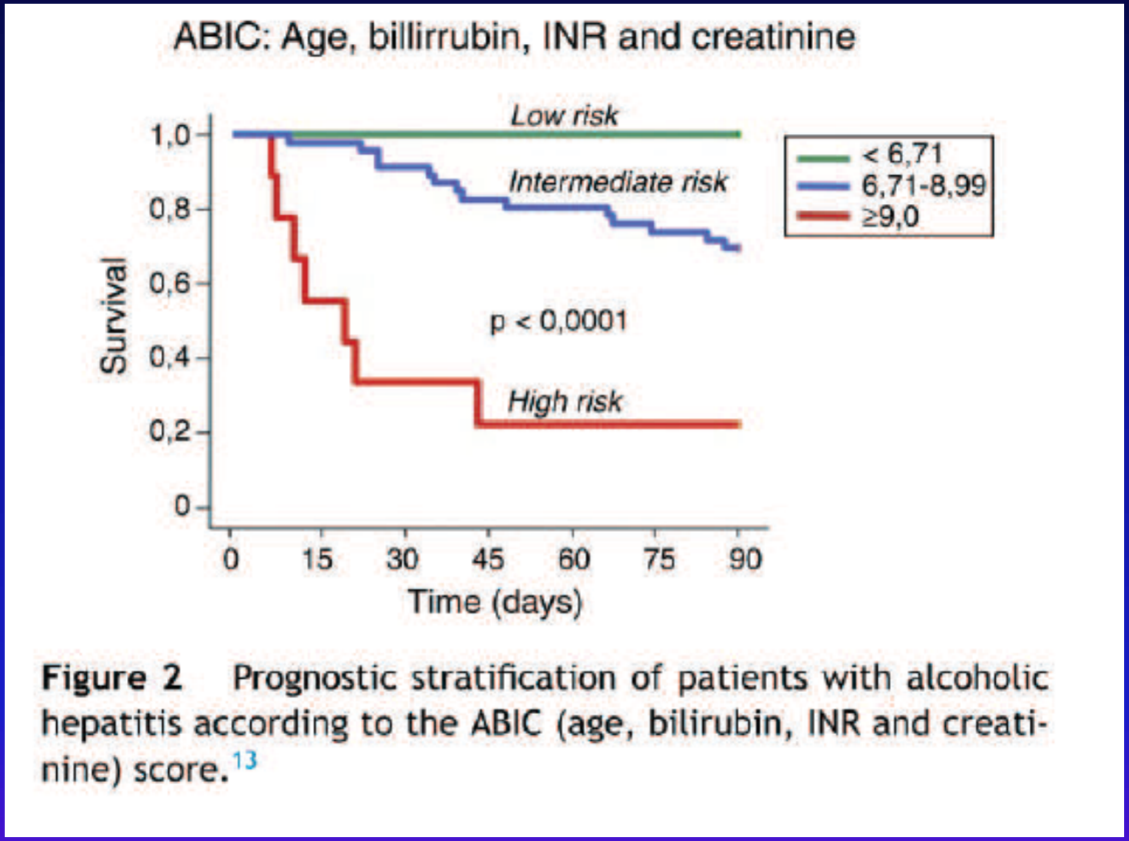


Figure 2 Prognostic stratification of patients with alcoholic hepatitis according to the ABIC (age, bilirubin, INR and creatinine) score.[13]

Dominguez et al; Am J Gastroenterol 2008

Casanova and Bataller; GastroenterolHepatol 2014

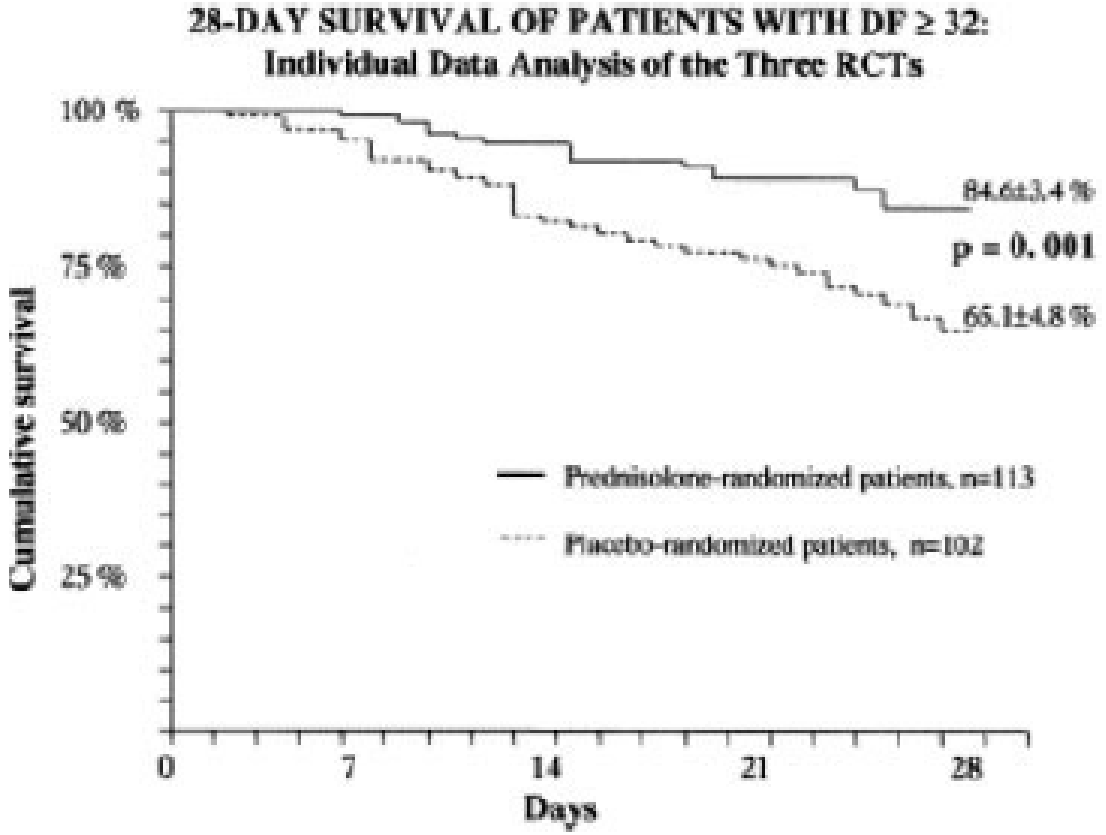


Figure 3. Twenty-eight-day survival in patients with discriminant function >32 treated with corticosteroids or placebo. From Mathurin P, Mendenhall CL, Carithers RL Jr, Raymond MJ, Maddrey WC, Garstide P, et al. Corticosteroids improve short-term survival in patients with severe alcoholic hepatitis AH: Individual data analysis of the last three randomized placebo controlled double blind trials of corticosteroids in severe AH. J Hepatol 2002;36:480-487.

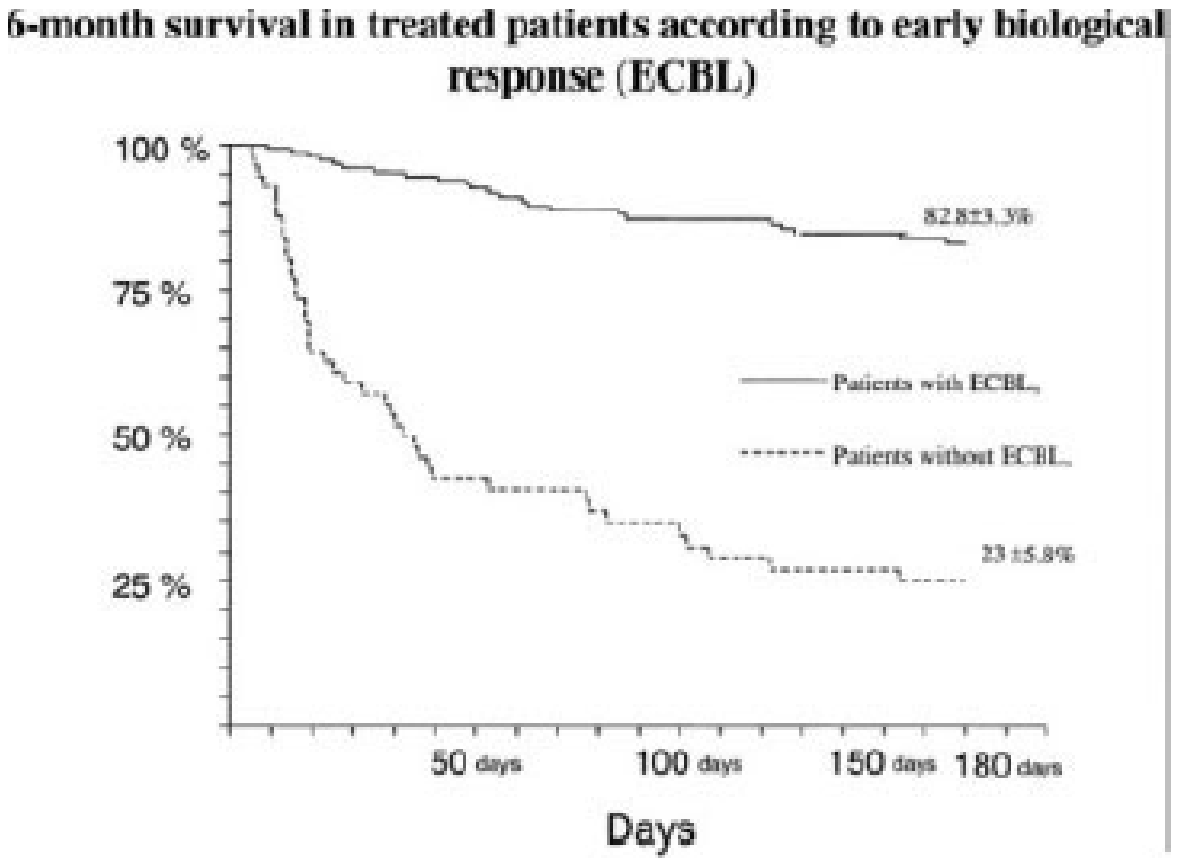
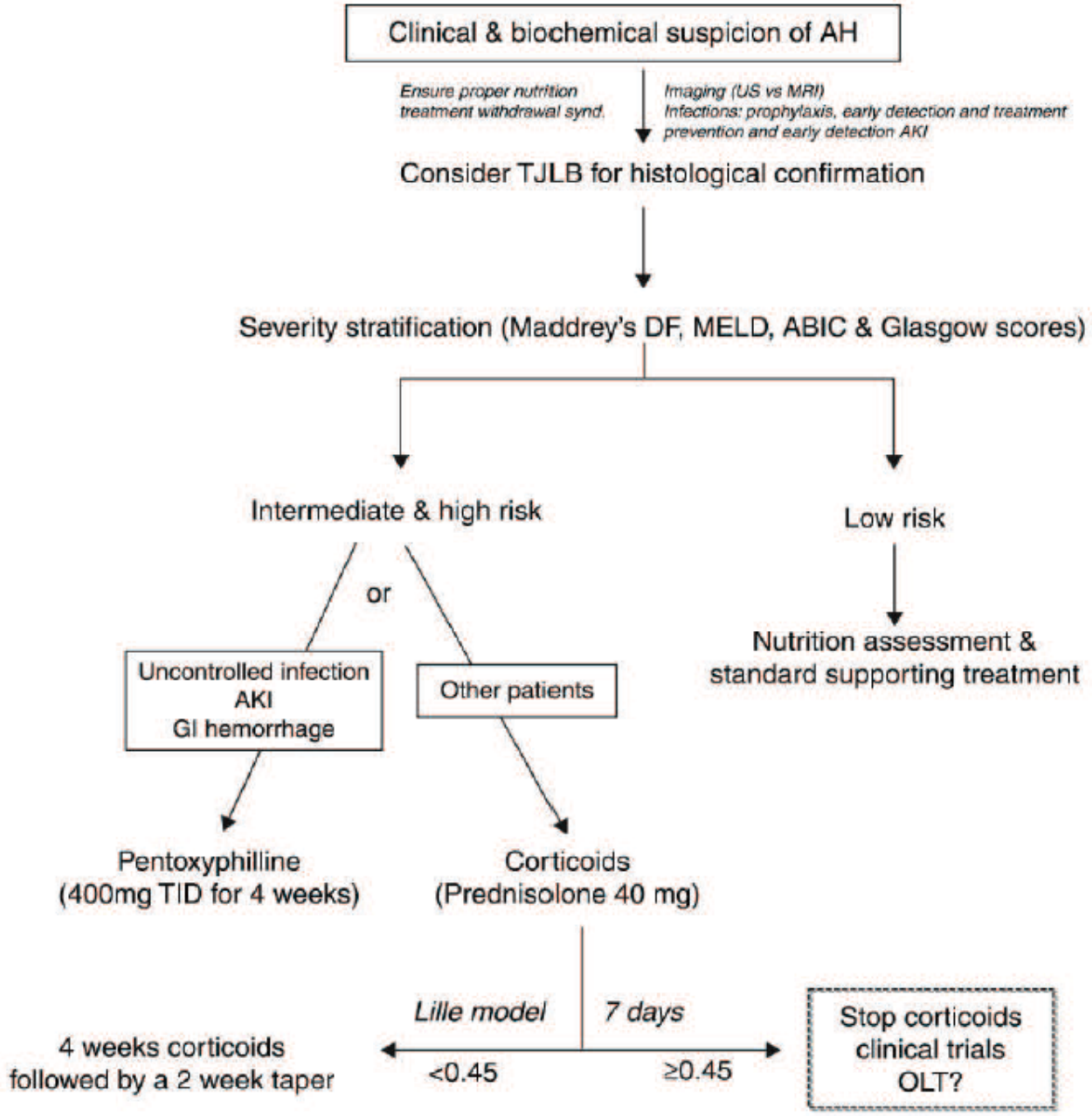


Figure 4. Six-month survival in patients treated with corticosteroids according to early biological response (ECBL). From Mathurin P, Abdelnour M, Ramond MJ, Carbonell N, Fartoux L, Serfaty L, et al. Early change in bilirubin levels is an important prognostic factor in severe alcoholic hepatitis treated with prednisolone. Hepatology 2003;38:1363-1369.



liver transplantation

Testino, Hepato-Gastroenterol 2008

Casanovaand Bataller, Gastroenterol Hepatol 2014

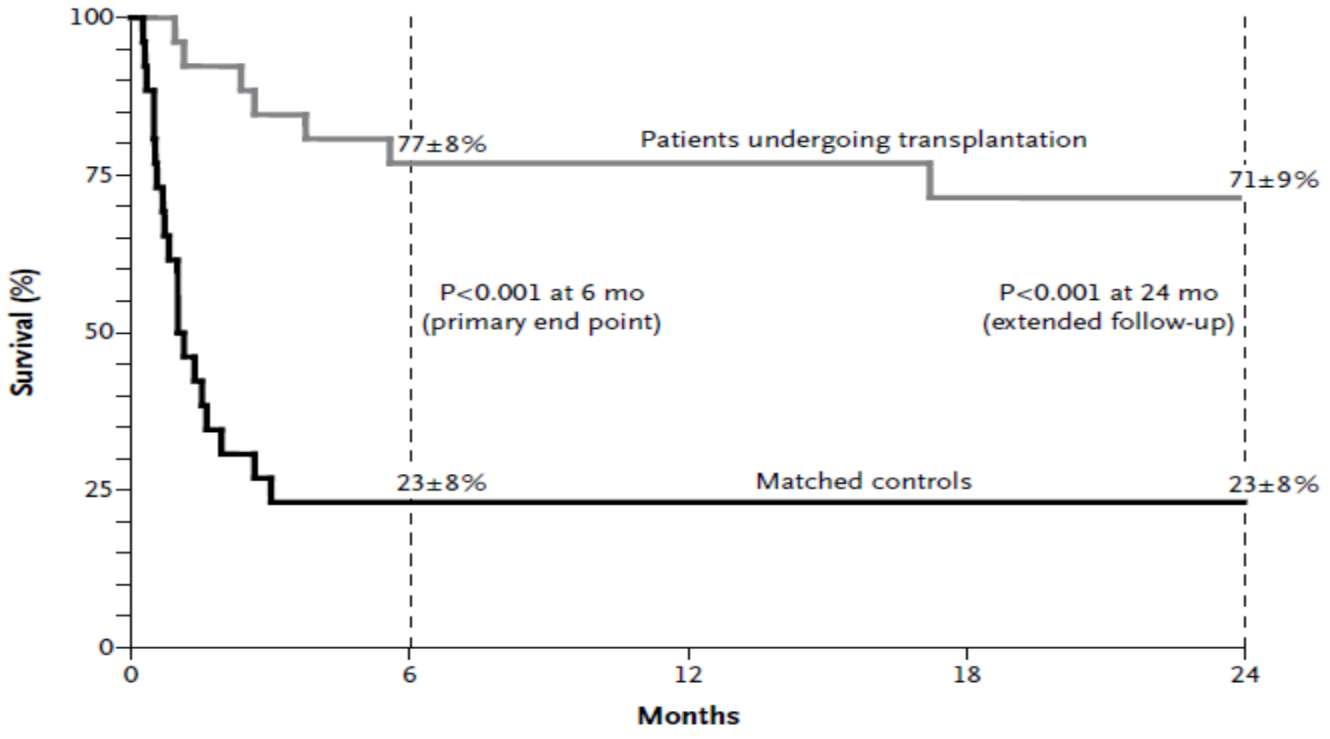
EARLY TRANSPLANTATION OF NON RESPONDERS TO STEROIDS IN SEVERE ALCOHOLIC HEPATITIS

6 – month survival was higher in the transplanted – non responders than in non transplanted –non responders controls :

83.3 +/- 8.7% vs 44.4 + /-11.7% p= 0.009

alcohol relapse: none was observed at 1 year, and only 1 relapsed at 917 days (3 units/week)

Shawcross and O' Grady, Lancet 2010



No. at Risk

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.

Mathurin et al, NEJM 2011

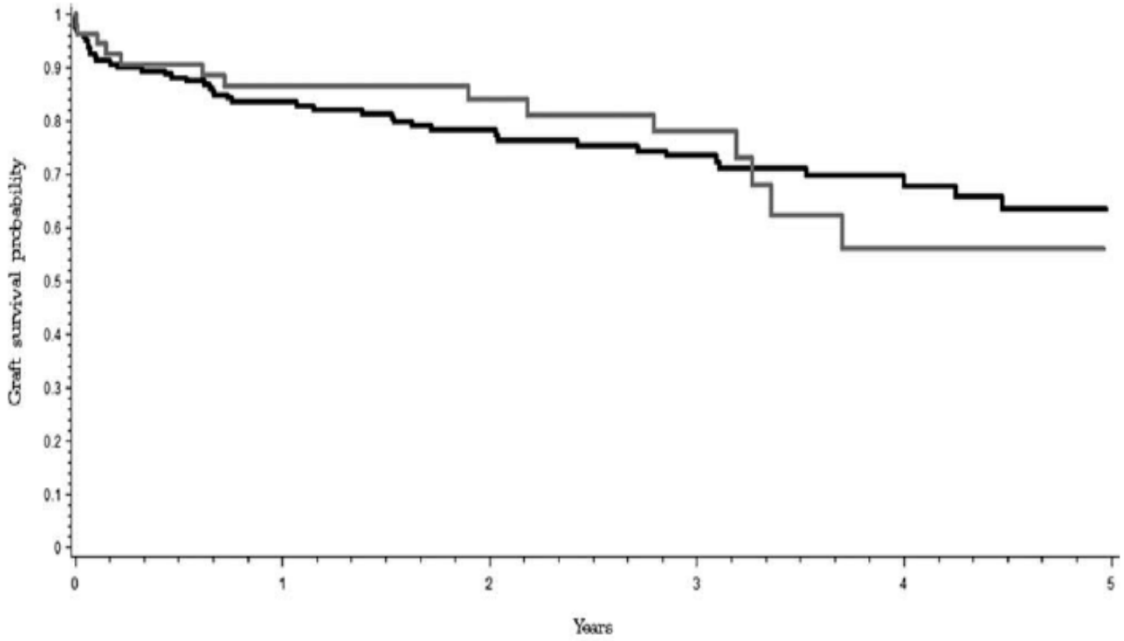
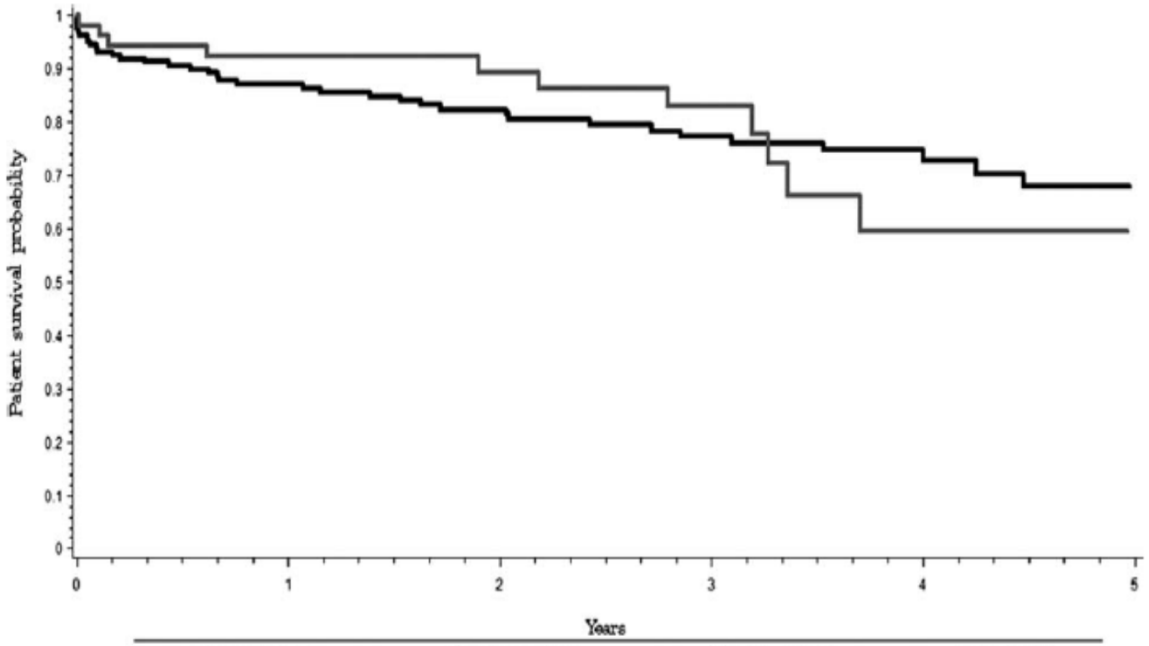


Fig. 2. Kaplan Meier survival curves comparing graft survival of patients transplanted for alcoholic hepatitis (gray line) and patients transplanted for alcoholic cirrhosis (black line). Results show similar graft survival between the two groups (Log rank $P = 0.97$).

Year of follow up	Alcoholic hepatitis	Alcoholic cirrhosis	Log Rank P
1 year	87	84	0.58
2 years	85	80	0.39
3 years	82	77	0.47
4 years	75	75	0.94
5 years	75	73	0.97

Singal et al, Hepatology 2012



Year of follow up	Alcoholic hepatitis	Alcoholic cirrhosis	Log Rank P
1 year	93	88	0.33
2 years	91	84	0.24
3 years	87	81	0.33
4 years	80	79	0.99
5 years	80	78	0.91

Fig. 3. Kaplan-Meier survival curves comparing patient survival of patients transplanted for alcoholic hepatitis (gray line) and patients transplanted for alcoholic cirrhosis (black line). Results show similar patient survival between the two groups (Log rank $P = 0.90$).

Singal et al, Hepatology 2012

Alcoholic Hepatitis and Liver Transplantation: Is an Abstinence of Six Months Necessary?

Gianni Testino and Paolo Borro

Department of Specialist Medicine, S. Martino Hospital, Genova, Italy

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To the Editor,

Forty-four percent of all deaths from liver disease are attributed to alcohol (1). Alcoholic liver disease (ALD) is the second most common diagnosis among patients undergoing liver transplantation (LT) in Europe and the Unites States. The outcome for patients transplanted for ALD is at least as good as that for most other diagnoses and better than that for HCV (2).

Forman *et al.* (3) evidenced a 5 year survival of 69.9% of HCV positive recipients and of 72% in HCV negative recipients transplanted for ALD. In HCV recipients, fibrosis/cirrhosis was present in 10-21% five years from LT. Reported rates of alcohol relapse ranged from 11.5-49%, although this fact was rarely considered a reason for graft failure in recipients with ALD. Graft dysfunction related to relapse ranged from 0 to 17%, although deaths related to relapse ranged from 0% to 5% (4). More recently, Tandon *et al.* (5) evidenced the risk of post-transplant problem drinking in 13% of cases. In this study there was no survival difference between problem drinkers and non-drinkers.

Alcoholic hepatitis (AH) is a clinical syndrome of jaundice and liver failure that generally occurs after decades of heavy alcohol use. The typical age of presentation is 40 to 60 years (6). The true incidence of AH is unclear. Its prevalence is around 20% among subjects who undergo liver biopsy and it is suspected in 10-35% of hospitalized alcoholics. Less severe forms of acute AH (AAH) frequently respond to alcohol abstinence, whereas the prognosis of severe AAH is poor; up to 40% die within 6 months. Cirrhosis co-exists in over 50% of cases and patients are at risk of variceal bleeding and hepatorenal syndrome (HRS) (7). Severe AAE non-responders to steroids have 6 months survival (approx. 25-30%) and in patients with HRS there is a 3-month mortality of more than 90% unless treated by LT (8-10).

In cases of severe AAH, LT is a therapeutic option in this setting but is rarely used. The reason for denying LT is that it requires abstinence from alcohol for six months before consideration for a transplant. This period is arbitrary and has never been shown to affect survival after LT (1). Even where there is evidence that shorter pre-listing abstinence correlates to shorter time to first drink post-transplant, an optimal period of pre-transplant abstinence remains unclear (2).

In our experience seven patients with severe AAE (Model End Stage Liver Disease over 21 and Maddrey Discriminant Function over 32) and type 1 HRS and non-responders to medical therapy, were submitted to transjugular intrahepatic portosystemic stent shunt (TIPS) and successively transplanted within five months of abstinence (median age 49 years) (unpublished data). None of the patients relapsed after a period of 5 years. Castell *et al.* (11) listed 22 patients for transplantation (median age 47 years) within 15 days of non-response to treatment and 18 patients were transplanted within 9 (range 5-13) days (2 died on the waiting list, 2 recovered). Non-responders to steroids were identified by a Lille score of 0.45 or higher, or worsening of liver function, seven days after presentation. Six-month survival was 83% (compared with 44% in a non-randomised case-matched control group). None of the patients relapsed in the first year although one patient relapsed after 917 days (1 unit/ three times week). Considering that patients who do not recover within the first 3 months of abstinence are unlikely to survive (12) in case of AAH, 3 months of alcohol abstinence may be more ideal than 6 months. Varma *et al.* (2) affirm that there is absence of enough evidence to support the 6 months sobriety. It is unclear whether this is an effective predictor for post transplant abstinence or simply a method of consistent selection popular with insurance companies. Shawcross and O'Grady (12) underlined that a teenager who develops liver failure after a deliberate paracetamol overdose, after taking ecstasy, or after contracting hepatitis B through irresponsible sexual behaviour will have open access to LT. Why should his or her peer who simply drank too much for a few months be treated differently? (12).

A strict application of a period of sobriety as a policy for transplant eligibility is unfair to non-responder patients, as most of them will have died prior to the end of the 6-month sober period (13). In our opinion, in case of severe AAH, subjects with a good social support, without psychotic or personality disorders, should be referred to LT if they still have decompensated liver disease and 3 months of abstinence.

Post-LT, patients with limited comorbidities and good social support should be offered individual cognitive behavioural therapy. Those with significant comorbidities and/or limited social support, should be offered multi-component programmes (multidimensional family therapy, functional family therapy, brief strategic family therapy) (14). The frequency of self-help groups, of which the best known is alcoholics anonymous, is mandatory. We agree with Kodyar *et al.* (15) that the lack of pre-LT abstinence alone should not be a barrier against being listed.

Hepato-Gastroenterology 2012; 59:00-00 doi 10.5754/hge11691

Alcoholism: Clinical and Experimental Research

Vol. **, No. *
**2013

Liver Transplantation in Alcoholic Patients

Gianni Testino, Silvia Leone, Alessandro Sumberaz, and Paolo Borro

In our experience, 7 patients (median age 49 years) with clinical evidence of severe AAH (MELD over 21 and DF over 32) and type 1 hepatorenal syndrome nonresponders to medical therapy have been submitted to transjugular intrahepatic portosystemic stent shunt (TIPS), and successively transplanted (30 to 45 days). Steroid therapy was contraindicated for renal failure. None patients (followed by our AU) relapsed after a period of 5 years (Testino et al., 2013).

Considering that patients with progressive ESLD who do not recover within the first 3 months of abstinence and patients with severe AAH are unlikely to survive, subjects with a good social support, without psychotic or personality disorders would be referred to LT if they still have decompensated liver disease and 3 months or less of abstinence.

Alcoholism: Clinical and Experimental Research, 2013

ASTENSIONE COME UNICO PARAMETRO ?

End Stage Liver Disease con MELD score > 19 senza recupero clinico-laboratoristico dopo circa 3 mesi di astensione

Epatite Alcolica Acuta Severa (DF > 32) non responder alla terapia medica o con complicanze (HRS) che ne peggiorano ulteriormente la prognosi

Testino G et al, Alcologia 2012

Consensus Conference – American Association for the Study of Liver Disease

A duration of 6 months of abstinence before liver transplantation should no longer be the definite rule and should not be considered the determining factor for graft access;

The term (pre-transplant) recurrence seems incorrect: it would be better to consider it as a relapse in alcohol dependence in order to differentiate it from isolated alcohol consumption;

An episode of alcohol intoxication does not necessarily translate into relapse;

Societal attitudes towards the patient must change. The alcoholic patient should be considered as suffering from a double pathology, both hepatic and alcoholic

Liver Transplantation, 2005

THE SEARCH FOR GENETIC RISK FACTORS FOR ALCOHOLIC LIVER DISEASE

Genetic variationmodulating addiction to alcohol

Genetic variation of alcohol-metabolising enzymes

Genetic variations involved in oxidative stress

Genetic variations controlling hepatic lipid storage

Genetic polymorphisms modulating endotoxin inflammation

Polymorphic variants of fibrosis-associated genes

Stickel and Hampe, Gut 2011

Recidivism (risk use) not necessarily reflects alcoholic liver disease. The dissociation may be because the transplanted liver changes the genetic susceptibility ……..

Burroughs, International Hepatology 2012

… reported rates of alcohol relapse range from 11.5% to 49%, although this fact was rarely considered a reason for graft failure in recipients with ALD.

Graft dysfunction related to relapse ranged from 0% to 17% although death related to relapse ranged from 0% to 5%

Cuadrado et al, Liver Transplantation 2005; DiMartini et al, Liver Transplantation 2006; De Gottardi et al, Arch Intern Med 2007; Burra P et al, Am J Transpl 2010; Lucey, Liver Transplantation 2011; Iruzubieta et al, WJG 2013

Cirrosi Epatica Alcol Correlata e Trapianto: Sopravvivenza

Europe:

84% at 1 year; 78% at 3 years; 73% at 5 years

USA:

92% at 1 year; 86% at 3 years; 86% at 5 years

Japan:

81.3% at 1 year; 78.5% at 3 years; 75.7% at 5 years

Testino G, 2014

CIRROSI EPATICA SCOMPENSTA E TRAPIANTO

DONAZIONE DA VIVENTE

Alcoholic Liver Disease

100% at 1 year; 91% at 3 years; 91% at 5 years

Non-Alcoholic Liver Disease

90% at 1 years; 86% at 3 years; 83% at 5 years

Kawaguchi et al; Hepatol Res 2013

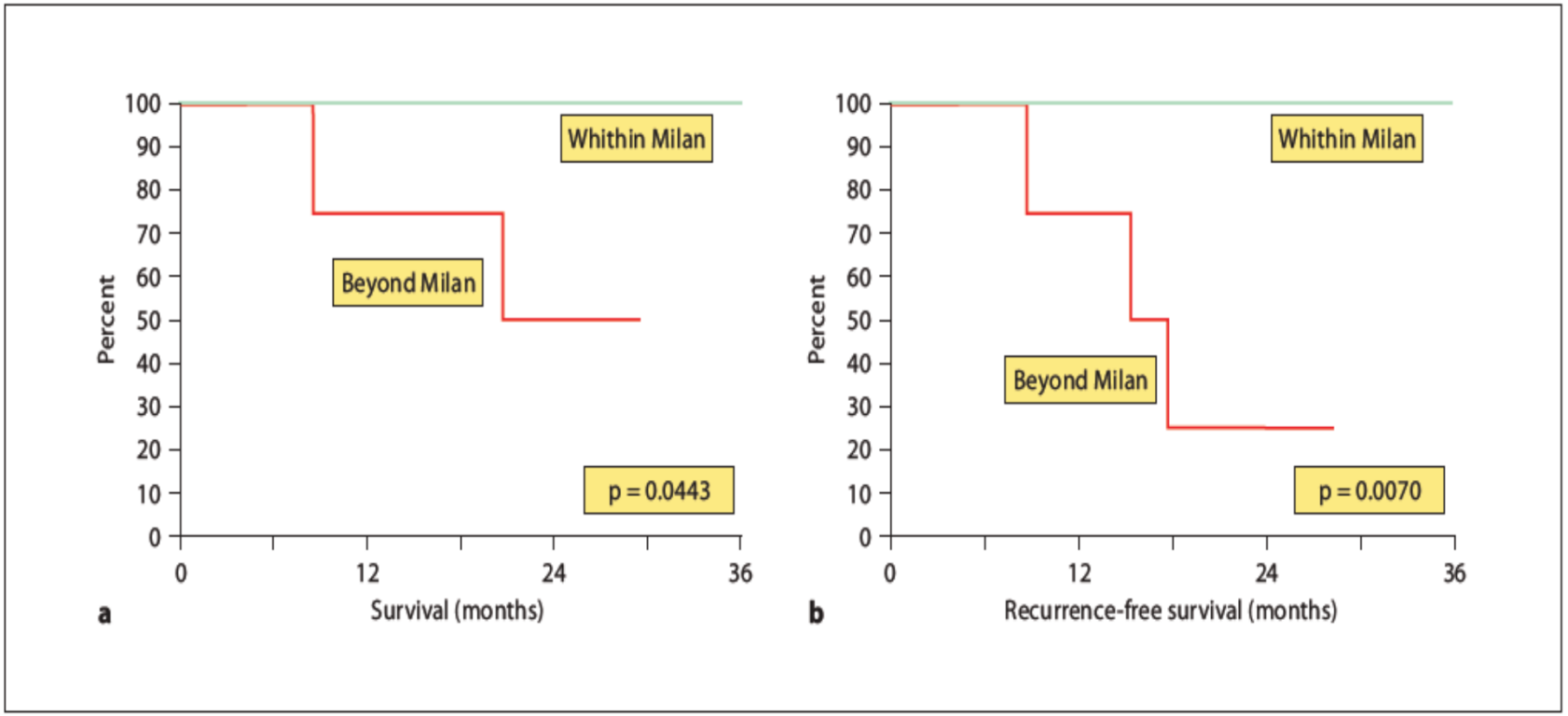

Fig. 2. Overall (**a**) and recurrence-free survival (**b**) rates in recipients within and beyond the Milan criteria.

Sotiropoulos et al, Eur Surg Res 2008

Table 7 Results in the literature on liver transplantation for alcoholic cirrhosis

Reference	*Period*	*Number*	*Follow up (months)*	*Survival (%)*				*Long term survivors*	*Recidivism (%)*	*Graft dysfunction related to recidivism (%)*	*Deaths related to recidivism (%)*
				1 year	*2 year*	*3 year*	*5 year*				
Bird and coworkers[3]	1980–1989	24	ND (4–84)	66				18	22	ND	0
Kumar and coworkers[2]	1982–1988	73	ND	74		62		52	11.5	2	2
Knechtle and coworkers[4]	1984–1990	41	ND	83			71	30	13	0	0
Berlakovitch and coworkers[7]	1982–1993	58	33	71			63	44	31	16	4.5
Osorio and coworkers[8]	1988–1991	43	21	100				37	19	ND	0
Raakow and coworkers[9]	1988–1994	78	25	96			85	ND	22	ND	2.5
Gerhardt and coworkers[10]	1985–1991	67	47		67 overall			41	49		4.4
Foster and coworkers[18]	1986–1994	88	49	79	75			63	22	17	5
Lucey and coworkers[11]	1987–1991	59	63	80			77	50	34		
Anand and coworkers[17]	1987–1994	39		79			79		13		
Gish and coworkers[6]	1988–1991	29	24	93				29	21	ND	0
Doffoel and coworkers[5]	1985–1991	75	29	80		68		57	26		
Pageaux and coworkers	1989–1994	53	42	75	69	67	62	47	32	4	2

ND, not determined.

Pageaux et al, Gut 1999

The focus on recidivism due to alcohol, rather than survival as the primary outcome after transplantation for alcoholic cirrhosis has been challenged

Burroughs, Int Hepatol 2012

Shawcross and O'Grady, Lancet 2010

Cause di morte dopo trapianto di fegato per cirrosi alcol-correlata

Patient	Transplant indication	Alcohol relapse	Cause of death	Survival (mo)	*Months after alcohol relapse
1	ALD	Yes	Metastatic dissemination of laryngeal epidermoid carcinoma	72	25
2	ALD	Yes	Sudden death	98	59
3	ALD	No	Hepatic metastases of pancreatic adenocarcinoma	102	—
4	ALD	Yes	Bone metastases of squamous pharyngeal carcinoma	95	36
5	ALD	No	Invasive bladder carcinoma	31	—
6	ALD	Yes	Acute myocardial infarction	93	48
7	ALD	Yes	Biliary sepsis	72	63
8	ALD	Yes	Acute stroke	91	36
9	ALD	No	Biliary sepsis	70	—
10	ALD	No	Acute myocardial infarction	90	—
11	ALD and HCC	Yes	Cerebral hemorrhage	14	10
12	ALD and HCC	No	Relapse of HCC with metastatic dissemination	57	—

Abbreviations: ALD, alcoholic liver disease; HCC, hepatocellular carcinoma.
* Time in months from alcohol relapse to the diagnosis of the clinical event that caused death.

Cuadrado Liver Transplantation 2005;4:420-426

P. Burra, XX Congresso Societa' Italiana di Alcologia; 2007

Aderenza alle prescrizioni mediche in pazienti con cirrosi alcol e non alcol-correlata

D. Canova & G. Germani, AISF 2007

	Alcol (n=67)	Non Alcol (n=67)	
			p
Mancata assunzione della terapia			
Si (qualche volta, spesso)	**31 (47%)**	**40 (58.8%)**	*n.s.*
No	36 (53)	27 (41.1)	
Assenza visite mediche			
Si (qualche volta, spesso)	**8 (11.7%)**	**8 (11.7%)**	*n.s.*
No	59 (88.2)	59 (88.2)	
Mancata esecuzione esami richiesti			
Si (qualche volta, spesso)	**6 (8.8%)**	**14 (20.5%)**	*n.s.*
No	61 (91.1)	53 (79.4)	

P. Burra, XX Congresso Societa' Italiana di Alcologia; 2007

TABLE 2. Multivariate Analysis of Pretransplant Risk Factors for Patient Survival in 195 Patients With ALC: A Proportional Hazards Analysis

Risk Factor	Risk Ratio	95% CI	*P* Value
Donor age ≥ 50 years	2.33	1.28-4.13	<0.01*
MELD score ≥ 19	1.91	1.07-3.55	0.03

*$P < 0.05$.

Egawa et al, Liver Transplantation 2014

CIRROSI EPATICA ALCOL CORRELATA

Molto frequente nei contesti ospedalieri (circa il 50% dei decessi dei paz. cirrotici e' alcol correlato)

(il 95% non viene valutato per trapianto e nel 40% dei casi di HCV/HBV consumo dannoso di alcol sottovalutato)

Eccellente condizione clinica da trapianto con sopravvivenza superiore alle altre condizioni

E' NECESSARIO UN CAMBIAMENTO

Rivalutazione del timing trapiantologico

Attivita' interdisciplinare personalizzata

Nuovo modo di lavorare per raggiungimento astensione – follow-up dell'astensione (sobrieta')

con coinvolgimento attivo delle UO Alcologia territoriali e delle Associazioni di auto-mutuo-aiuto

Testino G et al, Alcologia 2012

RISK SCORE

Severita' alcoldipendenza

Presenza di altre dipendenze *

Accettazione del problema da parte del candidato e dei familiari *

Aderenza al percorso assistenziale *

Consumo di alcol in famiglia

Assenza di disordini psichiatrici concomitanti *

Stabilita' e supporto sociale (famiglia, amici, lavoro) *

Presenza di figli

Frequenza ai gruppi di auto-mutuo-aiuto e accettazione di frequenza *

HBAR test (high risk alcoholism relapse); SCL 90 Score; ARRA*

Periodo di astensione (da ricoverato? a casa ?)

Presenza di una «reale rete costituita dalla collaborazione ospedale-territorio (attivita' multidisciplinare integrata) *

* Fattori considerati indispensabili

Pfitzmann et al, Liver Transplant 2007; Kotlyar et al, Am J Gastroenterol 2008;
Pilling et al, BMJ 2010; Burra P et al, Am J Transpl 2010; Brown, NEJM 2011;
Testino et al, DLD 2012; Burroughs, Int Hepatol 2012 ; *Rodrigue et al, Transpl Proc 2013

Risk Factors for Predicting Alcohol Relapse (I)

Alcohol drinking anamnesis (consumption habits: harmful drinking or mild/ moderate dependence

Drug abuse anamnesis

Family history of alcohol abuse/ dependence

Psychiatric comorbidities

HBAR test, SCL 90 score

Adherence to treatment: patients are asked to attend follow-up appointments

Ability to develop a therapeutic alliance, and to build good relationships with the transplant team

Social support (family, friends)

Risk factors for predicting alcohol relapse (II)

Adherence to behavioural support programs

Self-help group attendance and active participation

Period of abstinence before LT (five years !!!!!!)

Alcohol Unit attendance

Addiction specialist/ hepato-alcohologist

Testino et al, WJG 2014 in press

Alcohol and Alcoholism Advance Access published February 23, 2012

Alcohol and Alcoholism Vol. 0, No. 0, pp. 1–5, 2012 doi: 10.1093/alcalc/ags018

Characteristics of Alcoholics Attending 'Clubs of Alcoholics in Treatment' in Italy: A National Survey

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Abstract — Aims: To provide an overview of alcoholics attending a socio-ecological treatment programme [Clubs of Alcoholics in Treatment (CATs)] and to identify factors associated with abstinence and self-perceived improvement in lifestyle. **Methods:** A national sample of 7522 subjects (76% males and 24% females, mean age 53.2 ± 11.3 years ± SD) attending CATs was evaluated using a self-administered questionnaire completed at a weekly meeting in 2006. **Results:** Of participants, >70% reported no alcohol use in the last year and around 90% indicated no use in the previous month, whereas 4% of them declared no alcohol use before club attendance. Abstinence and lifestyle improvement were related positively to the number of years of club attendance but negatively to the presence of other problems in addition to the alcohol-related one. Moreover, being older or female was associated with more likely achievement of abstinence as well as with the perception of a better lifestyle. Finally, attending the club with one or more family members was associated with achievement of better lifestyle. **Conclusion**: These data provide an overview of alcoholics attending the CAT programme and are a first step toward developing a surveillance system. In addition, on the basis of this preliminary picture further research (notably longitudinal studies) can be planned considering this method and its effectiveness.

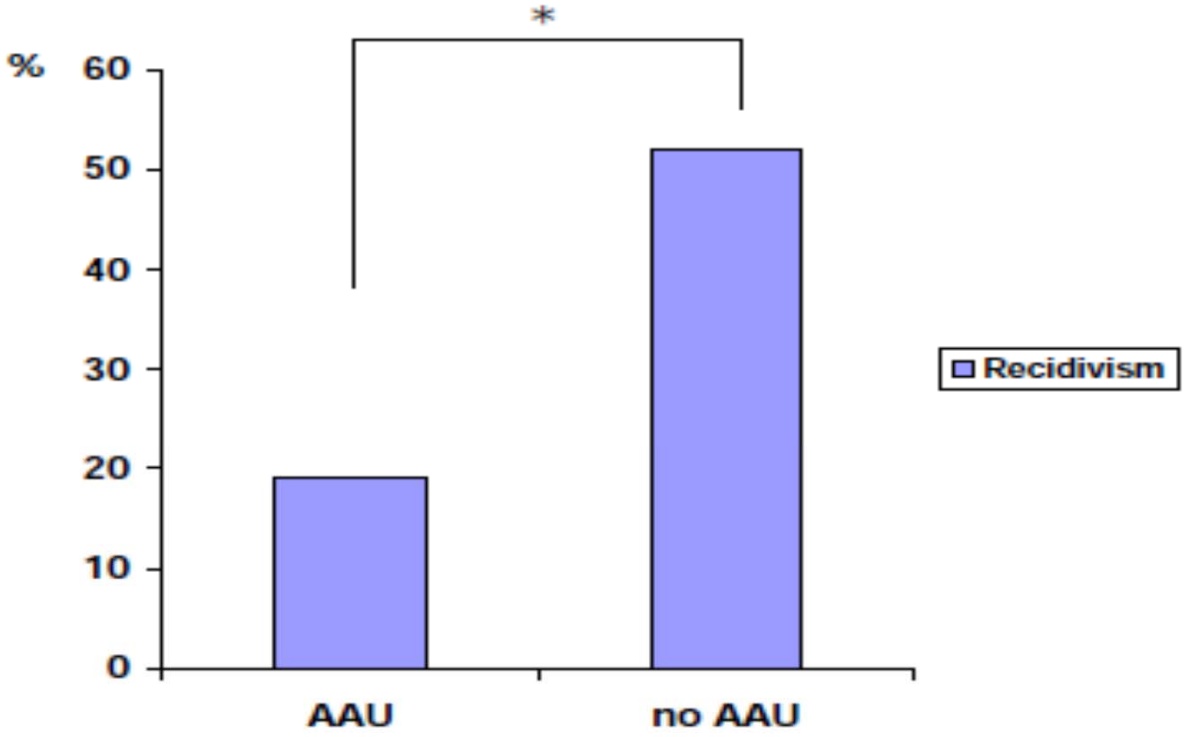

Fig. 2. Percentage of patients who showed recidivism after liver transplantation, and statistical comparison. *p = 0.005. AAU, Alcohol Addiction Unit.

Addolorato et al; Alcohol Clin Exp Res 2013

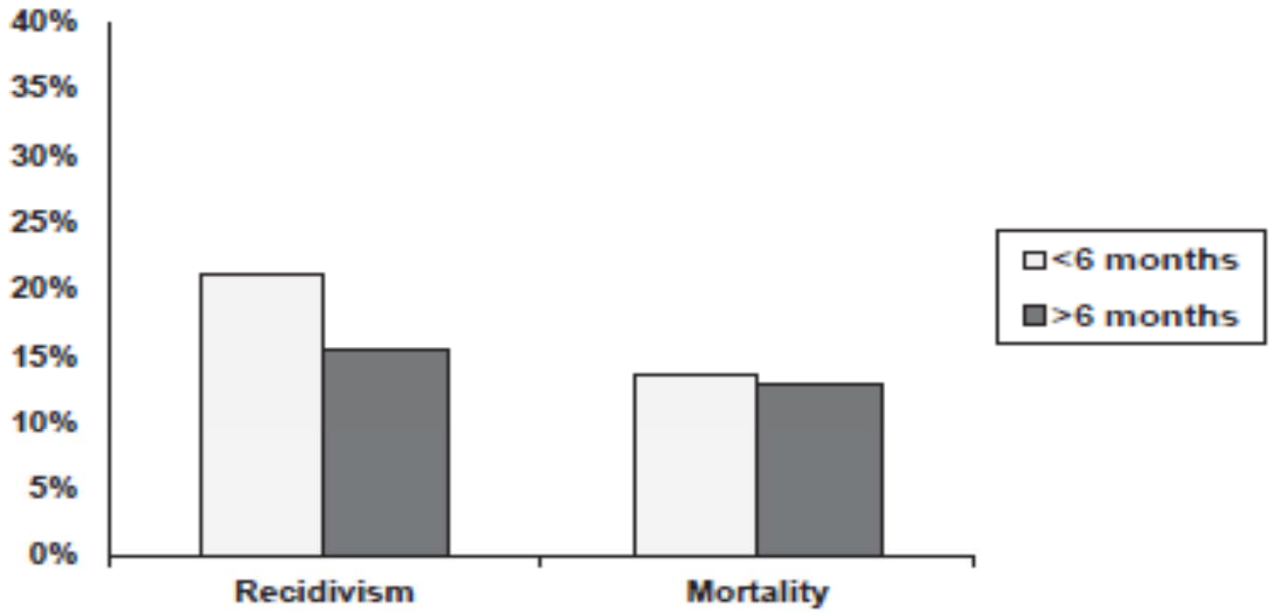

Fig. 4. Percentage of patients, followed at the Alcohol Addiction Unit (AAU), who showed recidivism, lapse, relapse, and mortality after liver transplantation, grouped on the basis of the pretransplant length of alcohol abstinence (>/<6 months; p = ns).

Addolorato et al; Alcohol Clin Exp Res 2013

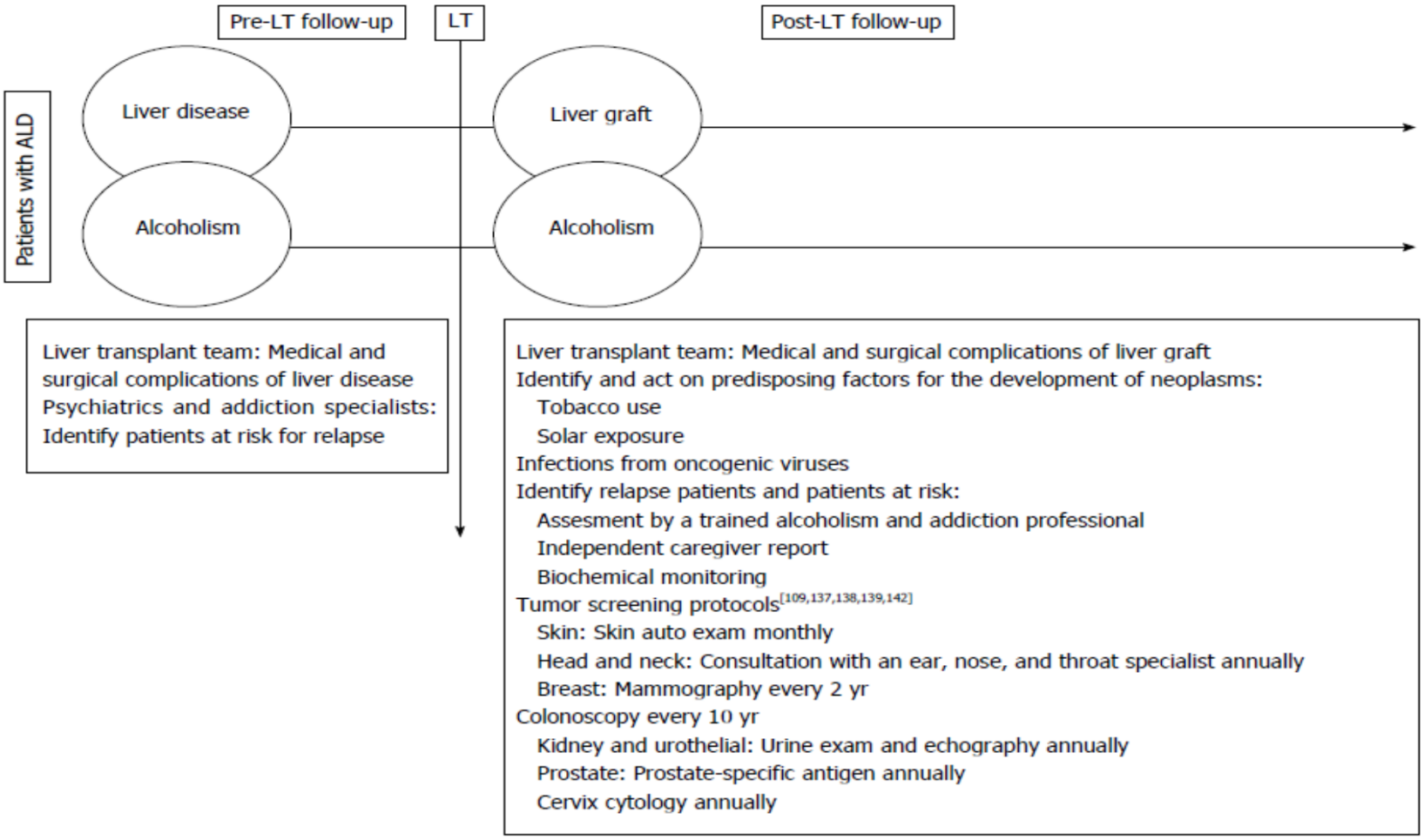

Figure 2 Proposed pre- and post-liver transplantation follow-up in alcohol liver disease. LT: Liver transplantation; ALD: Alcohol liver disease.

Iruzubieta et al; WJG 2013

HEPATO-ALCOHOLOGIST

Borro and Testino, Liver Int 2013

ACUTE ALCOHOLIC HEPATITIS, END STAGE ALCOHOLIC LIVER DISEASE AND LIVER TRANSPLANTATION: AN ITALIAN POSITION STATEMENT

WORLD JOURNAL OF GASTROENTEROLOGY, 2014 in press

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ALCOHOLIC LIVER DISEASE AND LIVER TRANSPLANTATION

1) Screening of the novo tumors after LT and prevention of cardiovascular complications

2) Child-Pugh class C

3) In case of ESLD with MELD < 19 six months of abstinence are required

4) In case of progressive ESLD (first visit) with MELD > 19, three months of abstinence are more ideal than six months in selected patients

5) In case of severe AAH, not responding to medical therapy (DF > 32 or MELD > 21), LT is mandatory in selected patients independently of the sober period achieved

6) The multidisciplinary transplant team must include an Addiction Specialist/ Hepato-Alcohologist

7) Patients have to partecipate to self-help groups

Testino G et al, World Journal of Gastroenterology 2014 in press

ALCOLDIPENDENZA E TRAPIANTO: UNA NUOVA VISIONE

DOPO TRIESTE (2012)

AK Singal et al; Clinical Gastroenterology and Hepatology 2013

JP Rice and MR Lucey; Current Opinion Organ Transplantation 2013

Addolorato et al; Alcohol and Clinical Exp 2013

P. Iruzubieta et al; World Journal of Gastroenterology 2013

Kawaguchi et al; Hepatol Research 2013

S. Masson et al; Transplantation International 2014

Abenavoli et al; World Journal of Gastroenterology 2014

H. Egawa et al; Liver Transplantation 2014

J Casanova and R. Bataller; Gastroenterologia and Hepatologia 2014

GA Berlakovich; WJG 2014

…. …there is no clear rationale for a defined period of abstinence before liver transplantation. The 6-month period is not based on prospectively gathered data but rather on custom and practice but its validity has been questioned as it is not evidenced based.

….the discussion concerning a fixed period of abstinence before transplantation might not be of relevance in clinical proctice and, therefore, lost of its importance.

In selected case (progressive ESLD, AAH) principles of medical ethics should take precedence over moral position, and the need for active and non-discriminatory treatment of these patients…

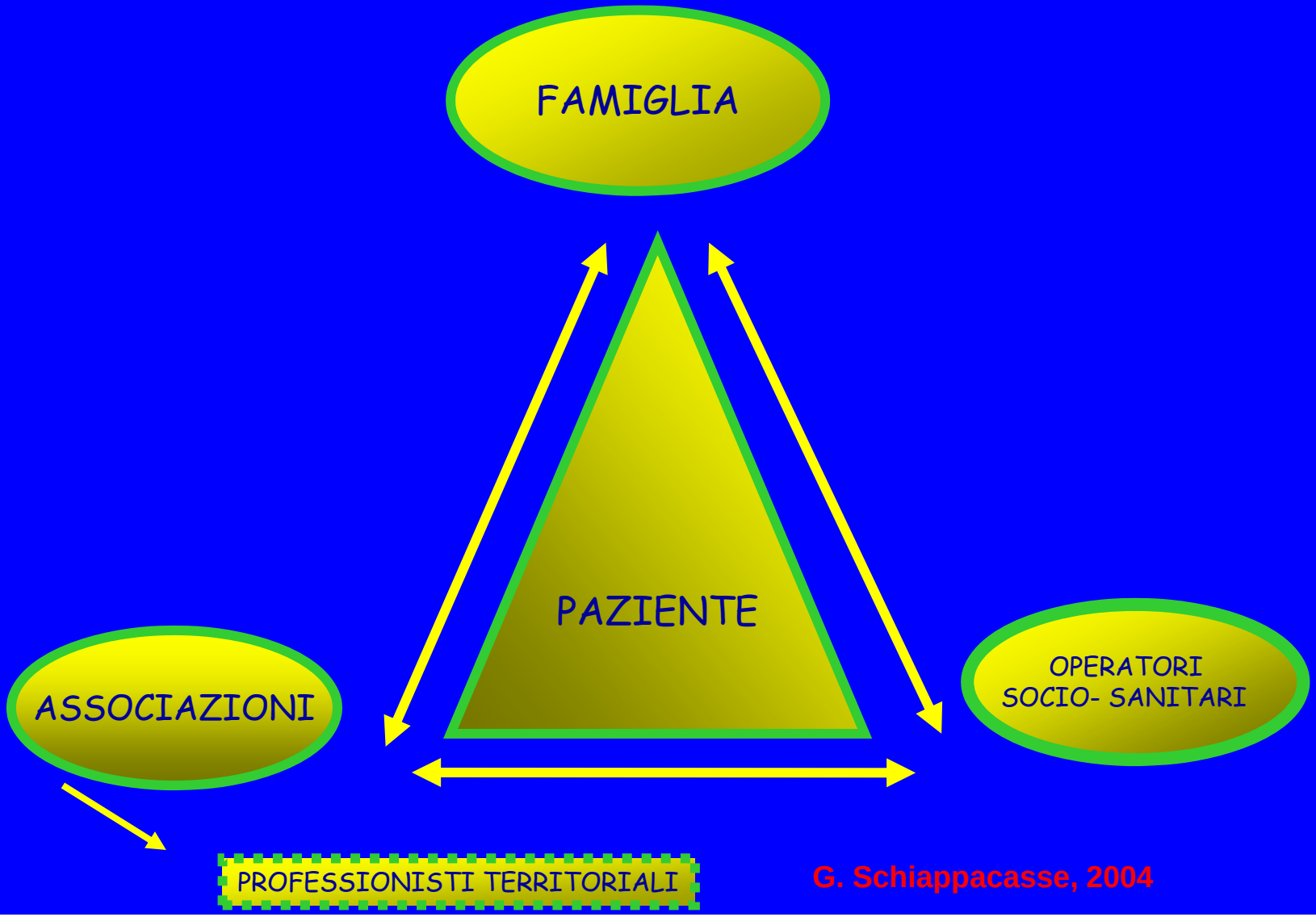
…the *biggest challenge* is the introduction of a multidisciplinary team, the presence of alcohologist and the interaction with the self-help groups

Berlakovich, WJG 2014

Donckier, Lucidi, Giusto et al; J Hepatol 2013

Testino, Burra, Bonino et al; WJG 2014, in press

OBIETTIVO



G. Schiappacasse, 2004

GIANNI TESTINO

ALCOL: BUGIE E VERITÀ

Tutti i rischi del bere

GRAZIE !!!

Pensiero Scientifico Editore, Roma, Dicembre 2013

www.pensiero.it/catalogo