

Actualités en Hépatologie

Hypertension portale
et fibrose hépatique
+ végétal

Hypertension portale

- Prévention primaire
- Propranolol et ascite

Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: A randomized controlled trial

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- Journal of Hepatology 2011 vol. 54 p 1161–1167

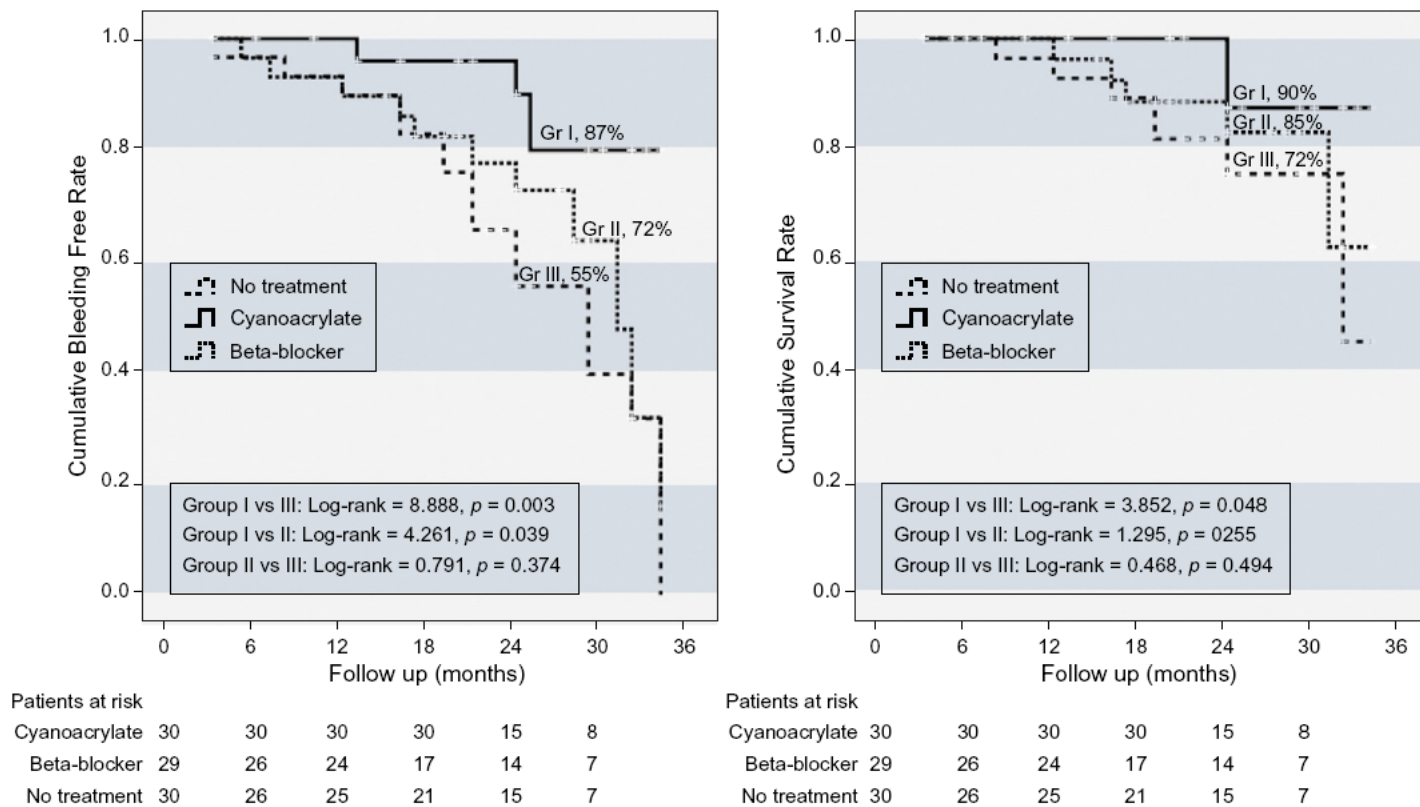


Fig. 1. Actuarial probability of freedom from bleeding from the gastric varices (A) and survival (B) in the endoscopic cyanoacrylate injection, beta-blockers, and no-treatment group.

- Conclusions:
- Primary prophylaxis is recommended in patients with large and high risk gastric varices to reduce the risk of first bleeding and mortality.
- Cyanoacrylate injection is more effective than beta-blocker therapy in preventing first gastric variceal bleeding.

Recommendations Baveno V

Prévention du 1^{er} épisode hémorragique

Patients avec varices gastriques

- En dépit de l'absence de données spécifiques d'études prophylactiques, les patients avec varices gastriques peuvent être traités avec NSBB (5,D).

LIVER FAILURE/CIRRHOSIS/PORTAL HYPERTENSION

**Controlled Trial of Ligation Plus Nadolol Versus Nadolol
Alone for the Prevention of First
Variceal Bleeding**

Gin-Ho Lo, Wen-Chi Chen, Huay-Min Wang, and Ching-Chang Lee

- HEPATOLOGY 2010;52:230-237

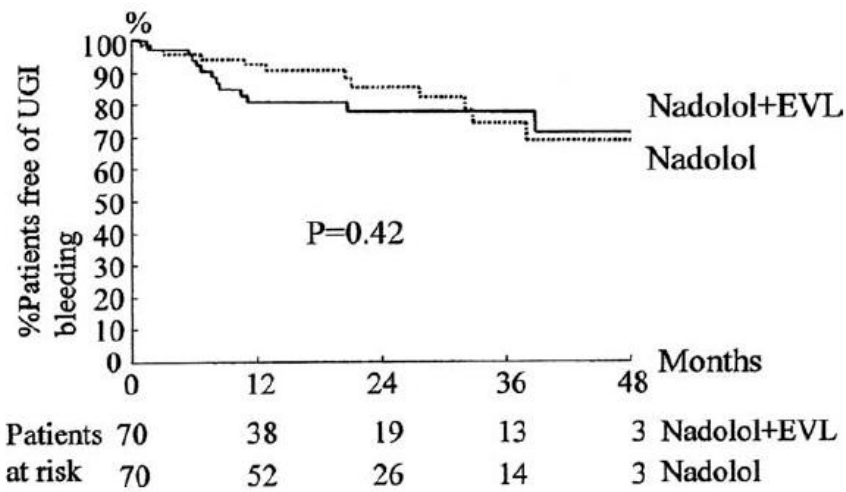


Fig. 2. The actuarial probability of free from bleeding from upper gastrointestinal tract in both groups.

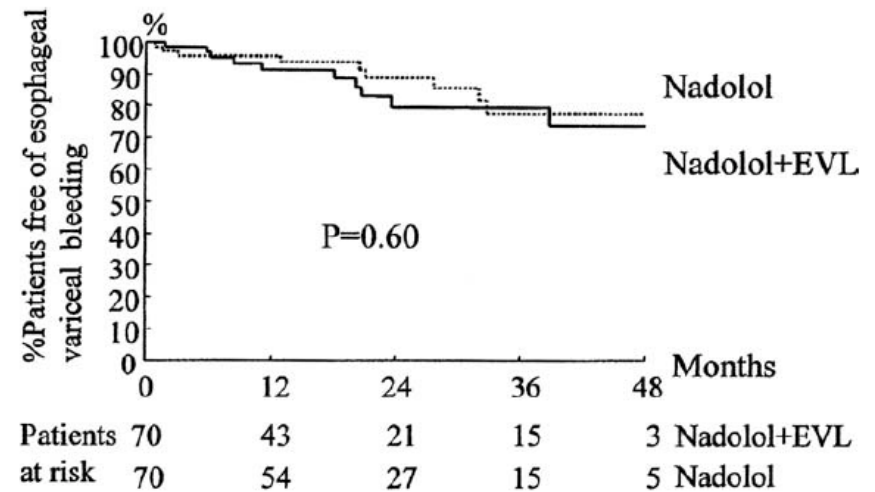


Fig. 3. The actuarial probability of free from first bleeding from esophageal varices in the two treatment groups.

- Conclusion:
- The addition of ligation to nadolol may increase adverse events and did not enhance effectiveness in the prophylaxis of first variceal bleeding.

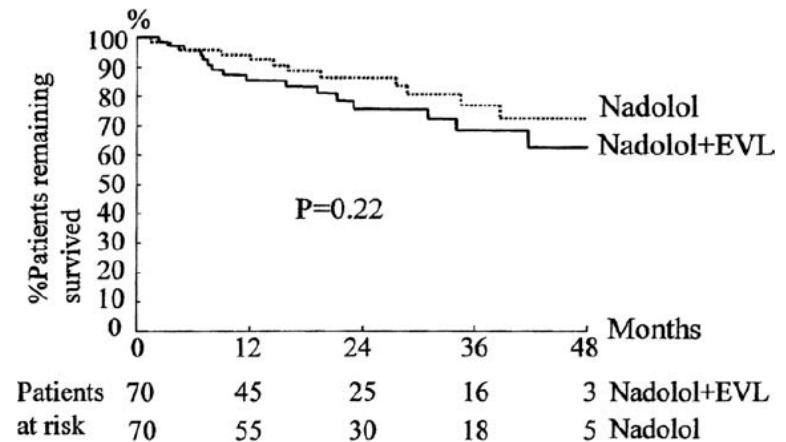


Fig. 4. The actuarial probability of survival in the two treatment groups.

Recommendations Baveno V

Prévention du 1^{er} épisode hémorragique

Patients avec varices de taille moyenne ou grande

- Les **NSBB** ou la **ligature élastique** des varices (LEV) sont recommandés pour la prévention de la première hémorragie par rupture de varices moyennes ou grandes (1a,A).
- Le choix du traitement devrait être basé sur l'expertise et les ressources locales, la préférence et les caractéristiques du patient, les effets secondaires et les contre-indications (5,D).
- Le **Carvedilol** est une alternative prometteuse (1b,A) qui nécessite des études complémentaires.
- Le traitement par shunt, la sclérothérapie endoscopique et le mono-nitrate d'isosorbide *seuls* ne devraient pas être utilisés en prévention de la première rupture de varices (1a,A).
- Il n'y a pas assez de données pour recommander l'utilisation des NSBB en combinaison avec le 5 mono-nitrate d'isosorbide (ISMN), la spironolactone ou la LEV pour la prévention primaire (1b, A).

New

New

Carvedilol for Portal Hypertension in Patients with Cirrhosis

Jaime Bosch

- **Recommendations** (HEPATOLOGY, Vol. 51, No. 6, 2010, 2214)
- At present, there is not enough evidence to recommend the use of carvedilol for treating portal hypertension in cirrhosis outside of clinical trials.
- Having said that, there are two situations where carvedilol may be the right beta-blocker for a patient with cirrhosis and portal hypertension.
- The first is the patient that requires treatment for portal hypertension and has **arterial hypertension** as a comorbidity. In this setting, carvedilol is probably the ideal beta-blocker and could be regarded as a first choice.
- The second situation is the patient who fails to exhibit an adequate decrease of HVPG during treatment with propranolol or nadolol. Available pharmacological options in this setting are the association of a second drug (isosorbide mononitrate, prazosin, or simvastatin) or to shift to carvedilol.

Deleterious Effects of Beta-Blockers on Survival in Patients With Cirrhosis and Refractory Ascites

Thomas Sersté,^{1,2,3} Christian Melot,⁴ Claire Francoz,^{1,2,5} François Durand,^{1,2,5} Pierre-Emmanuel Rautou,^{1,2}
Dominique Valla,^{1,2,5} Richard Moreau,^{1,2,5*} and Didier Lebrec,^{1,2,5*}

- HEPATOLOGY 2010;52:1017-1022

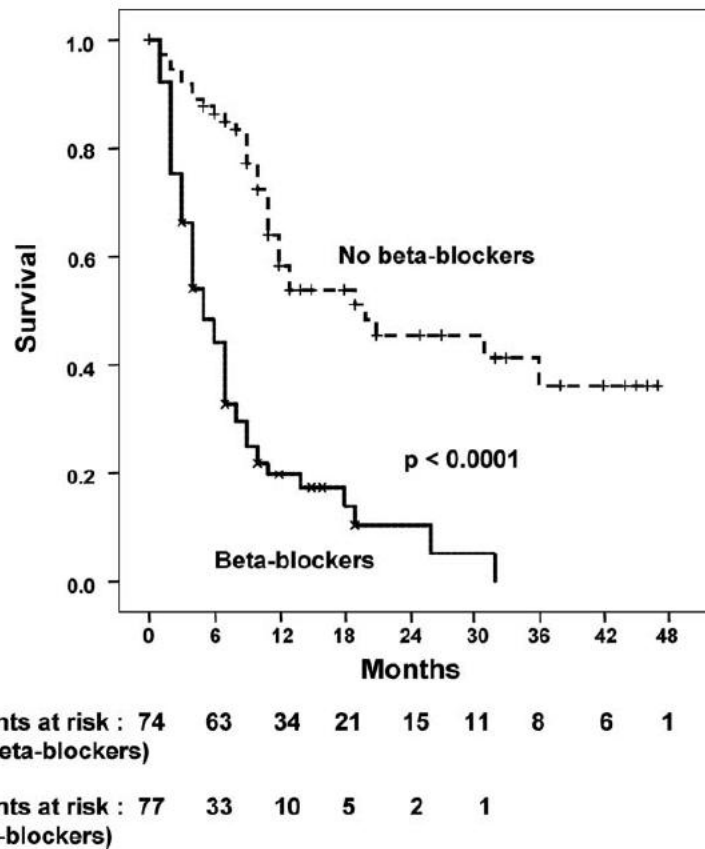


Fig. 2. Kaplan-Meier curves for the survival of patients with cirrhosis and refractory ascites who received beta-blockers and those who did not.

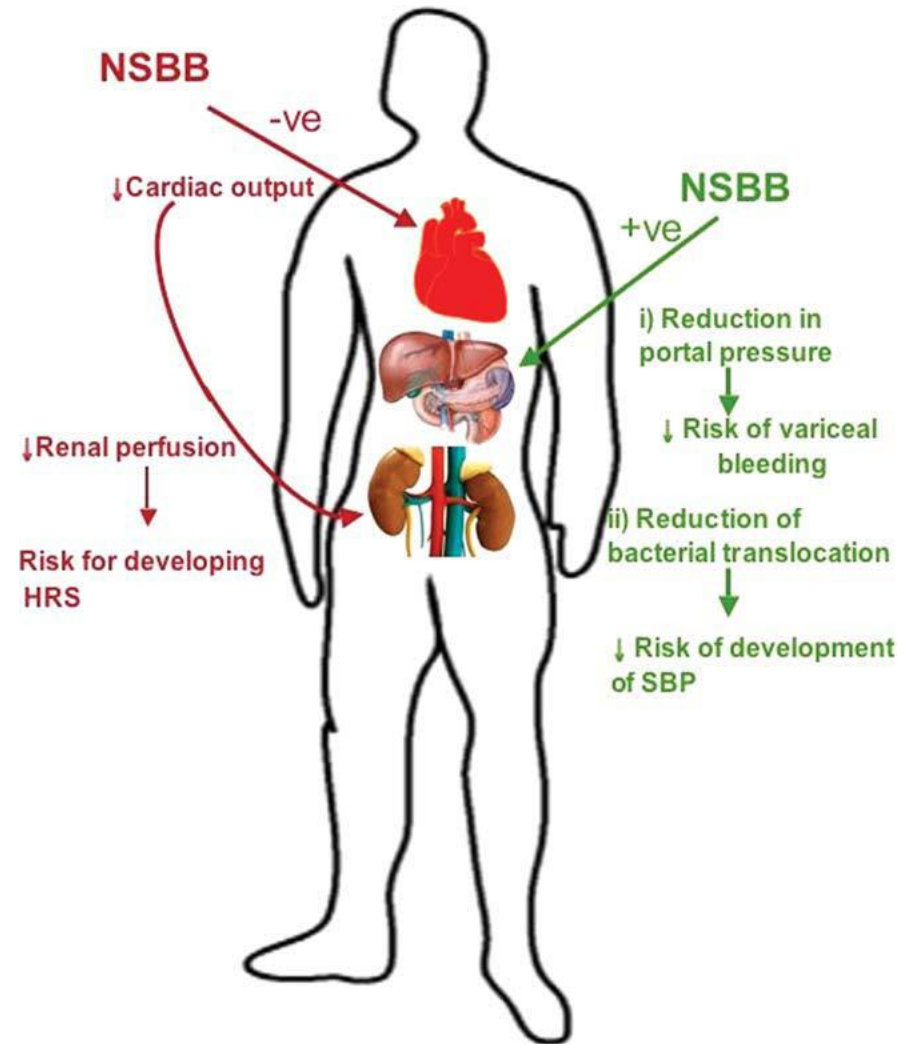
- **Conclusion:**
- The use of beta-blockers is associated with poor survival in patients with refractory ascites.
- These results suggest that betablockers should be contraindicated in these patients.

Analyses

- Hepatology. 2011 Apr;53(4):1412-3.
- Hepatology. 2011 May;53(5):1783.
- Hepatology. 2011 Apr;53(4):1411-2.
- Hepatology. 2011 Feb;53(2):715-6.
- Hepatology. 2011 Mar;53(3):1068-9.
- Hepatology. 2011 Jan;53(1):370-1.
- Hepatology. 2011 Jan;53(1):371-2.
- Hepatology. 2010 Sep;52(3):811-3.

Wong, Editorial Hepatology

- Patients with ascites who are on NSBBs should be monitored closely, and consideration should be given to discontinuing NSBBs when either sepsis or HRS develop.



- Non RCT
- The pronounced inhibitory effect of propranolol on cardiac function may explain the increased mortality.
- There is no impact of beta-blockers on ICU mortality in patients with cirrhosis resulting from severe sepsis or septic shock (GPS study).

- **Beta-blockers cause paracentesis-induced circulatory dysfunction in patients with cirrhosis and refractory ascites: A cross-over study.**
- Sersté T, Francoz C, Durand F, Rautou PE, Melot C, Valla D, Moreau R, Lebrec D.
- J Hepatol. 2011 (in press)
- Conclusions
- The use of beta-blockers may be associated with a high risk of PICD in patients with cirrhosis and refractory ascites.

Fibrose hépatique



VHC

Association of caffeine intake and histological features of chronic hepatitis C

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¹AP-HP, Service d'Hépatologie et de Gastroentérologie, Groupe Hospitalier Henri Mondor-Albert Chenevier, Créteil 94000, France; ²INSERM, U955, Créteil 94000, France; ³Université Paris-Est, Faculté de Médecine, UMR-S955, Créteil 94000, France; ⁴AP-HP, Service de Santé publique, Groupe Hospitalier Henri Mondor-Albert Chenevier, Créteil 94000, France; ⁵AP-HP, Service d'Anatomo-pathologie, Groupe Hospitalier Henri Mondor-Albert Chenevier, Créteil 94000, France; ⁶AP-HP, Service de Virologie, Groupe Hospitalier Henri Mondor-Albert Chenevier, Créteil 94000, France

Table 4. Stepwise logistic regression analysis of factors associated with Metavir activity grade $\geq$ A2.

	aOR*	95% CI	p
Caffeine consumption¹			
<225 mg/day	1		
225-407 mg/day	0.74	0.28-1.92	0.54
408-678 mg/day	0.32	0.12-0.85	0.022
>678 mg/day	0.28	0.10-0.75	0.011
Metavir fibrosis stage			
F0-F1	1		
F2-F4	13.3	5.4-32.7	<0.001
Steatosis			
Absent-mild	1		
Moderate-severe	2.43	1.01-5.88	0.049
Serum ALT level	1.01	1.00-1.02	0.005

*Adjusted odd ratio.

- By multivariate analysis, daily caffeine consumption greater than 408 mg/day was associated with a lesser risk of activity grade >A2 (OR = 0.32 (0.12–0.85)).
- Caffeine intake showed no relation with fibrosis stage.
- **Conclusions:**
- Caffeine consumption greater than 408 mg/day (3 cups or more) is associated with reduced histological activity in patients with CHC.
- These findings support potential hepatoprotective properties of caffeine in chronic liver diseases.

Coffee Consumption Is Associated With Response to Peginterferon and Ribavirin Therapy in Patients With Chronic Hepatitis C

NEAL D. FREEDMAN,* TERESA M. CURTO,[‡] KAREN L. LINDSAY,[§] ELIZABETH C. WRIGHT,^{||} RASHMI SINHA,* and JAMES E. EVERHART[¶] for the HALT-C TRIAL GROUP

- After adjustment for age, race/ethnicity, sex, alcohol, cirrhosis, ratio of aspartate aminotransferase to alanine aminotransferase, the *IL28B* polymorphism rs12979860, dose reduction of peginterferon, and other covariates, odds ratios for drinking 3 or more cups/day vs nondrinking were 2.0 (95% confidence interval [CI]: 1.1–3.6; *P* trend .004) for early virologic response, 2.1 (95% CI: 1.1–3.9; *P* trend .005) for week 20 virologic response, 2.4 (95% CI: 1.3–4.6; *P* trend .001) for end of treatment, and 1.8 (95% CI: 0.8–3.9; *P* trend .034) for sustained virologic response.
- **CONCLUSIONS:**
- **High level consumption of coffee (more than 3 cups per day) is an independent predictor of improved virologic response to peginterferon plus ribavirin in patients with hepatitis C.**

Multiple Effects of Silymarin on the Hepatitis C Virus Lifecycle

Jessica Wagoner,¹ Amina Negash,^{1*} Olivia J. Kane,^{2†} Laura E. Martinez,³ Yaakov Nahmias,⁴ Nigel Bourne,⁵ David M. Owen,⁶ Joe Grove,⁷ Claire Brimacombe,⁷ Jane A. McKeating,⁷ Eve-Isabelle Pécheur,⁸ Tyler N. Graf,⁹ Nicholas H. Oberlies,⁹ Volker Lohmann,¹⁰ Feng Cao,¹¹ John E. Tavis,¹¹ and Stephen J. Polyak^{1,2,3}

- HEPATOLOGY 2010;51:1912-1921
- **Conclusion:**
- Although inhibition of in vitro NS5B polymerase activity is demonstrable, the mechanisms of silymarin's antiviral action appear to include blocking of virus entry and transmission, possibly by targeting the host cell.

VHB

- **The Effect of Caffeine and Alcohol Consumption on Liver Fibrosis – A Study of 1045 Asian Hepatitis B Patients using Transient Elastography**
- Arlinking Ong^{1,2}, Vincent Wai-Sun Wong¹, Grace Lai-Hung Wong¹, Henry Lik-Yuen Chan¹
- Liver International (in press)

- ***Conclusion:***
- Caffeine intake does not affect liver stiffness in chronic HBV infected patients.
- Patients who drink coffee regularly tend to drink alcohol.
- Most chronic HBV infected patients do not have excessive alcohol consumption.
- The prevalence of advanced fibrosis among mild to moderate alcohol drinkers was low in this population.

- **Moderate coffee consumption reduces the risk of hepatocellular carcinoma in hepatitis B chronic carriers: a case-control study.**
- Leung WW, Ho SC, Chan HL, Wong V, Yeo W, Mok TS.
- J Epidemiol Community Health. 2011 Jun;65(6):556-8.

- Univariate and multivariate logistic regressions adjusting for age, gender, cigarette smoking, alcohol use, tea consumption and physical activity were conducted with dose-response analysis.
- **Results**
- Moderate coffee consumption significantly reduced the risk of HCC by almost half (OR 0.54, 95% CI 0.30 to 0.97) with a significant dose-response effect ($\chi^2(2)=5.41$, $df=1$, $p=0.02$), reducing the risk for moderate drinkers by 59% (OR 0.41, 95% CI 0.19 to 0.89).
- **Conclusion**
- The findings provided evidence to support the protective effect of coffee consumption in moderate quantities in HBV chronic carriers.

Café & OH

- Liver Int. 2010 Jul;30(6):867-70.
- **Interaction of alcohol intake and cofactors on the risk of cirrhosis.**
- Stroffolini T, Cotticelli G, Medda E, Niosi M, Del Vecchio-Blanco C, Addolorato G, Petrelli E, Salerno MT, Picardi A, Bernardi M, Almasio P, Bellentani S, Surace LA, Loguercio C.

- An alcohol intake of more than 3 units/day resulted associated with the likelihood of cirrhosis both in males (OR 4.3; 95% CI=2.5-7.3) and in females (OR 5.7; 95% CI=2.3-14.5).
- A multiplicative interaction on the risk of cirrhosis between risky alcohol intake and HBsAg or HCV-Ab/HCV-RNA positivity was observed.

- A reduction of cirrhosis risk was observed in subjects consuming more than 3 alcohol units/day with increasing coffee intake.
- The OR for the association with cirrhosis decreased from 2.3 (95% CI=1.2-4.4) in subjects drinking 0-2 cups of coffee/day to 1.4 (95% CI=0.6-3.6) in those drinking more than 2 cups/day.

- ***CONCLUSIONS:***

- In subjects with an alcohol intake >3 units/day the coexistence of HBV or HCV multiplies the risk of cirrhosis.

- Coffee represents a modulator of alcoholic cirrhosis risk.

Décrets, arrêtés, circulaires

TEXTES GÉNÉRAUX

MINISTÈRE DU TRAVAIL, DE L'EMPLOI ET DE LA SANTÉ

Décision du 1^{er} mars 2011 de l'Union nationale des caisses d'assurance maladie relative à la liste des actes et prestations pris en charge par l'assurance maladie

NOR : ETSU1120116S

Scores biologiques de fibrose hépatique

- “Evaluation d’une hépatite chronique C non traitée et sans comorbidité, chez l’adulte (hors diagnostic évident de cirrhose).
- Ces actes sont à réaliser dans le cadre d’une prise en charge spécialisée de la fibrose/cirrhose liée à l’hépatite chronique virale C.
- Ces actes sont réalisés dans le cadre de la stratégie diagnostique suivante, dans la limite d’une fois par an :
 - – en première intention : un test non invasif (un des trois scores ou l’élastographie impulsionnelle ultrasonore) ;
 - – en seconde intention (en cas de non-concordance entre le résultat du test réalisé en première intention et la clinique, ou d’échec technique/de non-interprétabilité de ce test) : un second test non invasif (autre que celui réalisé en première intention) en alternative avec une ponction biopsie hépatique.”
- Les actes 1000, 1001 et 1002 ne doivent pas être réalisés en cas de pathologie intercurrente susceptible d’interférer sur la valeur d’un ou plusieurs marqueurs du score et de perturber le résultat du calcul du score.

Excess Mortality in Patients with Advanced Chronic Hepatitis C Treated with Long-Term Peginterferon

Adrian M. Di Bisceglie,¹ Anne M. Stoddard,² Jules L. Dienstag,^{3,4} Mitchell L. Shiffman,⁵
Leonard B. Seeff,^{6,7} Herbert L. Bonkovsky,^{8,9} Chihiro Morishima,¹⁰ Elizabeth C. Wright,¹¹
Kristin K. Snow,² William M. Lee,¹² Robert J. Fontana,¹³ Timothy R. Morgan,^{14,15}
and Marc G. Ghany,⁷ for the HALT-C Trial Group

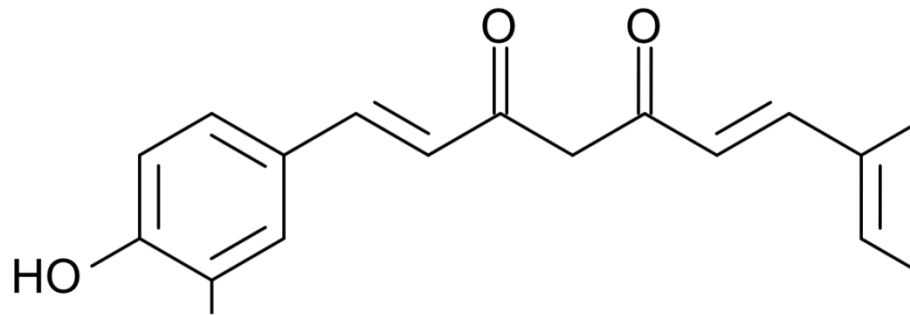
- HEPATOLOGY 2011;53:1100-1108
- Conclusion:
- Long-term maintenance peginterferon in patients with advanced chronic hepatitis C is associated with an excess overall mortality, which was primarily due to nonliver-related causes among patients with bridging fibrosis.

Plantes

- Pharm Biol. 2011 May 19. [Epub ahead of print]
- **Recent advances in herbal medicine for treatment of liver diseases.**
- Ghosh N, Ghosh R, Mandal V, Mandal SC.
- **Source**
- Dr. B.C. Roy College of Pharmacy and Allied Health Sciences, Durgapur, India.

- **Conclusion:**
- Out of the several leads obtained from plant sources as potential hepatoprotective agents, silymarin, andrographolide, neoandrographolide, curcumin, picroside, kutkoside, phyllanthin, hypophyllanthin, and glycyrrhizin have been established as potent hepatoprotective agents.
- The hepatoprotective potential of several herbal medicines has been clinically evaluated.
- Significant efficacy has been seen with silymarin, glycyrrhizin and Liv-52 in treatment of hepatitis, alcoholic liver disease and liver cirrhosis.

Curcumine



- La **curcumine** ou diféruloylméthane est le pigment principal du curcuma (*Curcuma longa*), aussi appelé safran des Indes.
- C'est un pigment polyphénolique (curcumoïde) qui donne une couleur jaune (c'est le colorant alimentaire E100).

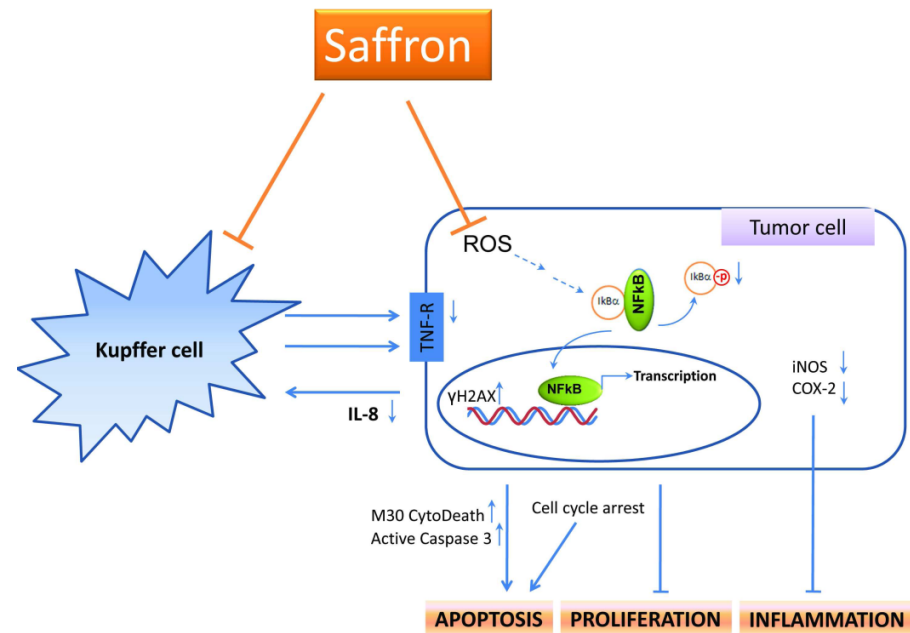
- 1: Zhang S, Chen S, Li W, Guo X, Zhao P, Xu J, Chen Y, Pan Q, Liu X, Zychlinski D, Lu H, Tortorella MD, Schambach A, Wang Y, Pei D, Esteban MA. Rescue of ATP7B function in hepatocyte-like cells from **Wilson's disease** induced pluripotent stem cells using gene therapy or the chaperone drug curcumin. Hum Mol Genet. 2011 Jun 4. [Epub ahead of print] PubMed PMID: 21593220.
- 2: Cerný D, Lekić N, Váňová K, Muchová L, Hořínek A, Kmoníčková E, Zídek Z, Kameníková L, Farghali H. Hepatoprotective effect of curcumin in lipopolysaccharide/-galactosamine model of liver injury in rats: Relationship to HO-1/CO antioxidant system. Fitoterapia. 2011 Jul;82(5):786-91. Epub 2011 Apr 30. PubMed PMID: 21545828.
- 3: Darvesh AS, Aggarwal BB, Bishayee A. Curcumin and Liver Cancer: A Review. Curr Pharm Biotechnol. 2011 Apr 5. [Epub ahead of print] PubMed PMID: 21466422.
- 4: Prakobwong S, Khoontawad J, Yongvanit P, Pairojkul C, Hiraku Y, Sithithaworn P, Pinlaor P, Aggarwal BB, Pinlaor S. Curcumin decreases **cholangiocarcinogenesis** in hamsters by suppressing inflammation-mediated molecular events related to multistep carcinogenesis. Int J Cancer. 2011 Jul 1;129(1):88-100. doi:10.1002/ijc.25656. Epub 2010 Nov 3. PubMed PMID: 20824699.
- 5: Karatepe O, Acet E, Battal M, Adas G, Kemik A, Altiok M, Kamali G, Koculu S, Catay A, Kamali S, Karahan S. Effects of glutamine and curcumin on **bacterial translocation in jaundiced rats**. World J Gastroenterol. 2010 Sep 14;16(34):4313-20. PubMed PMID: 20818815; PubMed Central PMCID: PMC2937112.
- 6: Yousef MI, Omar SA, El-Guendi MI, Abdelmegid LA. Potential protective effects of quercetin and curcumin on **paracetamol-induced** histological changes, oxidative stress, impaired liver and kidney functions and haematotoxicity in rat. Food Chem Toxicol. 2010 Nov;48(11):3246-61. Epub 2010 Sep 4. PubMed PMID: 20804811.

- 7: Hassell LA, Roanh le D. Potential response to curcumin in infantile hemangioendothelioma of the liver. *Pediatr Blood Cancer*. 2010 Aug;55(2):377-9. PubMed PMID: 20582974.
- 8: Rajagopalan R, Sridharana S, Menon VP. Hepatoprotective role of bis-demethoxy curcumin analog on the expression of matrix metalloproteinase induced by alcohol and polyunsaturated fatty acid in rats. *Toxicol Mech Methods*. 2010 Jun;20(5):252-9.
- 9: Rechtman MM, Har-Noy O, Bar-Yishay I, Fishman S, Adamovich Y, Shaul Y, Halpern Z, Shlomai A. **Curcumin inhibits hepatitis B virus** via down-regulation of the metabolic coactivator PGC-1alpha. *FEBS Lett*. 2010 Jun 3;584(11):2485-90. Epub 2010 Apr 29. Erratum in: *FEBS Lett*. 2010 Jul 16;584(14):3239. Har-Noy, Ofir [added]. PubMed PMID: 20434445.
- 10: Pinlaor S, Prakobwong S, Hiraku Y, Pinlaor P, Laothong U, Yongvanit P. Reduction of periductal **fibrosis** in liver fluke-infected hamsters after long-term curcumin treatment. *Eur J Pharmacol*. 2010 Jul 25;638(1-3):134-41. Epub 2010 Apr24. PubMed PMID: 20420820.
- 11: Baghdasaryan A, Claudel T, Kusters A, Gumhold J, Silbert D, Thüringer A, Leski K, Fickert P, Karpen SJ, Trauner M. Curcumin improves sclerosing cholangitis in Mdr2-/- mice by inhibition of cholangiocyte inflammatory response and portal myofibroblast proliferation. *Gut*. 2010 Apr;59(4):521-30. PubMed PMID: 20332524.
- 12: Li JM, LiYC, Kong LD, Hu QH. Curcumin inhibits hepatic protein-tyrosine phosphatase 1B and prevents hypertriglyceridemia and **hepatic steatosis** in fructose-fed rats. *Hepatology*. 2010 May;51(5):1555-66. Erratum in: *Hepatology*. 2010 Jul;52(1):402.
- 13: El-Agamy DS. Comparative effects of curcumin and resveratrol on aflatoxin B(1)-induced liver injury in rats. *Arch Toxicol*. 2010 May;84(5):389-96
- 14: van den Berghe PV, Stapelbroek JM, Krieger E, de Bie P, van de Graaf SF, de Groot RE, van Beurden E, Spijker E, Houwen RH, Berger R, Klomp LW. Reduced expression of ATP7B affected by **Wilson disease**-causing mutations is rescued by pharmacological folding chaperones 4-phenylbutyrate and curcumin. *Hepatology*. 2009 Dec;50(6):1783-95. PubMed PMID: 19937698.

NAFLD

- Hepatology. 2010 May;51(5):1555-66.
- **Curcumin inhibits hepatic protein-tyrosine phosphatase 1B and prevents hypertriglyceridemia and hepatic steatosis in fructose-fed rats.**
- Li JM, LiYC, Kong LD, Hu QH.
- CONCLUSION:
- Our data indicate that the mechanisms by which curcumin protects against fructose-induced hypertriglyceridemia and hepatic steatosis are its inhibition on PTP1B and subsequently improvement of insulin and leptin sensitivity in the liver of rats.
- This PTP1B inhibitory property may be a promising therapeutic strategy for curcumin to treat fructose-induced hepatic steatosis driven by hepatic insulin and leptin resistance.

A close-up photograph of a pile of bright red saffron threads and a single purple saffron flower resting on a piece of rough, light-colored stone. The threads are vibrant red and appear delicate and fibrous. The flower is a deep purple color with a yellow center. The stone surface is textured and uneven, providing a naturalistic background for the saffron.



- **Saffron: A potential target for a novel anti-cancer drug against hepatocellular carcinoma**
- Amr Amin et al, Hepatology (in press)
- **Conclusions:**
- The present study provides evidence that saffron exerts a significant chemopreventive effect against liver cancer through inhibition of cell proliferation and induction of apoptosis.
- This report also shows some evidence that saffron protects rat liver from cancer via modulating oxidative damage and suppressing inflammatory response.

Tabac

- Smoking as an Independent Risk Factor of Liver Fibrosis in Primary Biliary Cirrhosis
- Corpechot JH 2011 (in press)
- **Conclusions:**
- Smoking increases, in a dose-dependent fashion, the risk of liver fibrosis in PBC without apparent increase in the histological inflammatory activity, bile duct lesions, biochemical and immunological features of the disease.
- PBC patients should be strongly encouraged not to smoke.

Cigarette Smoking Exacerbates Nonalcoholic Fatty Liver Disease in Obese Rats

Lorenzo Azzalini,^{1*} Elisabet Ferrer,^{2*} Leandra N. Ramalho,³ Montserrat Moreno,¹ Marlene Domínguez,¹ Jordi Colmenero,¹ Víctor I. Peinado,² Joan A. Barberà,² Vicente Arroyo,¹ Pere Ginès,¹ Joan Caballería,¹ and Ramón Bataller¹

- HEPATOLOGY 2010;51:1567-1576
- ***Conclusion:***
- cigarette smoking causes oxidative stress and worsens the severity of NAFLD in obese rats. Further studies should assess whether this finding also occurs in patients with obesity and NAFLD.

Clearing the Smoke in Chronic Liver Diseases

- ZEIN, HEPATOLOGY 2010
- As hepatologists, we need to incorporate the intake of a more thorough smoking history during our evaluations, educate our patients on the effects of this modifiable risk factor on liver injury, and strongly recommend smoking cessation in all patients with CLD.

Table 1. Studies in Patients with CLD Investigating the Association Between Smoking and the Histological Severity of Disease

Authors	Condition	n	Association with Smoking	
			Histological Disease Activity*	Severity of Liver Fibrosis
Dev et al. ¹³	HCV	170	—	Yes
Pessione et al. ¹⁵	HCV	310	Yes	Yes
Hézode et al. ¹⁴	HCV	244	Yes	No
Tsochatzis et al. ¹²	HCV	176	—	Yes
Tsochatzis et al. ¹²	HBV	85	—	No
Yu et al. ¹⁶	HBV	1506	—	Yes
Corrao et al. ⁸	Cirrhosis	115	—	Yes
Zein et al. ¹⁷	PBC	269	—	Yes

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; PBC, primary biliary cirrhosis.

*A dash means “not reported” or “not applicable.”