

CIRROSI EPATICA 2018



16° corso
di aggiornamento
per il
medico
di base

26 – 28 settembre
2018
Mercato coperto
Giubiasco



Andrea De Gottardi, Epatologia, Bauchzentrum, Inselspital, Berna

Why does cirrhosis belong to Laennec?

Jalalyn M. Duffin, MD, FRCPC, PhD

Rene Theophile Hyacinthe Laennec (1781–1826): The Man Behind the Stethoscope



It is well known that Laennec gave cirrhosis its name from the Greek word *kirrhos* (tawny), in a brief footnote to his treatise *De l'auscultation médiate* (1819), but the eponym "Laennec's cirrhosis" is rarely used in France. This article explores the reasons why North American physicians commemorate a French chest specialist in their name for a hepatic lesion that had first been recognized in England more than a century earlier. It traces the content and fortunes of Laennec's essay on cirrhosis, part of an incomplete manuscript, including its eventual partial publication by a British editor in the original French. A survey of 19th-century literature on cirrhosis revealed that it was not until the publication of William Osler's textbook that the eponym came into common use. The geographic patterns of influence of Osler's book and the differing preoccupations of physicians on the two sides of the English Channel probably combined to result in the paradoxical employment of this eponym.

On sait que la cirrhose a été nommée par Laennec d'après le mot grec *kirrhos* (jaunâtre) dans un bref renvoi du traité *De l'auscultation médiate* (1819). Mais l'auteur prétend que l'appellation "cirrhose de Laennec" a peu cours en France. Elle s'attache à découvrir pourquoi les médecins nord-américains donnent le nom d'un ptisiologue français à une lésion déjà décrite en Angleterre plus d'un siècle auparavant. Elle retrace le texte et le devenir de l'essai de Laennec sur la cirrhose, partie d'un manuscrit inachevé, y compris la publication partielle en

divergentes des médecins de part et d'autre de la Manche qui expliqueraient le paradoxe terminologique précité.

René Théophile Hyacinthe Laennec (1781–1826) invented the stethoscope and made major contributions to the pathological understanding and diagnosis of diseases of the chest, yet his name is associated with atrophic, alcoholic cirrhosis of the liver. The eponym "Laennec's cirrhosis" is especially popular in the United States and in both English and French Canada. In France, Laennec's native country and the place most likely to laud his achievements, it is scarcely known. The following is a report on my investigation into what this pulmonary specialist contributed to hepatology and why his "achievement" seems to be recognized everywhere but in his homeland.

Laennec gave cirrhosis its name from the Greek word *kirrhos*, meaning tawny yellow. According to most medical history textbooks this baptism was first published in a footnote commenting on the incidental finding of yellow nodules in the liver of Jean Edmé, a patient described in the first and second editions of Laennec's treatise *De l'auscultation médiate*.^{1,2} Some historians cite this small digression as the first pathological description of the disorder, but they are mistaken. More detailed descriptions of cirrhosis had already been published by the British pathologists John Browne³ (1642–1700) and Matthew Baillie⁴ (1761–1823). Although these men had used different names for the lesion, both had recorded its appearance accurately, and Baillie had linked it to excessive alcohol consumption.

SOMMARIO

CIRROSI = EPATOPATIA CRONICA AVANZATA



DEFINIZIONE



CAUSE



DIAGNOSI



TRATTAMENTO

SOMMARIO

CIRROSI = EPATOPATIA CRONICA AVANZATA



DEFINIZIONE



CAUSE

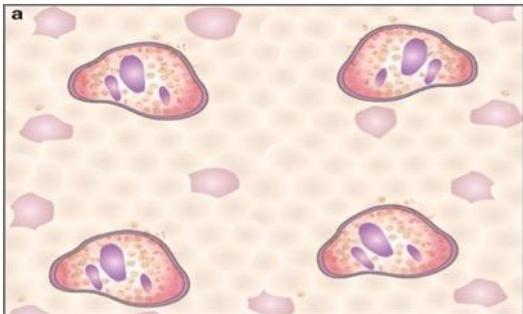


DIAGNOSI

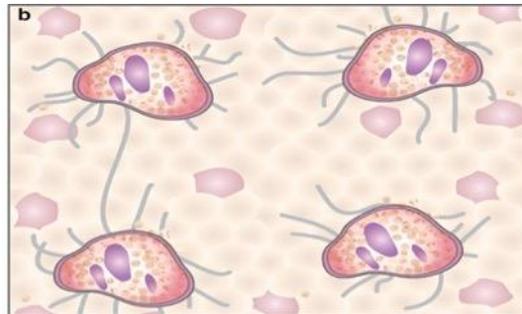


TRATTAMENTO

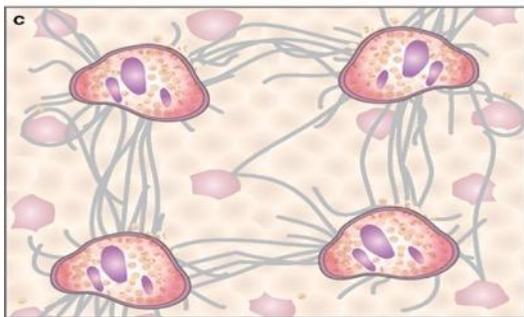
DEFINIZIONE



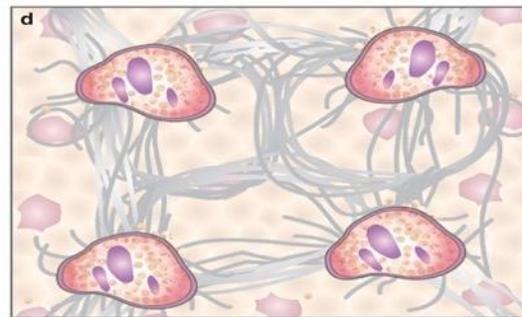
Fegato normale



Fibrosi porto-portale



Fibrosi porto-centrale

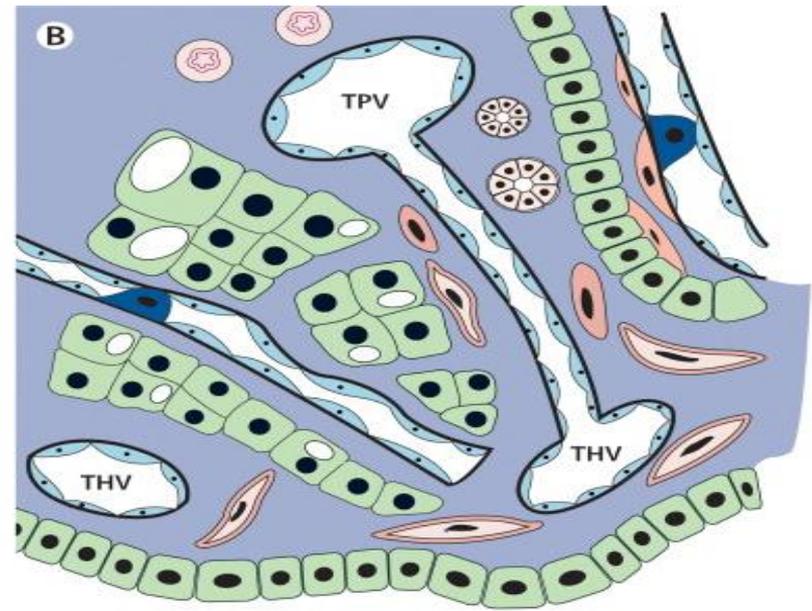
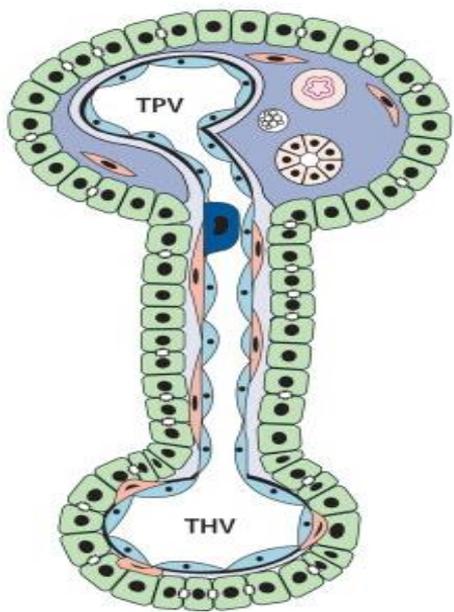


Noduli di rigenerazione

DEFINIZIONE

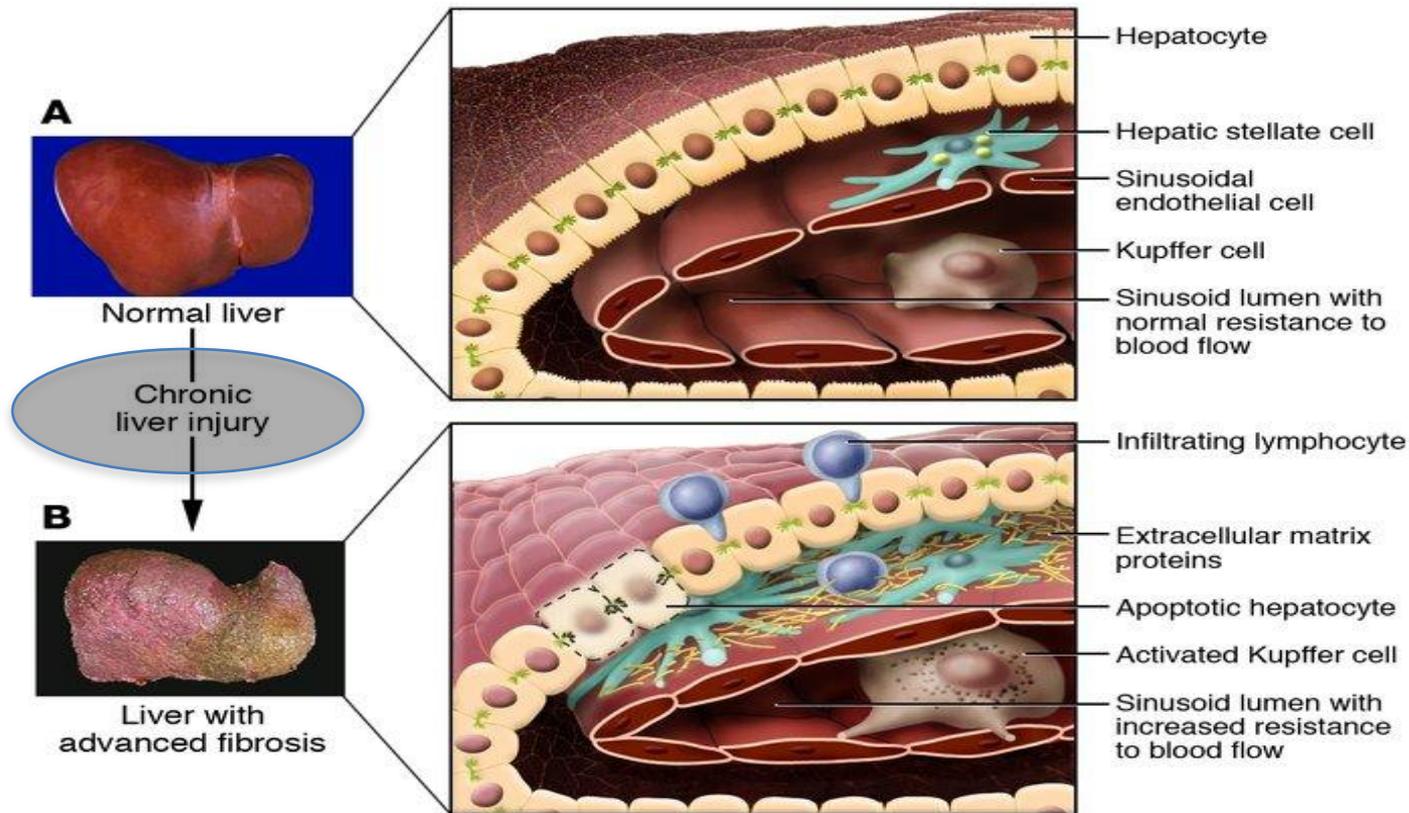
Fegato normale

Cirrosi

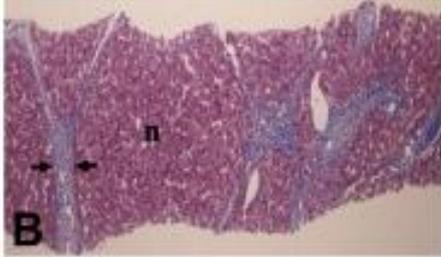


- Artery
- Bile duct
- Endothelium
- TPV Terminal portal vein
- THV Terminal hepatic vein
- Myofibroblast
- Regenerative nodule of hepatocytes*
- Fibrous tissue
- Kupffer cell
- Hepatic stellate cell

DEFINIZIONE



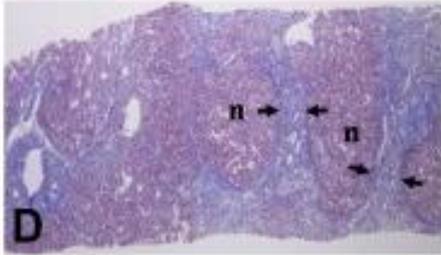
CIRROSI: CLASSIFICAZIONE DI LAENNEC



4A Cirrhosis, mild, definite, or probable **+++**

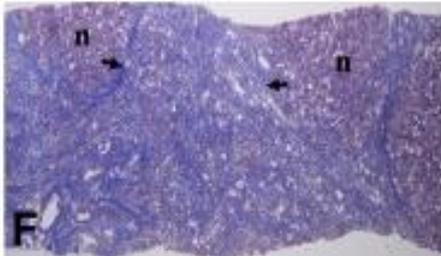
Marked septation with rounded contours or visible nodules

Most septa are thin (one broad septum allowed)



4B Moderate cirrhosis **++++**

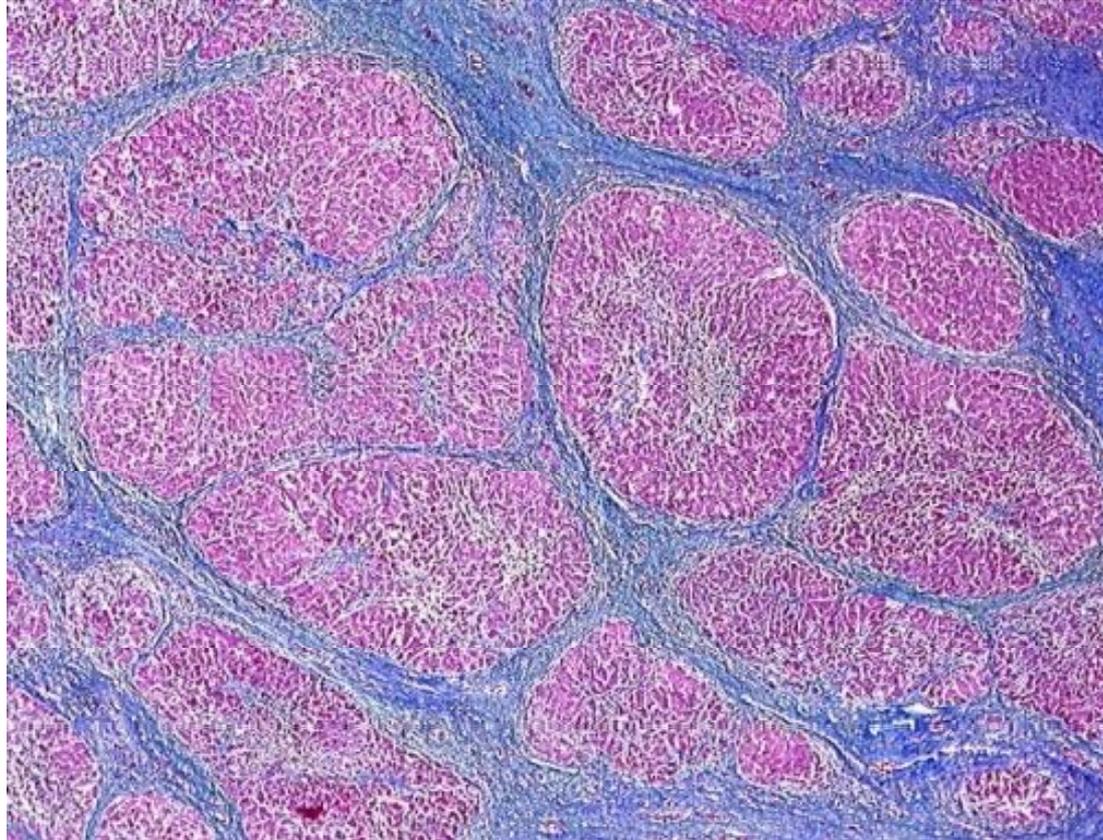
At least two broad septa, but no very broad septa and less than half of biopsy length composed of minute nodules



4C Severe cirrhosis **+++++**

At least one very broad septum or more than half of biopsy length composed of minute nodules (micronodular cirrhosis)

DEFINIZIONE



CLASSIFICAZIONE DELLA CIRROSI

	F1-F3	F4a	F4b	F4c
Istologia	F1-F3	F4a	F4b	F4c
Evoluzione	stabile	stabile	stabile	scompenso
Segni/Sintomi	assenti	assenti	assenti, varici	complicanze
Gradiente	< 6 mmHg	6-10 mmHg	10-12 mmHg	> 12 mmHg
Biologia	fibrogenesi	(micro)- trombosi	angiogenesi	carcinogenesi
Elastografia	8-14 KPa	← 14-75 KPa →		

Beyond “Cirrhosis”

A Proposal From the International Liver Pathology Study Group

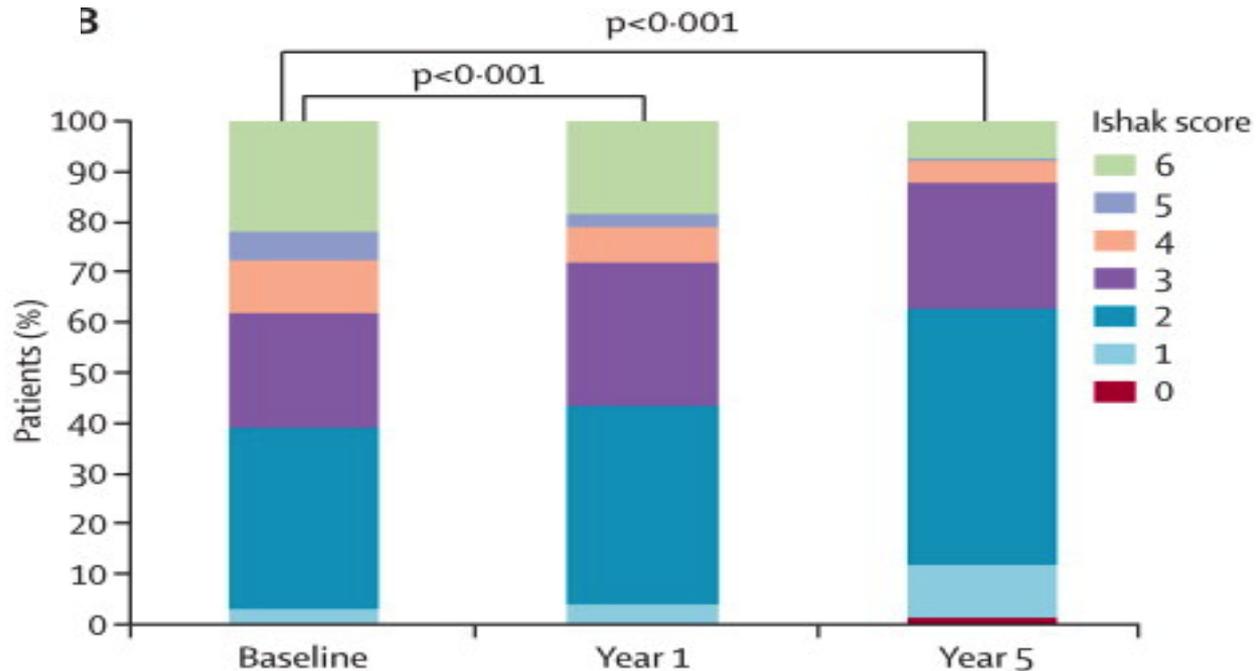
Prodromos Hytioglou, MD,¹ Dale C. Snover, MD,² Venancio Alves, MD,³ Charles Balabaud, MD,⁴ Prithi S. Bhathal, MD,⁵ Paulette Bioulac-Sage, MD,⁶ James M. Crawford, MD,⁷ Amar P. Dhillon, MD,⁸ Linda Ferrell, MD,⁹ Maria Guido, MD,¹⁰ Yasuni Nakanuma, MD,¹¹ Valerie Paradis, MD,¹² Alberto Quaglia, MD,¹³ Neil D. Theise, MD,¹⁴ Swan N. Thung, MD,¹⁵ Wilson M.S. Tsui, MD,¹⁶ and Dirk J. van Leeuwen, MD¹⁷

Am J Clin Pathol 2012;137:5-9

*„We recommend replacing the word **cirrhosis** with the term “**advanced stage**” when reporting the diagnosis of chronic liver diseases“.*

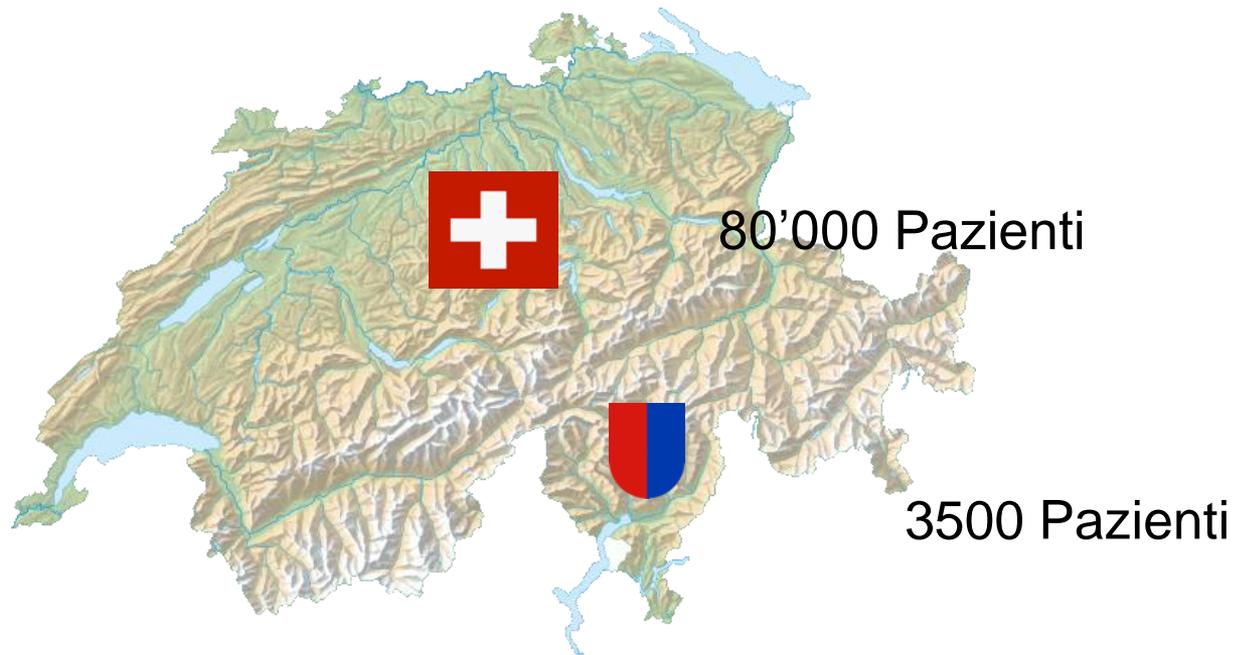
CIRROSI = CONDIZIONE REVERSIBILE

Pazienti HBV durante il trattamento con Tenofovir

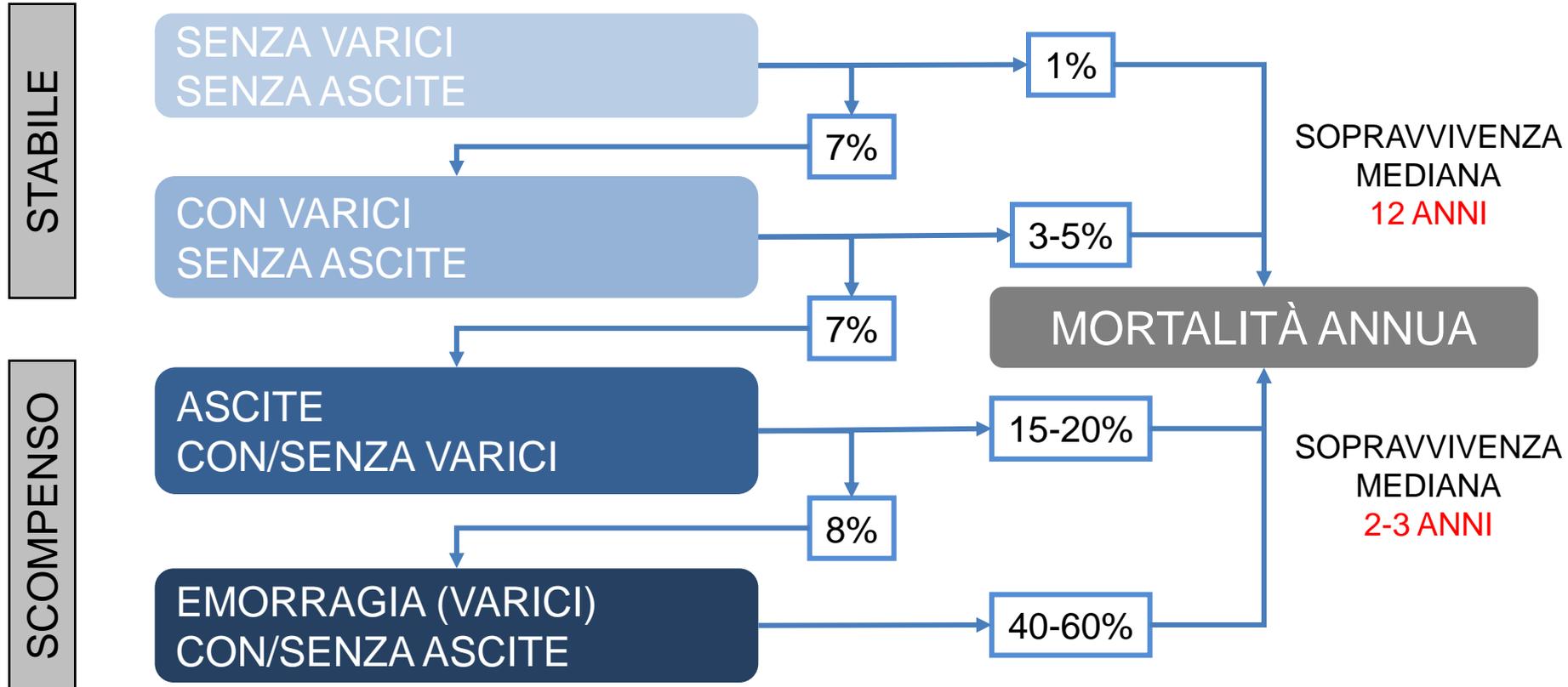


Prevalenza della cirrosi in Svizzera

0.15% - 1%



PROGNOSI NEI PAZIENTI CIRROTTICI



PROGNOSI NEI PAZIENTI CIRROTTICI

Child-Pugh

Bilirubina, Albumina, Quick, Ascite, Encefalopatia

	A (5-6)	B (7-9)	C (10-15)
1-YS	100%	80%	45%
2-YS	85%	60%	35%

MELD

Bilirubina, INR, Creatinina

	< 9	10-19	20-29	30-39	> 40
3-MS	98%	94%	80%	50%	28%

TAKE HOME MESSAGE 1

Cirrosi = Epatopatia Cronica Avanzata

Condizione reversibile

Scompenso = peggioramento della prognosi

SOMMARIO

CIRROSI = EPATOPATIA CRONICA AVANZATA



DEFINIZIONE



CAUSE

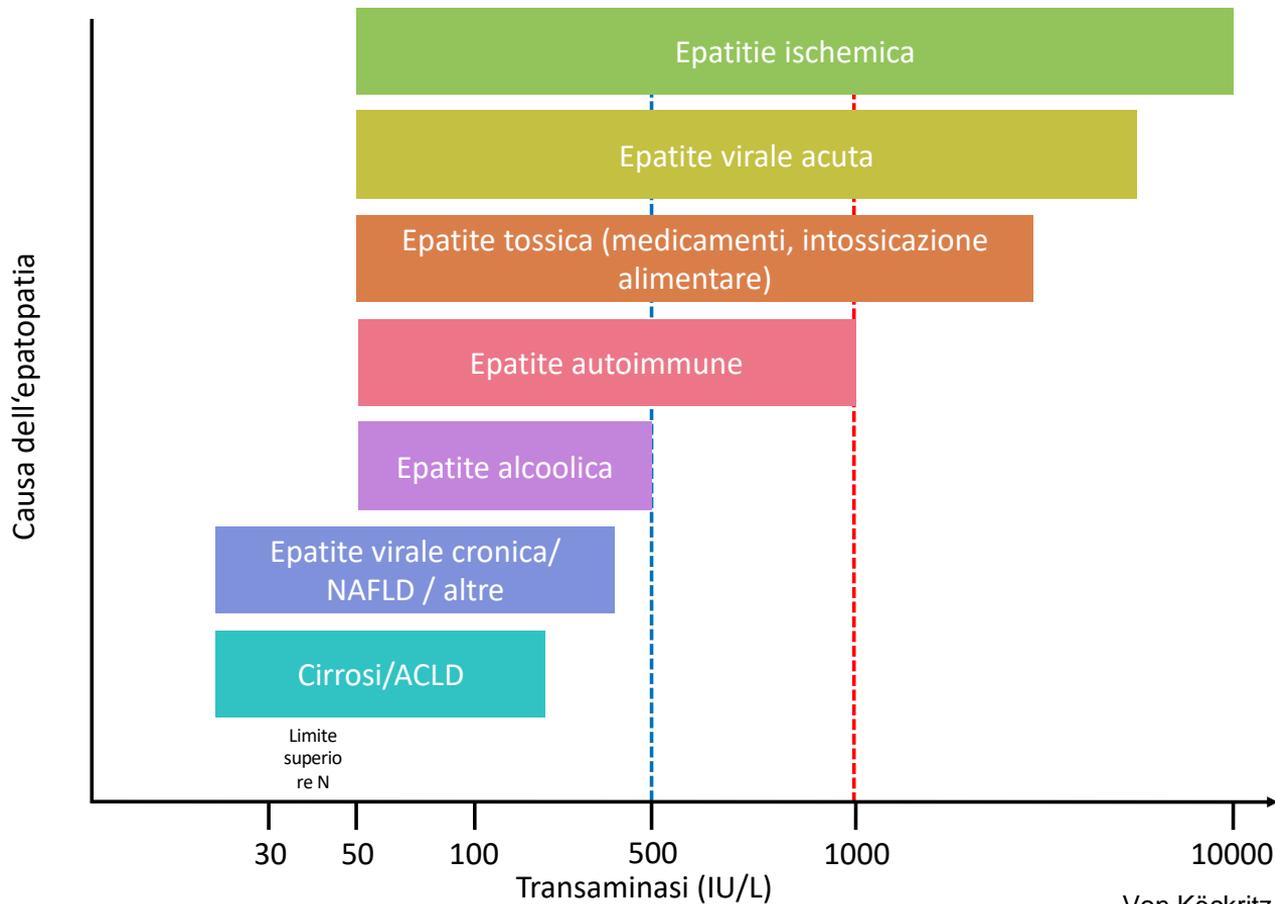


DIAGNOSI



TRATTAMENTO

CAUSE



CAUSE

EPATITE
VIRALE (B,C)

Anti-HCV, Anti-HBc, Anti-HBs, (HBs-Ag)

ALCOOL

marker-negativo!

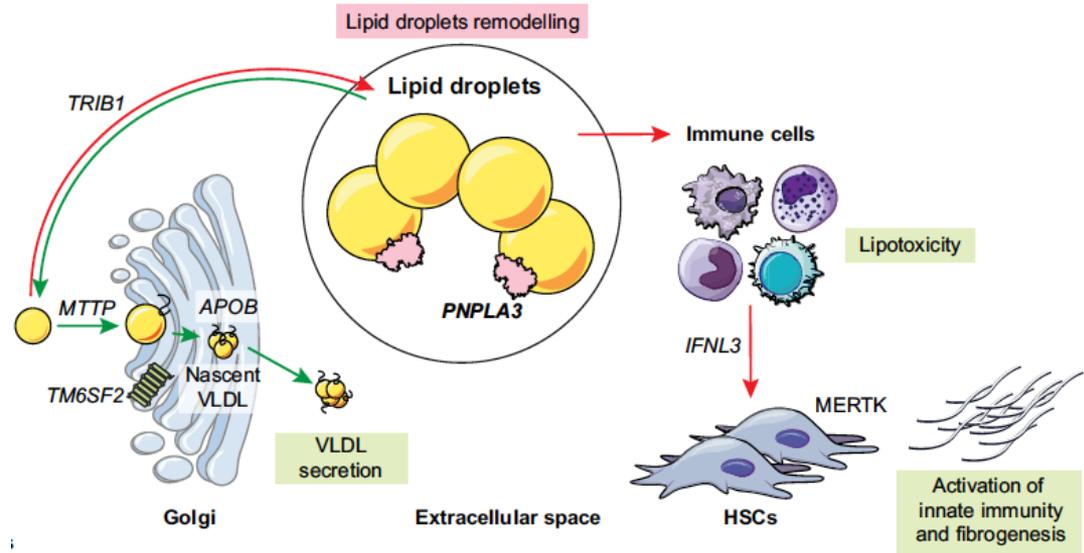
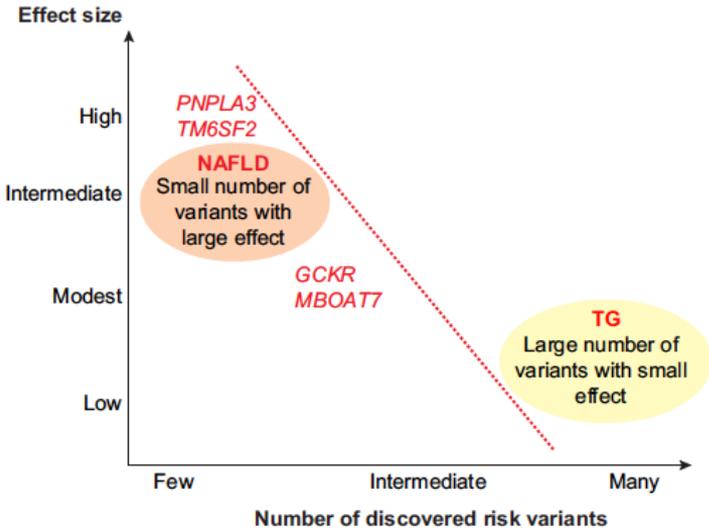
GGT, MCV, AST>ALT, ferritina,
Carbohydrate-Deficient-Transferrin (CDT),
Etil-Glucuronide

FEGATO GRASSO
(NAFLD)

marker-negativo!

Ecografia, Fibroscan (CAP), ferritina,
HOMA Score (insulina, glucosio),
PNPLA3, TM6SF2

CAUSE

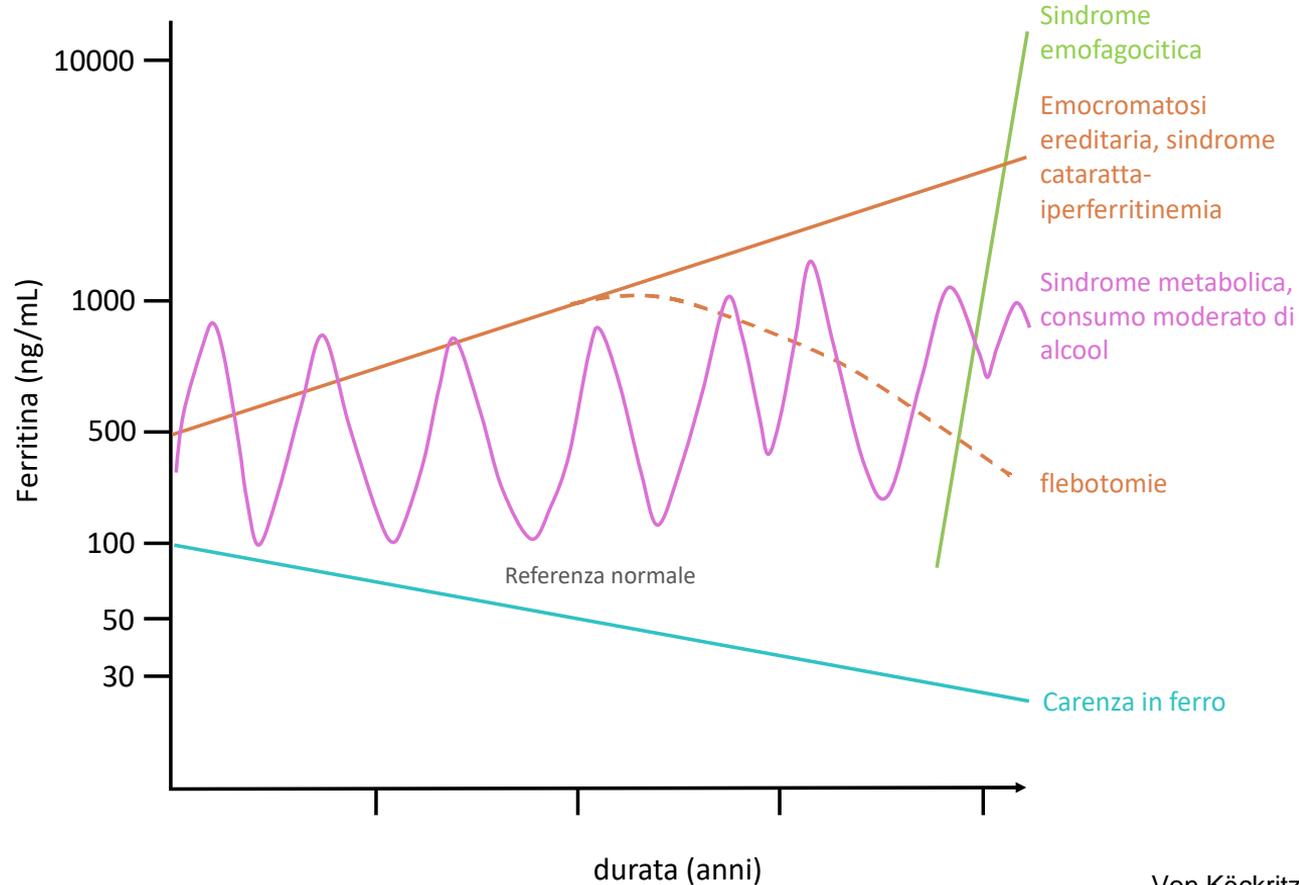


CAUSE

M. Wilson	Ceruloplasmina, rame urina 24h
Alfa-1 antitripsina	Alfa-1 AT, immunofenotipo
Epatite autoimmune	Autoanticorpi (ANA, SMA, LKM), IgG
Colangite biliare primaria	Anti-mitocondrio (M2), IgM
Emocromatosi	Saturazione della transferrina, ferritina, HFE C282Y, C282Y/H63D
Colangite sclerosante primaria	MRCP, pANCA

marker-negativo!

FERRITINA



SOMMARIO

CIRROSI = EPATOPATIA CRONICA AVANZATA



DEFINIZIONE



CAUSE



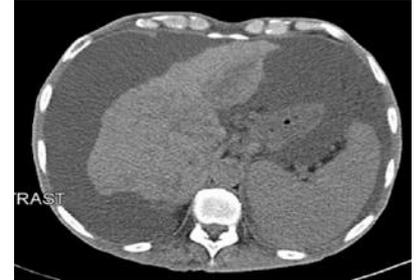
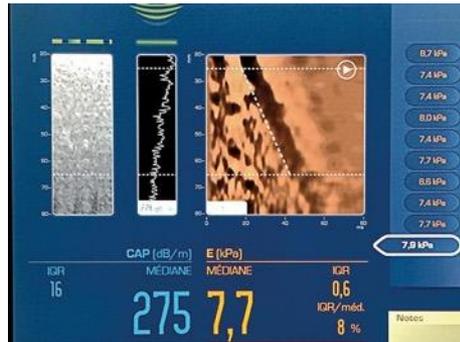
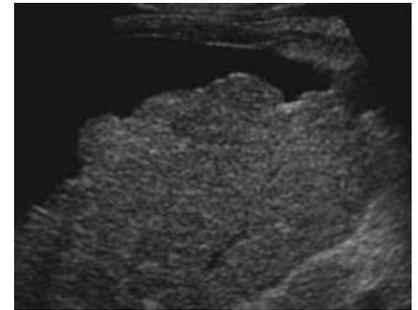
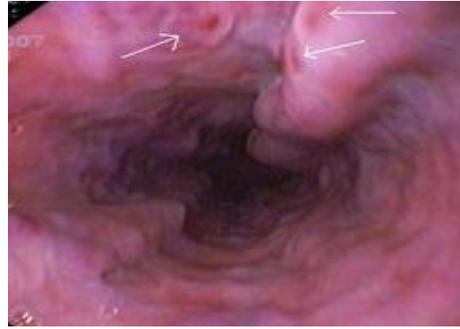
DIAGNOSI



TRATTAMENTO

DIAGNOSI

Quando sospettare un'epatopatia cronica avanzata



DIAGNOSI

Fibrosis-4 (FIB-4) Index for Liver Fibrosis ☆

Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.

When to Use ▾

Pearls/Pitfalls ▾

Why Use ▾

Age years

AST
Aspartate aminotransferase U/L

Platelet count $\times 10^9/L$ ↔

ALT
Alanine aminotransferase U/L

1.29 points

Fibrosis Stage: 0-1

FIB-4 scores <1.45 are 81% sensitive (NPV 90%) to rule out advanced fibrosis.

Copy Results 📄

Next Steps >>>



DIAGNOSI

SOSPETTO CLINICO DI CIRROSI

BASSO

Nessun segno o sintomo
Sintesi normale (Alb, Q)
Epatopatia di corta durata
Ecografia normale

INVESTIGAZIONI NON INVASIVE
FIB-4 + Fibroscan

**CIRROSI
ASSENTE**

ALTO

Segni clinici o sintomi presenti
Sintesi diminuita
Epatopatia di lunga durata
Ecografia patologica

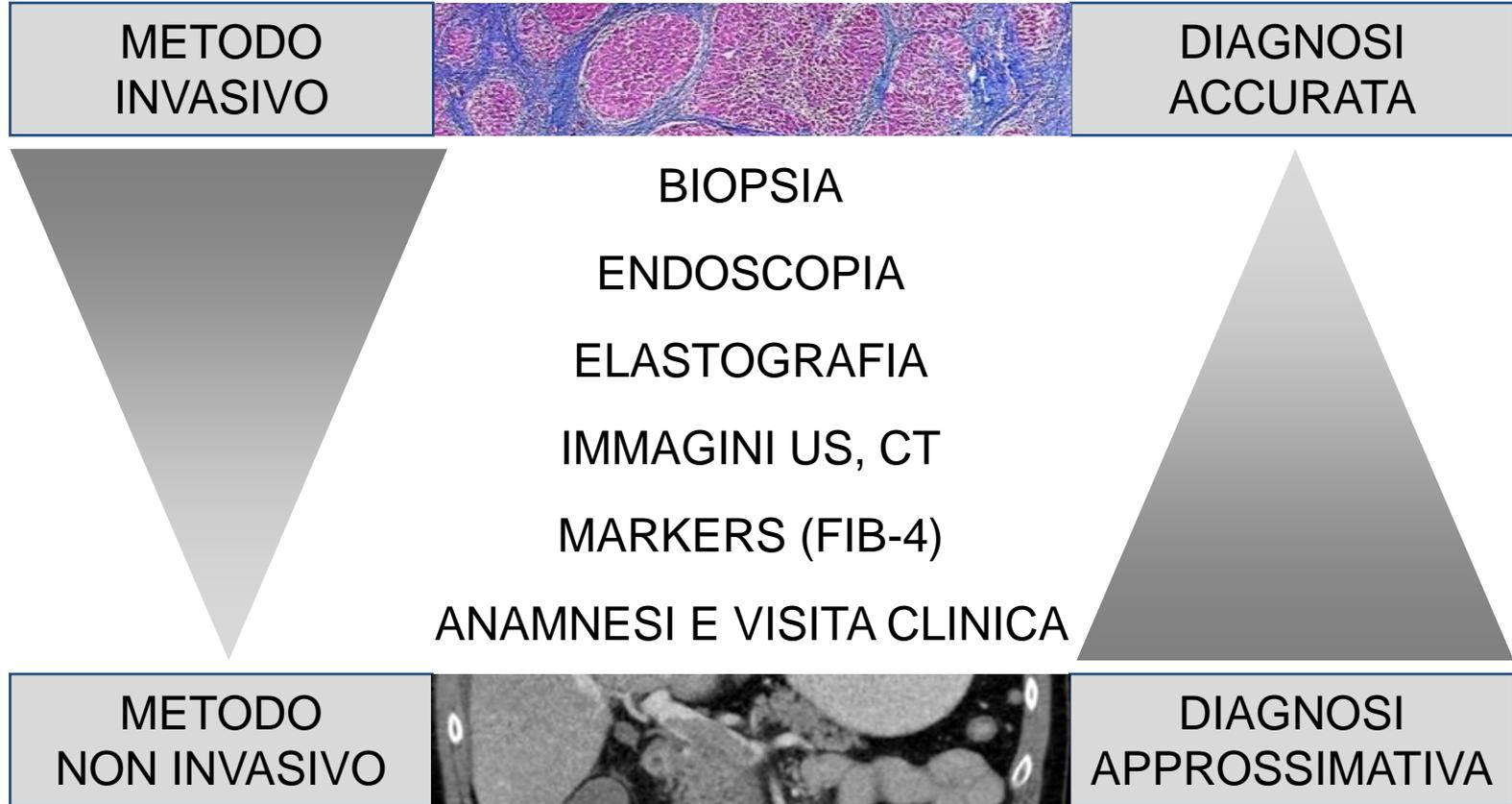
Conferma con FIB-4 + Fibroscan
BIOPSIA NON NECESSARIA

CIRROSI

DIAGNOSI NON CHIARA

BIOPSIA EPATICA

DIAGNOSI



TAKE HOME MESSAGE 2

Valori di laboratorio selezionati permettono di stabilire la causa dell'epatopatia (non sempre!)

La biopsia non è necessaria, se altri metodi permettono una diagnosi accurata

SOMMARIO

CIRROSI = EPATOPATIA CRONICA AVANZATA



DEFINIZIONE



CAUSE

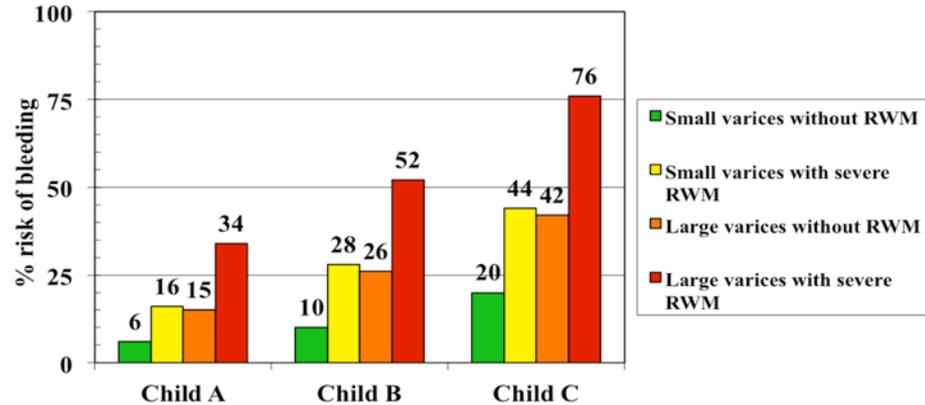
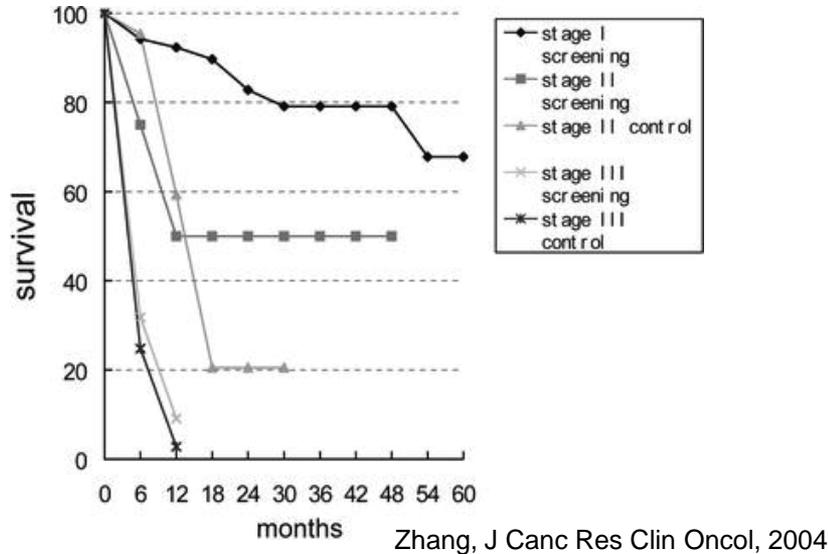


DIAGNOSI



TRATTAMENTO

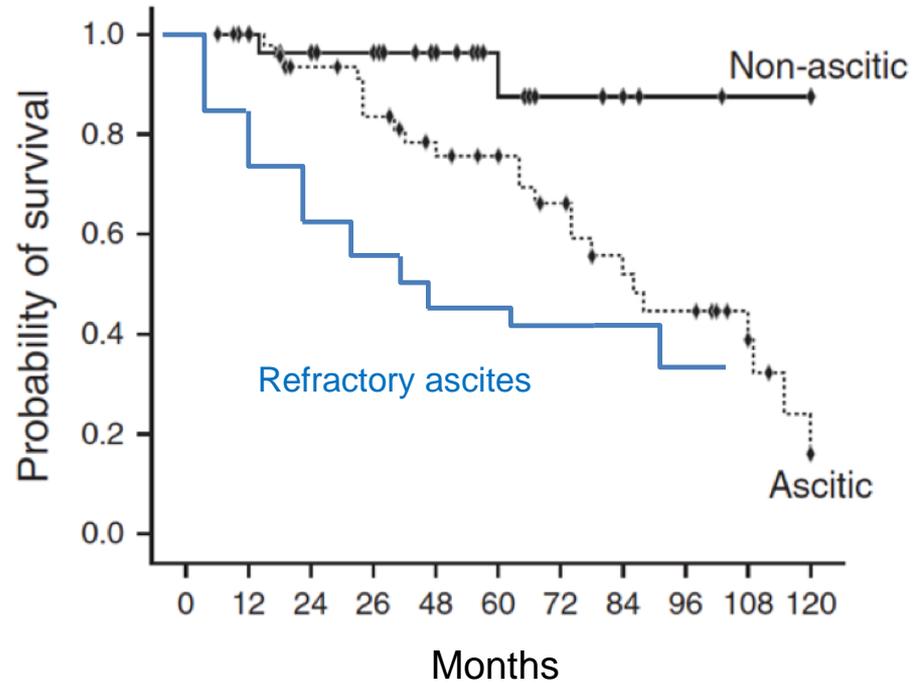
CIRROSI = EPATOPATIA CRONICA AVANZATA



1. Screening del carcinoma epatocellulare con ecografia ogni 6 mesi

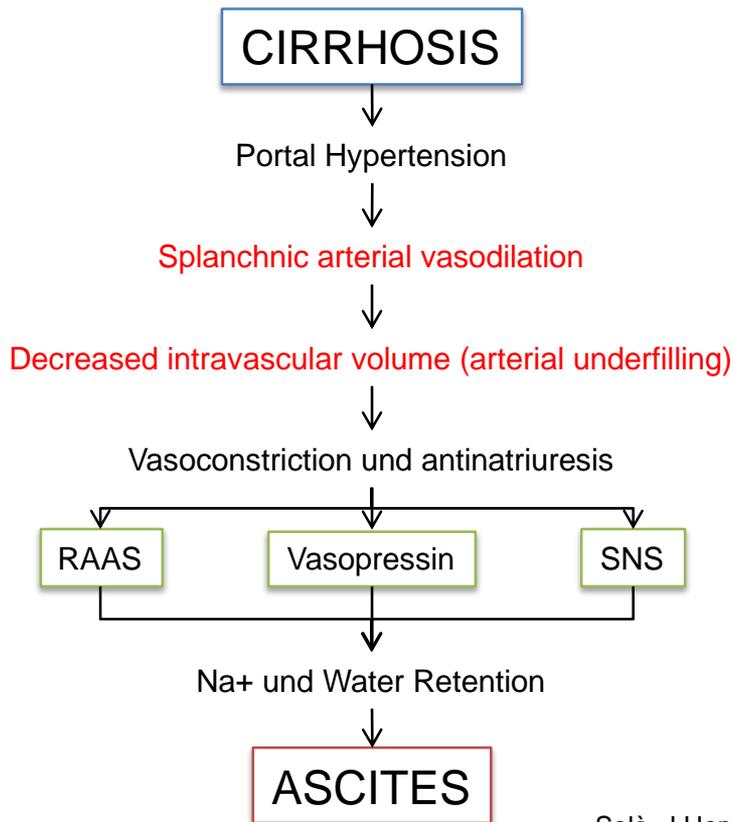
2. Ricerca di varici esofagee (gastroscopia) in particolare se trombociti < 150 G/L e Fibroscan > 20 KPa

ASCITE



ASCITE

Meccanismi



Possibili trattamenti

Trattamento della causa dell'epatopatia cronica avanzata, trapianto

Beta-bloccanti non selettivi, **Shunt Portosistemico Transgiugulare Intraepatico (TIPS)**

Albumina

Diuretici

Dieta povera in sale

Paracentesi
Alfapump

ASCITE

Paracentesi

possibile in studio/ambulatorio

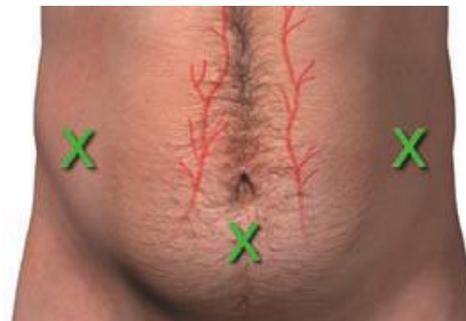
controllo ecografico facoltativo

complicanze molto rare

valori alti di INR non sono una
controindicazione

prudenza quando TC < 40 G/L

sostituzione con albumina (8 g/L)



TRATTAMENTO DELL'ASCITE

Spironolattone (Aldactone®) 100 mg -> 400 mg

o Eplerenone (Inspra®) 25mg -> 50 mg

Furosemide (Lasix®) 40 mg -> 160 mg

o Torasemide (Torem®) 10mg -> 40 mg

Controlli regolari (potassio e creatinina)

Dieta povera in sale (?)

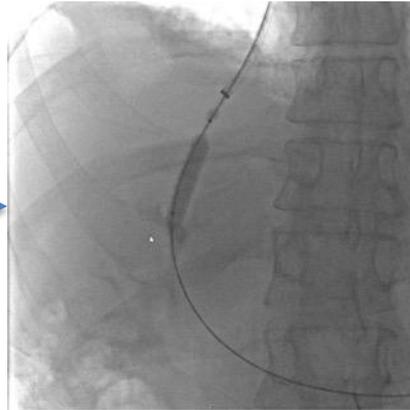
Evitare gli AINS (insufficienza renale)

TRATTAMENTO DELL'ASCITE

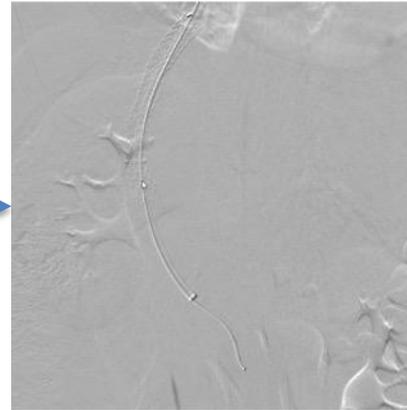
TIPS = transjugular intrahepatic portosystemic shunt



Vena porta



Dilatazione

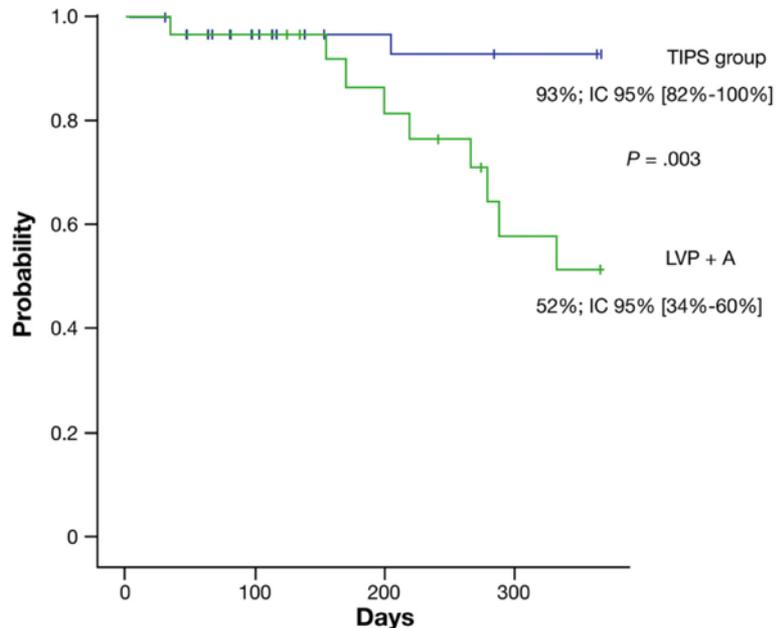


TIPS



Angiografia

TRATTAMENTO DELL'ASCITE



	0	100	200	300	360
TIPS group	29	27	27	25	24
LVP + A	33	27	16	9	8

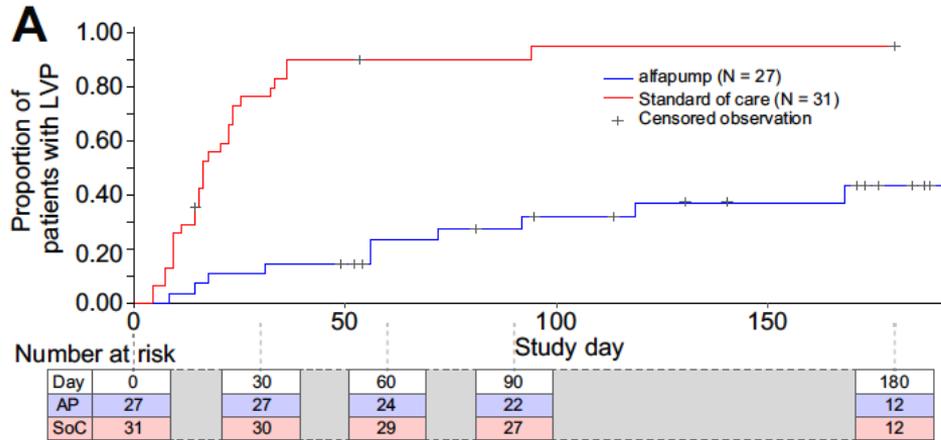
Outcome	TIPS (n = 29)	LVP+A (n = 33)
No. of paracenteses per patient, mean \pm SD	1 \pm 1	10 \pm 7 ^{***}
Volume extracted, L/patient, mean \pm SD	6 \pm 10	64 \pm 47 ^{***}
Albumin infusion, g/patient, mean \pm SD	39 \pm 70	550 \pm 458 ^{***}
Days in hospital, mean \pm SD	17 \pm 28	35 \pm 40 [*]
Patients with OHE, n	10	11
Episodes of OHE per patient, n, mean \pm SD	1.6 \pm 0.7	1.7 \pm 0.8
Patients with OHE grade >2, n	4	7
Patients with PHT-related bleeding, n	0	6 ^{**}
Patients with hernia-related complication, n	0	6 ^{**}
Patients with HRS, n	0	1
Patients with SBP, n	0	2
Patients with sepsis, n	5	9

Automated low flow ascites pump

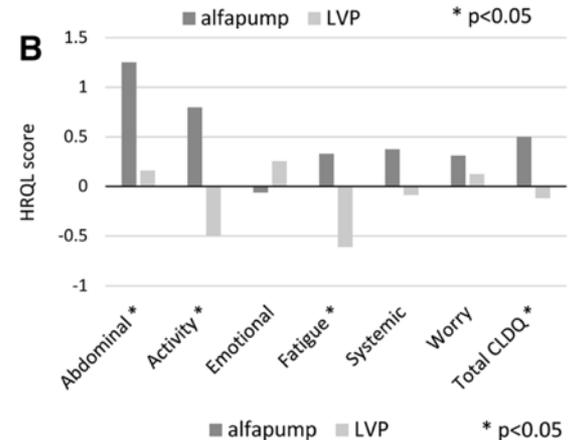
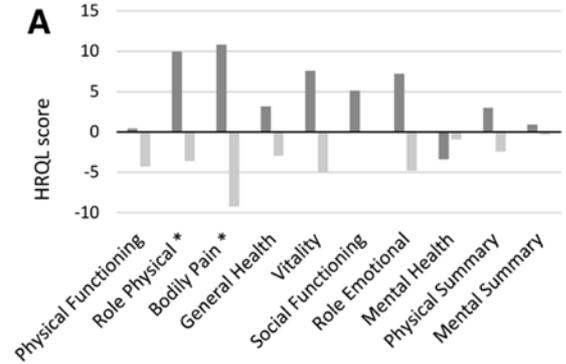


Automated low flow ascites pump

Studio randomizzato in 58 pazienti

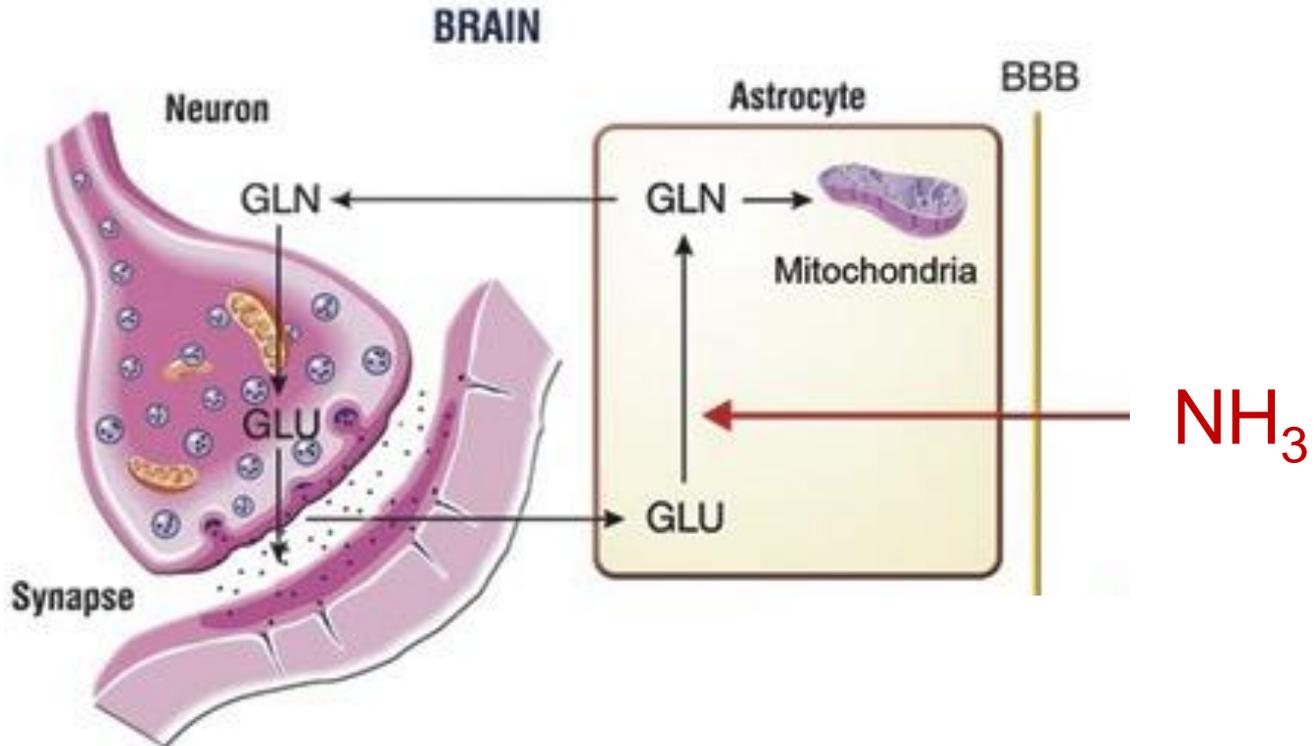


Bureau, J Hepatol, 2017



Stepanova, Qual Life Res, 2018

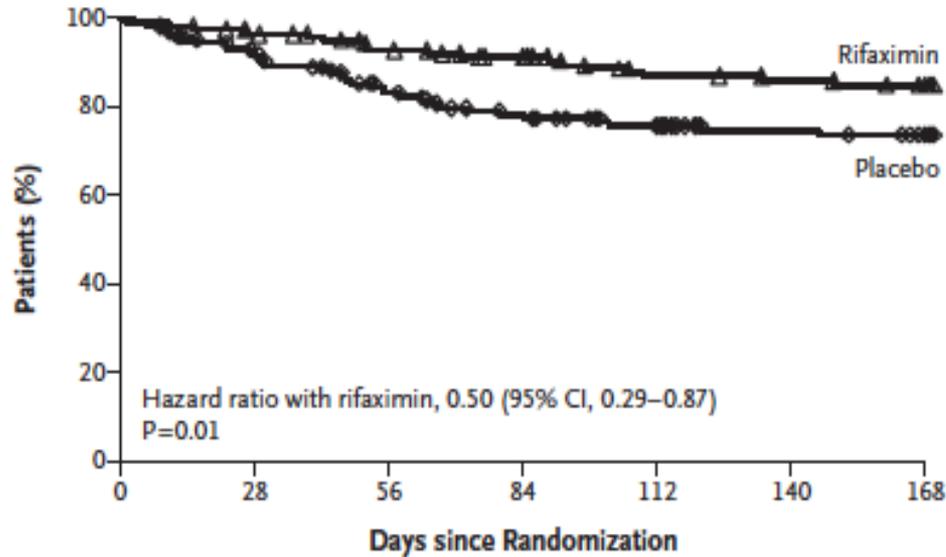
ENCEFALOPATIA EPATICA



La glutamina è osmoticamente attiva

ENCEFALOPATIA EPATICA

B Time to First HE-Related Hospitalization (Key Secondary End Point)



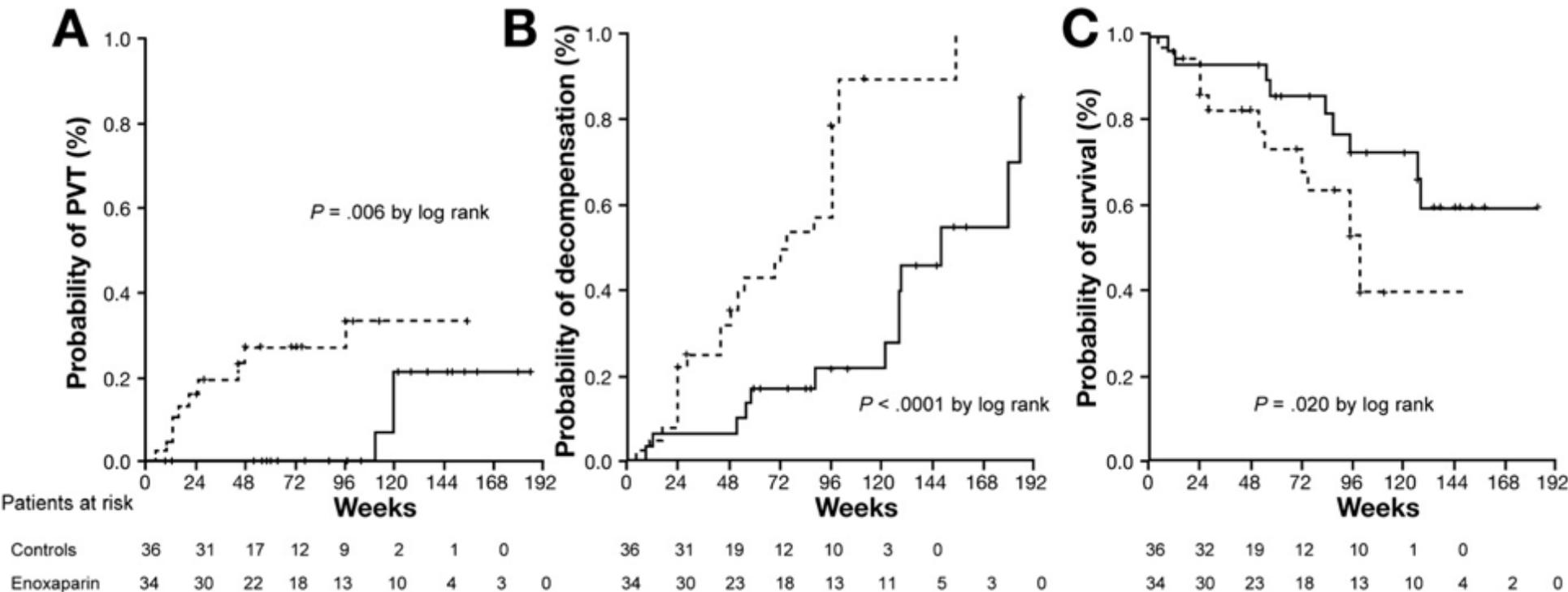
Rifaximina 550 mg 2/T
(Xifaxan)

Lactulosio 15 mL 3/T

Attenzione:

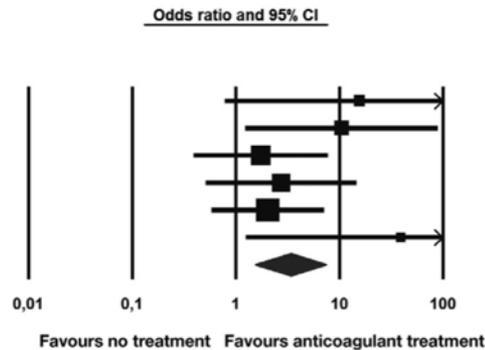
- *Trattare le possibili cause (infezioni, insuff. renale, emorragia GI)*
- *Evitare le benzodiazepine*

Anticoagulazione in pazienti cirrotici



Anticoagulazione in pazienti cirrotici

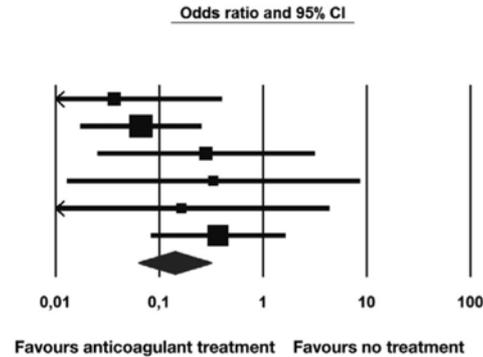
Meta-analisi sull'anticoagulazione nei pazienti cirrotici con una trombosi venosa portale



33 % 53 %

n = 217

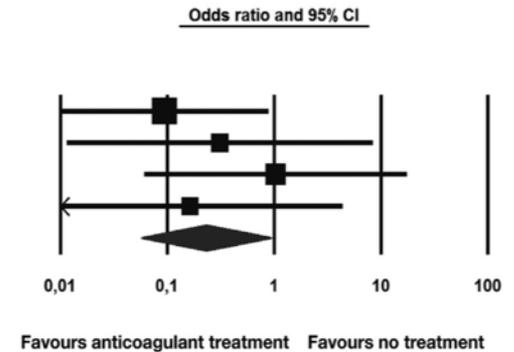
Ricanalizzazione
completa



9 % 33 %

n = 225

Progressione della
trombosi



2 % 12 %

n = 158

Emorragia da varici

TAKE HOME MESSAGE 3

Cirrosi = ecografia ogni 6 mesi e gastroscopia

Ascite e encefalopatia si possono trattare a casa

Possibile ruolo dell'anticoagulazione