Telfer Barclay Reynolds MD
Portal Hypertension Update

Bruce A. Runyon, MD FAASLD

Fellow of the Royal Society of Medicine

Special Hepatology Consultant to the IHS, Shiprock, NM

Clinical Professor of Medicine, UNM

Telfer Barclay Reynolds MD

- At USC 1944-2004=60 Years
- Dame Sheila Sherlock's 3rd Fellow
- Started USC Liver Unit 1954
  - John Wesley ~100 Beds
  - Rancho Los Amigos 86 Beds
- Lived to Care for Liver Patients
  - ~50 Years of Solo Consultation
  - ~10 Months/Year at Rancho
  - Fluid/Electrolyte Rounds
  - ER Early AM Scouting for Patients
- Inspired 100s of Trainees/Faculty

Disclosures

- Industry Affiliations: Author of Topics on Ascites, HRS & HypoNa in Cirrhosis in UpToDate
- Editor for Complications of Cirrhosis for UpToDate
- Off-Label Uses of Meds: Baclofen, Midodrine

Science

- Breakthrough Awards
- "Oscars for Scientists"
- Peter van Niewenhuizen
- "Science is a rock of truth in a sea of fake news"

Portal Hypertension

- Abstracts & News from AASLD/Backgr
- PP as a Target Awaits Noninv Measure
- MAP/Home BPs
- Meds: Overused/Underused
- Perfused Hepatic Mass
- Magical Numbers
- ODTAA Syndrome
- Recompensation
- Phrases To Use/Not Use
- Palliative Care/CofC

J Hepatol 2014;60:643-53
UpToDate
NEJM 2016;375:767-77
Liv Transp 2008;14:1100-6
JAMA 2006;295:2168-76

Really Big News

- LO3 Terlipressin 300 Pt RCT for Type 1 HRS, 200/100
- ~30% Response in Cr—2x Placebo Halves ICU LOS but 2x Sepsis
- Only 20% of Terli Needed RRT p TP
- Ikaria to Mallinckrodt
- Predicted to Get FDA Approval
- Perhaps Available Nov 2020
- Satellite Meeting

Hepatology 2019;70:1A-1380A
2348 Abstracts

Big News: Ascites PG

- New Practice Guideline/Guidance
- Chairman: Ray Kim
- Authors: Wong, Angeli, Gines, Garcia-Tsao, Mitra
- Ray Says to be Published Early 2020—Yeah Right
- Mine Took 2 Years to Get Published

Less Big News: Renal

- #98 RCT Oral NAC Prior to Contr CT
- 4 Doses of 1200 mg Prior & Day Of
- 6% vs 17% Contrast-Induced Neph
- Risk Factors for CIN: Cyst C, DM, Diur
- #305 Meta of 9 RCTs/620 Pts of Rx p LVP: Albumin, Terli, Midodrine, etc
- Midodrine x 3 Days was Superior to Albumin in Preventing PICD
- I Advise Giving Enough Midodrine to Get MAP >82. Go Up w Each Dose

Anti-Coagulation

- Olden Days: Never Considered It
- Italian RCT of Enoxaparin in Gastro 2012;143:1253-60 Survival Advantage
- New Data Global Coag: Nl, Hypo, Hyper
- #147 National Cohort: 2879 w Cirr
- Warfarin HR vs No AC: Death/Decomp 0.54
- DOACs HR 0.39
- DOACs vs Warfarin for Bleeding: HR 0.32
- #418 Retro Apixaban for New/Recent/Progr PVT: 68 Complete/Part Recan, 18% Bled

Anti-Coagulation

- #448 Retro Non-Cirr PVT, 161 Met Criteria
- 58% on DOACs vs Warf or LMWH
- 11% Bled, No Diff DOAC vs Traditional
- #794 Pharma Database: 16301 Pts
- Comp: No Increased Bleeding w AC or AP
- Decomp: HR 1.32 of Bleeding
- #802 Retro Fondaparinux vs LMWH for PVT
- 1/3 Fonda vs 2/3 LMWH
- Resolution of PVT at 36 mo: 77% vs 51%

Anti-Coagulation

- My Interpretation:
  - I Have Had Terrible Experience with Warf
  - Rule Out Malignant with Doppler of Clot
  - Individualize
  - Consider DOAC or LMWH for New/Progressive PVT
  - Usually No Time to Band Varices to Oblit
  - 2 Vein Clot: Pressure is Much Higher
  - MVT (Always Sx), Must Rx
  - Depends on Formulary

Imaging

- #150 Deep Learning of CT/MR in Detecting CS-PHT: 2 Prospective Cohorts, PP in 14 D
- 407 Pts with Cirrhosis & 272 Controls
- AUC vs PP: 0.94-0.998
- #241 Prospective Novel Quant of Surface Nodularity on Non Con MR vs PP: 153 Cirr vs 110. AUC for PHT 0.809, Se 0.820, Sp 0.704
- #399 House Officers Repeat CT Too Soon
- #425 Triph CT Rules Out Osteoporosis: NPV >90%

Imaging & Meds

- #805 Prospective Measurement of L & S Stiffness by MRE. C Index 0.948 in Predicting Esophageal Varices
- #55 National Database 31k Decomp: 51% Rec'd BB, Only 17% Took Them, NSAIDs Given to >10% of Pts w Ascites & >35% of HRS or SBP. 50% Opiates, 14% Benzos
- #744 National Database 131k Discharges of Cirr: 51% Received Opiates in House & 27% Discharged on Opiates
- Scary!

Medications in Cirrhosis

- Abnormal Metabolism
- Limited "Reserve"
- Weigh Risk vs Benefit of Each One
- Acetaminophen ≤4000 mg/d Is OK
  - Pts with Cirrhosis Tolerate Tylenol Better than Nls
  - Up to 44% of Nls Blip ALT up to 650 on 4000 mg/d
- Tramadol When Acetaminophen Is Not Enough

Clin Toxicol 2002;40:3-20
JAMA 2006;296:87-93
Hepatology 2004;40:10-15

Medications in Cirrhosis

- No NSAIDs x Rare 81 mg ASA
- Trazodone 100 mg or Hydroxyzine 25 mg HS (Hep 2004;40:10-15)
  - Rather Than Benzos for Insomnia
- Minimize Narcotics
- Minimize Benzos
- "It Is Not The Meds that I Prescribe that Will Help You. It is the Pills that You Actually Take"

Palliative Care

- 72% Poor Quality of Life
- 40% of Care Givers—"Major Deleterious Impact on Life"
- Distinct from Hospice—Limited Lifespan
- PC Goals: Provide End-of-Life Care, Alleviating Physical, Psychosocial, and Spiritual Pain Associated with Chronic Illness

Liver TP 2019;25:787-96
Liver TP 2019;25:859-69

Palliative Care

- #208 Palliative Care RN on Team: 21% of 287 Decompensated Referred
- #642 85% of Decomp Died in House, 70% in ICU. 60% Ventilated. 47% RRT. 31% Had PC Consult as Inpt, 5% as Outpt
- #743 <50% of PC Eligible Pts were Referred

Palliative Care

- Intubation: 48% vs 60%
- In-Hospital Death: 23% vs 74%
- 84% of Hospitals >300 Beds Have PC
- PC Can Be Continuity of Care
- Only 32% of Hepatologists Use Inpatient PC and only 11% Use Outpatient PC
- Why Not Think About It?
- Why Not Refer Early?
- Punt "Difficult Conversation"

Liver TP 2019;25:787-96
Liver TP 2019;25:859-69

NSBBs

- #100 mRNA Signature Predicted Response to BB
- #428 Retro of 393 Readm for HE: 90% of Pts who Ever Used BB vs 45% of Pts who Never Used BB

Propranolol & Ascites

- "Cirrhosis Cures Hypertension"
- Lebrec Told Us BB Do Not Decr BP
- Accumulating Data Suggesting Harm in Refractory Ascites
  - Prospective Study: 5 mo vs 20 mo Survival

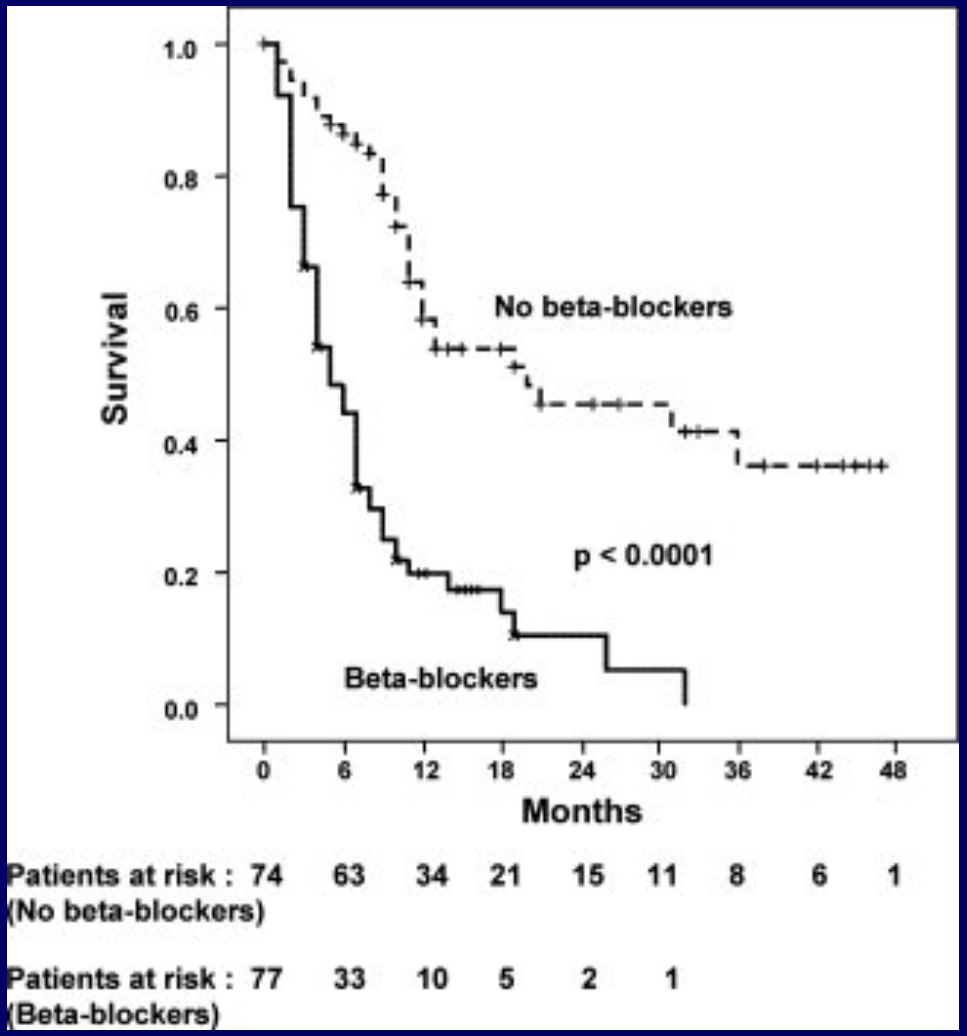
NEJM 1981;305:1371-4
Hepatol ogy 2010;52:1017-22
J Hepatol 2011;55:794-9
Gut 2012;61:967-9
J Hepatol 2014;60:643-53

Beta Blockers & Survival in Refractory Ascites

- 29 Years After Original RCT
- Prospective Non-Randomized Study of 151 Pts
- 51% on Propranolol
  - 88% on >40 mg Per Day
  - 47% on 160 mg Per day

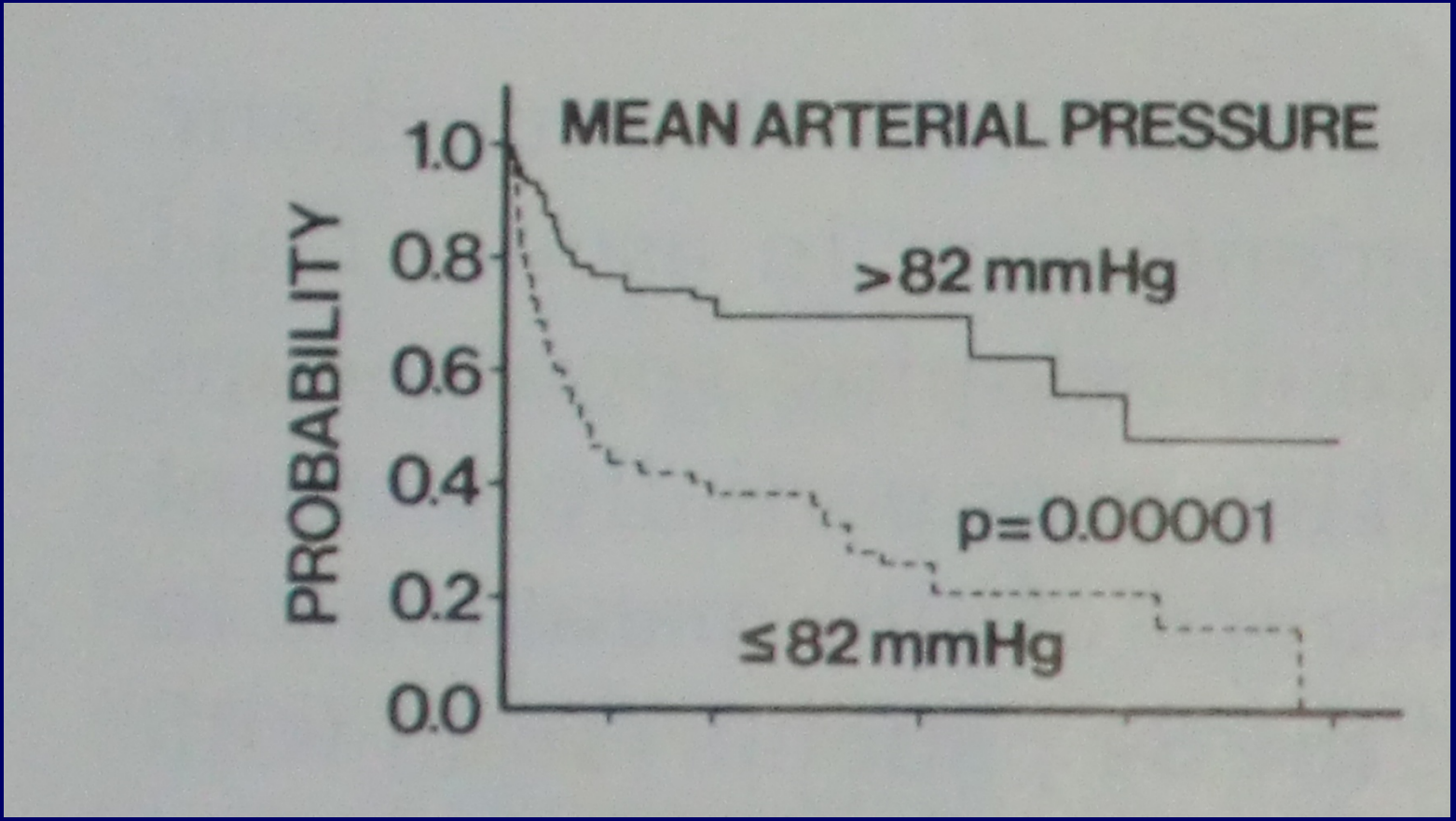
Hepatology 2010;52:1017-22

Beta Blockers & Survival in Refractory Ascites



Hepatology 2010;52:1017-22

BP & Survival in Cirrhosis

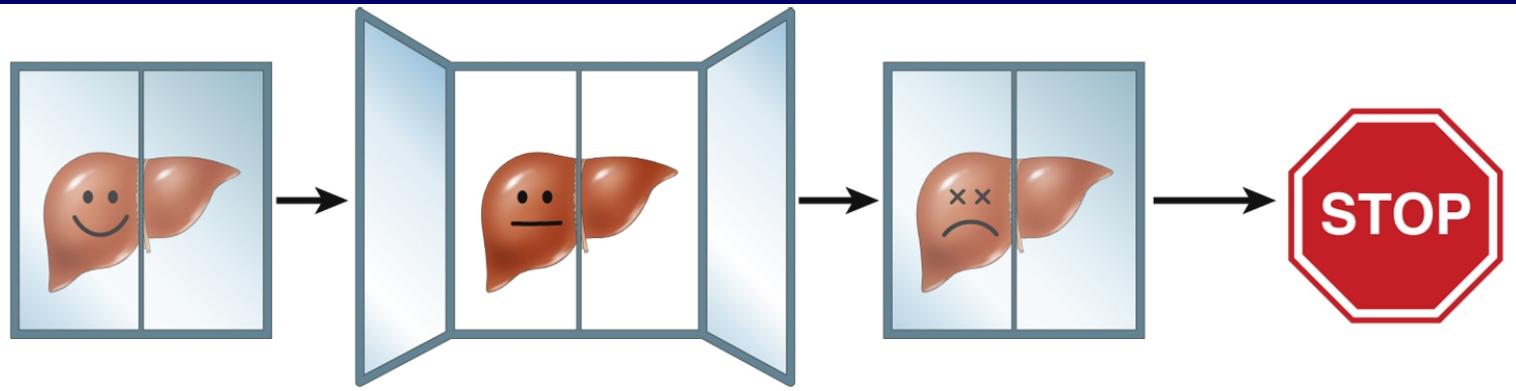


Gastroenterology 1988;94:482-7

Physicians Who Follow Their Own Patients:

- Know That Cirrhosis Cures Hypertension & Worsening Hypotension Is Problematic in Cirrhosis—Lebrec Was Wrong
- Monitor Blood Pressure
- Stop Propranolol or Other Anti-HTN When BP Drops
- Consider Banding of Varices—Power
- We Have To Be the Patient's Advocate
  - Stop BB When MAP $\leq$82, Mental Status Change, Rising Creatinine, SBP, Alc Hep

Beta Blocker "Window"



Early cirrhosis	Window opens	Window closes	Window does not re-open
• Beta-blockers are **not indicated** in early cirrhosis, may increase adverse events • Beta-blockers **may be indicated** for cardiovascular indications	• Beta-blockers are **indicated** for primary prophylaxis of variceal bleeding • Beta-blockers are **indicated** for secondary prophylaxis of variceal bleeding	• Beta-blockers are **contraindicated** under the following situations: ◦ Refractory ascites ◦ Systolic blood pressure < 100mm Hg ◦ Mean arterial pressure < 82mm Hg ◦ Acute kidney injury ◦ Hepatorenal syndrome ◦ **Spontaneous bacterial peritonitis** ◦ Sepsis ◦ Poor medical follow-up ◦ Patient noncompliance	

Gastroenterology 2014;146:1597-9

Learning from Experience

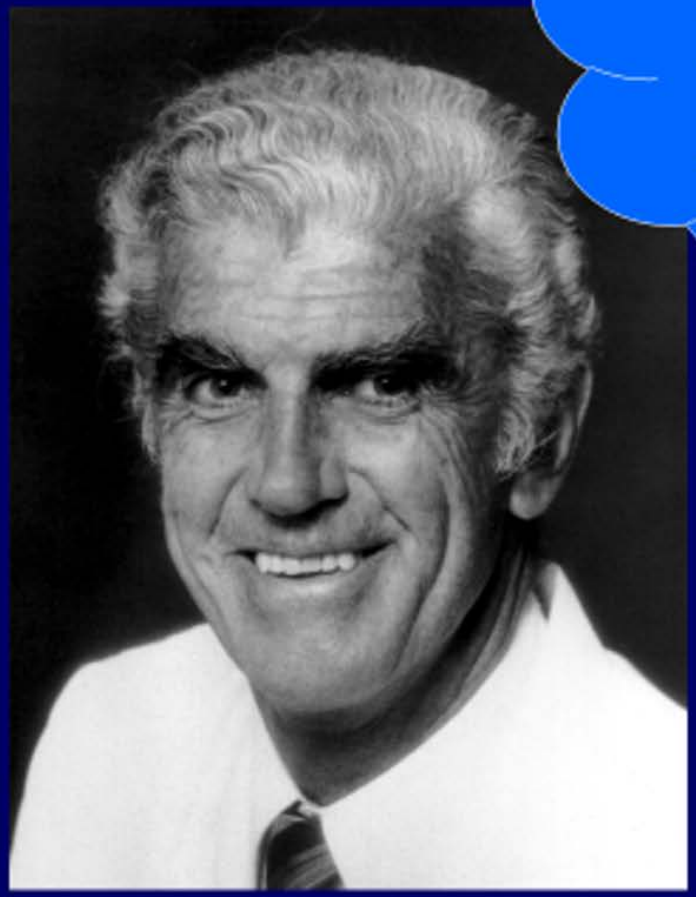
"We Must Discard Concepts That Have No Link with Experience"

Albert Einstein

"The True Test of Any Proposition is How Well It Correlates With Experimental Results And Produces a Practical Outcome"

Benjamin Franklin

"Science Commits Suicide When It Adopts a Creed" Thomas Huxley



The Patients Do The Teaching if We Just Pay Close Enough Attention

Learning from Experience

- "The Patients Do The Teaching if We Just Pay Close Enough Attention"
- Sir William Osler/Telfer Reynolds
- Enthusiasm of an MD for BBs is Inversely Related to Experience

MAP in ICU & Statins

- #1089 Nadir MAP Day 1: if <60, 43% Die, if ≥60, 7% Die
- Comment: 90/60=MAP of 70, Dangerously Close to 60
- The Bulk of Evidence Favors Statin Use in Cirrhosis: Only 22 Cases of DILI in 5 million Users in 8 Yrs Hepatology 2014;60:679-86
- Simvastatin Lowers HVPG: Gastroenterology 2009:136:1651-8

Predictors of Death

- #291 Retro 2693 Hosp Pts w Cirr: Adm Bicarb 14-17 OR of AKI 3.6, HRS 2.01, HE 1.69, GIB 1.56
- #411 Retro Cirr with Plt <50: <25k 70% Mort at 90 Days vs 30% at 25-50k. Outperformed MELD Na. I Readvised Ray Kim to Add Platelet to MELD

Simplicity

- "Simplicity is the Ultimate Sophistication"
- Da Vinci
- "Nature Loves Simplicity"
- Einstein

“Machine Learning”

- #187 Histology Using 68k Annotations & Gradient Boosting with Countless Decision Trees—Assess Fibrosis Throughout Bx
- #188 Bile Acid Profiles Predict Decomp in PSC
- #189 Predicting Dropout in HCC: Ascites
- #191 Predicting ASx Cirrhosis in Bariatric Surgery—Superior to Existing Non-Invasive Markers

Ownership

- The Hepatologist "Owns" the Patient
- We Approve/Not Drugs & Procedures
- Without TP, As Well As Pre & Post TP
- When You Transplant a Patient, You Marry Them with No Possibility of Divorce
- Try Finding Psych Services for the Poor
- We Are the Psychiatrist & Psychologist by Default

Physical Exam

- Forgotten/Not Taught Anymore
- LGFD—No Way. You Have to Do It
- Obesity Makes It Tough
- Look for Spiders, Palms, Collaterals
- May Be More Granular than Nodular
- Palpate Sub-Xiphoid for Left Lobe
- Get Your Own U/S: Butterfly $2000
- Home BPs
- Keep MAP >82

JAMA 2011;305:193-4
Gastroenterology 1988;94:482-7
Ann Int Med 2019;170:853-62

Overused Meds in Cirrhosis

- Rifaximin. Neomycin is Avail.
- Lactulose. Try Macrogol (PEG)
- Anti-Hypertensives—Taper/Stop
- Beta Blockers—RCTs of Compensated
  - Extrapolation to All Patients
  - No Stopping Rules Until 2015 & 2017
  - Keep MAP >82—Not 90/60
  - 90/60=MAP 70.
  - MAP <60=43% ICU Mort—2019 #1089

Overused Stuff in Cirrhosis

- ER/ED—NSAIDs, Benzos, etc.
- Benzo→Coma→Vent→Death in 63%
  - Hepatology 1996;23:1393-401
- ERC/No P P=Pancreatitis
- MR—I Use Only as Tie Breaker in Focal Lesions & R/In PSC or NRH
- Albumin—I Don't Believe Much

Underused Meds in Cirrhosis

- Baclofen to Reduce Alc Craving
- Midodrine to Keep MAP >82
- Consider Having Care Giver Phase in MiraLax and Phase Out Lactulose, if Patient is Intolerant
- 2-3 BMs/day Regardless of Med

News Flash: Baclofen for Alcohol Craving in ALD

- Most Studies of Drugs to Reduce Alcohol Consumption Excluded Pts with ALD—Duh!!
- Italian RCT of 84 Pts with ALD & Active Alcohol Intake: 90 Days
- Baclofen (5 mg po tid x 3 Days then 10 mg tid) Dramatically Reduced Alcohol Intake
- $4/Mo at CostCo=$40/year
- We Start Baclofen at End of Hospitalization for Alc Hep When It is Clear that Pt Will Survive & Continue Baclofen Indefinitely
- Baclofen Rec'd in Review

Lancet 2007;370:1915-22
Science 2011;332:653
Alc Alcoholism 2014;49:453-6
Hepatology 2019;70:410-7

Midodrine for Ascites

- BP Drops as Ascites Becomes Refractory
  - Nurses & Diuretics & FDA
- Midodrine: Oral Alpha Agonist
- Midodrine Can Increase BP & Improve Response to Diuretics
- Start at 7.5 mg tid & Go Up w Each Dose
- 40 Patient RCT for Refrac or Recurrent
  - Inc Uvol, UNa, MAP, SVR
  - Increased Control & **Survival**

J Hepatol 2007;46:213-21
Liver Int 2009;29:169-74
J Hepatol 2012;56:348-54

Underused Stuff in Cirrhosis

- Home BPs
  - Rx for Cuff or Consider Giving Cuff
- Measured Height
- Continuity of Care
- Care Coordination
- Palliative Care
- Variceal Banding

I Write a Lot of Rxs for These

Take Home Message

- Home BP Monitoring: Better
- Dozens of BPs
- I Am Usually the One Who Stops the AntiHTNs
- Weekly Visits (or Remote Monitoring) Initially When There is Ascites & Low BP

Perfused Hepatic Mass

- John Hoefs MD: USC then UCI
- 1970s til Today
- AKA: QLSS, SPECT LSS, Perfused Hepatic Mass, HepatIQ
- Tc Su Colloid LSS, Nuc Med
- Correlation c Lap Bxs, r=.9462 p<.001

Hepatol 1995; 22:1113-21
DDS 1995;40:552-60

ADVERTISEMENT

Type 2 diabetes: Reimbursement information
Information From Industry

Higher Vitamin D Levels and 'Markedly' Improved CRC Survival

Top Highlights in Hepatology: The Liver Meeting 2014

Express Scripts to Cover AbbVie HCV Drug, Drops Gilead Treatment

FDA Approvals > Medscape Medical News

FDA Clears Hepatiq Software for Quantifying Liver Disease

Megan Brooks | Disclosures

January 12, 2015

Comment | Print | Email

The US Food and Drug Administration (FDA) has approved software designed to help determine the severity of liver disease by quantitative analysis of nuclear medicine liver-spleen images.

The Hepatiq software, from Hepatiq LLC, calculates perfused hepatic mass, a measure of liver function.

The software automates the quantitative liver spleen scan shown to be an accurate predictor of clinical outcomes in the Hepatitis C Antiviral Long-term Treatment Against Cirrhosis trial, the company explains in a news release.

John Hoefs, MD, cofounder and chief operating officer of the company, developed the quantitative liver spleen scan methods to measure hepatic function, fibrosis, hepatic and spleen volume, and cirrhosis, whereas Dipu Ghosh, the company's chief executive officer, created the algorithms for automating the quantitative liver spleen scan techniques.

"As hepatologists," Dr Hoefs commented in the release, "we have needed and searched for a reliable, precise method of measuring liver

EDITORS' RECOMMENDATIONS

Noninvasive Alternatives to Assess Liver Fibrosis

Antidepressant-Induced Liver Injury Underestimated

Global Burden of Liver Disease Substantial

Topic Alert

Receive an email from Medscape whenever new articles on this topic are available.
Add Hepatitis C to My Topic Alert

DRUG & REFERENCE INFORMATION

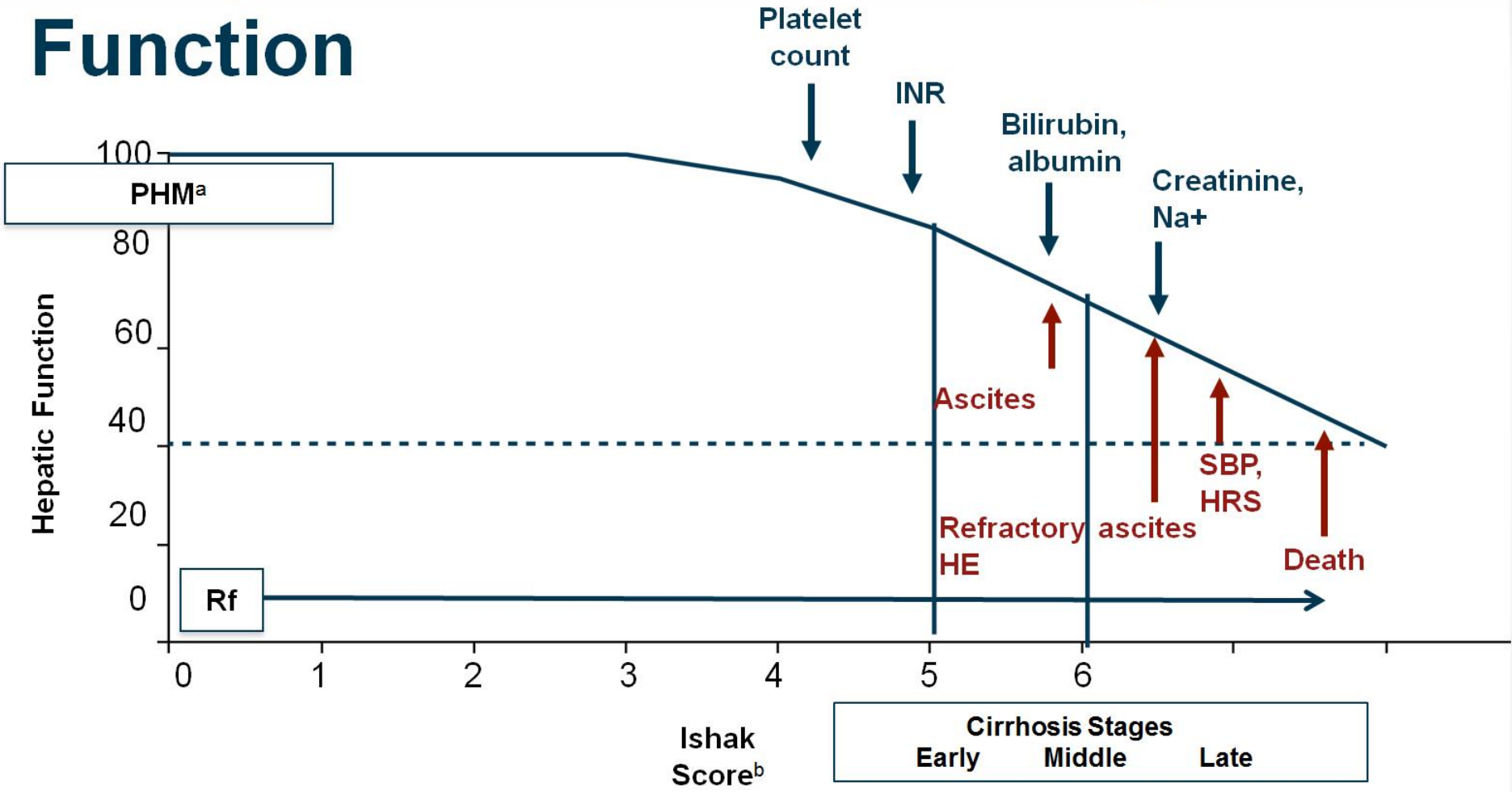
ADVERTISEMENT

MOST POPULAR ARTICLES

According to INTERNISTS

1. Chronic Fatigue Syndrome: Wrong Name, Real Illness
2. Vitamin D Screening: What About the Adult With Cognitive Changes?
3. Let's Stop the Unnecessary Treatment of Heart Disease
4. Order Antivirals Before Influenza Is Lab -Confirmed, CDC Says

Relationship Between Accumulation of Hepatic Scar Tissue and Hepatic Function



*An Rf >.2 units/year is a fast rate of progression

a. Everson GT, et al. *Hepatology*. 2012;55:1019-1029.[3]
b. Everhart JE, et al. *Hepatology*. 2010;51:585-594.[4]
c. Hoefs JC, et a. *Gastroenterology*. 2011;141:900-908.[5]

Magical Numbers in Hepatology

- MAP >82
- Platelet Count <160
- Max Spleen Size ≥12 cm
- Max PV Diameter >13 mm
- 30/30/30/3 Rule

ODTAA Syndrome

- Silent Cirrhosis on Imaging or Plt <160
- Then Ascites Develops
- Then HE When Treating Ascites
- “Wet & Wise or Dry & Demented” SS
- “Run” Elderly Wet
- Then EVGIB
- Treat all That
- Hope for Recompensation

Recompensation of Cirrhosis

- Not Much Page Space
- Occurs Most Impressively When Severe Inflammation is Present
- When Insult Stops, Inflammation Is Reduced
- Recompensation Can Occur

Recompensation of Cirrhosis

- Best: Due to Reversal of Underlying Liver Disease/PHT
- Control/Loss of Ascites
- Control/Loss of Hep Enceph
- Control/Loss of PHT-GIB
- Optimally: All Liver Meds D/C

Most Reversible Causes of Cirrhosis

- Alcoholic Hepatitis/Cirrhosis: Abstinence
- Reactivation of Hep B w Cirrhosis: Anti-Viral
- Autoimmune Hepatitis w Cirrhosis: Steroids, Then Aza

Recompensation

- "The Liver Takes a Lickin and Keeps on Tickin"
- "You Really Have to Work Hard to Wear Out Your Liver"
- "The Liver Suffers in Silence & Then Turns Up Its Toes"
- The Kidneys Are Wimps in Comparison

Liver Transplant

- "Get the Most Mileage Out of the Original Equipment"
- Decade in Transplant
- Recompensation is Vastly Superior
- Treat the Treatable: ALD, Hep B, AIH, Hep C (But Not Much Recompensation)
- "A Personality Transplant Does Not Come with a Liver Transplant"

Phrases to Use in Cirrhosis

- I am Worried—Long Pause
- I Wish….
- I Am Hoping for a Miracle Too
- vitaltalk.org
- Gain Framing—Emphasize Gains, if Pt Can Take Better Care of Him/Herself

Phrases Not to Use in Cirrhosis

- "There is Nothing Else We Can Do"—Hope Destroyer
- Medical Jargon
- Medical Acronyms
- Avoid Discussion of Loss of Life Expectancy—Brain Stalls Out

Liver Care Coordination

- Care Coordination Benefits Pts with Cirrhosis: Survival, Cost, LOS
- Hepatology Could Benefit from a "Culture Change" Relative to Liver Care Coordination
- "Liver Hospitalists"
- Maybe "Liver-Specific Palliative Care Providers"

J Hepatol 2013;59:203-4

Summary

- Terlipressin & New PG Coming
- Pendulum Swinging to AntiCoag PVT
- CT/MR May Be Surrogate/Replacement for Bx, HVPG, DEXA, Dare I Say EGD
- MAP/Home BPs
- Meds: Overused/Underused
- Perfused Hepatic Mass
- Magical Numbers
- Recompensation
- Phrases To Use/Not Use
- Consider Palliative Care/CofC