

# DDW: Liver Update

Patrick G. Northup, MD, MHS, FAASLD, FACG

Medical Director, Adult Liver Transplantation

NYU Langone Transplant Institute

Patrick.Northup@nyulangone.org

# Conflicts of Interest

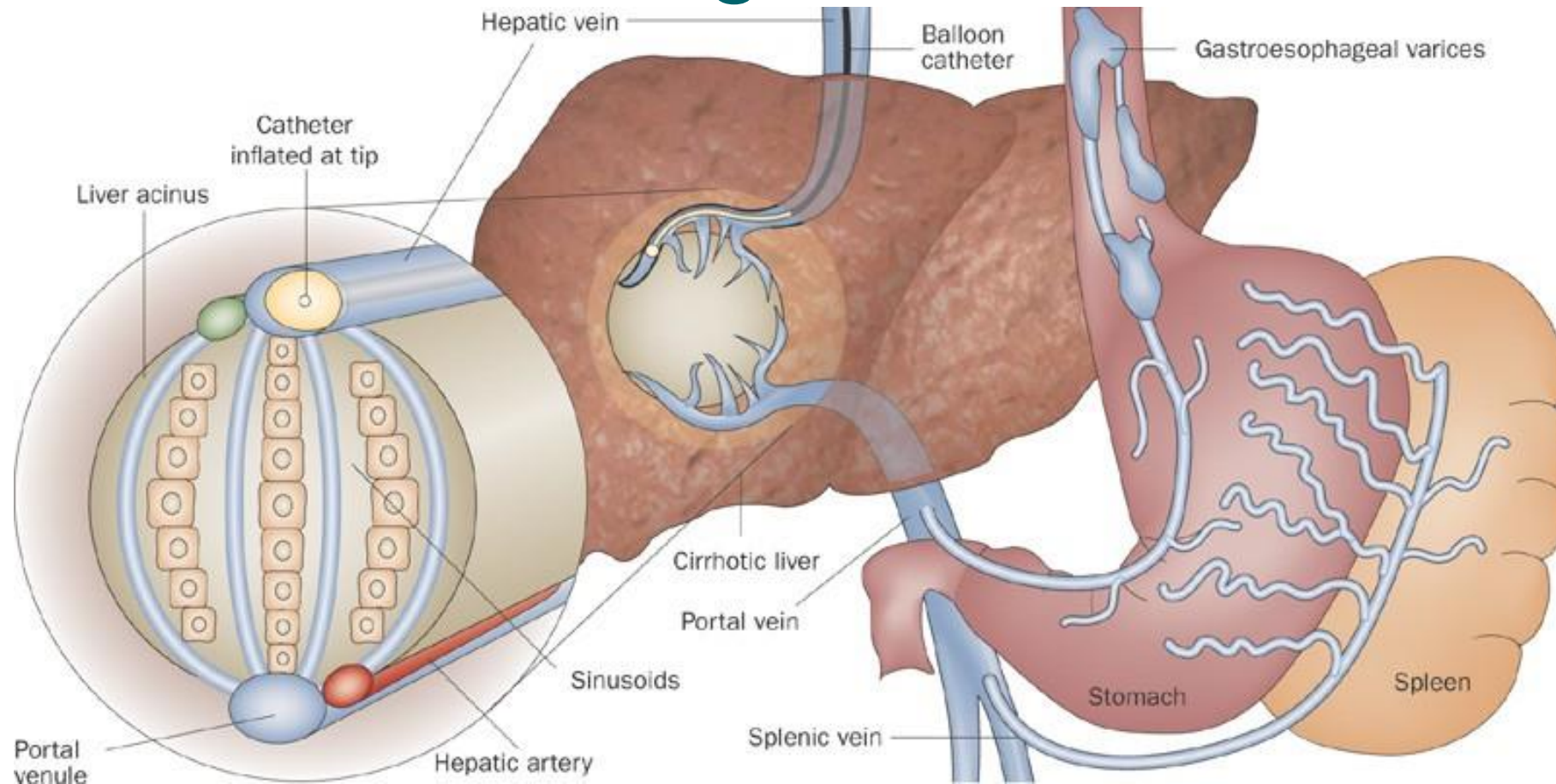
None to report

# Topics for Discussion Today

- Abstract 85: EUS guided portal pressure measurement
- Abstract 93: Statins and cholangitis in PSC
- Abstract Sa1467: FFP use in acute variceal bleeding
- Abstract 325: Lean NASH and cardiovascular disease

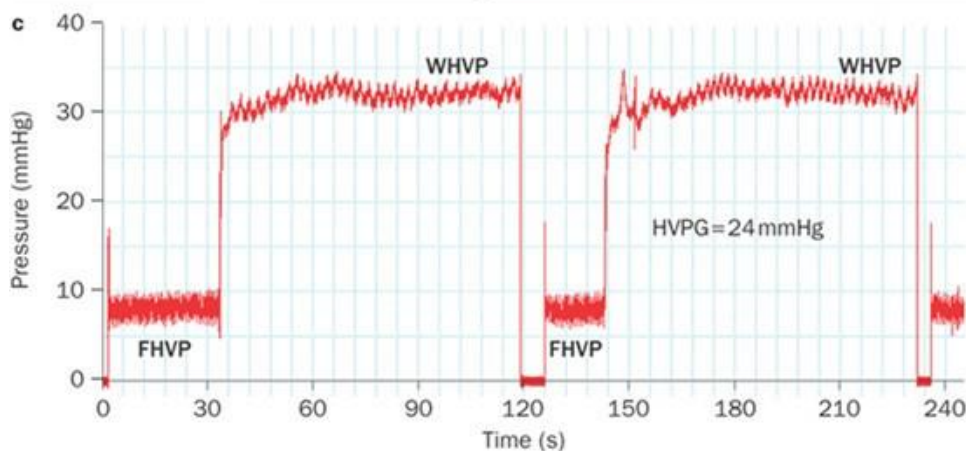
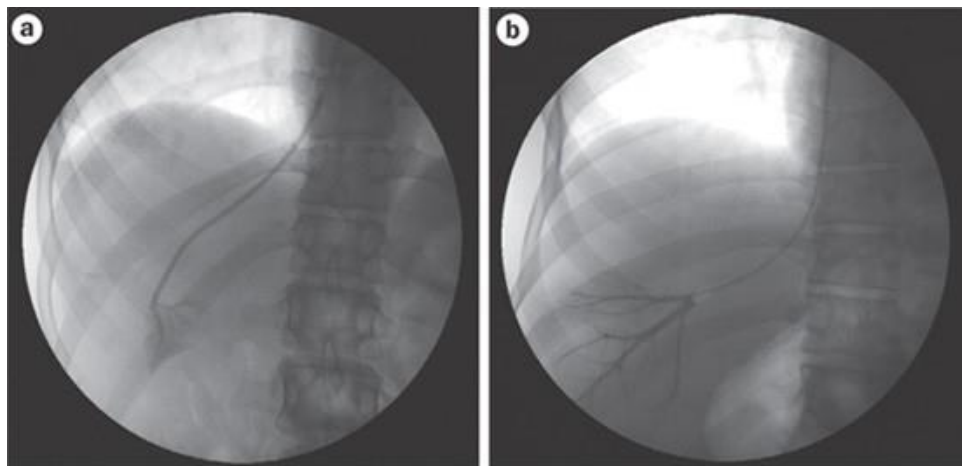
# EUS Guided Portal Pressure Measurements

# The HVPG is the gold standard



Bosch, et al., *Nat Rev Gastroenterol and Hep* 2009

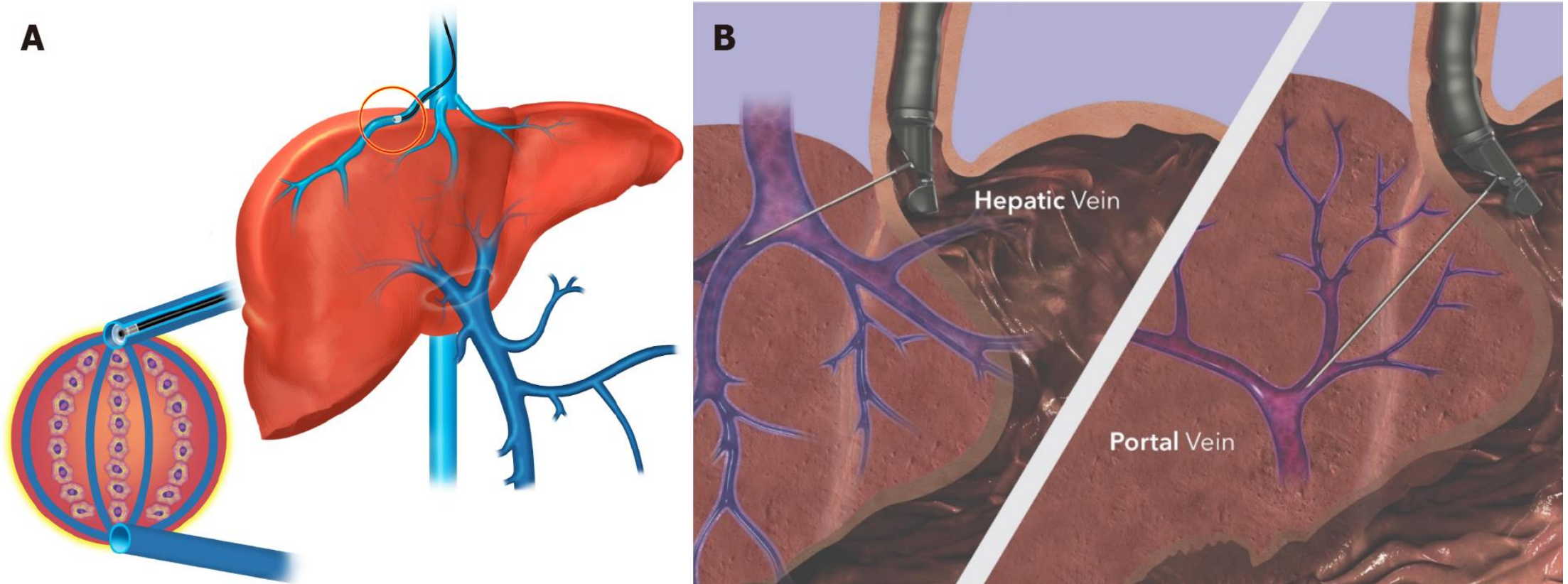
# The HVPG is the gold standard



- Mild portal hypertension: 5-9 mmHg
- Clinically significant portal hypertension: greater than 10 mmHg
- Risk of bleeding EVs: greater than 12 mmHg

Bosch, et al., *Nat Rev Gastroenterol and Hep* 2009

# EUS guided pressure measurement



Rudnick, et al., *World J Hepatol* 2021

# Abstract 85

PREDICTION OF LIVER HISTOLOGY AND CLINICAL PARAMETERS OF LIVER DISEASE USING EUS GUIDED PORTOSYSTEMIC PRESSURE GRADIENT MEASUREMENT: RESULTS FROM A US MULTI-CENTER ENDOHEPATOLOGY EXPERIENCE

Marc Monachese, Jennifer M. Kolb, Kenneth J. Chang, Alyssa Y. Choi, Sagar Shah, Thomas J. Wang, Ahmad Bazarbashi, Ali Zakaria, Pushpak Taunk, Ali M. Abbas, Pedro Cortés, Michael B. Wallace, Bhaumik Brahmhatt, Natalie Danielle Cosgrove, Wenjing Cai<sup>6</sup>, David P. Lee, Prashant Kedia, Marvin Ryou, Jason B. Samarasena



# Monachese, et al.

- 6 centers, 159 patients
- Mostly CP A cirrhosis
- Technical success was achieved in 156 patients (98.1%) with two (1.2%) procedure related adverse events (bleeding post liver biopsy).
- Higher mean PPGs were measured in patients with clinical features of portal hypertension
- esophageal varices (11mmHg vs. 2.75mmHg,  $p < .01$ )
- portal hypertensive gastropathy (10.5mmHg vs. 4.3mmHg,  $p < .01$ )
- thrombocytopenia (8.27mmHg vs. 3.99mmHg,  $p = < .01$ ).

# Monachese, et al.

PPG correlated “well” with commonly used scores for liver disease including

- FIB-4 (R=0.484,  $p < .01$ )
- APRI (R=0.30,  $p = 0.0003$ )
- MELD (R=0.28,  $p = .006$ )

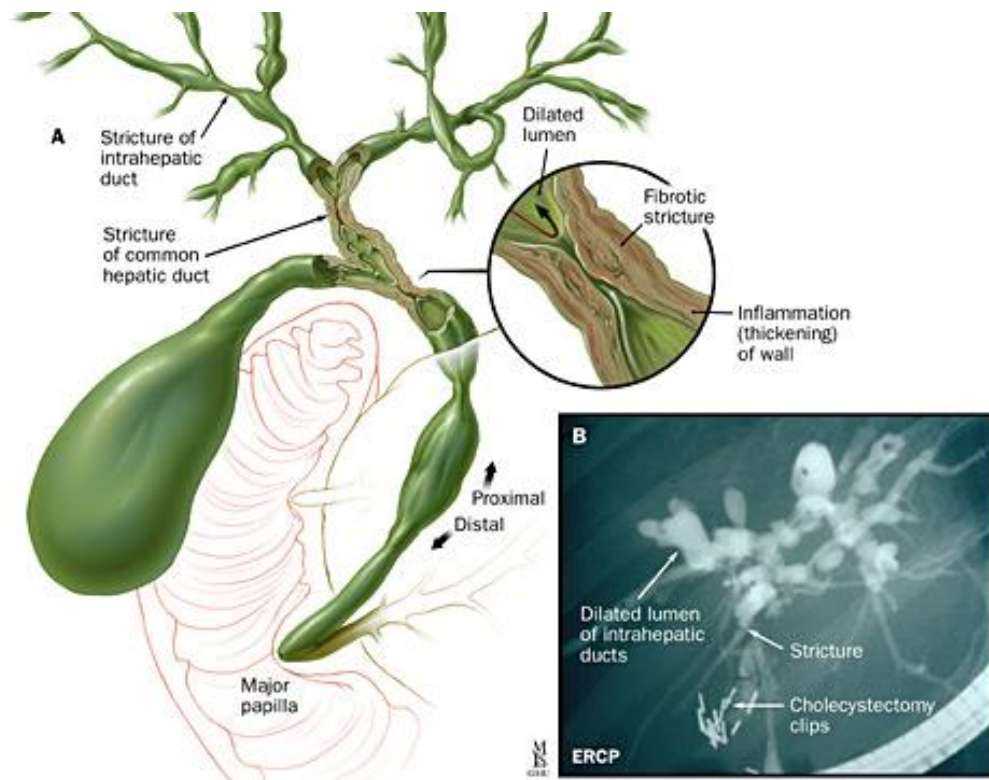
PPG did not correlate with TE (R= .005,  $p = 0.54$ )

## BOTTOM LINE:

EUS PPG was consistent with clinical features of cirrhosis but agreement with non-invasive validated studies is still to be determined

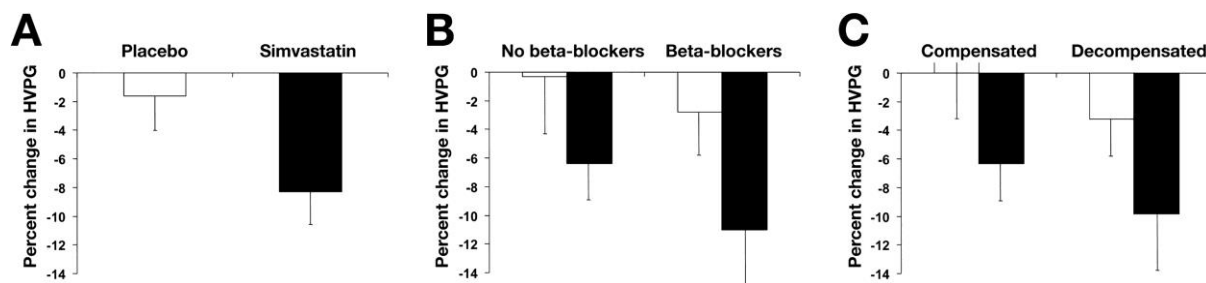
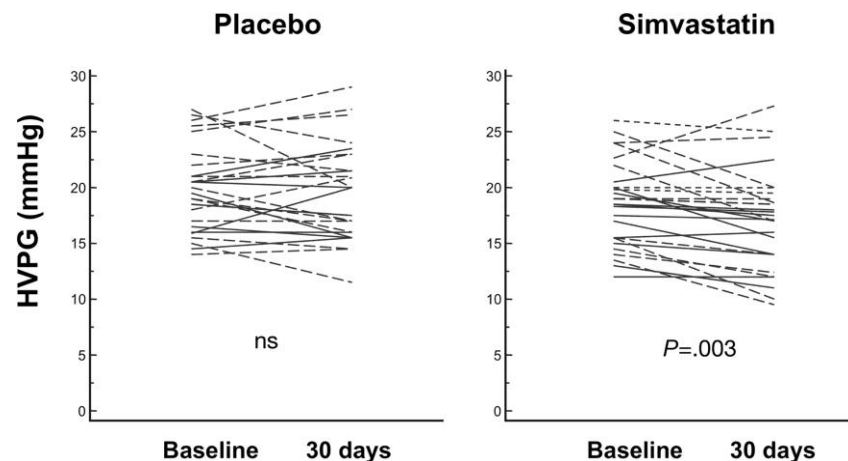
# Statins and Cholangitis in PSC

# Primary Sclerosing Cholangitis



- No approved therapies showing definitive benefit
- High dose UDCA trial stopped early and found harm in treatment group. Lindor *Hepatology* 2009

# Statins in Cirrhosis



- Statins improve HVPG in patients with cirrhosis but don't reduce rebleeding rates
- Potentially have a beneficial effect on survival in that population
- Statins do affect bile acid homeostasis and lipid composition

Abraldes, et al., *Gastroenterology* 2009

# Abstract 93

## STATINS PROTECT AGAINST THE RISK OF ACUTE CHOLANGITIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

Chiraag Kulkarni<sup>1</sup>, George Thomas Cholankeril<sup>2</sup>, Touran Fardeen<sup>1</sup>, Joseph K Rathkey<sup>1</sup>, Raja Samir Khan<sup>2</sup>, Soumya Murag<sup>3</sup>, Robert Lerrigo<sup>3</sup>, Ahmad Kamal<sup>3</sup>, Aijaz Ahmed<sup>1</sup>, Aparna Goel<sup>1</sup>, Sidhartha R. Sinha<sup>1</sup>

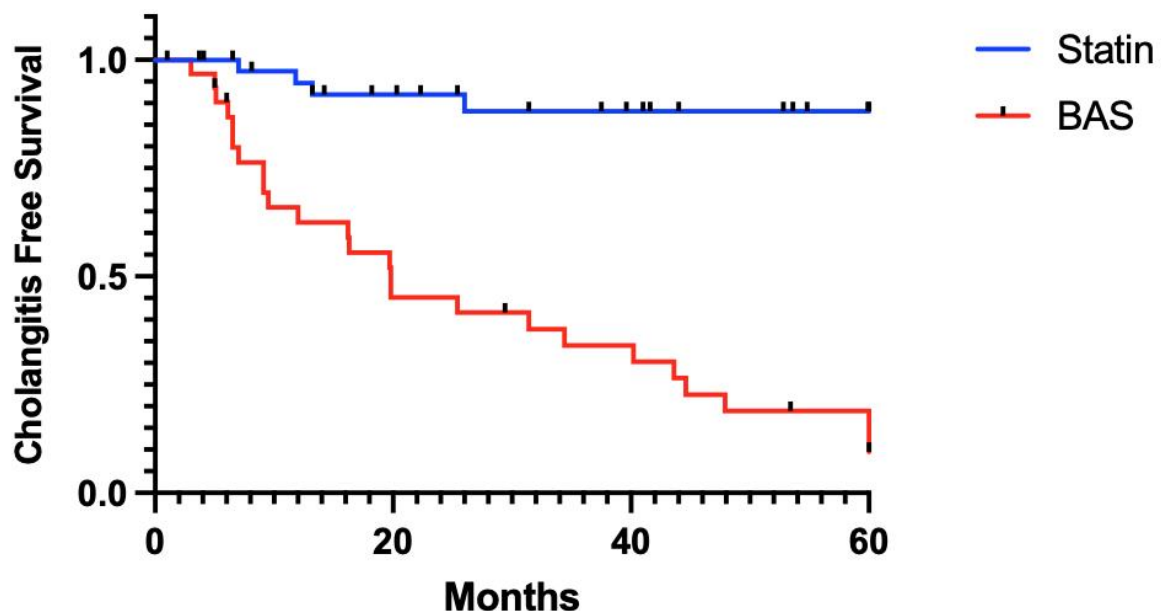
1. Stanford University, Stanford, California,
2. Baylor College of Medicine, Houston, Texas
3. Santa Clara Valley Medical Center, San Jose, California

# Kulkarni, et al.

- Three center retrospective review of 294 patients with PSC
- Compared those on statins to those on bile acid sequestrants (pruritis) with 30% developing cholangitis
- Statin therapy was associated with decreased odds of acute cholangitis (OR 0.22, 95% CI 0.07-0.62)
- Bile acid sequestrant use was associated with increased odds of acute cholangitis (OR 4.91, 95% CI 2.05-12.37).
- Statin therapy was associated with increased time-to-cholangitis, with an incidence of 8.6% at 36 months compared to 51.6% for patients not on statin therapy.

# Kulkarni, et al.

Figure 1. Time to cholangitis on statin and bile acid sequestrant therapy



## BOTTOM LINE:

- Non-randomized retrospective study with very different patient groups
- Interesting findings with some potential basis in pathophysiology but better studies are needed



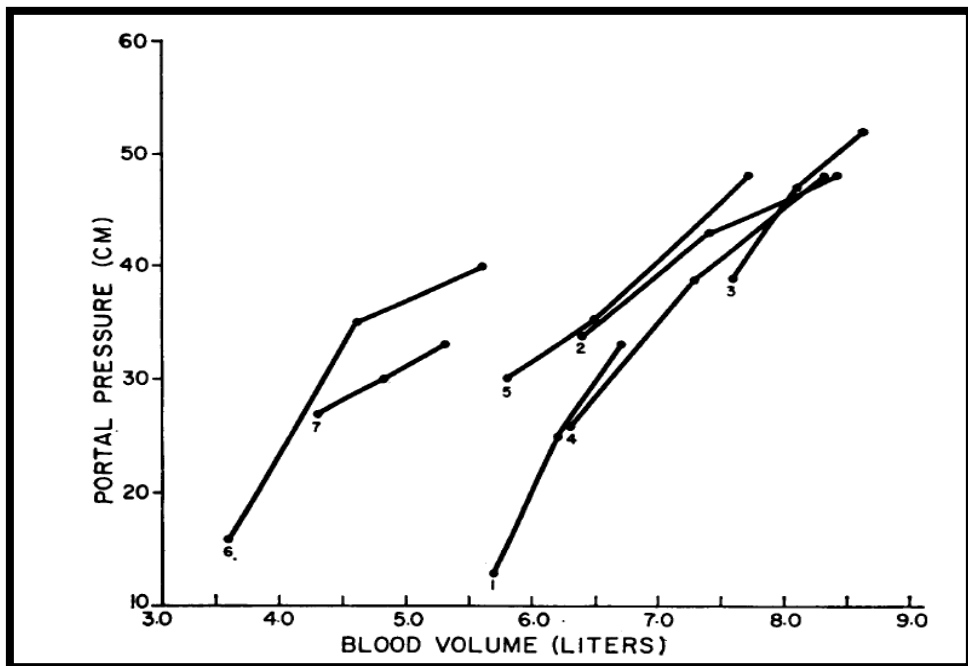
# FFP use in Acute Variceal Bleeding

# Fresh Frozen Plasma



- First developed as a battlefield therapy for hemorrhagic shock during WWI
- Each unit contains depleted amounts of clotting factors from a single unit donor
- Requires high volumes of transfusion for effective repletion of clotting factors (average 5-7 units over 3-4 hours)

# Fresh Frozen Plasma – Problems



- In cirrhosis, plasma volume expansion directly leads to increases in portal pressures
- Increased pressures lead to increased rebleeding rates Villaneuva, et al., *NEJM* 2013
- Practice guidelines recommend against the use of FFP

Zimmon and Kessler Gut 1974;15:99-101

# Fresh Frozen Plasma – Practice Guidelines

“..correcting the international normalized ratio (INR) by the use of fresh frozen plasma or factor VIIa is not recommended”

Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases

Garcia-Tsao, et al., *Hepatology* 2016

“...given the lack of effect of FFP on hemostatic capacity in the population of patients with cirrhosis, we advise against prophylactic FFP transfusion before common procedures”

Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases

Northup, et al., *Hepatology* 2021

# Abstract Sa1467

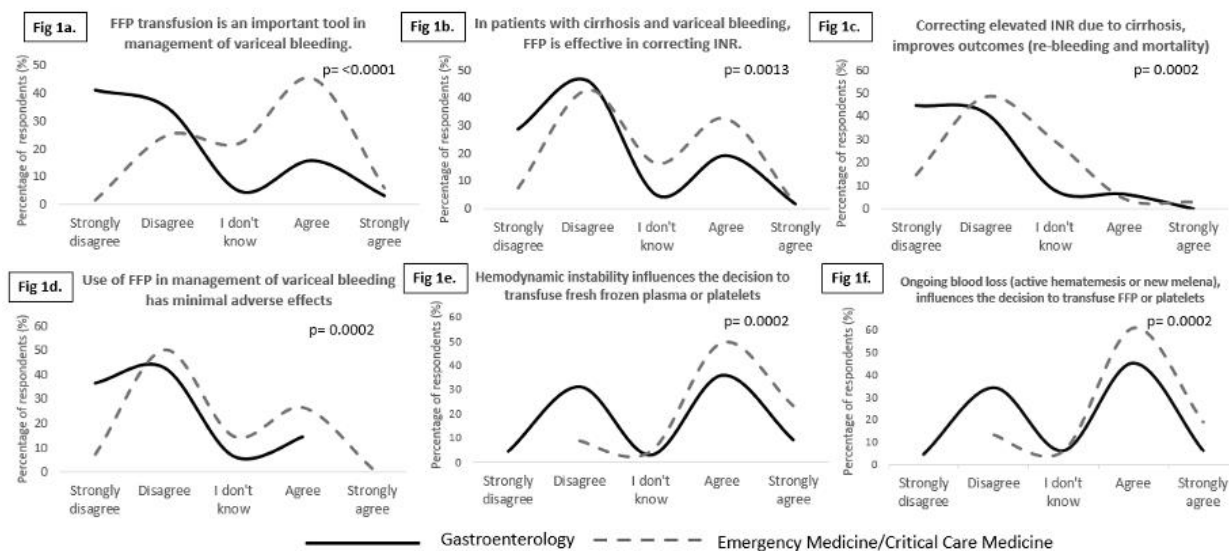
## PROVIDER PERCEPTIONS OF FRESH FROZEN PLASMA TRANSFUSION IN VARICEAL BLEEDING LAG BEHIND CURRENT EVIDENCE AND VARY ACROSS CLINICAL SPECIALTIES

Matthew J. Custodio, Kelly E. Diaz, Sartajdeep Kahlon, Andrew Canakis, Stephen H. Caldwell, Christine Campbell-Reardon, Jordan A. Spector, Pramod K. Guru, Reggie R. Thomasson, Michael F. Harrison, Eric Chak, Nathalie Helen Urrunaga, Zachary Fricker, Jonathan G. Stine, Arpan Mohanty

# Custodio, et al.

- Qualitative electronic survey sent to providers from four academic institutions in the U.S.
- Surveyed GI, critical care, and emergency medicine providers
- Only 22% GI and 32% EM/CCM providers felt that FFP was effective in correcting INR
- More GI providers felt that hemodynamic instability (36%) or ongoing blood loss (39%) did not warrant FFP transfusions as compared to EM/CCM providers

# Custodio, et al.



## BOTTOM LINE:

- There are significant differences between subspecialties in knowledge of efficacy and use of FFP in cirrhosis
- Specialty specific practice guidelines may not be read or adhered to by other specialties

# Lean NASH and Cardiovascular Disease








# NASH and Metabolic Syndrome



## Metabolic Syndrome

defined as 3 or more of the following

- Abdominal obesity 
- Elevated plasma triglycerides 
- Low plasma HDL cholesterol 
- Elevated blood pressure 
- Elevated fasting blood glucose 

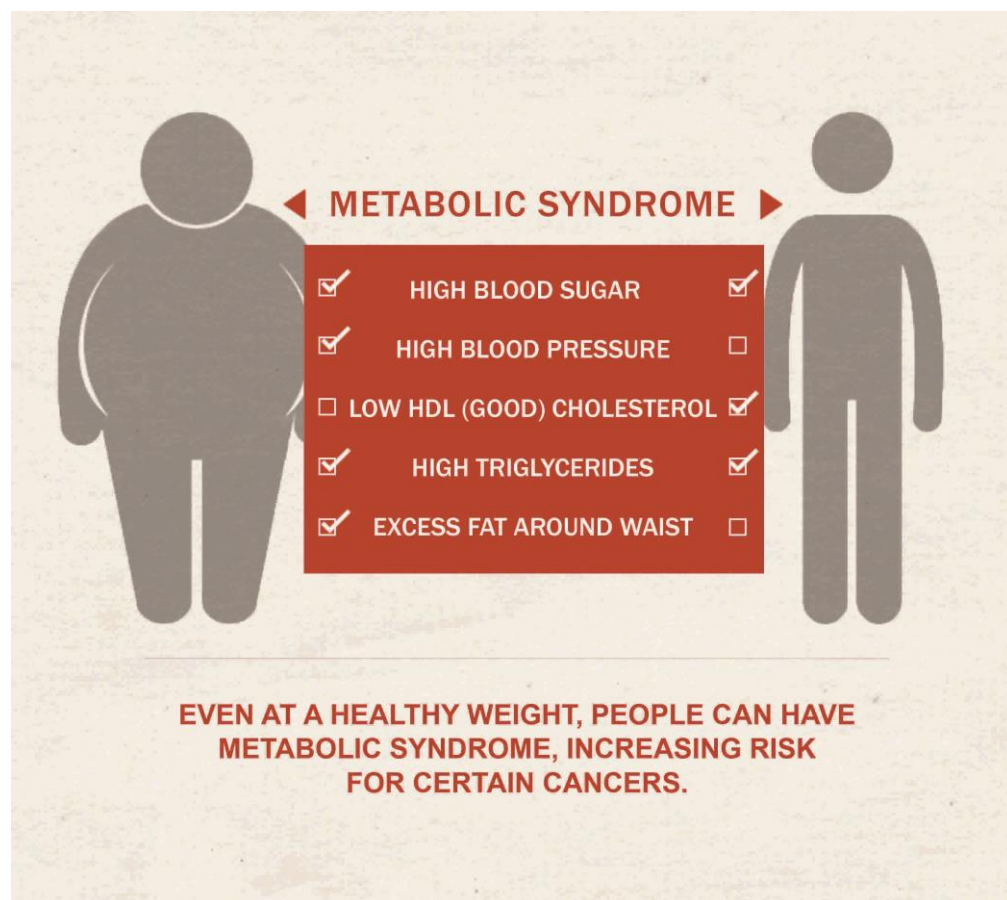
## Diseases Associated with Metabolic Syndrome

- Type 2 Diabetes
- Hypertension
- Non-alcoholic Fatty Liver Disease (NAFLD)
- Cardiovascular Events

## Drug Targets for Metabolic Syndrome

- Soluble Epoxide Hydrolase
- PPAR $\gamma$  / PPAR $\alpha$
- Farnesoid X Receptor
- Angiotensin Converting Enzyme
- Angiotensin Type 1 Receptor
- Dipeptidyl Peptidase 4
- Glucokinase

# “Thin” NASH



- Fructose ingestion may play an important role in development of NAFLD in lean subjects. A study found soft drink consumption to be significantly associated with hepatic steatosis, independent of metabolic risk factors *Abid, et al., J Hepatol 2009*
- Cholesterol intake was significantly higher in non-obese NAFLD patients than their obese NAFLD counterparts *Yasutake Scand J Gastroenterol. 2009*

# Abstract 325

HIGHER PREVALENCE OF CARDIOVASCULAR DISEASE AMONG LEAN VERSUS NON-LEAN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE DESPITE LOWER PREVALENCE OF ATHEROGENIC RISK AND METABOLIC DISEASES

Karn Wijarnpreecha<sup>1</sup>, Fang Li<sup>2</sup>, Vincent L. Chen<sup>1</sup>, Anna Lok<sup>1</sup>

1. University of Michigan, Ann Arbor, Michigan

2. The University of Texas Health Science Center at Houston

# Wijarnpreecha, et al.

- Retrospective cohort at UM of 10,220 patients with NAFLD
- 1,158 were lean (WHO definition)
- Lean patients had lower prevalence of cirrhosis, DM, hypertension, dyslipidemia,
- Lean patients had higher prevalence of peripheral vascular disease, cerebrovascular disease, and any cardiovascular disease

# Wijarnpreecha, et al.

Table 2 Logistic regression analysis of factors associated with prevalence of cardiovascular disease and cirrhosis

| Weight category             | Any cardiovascular disease |         | Coronary artery disease |         | Cerebrovascular accident |         | Cirrhosis       |         |
|-----------------------------|----------------------------|---------|-------------------------|---------|--------------------------|---------|-----------------|---------|
|                             | OR (95% CI)                | P value | OR (95% CI)             | P value | OR (95% CI)              | P value | OR (95% CI)     | P value |
| Lean (n= 1,158)             | <b>Referent</b>            |         | <b>Referent</b>         |         | <b>Referent</b>          |         | <b>Referent</b> |         |
| Overweight (n=2,560)        | 0.6 (0.5-0.8)              | <0.001  | 0.7 (0.6-0.9)           | <0.01   | 0.5 (0.4-0.7)            | <0.001  | 1.2 (0.8-1.9)   | 0.29    |
| Obesity class 1 (n=2,875)   | 0.6 (0.5-0.8)              | <0.001  | 0.7 (0.6-0.9)           | <0.01   | 0.6 (0.5-0.8)            | <0.001  | 1.4 (1.0-2.2)   | 0.07    |
| Obesity class 2-3 (n=3,789) | 0.6 (0.5-0.7)              | <0.001  | 0.6 (0.5-0.8)           | <0.001  | 0.4 (0.3-0.5)            | <0.001  | 1.5 (1.0-2.2)   | 0.06    |

Odds ratio (OR) adjusted for age, sex, race, smoking status, diabetes, hypertension, and dyslipidemia

## BOTTOM LINE:

- Lean patients with NALFD are likely at significantly higher cardiovascular risk than obese NAFLD despite traditional risk factors

# Thank you!

Patrick.Northup@nyulangone.org

