Post-AASLD Portal Hypertension Abstracts

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Financial Disclosures

- None

Update on the AASLD guidance document on patients with cirrhosis and portal hypertension

- Updated in 2016
- Focuses on portal hypertension, varices, and variceal hemorrhage
- Recognizes different stages of cirrhosis
  - Compensated cirrhosis: Those with mild PH vs with clinically significant portal hypertension
    - CSPH: Those with GEV and those without GEV
- Recommendations are now focused on…
  - Risk stratification
  - Individualization of care

AASLD 2017

- Hot topics at AASLD 2017 the Special Interest Group (SIG) session, parallel sessions, and the post-graduate course
  - Measuring portal pressure gradient
  - TIPs vs BRTO
  - Management of ectopic varices
  - Early TIPs

Diagnosis and Monitoring

Management

Prevention

Outline

- Case presentation
- AASLD abstracts (most were poster presentations, with one being an oral presentation)
- Questions

Case Presentation

- 54 yo man with history of alcoholic cirrhosis complicated by ascites who presents with hematemesis.
- His MELD is 13, Child class B
  - Labs: Tbili 1.5, Sodium 137, INR 1.5, Creatinine 1.0, Albumin 3.2
- The patient is taking diuretics for his ascites. His last EGD showed small esophageal varices.
- The patient is hemodynamically stable. He is resuscitated and is awaiting an upper endoscopy.

Questions arise

- Are noninvasive tests available to predict portal hypertension?
- Is our patient a candidate for early TIPS? Does MELD-Na vs MELD change prediction of mortality after TIPS?
- Was there a role to start beta blockers for primary prophylaxis?
- If TIPS is indicated, would he need a platelet transfusion?

Does Liver Stiffness Measurement and Controlled Attenuation Parameter predict portal hypertension, liver related events and overall mortality in individuals with cirrhosis?

Ahmed Hashim[1,2], Bethany Parnell[2], Yazan Haddadin[2], Lucia Macken[1], Stephen Bremner[1], Majella Keller[2], Alexandra File[2], Yvonne Gilleece[2], Jeremy Tibble[2], Sumita Verma[1,2]

[1]Brighton & Sussex Medical School, [2] Brighton & Sussex University Hospitals NHS Trust

Background: Liver stiff measurement (LSM) using transient elastography and controlled attenuation parameter (CAP) are established non-invasive tests for staging hepatic fibrosis and hepatic steatosis, respectively.

Aim: To establish the ability of LSM and CAP in predicting portal hypertension (PHT), liver-related events (LREs) and overall mortality in patients with cirrhosis.

Methods: Retrospective review of consecutive patients in outpatient setting who underwent Fibroscan for from 2013 to 2015, and follow up until 2017 or until death.

Definitions: Cirrhosis (≥ 13 kPa), PHT development of varices on endoscopy; LREs one or more of variceal bleeding, hepatic encephalopathy, ascites, hepatocellular cancer and/or need for transplantation.

Logistic regression analysis was performed.

1- Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, et al. (2008). Performance of transient elastography for the staging of liver fibrosis: a meta-

This work was sponsored by a research grant from the Dunhill Medical Trust

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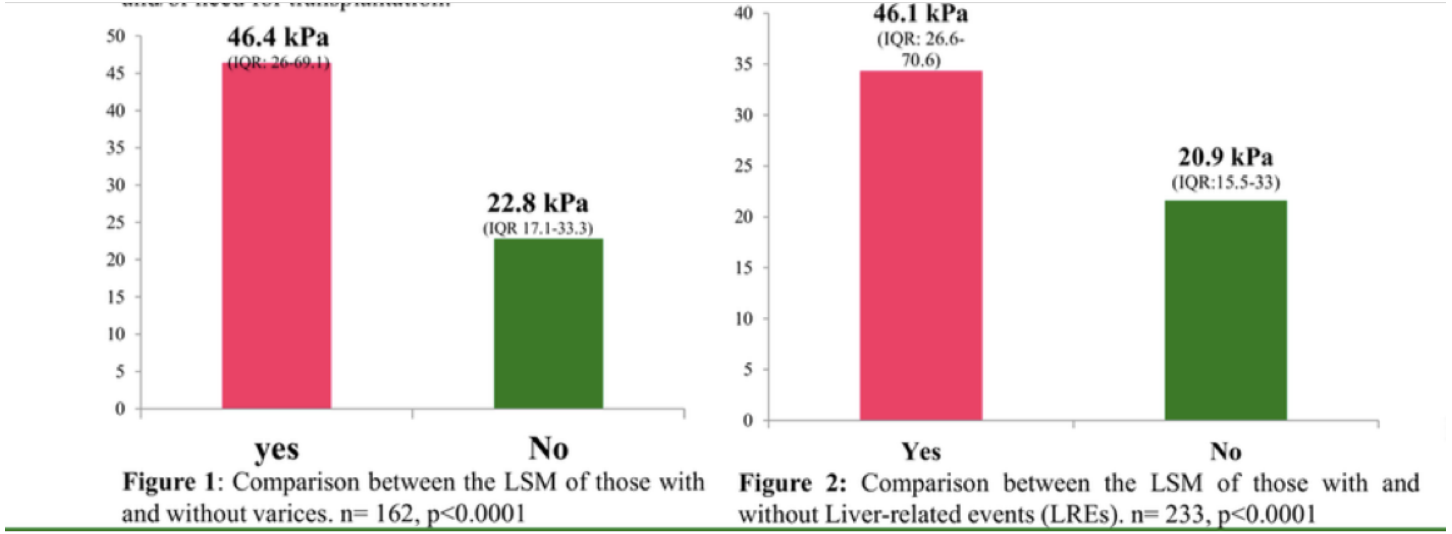


Figure 1: Comparison between the LSM of those with and without varices. n= 162, p<0.0001

Figure 2: Comparison between the LSM of those with and without Liver-related events (LREs). n= 233, p<0.0001

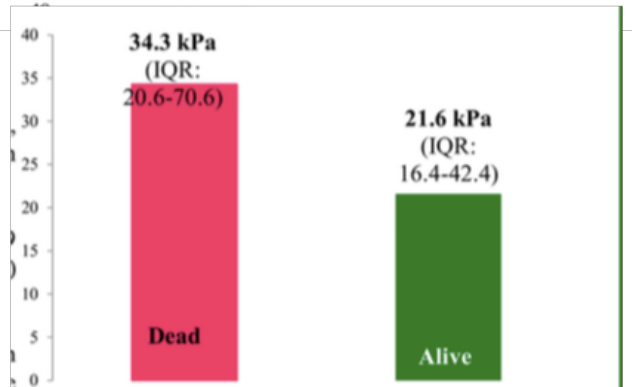


Figure 3: Comparison between the LSM of those who died vs alive n= 233, p<0.0036

•Thirty-four patients (14.6%) died within 15 months (IQR: 7-20). LSM in those who died were significantly higher than those that survived **(Fig. 3)**. CAP scores were significantly lower in survivors (230 ± 54 vs. 260± 59 dB/m, p=0.021). LSM (OR: 1.03, 95% CI: 1.01 – 1.05, p= 0.002) and comorbidities (OR: 2.75, 95% CI: 1.22 – 6.31, p= 0.015) were independent predictors of overall mortality.

Conclusion: Baseline LSM could potentially predict portal hypertension, LRE and overall mortality in individuals with cirrhosis. The lower CAP in survivors is another novel finding.

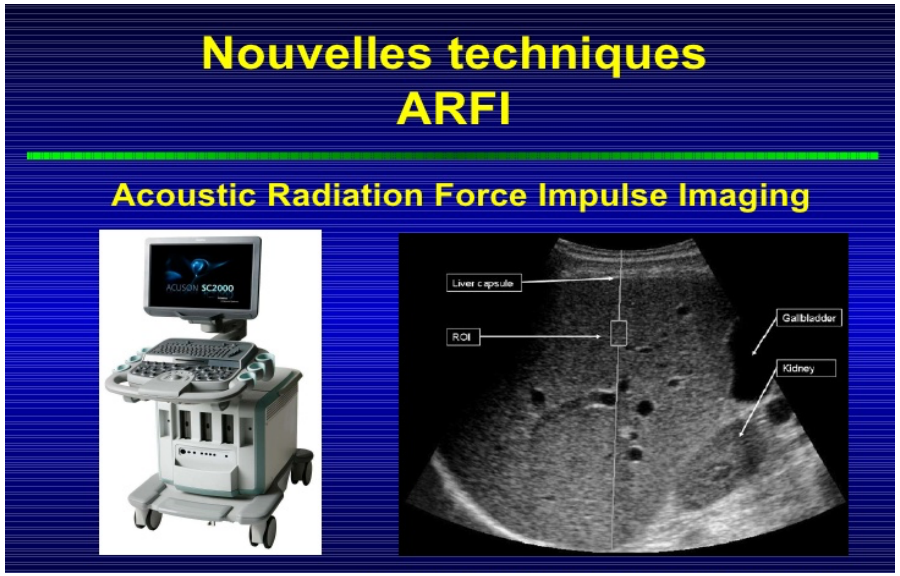
This work was sponsored by a research grant from the Dunhill Medical Trust

Spleen Stiffness

- Current European guidelines recommend to avoid screening EGD in patients with liver stiffness (LS) <20kPa and platelet >150,000 (1).
- Role of LS alone in predicting esophageal varices (EV) is controversial due to unsatisfactory diagnostic accuracy and lack of consistent results (2).
- Portal hypertension leads to spleen congestion and fibrosis, which is sufficient to increase organ stiffness (3).
- A recent meta-analyses found that spleen stiffness (SS) was superior to LS for predicting the presence of EV in patients with chronic liver disease, while the diagnostic accuracy of both LS and SS were limited in predicting severe EV (4).

1. De Franchis R. Expanding consensus in portal hypertension. Report of the Baveno VI Consensus Workshop: stratifying Risk and individualizing care for portal hypertension. J Hepatol 2015; 65:74—752.
2. Tripathi D, et al. UK guidelines on the management of variceal haemorrhage in cirrhotic patients. Gut 2015;65:1680-1704.
3. ABraldes JG, et al. Spleen stiffness: toward a noninvasive portal sphygmomanometer? Hepatology 2013;57:1278-1280.
4. Ma X, et al. Spleen stiff is superior to Liver Stiffness for Predicting Esophageal Varices in Chronic Liver Disease: a A Meta-Analysis. PLoS ONE 11(11):e0165786.

Acoustic Radiation Force Impulse Imaging



Acoustic Radiation Force Impulse(ARFI) imaging technology N=89

Method	F ≥ 2	F ≥ 2 ajusté	F ≥ 3	F = 4
AFRI-Imaging	0.81 (0.72 - 0.90)	0.83	0.91 (0.84 - 0.97)	0.91 (0.84 - 0.98)
Transient Elastography	0.83 (0.75 - 0.92)	0.85	0.90 (0.83 - 0.97)	0.91 (0.84 - 0.97)
FibroTest	0.83 (0.74 - 0.92)	0.85	0.91 (0.85 - 0.97)	0.83 (0.74 - 0.92)
APRI	0.75 (0.64 - 0.86)	0.77	0.77 (0.66 – 0.87)	0.70 (0.58 – 0.83)

- ARFI is similar to TE/Fibroscan but the attachment is to a regular ultrasound unit
- Both are one-dimensional scans but ARFI can see where you are placed in the ROI (region of interest)

Friedrich-Rust et al. Hepatology 2008.
Friedrich-Rust et al. Radiology 2009;252:595-604.
Lupsor et al. J Gastrointestin Liver Dis 2009;18:303-10.

Identification of Portal Hypertension and Prediction of Clinical Outcomes by Measuring Spleen Stiffness with Acoustic Radiation Force Impulse Imaging in Patients with Liver Cirrhosis

Yoshitaka Takuma, Youichi Morimoto, Hiroyuki Takabatake, Hiroshi Yamamoto, Shota Iwadow, Shuji Uematsu, Ryoichi Okamoto, Yasuyuki Araki

- **Aim**: To use acoustic radiation force impulse (ARFI) imaging to evaluate the significance of spleen stiffness (SS) as a predictor of mortality and decompensation.

- **Methods**: We measured SS, liver stiffness (LS), and hepatic venous pressure gradient (HVPG) in 60 cirrhosis patients, and analyzed correlations of SS, LS and HVPG using Spearman's rank-order correlation coefficient.

- In addition, we measured SS in 393 cirrhosis patients (280 compensated and 113 decompensated patients) and followed them prospectively.

- We examined the diagnostic accuracy of SS for predicting mortality and decompensation using the Cox proportional hazards model and compared SS with other non-invasive parameters using the Harrell's C-index.

- **Results:** The correlation coefficient between SS and HVPG (r = 0.876) was significantly better than that between LS and HVPG (r = 0.609, P < 0.0001).

- SS had a greater diagnostic accuracy for predicting mortality and decompensation compared with other parameters (the C-indexes for predicting mortality and decompensation were 0.824 and 0.843, respectively).

- An SS cutoff value of 3.43 m/s identified the death of patients with a 95.3% negative predictive value (NPV) and 75.8% accuracy. An SS cutoff value of 3.25 m/s identified patients with decompensation with a 98.8% NPV and 68.9 % accuracy.

- During follow-up (median, 44.6 months), 67 patients died, and 35 patients developed hepatic decompensation.

- In the multivariate analysis, SS was selected as an independent parameter associated with mortality after adjustment for alanine aminotransferase, serum sodium, and the model for end-stage liver disease score (MELD) ($p < 0.001$).

- SS was also selected as an independent parameter associated with decompensation after adjustment for Child–Pugh score and MELD ($P < 0.001$).

- **Conclusions:**
- SS is reliable and has better diagnostic performance than LS for identifying portal hypertension in liver cirrhosis, and SS is an excellent predictive marker for mortality and hepatic decompensation in cirrhosis patients.

Questions arise

- Are noninvasive tests available to predict portal hypertension?
- Is our patient a candidate for early TIPS? Does MELD-Na vs MELD change prediction of mortality after TIPS?
- Was there a role to start beta blockers for primary prophylaxis?
- If TIPS is indicated, would he need a platelet transfusion?

Comparison of MELD-Na and MELD scores in predicting survival following transjugular intrahepatic portosystemic shunt in patients with cirrhosis

Carrie E Hamilton[1], Ross Buerlein[2], Jacob Meindertsma[1], Zachary Henry[2], Neeral Shah[2]
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BACKGROUND

Model for End-stage Liver Disease (MELD) has been historically used for mortality prediction for patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) in patients with cirrhosis. Serum sodium has been shown to be an independent prognostic factor in patients with cirrhosis, and has been implemented into the MELD score to create MELD-Na.

MELD-Na has been adapted by UNOS for organ allocation in transplantation. However, there is limited data on the effect of MELD-Na on predicting mortality after TIPS.

AIM

We aim to determine the prognostic ability of MELD-Na in predicting death at 30 days and 90 days following TIPS in patients with cirrhosis.

METHODS

We conducted a retrospective chart review of all cirrhosis patients undergoing TIPS for the indication of refractory ascites or hepatic hydrothorax or prophylaxis for recurrent esophageal variceal bleeding between February 2011 and July 2016 at a single tertiary referral center in the United States.

Exclusion criteria included emergent TIPS performed for control of active variceal bleeding following two endoscopic failures within a 24 hour period, history of liver transplantation, active malignancy, and active infection.

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Table 1: Patient Characteristics (n=243)

	Death at 90 days (n = 31)	Alive at 90 days (n = 203)	P value
Age	63	56	0.002
Male Sex	54.8%	63.1%	0.38
Etiology of cirrhosis			0.07
EtOH	6.9%	93.1%	
HCV	9.8%	90.2%	
NASH	12.5%	87.5%	
AIH	14.3%	85.71%	
Other	25%	75%	
MELD	17	13	<0.0001
MELD-Na	21	14	<0.0001
Serum albumin	2.8	3.1	0.01
Indication for TIPS			0.02
Volume Overload	83.9%	62.3%	
Variceal bleeding	16.1%	37.7%	
Change in PS gradient (mmHg)	9.8	9.3	0.61

Table 2: Univariate predictors of 30 day and 90 day mortality

	30 day mortality	P-value	90 day mortality	P-value
MELD	1.15	<0.01	1.154	<0.01
MELD-Na	1.151	<0.01	1.165	<0.01
RV systolic dysfunction	7.215	<0.01	4.917	0.03
Diastolic dysfunction	3.069	0.05	N/A	

Figure 1. AUROC for MELD-Na as predictor of 90-day mortality after TIPS

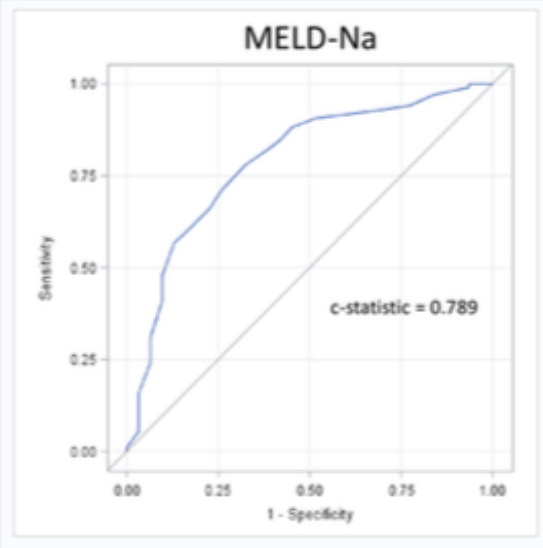

Table 3: Multivariate predictors of 30 day and 90 day mortality

	30 day mortality	P-value	90 day mortality	P-value
MELD-Na	1.165	<0.01	1.165	<0.01
RV systolic dysfunction	5.195	0.03	N/A	
Diastolic dysfunction	5.754	0.004	N/A	

CONCLUSIONS

To date, this is the largest study in the literature assessing the effect of MELD-Na on mortality following TIPS.

Our study shows that MELD-Na significantly predicts 90-day mortality following TIPS, and it does so with a higher c-statistic than that previously reported in the literature with MELD alone.

Additionally, a MELD-Na above 22 predicts the highest risk of mortality at 90 days.

Questions arise

- Are noninvasive tests available to predict portal hypertension?
- Is our patient a candidate for early TIPS? Does MELD-Na vs MELD change prediction of mortality after TIPS?
- Was there a role to start beta blockers for primary prophylaxis?
- If TIPS is indicated, would he need a platelet transfusion?

Non-selective beta-blockers and acute kidney injury related in decompensated cirrhosis

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AASLD THE LIVER MEETING® 2017 WASHINGTON, DC OCTOBER 20-24

Background: Non-selective beta-blockers (NSBB) use in patients with decompensated cirrhosis (DC) is controversial. It has been suggested that NSBB in DC predisposes to acute renal injury (AKI), leading to negative evolution and outcomes.

AIM

Evaluate the risk of developing AKI in NSBB users in decompensated cirrhosis and associated mortality.

Methods: We compared 105 patients (59±15.2 years, women: 65%, MELD: 19.0±7.3), Hepatitis C was the most frequent etiology (32.4%), followed by cryptogenic (22.9%). At admission 67 (63.8%) were NSBB+ and 38 (33.2%) NSBB-.

Figure 1: Mortality of NSBB+ / NSBB- 1st and 6th month.

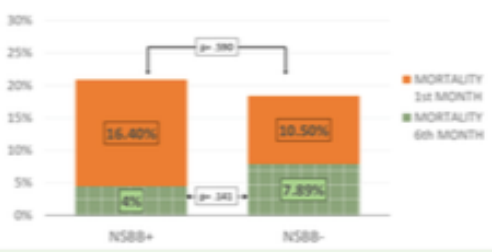

Table 1. Serum Creatinine Levels (mg/dl) of NSBB+ y NSBB-: basal, at admission, hospital stay and discharge.

Group	Basal creatinine	At admission creatinine	Hospital stay creatinine	Hospital discharge creatinine
NSBB +	0.95 ± 0.64	1.56 ± 1.15	1.41 ± 1.05	1.31 ± 1.62
NSBB -	0.96 ± 0.26	1.34 ± 0.61	1.25 ± 1.00	1.30 ± 1.87
p (<0.05)	0.886	0.26	0.44	0.96

CONCLUSION

The development of AKI was similar between both groups without statistical difference. We did not observe differences in mortality.

The results suggest that the use of NSBB on DC at admission is safe, it does not increase the frequency of AKI, neither mortality. However it is necessary to increase the number of patients.

Questions arise

- Are noninvasive tests available to predict portal hypertension?
- Is our patient a candidate for early TIPS? Does MELD-Na vs MELD change prediction of mortality after TIPS?
- Was there a role to start beta blockers for primary prophylaxis?
- If TIPS is indicated, would he need a platelet transfusion?

Superiority of Avatrombopag (AVA) to Placebo (PBO) for the treatment of Chronic Liver Disease (CLD) – Associated Thrombocytopenia (TCP) in Patients Undergoing Scheduled Procedures: Results of 2 Randomized, PBO Controlled Phase 3 Studies

Norah Terrault, Francesco Bibbiani, Yi-Cheng Chen, Namiki Izumi, Zeid Kayali, Jose R Lazcano Soto, Paul Mitrut, Wong Young Tak, Tare I Hassanein

- Severe thrombocytopenia (Platelet <50) is common in patients with chronic liver disease
- Platelet transfusions current standard of care to reduce risk of bleeding during invasive procedures in these patients
  - Associated with risk of transfusion reactions, infections, and induction of platelet refractoriness
- No pharmacological treatments are currently licensed for this indication.

ADAPT-1 & ADAPT-2 : Primary endpoint

- Need for platelet transfusions

- Higher proportion of patients in the AVA group did NOT require platelet transfusion or any rescue procedure for bleeding compared to placebo
  - This was true in both patient groups with baseline platelets <40 (66%, 69%) vs placebo (23%, 35%) $p<0.0001$
  - Those with 40 to <50 (88%, 88%) vs placebo (38%, 33%) $p<0.0001$

ADAPT-1 & ADAPT-2 trials: Secondary endpoint

- Proportion of patients who achieved platelet counts > or = 50 on procedure day

- 69% and 67% of patients with baseline platelet count <40 on AVA achieved platelet counts > or = 50 on procedure day compared to 4% and 7% in the placebo group (ADAPT-1 & ADAPT-2 trials)

- 88% and 93% of patients with baseline platelets of 40 to <50 in the AVA group achieved platelet counts > or =50 on procedure day compared to 21% and 39% in the placebo group

Question 1:

- True or False.

- A patient with decompensated cirrhosis and refractory ascites should remain off nonselective beta blockers for primary variceal bleed prophylaxis.

Question 2:

- 54 yo man with history of alcoholic cirrhosis complicated by ascites, who presents with hematemesis and confusion. His MELD is 13, Child class C. The patient is hemodynamically stable.
- EGD shows large esophageal varices, no other source of GI bleed. Endoscopic ligation is performed.

- What is the next course of action?
  - A. Return in 2 weeks for variceal surveillance
  - B. Start NSBB upon discharge
  - C. Early TIPs
  - D. A & B
  - E None of the above

Question 3, original case presentation:

- 54 yo man with history of alcoholic cirrhosis complicated by ascites, who presents with hematemesis. His MELD is 13, Child class B. The patient is hemodynamically stable. He has been placed on a PPI drip, ocreotide drip, and antibiotics.
- EGD shows large fundic varix with a nipple sign.

- What is your next step?
- A. Perform a CT or MRI
- B. Perform variceal ligation
- C. Inject cyanoacrylate
- D. Perform balloon retrograde transvenous obliteration (BRTO)
- E. Perform a TIPs

Questions arise

- Are noninvasive tests available to predict portal hypertension?
  - Yes, may help to avoid more invasive procedures like EGD and HVPG measurements
- Is our patient a candidate for early TIPS? Does MELD-Na vs MELD change prediction of mortality after TIPS?
  - He is Child Class B with fundic varices and ascites. Although there's thought that BRTO is a better option for gastric varices compared to TIPS, this patient has MELD <18, ascites, varices with high risk stigmata, early TIPs may be a good option for him.
- Was there a role to start beta blockers for primary prophylaxis?
  - Yes
- If TIPS is indicated, would he need a platelet transfusion?
  - AVA would be a great option for him if his platelets <50,000

Thank you