

ELASTOGRAPHY IN AUTOIMMUNE AND CHOLESTATIC LIVER DISEASE

UCL

International Hepatology Ultrasound Course

Royal Free Hospital

26-28th February 2026

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AUTOIMMUNE HEPATITIS

- The natural history of autoimmune hepatitis is often non linear and might change from an indolent form with mild fibrotic changes to progressive parenchymal sclerosis and cirrhosis with portal hypertension.
- It might be characterized by inflammatory flares or an aggressive pattern with diffuse necrosis which may lead to acute/subacute liver failure or cirrhosis.
- The timing of treatment and response leads to the residual parenchymal appearance and functional reserve.

ULTRASOUND APPEARANCE IN AUTOIMMUNE LIVER DISEASE

Extremely variable depending, the onset and severity of inflammation, the stage of disease, the timing of treatment

- Homogeneous heterogeneity of liver parenchyma
- Often reactive nodes are present at the liver hilum
- Heterogeneous heterogeneity of liver parenchyma
- Retracted segments with compensatory hypertrophy
- ‘usual cirrhotic appearance’

AUTOIMMUNE HEPATITIS

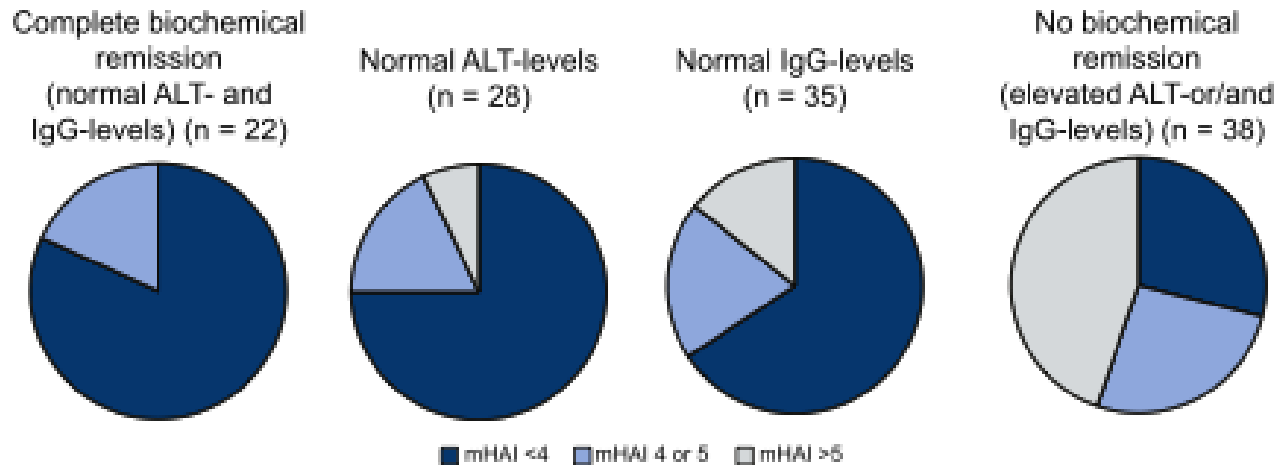
- Liver stiffness has been reported to be very high in AIH, likely to be secondary to inflammation*
- Fibrosis and cirrhosis can be reversible in this setting and elastography is a reliable follow-up tool to monitor also disease activity**

*Hartl et al. Transient elastography in autoimmune hepatitis: Timing determines the impact of inflammation and fibrosis. *J Hepatol.* 2016; 65(4):769-775

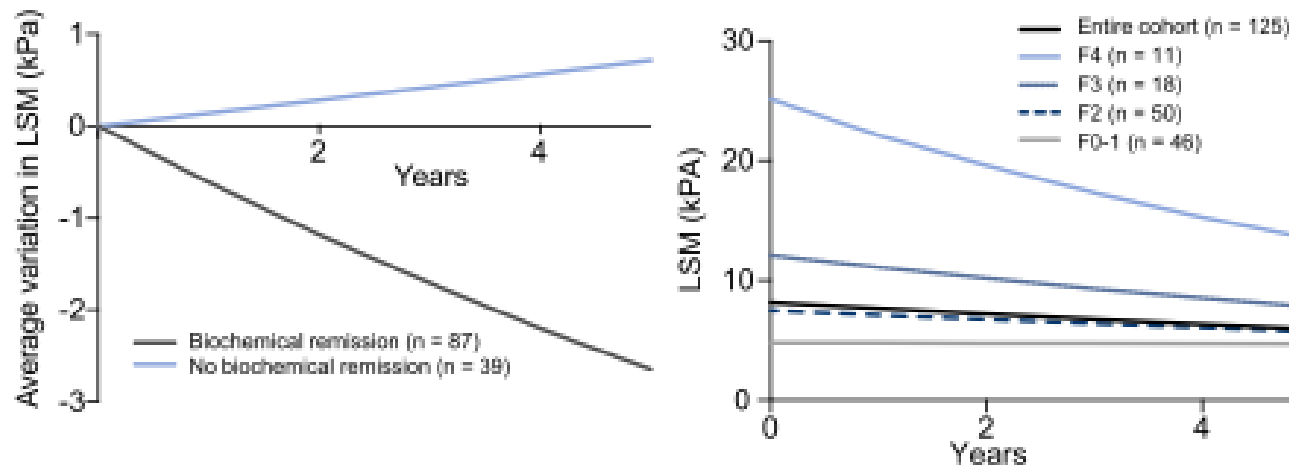
**Hartl et al. Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis.

J. Hepatol. 2018, 68, 754–763

Histological disease activity in dependence of biochemical remission in autoimmune hepatitis



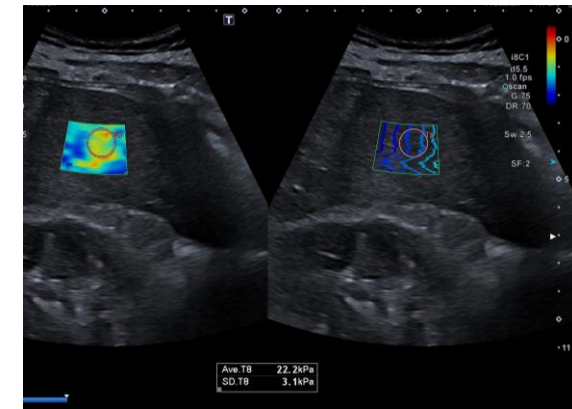
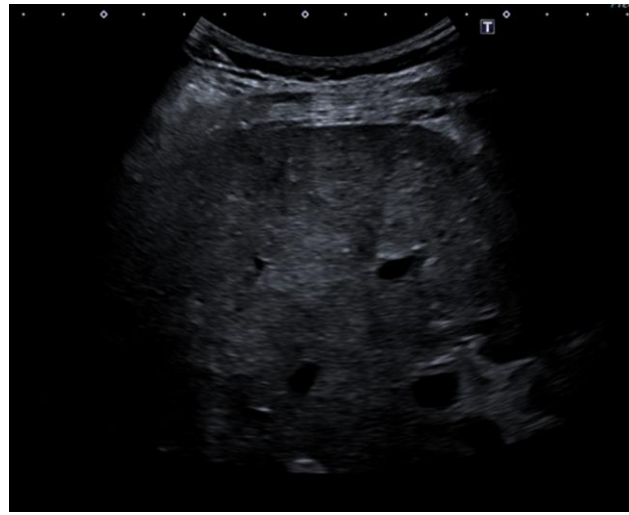
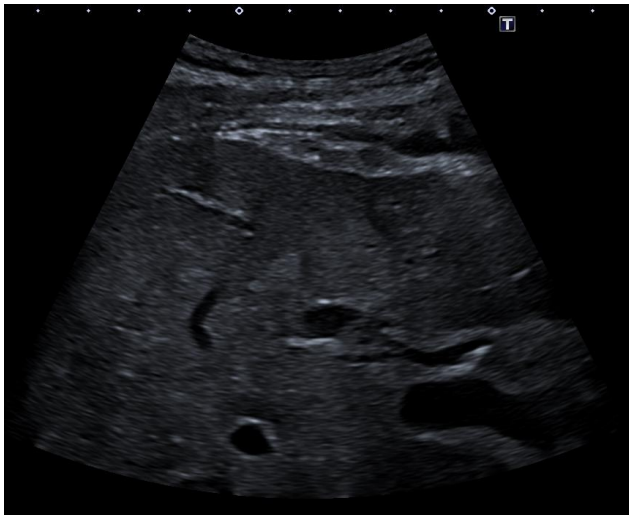
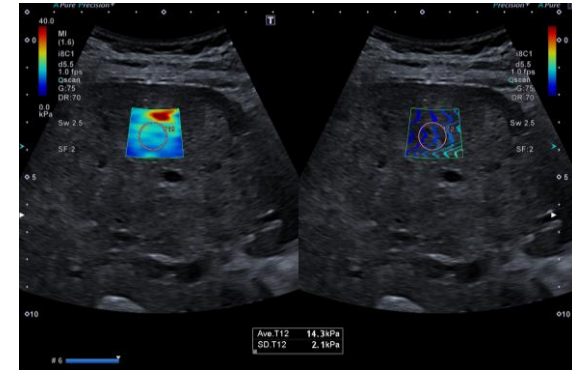
Changes of liver stiffness measurement (LSM) in dependence of complete biochemical remission and fibrosis stage



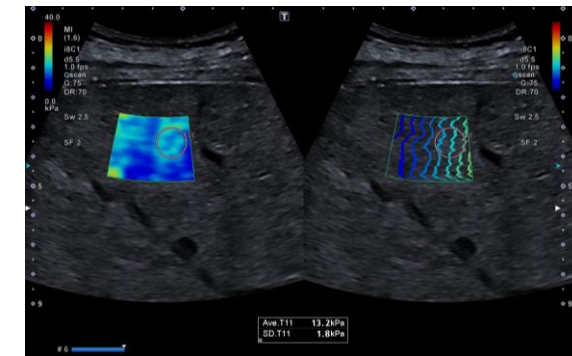
**Hartl et al. Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis. J Hepatol. 2018, 68, 754–763

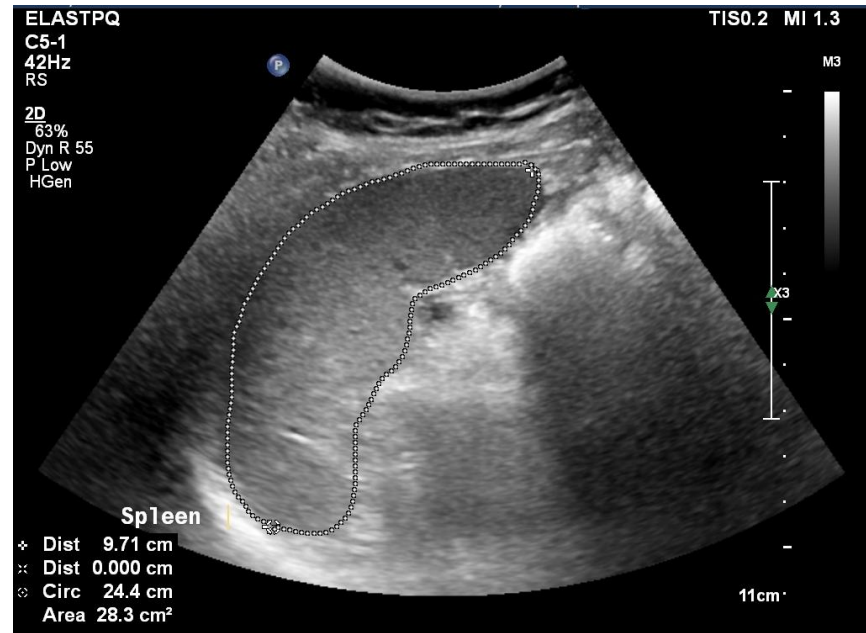
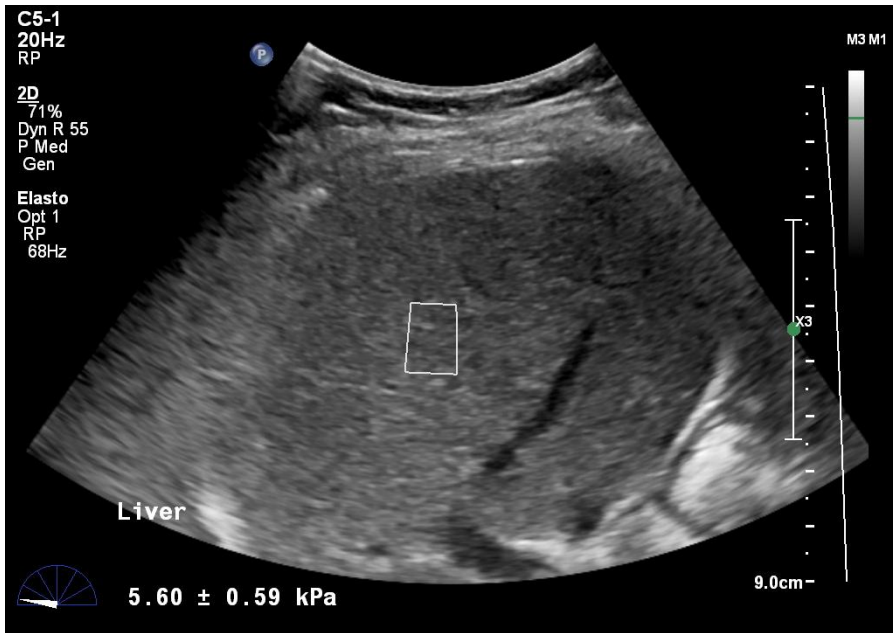
ACUTE AUTOIMMUNE HEPATITIS



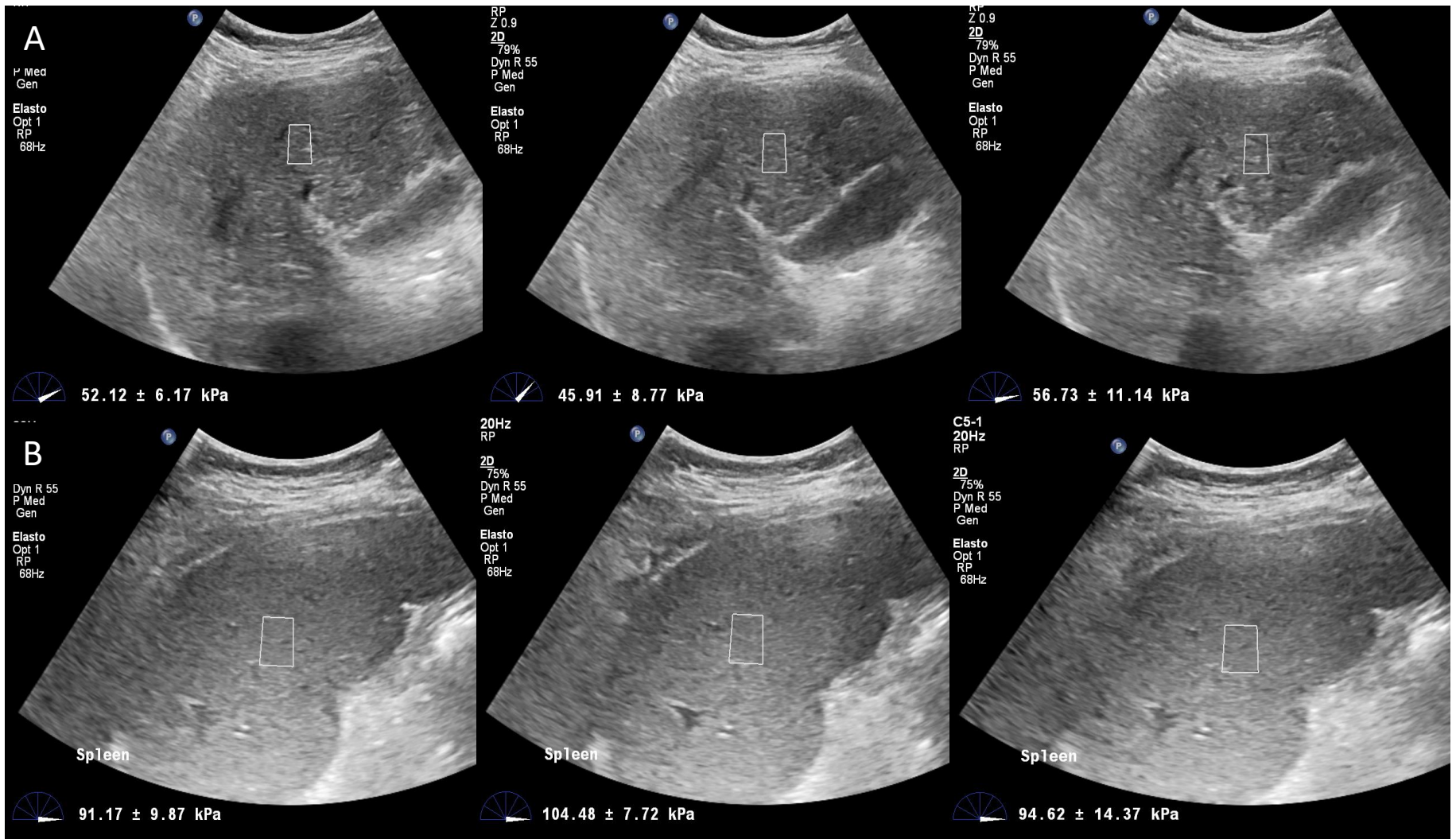


AIH related liver disease. There are signs of parenchymal heterogeneity. Liver elastography shows increased stiffness values that are different according to where the measurement is acquired. These result reflect the heterogeneous distribution of the inflammatory changes that can occur in autoimmune hepatitis.

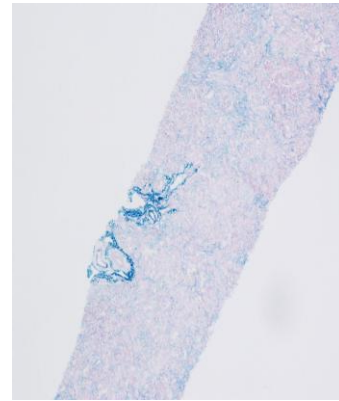
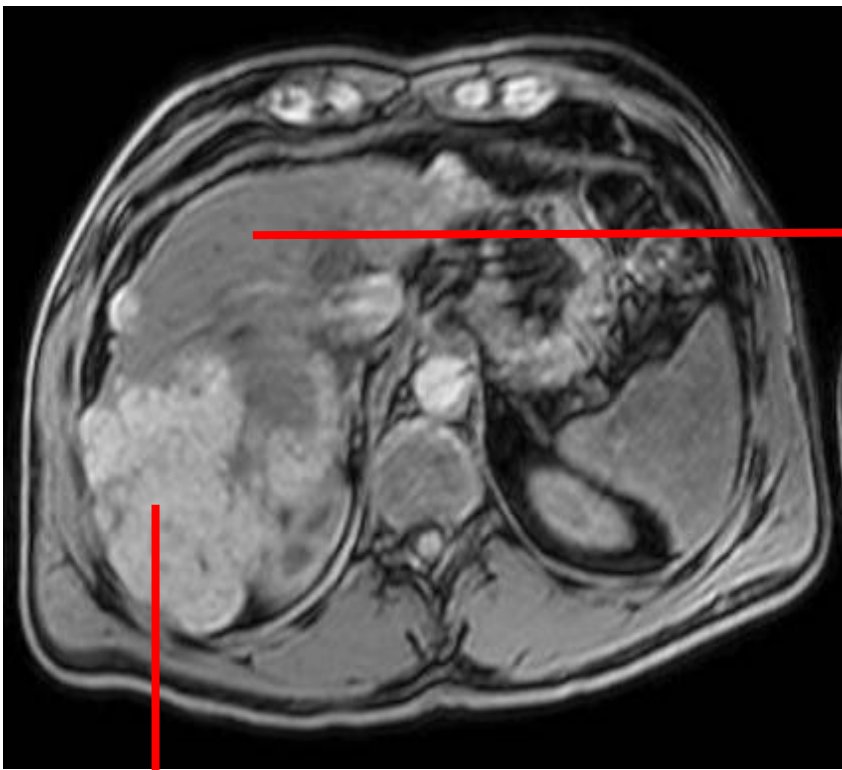




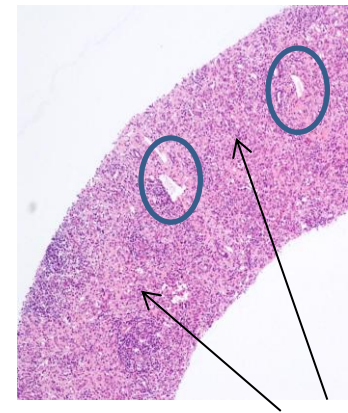
AIH related liver disease. There are signs of parenchymal heterogeneity and the left liver lobe is atrophic. Spleen is normal in size. Liver elastography shows normal stiffness values. These results show that this patient had a severe previous hepatitis that is now in remission as proven by the stiffness values and normal biochemistry (not shown).



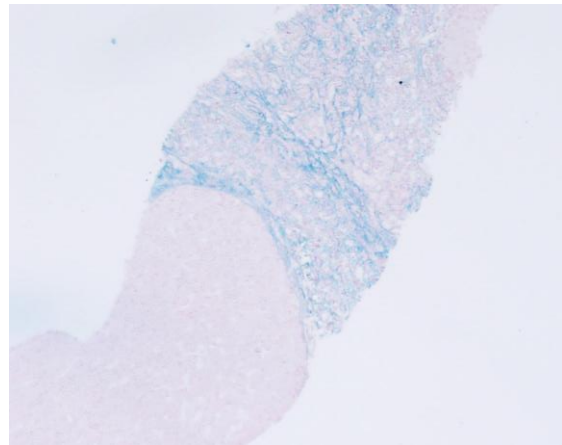
AIH related cirrhosis. Both liver (A) and spleen (B) elastography confirm stiffness values compatible with clinically significant portal hypertension.



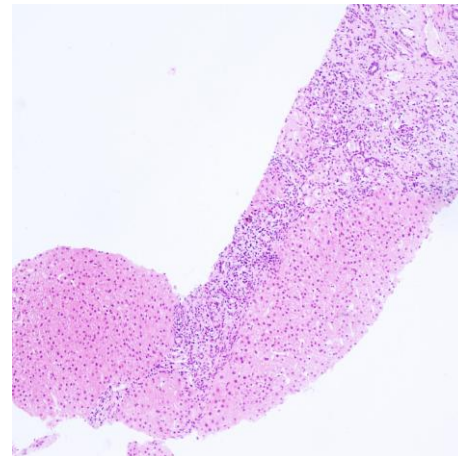
Little elastification of the areas with panacinar necrosis. Portal tracts highlighted by dense well-formed elastin



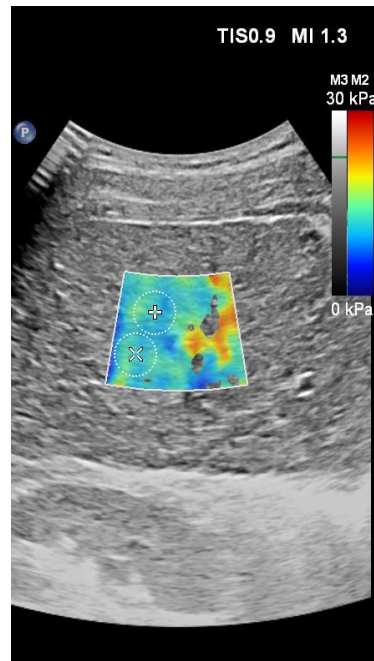
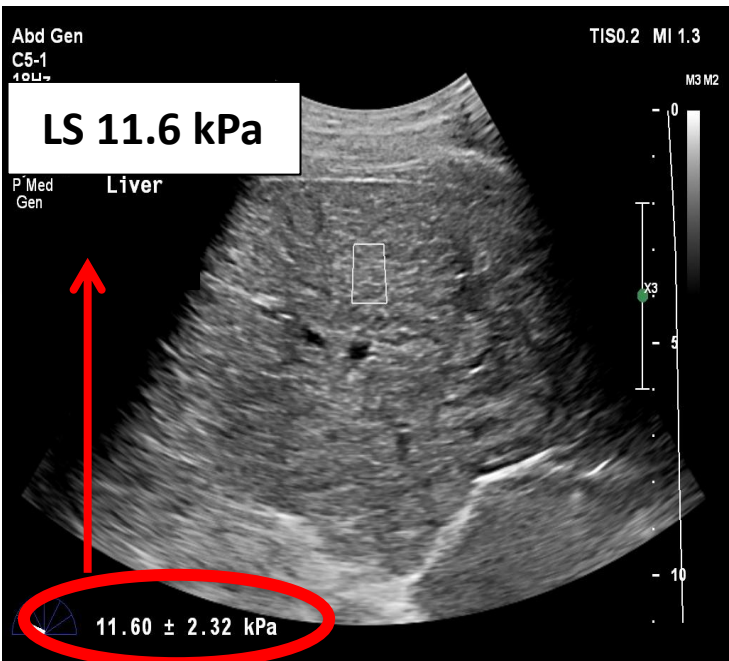
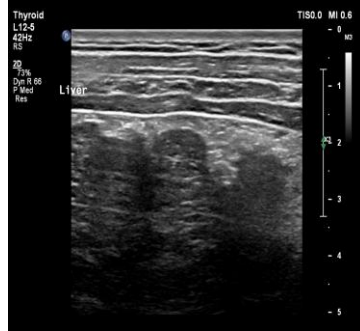
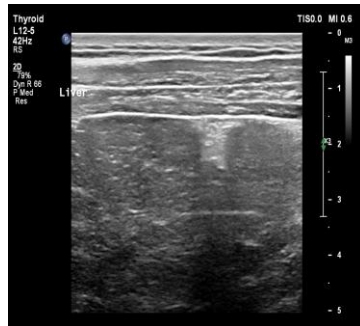
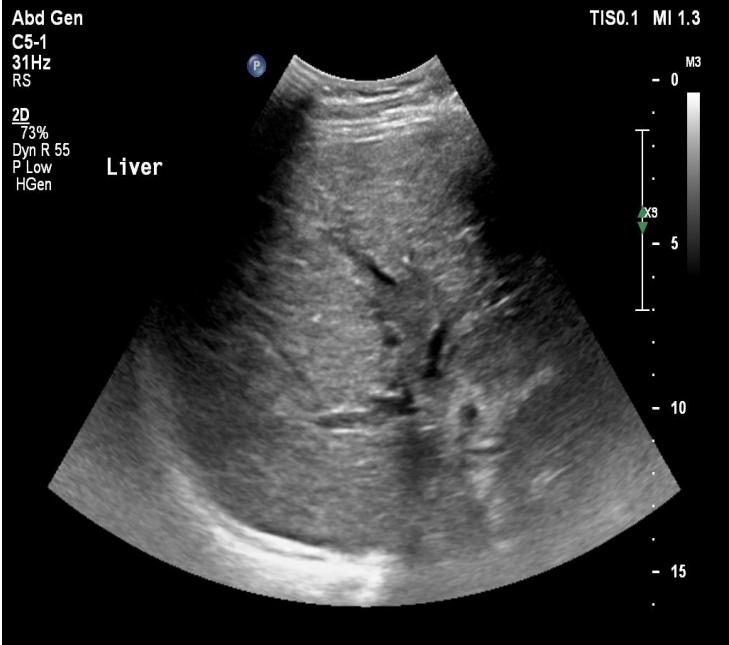
Panacinar necrosis. Basic underlying lobular architecture preserved with identifiable portal tracts



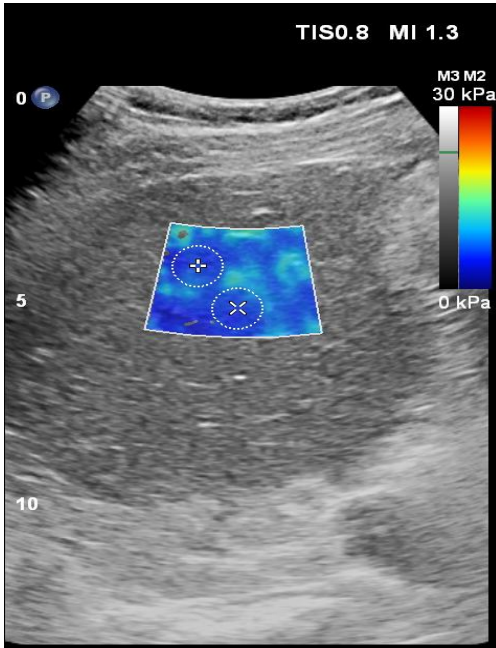
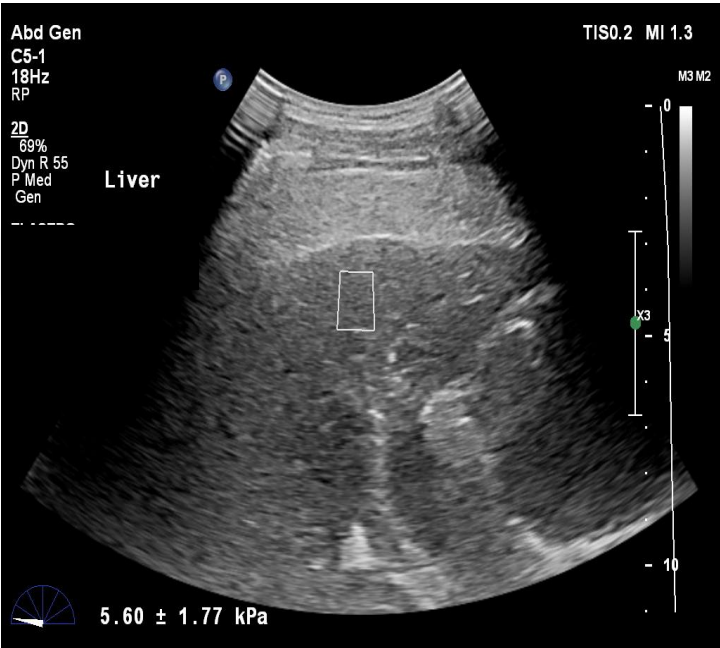
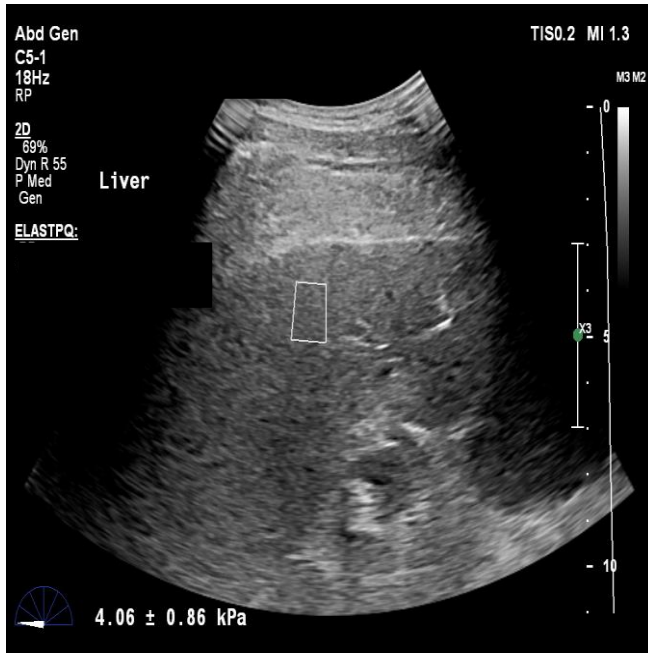
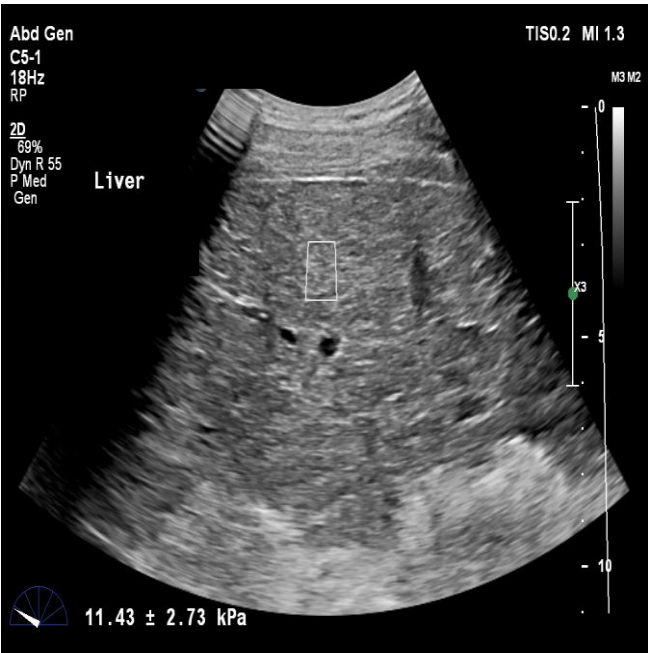
Elastified panacinar necrosis with regenerating nodules



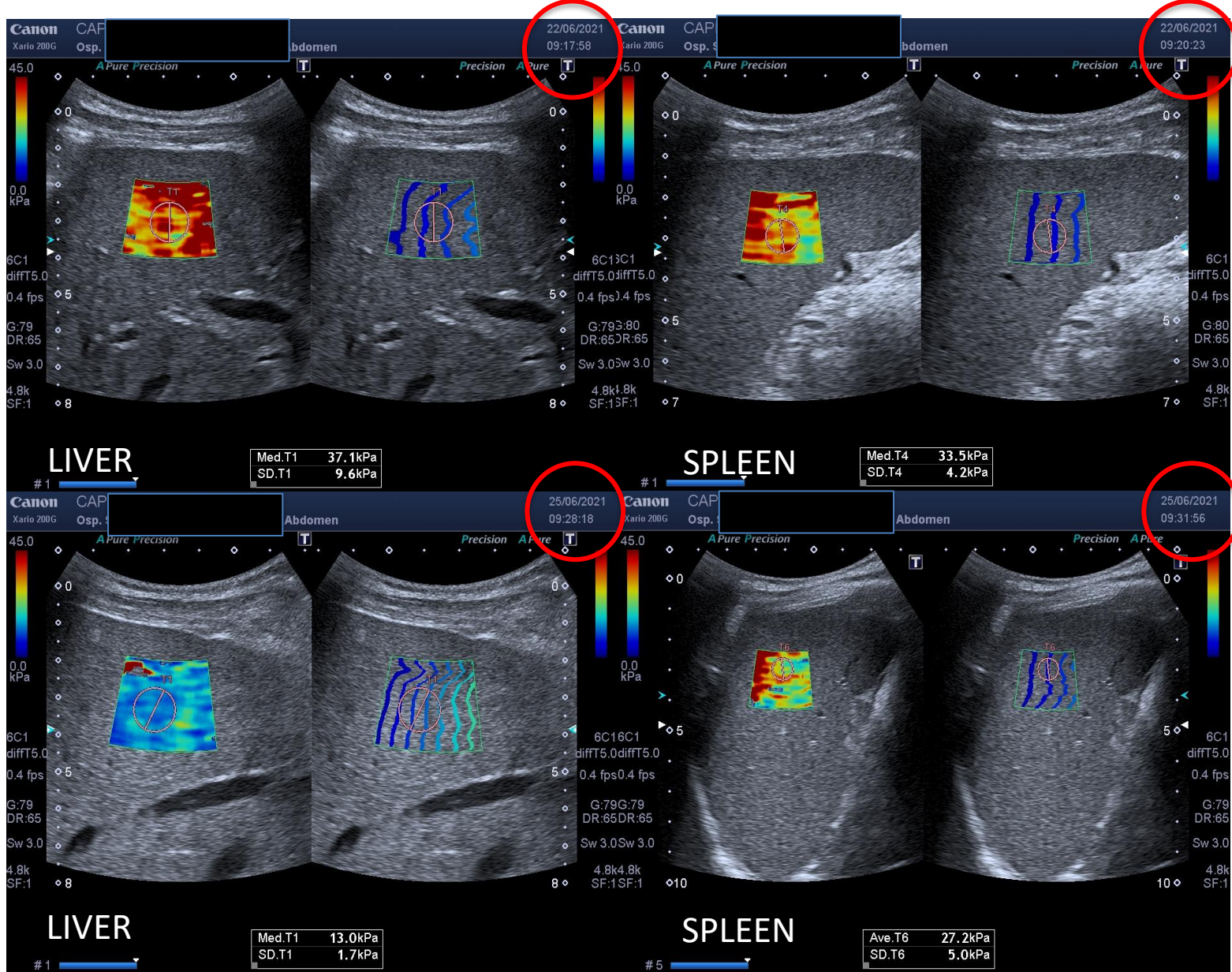
Hepatocyte nodules separated by thick fibrous septa with marked ductular proliferation and a mild, mainly lymphoplasmacytic inflammatory infiltrate



LS 11.01 kPa
LS 11.05 kPa



LS 5.82 kPa
LS 6.06 kPa



Patient with autoimmune hepatitis with a significant flare of inflammation. Spleen stiffness is slightly increased but not significantly. After a few days of immunosuppressive treatment LS is reduced considerably. Spleen stiffness is also reduced. No signs of portal hypertension.

TAKE HOME MESSAGES ON AUTOIMMUNE HEPATITIS

- The natural history of autoimmune hepatitis is very variable
 - It might be characterized by inflammatory flares or an aggressive pattern with diffuse necrosis which may lead to acute/subacute liver failure or cirrhosis.
 - The timing of treatment and response leads to the residual parenchymal appearance and functional reserve.
 - The ultrasound features are very variable and there might be a significant discrepancy between the heterogeneity and stiffness values
 - Delta stiffness values are important to evaluate treatment response and the presence of increased liver stiffness results should be considered related to fibrosis once biochemical remission is obtained

AUTOIMMUNE HEPATITIS

- Complete biochemical remission is a reliable surrogate of low histological disease activity.
- Patients with autoimmune hepatitis have a high chance of fibrosis regression if inflammation is suppressed.
- Transient elastography is a non-invasive tool to monitor fibrosis development in autoimmune hepatitis.
- Elastography is a potential tool to improve treatment monitoring and response in patients with autoimmune hepatitis.

PRIMARY BILIARY CHOLANGITIS

- Autoimmune liver disease
- Affects the distal bile ducts with inflammation and periductal fibrosis
- Patchy distribution of fibrosis
- Presinusoidal portal hypertension
- Cirrhosis
- There are many phenotypes

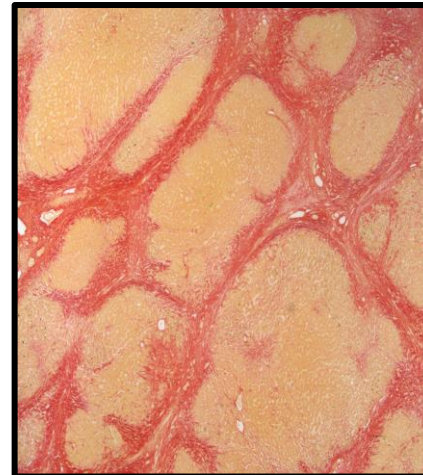
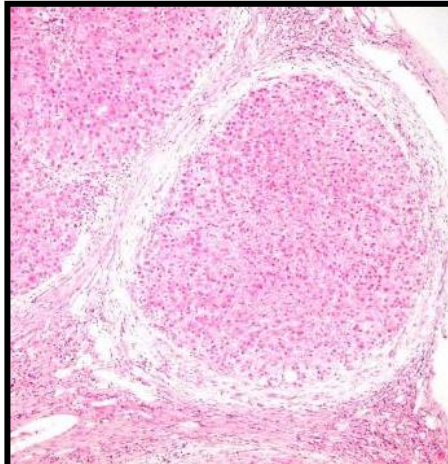
PRIMARY BILIARY CHOLANGITIS

*F1 ≥ 7.1
kPa

F2 ≥ 8.8 kPa

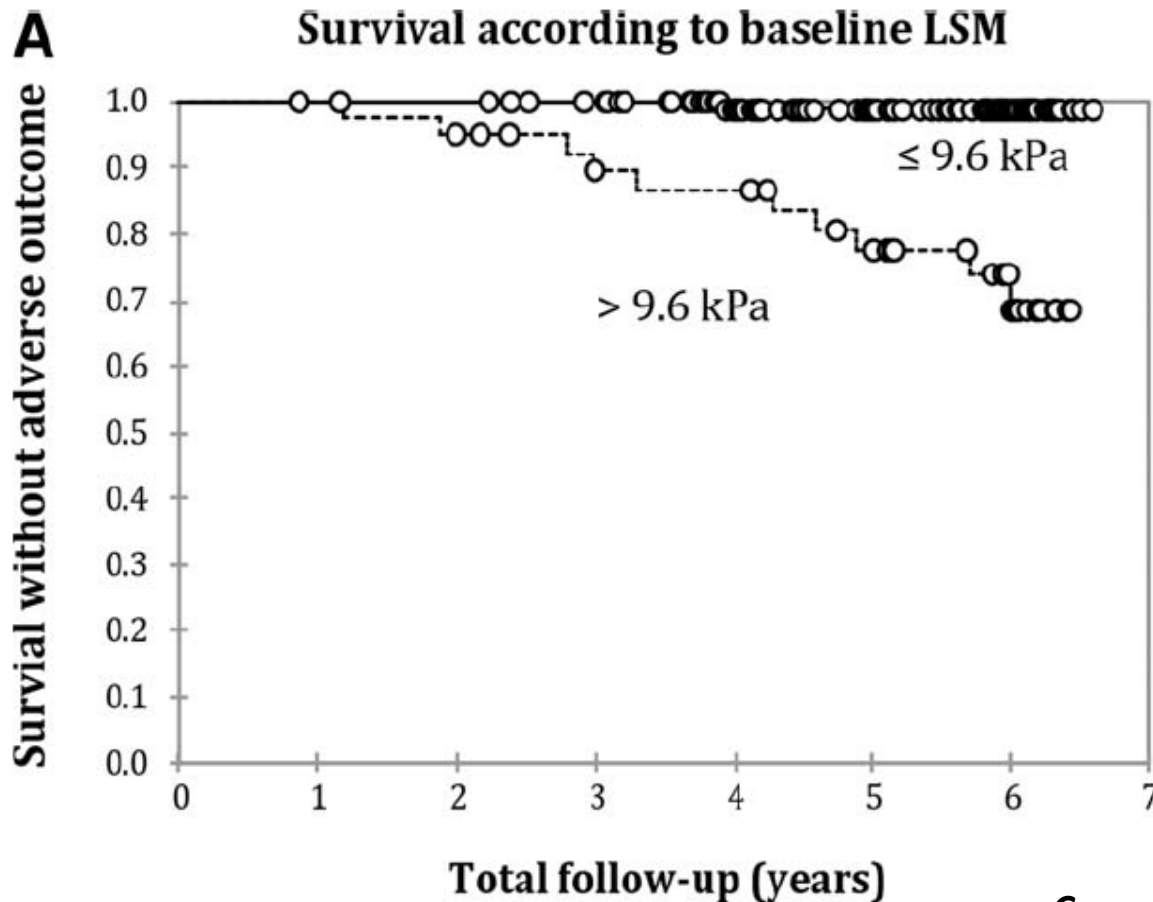
F3 ≥ 10.7 kPa

F4 ≥ 16.9
kPa

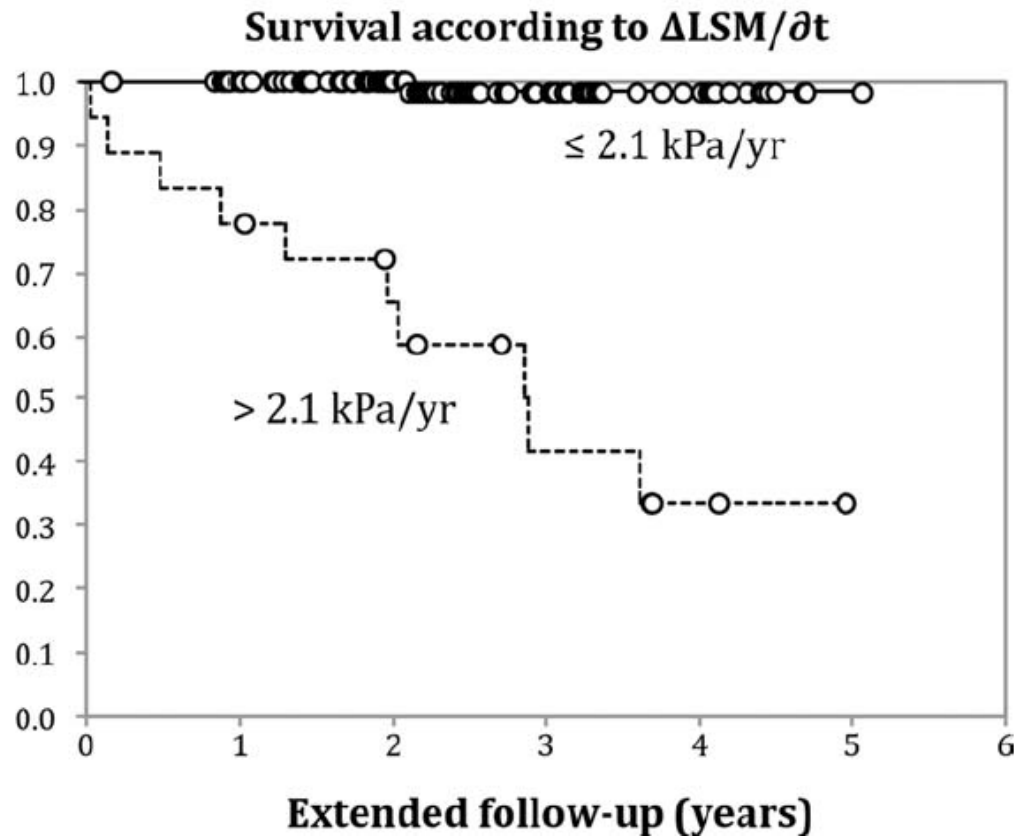


*Corpechot et al. Noninvasive elastography-based assessment of liver fibrosis progression and prognosis in primary biliary cirrhosis. *Hepatology*. 2012;56(1):198-208

Noninvasive Elastography-Based Assessment of Liver Fibrosis Progression and Prognosis in Primary Biliary Cirrhosis

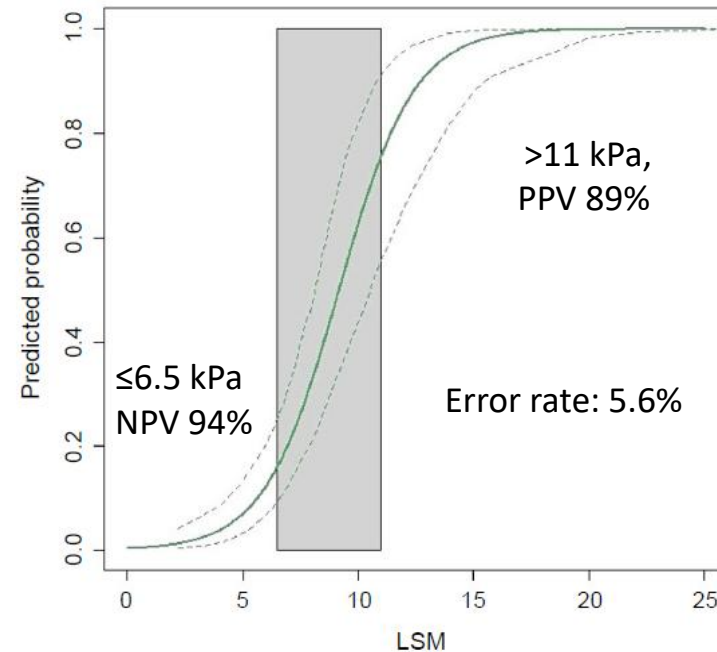
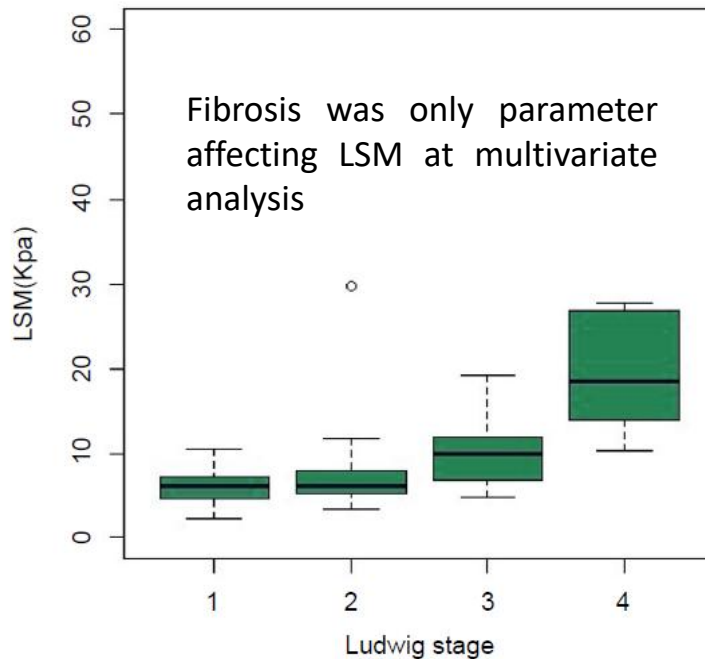


Noninvasive Elastography-Based Assessment of Liver Fibrosis Progression and Prognosis in Primary Biliary Cirrhosis



A cut-off value of 2.1 kPa/year was associated with an 8.4-fold increased risk of liver decompensations, liver transplantations, or deaths

Accuracy of Transient Elastography in Assessing Fibrosis at Diagnosis in Naïve Patients With Primary Biliary Cholangitis: A Dual Cut-Off Approach



In patients with LSM between these two cutoffs, VCTE is not reliable and liver biopsy should be evaluated for accurate disease staging.

Liver stiffness measurement by vibration-controlled transient elastography improves outcome prediction in primary biliary cholangitis

- Multicentre study
- 23 centres
- 3985 pts (2740 derivation, 568 validation cohort)

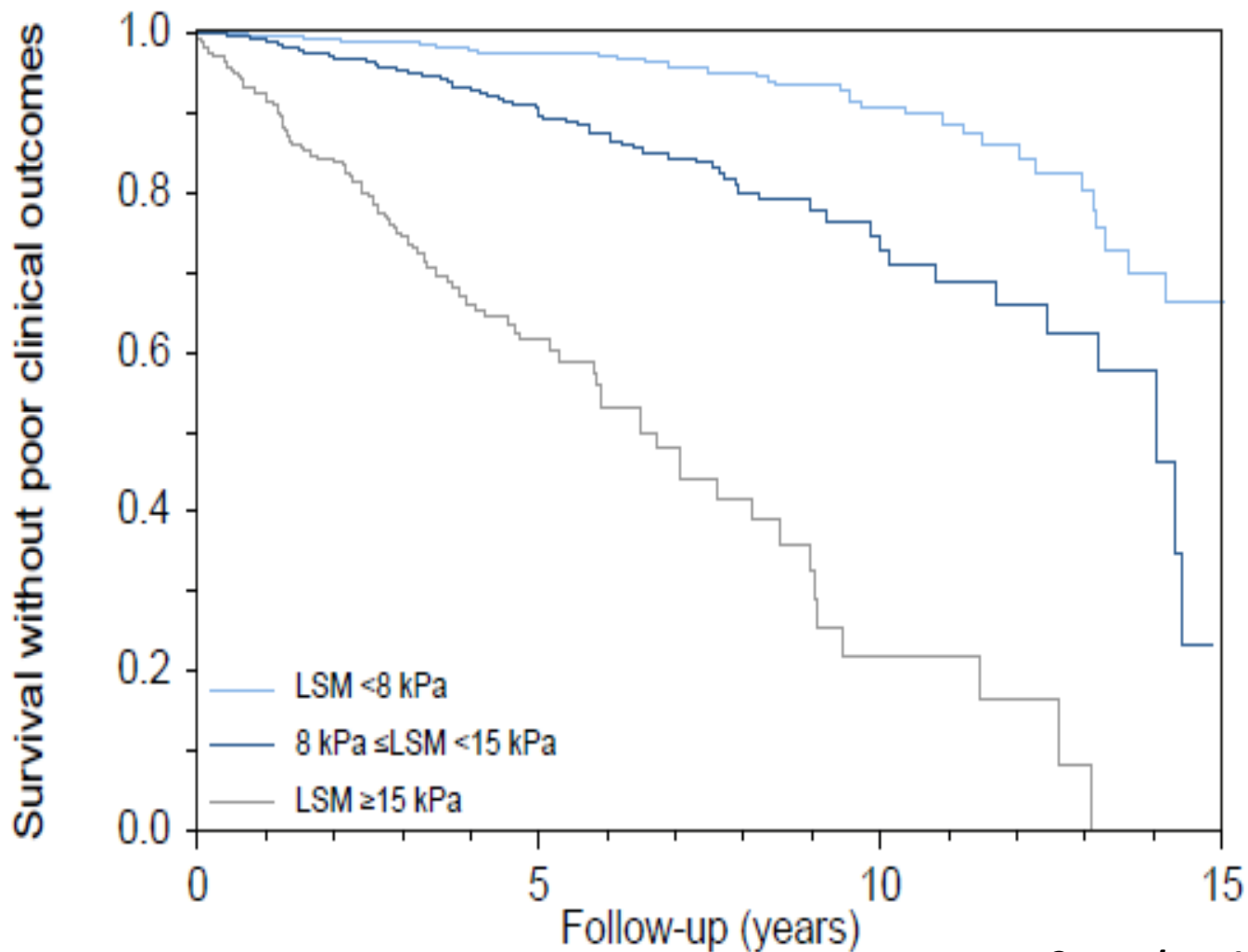


- LSM ≤ 8 kPa Low risk

- LSM 8-15 kPa Intermediate risk

- LSM > 15 kPa High risk

Liver stiffness measurement by vibration-controlled transient elastography improves outcome prediction in primary biliary cholangitis



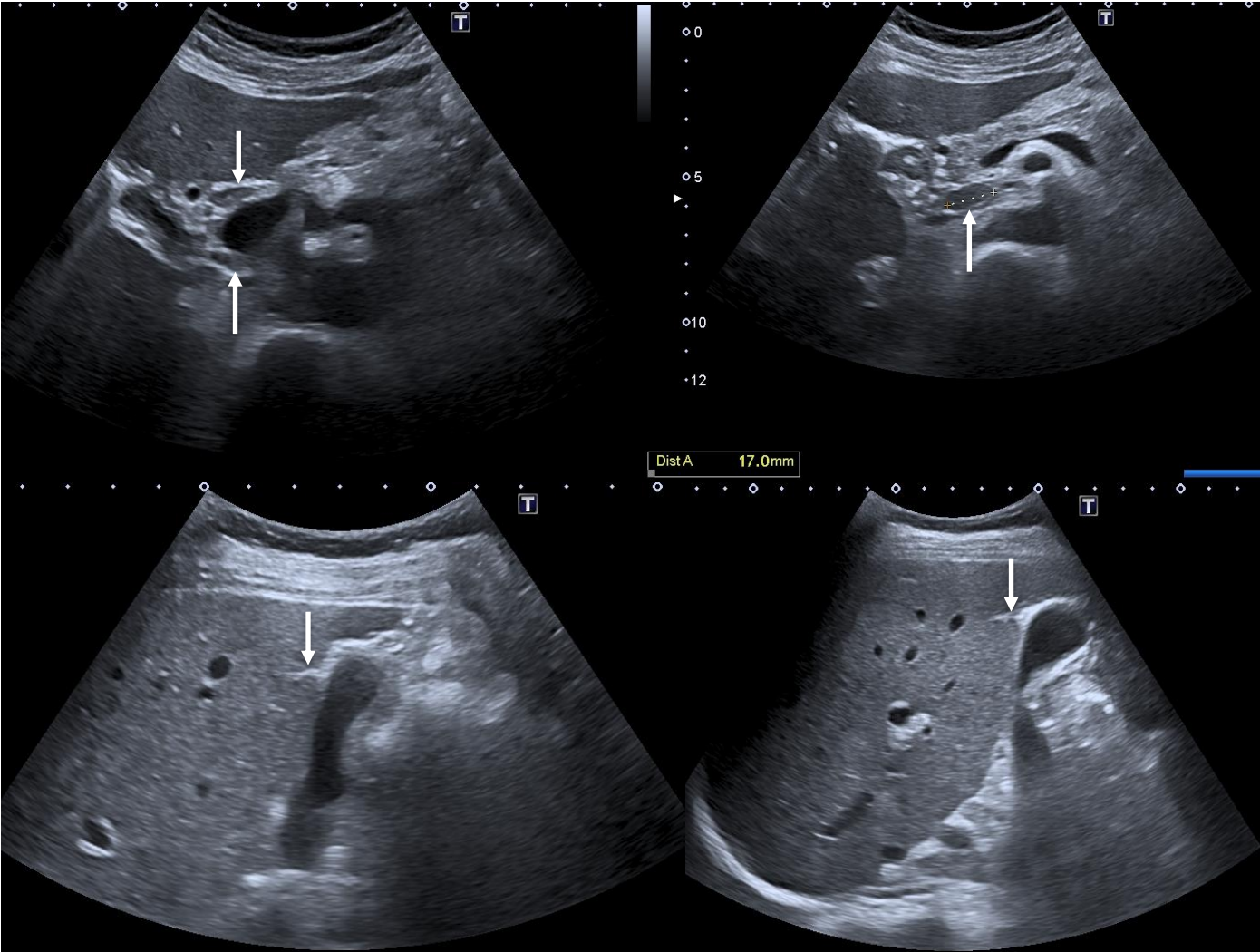
PORTAL HYPERTENSION IN CHOLESTATIC LIVER DISEASE

Non-Invasive Prediction of High-Risk Varices in Patients with Primary Biliary Cholangitis and Primary Sclerosing Cholangitis

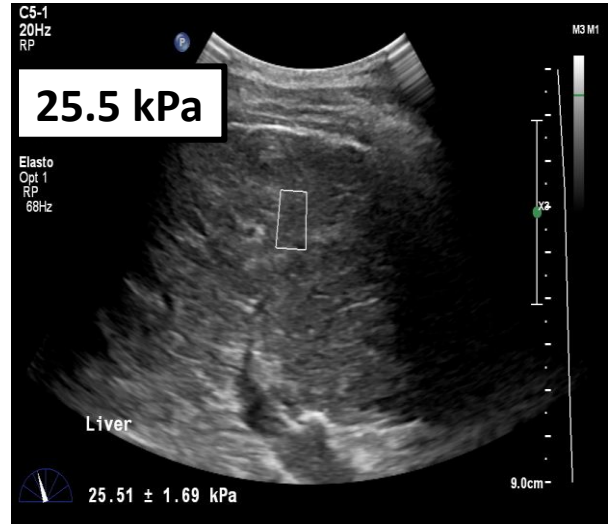
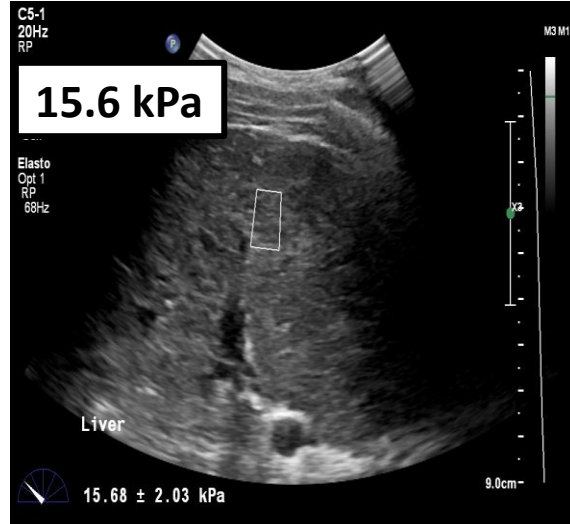
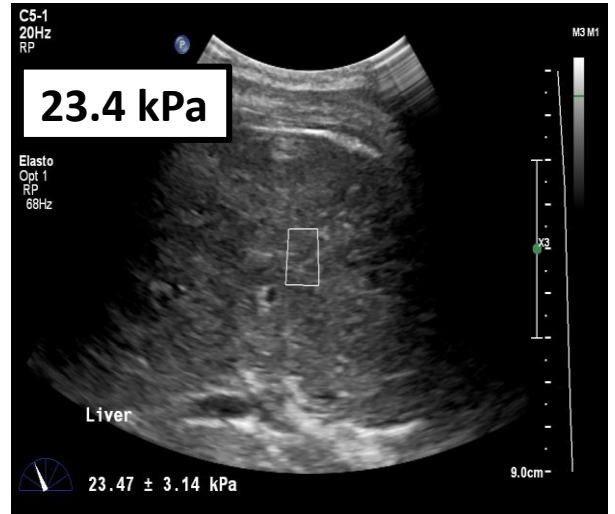
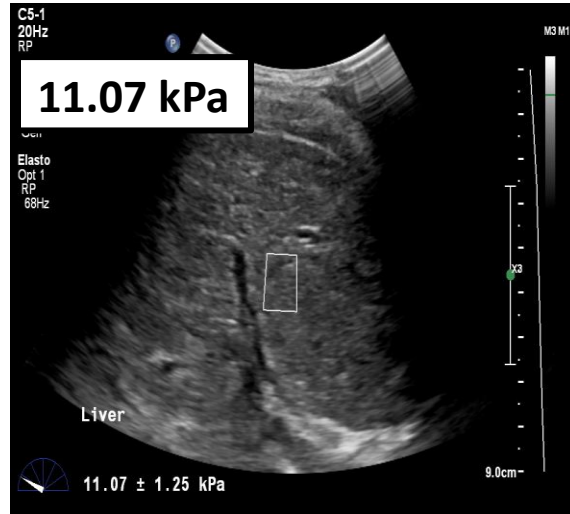
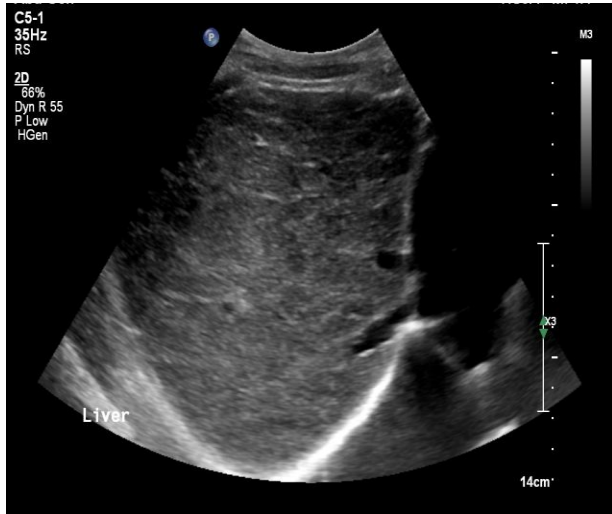
Carlos Moctezuma-Velazquez, MD, MSc¹, Francesca Saffiotti, MD^{2,3}, Stephanie Tasayco-Huaman, MD^{4,5}, Stefania Casu, MD⁶, Andrew Mason, MD, MBBS¹, Davide Roccarina, MD, PhD², Victor Vargas, MD^{4,5}, Jan-Erick Nilsson, MD¹, Emmanuel Tsochatzis, MD, PhD², Salvador Augustin, MD^{4,5}, Aldo J. Montano-Loza, MD, PhD¹, Annalisa Berzigotti, MD, PhD⁶, Douglas Thorburn, MD, PhD², Joan Genesca, MD, PhD^{4,5} and Juan Gonzalez Abraldes, MMSc¹

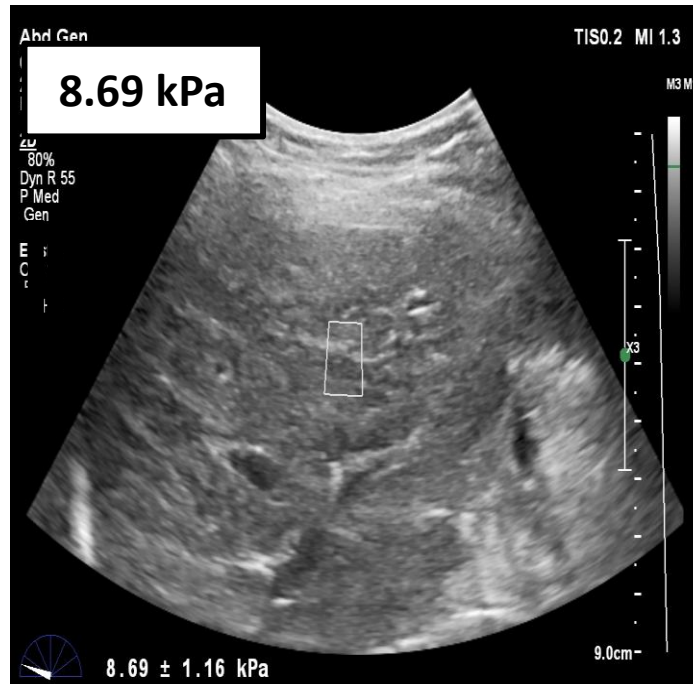
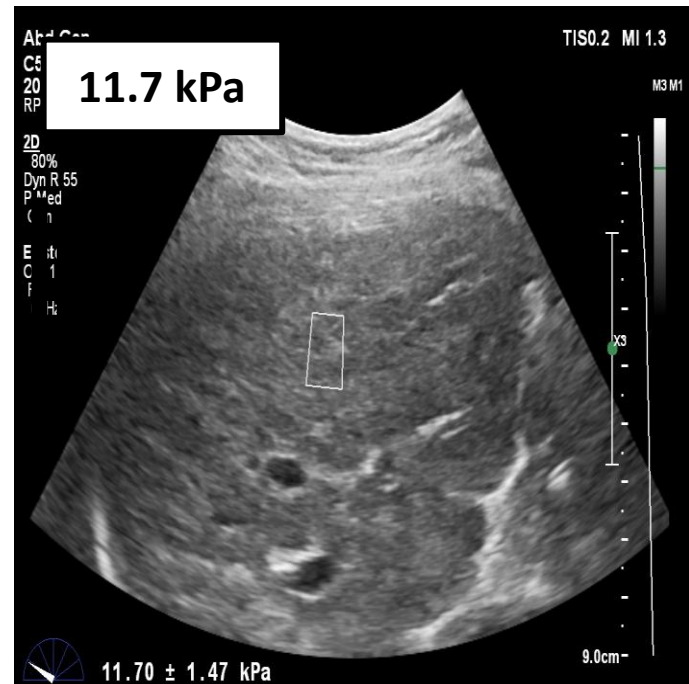
LS <20 kPa and platelet count >150000/mm³ and extended criteria LS < 25 kPa and platelet count > 110000/mm³ can be applied however the false negative rate in this PBC population was > 5%.

PRIMARY BILIARY CHOLANGITIS



PRIMARY BILIARY CHOLANGITIS





Discrepancy between the liver irregular echostructure/morphology and stiffness values which are relatively “low” and variable liver stiffness

C5-1
31Hz
RS

2D
64%
Dyn R 55
P Low
HGen

M3



16cm

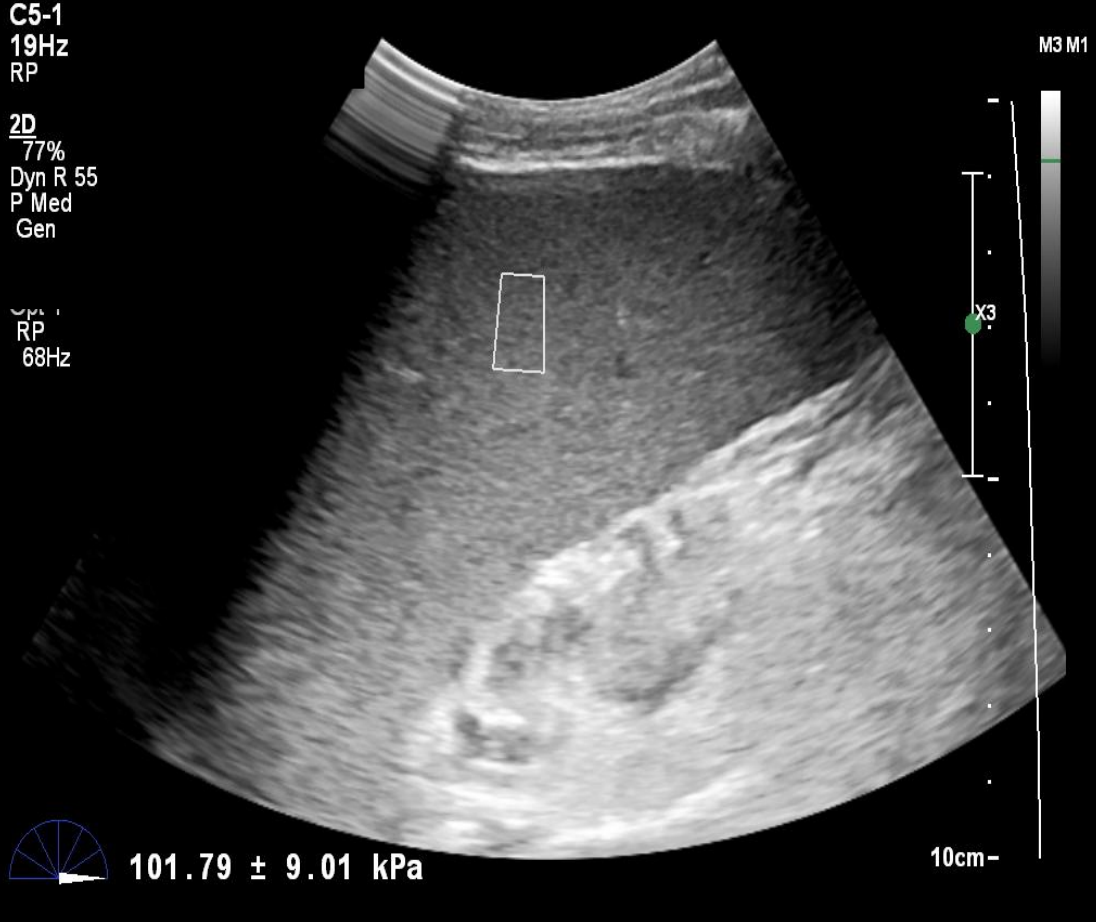
CPH and PBC LIVER STIFFNESS

Stiffness Measurements

Sample 1	[41.69] kPa	5	[16.37] kPa	9	[10.55] kPa
2	[20.74] kPa	6	[17.29] kPa	10	[40.30] kPa
3	[32.74] kPa	7	[24.36] kPa		
4	[13.77] kPa	8	[41.24] kPa		

Stiffness Calculations

Stiffness Avg	[25.91] kPa
Stiffness Std	[11.47] kPa
Stiffness Med	[22.55] kPa



PBC

SPLEEN

STIFFNESS

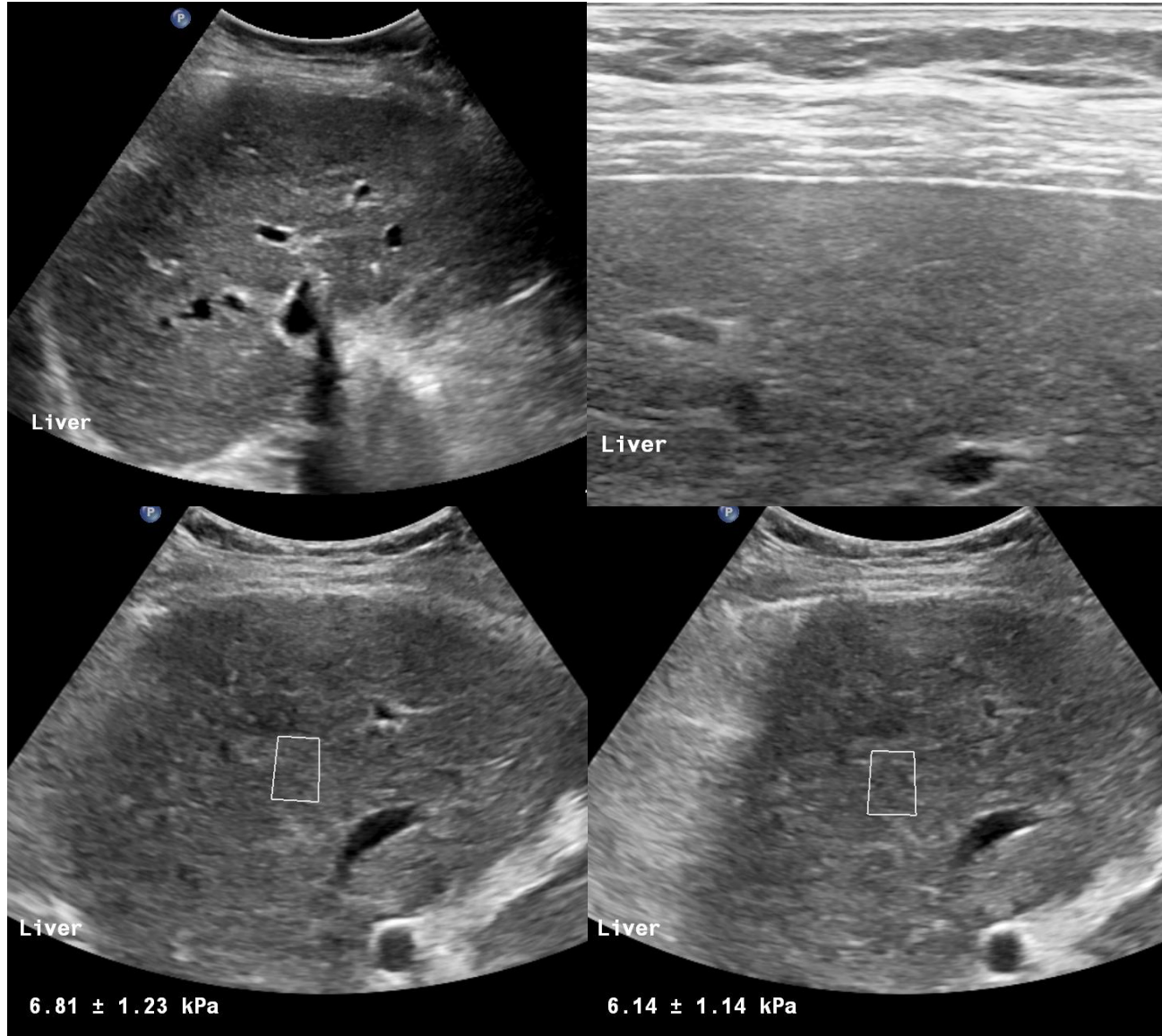
Stiffness Measurements

Sample 1	[105.41] kPa	4	[92.78] kPa	7	[60.55] kPa
2	[101.79] kPa	5	[159.71] kPa		
3	[83.34] kPa	6	[100.28] kPa		

Stiffness Calculations

Stiffness Avg	[100.55] kPa
Stiffness Std	[27.98] kPa
Stiffness Med	[100.28] kPa

PRIMARY BILIARY CHOLANGITIS



PRIMARY BILIARY CHOLANGITIS

- The available data is scarce compared to other aetiologies but provides clinical guidance
- However there is high variability due to the patchy distribution of fibrosis and liver stiffness per se might in some cases underestimate fibrosis
- Presinusoidal portal hypertension should always be suspected.

CONCLUSIONS - PBC

- There is evidence of a good correlation between liver fibrosis and elastography.
- Elastography is of prognostic significance in PBC
- Elastography is useful in monitoring treatment response
- The use of extended Baveno criteria can be applied to cholestatic liver disease. But in the PBC population it carried a FNR >5%. The accuracy is good but caution is advised* and more studies are needed.

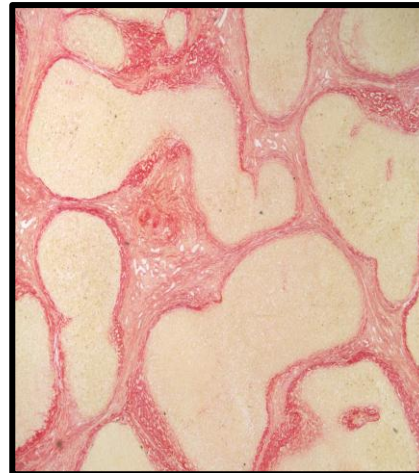
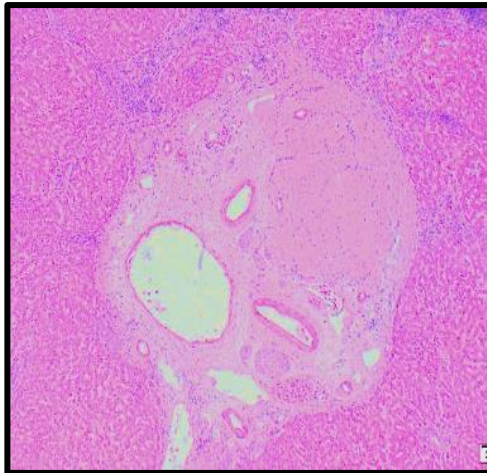
PRIMARY SCLEROSING CHOLANGITIS

*F1 \geq 7.4 kPa

F2 \geq 8.6 kPa

F3 \geq 9.6 kPa

F4 \geq 14.4 kPa

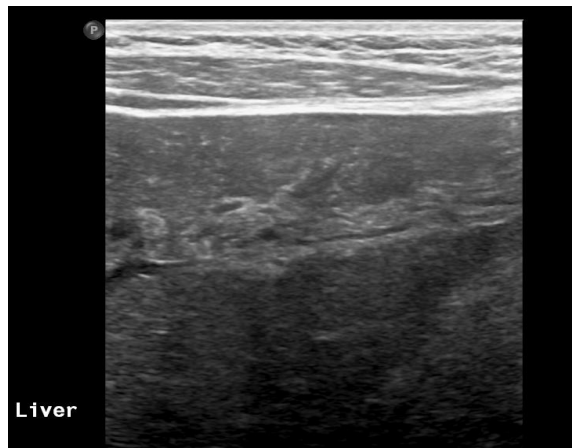
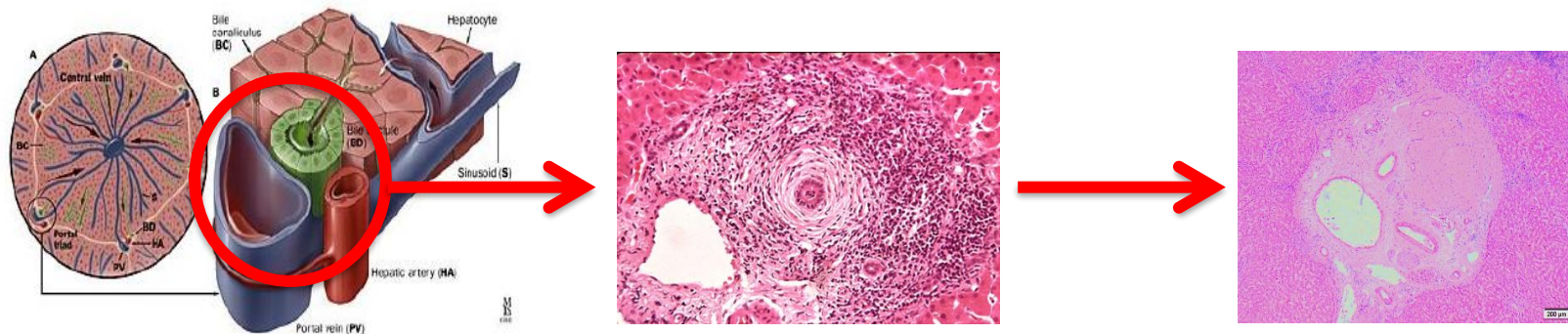


*Corperchot et al. Baseline values and changes in liver stiffness measured by transient elastography are associated with severity of fibrosis and outcomes of patients with primary sclerosing cholangitis. *Gastroenterology* 2014;146(4):970-9.

PRIMARY SCLEROSING CHOLANGITIS

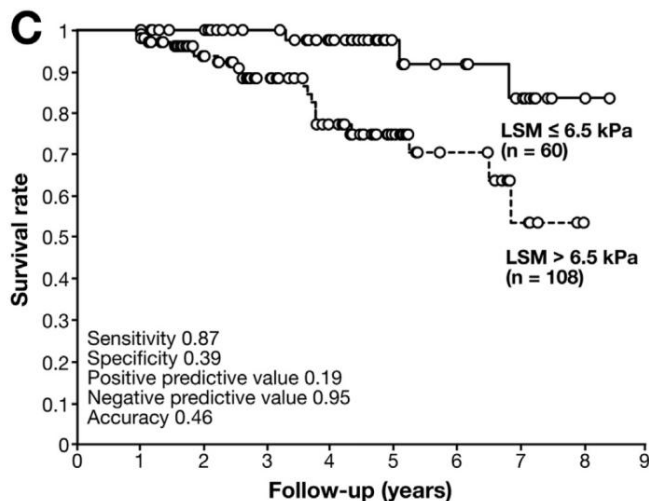
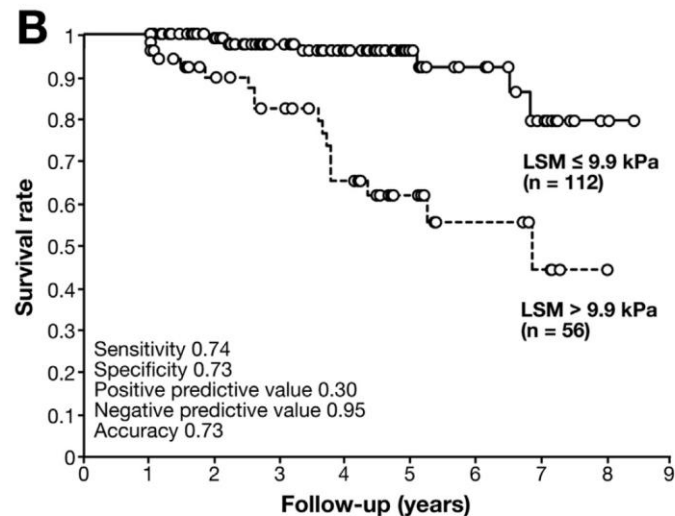
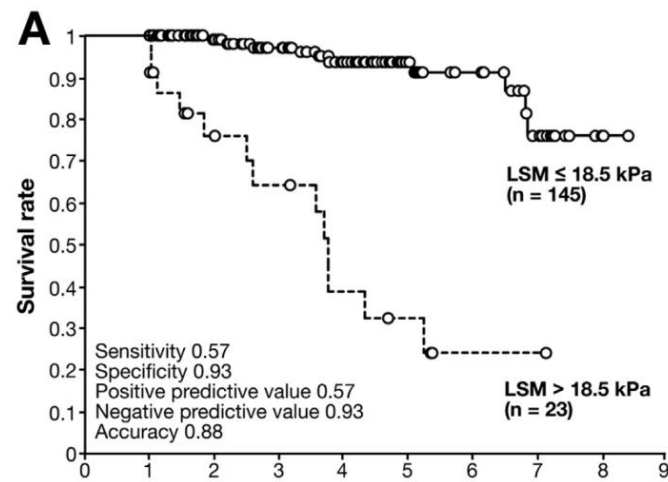
- Chronic cholestatic liver disease of unknown cause
- Inflammation of the intra and/or extra-hepatic bile ducts which leads to biliary fibrosis
- It is typically a segmental/regional disease
- Periportal fibrosis
- Cirrhosis

BILIARY FIBROSIS IN PRIMARY SCLEROSING CHOLANGITIS



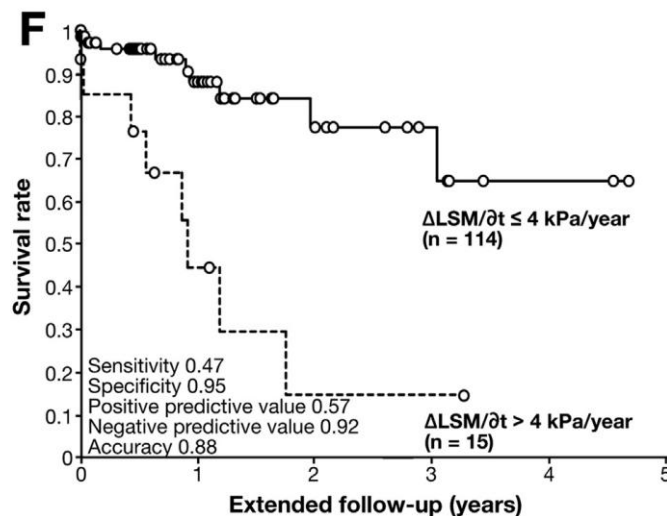
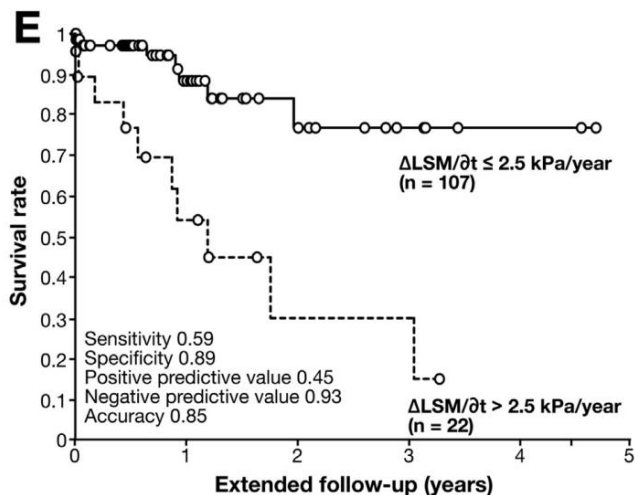
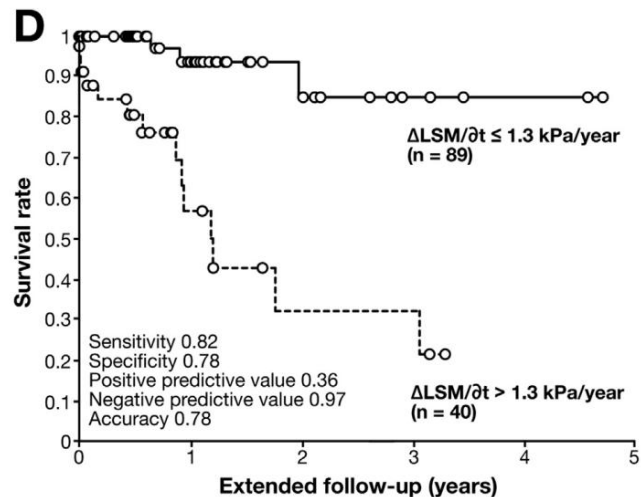
Baseline Values and Changes in Liver Stiffness Measured by Transient Elastography Are Associated With Severity of Fibrosis and Outcomes of Patients With Primary Sclerosing Cholangitis

Christophe Corpechot,^{1,2} Farid Gaouar,¹ Ahmed El Naggar,¹ Astrid Kemgang,^{1,2} Dominique Wendum,³ Raoul Poupon,^{1,2} Fabrice Carrat,⁴ and Olivier Chazouillères^{1,2}

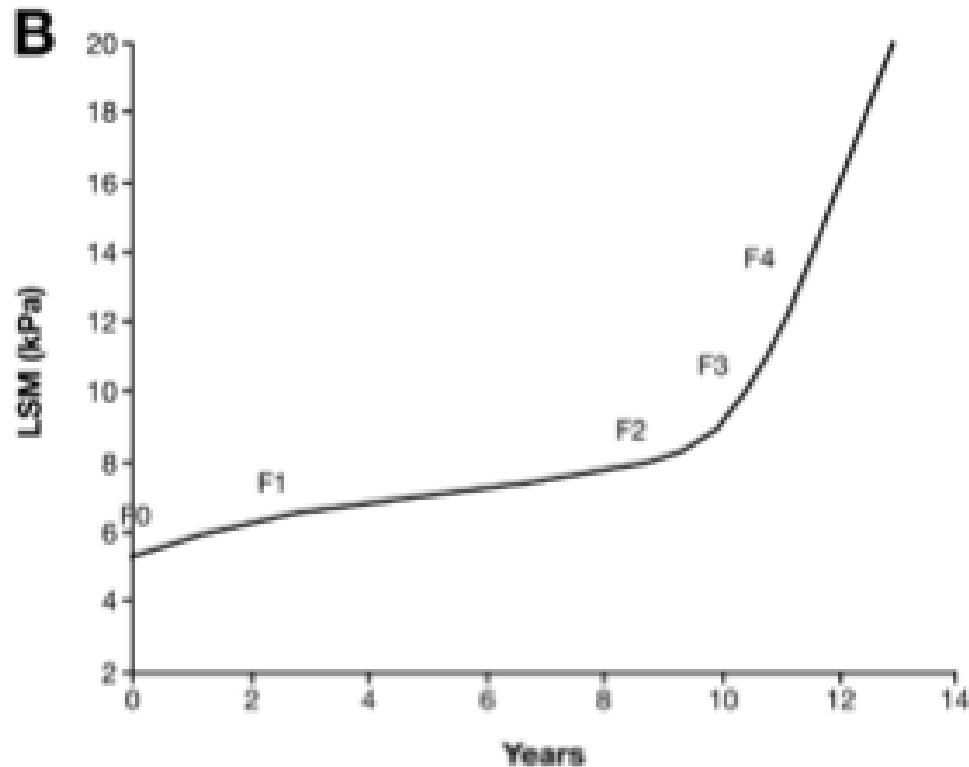


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STIFFNESS PROGRESSION RATE IN PRIMARY SCLEROSING CHOLANGITIS



Changes in Liver Stiffness in a continuous process extrapolated from the means of progression rate.

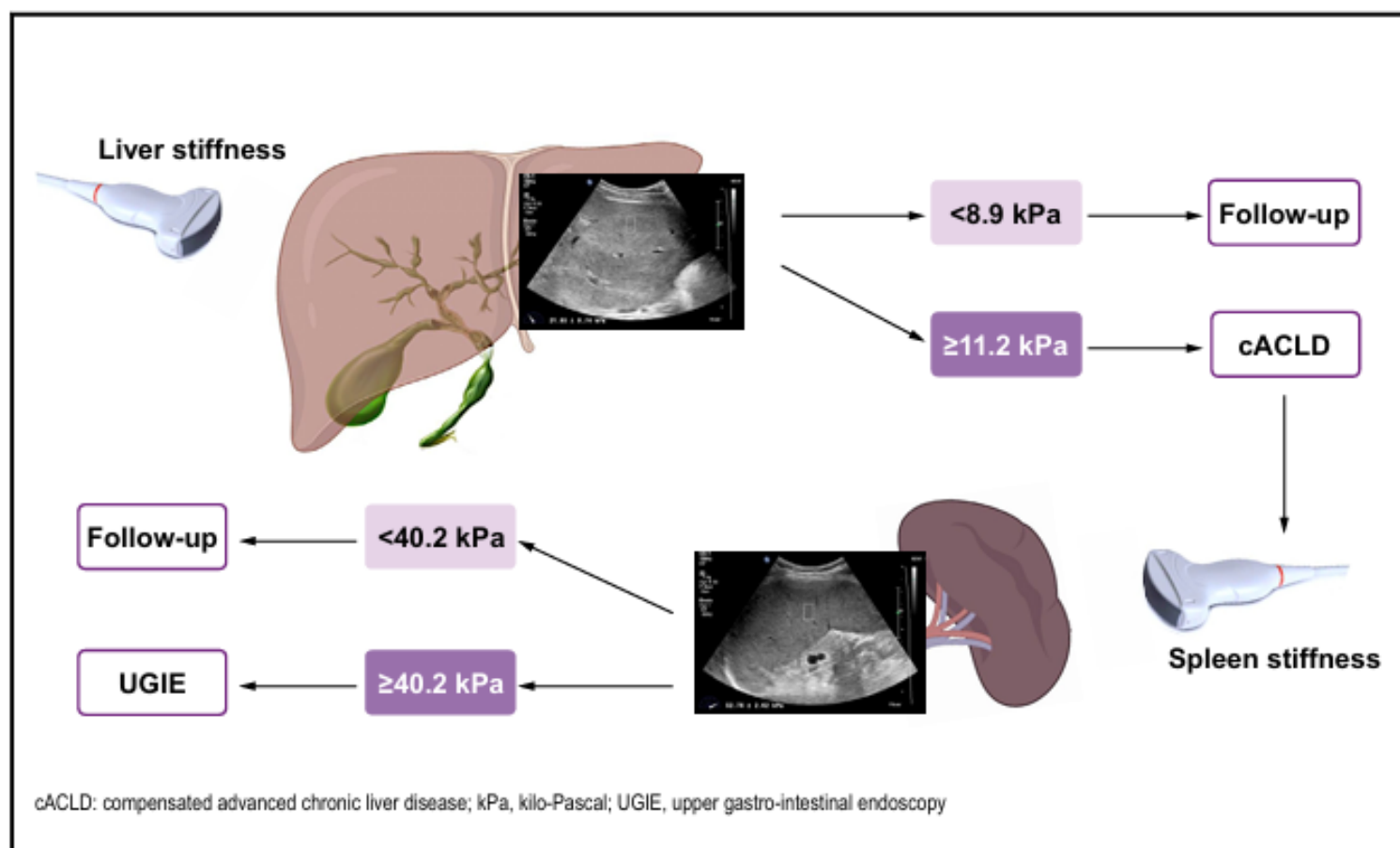
PROGNOSTIC RELEVANCE OF LIVER STIFFNESS IN PRIMARY SCLEROSING CHOLANGITIS

Patients with either LSM >11.1 kPa or DLSM/vt >1.5 kPa/y are at very high risk of death, liver transplantation, or hepatic complications within a 4-year period.

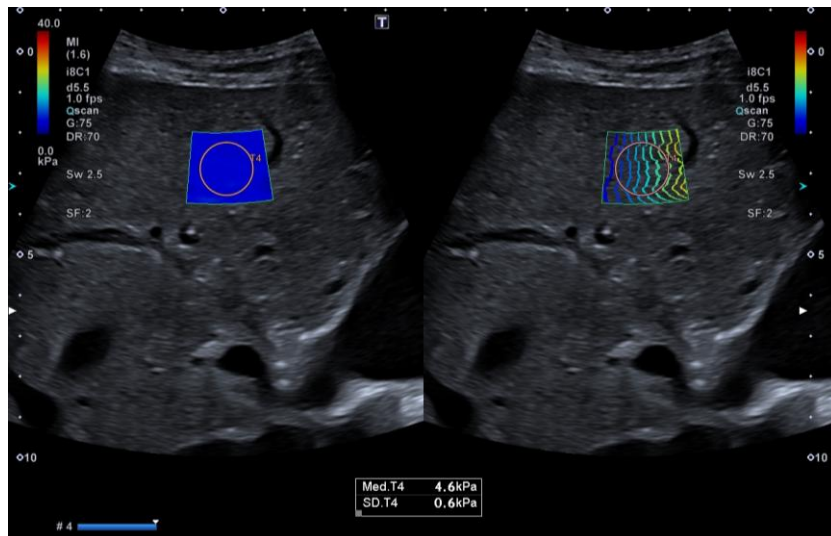
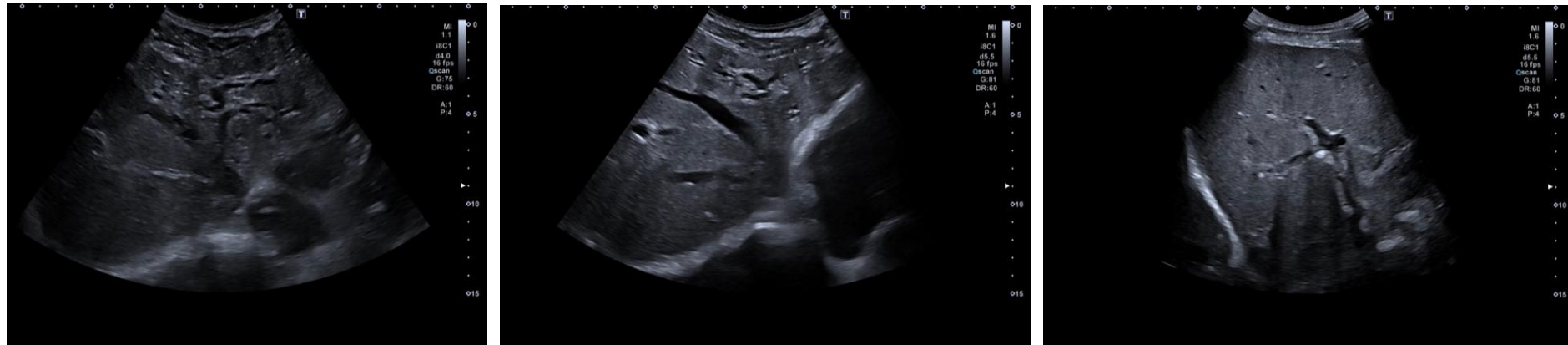
Utility of ElastPQ point-shear wave elastography in the work-up of patients with primary sclerosing cholangitis

Authors

Daive Roccarina, Francesca Saffioti, Matteo Rosselli, Aileen Marshall, Massimo Pinzani, Douglas Thorburn

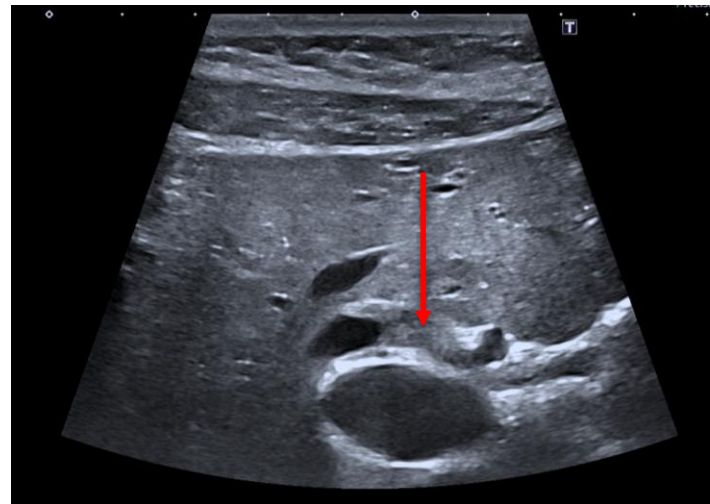
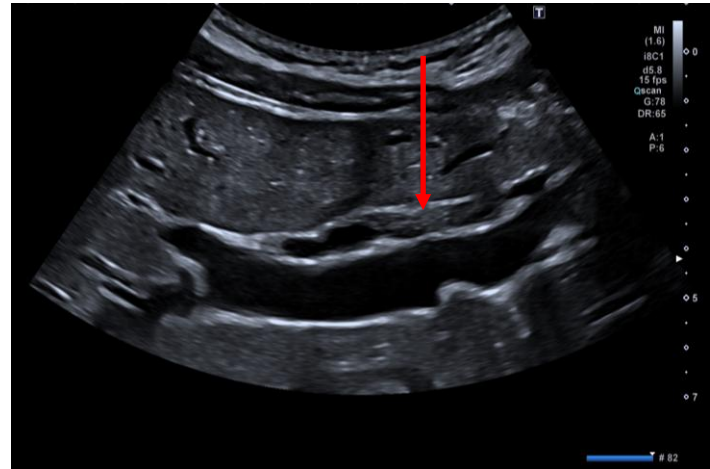
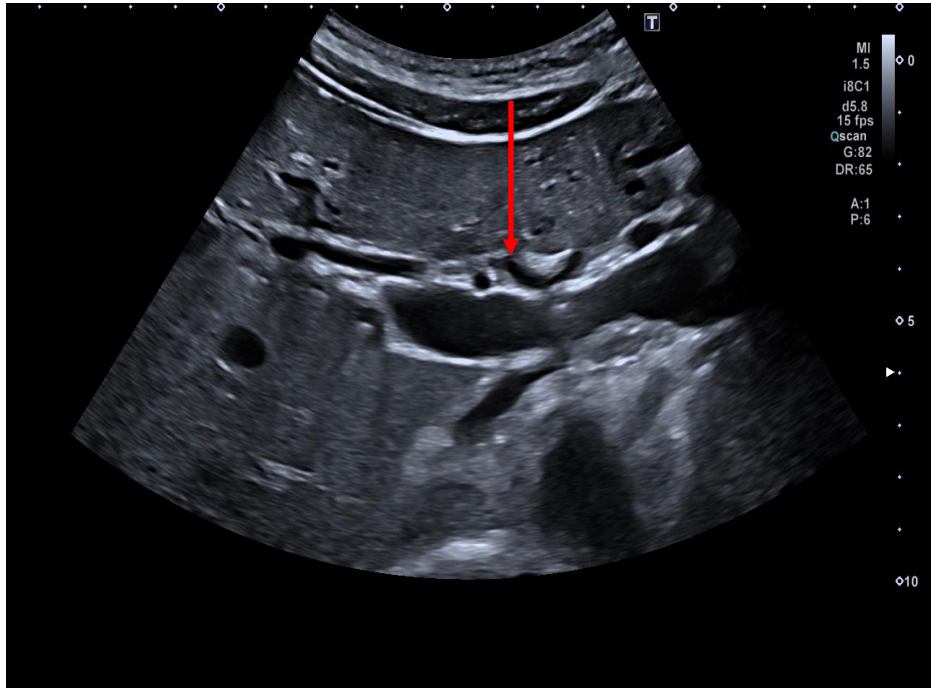


BILIARY INVOLVEMENT IN PSC HAS OFTEN AN IRREGULAR DISTRIBUTION

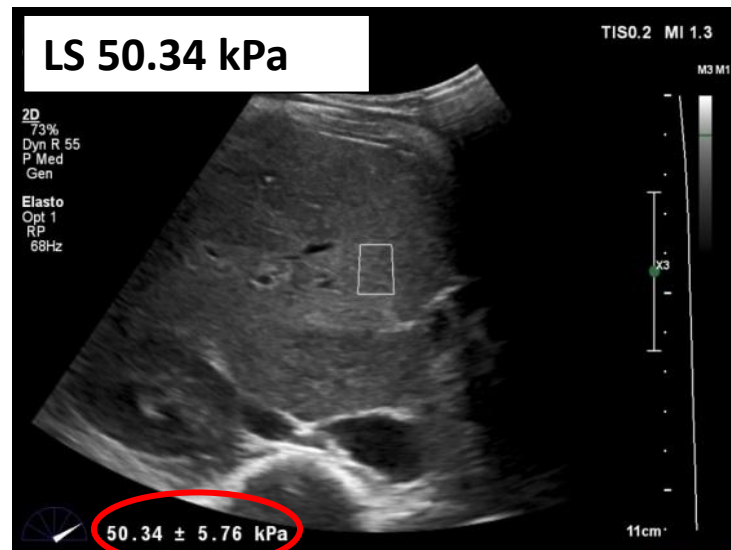
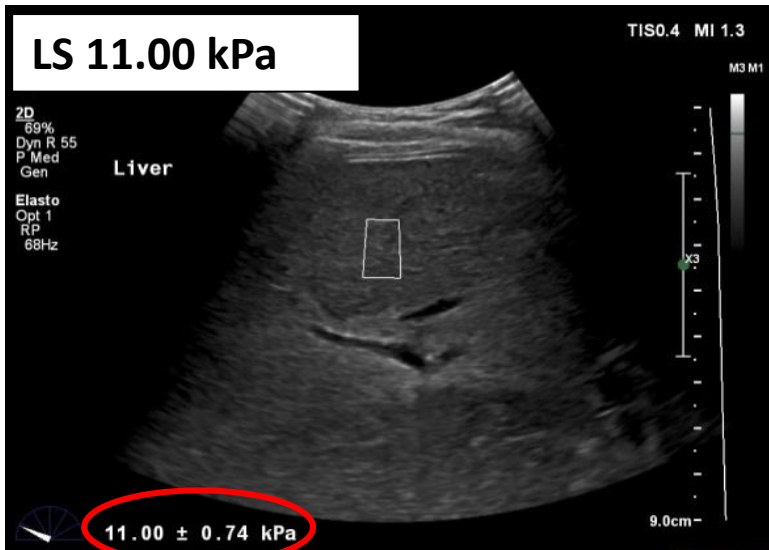
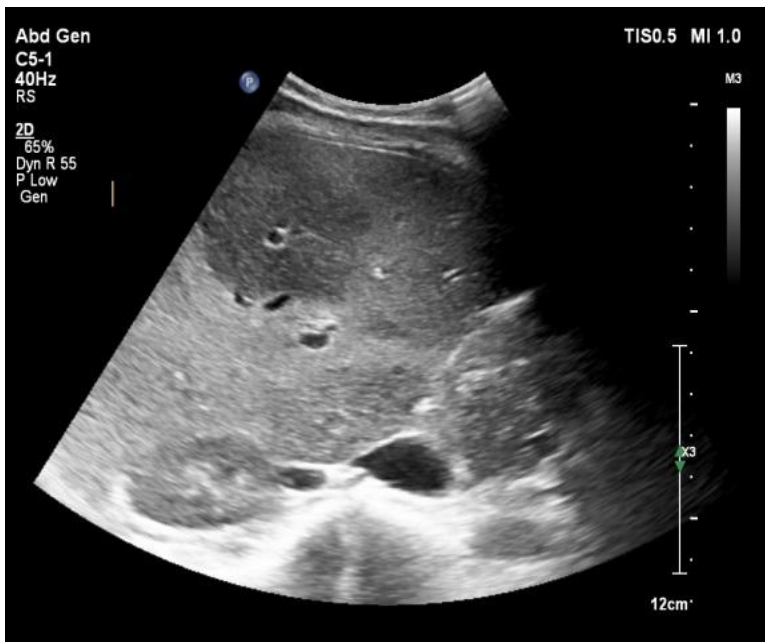


PATIENT WITH PSC

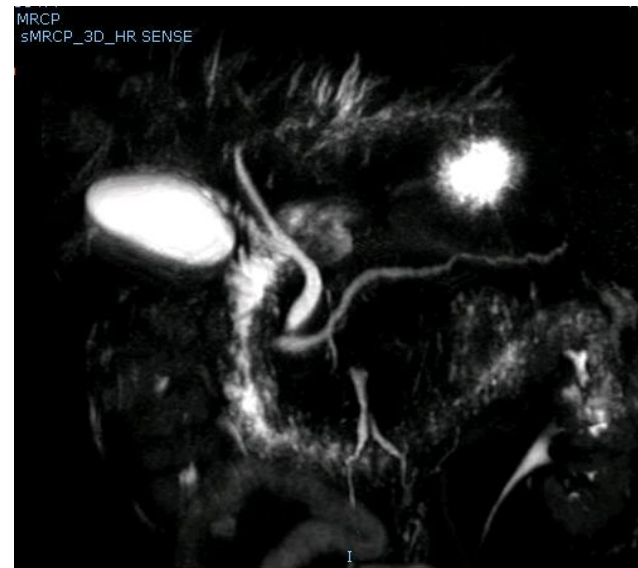
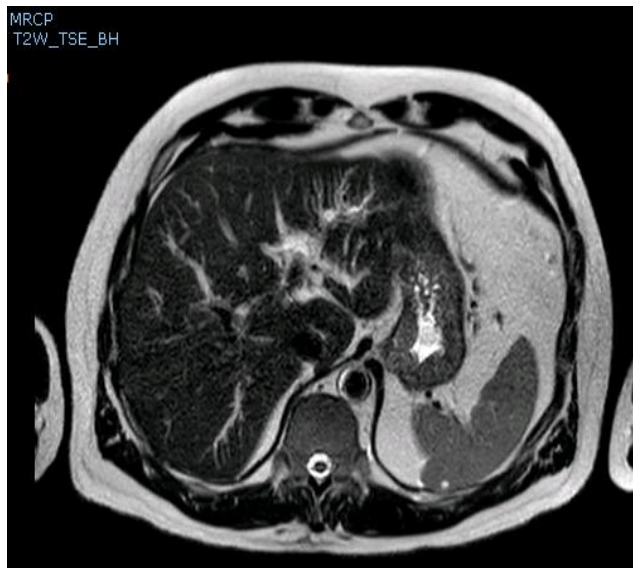
There is a more extended involvement of the left biliary ducts than the right ones. Liver stiffness value is normal because the right liver lobe is not involved.



The common bile duct (red arrows) is not dilated but has very thickened walls. Note that the thickening is not equally present along the whole tract of the CBD



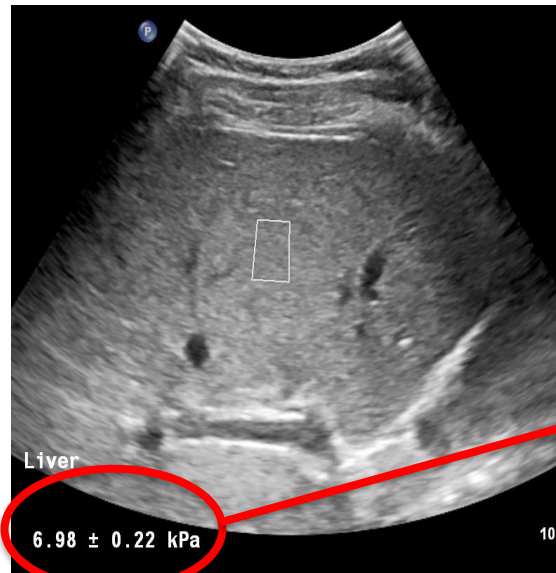
The liver is slightly dysmorphic with patchy echogenic areas. Thickening and strictures are not macroscopically visible on ultrasound but the parenchymal changes together with increased liver stiffness results are an expression of underlying biliary fibrosis in this case of small duct PSC



PATIENT WITH PSC. left lobe involvement of the biliary system and sparing of the right liver lobe. Liver stiffness value is normal because the right liver lobe is not involved. The differences in the biliary tree can be appreciated well on ultrasound as it is shown for comparison on MRCP



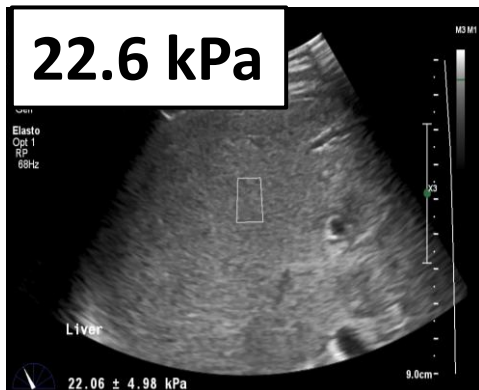
PATIENT WITH PSC, left lobe involvement of the biliary system and sparing of the right liver lobe. Liver stiffness value is normal because the right liver lobe is not involved

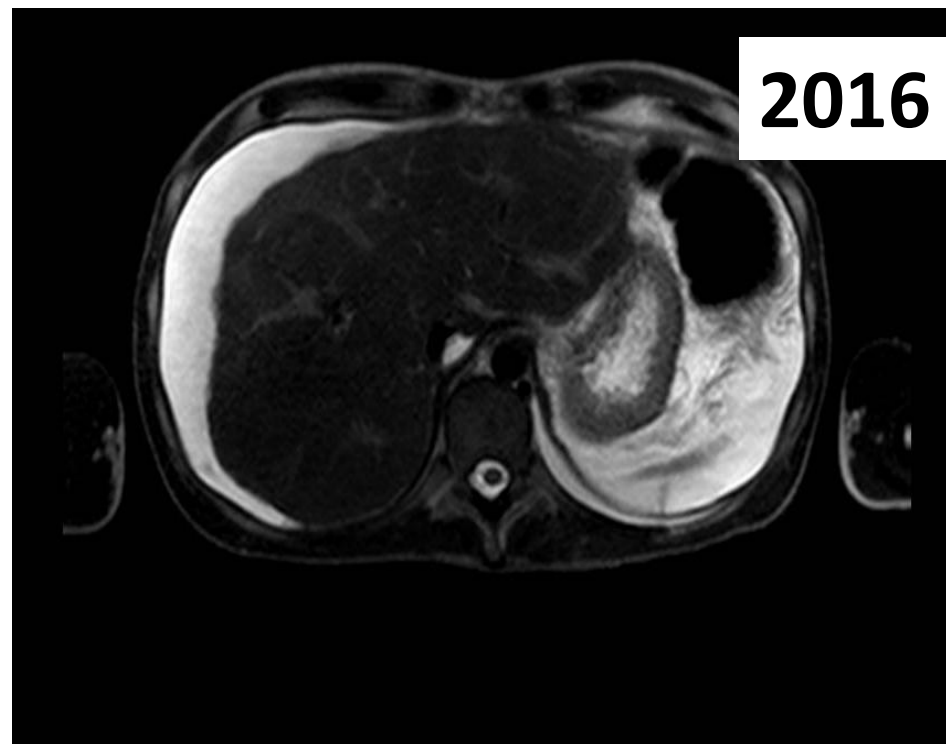
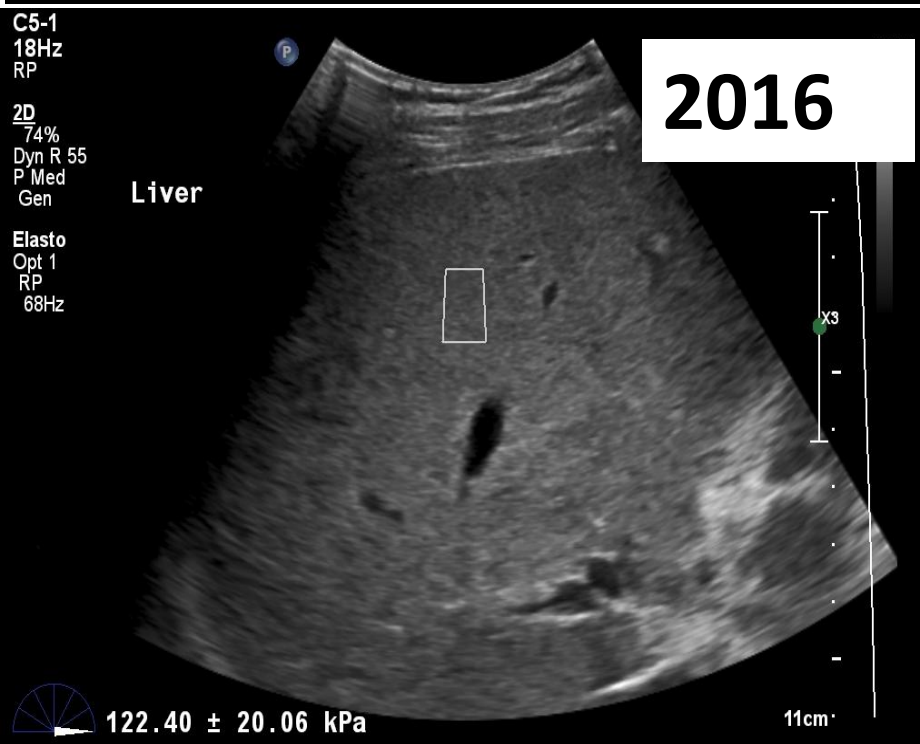
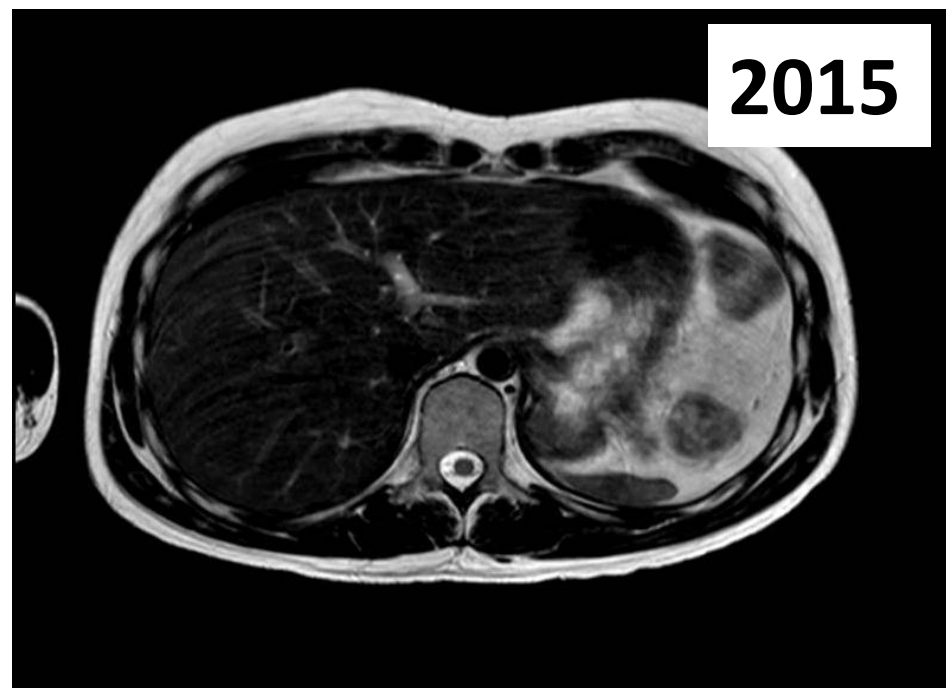
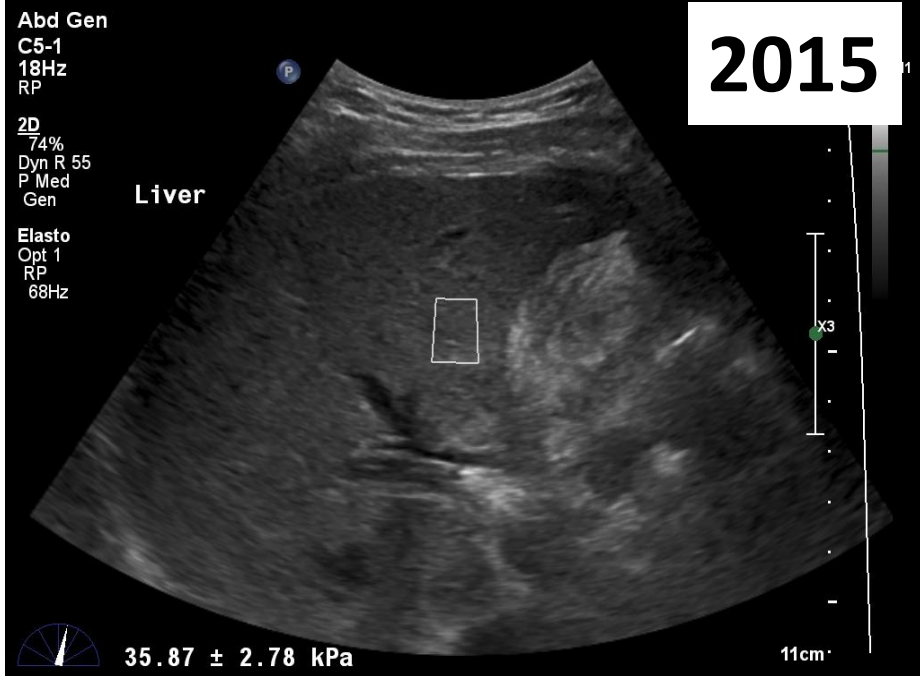


6.9 kPa

PATIENT WITH PSC AND DISSOCIATION OF THE BILIARY TREE

Please note that when such discrepancies in liver stiffness are found it is crucial to always evaluate liver parenchyma with second level imaging since increase stiffness can also be secondary to underlying malignancy/infiltrative disease





PRIMARY SCLEROSING CHOLANGITIS

- There is evidence of correlation between defined stiffness values and fibrosis
- Stiffness measurement follow up might provide prognostic information
- The best cutoff values (with pSWE) to rule in and out cACLD are a liver stiffness of 8.9 kPa and 11.3 kPa and a spleen stiffness >40.2 kPa is accurate to rule in the presence of varices in this population of patients.
- Cholestasis has a high impact on stiffness values and we do not know for sure how much of it is due to inflammation or established fibrosis
- The segmental distribution of disease might underestimate the severity of PSC if we rely on stiffness values which might have sampled a “normal” area of liver parenchyma.
- Spleen stiffness has potentially the added value to not be influenced by cholestasis and be more reliable in the assessment of portal hypertension



THANK YOU!

