

# The asymmetry of the liver and spleen stiffness measures between patients with chronic hepatitis B and D reflects important clinic-pathologic differences

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## Introduction

- Chronic HDV infection increases the pathologic burden in patients (pts) with chronic HBV infection worsening clinical outcomes<sup>1</sup>
- Liver stiffness measurement (LSM) is a non-invasive tool widely used to assess the burden of liver disease and spleen stiffness measurement (SSM) has been shown to be related to portal hypertension<sup>2</sup>.
- We measured LSM and SSM in a single centre cohort of pts with chronic hepatitis B (CHB) and D (CHD), in order to point out potential added values of the SSM in this clinical setting.

## Material and Methods

**Study population:** We enrolled consecutively 119 HBsAg+ pts attending regular follow-up at the Hepatology Unit of Pisa University Hospital: 71 pts with CHB [30(42.3%) with cirrhosis] and 48 pts with CHD [27(56.3%) with cirrhosis]. Fifty-two (73.2%) CHB were treated with nucleos(t)ide analogues (NUCs) and 15 (31.3%) CHD pts with Bulevirtide (BLV).

**Data collection:** Ultrasound scan, LSM and SSM (FibroScan®, Echosens, France) were performed on the same day. Liver biochemistry and virological assays were performed within one week since the physical examination of the pts.

**Statistical Analysis:** Statistical analysis were performed using X<sup>2</sup> test, Mann-Whitney/ Kruskal-Wallis test, Spearman correlation test and multiple regression analysis.

Table 1: Demographic, clinical and laboratory characteristics of study cohort

Variables		HBV N = 71	HDV N = 48	P
Age	Yrs	58.9 (28.9-86.4)	47.8 (20.2-74.8)	<0.001
Gender	F	17 (23.9)	21 (43.8)	0.038
	M	54 (76.1)	27 (56.3)	
Country	Italy	52 (73.2)	18 (37.5)	<0.001
	Other	19 (26.8)	30 (62.5)	
BMI	Kg/m <sup>2</sup>	24.9 (18.8-51.8)	24.6 (17.3-43.1)	0.497
Cofactors	MASLD	22 (31.0)	21 (43.8)	0.220
	HCV (SVR)	4 (5.6)	5 (10.4)	0.539
	Alcohol	9 (12.7)	5 (10.4)	0.932
Cirrhosis	Yes	30 (42.3)	27 (56.3)	0.189
	No	41 (57.7)	21 (43.8)	
NUC Therapy	Yes	51 (71.8)	34 (70.8)	1.000
	No	20 (28.2)	14 (29.2)	
HBsAg	Log IU/mL	2.61 (-0.70 / 5.07)	3.65 (-0.70 / 4.75)	<0.001
ALT	U/L	19 (5 - 219)	27 (9 - 160)	0.001
PLTs	n/mm <sup>3</sup>	187 (20 - 489)	176 (33 - 341)	0.066

Table 2: Bivariate correlation between LSM, Spleen diameter, platelets count (PLTs) and SSM by aetiology and stage

		Overall n=119	Cirrhosis n=57	HBV n=71	HBV Cirrhosis n=30	HDV n=48	HDV Cirrhosis n=27
LSM	ρ	0.567	0.579	0.465	0.432	0.761	0.799
	P	<0.001	<0.001	<0.001	0.022	<0.001	<0.001
median	kPa	7.2	10.5	6.2	9.7	8.1	13.3
SD	ρ	0.534	0.537	0.489	0.524	0.643	0.647
	P	<0.001	<0.001	<0.001	0.004	<0.001	<0.001
median	cm	11.5	12.8	11.0	12.1	12.0	13.0
PLTs	ρ	-0.538	-0.666	-0.498	-0.638	-0.617	-0.726
	P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
median	num	180	132	187	142	176	106

## Reference

1. EASL Clinical Practice Guidelines on hepatitis delta virus. European association for the Study of the Liver. J Hepatol 2023;79(2):433-460
2. Baveno VII - Renewing consensus in portal hypertension, de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022 Apr;76(4): 959-974.

## Results

- **Table 1** shows the comparison of demographic, clinical and laboratory features in CHB and CHD pts. **Table 2** shows the correlations between LSM, Spleen diameter (SD), platelet count (PLTs) and SSM.
- **In CHD pts, SSM correlated better with LSM**, overall ( $\rho=0.761$  vs  $\rho=0.465$ ) and in cirrhotics ( $\rho=0.799$  vs  $\rho=0.432$ ), and **with SD**, overall ( $r=0.643$  vs  $r=0.489$ ) and in cirrhotics ( $r=0.647$  vs  $r=0.524$ ). Also the correlation between **SSM and PLTs was stronger in CHD pts**, overall ( $r=-0.617$  vs  $r=-0.498$ ) and in cirrhotics ( $r=-0.726$  vs  $r=-0.638$ ).
- **Median LSM** was significantly **lower in CHB** compared to CHD pts [6.2 (2.8-71) vs 8.1 (2.8-33.1) kPa,  $p=0.004$ ], whereas **SSM values** were **similar** between the two group [25.6 (9.3-87.6) vs 26.8 (4.8-100) kPa,  $p=0.569$ ].
- **SD** showed no significant difference between CHB and CHD pts [11.0 (7.0-18.0) cm vs 12.0 (6.5-23.0) cm,  $p=0.079$ ]. **PLTs** showed a trend to lower values in CHD pts [176 (33-341) vs 187 (20-489),  $p=0.066$ ].
- Overall, the **SSM/LSM ratio** was **significantly lower in CHD pts** [2.98 (1.00-9.64) vs 3.88 (1.09-16.25),  $p=0.003$ ] (**Figure 1a**), as well as the **SD/LSM ratio** [1.33 (0.36-3.89) vs 1.78 (0.21-4.08),  $p=0.007$ ] (**Figure 2a**).
- Analysing **cirrhotic pts only**, **LSM** was significantly **lower in CHB pts** [9.7 (3.7-71) vs 13.3 (5.6-33.1) kPa,  $p=0.022$ ], and **SSM similar** in both groups [34.0 (9.9-87.6) vs 33.3 (14.5-100) kPa,  $p=0.842$ ]. The **SSM/LSM ratio** (**Figure 1b**) remained significantly **lower in CHD pts** [2.55 (1.28-5.14) vs 3.55 (1.09-14.45),  $p=0.009$ ], whereas the SD/LSM did not (**Figure 2b**).

Figure 1: Ratio between SSM and LSM in CHB vs CHD patients overall (A) and in cirrhotics (B)

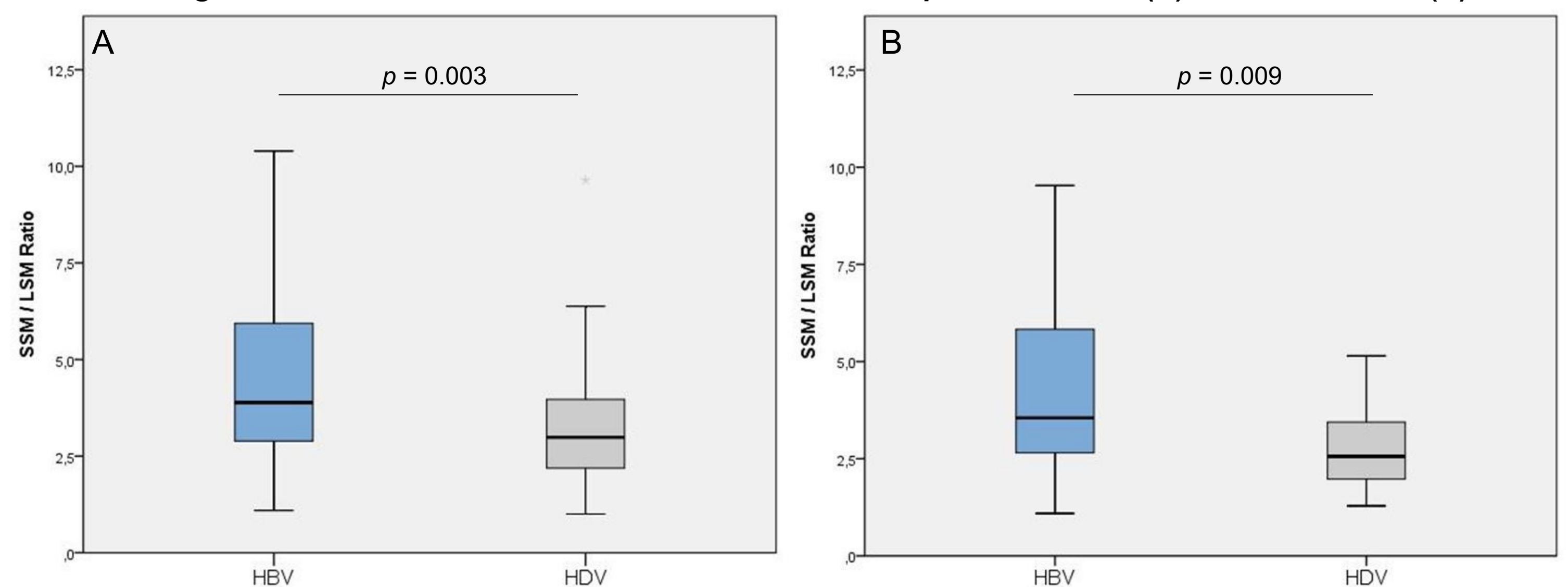
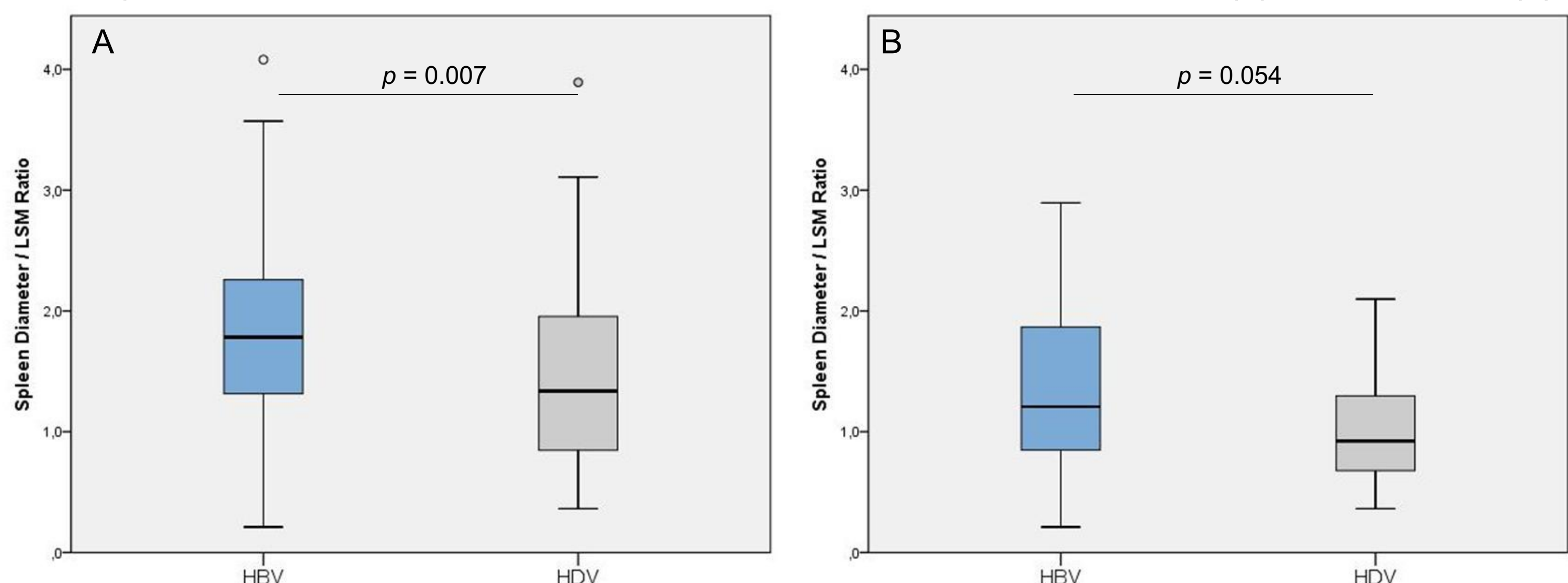


Figure 2: Ratio between Spleen diameter and LSM in CHB vs CHD patients overall (A) and in cirrhotics (B)



## Conclusion

- The combined measurement of LSM and SSM pointed out different characteristics of the liver disease, as the lower LSM found in CHB than in CHD pts (6.2 vs 8.1 kPa) and the stronger correlation between SSM and LSM in CHD ( $\rho=0.761$  vs 0.465), may depend on the higher rate of CHB pts with ongoing effective antiviral treatment (73.2% vs 31.3%).
- Interestingly, in cirrhotic CHB pts with suppressed HBV replication, the SSM was similar to that of CHD pts, suggesting that in this setting SSM may better assess the presence of clinically significant portal hypertension.
- Further follow-up is required in CHD pts treated with current antiviral therapies to determine the effects of these treatments on disease progression.