Dynamics of Splenic Transient Elastography in Patients With Alcohol Use Disorder

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INTRODUCTION: **Splenic stiffness (SS) measurement (SSM) is an evolving noninvasive assessment to evaluate portal hypertension. Studies with respect to SSM in patients with alcohol use disorder are limited.**

METHODS: **We studied patients seeking treatment for alcohol use disorder in an inpatient treatment protocol at the National Institutes of Health and parsed SSM into 3 groups based on degree of change.**

RESULTS: **The improved SS group had statistically higher initial SSM and a nonstatistically increased liver stiffness measurement compared with others.**

DISCUSSION: **SS is dynamic in a subset of patients immediately after alcohol cessation, and improved SS is associated with a normalization of platelet count.**

KEYWORDS: splenic stiffness; liver stiffness; noninvasive liver disease assessment; alcohol; alcohol use disorder

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INTRODUCTION

Splenic stiffness (SS) is a noninvasive liver disease assessment used to predict portal hypertension and complications (1). Studies are heterogenous and inconclusive over superiority of SS measurement (SSM) over liver stiffness measurement (LSM) (2). However, there are data that SSM by transient elastography may have a stronger correlation with hepatic venous pressure gradient than LSM in patients with portal hypertension (3,4).

Patients with alcohol use disorder (AUD) are at higher risk of developing alcohol-associated liver disease (ALD) (5). SS has been shown to be dynamic in response to treatment, with a study showing a significant decrease in SS after hepatitis C virus treatment and a nonsignificant decrease in patients with ALD in the immediate period after alcohol cessation (6). There is a gap in the literature in measuring SS in patients with AUD after acute cessation without established ALD.

METHODS

Patients seeking treatment for AUD from January 2017 to August 2022 were enrolled per protocol in a 4-week interdisciplinary inpatient treatment program at our institution. Inclusion criteria for this natural history protocol included adults aged 18 years or older, willingness to undergo blood testing, genetic testing, and radiology imaging over the study period. Laboratory values were collected on all patients at admission, weeks 2, and 4 per protocol.

Patients were evaluated by the hepatology service with serial vibration-controlled transient elastography (FibroScan, Echosens) performed for LSM and SSM at weeks 1, 2, and 4 with patients in a fasting state. Patients with a minimum of 2 SSMs at least 14 days apart were included in this analysis with the week 4 SSM as the primary comparator. Patients were categorized into 3 groups based on SS changes with a threshold of change in SSM of 15 or more kPA: (A) improved ($<$15 kPa), (B) static (within +/− 15 kPa range), and (C) worsened ($>$15 kPa).

For continuous variables, groups (A and B) and (B and C) were compared using analysis of variance with Dunnett's correction (SAS proc Generalized Linear Model). Group A (improved) was compared with the combined groups B and C by a *t* test with equal variances or unequal variances if the variances were different (SAS proc TTEST). The Fisher exact test was used for percentages (SAS proc FREQ).

RESULTS

One hundred twenty-four patients underwent SSMs during the study period, with 69 completing a minimum of 2 SSMs at least 14 days apart. Fifty-one patients had static SS, 9 had improved SS, and 9 had worsened SS during the study period based on an SSM threshold of 15 kPa (Table 1).

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Table 1. Characteristics of patients with improved, static, and worsened splenic stiffness

	Improved N = 9 (A)	Static N = 51 (B)	Worsened N = 9 (C)	C vs B *P* value[a]	A vs B *P* value[a]	A vs others *P* value[b]
Demographics[c]						
Age at admission, yr	55 (12)	44 (12)	45 (13)	0.94	0.033*	0.017*
Male sex, n (%)	9 (100)	32 (63)	7 (78)			0.049*
White race, n (%)[d]	7 (77)	33 (65)	5 (56)			0.48
Black race, n (%)	2 (22)	11 (22)	3 (33)			
Other race, n (%)	0 (0)	7 (14)	1 (11)			
Initial laboratory values[c]						
ALT	31 (15)	53 (47)	61 (57)	0.33	0.88	0.006*
AST	48 (24)	76 (88)	77 (53)	0.99	0.55	0.044*
Total bilirubin	0.71 (0.31)	0.73 (1.36)	0.49 (0.19)	0.82	0.99	0.91
Alkaline phosphatase	90 (22)	85 (36)	86 (38)	0.99	0.92	0.72
Platelets	164 (54)	235 (109)	183 (66)	0.29	0.10	0.011*
INR	1.11 (0.15)	1.01 (0.12)	1.06 (0.06)	0.45	0.056	0.040*
Albumin	4.20 (0.37)	4.49 (0.37)	4.66 (0.46)	0.41	0.081	0.026*
GGT	103 (66)	257 (482)	228 (206)	0.98	0.53	0.019*
Creatinine	0.83 (0.18)	0.73 (0.15)	0.85 (0.39)	0.20	0.34	0.28
Glucose	113 (21)	100 (23)	104 (23)	0.83	0.23	0.14
Ferritin	455 (655)	412 (707)	695 (1,313)	0.55	0.99	0.99
CRP	2.41 (1.70)	4.31 (8.74)	1.82 (1.84)	0.60	0.74	0.21
ESR	11.0 (11.6)	10.6 (10.0)	14.0 (9.2)	0.58	0.99	0.98
Fib-4 score	2.89	1.95	2.42			
Final laboratory values[c]						
ALT	33 (14)	29 (18)	42 (26)	0.12	0.75	0.70
AST	31 (7)	26 (14)	33 (15)	0.30	0.55	0.22
Total bilirubin	0.46 (0.21)	0.49 (0.87)	0.32 (0.13)	0.79	0.99	0.93
Alkaline phosphatase	73 (21)	71 (28)	74 (35)	0.93	0.98	0.90
Platelets	233 (85)	268 (79)	230 (82)	0.35	0.40	0.31
Albumin	3.83 (0.36)	4.08 (0.43)	4.07 (0.47)	0.99	0.20	0.11
GGT	60 (35)	89 (118)	110 (116)	0.84	0.72	0.10
Creatinine	0.80 (0.18)	0.78 (0.16)	0.88 (0.36)	0.31	0.95	0.94
Glucose	98 (8)	99 (15)	95 (6)	0.71	0.99	0.99
Ferritin	172 (123)	173 (185)	234 (267)	0.62	0.99	0.88
CRP	1.68 (1.27)	3.95 (6.74)	3.26 (2.25)	0.94	0.50	0.021*
ESR	11.9 (8.7)	14.8 (11.2)	24.1 (20.5)	0.08	0.76	0.34
Fib-4 score	1.27	0.79	1.00			
Transient elastography[c]						
Interval first to last scan, d	20.4 (1.3)	19.7 (3.2)	20.3 (0.9)	0.78	0.71	0.28
Week 1						
LSM, kPa	19.1 (27.4)	8.0 (10.2)	9.1 (5.0)	0.97	0.044	0.27
Liver CAP	258 (55)	258 (58)	276 (36)	0.60	0.99	0.87
SSM, kPa	54.9 (16.7)	18.7 (12.3)	17.2 (6.5)	0.93	<0.001*	<0.001*
Week 4						
LSM, kPa	16.3 (22.4)	7.7 (10.1)	8.1 (6.8)	0.99	0.097	0.29

Table 1. (*continued*)

	Improved N = 9 (A)	Static N = 51 (B)	Worsened N = 9 (C)	C vs B *P* value[a]	A vs B *P* value[a]	A vs others *P* value[b]
Liver CAP	227 (73)	238 (55)	232 (57)	0.95	0.84	0.63
SSM, kPa	18.4 (13.4)	18.9 (13.3)	45.4 (15.2)	<0.001*	0.99	0.44

ALT, alanine aminotransaminase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GGT, gamma-glutamyl transferase; INR, international normalized ratio; LSM, liver stiffness measurement; SSM, splenic stiffness measurement.
[a]*P* value for worse vs static or better vs static adjusting for multiple comparisons using Dunnett's correction.
[b]*P* value for better vs same or worse from *t* test with unequal variances or Fisher exact test.
[c]Mean (SD) or n (%).
[d]*P* value is for White race vs others.
**P* value <0.05 denotes statistical significance.

Patients with improved SS were significantly older (54.6 years) than patients who did not improve (54.6 vs. 44.3, $P = 0.017$). On initial laboratory evaluation, patients with improved SS had lower mean aspartate aminotransferase (48 vs. 76, $P = 0.044$), higher mean international normalized ratio (1.11 vs 1.01, $P = 0.040$), lower mean albumin (4.20 vs 4.51, $P = 0.026$), and lower mean platelets (164 vs 227, $P = 0.011$) compared with those who did not improve. Although platelets increased in patients with improved SS, with a mean change of 68.9 (SD 82) compared with those who did not improve (mean change 35 [SD 95]), this difference was not significant, $P = 0.31$. Final laboratory values at 4 weeks reported lower C-reactive protein (1.68 vs 3.85, $P = 0.021$) in patients with improved SS compared with those who did not.

The improved SS group had statistically higher week 1 SS (54.9 kPa) compared with the static SS group (18.5 kPa, $P < 0.001$). As expected, patients who did not improve had higher SS kPa at week 4 (Figure 1). Improved SS patients also had increased LS at weeks 1 and 4, although this difference was not significant ($P = 0.27$ and 0.29, respectively).

DISCUSSION

Our results suggest that in some patients, SS is dynamic in the immediate period after alcohol cessation. SS improves in a subset of patients in the period directly after alcohol cessation. Patients with improved SS had higher initial mean SS and LS, although the difference in LS was not statistically significant. Improvement in SS was associated with normalization of platelet count. The improvement in thrombocytopenia in the subgroup may be related to transient and improved portal hypertension as well as the direct bone marrow toxicity of alcohol. Patients with improved SS had significantly lower final C-reactive protein, suggesting that acute inflammation may play a role in improved SS.

Our results differ from a study of SS in patients with ALD. In this study, the mean follow-up interval between SS was 5.3 days compared with ours of 20.4 days. In this study, patients experienced a mean decrease of −4.5 kPa, with patients with ALD not demonstrating a significant decrease in SS after alcohol withdrawal (6).

Our data must be interpreted in the context of the study design. As most patients had static SS, we had a small sample size of those with dynamic SS. As such, differences in SS and LS were mostly insignificant, likely because of inadequate sample size. Another limitation of the study was intrinsic to our patient population with AUD because most patients did not have a diagnosis or manifestations of decompensated cirrhosis. Larger studies are needed to better understand the role of SS in AUD and early ALD. In conclusion, a subset of patients with AUD experience dynamic changes in SS in the period immediately after alcohol cessation.

CONFLICTS OF INTEREST

Guarantor of the article: Theo Heller, MD.

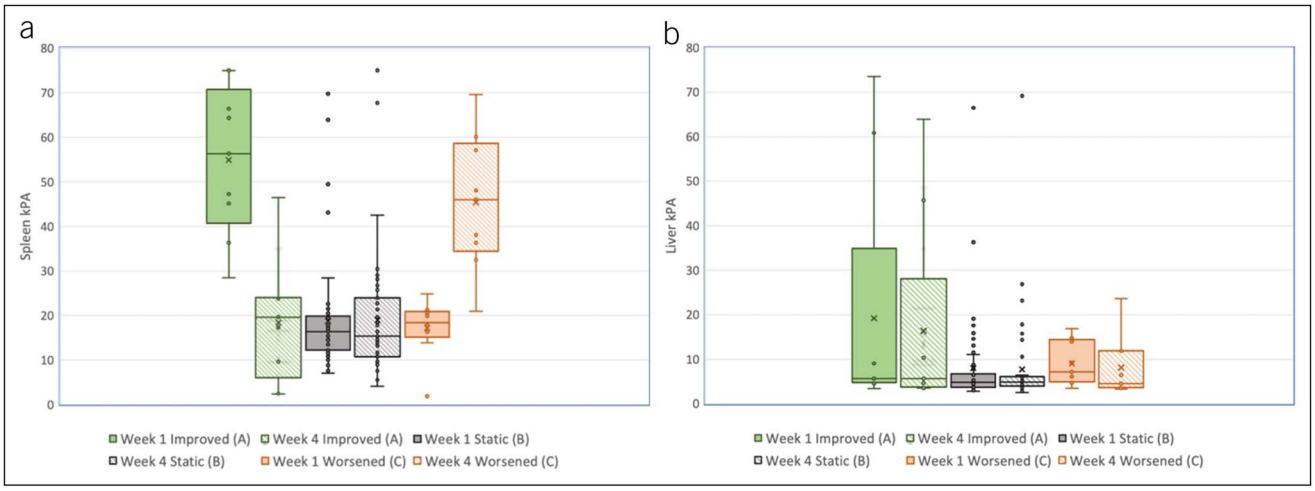

Figure 1. (**a**) SS at weeks 1 and 4 by improved, static, and worsened SS. (**b**) LS at weeks 1 and 4 by improved, static, and worsened SS. LS, liver stiffness; SS, splenic stiffness.

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Potential competing interests: None to report.

Study Highlights

WHAT IS KNOWN

- ✓ Splenic stiffness noninvasively predicts portal hypertension in liver disease.

WHAT IS NEW HERE

- ✓ Splenic stiffness can fluctuate in some patients acutely after alcohol cessation.
- ✓ Improvement in splenic stiffness is associated with normalization of platelets.

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