Changes in Transient Elastography with Glucagon-like Peptide-1 Receptor Agonist Use in Metabolic Dysfunction-Associated Steatotic Liver Disease

Nazar Akhverdyan[1], Amanda Wieland MD[2], Shelby Sullivan MD[3], Mark Lindsay NP[4], Sheila Swartwood NP[2], Gretchen Arndt NP[4], Laura Katherine Kaizer MPH[5], Thomas Jensen MD[4]

1. University of Colorado School of Medicine, Aurora, CO, USA
2. Division of Hepatology, University of Colorado School of Medicine, Aurora, CO, USA
3. Division of Gastroenterology, University of Colorado School of Medicine, Aurora, CO, USA
4. Division of Endocrinology, University of Colorado School of Medicine, Aurora, CO, USA
5. Department of Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

University of Colorado Anschutz Medical Campus

Introduction

- Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is characterized by hepatic fat accumulation in the absence of heavy alcohol consumption or other secondary causes of hepatic steatosis.
- MASLD has increased in global prevalence to 20-30% and is projected to become the leading cause of liver transplantation in the United States.
- Recent guidelines by the American Association of Clinical Endocrinology recommend the use of Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RAs) in the treatment of MASLD.
- The aim of this study is to investigate the effectiveness of GLP-1RA use on liver steatosis and fibrosis in patients with MASLD as measured by changes in Vibration Controlled Transient Elastography (VCTE) and other metabolic parameters in a real-world clinical scenario.
- In addition, we assessed whether improvements in hepatic steatosis, based on CAP change value previously described in the literature, was associated with improvements in liver fibrosis.

Methods

- A retrospective analysis was performed of patients with MASLD from the UCHealth Multidisciplinary Fatty Liver Clinic, Endocrinology Clinic, and Hepatology Clinic who underwent VCTE (Fibroscan) separated by 6 months
- Exclusion criteria: excessive alcohol consumption (> 21 drinks/week for males, > 14 drinks/week for females), viral hepatitis, drug-induced liver disease, other secondary causes of liver disease.
- Changes in Controlled Attenuation Parameter (CAP), Liver Stiffness Measurement (LSM), weight, BMI, blood pressure, liver enzymes, A1c, and lipid values were compared between GLP-1RA Users (N=48) vs Non-Users (N=42) and Responders (N=51) vs Non-Responders (N=39) (based on CAP change of > 38 dB/m).
- Laboratory studies and anthropomorphic data were collected within 3 months of the initial and follow up Fibroscan.
- Statistical analysis was conducted using two sample t-tests, Wilcoxon rank sum tests, and simple linear regression models.
- This study was approved by the Colorado Multiple Institutional Review Board (COMIRB).

Results

Table 1. Comparison of Clinical Parameters in GLP-1 Receptor Agonist Users vs Non-Users

Measure	*GLP1 Users Pre*	*GLP1 Users Post*	*GLP1 Users Change*	*GLP1 Non-Users Pre*	*GLP1 Non-Users Post*	*GLP1 Non-Users Change*	*p-value*
Weight (kg)	93.9 (18.0)	86.3 (16.1)	-7.5 (9.1)	93.0 (16.9)	89.8 (17.8)	-3.1 (6.9)	0.011
BMI (kg/m2)	33.0 (5.4)	30.3 (4.7)	-2.7 (3.2)	32.3 (5.0)	31.2 (5.1)	-1.1 (2.5)	0.013
Systolic Blood Pressure	126.2 (15.4)	121.4 (14.5)	-4.8 (18.1)	135.4 (18.8)	124.2 (18.3)	-11.1 (19.7)	0.132
Diastolic Blood Pressure	74.5 (8.8)	71.8 (10.4)	-2.6 (12.7)	76.7 (8.5)	72.5 (9.4)	-4.4 (9.4)	0.461
ALT	40.0 (26.0, 68.0)	22.0 (17.0, 31.0)	-15.0 (-33.0, -2.0)	45.0 (25.5, 64.0)	32.0 (24.0, 55.0)	-3.0 (-18.0, 4.0)	0.019*
AST	28.0 (21.0, 40.0)	21.0 (18.0, 25.0)	-4.0 (-17.0, -1.0)	33.5 (22.0, 40.5)	29.0 (21.0, 37.0)	1.0 (-10.0, 6.0)	0.025*
Total Cholesterol	170.5 (43.1)	147.8 (39.0)	-22.6 (39.5)	175.2 (48.6)	147.3 (40.7)	-27.9 (43.0)	0.696
LDL Cholesterol	91.0 (59.0, 120.5)	79.0 (49.5, 102.5)	-3.0 (-42.0, 14.0)	92.0 (58.0, 134.0)	75.0 (53.0, 108.0)	-17.0 (-48.0, 11.0)	0.555*
Triglycerides	192.1 (98.2)	147.6 (84.2)	-48.1 (107.5)	217.3 (149.7)	175.0 (57.9)	-35.0 (145.5)	0.762
HDL Cholesterol	41.4 (8.9)	44.5 (10.5)	3.1 (8.3)	38.1 (12.4)	41.0 (12.0)	2.9 (6.7)	0.919
Non-HDL	128.5 (40.3)	103.3 (38.6)	-25.2 (36.5)	137.1 (48.7)	106.3 (36.1)	-30.8 (41.7)	0.664
Hemoglobin A1c	7.0 (5.9, 8.8)	6.0 (5.6, 7.0)	-0.7 (-1.3, -0.2)	6.7 (6.3, 7.9)	6.9 (6.2, 7.3)	0.0 (-1.0, 0.6)	0.026*
LSM	6.9 (4.8, 9.3)	5.8 (4.4, 7.4)	-0.6 (-3.8, 0.7)	7.7 (5.5, 10.4)	6.7 (5.2, 8.5)	-0.5 (-2.2, 1.5)	0.493*
CAP	336.0 (37.8)	274.1 (63.0)	-61.6 (57.9)	333.0 (39.8)	303.9 (56.3)	-28.8 (62.7)	0.012

Figure 1. Percent Weight Change in GLP-1RA Users vs Non-Users

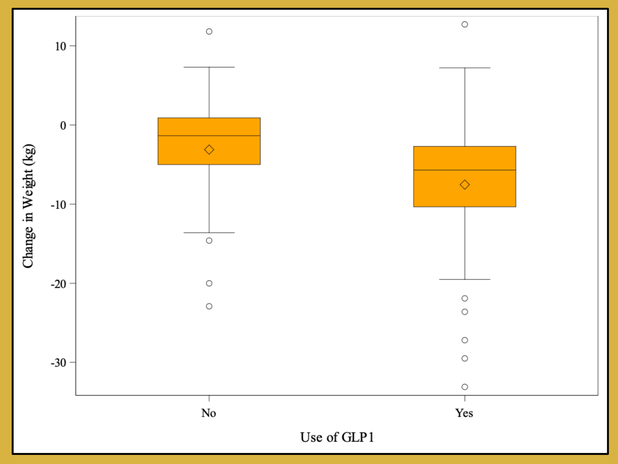


Figure 3. Relationship between percent weight change and change in CAP differentiated by GLP-1RA use

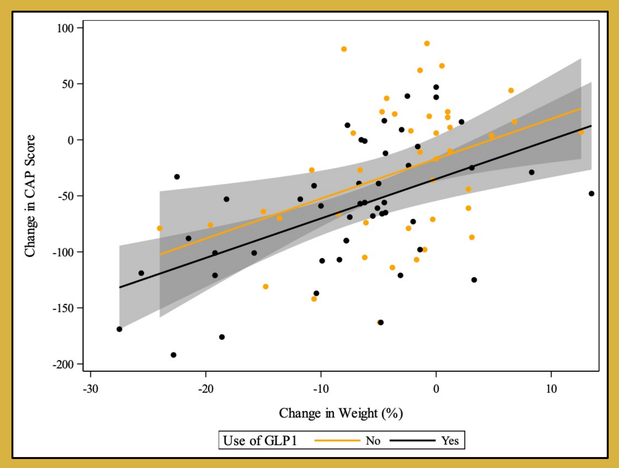


Table 2. Comparison of Clinical Parameters in Responders vs Non-Responders

Measure	*Responders Pre*	*Responders Post*	*Responders Change*	*Non-Responders Pre*	*Non-Responders Post*	*Non-Responders Change*	*p-value*
Weight (kg)	92.2 (17.0)	83.9 (15.4)	-8.4 (8.6)	95.1 (18.0)	93.4 (17.5)	-1.7 (6.5)	<.001
BMI (kg/m2)	32.4 (4.9)	29.5 (4.0)	-3.0 (3.0)	33.0 (5.7)	32.4 (5.5)	-0.6 (2.3)	<.001
Systolic Blood Pressure	129.5 (18.6)	119.5 (17.0)	-10.0 (19.3)	131.9 (16.3)	127.3 (14.5)	-4.6 (18.4)	0.196
Diastolic Blood Pressure	75.1 (8.4)	69.9 (11.2)	-5.2 (11.8)	76.2 (9.1)	75.3 (6.7)	-0.9 (10.0)	0.075
ALT	39.5 (25.0, 65.0)	24.0 (17.0, 32.0)	-9.0 (-38.0, 1.0)	45.0 (26.0, 68.0)	44.0 (24.0, 61.0)	-2.0 (-20.0, 1.0)	0.078*
AST	27.0 (21.0, 40.0)	21.0 (18.0, 25.0)	-4.0 (-15.0, 2.0)	35.0 (23.0, 45.0)	29.0 (20.0, 40.0)	-2.0 (-16.0, 4.0)	0.316*
Total Cholesterol	171.6 (44.6)	140.7 (41.7)	-30.9 (36.7)	173.1 (45.8)	159.4 (32.1)	-13.7 (44.9)	0.206
LDL Cholesterol	92.0 (58.0, 130.0)	68.0 (46.0, 93.0)	-16.0 (-48.0, 1.0)	85.5 (63.0, 118.5)	94.5 (78.0, 108.5)	11.0 (-31.0, 26.0)	0.042*
Triglycerides	188.0 (81.6)	139.1 (70.2)	-48.8 (90.5)	222.8 (162.3)	187.6 (79.0)	-34.6 (162.3)	0.750
HDL Cholesterol	41.9 (9.7)	44.6 (11.2)	2.7 (8.0)	37.6 (10.9)	41.1 (10.8)	3.6 (7.3)	0.722
Non-HDL	129.1 (39.8)	96.1 (39.8)	-33.0 (32.1)	135.5 (49.2)	118.3 (28.7)	-17.3 (45.7)	0.237
Hemoglobin A1c	7.0 (6.2, 8.7)	6.0 (5.6, 7.1)	-0.8 (-1.3, -0.3)	6.7 (6.2, 8.0)	6.9 (6.2, 7.3)	0.3 (-0.9, 0.6)	0.001*
LSM	7.6 (5.0, 9.4)	5.4 (4.1, 7.2)	-1.3 (-4.2, 0.1)	6.8 (5.2, 9.5)	7.2 (5.7, 9.3)	0.3 (-0.6, 2.4)	<.001*
CAP	341.7 (35.7)	250.5 (44.5)	-91.0 (38.1)	325.3 (40.7)	337.1 (43.4)	12.0 (30.6)	<.001

Figure 2. Percent Weight Change in Responders vs Non-Responders

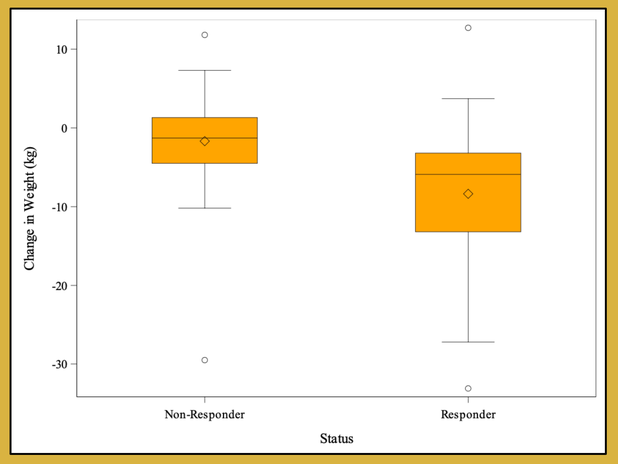
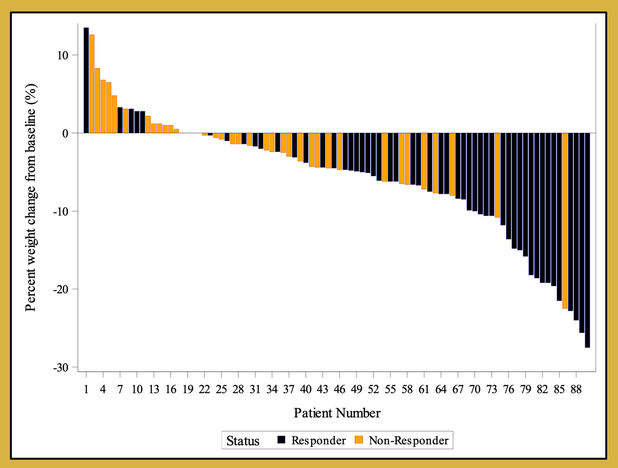


Figure 4. Waterfall plot demonstrating percent weight change from baseline of all patients (n=96) based on responder status



- There was a significant improvement in CAP (-61.6% vs -28.8% p=0.012) in GLP-1RA users vs nonusers, although LSM was not significantly different (-0.6 kPa vs -0.5 kPa p=0.493).
- Weight (-7.5% vs -3.1% p=0.011), BMI (-2.7% vs -1.1% p=0.013), ALT (-15 U/L vs -3.0 U/L p=0.019), AST (-4.0 U/L vs 1.0 U/L p=0.025), and A1c (-0.7 vs 0.0 p=0.026) were significantly improved in GLP-1RA users than nonusers.
- Weight (-8.4% vs -1.7% p<0.001), BMI (-3.0% vs -0.6% p<0.001), LDL (-16.0 vs 11.0 p=0.042), and A1c (-0.8 vs 0.3 p=0.001) were significantly improved in responders than non-responders.
- % weight change and GLP-1RA use were significantly associated with changes in CAP score. In the single variable models, CAP score increased by 3.82 units (95% CI: 2.42, 5.22) for every 1% increase in percent weight change. Additionally, GLP-1RA users averaged a 32.81 unit (95% CI: -58.01, -7.55) decrease in CAP score compared to nonusers.
- However, in the full model that included % weight change and GLP-1RA use, GLP-1RA use was no longer significantly associated with changes in CAP score (p=0.132).

Conclusions

- GLP-1RA use is associated with improvements in CAP score, weight, liver enzymes, and A1c.
- Weight loss with GLP-1RA use is the likely mechanism for liver improvement.
- The CAP change cutoff of >38 dB/m is linked to weight loss as well as improvements in LSM and metabolic parameters, suggesting the utility of VCTE in the surveillance of fatty liver disease.
- Limitations: retrospective design, small sample size (n = 96), short follow-up duration (1 year)

References Funding/COI Statements

The authors received no financial support. The authors report no conflicts of interest.

Scan me!