# Effects on Liver Stiffness Following Treatment of Hepatitis C with Direct Acting Antivirals as Evaluated by Vibration Controlled Transient Elastography

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## Background

Liver stiffness is now widely employed as a surrogate measure for liver fibrosis and staging of liver disease. Subsequently, vibration controlled transient elastography (VCTE) is becoming more commonly accepted and utilized to evaluate liver stiffness, likely driven by its dependable diagnostic accuracy and ease of use. This non-invasive technique allows for safer data collection as compared to traditional methods of liver staging such as liver biopsy, and more accurate interpretation compared to biochemical staging allowing for effective trending of liver staging over time. The advent of direct acting antiviral (DAA) based therapy has revolutionized the management of Hepatitis C virus (HCV) infection with high cure rates for all genotypes. Longitudinal studies have demonstrated reduction in hepatic decompensation, hepatocellular carcinoma, and survival benefits after sustained virologic response (SVR); however, there is little data to assess the immediate effects on liver stiffness/staging after achieving SVR. The objective of this study is to evaluate the effect of SVR after DAA based therapy for HCV on liver stiffness as measured by VCTE.

## Methods

This is a retrospective chart review study conducted at the W. G. Hefner VA Medical Center, Salisbury, NC from December 2013 to March 2016. All HCV patients who had undergone VCTE at least 6 months apart were reviewed. VCTE was performed by trained nursing staff and fasting >2 hours prior to VCTE was ensured in both groups. The Treatment Group (n=25) consisted of HCV infected patients who were treated with a DAA based regimen, achieved SVR, and had VCTE evaluation before treatment and after SVR. The Control Group (n=64) consisted of HCV infected patients who were not being treated for HCV and had two VCTE data points over time. VCTE data reported as kilopascal (kPa) were compared to assess trend.

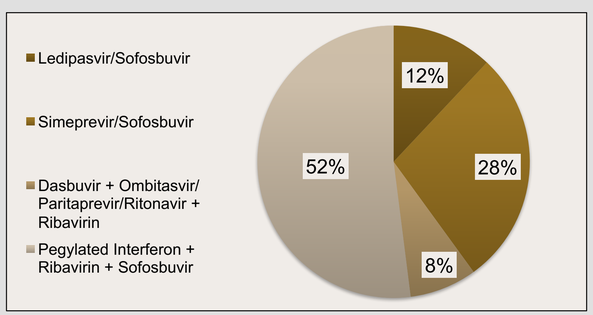


***Figure 1:*** *Treatment regimens used*

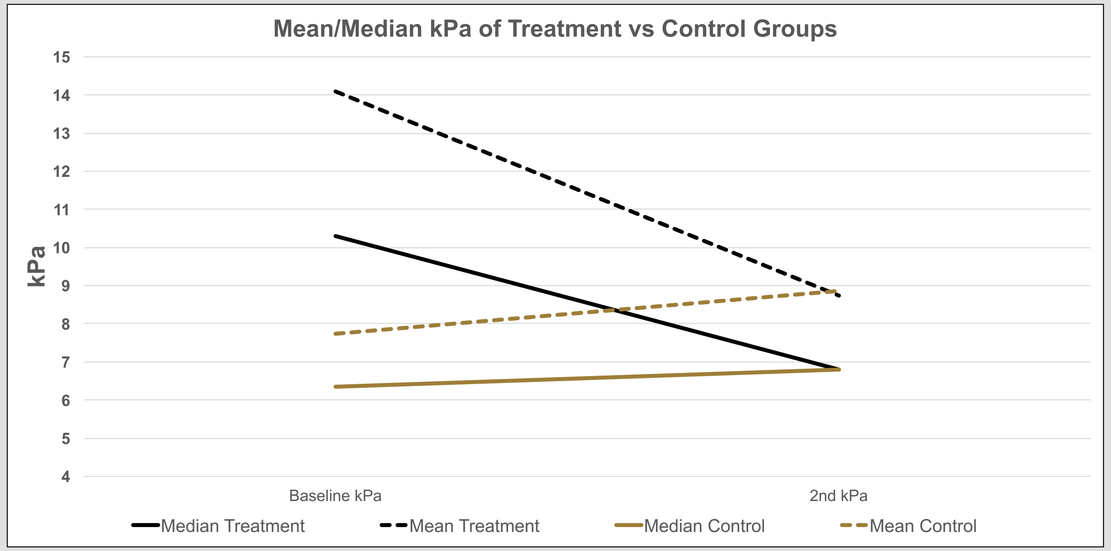


***Figure 2:*** *Mean and Median kPa data as compared between Treatment Group and Control Group*

| Group | Observation | Mean | Std Dev | Median | Minimum | Maximum |
|---|---|---|---|---|---|---|
| **Control (n=64)** | kPa Baseline | 7.7 | 5.6 | 6.4 | 3.3 | 43.6 |
| | kPa Follow Up | 8.9 | 7.6 | 6.8 | 3.3 | 45.7 |
| | Change | 1.1 | 4.5 | 0.5 | -8.1 | 24.9 |
| | Percent Baseline | 117.3 | 51.9 | 108.4 | 38.2 | 361.0 |
| | Percent Change | 17.3 | 51.9 | 8.4 | -61.8 | 261.0 |
| **Treatment (n=25)** | kPa Baseline | 14.1 | 7.6 | 10.3 | 7.6 | 38.0 |
| | kPa Post-Treatment | 8.7 | 5.8 | 6.8 | 4.4 | 28.0 |
| | Change | -5.4 | 7.3 | -3.4 | -29.7 | 10.4 |
| | Percent Baseline | 66.7 | 28.8 | 64.5 | 21.84 | 159.1 |
| | Percent Change | -33.5 | 28.8 | -35.5 | -78.2 | 59.1 |

***Figure 3:*** *In the control group, kPa increased by a mean of 1.1 (17.3%) and median of 0.5 (8.4%). In the treatment group, kPa decreased by a mean of 5.4 (33.5%) and median of 3.4 (35.5%). Using a Wilcoxon Rank Sum test, the percent change from baseline was significantly different between the control and treatment groups (p=<0.0001).*

| | Stage by kPa[1] | n | Improved kPa n (%) | Avg Days from SVR to 2nd VCTE | Avg Days Between VCTE |
|---|---|---|---|---|---|
| Treatment | F0-1 | 0 | N/A | N/A | N/A |
| | F2 | 8 | 7 (88%) | 267 | 509 |
| | F3 | 8 | 8 (100% | 220 | 472 |
| | F4 | 9 | 8 (89%) | 231 | 510 |
| Control | F0-1 | 41 | 14 (34%) | N/A | 404 |
| | F2 | 15 | 8 (53%) | N/A | 409 |
| | F3 | 3 | 2 (67%) | N/A | 396 |
| | F4 | 5 | 1 (20%) | N/A | 420 |

***Figure 4:*** *Number of patients with improved stiffness (kPa) and average time (measured in days) between Vibration Controlled Transient Elastography (VCTE) data. [1]Staging cut-offs as per Bonder and Afdhal, Curr Gastoenterol Rep (2014) 16:372*

## Results

Liver stiffness improved in 92% (23/25) of the Treatment Group (T) and only 39% (25/64) of the Control Group (C). When accounting for differences in baseline kPa (using the least squares mean method), our model estimates an absolute difference of 5.1 kPa between C (10.2 kPa) and T (5.2 kPa) at time of follow up (p=0.0004, 95% confidence interval 2.3, 7.8). Review Figure 3 for further details.

## Conclusions

Successful treatment of HCV with SVR after DAA therapy results in a significant improvement in liver stiffness. It is not possible to determine to what extent reduction in liver stiffness was as a result of improvement in liver fibrosis vs reduction in necroinflammatory aspect of hepatitis C.

## Limitations

- Baseline fibrosis stage between control and treatment groups was quite disparate secondary to institution driven selection bias (prioritized treating advanced stage disease)
- Background rates of fatty liver disease and the contributions of non-alcoholic steatohepatitis could not be assessed as Controlled Attenuation Parameter was not performed
- Significant proportion of treatment patients received concurrent therapy with Peg-IFN/Riba
- Small treatment group