# SEVERITY AND CORRELATES OF LIVER FIBROSIS ASSESSED BY ELASTOGRAPHY ARE DIFFERENT BETWEEN HEPATITIS C-INFECTED PEOPLE WHO INJECT DRUGS AND PATIENTS INFECTED BY OTHER ROUTES.

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## Background & Aim

Hepatitis C virus (HCV) infection is a major worldwide health problem. People who inject drugs (PWID) account for a large burden of HCV in most developed nations, with >50% of existing and >75% of new infections attributed to injecting illicit drugs.

The advent of direct acting antivirals (DAAs) for HCV treatment promises a cure for all. Although wide access to interferon-free DAAs, the high costs associated with these agents necessitate prioritization of patients for treatment. Given the high risk for HCV transmission among PWID and the fact that cure after DAA therapy eliminates infectiousness, international recommendations have suggested that PWID are a high priority for treatment. A better understanding of factors associated with advanced liver disease would help inform public health policymaking targeting PWID. However, data on the liver disease burden and drivers of liver fibrosis in HCV-infected PWID remains limited.

Transient elastrography (TE) has been demonstrated to be an accurate non-invasive method for staging liver fibrosis in patients infected with HCV.

Using TE, we aimed to compare the stage of the liver disease and its correlates between HCV-infected PWID and patients infected through other routes (non-PWID).

## Patients and Methods

Consecutive HCV-viremic patients (n=280; PWID/non-PWID: 137/143) undergoing successful liver stiffness measurements (2009-2015) were retrospectively reviewed. Liver stiffness values were stratified according to established cut-offs (7, 9.5, 12 kPa for significant, advanced fibrosis, cirrhosis respectively). Multivariate logistic regression was used to assess predictors correlating with presence of advanced fibrosis (liver stiffness >9.5kPa). The statistical analyses were performed using SPSS statistics version 22 (SPSS, IBM, Chicago, IL, USA).

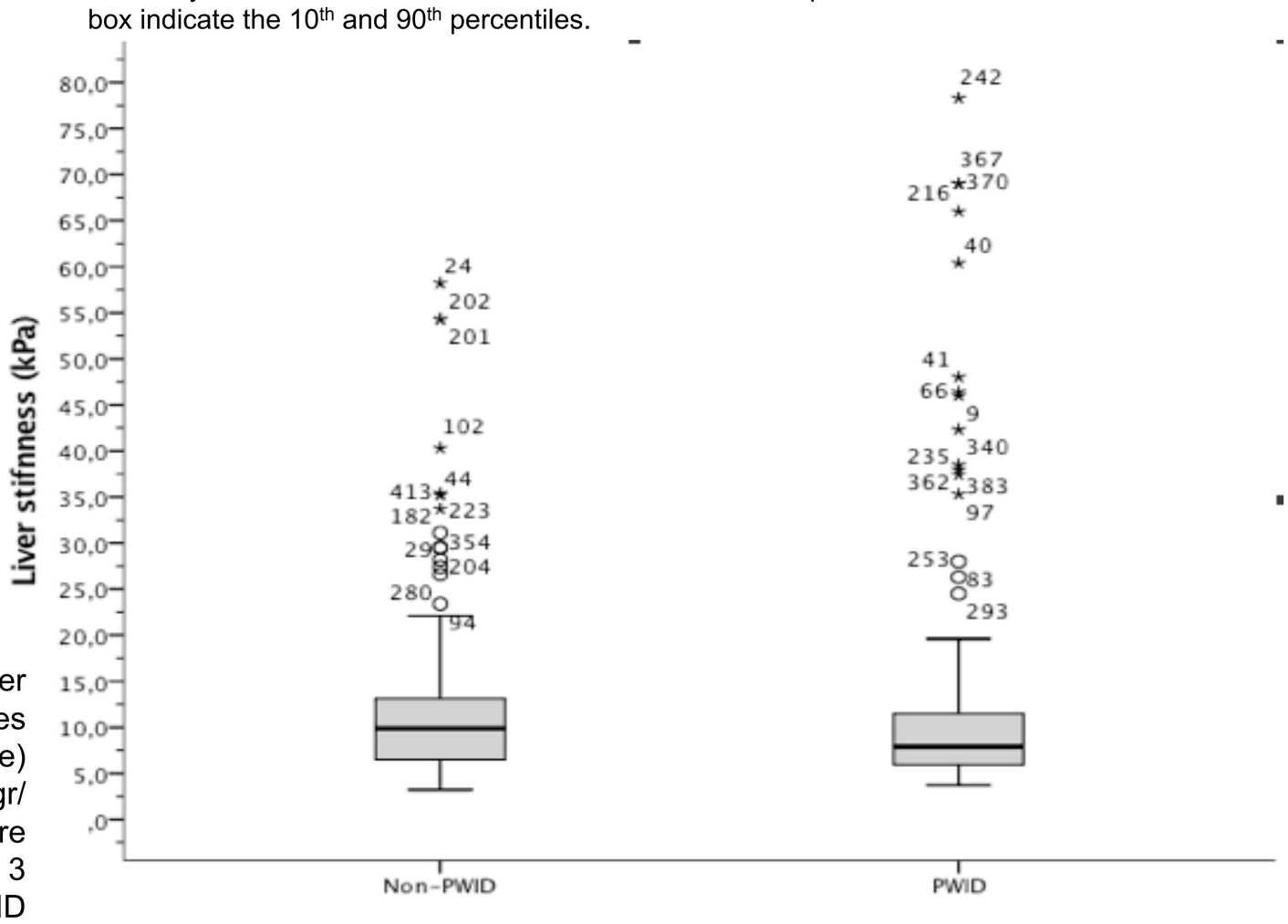
## Results

PWID were more frequently males, younger, and had a lower mean body mass index and lower prevalence of comorbidities (diabetes, hypertension, coronary artery disease, heart failure) compared to non-PWID (Table 1). Excessive alcohol use (>40gr/day), history of smoking, and psychiatric comorbidities were significantly more prevalent among PWID. Genotype 3 predominated in PWID (48.3%) and genotype 1 in non-PWID (43.7%).

**Table 1.** Comparison of demographic and clinical characteristics between PWID and non-PWID

| | PWID | Non-PWID | P-value |
|---|---|---|---|
| **Age, mean (SD)** | 41.7 (10.6) | 50.2 (15.1) | 0.0001 |
| **Male Gender (%)** | 78.8 | 55.9 | 0.0001 |
| **Born in Greece (%)** | 93.2 | 65.6 | 0.0001 |
| **BMI, mean (SD)** | 25 (3.5) | 26.4 (4.5) | 0.005 |
| **History of smoking (%)** | 85.2 | 38.5 | 0.0001 |
| **Alcohol>40gr/day (%)** | 37.3 | 19.1 | 0.0001 |
| **Diabetes (%)** | 3.7 | 11.1 | 0.002 |
| **Arterial Hypertension (%)** | 6.6 | 21.7 | 0.0001 |
| **Heart Failure (%)** | 0 | 3.6 | 0.02 |
| **CAD (%)** | 6.8 | 18.8 | 0.02 |
| **Kidney Failure (%)** | 0.6 | 2.1 | NS |
| **Psychiatric Disease** | 22.4 | 9 | 0.002 |
| **Genotype 1/4 (%)** | 51.1 | 71.6 | 0.0001 |
| **HCV-RNA>800.000 IU/ml (%)** | 58.2 | 56.3 | NS |
| **ALT<ULN (%)** | 26.1 | 25.7 | NS |
| **Treatment naive (%)** | 77.9 | 72.9 | NS |

**Figure 1.** Liver stiffness measurements in PWID and non-PWID. In the box plots, the boundary of the box closest to zero indicates the 25th percentile, a black line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers above and below the box indicate the 10th and 90th percentiles.




Liver stiffness measurements in PWID and non-PWID groups are graphically represented in Figure 1. Overall, PWID had lower median liver stiffness compared to non-PWID [7.9kPa (IQR:5.9-11.5) vs 9.9kPa (IQR:6.4-13.1); p=0.049]. The prevalence of significant (≥F2) fibrosis (PWID 58.4%; non-PWID 69.2%, P=0.06), advanced (≥F3) fibrosis (PWID 36.5%; non-PWID 51.7%, P=0.01) and cirrhosis (F4) (PWID 19.7%; non-PWID 30.1%, P=0.05) was lower in PWID compared to non-PWID. Multivariate analysis was carried out to assess predictors of advanced fibrosis including all variables in Table 1. Older age was the only factor associated with advanced fibrosis in non-PWID (OR:1.05, 95%CI:1-1.10, P=0.04). In PWID, older age (OR:1.09, 95%CI: 1.03-1.15, P=0.004), male gender (OR:6.32, 95%CI: 1.37-29.26, P=0.02), alcohol use (OR:3.60, 95%CI:1.12-11.49, P=0.03) and smoking (5.16, 95%CI: 1.32-20.05, P=0.02) were independently associated with advanced fibrosis.

## Conclusions

Distinct epidemiological and liver disease features, including predominance of non-advanced fibrosis stages, should be taken into account in designating HCV elimination policies targeting PWID. Smoking and alcohol cessation counseling is also important, as both appear to be relevant co-factors of liver disease in PWID.