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Utility of Non-Invasive Testing for Fibrosis Assessment in Patients with End Stage Renal Disease

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BACKGROUND

Non-alcoholic fatty liver disease (NAFLD) risk factors (below) have an increased prevalence in end stage renal disease (ESRD).

- Obesity (BMI ≥ 30)
- Diabetes Mellitus (DM)
- Hypertension (HTN)
- Dyslipidemia (DL)

May patients with ESRD have normal liver enzymes and therefore do not have further testing to evaluate for NAFLD. Therefore, the prevalence and severity of NAFLD in ESRD is unknown.

The goal of study was to assess utility of non-invasive testing (NIT) including transient elastography (TE) for liver stiffness (LS), controlled attenuated parameter (CAP) for steatosis, Fibrosis-4 (FIB-4), AST to platelet ratio (APRI) and NAFLD Fibrosis score (NFS) (**Table 1**) for assessment of NAFLD in patients with ESRD undergoing renal transplant (RT) evaluation.

METHODS

Retrospective analysis with the demographic, clinical, and laboratory data was collected within 12 weeks of TE.

Primary outcomes evaluated for advanced fibrosis (AF, ≥F3) (defined as TE ≥ 9 kPa) and steatosis (defined as CAP ≥ 263 dB/m).

Univariate and multivariate analysis was performed to identify factors associated with AF and steatosis.

In those with available liver histology, utility of LS, FIB-4 and NFS to predict AF was assessed.

Table 1. Formulas for Selected Non-Invasive Tests

Non-invasive tests	Formula
APRI	[(AST/normal AST)/platelet count (103/mL)] x 100
FIB-4	[age(years) x AST)/(platelet count (103/mL)) x √ ALT]
NFS	-1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio – 0.013 × platelet (×109/L) – 0.66 × albumin (g/dL)

RESULTS

- Comorbidities of metabolic syndrome were common with HTN being the most prevalent followed by DM and DL (**Table 2**).
- AF and steatosis were observed in 21% and 25%, respectively (**Table 3**).
- Patients with steatosis were found to have higher BMI ($p < 0.0001$) and obesity ($p < 0.001$).
- NFS showed reasonable accuracy to detect AF, however, did not correlate with TE in identifying fibrosis.

Table 2. Demographic and median clinical values of study population

Characteristic	Patient cohort (n=171)	Characteristic	Patient cohort (n=171)
Age	56 years	Diabetes	47%
Male	65%	Hypertension	96%
Black	60%	Dyslipidemia	56%
Non-Hispanic	99%	AST (IU/L)	31
BMI	28.9	ALT (IU/L)	29
BMI ≥ 30	36%	Platelets x 10^3/mL	215

Table 3. Assessment of each non-invasive test to identify advanced fibrosis and steatosis (%, mean (SD), Median (IQR))

Non-invasive tests	Established cut offs	Results
Transient Elastography (TE)	LS kPa	8.3 (7.1), 6.5 (4.7-8.9)
	LS IQR/med	13.2 (5.4)
	LS ≥ 9	21%
	CAP dB/m	232 (61)
	CAP IQR	40 (20)
	CAP ≥ 263 dB/m	25%
	Probe (M/XL)	62%/38%
AST Platelet Ratio Index (APRI)	APRI	0.35 (0.39), 0.025 (0.016-0.37)
	APRI > 1.5	1.8%
Fibrosis-4 Score (FIB-4)	FIB-4	1.97 (1.33), 0.72 (1.07-2.37)
	FIB-4 > 2.67	15%
Non-alcoholic fatty liver disease fibrosis score (NFS)	NFS	-0.408 (1.61), -0.385 (-1.56-0.51)
	NFS > 0.65	23%

DISCUSSION

Summary and Conclusions:

- Features of the metabolic syndrome in those presenting for RT evaluation are common.
- Despite normal liver enzymes, AF and steatosis were common.
- NFS identified fibrosis more so than APRI and FIB-4 as it includes components of metabolic syndrome in it's formula.
- It is of utmost importance to identify those patients with advanced fibrosis in ESRD as this may help gauge risk of hepatic decompensation post renal transplantation.
- TE and NFS showed good NPV but only moderate ability to predict advanced fibrosis → **optimal to detect patients who lack significant fibrosis.**
- Long-term follow-up following RT in this population are needed to determine the clinical significance of our findings.

Limitations:

Non-invasive tests may under represent of fibrosis as certain serological markers such as AST and ALT may not be elevated in these patients.
Timing of when to perform TE must be considered in the ESRD population (post-HD is preferred so that volume will not interfere with results).

Future Directions:

Multi-center study to further stratify a more global consensus with regards to a preferred modality of testing across all ethnicities.
Only 14 patients in this study had biopsies available for correlation; may benefit from further correlation with biopsies.

ACKNOWLEDGEMENTS

Department of Gastroenterology, Nutrition and Hepatology
Department of Internal Medicine
Department of Nephrology
Hume-Lee Transplant Center

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- May patients with ESRD have normal liver enzymes and therefore do not have further testing to evaluate for NAFLD. Therefore, the prevalence and severity of NAFLD in ESRD is unknown.
- The goal of study was to assess utility of non-invasive testing (NIT) (see below; Table 1) for assessment of NAFLD in patients with ESRD undergoing renal transplant (RT) evaluation.
  - Transient elastography (TE) for liver stiffness (LS)
  - Controlled attenuated parameter (CAP) for steatosis
  - Fibrosis-4 (FIB-4)
  - AST to platelet ratio (APRI)
  - NAFLD Fibrosis score (NFS)

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