Renal Artery Resistive Index and Estimated Glomeruler Filtration Rate in Patients with Non-alcoholic Fatty Liver Disease

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Introduction:

Non-alcoholic fatty liver disease (NAFLD) is commonly observed and is a vital health problem that can affect up to one-third of the adult population worldwide ,The key pathophysiological factor triggering NAFLD liver damage is insulin resistance.There is now increasing clue that NAFLD is a multisystem disorder, influencing the cardiovascular system and endocrine organs (4). NAFLD is also potentially due to an important load of renal changing and chronic kidney disease With the estimated glomerular filtration rate (eGFR), which is a quantification of the kidney's capability to purify the blood, we can predict approximate renal changes and chronic renal disease prognosis and clinical outcomes The renal resistive index (RR), pulsatility index (PI), systolic/diastolic ratio (S/D), peak systolic velocity (PSV), and end-diastolic velocity (EDV) are estimated by renal color Doppler USG, which shows renal hemodynamic changes. Among these parameters, the most common in clinical use is the RRI

Our aim in this study was to investigate renal hemodynamic changes and Egfr levels and to query their clinical usability in patients with NAFLD.

Material and Methods

his study was a retrospective study from January 2015 to July 2017 in our hospital. A total of 69 patients with NAFLD and 50 age and gender-matched healthy controls were included. Patients with chronic, systemic disease, vitamin and mineral deficiency and continuous medication were excluded from this study. Local ethics committee approval was obtained for this study. The results consisted of four parameters: I. Clinical features, II. Laboratory data, III. Upper Abdominal USG, and IV. Renal gray scan USG and hemodynamic properties (revealed by Doppler USG as stated in the guidelines considered by the Asia-Pacific Working Party) NAFLD was diagnosed by the existence of fatty liver and it was figured as the presence or absence of hepatic steatosis by an USG scan, determinated by general radiologist using the standard method. The existance of increased echogenicity of the liver correlated to the renal cortex of the NAFLD patients and the healhty control group were notedThe kidney function level was defined by the Estimated Glomerular Filtration Rate (eGFR), which was evaluated by the formula developed and validated in the Modification of Diet in Renal Disease (MDRD) study (13). The MDRD formula is as following: eGFR = 186 x SCr-1.154 x age-0.203 x 1.233 (Turkish) x 0.742 (if female).

Statistical Analysis ;Statistical analysis was performed with SPSS version 14 (Chicago, Illinois). Continuous variables were given as arithmetic mean ± standard deviation, and categorical variables were defined as a percentage. Normally distributed data were analyzed using the independent test. Abnormally distributed data were analyzed via the Mann Whitney U test. The Spearman test was used for correlation analysis. To determine the accuracy and respective best cut-off values of RRI for predicting patients with NAFLD, ROC curves and their corresponding AUC were used. The linear regression analysis was performed to determine the independent relationship between eGFR, RRI, and other parameters. A 2-sided P <0.05 was considered significant.

Results

No significant difference was detected between the groups for age, sex, and body mass index (Table 1,2) In the patient group, the RRI was 0.64±0.06, and the eGFR was 86.52±22.01 (mL/min/1.73m^2), while in the control group, the RRI was 0.61±0.05, and the eGFR was 95.40±20.21 (mL/min/1.73m^2).(figure 1) Compared to the control group, the patient group had significantly different RRI and eGFR values. There was a negative correlation between the RRI and eGFR (P_{RRI}=0.003 and P_{eGFR}=0.025) (figure2)There was a negative correlation between RRI and eGFR (r=-0.347, P=0.003) An ROC curve analysis proposed that the optimum RRI cut-off value for patients with NAFLD is 0.62, with 65% sensitivity and 60% specificity (AUC=0.663, 95 % confidence interval=0.564-0.762, p=0.002).There was an independent relationship between RRI and eGFR in the linear regression analysis (β=-0.301, P=0.015). (figüre 3

Table 1. Thesociodemographic and laboratory parameters in two groups

	NAFLD patients (n=69)	Controls (n=50)	P value
Age (years)	48.1 ± 14.9	47.0 ± 14.8	0.802
Gender (M/F), n (%)	41 (15.4) / 28 (40.6)	21 (42)/ 29 (58)	0.003
BMI (kg/m^2)	28.69 ± 4.35	28.97 ± 6.14	0.013
Hb (g/dl)	15.07 ± 1.67	13.74 ± 2.28	0.632
WBC (10^3/L)	7.78 ± 1.97	6.87 ± 1.59	0.010
BUN	12.17 ± 3.55	12.63 ± 5.01	0.802
Creatinine	0.92 ± 0.13	0.85 ± 0.12	0.003
RRI	0.64 ± 0.06	0.61 ± 0.05	0.003
eGFR, mL/min/ 1.73m^2	86.52 ± 22.01	95.40 ± 20.21	0.025

	NAFLD patients (n=69)	Controls (n=50)	P value
TC (mg/dL)	225.89 ± 86.48	217.83 ± 60.07	0.616
TG (mg/dL)	180.67 ± 106.59	103.26 ± 35.45	0.010
LDL-c (mg/dL)	132.70 ± 42.42	126.76 ± 57.03	0.651
HDL-c (mg/dL)	43.68 ± 8.30	52.00 ± 7.97	<0.001
Renal long axis, mm	112.35 ± 8.46	109.05 ± 9.97	0.060
Renal short axis, mm	48.49 ± 6.09	43.69 ± 5.96	<0.001
RPT, mm	12.02 ± 1.38	12.14 ± 1.79	0.707

Table 2. RRI and correlation analysis of other parameters in NAFLD patients

	r value	P value
WBC	0.031	0.562
TC	0.014	0.922
HDL-c	0.049	0.738
TG	0.039	0.768
LDL-c	0.031	0.837
Age	0.500	<0.001
BMI	0.095	0.435
BUN	0.112	0.387
Creatin	0.046	0.709
Hb	0.248	0.046

Table 3 Linear Regression Analysis for eGFR in patients with NAFLD

Independent Variables	Beta Regression Coefficient	p value
BUN	**-0.097**	**0.438**
Creatinine	-0.686	<0.001
BMI	-0.223	0.074
TC	0.477	0.749
TG	**-0.299**	**0.596**
WBC	-0.159	0.238
HB	0.194	0.160
PLT	-0.217	0.153
RRI	-0.301	0.015

Figure 1.

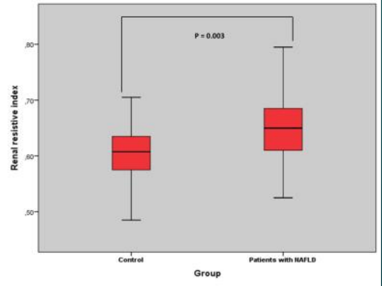


Figure 2.

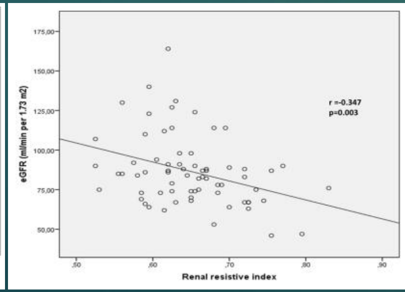
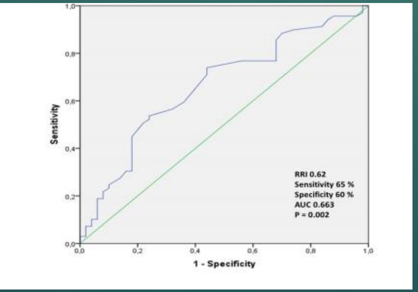


Figure 3



Discussion –Conclusion

In this study, we aimed to investigate the correlation between RRI values and eGFR levels in patients with NAFLD. We showed that the RRI values increased and the eGFR levels decreased in patients with NAFLD compared to the control group. There was an inverse relationship between the RRI and eGFR in patients with NAFLD.

The eGFR is a very common, useful, and easily applied indicator of renal function and clinical prognosis of patients in daily routine clinical practice Based on the current literature, the presence and/or severity of NAFLD is thought to be significantly associated with reduced eGFR.

Chen et al. showed that in patients with NAFLD, the reduction in eGFR was higher than in those without NAFLD. Hsieh et al. reported a significant relationship between the increased fibrosis score and decreased eGFR in patients with NAFLD. Jang et al. evaluated that the reduction in the NAFLD-related eGFR was higher in patient with a high NAFLD fibrosis score. They also stated that NAFLD was independently associated with progression to chronic kidney disease. In addition, some of these studies showed a positive relationship between histological severity and increased kidney disease, regardless of the risk factors in patients with NAFLD Insulin resistance in the development of NAFLD is considered the hepatic manifestation of metabolic syndrome, which is closely related to obesity, hypertension, dyslipidemia, and type 2 diabetes mellitus Afşar et al. showed that increased insulin resistance is independently associated with an increased RRI.

Trovato et al. found that abdominal obesity and hypertension were among the significant variables leading to a high RRI in a multiple linear regression analysis. Bruno et al. revealed that the RRI was higher in patients with diabetes and hypertension compared to the control group. In another study,Afşar et al. demonstrated with a multivariate regression analysis that an increased RRI in patients with type 2 diabetes mellitus was associated with a decreased 24-hour creatine clearance.

Despite the increasing evidence that the risk of kidney disease is high in NAFLD, the factors in the etiology have not been fully clarified. The factors that increase the risk of chronic kidney disease in NAFLD are thought to be lipotoxicity, increased oxidative stress, mitochondrial dysfunction, reactive oxygen radicals, inflammatory and proinflammatory cytokine pathways, and the renin-angiotensin-aldosterone system However, additional systemic diseases seen during the disease and/or included in its etiology also increase the risk of renal disease. After all these processes, renal damage also increases the risk of NAFLD This vicious cycle can result in renal parenchymal damage and hemodynamic changes

Shen et al. (26) revealed that the eGFR was lower in patients with NAFLD compared to that in the control group. Catalano et al. (27) demonstrated that the RRI was high in NAFLD and the eGFR decreased. In our study, the higher RRI in patients with NAFLD compared to the control group, lower eGFR, negative correlation between the RRI and eGFR, and determination of the relationship between the RRI and eGFR with a linear regression analysis suggested that the increased RRI in patients with NAFLD may be a useful indicator in the assessment of decreased kidney function

In conclusion, there are many more studies about NAFLD 's systemic effects except liver. NAFLD is potentially due to an important load of renal changing and chronic kidney disease. In this study suggested that the RRI may be an indicator of renal function, such as with the eGFR, in patients with NAFLD. Multicenter prospective studies involving more patients are needed in this regard.

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