Ageing rates and oxidative stress in patients with non-alcoholic fatty liver disease and profound insulin resistance

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Introduction

Redox imbalance can be both a cause and a consequence of many metabolic pathologies, including non-alcoholic fatty liver disease (NAFLD) and insulin resistance (IR) [1-3]. At the same time, disruption of the synthesis of free radicals and the work of antioxidant systems is one of the key mechanisms of the development of premature aging [4, 5]. On the one hand, the presence of metabolic disorders contributes to the formation of accelerated aging rates. On the other hand, disturbed rates of aging contribute to the emergence and progression of existing metabolic disorders [6]. Therefore, understanding the interrelated changes in IR, OS and rates of aging in patients with NAFLD may be useful for the development of tools for the prevention of premature aging in this group of patients. Data regarding ageing rates and redox markers in NAFLD patients based on the IR level is limited.

Aim

The aim of our study was to evaluate the parameters of oxidative stress (OS) and aging rates in patients with NAFLD and IR of various severity.

Method

Our study included **82 patients with NAFLD** with a mean age of 48.5 [41.0;57.0] years (62.5 % women) and comparison group of **62 patients without NAFLD** with a mean age of 49.0 [38.4;54.9] years (64.6 % women).

Patients were divided into subgroups according to IR index (HOMA-IR): patients **without IR** (n = 22 and n = 28 with/without NAFLD accordingly), with HOMA-IR less than 3 times the upper limit of normal (ULN) (**HOMA-IR <3 * ULN**) (n = 32 and n = 34) and with HOMA-IR 3 times higher than ULN (**HOMA-IR >3 * ULN**) (n = 28, present only in NAFLD group).

Markers of OS included content of total hydroperoxides (THP) and total antioxidant activity (TAA), measured using colorimetric method. Ageing rates were estimated based on the difference between biological age calculated according to the M. Levine et al. (2018) and calendar age for each patient.

Conclusions

NAFLD patients with HOMA-IR >3 * ULN had higher ageing rates compared with NAFLD patients with lower HOMA-IR level or without IR, probably due to higher levels of THP. IR emergence in NAFLD patients most likely mediated by the increased OS. The data obtained can be useful for the prevention of accelerated aging rates in patients with NAFLD.

References

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Results

*Analysis of studied parameters in patients with NAFLD and HOMA-IR >3 * ULN revealed significant higher levels of glucose, alkaline phosphatase and THP compared to NAFLD patients with HOMA-IR < 3 * ULN (p = 0,015, p = 0,014 and p = 0,004) and NAFLD patients without IR (p = 0,004 p = 0,036 and p = 0,046). No such differences were observed between NAFLD patients without IR and with HOMA-IR < 3 * ULN . In addition, NAFLD patients with HOMA-IR >3 * ULN had higher ageing rates compared with NAFLD patients without IR. Such data indicate the appearance of impaired glucose tolerance, pronounced increase in the activity of oxidative processes and, as a result, noticeable increase in the rate of aging in NAFLD patients with profound IR only.*

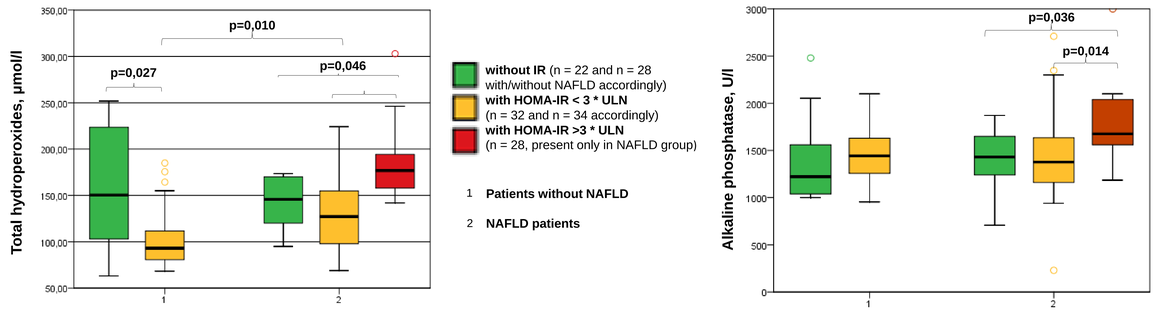
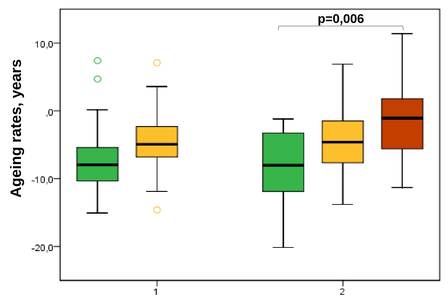


Figure. Comparison of the levels of total hydroperoxides, alkaline phosphatase and groups of patients with non-alcoholic fatty liver disease and different levels of insulin resistance

*In patients with HOMA-IR <3 * ULN the presence of NAFLD was characterized by significantly higher levels of THP (p = 0.010), while a comparison of the same indicator among patients without IR did not reveal differences depending on the presence of NAFLD.*



*In patients **without NAFLD** higher THP levels were observed in the absence of IR (p = 0,027). Available data indicate that insulin suppresses, while elevated glucose levels increase lipid peroxidation. So hyperinsulinemia in patients without NAFLD with mild IR and normal glucose levels may be the reason for lower THP levels.*

*In patients **with NAFLD** IR is probably not the cause but rather a consequence of redox disturbances, so higher IR levels are accompanied by higher THP levels.*

DOI: 10.3252/pso.eu.EASLCONGRESS.2023