

January 30, 2017

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 31075-REVISED Poggiogalle et al.doc).

**Title:** NAFLD connections with fat- free tissues. A focus on bone and skeletal muscle

**Authors:** Eleonora Poggiogalle, Lorenzo Maria Donini, Andrea Lenzi, Claudio Chiesa, Lucia Pacifico

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 31075

The manuscript has been revised according to the suggestions of the reviewer.

Reviewer #1

- As suggested by the reviewer, we have included into the new text a paragraph on the relationship between physical inactivity and NAFLD and osteoporosis and sarcopenia (beginning on page 11 line 20 and ending on page 12, line 20), and have added new references (references # 95-105) to this paragraph:

***“Physical inactivity***

Sedentariness is a well- known risk factor for weight gain and the consequences related to excess fat, including the onset of fatty liver<sup>[95]</sup>. Indeed, lifestyle interventions, combining dietary interventions and physical activity, have been demonstrated to be beneficial in terms of liver fat reduction, due to weight loss. Interestingly, mounting evidence supports an exercise effect and a physical fitness role *per se* in the pathophysiology of NAFLD<sup>[96]</sup>. In fact, based on pooled data from six studies, a recent meta-analysis revealed that exercise alone (versus non-exercise control, without any dietary intervention) was sufficient to determine a significant decrease of the intrahepatic lipid content, even in the absence of weight change, or

minimal weight loss<sup>[97]</sup>.....

- We have modified the sentence on page 4 of previous manuscript to read “The association between NAFLD and decreased BMD has been reported in both genders, and also confirmed in children and adolescents, in the majority of the studies, with few exceptions<sup>[13,16,20]</sup>. .... Bhatt and coll. assessed BMD in different skeletal segments, and surprisingly, found higher BMD values in some bone sites (namely, trunk, pelvis, spine, and also whole body BMD) in adult subjects with NAFLD compared to controls<sup>[16]</sup>. In this study, participants with NAFLD had a higher BMI and a higher body fat than controls, and any adjustments for either BMI or body fat were not considered in the comparison of BMD between groups: this may account for the discrepant results obtained<sup>[16]</sup>. ”

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Lucia Pacifico, MD,  
Corresponding Author  
E-mail: lucia.pacifico@uniroma1.it