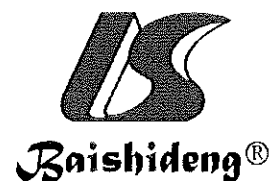


Format for ANSWERING REVIEWERS

September 19, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11672-edited 9.14.14.docx).

Title: Cardiac adipose tissue and its relationship to Diabetes mellitus and Cardiovascular disease

Author: Adam M. Noyes, Kirandeep Dua, Ramprakash Devadoss and Lovely Chhabra

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11672

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated throughout.

2. Revision has been made according to the suggestions of the reviewer (highlighted in text):

(1): "The serum profile of coronary artery bypass grafting (CABG) patients showed..."

(2) "...BMI-matched controls..."

(3) "...nitric oxide (NO) synthesis..." (changed later nitric oxide to "NO")

(4) "EAT accumulation was seen to strongly correlate with serum fibroblast growth factor 21 (FGF21), which is known to improve insulin sensitivity despite an increment in its serum levels in T2DM patients. Thus, excessive EAT in T2DM patients may exert bivalent, unfavorable and adaptive effects on progression of cardiovascular diseases."

(5) "The best imaging tool for quantification of both EAT and PAT remains uncertain. Their thicknesses and volumes can be evaluated by echocardiography, computed tomography (CT) or magnetic resonance imaging (MRI).(24, 29) Due to distinct attenuation values of fat on chest or cardiac CT and MRI, EAT and PAT are both readily identified with ability to calculate the tissue volume and thickness. Furthermore, MRI accurately correlates with EAT and PAT seen on echocardiography imaging.(30) "

(6) "The Multi-Ethnic Study of Atherosclerosis (MESA) study"

(7) "voltage-independent PWI"

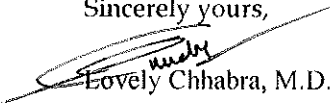
(8) "Management of EAT and PAT"

As excessive cardiac adipose tissue have correlations with poor cardiovascular outcomes, research into possible reversal of the tissue has been studied. Weight loss through bariatric surgery and calorie restriction has shown a corresponding decrease in EAT volume and thickness. EAT thickness decreased in obese subjects who underwent an aggressive 6-month long weight loss program (mean 20 kg) by adhering to a very low-calorie diet (900 kcal/day).(79) Similarly, weight loss after bariatric surgery (average weight loss of 40 kg) was associated with a decrease in EAT thickness.(80) Conversely, the compared effects of pioglitazone and metformin treatment in T2DM patients demonstrated an increase in PAT volume in pioglitazone-treated patients after 24-weeks.(81) Nonetheless, the correlation between increased cardiac adipose tissue has been associated with several features of metabolic syndrome, including fasting insulin. (82) Further studies are needed to show the effects of controlling these measures with changes in size of the cardiac adipose tissues."

3 References and typesetting were corrected

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

Sincerely yours,



Lovely Chhabra, M.D.

Department of Cardiology

80 Seymour Street, Hartford, Connecticut, USA, 06102

Email: lovids@hotmail.com

Tel: +1-860-545-5000/ Fax: +1-888-598-6647