Author’s response to reviews

Title: Impact of body mass index and fat distribution on sex steroid levels in endometrial carcinoma: a retrospective study.

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Answer to questions of the editor

Question 1. when was the blood drawn? (days, weeks, months after the operation?, was there any kind of a protocol for blood donation?)

Answer: Thank you for permitting us to clarify this issue. Blood was drawn according to the Radboudumc biobank protocol at the last preoperative visit at the outpatient clinic, which took place within 4 weeks before surgery. We improved the text on page 7, line 123 (highlighted in red).

Question 2. was this fasting blood donation? at one time point?

Answer: the Radboudumc biobank protocol did not require a fasting blood sample. Therefore, the blood samples will most likely be non fasting, although we cannot exclude to have drawn
fasting blood samples in individual cases. Also blood sample donation occurred throughout the day and not on a specific time point. Although we agree that this could be a limitation of our analysis, estradiol, which was the most important sex steroid analyzed, has stable levels throughout the day in postmenopausal women, independent of fasting status (1). Therefore, it will only have minimal influence on the reported results. For lipids however, serum levels are influenced by fasting status, although levels are relatively stable throughout the day (2). Consequently, the protocol for blood sample donation might have hampered the analysis of lipids in relation to fat distribution measurements. We changed the manuscript on page 15, line 250-255 accordingly.

Question 3. as - except for operation - the patients were untreated for endometrial cancer, what is the expected difference in serum hormone levels to patients who have no endometrial cancer but for instance same BMI?

Answer: see answer to question 4

Question 4. if you expect a difference to matched patients without endometrial cancer I would suggest to add this group (this will not take too much of time or work but will improve the paper - I just wonder whether there is any rationale that serum hormone levels are different in a matched population without endometrial cancer… but this is your crucial point in this paper…)

Answer: We would like to answer question 3 and 4 simultaneously. These are intriguing questions that touch to the core message of our article. The study performed by Audet et al has shown that levels of sex steroids were higher in endometrial cancer patients (n=126) compared to matched healthy postmenopausal women without endometrial cancer (n=110) after correction for differences in BMI (3). Therefore we decided to focus on the association between fat distribution and sex steroid serum levels in endometrial cancer patients. Results of our study demonstrate that the type of fat distribution adds relevant information to BMI and suggest that subcutaneous fat may be more important than visceral fat in production of estradiol.

Reference
