Letter by Lecoultre and Tam Regarding Article, “Increased Adipose Tissue Oxygen Tension in Obese Compared With Lean Men Is Accompanied by Insulin Resistance, Impaired Adipose Tissue Capillarization, and Inflammation”

To the Editor:

At odds with recent reports and reviews implicating adipose tissue (AT) hypoxia as a factor inducing AT dysfunction,1–4 Goossens et al5 published in Circulation a very elegant study suggesting that the impaired responsiveness of AT blood flow in obese patients is accompanied by reduced oxygen extraction and mitochondrial dysfunction leading to impaired tissue oxygen consumption. As a result, AT oxygen partial pressure is paradoxically higher in obese (≈67 mm Hg) versus lean (45 mm Hg) subjects, a condition referred as hyperoxic as opposed to normoxic. Interestingly, in both groups, Goossens et al reported wide ranges of PO2 (20–90 mm Hg; Figure 3).5 Moreover, in response to the vasodilator isoprenaline, AT oxygen tensions transiently rose up to 100 mm Hg (Figure 1). Should these values be considered as hyperoxia, or do they simply reflect the flexibility and normal physiological range of AT PO2 in response to changes in blood flow?

At sea level, oxygen partial pressure in the inspired air is roughly 160 mm Hg, dropping and physiologically decreasing at each step of the oxygen cascade until reaching 1 to 2 mm Hg within the mitochondria of many tissues. At the mitochondrial level, an oxygen tension as low as 1 to 2 mm Hg might therefore be considered as normoxic, whereas that would clearly not be the case at the pulmonary or arterial levels, where it is expected to be 100 mm Hg at sea level. Subcutaneous AT mean oxygen tension has been reported to vary between 45 and 55 mm Hg (range 20–80 mm Hg) in the nonobese and between 45 and 67 mm Hg (range 20–90 mm Hg) in the obese in vivo.3–5 Of importance, oxygen tension in obese patients’ AT overlap with control subjects’ AT, suggesting that differences in AT PO2 are linked to body mass index or body fatness rather than true physiological hypo- or hyperoxia. This is also supported by the absence of hallmarks of hypoxia (ie, HIF-1α or HIF-1β target gene expression) at the lowest but likely normoxic oxygen tensions.5 As pointed out by Goossens et al, such levels moreover remain higher than the levels of hypoxia (ie, 1%) typically used in cell culture models of hypoxia-induced AT dysfunction.

To first address the question of whether obese AT is hypoxic or hyperoxic and whether it affects AT function, the normal range of oxygen tension in AT needs to be defined. Definitions may include oxygen tension levels and cellular responses in the AT and other tissues. For example, the threshold of PO2 at which HIF-1α is stimulated may be used as a true physiological index of hypoxia rather than claiming hyper- or hypoxia when comparing relative tissue PO2 in 2 groups of subjects or animals. Only then will terms such as hypoxia or hyperoxia make sense.

Regardless, we agree that the data reported herein are of very high importance to the field of obesity and insulin sensitivity research. Using integrated physiological approaches, the authors suggest that beyond oxygen tension, impaired oxygen fluxes within the AT affect AT function and inflammation, therefore influencing whole-body insulin sensitivity.

Disclosures

None.

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References

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