Featured Young Investigators' Recent Study in *Microcirculation**

Visceral adipose microvascular function in morbid obesity: a pathway to disease

Featuring: ***Austin Robinson*** *(Ph.D. student) and* ***Ivana Grizelj*** *(junior faculty) in the laboratory of Shane Phillips at the University of Illinois, Chicago.*

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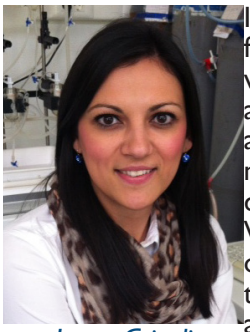
The importance of our study, Reduced Flow- and Acetylcholine-Induced Dilations in Visceral Compared to Subcutaneous Adipose Arterioles in Human Morbid Obesity, lies in that we found reduced endothelium-dependent, acetylcholine (AChID) and flow-induced (FID), vasodilator capacity in resistance arteries (RAs) derived from the visceral adipose tissue (VAT) of morbidly obese women in comparison to RAs obtained from their subcutaneous adipose tissue (SAT). In addition we found that usual mediators of dilation Nitric Oxide (NO), Prostaglandins (PGI_2), and Hydrogen Peroxide (H_2O_2) did not regulate dilatory function in VAT RAs, while in SAT RAs they have very important role in endothelium-dependent dilation.



Ivana Grizelj

In order to assess vasodilator function we subjected micro vessels to AChID and FID with and without pharmacological agents. We used fluorescent microscopy to quantify production of NO and H_2O_2. While the principal mediator of vasodilation is specific to the size and depot of the artery, it is generally NO. However obesity is associated with greater cardiovascular risk due to increased production of reactive oxygen species (ROS) which can decrease bioavailability of NO. Therefore, we postulated that PGI_2 and H_2O_2 may contribute to dilator function of RAs in morbidly obese subjects, since these compounds confer compensatory vasodilation in conditions of reduced NO bioavailability, e.g. in obesity.

As expected, VAT RAs demonstrated reduced sensitivity to AChID and FID compared to micro vessels from SAT of the same patients. While SAT RAs were responsive to inhibition of either NO, PGI_2 or H_2O_2, VAT RAs were not responsive. A combined blockade of NO and PGI_2 did result in a significant reduction in dilatory function in VAT, suggesting that even in the impaired vasodilator state COX metabolites or NO may serve to partially compensate when either of the other vasodilator pathways is blocked. These findings were corroborated by fluorescence experiments which indicated SAT RAs produce more NO and H_2O_2 than VAT RAs under static and flow conditions.

Austin Robinson

Our results support previous findings of impaired vasodilator function in VAT RAs relative to SAT[1] and that the microcirculation of visceral fat in obesity displays impaired vasodilator function compared to healthy weight adults[2]. It is also known that VAT accumulation is associated with heightened inflammation that may contribute to propensity for cardiovascular dysfunction. Taken together these findings suggest that morbid obesity is associated with reduced perfusion to the VAT which may evoke inflammatory and other deleterious paracrine factors associated with tissue hypoxia. As our patients in this study were morbidly obese women, what remains unknown is the level of obesity that must occur before these deleterious changes transpire, potential sex differences, and mechanistic underpinnings that cause microcirculatory dysfunction in VAT.

Shane Phillips

1) Farb MG, Ganley-Leal L, Mott M, Liang Y, Ercan B, Widlansky ME, Bigornia SJ, Fiscale AJ, Apovian CM, Carmine B, et al. Arteriolar function in visceral adipose tissue is impaired in human obesity. Arterioscler Thromb Vasc Biol 32: 467–473, 2012.

2) Virdis A, Santini F, Colucci R, Duranti E, Salvetti G, Rugani I, Segnani C, Anselmino M, Bernardini N, Blandizzi C, Salvetti A, Pinchera A, Taddei S. Vascular generation of tumor necrosis factor-alpha reduces nitric oxide availability in small arteries from visceral fat of obese patients. J Am Coll Cardiol 58: 238–247, 2011.

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