Obesity is associated with elevated risk of cardiovascular events, diabetes, arterial hypertension and cancer and has become a worldwide problem affecting developed and developing countries. Experimental, clinical and epidemiological data indicate that not the amount but the distribution of fat is an important determinant. In animal models, we have investigated effects of dietary interventions and physical exercise on total body fat, aorta eNOS and iNOS expression, microvascular reactivity in response to acetylcholine and sodium nitroprusside, functional capillary density, capillary recruitment and macromolecular permeability on cheek pouch or cremaster muscle preparations. In obese patients, we have investigated whether functional microvascular parameters were correlated with clinical-anthropometrical data and if these parameters would influence obesity-related metabolic disorders, especially glucose homeostasis, in young overweight/obese women. Our results have shown that high fat diet elicits an increase on visceral fat deposition, microvascular dysfunction and insulin resistance in hamsters. In patients we could find a direct correlation between post-load plasma glucose and the time to reach peak red blood cell velocity linking microvascular parameters with metabolic variables and suggesting a key role for microcirculation in obesity-related metabolic disorders. Oxidative stress, inflammation and renin-angiotensin system are also involved on microvascular dysfunction.