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Visceral adipose inflammation in obesity: relationship with circulating inflammation and bariatric surgery outcomes

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Introduction

- Obesity is characterized by a chronic low-grade inflammatory state, with an increased production of pro-inflammatory markers, which could participate to neuropsychiatric comorbidity in this condition. The precise characterization of the inflammatory profile of obese subjects is therefore essential.

- Obesity-related systemic inflammation is believed to originate from the adipose tissue, in particular the visceral adipose tissue.

The specific characterization of the inflammatory profile of obese subjects, associating systemic and adipose markers of inflammation, is still needed so as the question whether adipose and systemic inflammatory profiles/specificities in obesity influence the outcome of bariatric surgery on weight reductions.

➔ The present study aimed at assessing the association of adipocytokines expression with immune cells in the visceral adipose tissue of obese patients, and their relationship with systemic inflammation.

➔ Moreover, this study investigated the association of systemic and adipose inflammation before surgery with surgery-induced weight loss.

Patients and methods

Patients

Thirty-seven severely or morbidly obese patients (body mass index (BMI) > 35-40 kg/m²) awaiting for surgical treatment of obesity were included. Twenty-eight patients (76%) were successively followed at 1-3 months after surgery (mean time: 1.3 months) and twenty-five (68%) were followed after six months after bariatric surgery (range: 6-14 months, mean time: 10.6 months).

Weight and BMI were collected before and after bariatric surgery.

Circulating concentrations of inflammatory markers

Fasting blood samples were collected before surgery for the measurement of high-sensitivity (hs) interleukin-6 (hsIL-6), hs tumor necrosis factor- α (hsTNF-α), hs C-reactive protein (hsCRP), leptin and neopterin by ELISA.

Adipose tissue gene expression of inflammatory and immune cells markers

Samples of visceral adipose tissue were taken during bariatric surgery for the measurement by qRT-PCR of gene expression of:

- Adipocytokines: IL-6, IL-1ra, TNF-α , IL-10, IL-1β, leptin, MCP-1
- Macrophage markers: CD11B (macrophages), CD11C (M1), CD206 (M2)
- T cell markers: CD3e (T cells), CD8A (cytotoxic), TBX21 (Th1), GATA3 (Th2), FOXP3 (regulatory).

Statistics

HsIL-6, hsTNF-α, neopterin, and leptin values were log transformed. Correlation analyses and multiple linear regression analyses were controlled for obesity-related comorbidities (e.g., T2D, OSA, HTA, hepatic steatosis) and, when appropriate, for time at follow-up.

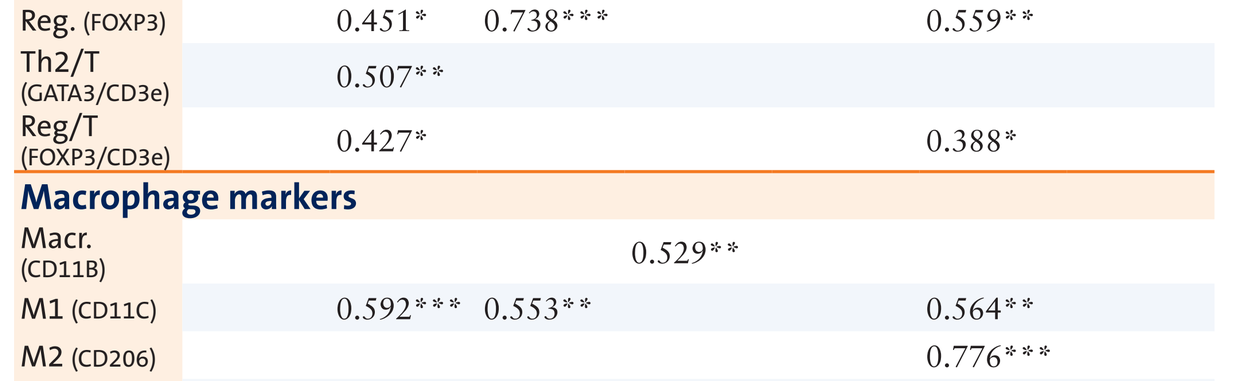
Results

Relationships between adipocytokines and immune cell subpopulations markers in the visceral adipose tissue

	IL-6	IL-1ra	TNF-α	IL-10	IL-1β	Leptin	MCP-1
Adipocytokines							
IL-1β	0.622***		0.364*	0.439*			0.760***
MCP-1	0.565***			0.518**	0.760***		
Leptin		0.564***					
T-Cell markers							
T cells (CD3e)		0.368*	0.683***			0.521**	
Cytotoxic (CD8A)			0.654***				
Th1 (TBX21)			0.449*				
Th2 (GATA3)		0.585**				0.506**	
Reg. (FOXP3)		0.451*	0.738***			0.559**	
Th2/T (GATA3/CD3e)		0.507**					
Reg/T (FOXP3/CD3e)		0.427*				0.388*	
Macrophage markers							
Macr. (CD11B)				0.529**			
M1 (CD11C)		0.592***	0.553**			0.564**	
M2 (CD206)						0.776***	
M1/M (CD11C/11B)		0.580***	0.511**			0.382*	
M2/M (D206/11B)		0.387*		- 0.393*		0.714***	

Expression of macrophage and T-cell markers were related to adipocytokines expression in the visceral adipose tissue, supporting the role of macrophages and T cells in adipose inflammation.
The absence of association of IL-6, IL-1 or MCP-1 with immune cell markers suggests that they may primarily originate from adipocytes.

Association between the visceral adipose inflammatory state before bariatric surgery and surgery-induced weight loss



The inflammatory state in the visceral adipose tissue predicted the magnitude of bariatric surgery-induced decrease in BMI.
Higher pro-inflammatory profile and lower anti-inflammatory profile was related to lower reduction in BMI.

Relationship of gene expression of inflammatory and immune cell markers in the visceral adipose tissue with circulating inflammatory markers

	Circulating inflammatory markers				
	hsCRP	hsIL-6	hsTNF-α	Leptin	Neopterin
Pro-inflammatory markers					
IL-6					- 0.372*
IL-1β					- 0.466**
Th1/T (TBX21/CD3e)		0.427*			
Anti-inflammatory markers					
IL-1ra			- 0.487**		
Th2 (GATA3)			- 0.455*		
Th2/T (GATA3/CD3e)			- 0.468**		
M2/Macr (CD206/CD11B)			- 0.517**		

The inflammatory state of the visceral adipose tissue was associated with circulating levels of inflammatory markers, consistent with the contribution of the adipose tissue to obesity-related inflammation.

The absence of relationship between systemic and adipose IL-6 or TNF-α suggests that circulating concentrations of IL-6/TNF-α do not directly reflect their release per se by the adipose tissue.

Conclusion

- The present study are in line with recent data suggesting the contribution of T cells, in addition to macrophages, to the adipose inflammatory state.

- In addition, our results indicate significant association between the inflammatory state of the visceral adipose tissue and circulating concentrations of inflammatory markers in obese patients, supporting the notion that **low-grade inflammation in obesity relies, at least partially, on adipose inflammation.**

- Importantly, higher pro-inflammatory profile of the visceral adipose tissue was associated with reduced weight loss, while higher adipose anti-inflammatory profile was related to greater weight loss, one to three months after bariatric surgery. This association was still apparent at later stages after surgery, although to a lesser extent probably because of the additional involvement of lifestyle factors.

- These results suggest that visceral adipose inflammation may modulate the efficacy of bariatric surgery on weight reduction, with **increased adipose inflammatory processes associating with reduced success of the intervention.** The basal inflammatory state of the visceral adipose tissue may therefore represent one of the biological predictors of surgery-induced weight loss in obese patients.

- Future studies are needed in order to assess the role of adipose inflammation, in conjunction with systemic inflammation, in neuropsychiatric symptoms associated with obesity and in behavioral changes after bariatric surgery.

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