

Pentraxin 3: A Biomarker Link between Inflammation and Cardiovascular Risk among Obese Children

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The relationship between obesity and atherosclerosis is well-documented even since the adulthood. Recently, pentraxin 3 (PTX3) has been shown to be associated with acute coronary syndrome in adults; however, it is unclear when the risk of heart disease begins in childhood obesity¹ and study by Dervisoglu P et al.² successfully estimated the relationship and predictive value for cardiovascular risk since childhood by this novel biomarker PTX3.

PTX3 is a mediator of subclinical inflammation in atherosclerosis and cardiovascular diseases.³ It has the predictive value as an inflammatory biomarker in overweight and obese children. Three groups were evaluated: overweight, obese and healthy control children. The mean PTX3 level was significantly higher in the overweight and obese groups compared to the control group. It was significantly correlated with carotid intima media thickness and epicardial adipose tissue thickness in the overweight group. In receiver operating characteristic analysis, the optimal cut-off value for PTX3 in the obese group was 9.321 ng/mL, with acceptable sensitivity and specificity rate.²

Obesity is a growing issue in childhood worldwide. The presence of comorbidities with obesity, including hypertension, dyslipidemia, impaired glucose metabolism and atherosclerosis further increases an individual's

risk.⁴ Obesity is associated with systemic inflammation, resulting from the secretion of hormones, cytokines and chemokines from adipose tissue. Several novel biomarkers of systemic inflammation which may affect the outcome of cardiovascular disease and can be therapeutic targets. Pentraxins are one of the mediators secreted during systemic inflammation, synthesized by several different genes and by different protein sizes (i.e., short and long arms). C-reactive protein (CRP) is a well-known short pentraxin, which increase during the acute phase of inflammation. In the study in this Journal, the author established that PTX3 can be another target for prevention of atherosclerosis among obese children.

PTX3 was the first identified long pentraxin family proteins and has been shown to increase with inflammatory response, including tumor necrosis factor, interleukin 1 β and lipopolysaccharide stimulation.⁵ PTX3 can be a more useful target for atherosclerosis probably because it is predominantly secreted from macrophages and vascular endothelial cells; however, CRP is produced differently by hepatocytes.^{6,7}

This is the first study to assess PTX3 levels in children, showing that PTX3 levels were significantly higher in overweight and obese children compared to healthy controls. The optimal cut-off value for PTX3 levels in the obese group was 9.321 ng/mL and 9.263 ng/mL for the overweight group.

In this current study, the authors first reported that PTX3 levels were higher in the overweight and obese groups than in the controls, but they also found that there was no significant difference between the overweight and obese groups. This may suggest that PTX3 starts to increase in the overweight period, which is the initial stage of obesity. These findings may be attributed to the subclinical inflammation associated with overweight and obesity and the secretion of PTX3 from vascular cells secondary to the inflammatory response.⁸ In

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addition, this study interestingly reported that epicardial adipose tissue thickness (EATT) and carotid intima-media thickness (CIMT) were higher in the overweight and obese groups, and PTX3 was positively correlated with these thickness parameters only in the overweight group. From Figure 1, we could thus propose that subclinical inflammation starts during the overweight period, grows severe during the obese period, and becomes more stable in obesity.

Interestingly, childhood obesity may cause autonomic nervous system imbalance, characterized by reduced parasympathetic modulation.^{9,10} In the current analysis, PTX3 was also found positively correlated with the heart rate in the obese groups, indicating that childhood obesity is characterized by reduced parasympathetic activity, resulting in sympathetic activity dominance.

In this novel and interesting pediatric population study, the authors provided new evidence that serum PTX3 levels may be used to assess cardiovascular risk in overweight children, providing a window for early interventions and prevention for future cardiovascular diseases.

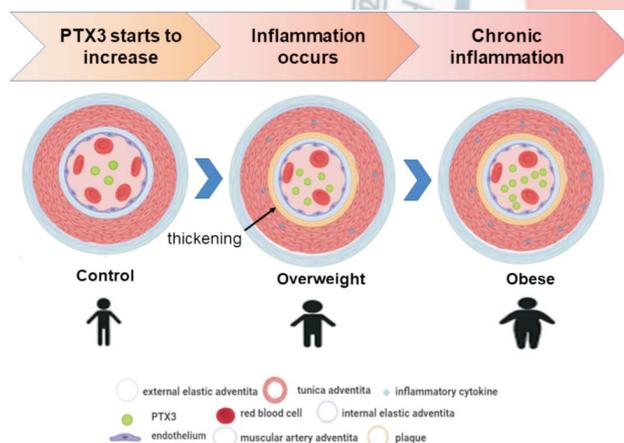


Figure 1. The illustration of progress CIMT in obese children. Secretion of PTX3 from vascular cells was highly correlated with CIMT attributed to the subclinical inflammation. Subclinical inflammation starts during the overweight period and becomes more severe during the obese period, and then gradually becomes more stable in obesity. CIMT, carotid intima-media thickness; PTX3, pentraxin 3.

CONFLICT OF INTEREST

All the authors declare no conflict of interest.

REFERENCES

1. Kume N, Mitsuoka H, Hayashida K, Tanaka M. Pentraxin 3 as a biomarker for acute coronary syndrome: comparison with biomarkers for cardiac damage. *J Cardiol* 2011;58:38-45.
2. Dervisoglu P, Elmas B. Pentraxin 3 as a marker for cardiovascular disease risk in overweight and obese children. *Acta Cardiol Sin* 2021;37:177-83.
3. Norata GD, Marchesi P, Pulakazhi Venu VK, et al. Deficiency of the long pentraxin PTX3 promotes vascular inflammation and atherosclerosis. *Circulation* 2009;120:699-708.
4. Vos MB, Welsh J. Childhood obesity: update on predisposing factors and prevention strategies. *Curr Gastroenterol Rep* 2010;12:280-7.
5. Bonacina F, Baragetti A, Catapano AL, Norata GD. Long pentraxin 3: experimental and clinical relevance in cardiovascular diseases. *Mediators Inflamm* 2013;2013:725102.
6. Abderrahim-Ferkoune A, Bezy O, Chiellini C, et al. Characterization of the long pentraxin PTX3 as a TNFalpha-induced secreted protein of adipose cells. *J Lipid Res* 2003;44:994-1000.
7. Inrona M, Alles VV, Castellano M, et al. Cloning of mouse PTX3, a new member of the pentraxin gene family expressed at extrahepatic sites. *Blood* 1996; 87:1862-72.
8. Mantovani A, Valentino S, Gentile S, et al. The long pentraxin PTX3: a paradigm for humoral pattern recognition molecules. *Ann N Y Acad Sci* 2013;1285:1-14.
9. Souza N, Rossi R, Vanderlei F, et al. Heart rate variability in obese children. *J Hum Growth Dev* 2012;22.
10. Dangardt F, Volkmann R, Chen Y, et al. Reduced cardiac vagal activity in obese children and adolescents. *Clin Physiol Funct Imaging* 2011;31:108-13.