

METABOLIC SYNDROME IN CHILDREN: CARDIOVASCULAR CONSEQUENCES

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Introduction
Pediatric metabolic syndrome (MetS) is an association of at least 2 cardiovascular risk factors (*hypertriglyceridemia, low HDL-cholesterol levels, hypertension, hyperglycemia*) in children with abdominal obesity. The individual components of MetS have a shared pathophysiology and determine a future risk of the most common cause of mortality among adults - *cardiovascular disease*.

Purpose
Elucidating the pathophysiological mechanisms and the clinical features of MetS in children to prevent adult cardiovascular disease.

Material and Methods
This literature review is based on 150 scientific articles recently published on PubMed.

Results
Table 1. Comparison of Key Published MetS Definitions for Children and Adolescents. (Wang HH et al. Novel insights into the pathogenesis and management of the metabolic syndrome. *Pediatr Gastroenterol Hepatol Nutr.* 2020;23(3):189–230.)

	IDEFICS (2012) 2-11 y	IDF (2007) 10-15 y	IDF (2007) ≥ 16 y	NCEP ATP III by Cook et al. (2003)
Defining criterion	Each category counts as one risk criterion	Central obesity and at least 2 of remaining 4 criteria	Central obesity and at least 2 of remaining 4 criteria	≥3 criteria
Obesity (WC)	≥90th %	≥90th % or adult cutoff if lower	≥90 cm for men, ≥80 cm for women	≥90th %
Glucose intolerance (fasting glucose)	HOMA-index ≥ 90th % or fasting glucose ≥ 90th %	≥100 mg/dL (>5.6 mmol/L) or known type 2 diabetes mellitus	≥100 mg/dL or previous diagnosed type 2 diabetes	≥110 mg/dL (≥6.1 mmol/L)
Dyslipidemia (triglycerides)	≥ 90th %	≥150 mg/dL	≥150 mg/dL or specific treatment for this lipid abnormality	≥110 mg/dL
Dyslipidemia (HDL-C)	≤ 10th %	<40 mg/dL (1.03 mmol/L)	<40 mg/dL for men, <50 mg/dL for women, or specific treatment for this lipid abnormality	≤40 mg/dL (1.03 mmol/L; all ages and sexes, NCEP)
High BP	SBP ≥ 90th % or DBP ≥ 90th %	SBP ≥130 mm Hg or DBP ≥85 mm Hg	SBP ≥130 mm Hg or DBP ≥85 mm Hg or treatment of previously diagnosed hypertension	≥90th percentile (age, sex, and height specific)

BP - blood pressure; HDL-C - high-density lipoprotein cholesterol; WC - waist circumference; IDF - International Diabetes Federation; IDEFICS - identification and prevention of dietary- and lifestyle-induced health effects in children and infants; NCEP - National Cholesterol Education Program; ATP - Adult Treatment Panel; IDF - International Diabetes Federation.

- The pathophysiology of MetS is determined *genetically*, by *environmental factors* and *lifestyle*, and defined by the following *mechanisms*: insulin resistance, central obesity, proinflammatory and prothrombotic status, adipocyte dysfunction.
- The *dynamic evaluation* of children with MetS registers an uncertain character of the diagnosis as they grow older and a more favorable prognosis than in adults. However, MetS in children is linked to *structural and functional changes of the cardiovascular system* such as pulmonary hypertension, increased thickness of the intima-media of the carotid artery, arterial stiffness and increased size of the left atrium and ventricle.

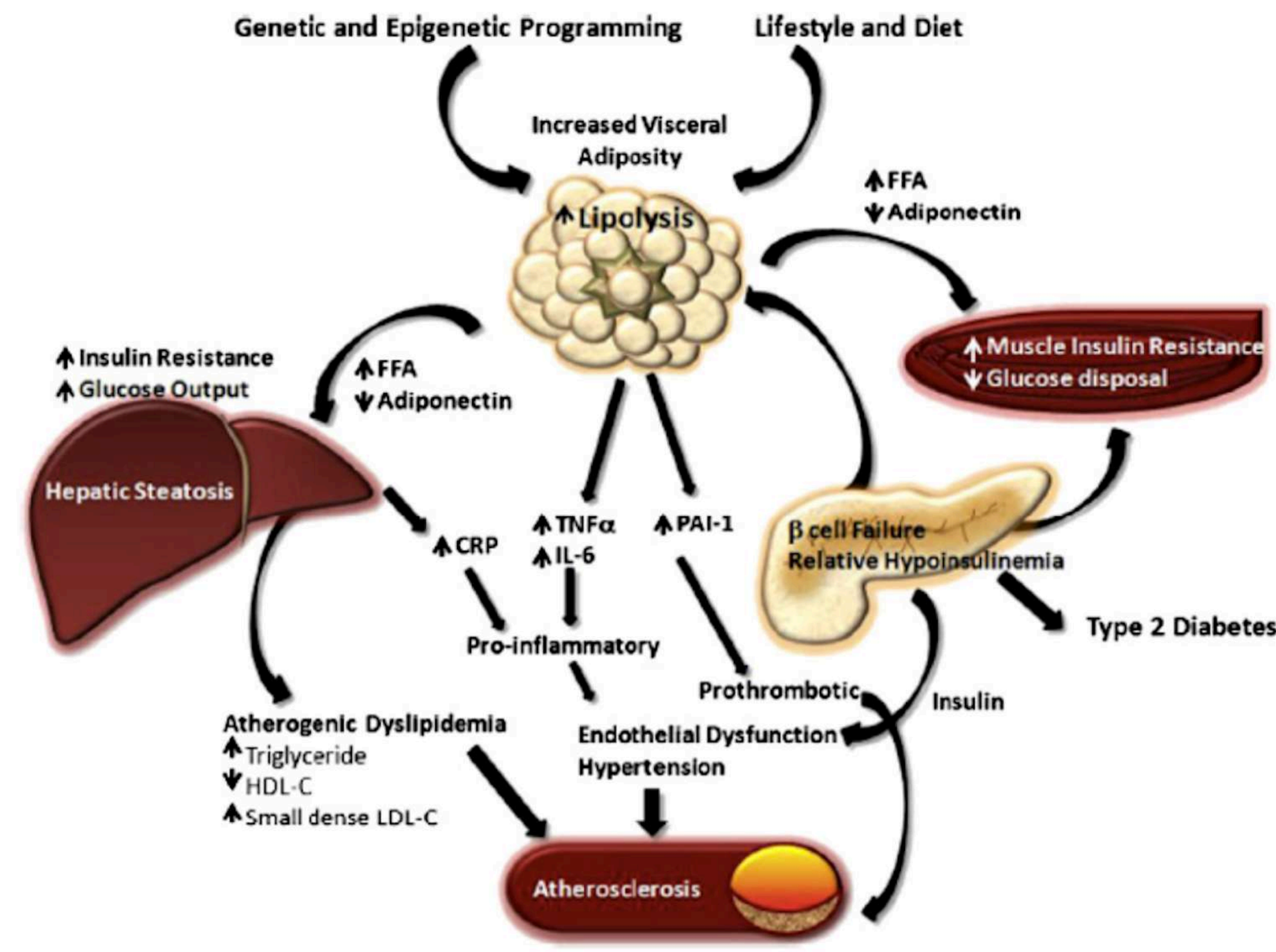


Figure 1. Proposed mechanisms for the clustering of MetS components and the increased risk of type 2 diabetes mellitus and CVD. CRP - C-reactive protein; FFA - free fatty acids; IL-6 - interleukin 6; LDL-C - low-density lipoprotein cholesterol; PAI-1 - plasminogen activator inhibitor 1; TNF α - tumor necrosis factor α. (Samson SL, Garber AJ. *Metabolic syndrome. Endocrinol Metab Clin North Am.* 2014;43(1):1–23.)

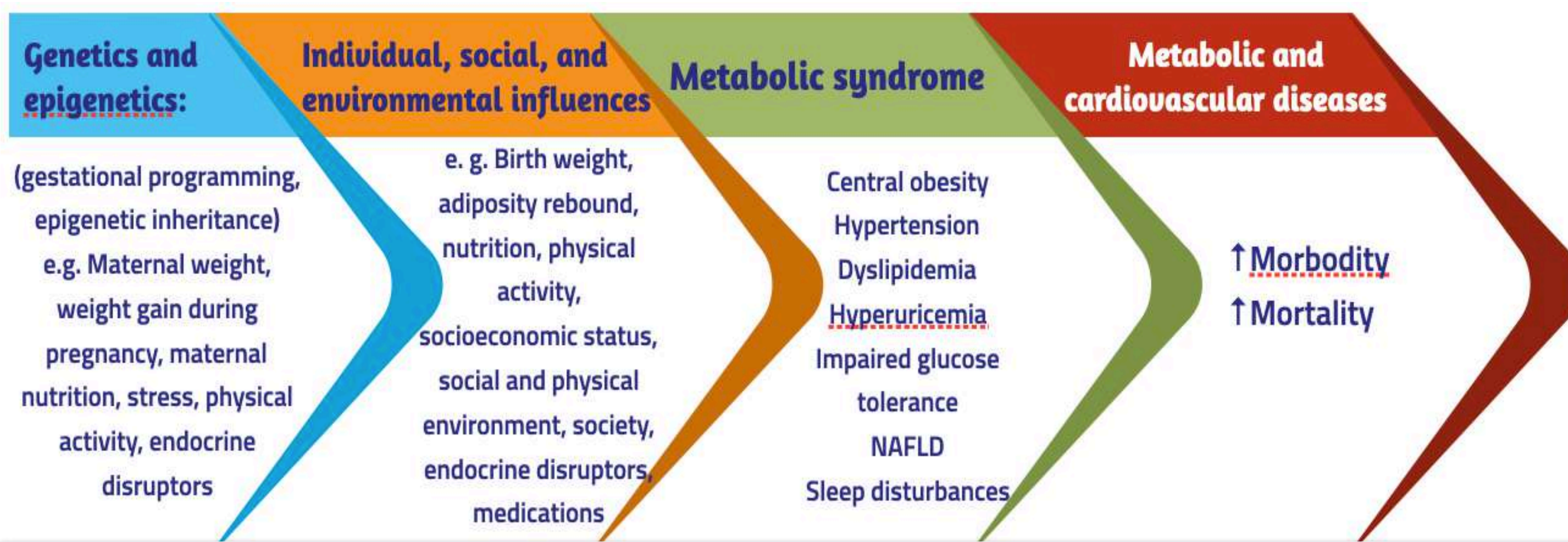


Figure 2. Risk factors and consequences of the MetS. NAFLD - non-alcoholic fatty liver disease (Bussler S, Penke M, Flemming G, Elhassan YS, Kratzsch J, Sergeev E, et al. *Novel insights in the metabolic syndrome in childhood and adolescence. Horm Res Paediatr.* 2017;88(3–4):181–93.)

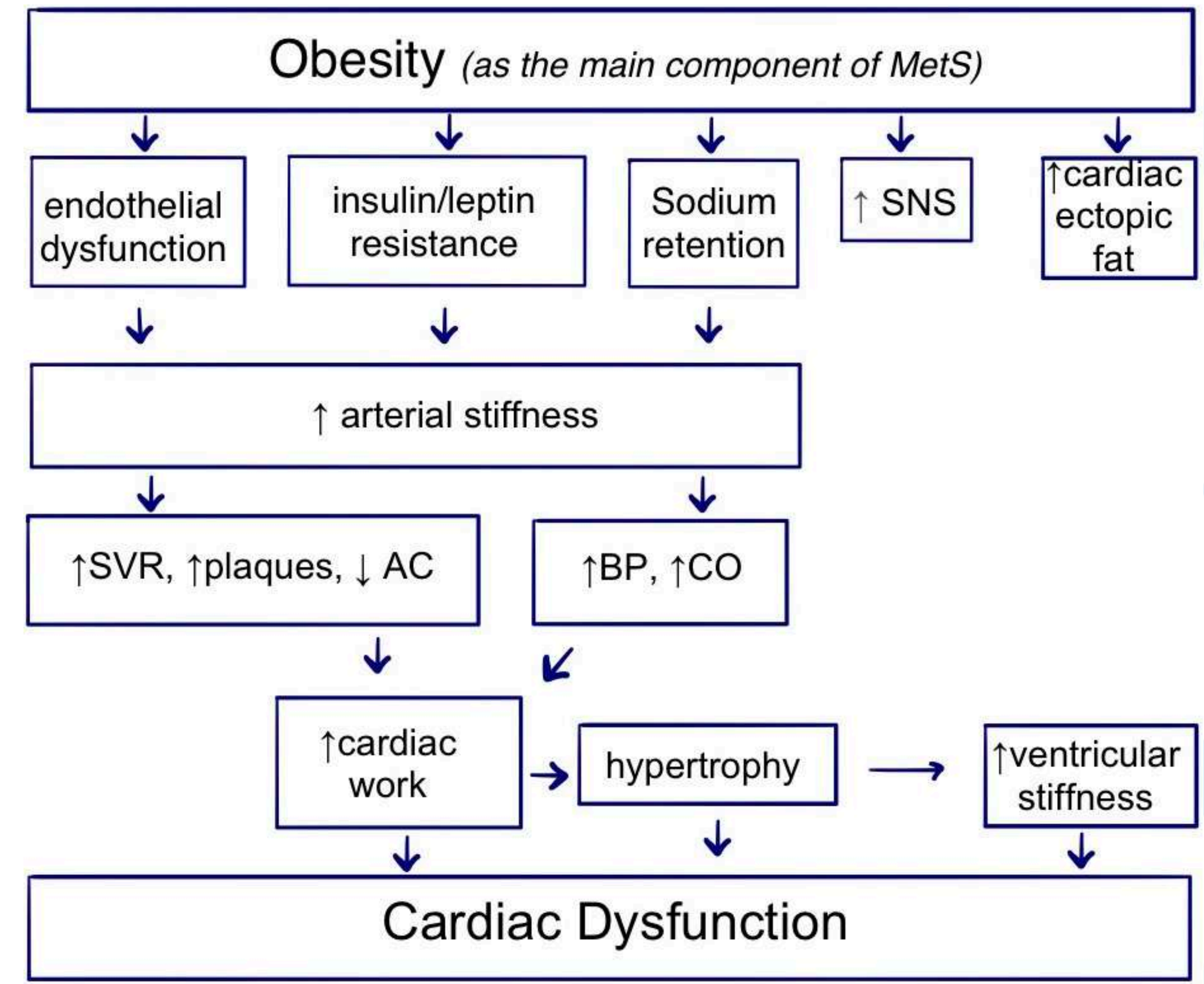


Figure 3. Obesity-Related Mechanisms of Cardiovascular Dysfunction in Children. AC - arterial compliance; BP - blood pressure; CO - cardiac output; SNS - sympathetic nervous system activity; SVR - systemic vascular resistance. (Cote AT, Harris KC, Panagiotopoulos C, Sandor GGS, Devlin AM. *Childhood obesity and cardiovascular dysfunction. J Am Coll Cardiol.* 2013;62(15):1309–19.)

Conclusion
MetS is primarily generated by increased visceral adiposity and ensuing insulin resistance. The subsequent metabolic complications including hypertension, dyslipidemia, and impaired glucose tolerance lead to the development of atherosclerosis and cardiovascular disease. Although the clinical benefit of identifying MetS in children is a controversial topic, the serious cardiovascular consequences of MetS require early intervention in diagnosis and treatment to reduce cardiovascular risk.

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