

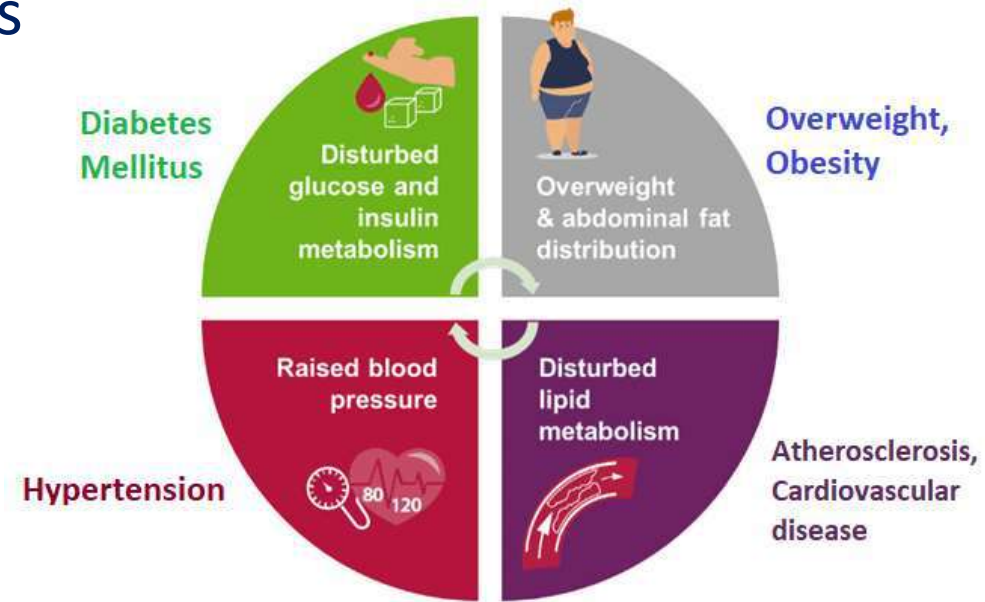
CARDIOMETABOLIC SYNDROME: An Emerging Global Health Issue

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Cardiometabolic Syndrome

Cardiometabolic syndrome (CMS) is a constellation of metabolic dysfunctions characterized by insulin resistance and impaired glucose tolerance, atherogenic dyslipidemia, hypertension and intra-abdominal adiposity (IAA)



Cardiometabolic Syndrome

- The disorder has received multiple names, including
 - Syndrome X,
 - Dysmetabolic syndrome,
 - Plurimetabolic syndrome,
 - Insulin resistance syndrome,
 - and finally, CMS
- CMS is now recognized as a disease entity by the American Society of Endocrinology (ASE), National Cholesterol Education Program (NCEP), and World Health Organization (WHO).

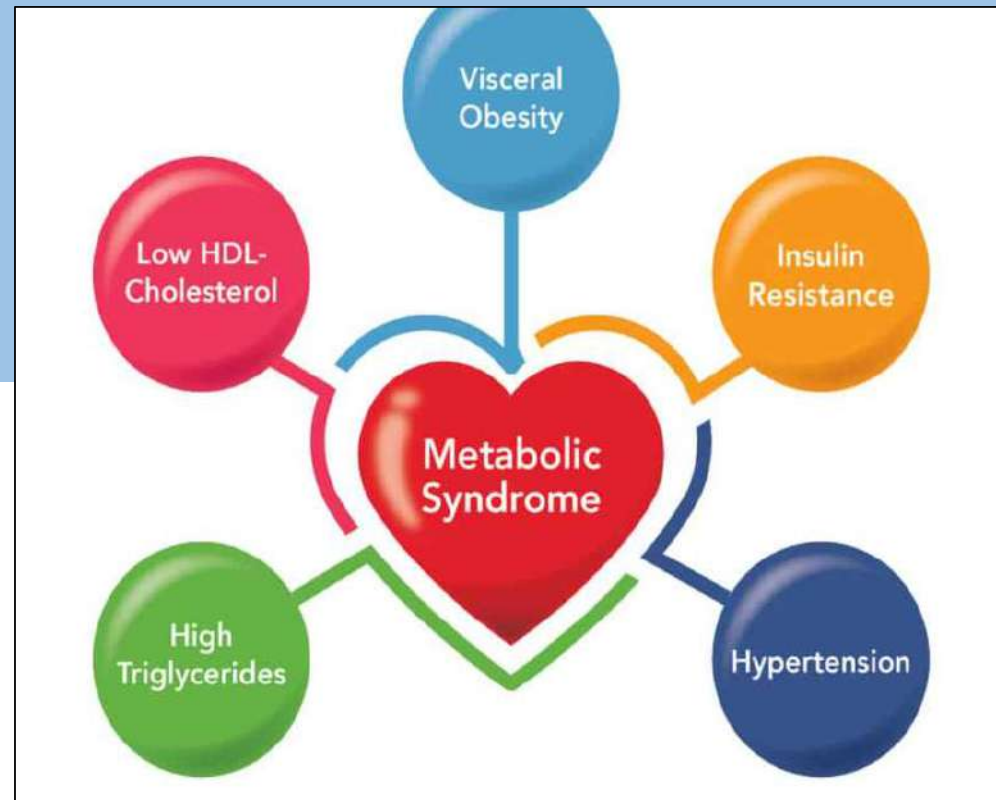
Cardiometabolic Syndrome

These cardiovascular and metabolic derangements individually and interdependently lead to a substantial increase in cardiovascular disease (CVD) morbidity and mortality, making the CMS an established and strong risk factor for premature and severe CVD and stroke.

The risk of CHD, MI & stroke is much higher in persons who have CMS than in those without the syndrome.



Metabolic syndrome is defined as having at least 3 of 5 components:



'Metabolic syndrome' label is imprecise, but cardiometabolic risk is real.

Cardiometabolic syndrome includes the relationship of a number of additional metabolic factors such as prothrombotic factors, inflammation & beyond to CV disease.

The most widely used clinical criteria for diagnosing the cardiometabolic syndrome are those proposed by the World Health Organization and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)

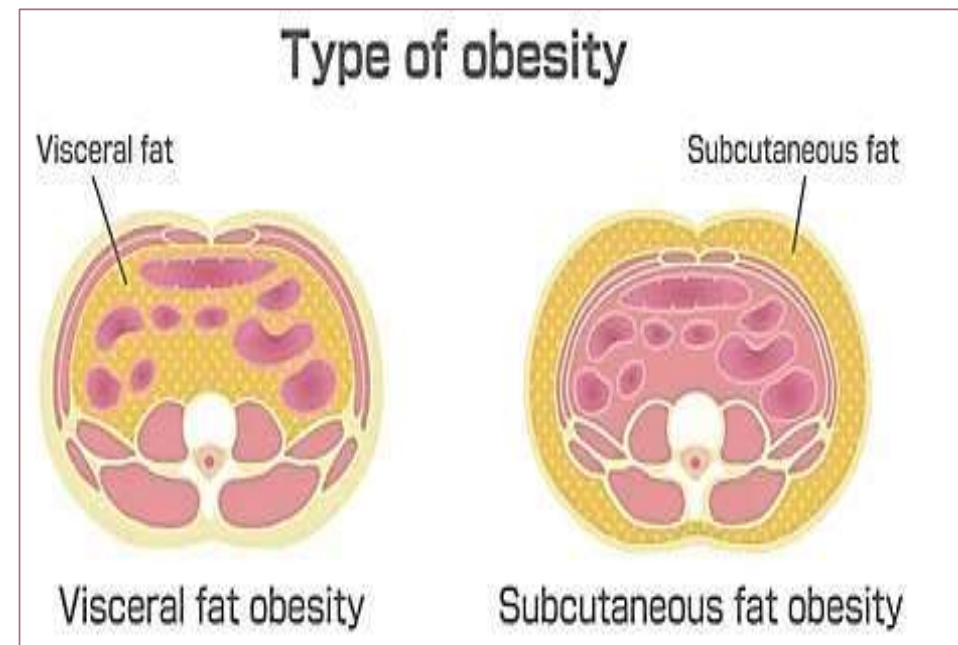
	NCEP ATP III	WHO
Fasting blood glucose	≥100 mg / dL	IFG / IGT / T2DM
Abdominal obesity Men Women	>102 cm WC >88 cm WC	Waist-to-hip ratio >0.90 (or BMI ≥ 30 kg /m ²) Waist-to-hip ratio >0.85 (or BMI ≥ 30 kg /m ²)
Triglycerides	≥150 mg / dL	≥1.7 mmol/L
HDL Cholesterol Men Women	<40 mg / dL <50 mg / dL	<0.9 mmol /L <1.0 mmol/L
Blood pressure	≥130 / 85 mm Hg	≥140 / 90 mm Hg
Microalbuminuria	-	Yes

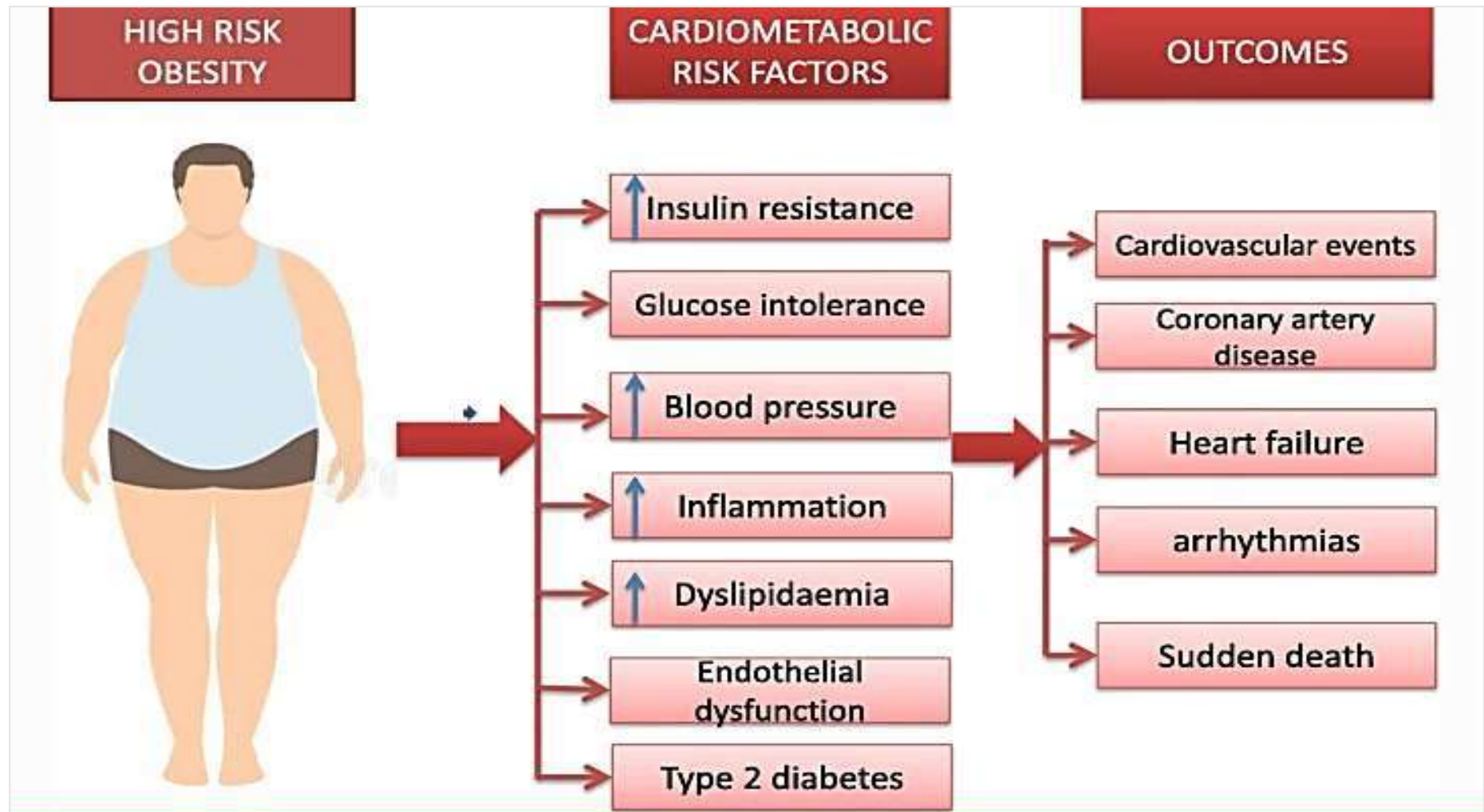
Prevalence

- Data from the Third (NHANES III), the overall age adjusted prevalence of CMS was 24% in the US adult population.
- The frequency of CMS increases dramatically in both sexes between the third and the sixth decades of life and appears to plateau thereafter

Pathophysiology

- At the cellular level, visceral obesity is the result of imbalance between energy intake and expenditure.
- Visceral fat is metabolically active tissue that produces various pro-inflammatory and prothrombotic cytokines
- Defective oxidative metabolism mainly impaired mitochondrial function is involved in visceral fat gain and the development of insulin resistance.



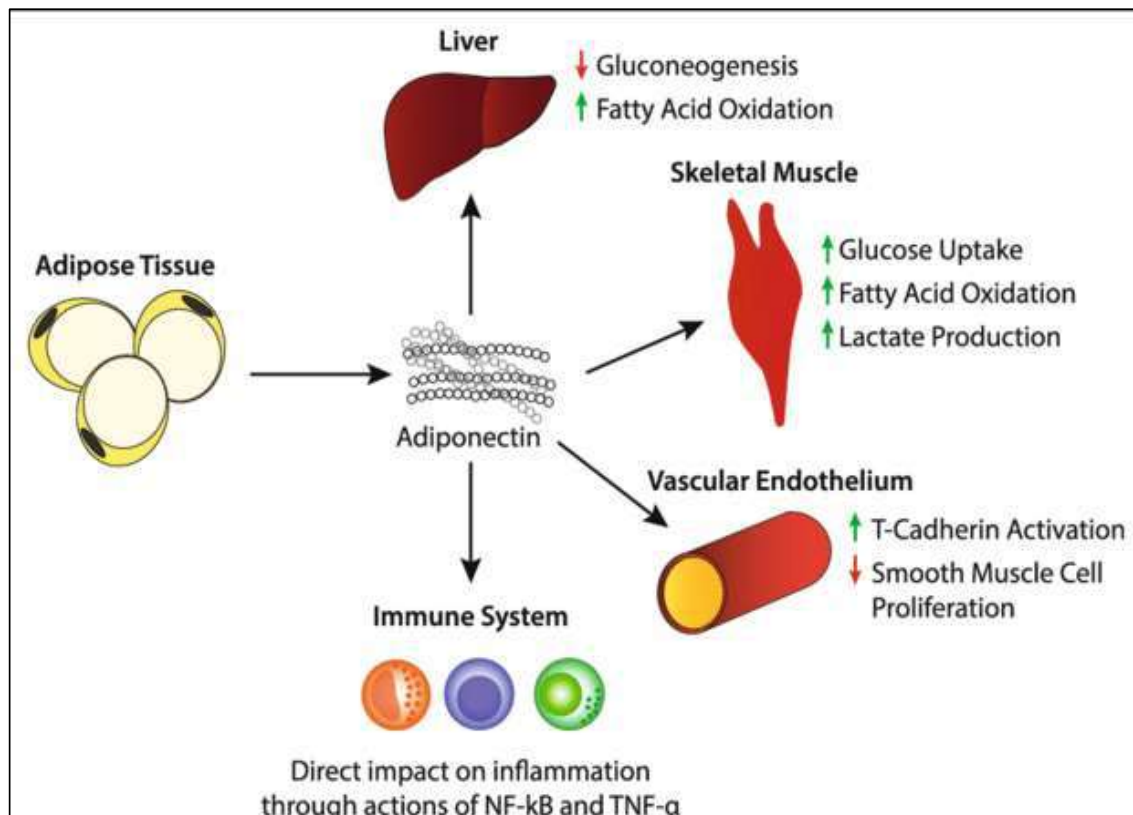


Relationships between high-risk obesity, intermediate cardiometabolic risk factors, and cardiovascular outcomes (obesity phenotypes, diabetes, and cardiovascular diseases)

Pathophysiology (cont)

- Various studies have shown that the alterations in number or density of mitochondria and its oxidative mechanism are associated with development and progression of metabolic syndrome
- Similarly, insulin resistance seems to be associated with a decrease in the mitochondria to nuclear DNA ratio in adolescents
- **Adiponectin**, a hormone from adipose tissue has shown to possess cardioprotective effects. It has anti-inflammatory and anti-atherogenic properties.

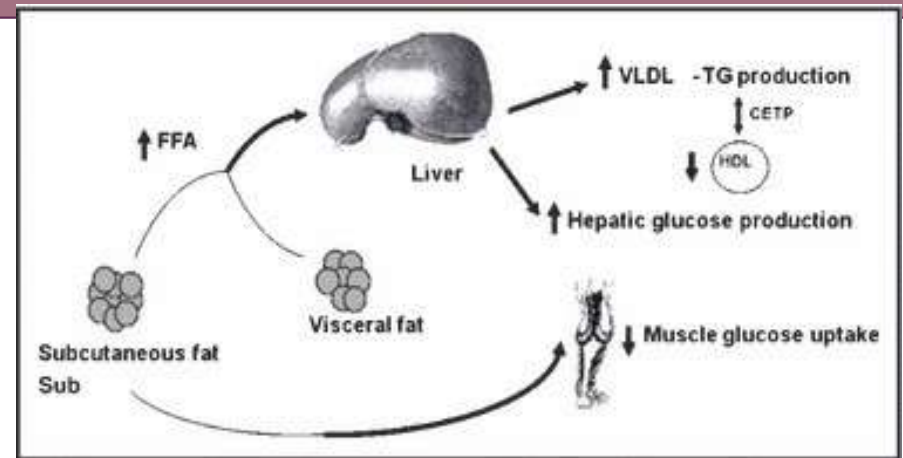
Pathophysiology (cont)



- The hypothesis that **hypoadiponectinaemia** may explain the pathophysiology of metabolic syndrome.
- Low level of adiponectin has been found in patients with diabetes, dyslipidemia and obesity.

Pathophysiology (cont)

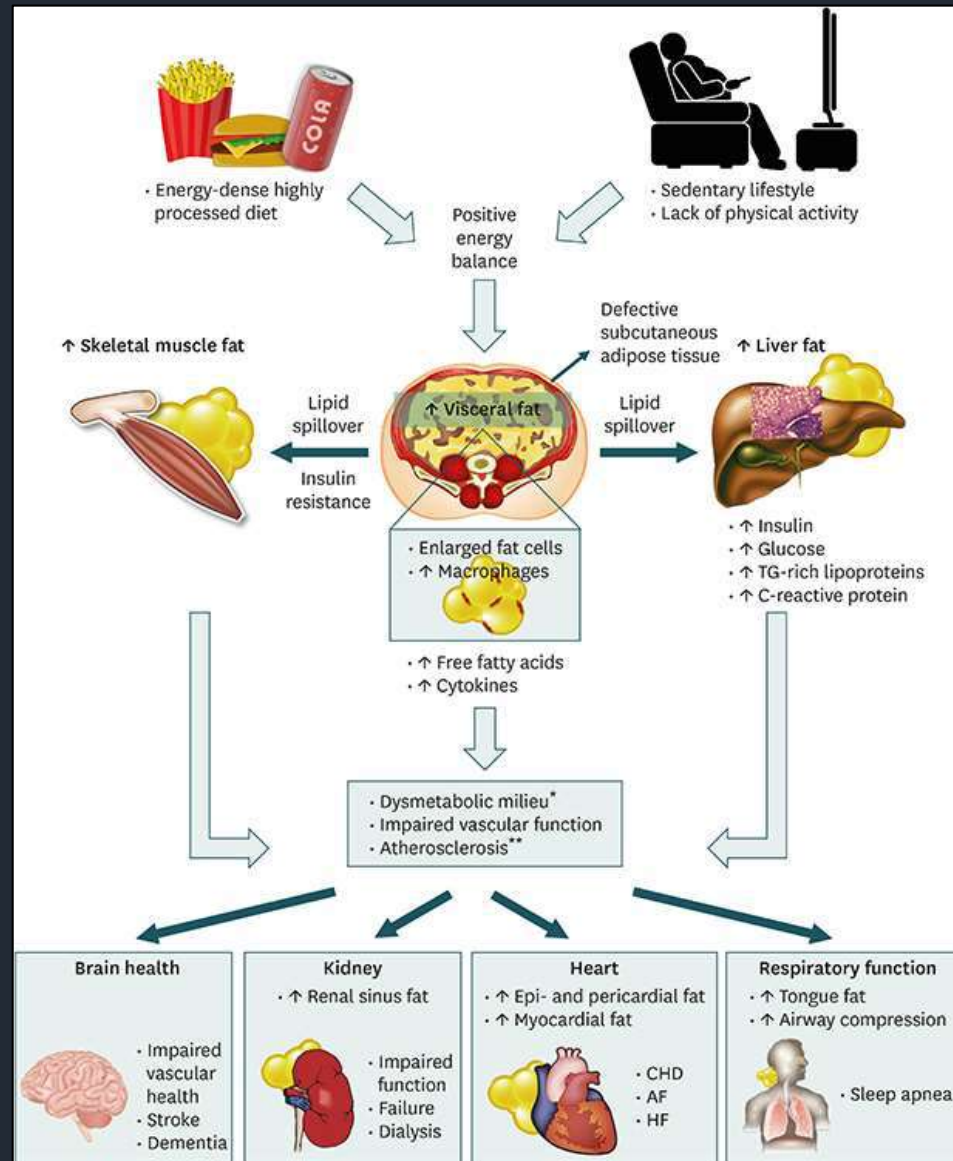
- Insulin resistance in adipose tissue stimulate an increase in lipolysis & free fatty acids release in blood stream which reduces glucose transport into the muscles.



- In addition, increased free fatty acid delivery to the liver can increase hepatic VLDL triglyceride production and plasma triglyceride concentration.
- An increase in plasma triglycerides increases HDL clearance and decreased plasma HDL concentration.

Pathophysiology (cont)

- Among the CMS risk factors, the relation between insulin resistance and HTN is well established. Several different mechanisms are proposed.
- First, insulin is a vasodilator when given intravenously to people of normal weight with secondary effects on sodium reabsorption in the kidneys. In the setting of insulin resistance the vasodilatory effect of insulin can be lost, while the renal effect on sodium reabsorption is preserved.
- Hyperinsulinaemia may result in increased sympathetic nervous system activity and contribute to the development of Hypertension, a risk factor for CMS.



What are the cardiometabolic risk factors?

Abnormal lipids

Smoking

Hypertension

Diabetes

Abdominal obesity

Psychosocial stress

Lack of consumption of fruits & vegetables

Lack of moderate alcohol consumption and

Lack of physical activity

Global cardiometabolic risk*



* working definition

Gelfand EV *et al*, 2006; Vasudevan AR *et al*, 2005

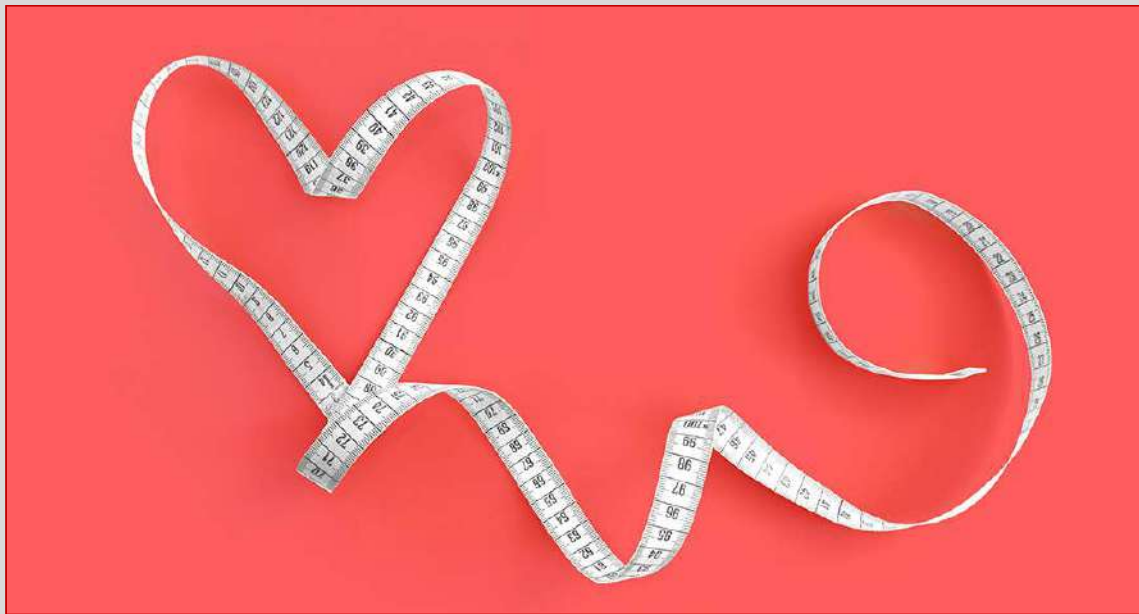
Treatment Challenges



The current approach to the treatment of CMS includes aggressive control of classical risk factors, including dyslipidaemia, hypertension, diabetes and smoking.

However there is a major clinical need to address cluster risk factors which include high plasma insulin, intra-abdominal obesity, prothombotic & proinflammatory cytokines.

Public Health Approach



- Public Education
- Screening for at risk individuals
 - Body habitus/activity
 - Family history
 - Smokers
 - Blood pressure
 - Blood sugar/HbA1c
 - Lipid profile

Lifestyle Modification – Is it Important?

- Diet
- Exercise
- Weight Loss
- Smoking Cessation



Exercise

- Improves CV fitness,
- Weight control,
- Sensitivity to insulin,
- Reduces incidence of DM



Weight loss of 7% Body Weight will:

- Improves lipids,
- Insulin sensitivity,
- BP levels,
- Reduces incidence of diabetes

Brisk walking - 30 min./day
10% reduction in body wt

Lifestyle Modification (Cont)

Healthy lifestyle changes can help prevent or delay serious health problems.

- Healthy diet: Healthy eating plans, DASH diet & Mediterranean diet, emphasizing eating vegetations, fruits, high fiber whole grains & lean protein.
- Reducing or managing stress, physical activity, meditation, yoga and other programs can help to handle stress and improve your emotional & physical health



Smoking Cessation

Both passive and active exposure harmful

A major risk factor for:

- Insulin resistance and metabolic syndrome
- Macrovascular disease (PVD, MI, Stroke)
- Microvascular complications of diabetes
- Pulmonary disease

Smoking cessation counseling

- Consider group therapy & medication support (nicotine replacement, bupropion, varenicline)



Pharmacological Interventions



BP Control – How Important?

- Goal: BP < 130/80
- Conclusively proved the increased risk of CVD with long-term sustained hypertension
- 40% reduction in stroke with control of HTN

Optimize Blood Pressure-

- Initiate behavioral changes: regular exercise, improve diet quality including salt restriction
- If target BP is not achieved after behavioral changes, consider pharmacotherapy

Pharmacological Interventions



Diabetes Control- How Important?

- For every 1% rise in HbA1c there is an 18% rise in risk of cardiovascular events & a 28% increase in peripheral arterial disease
- Evidence is accumulating to show that tight blood sugar control in both Type 1 and Type 2 diabetes reduces risk of CVD

Optimize blood glucose levels

- Initiate behavioral changes: regular exercise, improve diet quality
- If HbA1c <6.5% is not achieved after behavioral changes, consider pharmacotherapy

Optimize Lipid levels

Lipid Control- How Important?

- Goals : HDL > 40mg%, LDL < 100 mg/dl, TG < 150mg%
- Studies shows 24-37% reduction of CVD risks with the use of Statins & Fibrates

Initiate behavioral changes first, then pharmacotherapy if necessary

- Regular exercise & Improve diet quality

Pharmacotherapy

- High risk: initiate statin treatment immediately
- Intermediate risk
 - If LDL-C > 3.5mmol/L, initiate statin treatment
 - If CRP > 2mg/L; start statin (if age appropriate)
 - If multiple CMR factors, initiate statin treatment
- Low risk: observe & if LDL-C > 5.0 mmol/L, initiate statin treatment

Weight Loss Surgery



- The use of weight loss surgery in the clinical management of T2DM in severely obese persons has been recommended. Some clinicians believe it is better to use surgery very early in the course of the disease in order to anticipate clinical deterioration. Others suggest a delayed approach to surgery only in patients not adequately controlled pharmacologically.
- Obesity management strategy can be challenging & it is now generally believed that behavioral modification, dietary macronutrient composition & physical activity are key components that affect CMS management.

Conclusion

- **Cardiometabolic syndrome is a key driver of cardiovascular events. Owing to the high prevalence of cardiometabolic risk factors, prompt assessments with appropriate treatment in primary care are needed to help reduce future complications.**
- **Addressing CMR is not only about counseling patients but rather targeting health promotion efforts to prevent disease.**
- **The key treatments involve behavior change, exercise programme, vascular protective measures such as pharmacotherapy & bariatric surgery for weight reduction might be needed for patients at high risk.**

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THANK YOU