Managing 'metabolic syndrome' and multiple risk factors

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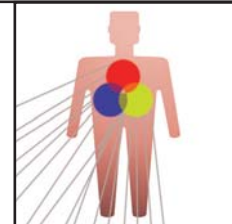
BACKGROUND Risk factors tend to cluster and are shared across common diseases seen in general practice. The **'metabolic syndrome'** is a cluster of fasting hyperglycaemia, abdominal adiposity, dyslipidaemia and hypertension. This syndrome is associated with both insulin resistance and behaviourally modifiable risk factors such as smoking, physical activity and unhealthy diet.

OBJECTIVE This article aims to provide pragmatic guidance on conditions that are lifestyle based and present as a number of disease states that require multiple interventions. Management of comorbidity and multiple risk factors is discussed using a case vignette.

DISCUSSION Metabolic disease states have common bases and their management is directed toward identifying all the risk factors, establishing absolute risk and intervening sequentially.

Case history - Clive
Clive enjoys life to the full. At 58 years of age he is an overweight, retired real estate agent who likes nothing better than long, 'boozy' lunches at his golf club; he has never been known to venture out onto the fairways though. Clive has been hypertensive for at least 20 years (his readings usually in the vicinity of 150/100 mmHg) but he never takes his medication. His body mass index (BMI) is 30 and his waist hip ratio is 1.2. A recent fasting blood glucose was 9.8 mmol/L and his total cholesterol was 6.4 mmol/L with a HDL of 0.8 mmol/L. He quit smoking 3 years ago during his wife's first pregnancy. Last week, Clive noticed for the first time, a heavy feeling in his jaw as he climbed the small number of clubhouse stairs.

One would wonder about the aphorism of 'enjoying life to the full' associated with Clive's behaviours. His life story is almost certainly replete with poor exercise tolerance, difficulties at home with his wife and young child associated with his drinking and absences, and the personal discomfort of a large frame.

The case history is well known to all general practitioners. Using probability diagnosis the red light of ischaemic heart disease is flashing and there is a need to organise immediate management of what is very likely a new onset unstable angina. Clive is a lucky man, as coronary heart disease is the commonest cause of sudden death in Australia.[1]

Clive's coronary disease is underwritten by metabolic syndrome or 'syndrome X':
- fasting hyperglycaemia

Table 1. Definition of the metabolic syndrome[3]

Metabolic syndrome is defined by the World Health Organisation as:

At least one of
- Type 2 diabetes
- Impaired glucose intolerance
- Insulin resistance

Plus at least two of
- Hypertension (BP 140/90 mmHg)
- Obesity (BMI 30 kg/m^{2}, or waist-hip ratio >0.90 for men, >0.85 for women)
- Hypertriglyceridaemia (1.7 mmol/L) or low serum HDL level (<0.9 mmol/L for men, <1.0 mmol/L for women)
- Microalbuminuria (albumin creatine ratio >2.5 mg/mmol for men, >3.5 mg/mmol for women)

BP = blood pressure BMI = body mass index HDL = high density lipoprotein
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Figure 1. New Zealand cardiovascular risk calculator[8]

- obesity (abdominal adiposity)
- dyslipidaemia (low HDL and high triglycerides), and
- hypertension.[2]

Diagnostic criteria are shown in *Table 1*.[3] The pathophysiology underlying this syndrome is insulin resistance.[4,5] The classification as a syndrome recognises that the components are comorbidities and share behavioural traits, environmental influences and outcomes. The syndrome probably affects at least 25% of adults (40% over the age 40 years) and is particularly 'fuelled' by increasing central overweight measured by waist circumference.[5]

Clive's further management is relatively straightforward as he is likely to have overt coronary disease, and is by definition at very high risk of further adverse cardiovascular events such as a myocardial infarction and therefore requires aggressive therapy underwritten by attention to his lifestyle.

However, the approach I wish to take is what one would do with Clive if he had presented the week before he had his episode of angina where he still has vascular disease but it is not yet clinically evident.

Hypertension

Clive has long been recognised as having hypertension. Hypertension was the first of the cardiovascular disease (CVD) risk factors identified and the first to be conclusively proven to benefit from therapeutic drug intervention.[6,7] The success of this strategy has led to the identification and effective therapeutic intervention for other risk factors such as dyslipidaemia. Individual risk factors were recognised as important but it is evident that the interaction of these factors is what really establishes an individual's risk of having a heart attack or stroke. This absolute risk is usually expressed as a percentage and represents the probability of having a cardiovascular or coronary heart disease event over a specified period of time, usually 5 or 10 years. This concept has reached its logical extension with studies such as HOPE demonstrating the benefit of a blood pressure lowering agent, here the angiotensin converting enzyme (ACE) inhibitor ramipril, for subjects who were not hypertensive but were at high absolute cardiovascular event risk.[8]

Assessing cardiovascular risk

To assess absolute risk in individuals without overt CVD one needs to assess an individual's CVD risk factors. The most important drivers of risk are age and gender. While it is simple to estimate Clive's risk in relative terms, ie. compared to other men his age, it is difficult to estimate his absolute risk without the aid of tools. Several of these aids are available such as the popular paper based 'New Zealand absolute risk calculator' (*Figure 1*).[9] Modifiable risk factors needed to establish absolute risk using this tool are:
- smoking (the most important modifiable risk factor)
- the presence of diabetes
- blood lipid fractions, and
- blood pressure.

A recent study identified that 87–100% of subjects presenting with fatal coronary heart disease or a nonfatal acute myocardial infarction had at least one of these risk factors elevated.[10] Clive's doctor, though unable to convince him to take his blood pressure lowering medication, has managed the most important lifestyle change of ceasing smoking and has associated this
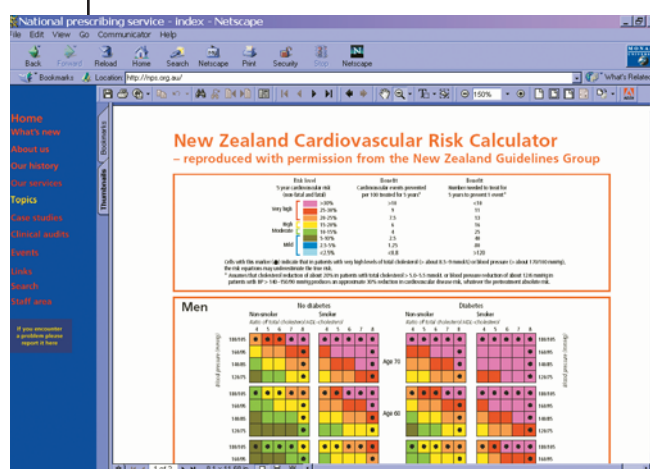
with an important life event, the birth of his child. Other lifestyle risk factors for hypertension that need addressing are his:

- weight
- alcohol intake
- physical inactivity, and
- diet (encourage low alcohol, low salt, low saturated fats, high fibre, and increased intake of fresh fruit, vegetables and fish).[11]

Diabetes and dyslipidaemia

Tests reveal that Clive has diabetes and dyslipidaemia. Diabetes is an important risk factor for heart disease. The hyperglycaemia may be associated with the symptoms of diabetes and the long term microvascular complications such as retinopathy and peripheral neuropathy, but it is the macrovascular disease that will kill or incapacitate patients such as Clive. Therefore, Clive's risk factor management must be as aggressive as it would be if he was known to have CVD. This is perhaps the key to Clive's management and could well have prevented his episode of angina.

Using the 'New Zealand absolute risk calculator' we can estimate Clive's absolute risk of having a fatal or nonfatal cardiovascular event in the subsequent 5 years as greater than 30% – a very high risk. If Clive is a betting man he can be told he is at short odds – about 3 to 1 – of having a heart attack, stroke or angina in the next 5 years. Therapy will not prevent all events. From a doctor's perspective the number of 'Clives' we would need to treat to prevent such an event is less than ten. If Clive was unconvinced that he required his blood pressure medication in the past, perhaps he will be willing today after receiving this information.

Managing Clive's comorbidities

Clive obviously has a number of things that need attending to, including his weight problem. The way to ensure that Clive reduces his risk could be to give him:

- an exercise regimen
- an oral hypoglycaemic
- a combination of blood pressure lowering medications
- low dose aspirin
- a statin
- pamphlets on 'how to lower your cholesterol', 'how to lower your blood pressure', 'diabetes and you', 'losing weight'
- a bottle for a 24 hour urine collection, and
- appointments with a diabetes educator, dietician, podia-

Table 2. 10 step guide to clinical management of weight in adults[14]

1. Discuss weight with patient and whether measurements should be taken then
2. Assess and treat comorbidity associated with weight and determine need to lose weight
3. Ascertain readiness and motivation to lose weight
4. Assess why energy imbalance has occurred
5. Assess how energy imbalance has occurred
6. Determine the level of clinical intervention required
7. Devise goals and treatment strategies with patient
8. Prescribe or refer for dietary and physical activity advice
9. Prescribe medication or refer for obesity surgery, and/or conduct or refer for behaviour modification as determined appropriate
10. Review and provide regular assistance for weight management and maintenance of weight change, and change program as required

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trist, ophthalmologist, endocrinologist and a cardiologist. He may well require all of these, but a structured and stepped intervention using a chronic care model is more likely to reach therapeutic goals.[12]

Stepped intervention

Our first priority should be education and understanding, and the establishment of a good therapeutic relationship. We should also aim to control his risk factors over months rather than weeks. It would be reasonable to re-establish blood pressure lowering therapy in preference to other drug therapies as a first step. With his approval, it would also be reasonable to involve Clive's wife at a later review (many older men do not cook and therefore his wife may need to be informed of dietary restrictions).

Medication

Because of Clive's high absolute risk, drug therapy is indicated from the outset. Introduce medication stepwise and commence at low doses substituting other agents when there is no response or intolerable side effects. Titrate up or add a second low dose agent when there is a partial response. Combination therapy is usually needed to control hypertension. Encourage adherence to therapy when there is a good response and treat to goals where possible. If this is not possible, we must live with therapeutic compromise rather than risk losing patient adherence altogether. However, treat goals as goals, and don't partially treat with the attitude that, for example, the blood pressure is lower than it

was before. Remember that there is a continuous relationship between blood pressure and mortality.[13]

Behavioural modification

Always have behavioural modification as first line therapy even where, as in Clive's case, drug therapy is indicated from the outset. If you do not pay attention to the lifestyle factors they may have adverse consequences as risk factors themselves, may contribute to other risk factors, or may reduce the effectiveness of drug therapy. Behavioural modification also has beneficial effects on other noncardiovascular conditions. Strategies to address Clive's obesity are contained in the 'National Health and Medical Research Council's overweight and obesity in adults guidelines' (*Table 2*).[14]

Lack of physical activity can be identified and addressed by 'green prescribing' programs such as 'active script' or as part of an integrated program such as 'SNAP' which addresses smoking, nutrition, alcohol and physical activity.[15,16]

Conclusion

It is unlikely that, given Clive's angina was fated to occur the week after we saw him, we would have prevented it on this occasion; although it is interesting to speculate what would have happened if Clive's antihypertensive medication was a beta blocker or calcium channel blocker. Is it better to mask a condition or establish it as overt? Irrespective of this, a duly informed Clive may well have recognised the significance of his exertion jaw discomfort and presented to an emergency department or other medical facility forthwith rather than waiting a week with the risk of joining the men who 'died before their time'.

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