Achieving effective risk-factor modification in men

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Urological complaints in men provide healthcare professionals with an opportunity to modify risk factors, thus not only averting the progression of prostate cancer and benign prostatic hyperplasia (BPH), but also reducing the hazards of cardiovascular events in men presenting with erectile dysfunction (ED).

The concept of ‘risk’ is not well appreciated by most men. In the business world, risk, when adroitly judged, can lead to significant rewards. By contrast, most men tend to be somewhat risk averse, not only financially, but also more importantly in terms of approaching their health. Attitudes between the sexes vary, as does their willingness to seek medical help and advice. Women tend to seek help earlier and are much more likely to confide in friends and relatives.

When men eventually do present to us in the surgery or clinic, we need to take the opportunity to think about their future risk and modify those things that are modifiable.

From middle age onwards we all carry a complex portfolio of risk factors, including our family history, which are modified by our environment and lifestyle. For some of us, these factors will translate into premature morbidity and mortality.

Risk prediction has become a hot topic, not only in cardiovascular disease, but also in localised prostate cancer, BPH and ED, and there are major opportunities to advise corrective treatment and/or lifestyle modification accordingly.

PROSTATE CANCER

A subgroup of patients presenting with localised prostate cancer can certainly be stratified as high risk. Traditionally, this category has been based on the presenting prostate-specific antigen (PSA) level and the Gleason score, but recently D’Amico et al. identified the rate and extent of PSA rise (PSA kinetics or velocity) before diagnosis as another important variable. Patients identified as high risk in this respect should clearly be given priority for potentially curative therapy, such as radical prostatectomy, after the risks and benefits have been clearly explained to them, as their prognosis with no intervention is poor.

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TALKING POINTS

BENIGN PROSTATIC HYPERPLASIA

Although the risks associated with BPH are not life-threatening, progression of this disorder can certainly diminish the quality of life. Moreover, if acute urinary retention (AUR) develops, severe distress can result, which has been shown to persist for many months after the actual event. The risk factors for BPH progression and AUR have been identified as:
- severe lower urinary tract symptoms
- a prostate volume >30ml
- an elevated PSA level (which in the absence of prostate cancer can serve as a surrogate for prostate volume).

The 5-alpha-reductase inhibitors finasteride and dutasteride have both been shown to reduce the risk of AUR by more than half when matched against placebo. Finasteride in combination with the alpha-blocker doxazosin was more effective in the Medical Therapy of Prostatic Symptoms study than either agent alone in preventing progression, which was defined as an increase in symptom score of more than four points, the need for surgery, or the development of complications such as AUR.

CARDIOVASCULAR DISEASE AND ERECTILE DYSFUNCTION

Evidence is also steadily accruing that ED might be a harbinger of coronary artery disease and therefore risk of subsequent myocardial infarction. Certainly, the two conditions share similar risk factors. As the mean diameter of the penile artery is only a small fraction of that of the coronary vessels, atheroma in the former might be a harbinger of coronary artery disease, and therefore risk of subsequent myocardial infarction. The risk factors for BPH progression and AUR have been identified as:

Regular moderate to intense physical exercise is well known to reduce the risk of cardiovascular disease and is beneficial for secondary prevention. In addition to this, there is good evidence that increasing physical activity can reduce the risk of certain types of cancer, osteoporosis, type 2 diabetes, depression, obesity and hypertension. If diabetes mellitus is identified, there should be active intervention.

CHOLESTEROL LOWERING

It has become understood that exercise and weight reduction alone will yield beneficial effects on lipid profiles and blood pressure, and improve ED. However, if total and low-density lipoprotein (LDL) cholesterol are significantly elevated, there is now abundant evidence that lowering these with a statin will result in a significant reduction in cardiovascular risk.

Statins have various pleiotropic effects, with vasculoprotective and cardioprotective activity, which might be attributable, at least in part, to inhibition of vascular smooth muscle cell proliferation and the way they accelerate re-endothelialisation. Their beneficial effects on endothelial cells and on endothelial cell function appear to be related to improved nitric oxide (NO) bioavailability.

Statins induce stability of endothelial NO synthase mRNA in endothelial cells, and promote endothelial NO synthase activity through a PI3K/Akt-dependent pathway, which is the common signal-transduction pathway shared by growth factors such as vascular endothelial growth factors or fibroblast growth factors. Statins might influence re-endothelialisation by their effects on mobilising, differentiating and improving the survival of endothelial progenitor cells. It has been proposed that these mechanisms might all contribute to the improved NO bioavailability.

A recent meta-analysis revealed that a 1mmol/l reduction in LDL cholesterol translated into an 18 per cent reduction in heart attack or stroke. Intriguingly, there is also emerging evidence that statins might not only reduce PSA levels but also offer some chemopreventive protection against prostate cancer. In addition, it might be expected that statins would be beneficial in ED; preliminary data on the beneficial effect of statins on patients with ED were reported recently.

LIFESTYLE MODIFICATION

An increased waist circumference and/or body mass index is significantly associated with increased cardiovascular risk, as well as all the other deleterious components of the metabolic syndrome, including diabetes mellitus. Exhortation by clinicians to adopt a more sensible diet and to increase the amount of regular vigorous exercise is therefore in order. This should help our patients get to a better PLACE (see Figure 1). The beneficial effect of a high intake of fruit and vegetables has been reinforced by a recently published meta-analysis.

CONCLUSIONS

The conclusions to be drawn from these data seem clear. Primary care physicians and urologists, when assessing their patients with cardiovascular risk, prostate cancer, BPH or ED, should be thinking not only about the ‘here and now’, but also the future prospects for the given individual, providing them with the information to make personal choices and get control.

Risk-factor modification, including smoking cessation advice, is now a routine component of cardiovascular and diabetes management, and a similar approach could be adopted in men with urological complaints to avert the progression of prostate cancer and BPH, and also to reduce the hazards of cardiovascular events in men presenting with ED. Significant risk reduction in all these disorders can be achieved with timely lifestyle modification, pharmacotherapy and surgical intervention.
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REFERENCES