Obesity in men Reproductive and lower urinary tract complications

GARY WITTERT MB Bch, MD, FRACP, FRCP, FAAHMS

Obesity in men has deleterious effects on reproductive and lower urinary tract function as well as important implications for chronic disease risk. A focus on common sexual and lower urinary tract symptoms by healthcare providers affords an opportunity for prevention or early detection and management of chronic disease in men.

Based on Australian Bureau of Statistics 2011–2012 data, the prevalence of overweight and obesity is similar in males and females aged 2 to 17 years, but is higher in adult men (70%) than adult women (56%).¹ Furthermore, the proportion of men with severe and very severe obesity is increasing rapidly.^{2,3} Obesity is now the second highest contributor to burden of disease in Australia, and ahead of smoking (AIHW).

Most descriptions of the complications of obesity tend to focus on a 'generic human' with little attention to differences between men and women. Obesity has deleterious effects on sexual, reproductive and lower urinary tract function in men that have, until relatively recently, been largely ignored. These effects are the focus of this brief article, together with factors that interact with obesity to determine outcome, and the optimising of healthcare service provision for such men.

Obesity-associated functional hypogonadism

Obesity, particularly when the excess adipose tissue is predominantly visceral and associated with metabolic abnormalities, induces a form of functional secondary hypogonadism

MedicineToday 2017; 18(9): 69-70

Professor Wittert is Head, Discipline of Medicine, and Director of the Freemasons Foundation Centre for Men's Health, University of Adelaide, and Senior Principle Research Fellow at South Australian Health and Medical Research Institute, Adelaide, SA.

OBESITY IN MEN: PRACTICE POINTS

- Reproductive consequences and lower urinary tract symptoms (LUTS) are common in men with obesity.
- Obesity in men leads to alterations in sperm that affect reproductive capacity and transmits chronic disease risk to subsequent generations.
- Particularly in men with obesity, LUTS should not be assumed to be related to the prostate. It is a marker of the presence and/or risk of systemic disease.
- The risk of obesity-associated comorbidities is higher in men who are socially disadvantaged, live in a rural or remote location or have limited functional health literacy. Programs for health promotion should be designed to reach these subgroups, as well as Aboriginal and Torres Strait Islander men and migrants.
- There is considerable evidence to support the health benefits of a high-quality nutrient-rich diet, as well as for regular physical activity, elimination of harmful behaviours and ingested toxins (e.g. smoking, binge drinking), and management of stress, anxiety and depression.
- Substantial favourable outcomes are achievable by optimal treatment of comorbidities such as hyperlipidaemia, hypertension and diabetes, even if there is no loss of weight.

characterised by low serum total testosterone and sex hormone binding globulin (SHBG) concentrations with luteinising hormone and follicle-stimulating hormone concentrations in the mid- or low-normal range. There is some evidence that the reduced testosterone interacts with obesity, age and other risk factors, in a 'feed forward manner' to accelerate progression of milder abnormalities of glucose metabolism to type 2 diabetes. Testosterone increases in response to weight loss and the magnitude of the increase in testosterone is proportional to the amount of weight lost.⁴ At the current time, treatment with testosterone is not appropriate for obesity related low testosterone since neither its efficacy nor safety are established.⁵ Indications for the use of testosterone may change when the T4DM trial (www.t4dm.org.au) reports in early 2019.

Sperm quality and function, and intergenerational transmission of chronic disease risk

Men with obesity are more likely to have abnormalities in the morphology and function of their sperm, high levels of reactive oxygen species in seminal fluid, vulnerability of the sperm to oxidative damage and reduced pregnancy rates as compared with normal weight men.6-8 Obesity may also produce epigenetic changes to sperm DNA9 and alter the pattern of microRNAs in sperm.¹⁰ These alterations to sperm not only affect reproductive capacity but transmit chronic disease risk to subsequent generations. The extent to which this is attributable to obesity in and of itself, or associated comorbidities such as abnormal glucose metabolism, and obstructive sleep apnoea (OSA), dietary pattern and other lifestyle behaviours, and/ or environmental exposures is unclear.11

Lower urinary tract symptoms

Men with obesity have an increased prevalence and severity of both voiding (difficulty initiating urination, poor stream, incomplete emptying, after-dribble) and storage (frequency, urgency, nocturia, incontinence) type lower urinary tract symptoms (LUTS). Although enlargement of the prostate is more common in men with obesity and the metabolic syndrome, and may be causally associated with these symptoms, there is no direct association between the size of the prostate and the presence of any of the symptoms. The presence of LUTS should prompt a search for systemic factors, apart from obesity, now known to be independently associated with LUTS. These factors include, but are not limited to, hypertension, abnormal glucose metabolism, OSA, insufficient physical activity, depression, sex steroid levels, medication use (e.g. thiazide diuretics) and caffeine intake;12,13 the presence of LUTS should prompt their consideration. When nocturia is present OSA, which affects one in two men over the age of 50 years and which may be severe in the absence of sleepiness, should

be excluded.¹³ There are also strong bi-directional associations between depression and LUTS and erectile dysfunction and LUTS and the three conditions and OSA.¹⁴ Comorbid depression in men tends to present predominantly with somatic complaints. Furthermore, LUTS are a marker of risk for incident type 2 diabetes and cardiovascular disease.¹⁵

Other factors interact with obesity to increase risk

As indicated above, numerous factors, independent of and presumably also interacting with obesity, affect sexual, reproductive and lower urinary tract function in men. These include diet quality, physical activity, comorbidities, substance use, other lifestyle behaviours and occupation and environmental risk factors. The effects of obesity also interact with sociodemographic factors to influence disease risk. Men who are socially disadvantaged (low income, unemployed, separated, victims of racial and ethnic disparity), located in rural and remote locations, and/or have limited functional health literacy have a higher risk of obesity-associated comorbidities.16,17

Furthermore, the outcomes for men affected by obesity are determined by their utilisation of health services. The often-held notion that 'men don't go to the doctor' is incorrect. Approximately 90% of men over the age of 40 years visit their GP at least once a year.¹⁸ Those men with chronic disorders, including depression, attend (appropriately) more frequently.19 By contrast, men tend to go to their GP less frequently specifically for preventative health care. When they do go for an acute problem most feel that other issues, not directly associated with the acute problem, are not addressed. Men are reluctant to raise issues peripheral to the immediate reason for attendance, but they still want to be asked and are happy to talk if they feel time is available.20

Implications for management

Every visit by a man to a healthcare provider should be treated as an opportunity for prevention or early detection and management of chronic disease. Enquire about LUTS, erectile dysfunction, health behaviours, work and personal stress, sleep, and symptoms of depression. Also ask if there are any other issues they would like to address. Measure height (if not done previously), weight, waist circumference and blood pressure. Use those data to guide further investigation and schedule a subsequent appointment making sufficient time to address the issues.

As with provision of services, programs for health promotion should be designed to reach specific subgroups of men, including Aboriginal and Torres Strait Islander men, migrants, and men in rural, remote or disadvantaged situations.

In general, weight loss improves obesity-related comorbidities and/or risk of their occurrence. Modest weight loss is relatively easy to achieve in men. However, while it may be possible to maintain some of the weight lost, substantial weight loss is seldom maintained by behavioural intervention alone. Furthermore, eating less of a bad diet may not produce a favourable outcome irrespective of weight lost.²¹ On the other hand, the health benefits of a high-quality nutrient-rich diet,²² regular physical activity,^{23,24} elimination of harmful behaviours and ingested toxins (e.g. smoking, binge drinking), management of stress, anxiety and depression,²⁵ and optimal treatment of comorbidities such as hyperlipidaemia, hypertension and diabetes even if there is no loss of weight, are substantial and achievable. MT

References

 Australian Bureau of Statistics. Australian Health survey: biomedical results for chronic diseases, 2011-12. Canberra: ABS; 2013.

 Neovius M, Teixeira-Pinto A, Rasmussen F. Shift in the composition of obesity in young adult men in Sweden over a third of a century. Int J Obes (Lond) 2008; 32: 832-836.

3. Howard NJ, Taylor AW, Gill TK, Chittleborough CR. Severe obesity: investigating the sociodemographics within the extremes of body mass index. Obes Res Clin Pract 2008; 2: I-II.

4. Grossmann M. Low testosterone in men with

Downloaded for personal use only. No other uses permitted without permission. © MedicineToday 2020.

type 2 diabetes: significance and treatment. J Clin Endocrinol Metab 2011; 96: 2341-2353.

5. Yeap BB, Grossmann M, McLachlan RI, et al. Endocrine Society of Australia position statement on male hypogonadism (part 1): assessment and indications for testosterone therapy. Med J Aust 2016; 205: 173-178.

 Bakos HW, Henshaw RC, Mitchell M, Lane M.
Paternal body mass index is associated with decreased blastocyst development and reduced live birth rates following assisted reproductive technology. Fertil Steril 2011; 95: 1700-1704.

7. Tunc O, Bakos HW, Tremellen K. Impact of body mass index on seminal oxidative stress. Andrologia 2011; 43: 121-128.

8. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online 2015; 31: 593-604.

9. Donkin I, Versteyhe S, Ingerslev LR, et al. Obesity and bariatric surgery drive epigenetic variation of spermatozoa in humans. Cell Metab 2016; 23: 369-378.

10. Lee S, Lim S, Ham O, et al. ROS-mediated bidirectional regulation of miRNA results in distinct pathologic heart conditions. Biochem Biophys Res Commun 2015; 465: 349-355.

 Day J, Savani S, Krempley BD, Nguyen M, Kitlinska JB. Influence of paternal preconception exposures on their offspring: through epigenetics to phenotype. Am J Stem Cells 2016; 5: 11-18.
Martin S, Lange K, Haren MT, Taylor AW, Wittert G; Members of the Florey Adelaide Male Ageing Study. Risk factors for progression or improvement of lower urinary tract symptoms in a prospective cohort of men. J Urol 2014; 191: 130-137.

13. Martin SA, Appleton SL, Adams RJ, et al. Nocturia, other lower urinary tract symptoms and sleep dysfunction in a community-dwelling cohort of men. Urology 2016; 97: 219-226.

 Martin S, Vincent A, Taylor AW, et al. Lower urinary tract symptoms, depression, anxiety and systemic inflammatory factors in men: a population based cohort study. PLoS One 2015; 10: e0137903.
Kupelian V, Araujo AB, Wittert GA, McKinlay JB. Association of moderate to severe lower urinary tract symptoms with incident type 2 diabetes and heart disease. J Urol 2015; 193: 581-586.

16. Li JJ, Appleton SL, Wittert GA, et al. The relationship between functional health literacy and obstructive sleep apnea and its related risk factors and comorbidities in a population cohort of men. Sleep 2014; 37: 571-578.

17. Lam LT, Yang L. Is low health literacy associated with overweight and obesity in adolescents: an epidemiology study in a 12-16 years old population, Nanning, China, 2012. Arch Public Health 2014; 72: 11.

 Holden CA, Jolley DJ, McLachlan RI, et al. Men in Australia Telephone Survey (MATeS): predictors of men's help-seeking behaviour for reproductive health disorders. Med J Aust 2006; 185: 418-422.
Atlantis E, Lange K, Goldney RD, et al. Specific medical conditions associated with clinically significant depressive symptoms in men. Soc Psychiatry Psychiatr Epidemiol 2011; 46: 1303-1312.
Smith JA, Braunack-Mayer AJ, Wittert GA, Warin MJ. Qualities men value when communicating with general practitioners: implications for primary care settings. Med J Aust 2008; 189: 618-621. 21. Khoo J, Piantadosi C, Duncan R, et al. Comparing effects of a low-energy diet and a highprotein low-fat diet on sexual and endothelial function, urinary tract symptoms, and inflammation in obese diabetic men. J Sex Med 2011; 8: 2868-2875. 22. de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999; 99: 779-785. 23. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006; 174: 801-809.

Simon RM, Howard L, Zapata D, Frank J,
Freedland SJ, Vidal AC. The association of exercise with both erectile and sexual function in black and white men. J Sex Med 2015; 12: 1202-1210.
Brieler JA, Lustman PJ, Scherrer JF, Salas J,
Schneider FD. Antidepressant medication use and glycaemic control in co-morbid type 2 diabetes and depression. Fam Pract 2016; 33: 30-36.

COMPETING INTERESTS: Professor Wittert has received speaking fees from Roche, Amgen, Bayer, AstraZeneca, Merck Serono, Merck Sharpe and Dohme, Novo Nordisk, Besins and Abbvie. He has received research support from Bayer-AG, Eli-Lilly, Lawley, ResMed foundation, and Weight Watchers. He is Independent Chair of the Weight Management Council of Australia, Editor-in-Chief of *Obesity Research and Clinical Practice* (Elsevier) and International Advisor for 'ClinicalKey' (Elsevier).