Academic Article

The impact of obesity on urological disorder

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Abstract

The global obesity epidemic is chief among these trends in modern medical discourse. Data from the National Center for Health Statistics estimate that 39.8% of U.S. adults aged 20 years and over were obese in the year 2015 to 2016.[1] Urology is a surgical discipline that spans a variety of anatomical and metabolic systems, and is constantly influenced by global health trends in both subtle and apparent ways.

Obesity, defined as a body mass index ≥ 30 kg/m2 in adults by the National Institutes of Health, is associated with an increased risk for a number of health conditions, including hypertension, unfavorable lipid level, and diabetes mellitus.

More recently, there has been greater interest in the effects of obesity on a variety of benign and malignant urologic conditions. Obesity has been shown to have an effect on urolithiasis; benign prostatic hyperplasia and lower urinary tract symptoms; female incontinence, overactive bladder and pelvic prolapse; male hypogonadism; and male sexual function and infertility. These urologic diseases have a considerable impact on patients' quality of life.

Furthermore, dietary or lifestyle modification and other public health measures directed at reducing weight may reduce the incidence of urologic illnesses. More studies are necessary to determine the therapeutic effects of weight loss and dietary modification on the incidence and progression of benign and malignant urologic conditions.

Keywords: Urological disorder, Obesity, Urology

Introduction

Urology is a surgical discipline that spans a variety of anatomical and metabolic systems, and is constantly influenced by global health trends in both subtle and apparent ways. The global obesity epidemic is chief among these trends in modern medical discourse. Data from the National Center for Health Statistics estimate that 39.8% of U.S. adults aged 20 years and over were obese in the year 2015 to 2016. [1]

Over 60% of the U.S.population is obese or overweight. Obesity in adults is defined as a body mass index greater than 30. It is widely recognized that obesity influences the severity and prevalence of many pathologies. Urological diseases are no exception, and urologists should implore patients to eat well, exercise and maintain a healthy weight as it pertains to both their overall and urological health. Benign urological diseases influenced by obesity include nephrolithiasis, benign prostatic hyperplasia, male infertility, erectile dysfunction, stress urinary incontinence and OAB.

Additionally there has been clinical and biochemical research into the impact of obesity on urological malignancies. Clinical trends and specific pathophysiology will be addressed where applicable. Perioperative considerations such as patient positioning, perioperative complications and anesthesia factors will also be discussed.

Benign Urology

Nephrolithiasis. The incidence of nephrolithiasis has been positively associated with BMI in several studies. One large prospective study observed a RR of 1.3 to 2.1 for BMI over 30 when compared to BMI 21 to 22.9.[2] Subgroup analysis suggests a continuous positive relationship between RR of stone events and BMI.

The mechanism of this relationship has not been completely elucidated, but several theories have been investigated. Obesity associated insulin resistance has been implicated in calcium stone formers. Compensatory hyperinsulinemia leads to metabolic alterations that may contribute to stone formation. Insulin resistance reduces renal ammonium buffering and promotes aciduria. Gouty diathesis, hypocitraturia and hyperuricosuria were the most common urine abnormalities observed in obese stone formers. Increased body size has been associated with hypercalciuria and hyperoxaluria as well. [3,4]

Obesity may increase the risk of uric acid stones. One large study demonstrated that men weighing over 120 kg excreted 37% more uric acid than those weighing less than 100 kg.5 Metabolic syndrome associated acidosis and resulting aciduria predispose obese patients to uric acid stone formation (fig.1). Dietary habits associated with obesity (e.g. excess ingestion of animal protein) reduce urine pH and may contribute to uric acid stone formation.

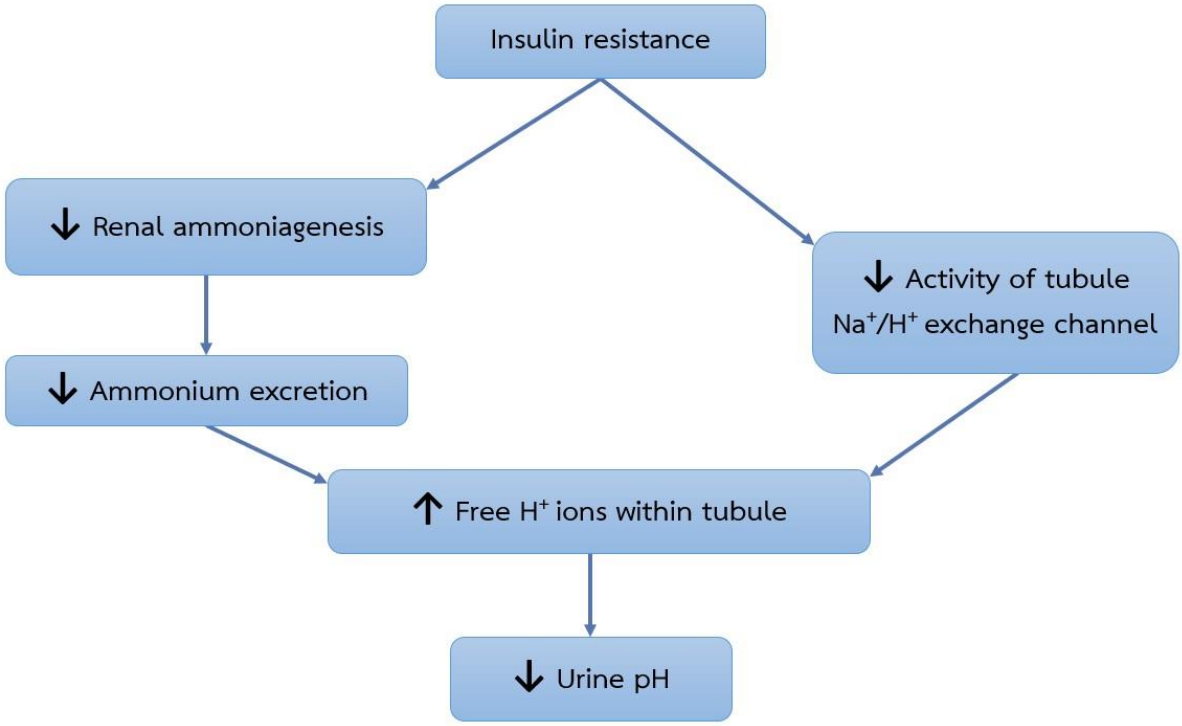

Figure 1. Urine acidification in setting of metabolic syndrome. [5]

Bariatric bypass surgery (e.g. Roux-en-Y) is associated with changes in nutrient absorption that promote urinary stone formation. Decreased fat absorption secondary to shortened gut transit time and subsequent decreased fat emulsification result in saponification of calcium. Small bowel-free oxalate and resulting increased oxalate absorption lead to hyperoxaluria and elevated calcium stone risk. Even though gastric bypass surgery has been shown to decrease insulin resistance and body mass, it is important to recognize this surgical history as a risk factor for stone formation.[6]

General challenges of operating on the obese patient will be further discussed; however, there are important nephrolithiasis specific surgical challenges. Fluoroscopic visualization of stones for targeting during extracorporeal shock wave lithotripsy can be compromised by the increased stone-to-skin distance seen in obese patients. Obese patients have lower stone-free rates after ESWL® with a 3-month stone-free rate of 68% in obese patients vs 80% to 85% for non-obese patients.[7] Ureteroscopy has demonstrated similar stone-free rates when comparing obese and non-obese patients.[8] PCNL will be discussed in a later section.

Erectile dysfunction. Erectile dysfunction is a common urological pathology and has been positively associated with obesity. Central obesity is an independent risk factor for ED.[9] Additionally weight loss through lifestyle modification has been shown to improve International Index of Erectile Function scores with restoration of erectile function in men with baseline ED.[10]

The pathophysiology of erectile dysfunction in obesity is likely multifactorial. It is known that obesity is an independent risk factor for cardiovascular disease, which, in turn, is the most common etiology of ED. Obesity is a state of chronic inflammation in which oxidative stress leads to endothelial damage, cardiovascular

disease and reduction of end organ arterial blood flow. Free radicals may deactivate nitric oxide, reducing the smooth muscle vascular dilatation required for tumescence tumescence.[10] Levels of inflammatory markers such as C-reactive protein and interleukins are elevated in obese men with ED (fig.2). [11]

Adipose tissue harbors aromatase, which peripherally converts androgens into estrogens. Obese men have lower levels of circulating androgens possibly potentiating erectile dysfunction in conjunction with the cardiovascular and endothelial risks described.[12]

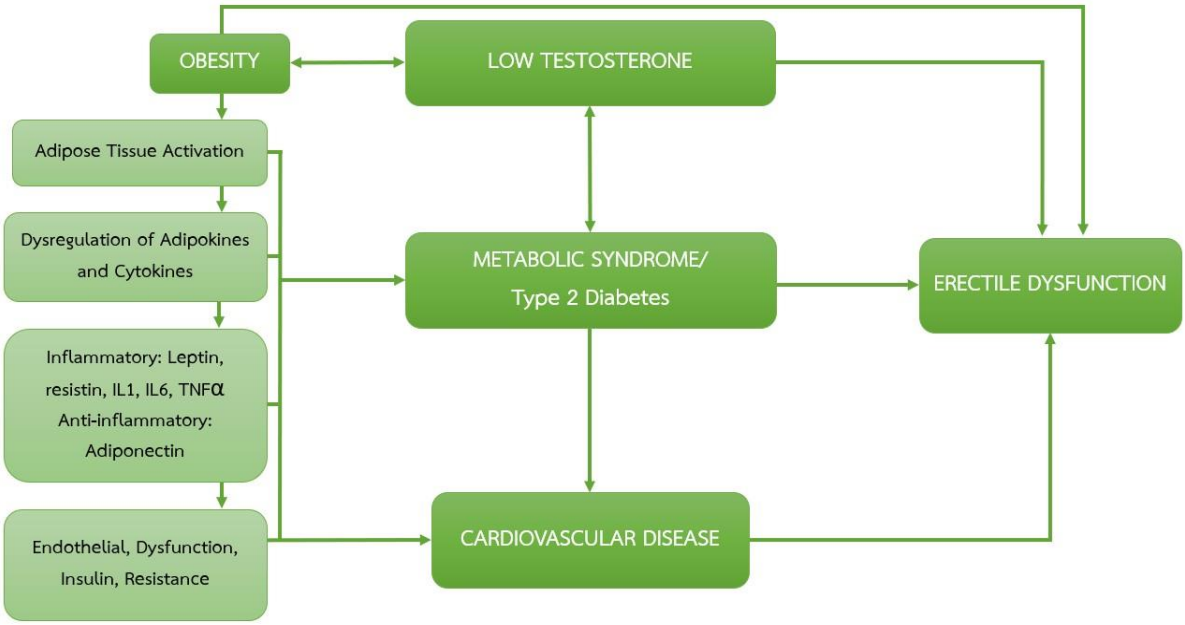

Figure 2. Mechanisms of obesity in erectile dysfunction.[12] TNF, tumor necrosis factor.

Infertility. Infertility, defined as the absence of conception after 1 year of unprotected intercourse, has been associated with obesity in both men and women. Briefly the interconnectivity between obesity, insulin resistance and polycystic ovary syndrome has been well described regarding irregular menstrual cycle, anovulation and resultant infertility. About 30% of infertility cases are so-called male factor. In males multiple mechanisms have been implicated in increased rates of infertility seen in the obese population. The odds of infertility increase by 10% with each 9 kg of weight gain over a BMI of 25.[12]

Hypotestosteronemia secondary to peripheral aromatization in the obese patient is thought to be a driving factor. Additionally lower sex hormone binding globulin levels are seen in obese patients, facilitating aromatization of free testosterone to estrogen. Increased circulating estrogen blunts the cyclic hypothalamic secretion of luteinizing hormone and follicle-stimulating hormone. Resultant reduction in the follicle-stimulating hormone-to-luteinizing hormone ratio impairs sperm maturation, and aberrant semen parameters are observed. Obesity associated peripheral insulin resistance is also thought to play a role by increasing proinflammatory cytokines,

which, in turn, have a blunting effect on the gonadotropic-releasing hormone axis. More common in obese patients, obstructive sleep apnea is an independent risk factor for both erectile dysfunction and infertility. Fragmented sleep results in decreased early morning testosterone levels, causing GnRH axis disruption as previously described.[13] Leptin, an energy management hormone associated with adipose tissue, may impact the GnRH axis as well. Elevated leptin levels have been associated with decreased testosterone secretion from Leydig cells in rats.[14] In humans there is evidence that Sertoli cells, which express leptin receptors, may alter their acetate secretions in response to leptin levels, thus impacting spermatogenesis.[15]

Overall, it is important to consider that the obesity related mechanisms of infertility are generally reversible with weight loss, improved diet and exercise. Particularly weight loss and reduction in adipose tissue volume decrease leptin levels, peripheral aromatization, metabolic endocrinopathy and subsequent impact on the GnRH signaling pathways.[16]

Benign prostate hyperplasia. The potential link between BPH/LUTS and obesity has been studied in some depth. Validated symptom scores do not often correlate to the degree of gland hyperplasia, making this disease particularly difficult to study.

Non-surgical therapies are targeted at reducing symptoms but the most effective of these, a1-blockers, do not impact the prostate size or prevent progression of disease. Patients respond variably to currently available therapies, highlighting the need to identify modifiable risk factors. Despite this variability, a strong positive link has been observed between obesity and BPH. Some studies focus on validated symptom scoring tools, while others focus on anatomical metrics, such as prostate size.

As in the previously discussed pathologies, the increased estrogen-to-androgen ratio in obese patients may play a role. Benign prostate tissue expresses estrogen receptors. In tissue models prostate growth and growth inhibition can be modulated with estrogen and selective estrogen receptor modulators. Study of the complex sex hormone mediated molecular pathways potentiating BPH suggests that estrogens from testosterone aromatization mediate BPH through action on Era (proliferative) and ERβ (antiproliferative) target receptors.

Despite tissue studies showing reduction of indices of growth, proliferation and cell size with use of selective estrogen receptor modulators and aromatase inhibitors, to date there has not been evidence of clinical significance. Long-term data on prevention and prostate growth kinetics with the use of these medications is an area of potential further study.[17]

Patients with BPH and metabolic syndrome have increased prostate growth when compared to those without metabolic syndrome. Increased obesity and resultant increased insulin resistance, hyperinsulinemia and impaired insulin mediated glucose uptake may directly potentiate BPH, although the mechanism of this has yet to be elucidated. Some molecular studies have demonstrated that basic fibroblast growth factors 1 and 2 present in prostate stromal tissue may modulate prostate growth.[18,19]

BPH is sometimes described as a disease of inflammation. It has been shown that prostate inflammation as seen on histological evaluation correlates strongly with LUTS. Patients with higher waist-to-hip ratios have higher levels of inflammation. This association is independent of

prostate size, which did not appear to influence levels of inflammation directly. In fact, 1 study showed a 7-point AUA symptom score increase in patients with severe vs mild prostate inflammation on histological evaluation.[20] Figure 3 depicts potential mechanisms of obesity in BPH/LUTS.[21]

Although prostate size has not been shown to predict or correlate to the clinical severity of LUTS, the link between obesity and prostate size has been investigated. Studies almost universally show that there is a positive link between multiple metrics of obesity and prostate size. Increased waist circumference and waist-to-hip ratio have consistent positive association with prostate size, even in studies that do not show BMI as an independent risk factor for BPH. Sedentary lifestyle and Western diet are associated with larger prostate size as well. While decreasing weight and increasing activity have not been found to reverse prostate enlargement, these may be considered important potential targets for primary prevention of BPH.[22]

Urinary incontinence. Obesity has been implicated in the pathogenesis of both SUI and OAB.[23] Obese women with stress urinary incontinence have increased intra-abdominal pressure, leading to reduced sphincter tone from weakening of pelvic floor musculature and innervation. Weight loss through both lifestyle modification and bariatric surgery has been shown to improve SUI in female patients. Even though obesity increases SUI surgical correction failure, obese patients may benefit from surgical correction, which should be offered if indicated.[24]

OAB, observed in both men and women, is a more complex clinical entity with multiple molecular pathways linked to obesity. The metabolic syndrome is again implicated here. In mouse models obesity induced insulin resistance and hyperinsulinemia inhibit the PI3K/AKT/eNOS pathway, resulting in increased voiding frequency, non-voiding detrusor contractions and impaired bladder relaxation. In rat studies metabolic syndrome increases muscarinic receptor expression on the urothelium with associated detrusor overactivity.[23], [25]

In a randomized controlled trial with 6-month follow-up female patients in intensive weight loss programs (8.0% vs 1.4% mean weight loss) experienced a 70% reduction in all incontinence (stress and urge) episodes compared to controls.[26] Further clinical investigation is required to demonstrate novel drug targets that may have efficacy specifically in obese and overweight populations.

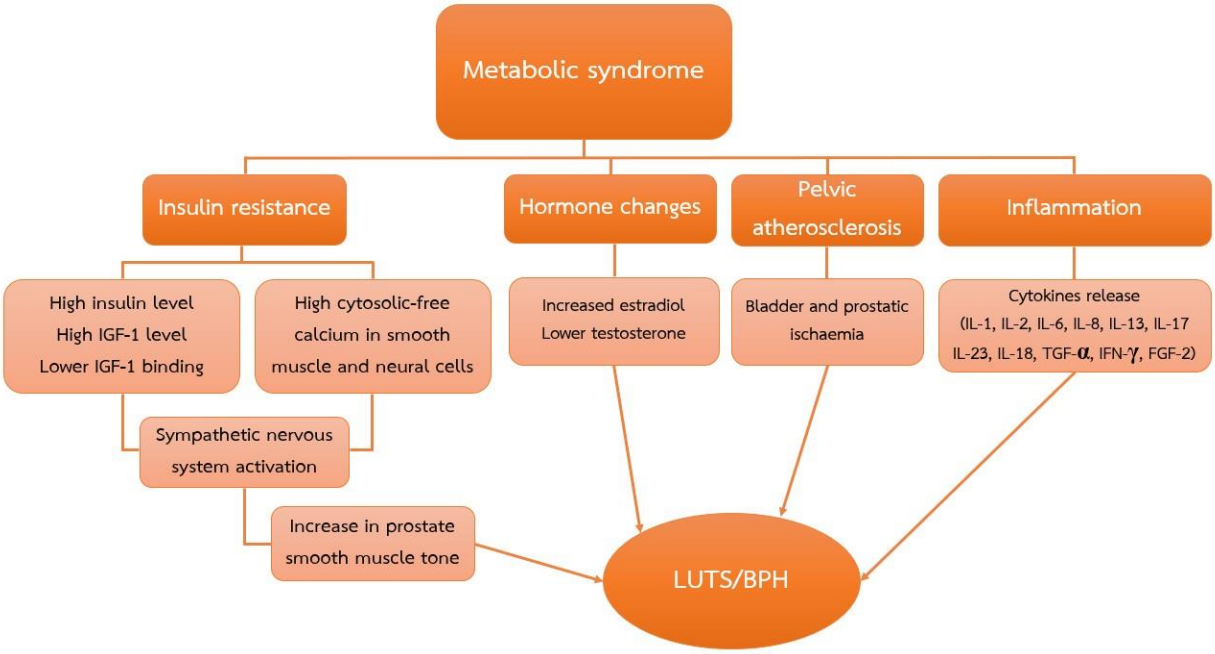

Figure 3. Mechanisms of metabolic syndrome in BPH.22, fibroblast growth factor (FGF), Interferon (IFN), transforming growth factor (TGF)

Urological Malignancy

The physiological changes of obesity have oncologic implications described both epidemiologically and biochemically. It is critical to appreciate the mechanisms by which obesity is a tumorigenic state both for better patient counseling and to identify novel drug targets for future oncologic treatment. Described mechanisms of obesity in tumorigenesis will first be addressed, after which the discussion will focus on clinical data surrounding obesity in specific genitourinary cancers. A complex interplay between environment and genetics underlies the pathogenesis of obesity related malignancies. As in benign urological processes, mechanisms including chronic hyperinsulinemia, altered sex steroid circulation and aberrant metabolism are discussed.

Several epidemiological studies have demonstrated an increased incidence of cancer in obese individuals. A large study of women in the United Kingdom revealed increased risk of endometrial cancer, esophageal cancer, kidney cancer, leukemia, multiple myeloma, pancreatic cancer, non-Hodgkin lymphoma, ovarian cancer, breast cancer (in postmenopausal women) and colorectal cancer (in premenopausal women) in obese women.[27]

Chronic hyperinsulinemia and insulin resistance associated with metabolic syndrome is the primary biochemical hypothesis for obesity related tumorigenesis.[28] Hyperinsulinemia creates a cellular environment that favors tumor development.[29] Insulin growth factor binding proteins 1 and 2 (IGFBP1 and IGFBP2) are downregulated in hyperinsulinemia, increasing levels of unbound bioactive insulin-like growth factor 1. IGF-1, after binding the IGF-1 receptor, initiates a cascade of mitogenic, antiapoptotic and proangiogenic processes. This is mainly orchestrated through extracellular signal regulated kinase and phosphatidylinositol-3 kinase pathways.[30] It has been shown that activation of the insulin-IGF pathway causes redistribution of cell surface proteins from adherens junctions to the

cytoplasm, which is a hallmark of cell migration and tumorigenesis.[31] Overall, the chronic activation of the insulin IGF pathway is likely a primary driver of tumor formation in the setting of obesity.

Adipocytes have robust endocrine and metabolic activity that impacts cancer formation. The 2 adipokines (adipocyte derived signaling molecules) most studied in cancer development are leptin and adiponectin. Leptin is regulated by insulin and IGF-1, by positive and negative regulation, respectively.[32] Leptin deficient mice overfeed and become hyperinsulinemic as well as diabetic.[33] Leptin has widespread mitogenic effects appearing to work synergistically with vascular endothelial growth factor, an important factor in many malignancies, particularly renal cancer. Adiponectin is antiproliferative, proapoptotic, and antiangiogenic by induction of p53 and Bax expression with BCl-2 suppression, thus promoting a well regulated cell cycle.[34] Adiponectin levels negatively correlate with BMI. Insulin and estrogens suppress adiponectin secretion. Thus, with chronic hyperinsulinemia and aromatization seen in obesity, adipokine homeostasis is disrupted, leading to a proneoplastic environment. In chronic inflammatory states such as obesity elevated acute phase reactants such as cytokines and C-reactive protein contribute to the development of insulin resistance, type 2 diabetes mellitus and obesity related atherosclerosis, likely additionally enhancing the tumorigenic mechanisms discussed above with respect to chronic hyperinsulinemia, sex steroid profile and adipokines.[35]

Prostate cancer. PCa is the most common urological malignancy and there has been much study into its characteristics in the obese patient. The exact influence of obesity on PCa incidence is unclear, with metanalyses showing inconclusive data due to variable findings. There are, however, several clinically important detection biases that providers must be aware of with respect to PCa screening in obese men.[36] Prostate specific antigen values are 7%, 14% and 18% lower in overweight, obese and severely obese men, respectively.[37] These findings suggest lower sensitivity of PSA in obese patients concerning enough that thought has been applied to developing a weight based correction for PSA.[38] Digital rectal examinations can be anatomically challenging in obese patients, leading to detection failure of clinically important tumors.[39]

Outcomes with respect to biochemical recurrence and disease specific mortality suggest that prostate cancer in obese men is more aggressive. Several studies have suggested shorter time to biochemical recurrence after both radical prostatectomy and external beam radiation in obese men.[40] Additionally men with higher BMI have a higher risk of disease progression to castrate resistant metastatic PCa and higher PCa specific mortality.[41] The association between increased circulating IGF-1 levels and clinically significant PCa has been described.[42] Men with obesity can have hypotestosteronemia, which, in turn, has been linked to more aggressive phenotypes of PCa.[43] No consensus has been achieved on associations found between leptin or adiponectin levels and PCa incidence or outcomes, although this is an active area of research.[44] Figure 4 summarizes the mechanisms by which a more aggressive PCa phenotype may be seen in obese men.[37]

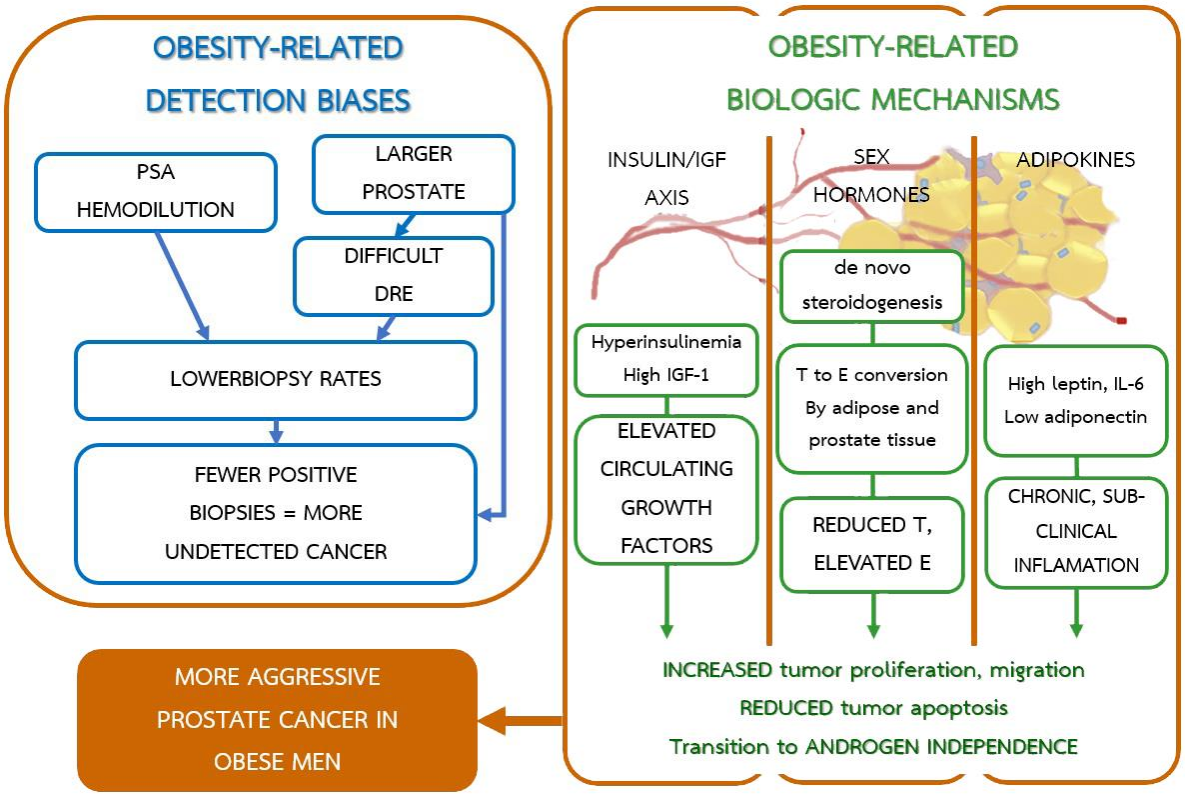

Figure 4. Impact of obesity on prostate cancer detection and pathogenesis.[37] DRE, Digital rectal examination. E, estrogen. T, testosterone.

Renal cancer. Renal cancer has been positively associated with obesity. A longitudinal study of 363,992 Swedish men revealed that men with increased BMI have up to double the risk of RCC compared to normal weight peers.[45] Obesity is also a risk factor for hypertension. A direct association of blood pressure and risk of renal cell cancer was also seen in this cohort. Interestingly there was no correlation between BMI or hypertension with risk of upper tract urothelial cancers of the renal pelvis. Early literature has suggested that obesity does not confer RCC risk in female populations; however, a large quantitative review concluded that the increased relative risk of RCC is seen equally between men and women with elevated BMI.[46] Other studies have demonstrated that hypertension is an independent risk factor for RCC and should be a component of patient counseling on modifiable risk factors with respect to RCC risk in the obese patient, who is often hypertensive.[47]

Bladder cancer. Bladder cancer treatment, both surgical and medical, has high morbidity when compared to treatment for other urological cancers, especially for advanced disease. In patients with muscle invasive bladder cancer undergoing radical cystectomy and pelvic lymphadenectomy, obesity is associated with higher perioperative complications as well as reported worse oncologic outcomes, such as disease recurrence, cancer specific mortality and overall mortality. Several studies report that patients with higher BMI present with higher stage and grade bladder cancer. Retrospective studies

highlight that increased BMI is associated with higher risk of lymphatic vessel invasion and lymph node metastasis. Although the mechanism is unclear, obesity is associated with poor clinical outcomes for bladder cancer, even when controlling for tumor stage and grade.[48]

Other malignancies. Interestingly there is seemingly no association between BMI and testicular germ cell tumors. A large meta-analysis comparing body size and testicular cancer risk concluded that height, but not BMI, conferred a higher risk of testicular cancer to young adults.[49]

Obesity has been well described as a risk factor for penile cancer. Penile cancer is a rare cancer worldwide. The mechanism for tumorigenesis is squamous metaplasia secondary to human papillomavirus infection or inflammation. The risk of invasive penile cancer has been observed to double with every 5-unit increase in BMI. Several mechanisms are suggested for the development of penile cancer specifically in obesity, which include inflammation secondary to poor genital hygiene, smegma accumulation and functional phimosis.[50] It is important to consider obesity as an additional modifiable risk factor in prevention of penile squamous cell carcinoma.

Preoperative Considerations

Obesity related physiological changes. Obesity related physiological changes in respiratory and cardiovascular function impact the delivery and maintenance of anesthesia. These are important considerations in the urology patient.

Obesity associated respiratory changes are a consequence of restricted lung volumes and limited chest wall movement as well as increased metabolic activity of excess adipose tissue.[51,52] Obese patients subsequently develop increased work of breathing, oxygen consumption and CO2 production. Ventilation/ perfusion mismatch may also arise as a function of reduced functional residual capacity, resulting in right to left shunting and hypoxia.[53]

Obesity associated cardiovascular changes are a function of increased cardiac output, resulting in cardiac remodeling and increased risk of both right and left heart failure. Obese patients have increased circulating blood volume with decreased systemic vascular resistance compared to age matched nonobese patients. Cardiac output subsequently increases as a component of increased stroke volume. As a function of time, increased cardiac output results in left heart remodeling and hypertrophy, contributing to heart failure with preserved ejection fraction. Right heart failure may also occur secondary to hypercapnia associated with obstructive sleep apnea.[54,55] Induction and maintenance of anesthesia relies on the intricate interplay of circulating free anesthetic concentration balanced with bound and lipid stored concentrations. Drug dosing in the obese patient is modified by the increase in lean body weight, cardiac output and blood volume, resulting in changes in peak plasma concentrations, half-life and drug clearance. The interplay of each of these factors is beyond the scope of this review, but it is important to understand that the obese patient may not respond to usual anesthetic protocols in a predictable fashion.[56]

Management of anesthesia and choice of airway. Non-invasive blood pressure monitoring in obese patients is often complicated by poorly fitting blood pressure cuffs. For obese patients cuffs are often placed in alternate locations for better fit; however, the impact on blood pressure monitoring during anesthesia is not well studied. In procedures where hemodynamic shifts or accurate blood

pressure monitoring are essential, invasive arterial blood pressure monitoring may be utilized.[57]

Choice of airway in the obese urology patient is an important consideration that may impact duration under anesthesia and operative time. Face mask ventilation is often technically difficult secondary to difficult mask fit and airway obstruction related to excess oropharyngeal tissue or enlarged tongue. Face mask ventilation should be limited to preoxygenation prior to controlled intubation and to brief procedures (e.g. examination under anesthesia).[58]

The choice of airway in laparoscopic and open genitourinary surgery in both the obese and non-obese patient is endotracheal intubation. However, given the large breadth of endoscopic and minor procedures under anesthesia, the choice of supraglottic airway vs endotracheal intubation is often considered by urologists. Obese patients are more likely to require intubation than supraglottic airway (e.g. laryngeal mask airway) secondary to high airway pressures and poor supraglottic airway seal.[59] Universal recommendations do not exist when choosing between supraglottic airway and endotracheal intubation. Second generation laryngeal mask airways provide added ventilation control and increased airway pressures, which are useful in obese patients but are uncommonly utilized.[60] With the increased frequency of endotracheal intubation the obese patient may require prolonged anesthetic time, which may limit the ability to safely perform urological procedures in the outpatient surgical center setting.

Patient positioning: For the obese patient surgical positioning poses unique concerns for both urologists and anesthesiologists. Independent of position, obese patients are at increased risk for nerve/tissue damage and rhabdomyolysis. Care should be taken to minimize these risks. We will highlight these unique concerns as well as several procedure specific modifications that can be utilized in the obese patient. Supine or Trendelenburg Position: With increased intraabdominal contents against the diaphragm, lung volumes are decreased and the work of breathing is increased. Cardiac output increases secondary to increased venous return. For obese patients, who already have increased oxygen demand, Trendelenburg position may cause rapid desaturation and pulmonary shunting during apneic periods.

Prone: Obese patients in the prone position may have improved respiratory function and increased functional residual capacity compared to the supine position secondary to decreased diaphragmatic pressure. Patient support is critical to adequate ventilation. Care should be taken to place supports under the patient's chest and pelvis rather than the abdomen to avoid elevated intrabdominal pressure. In obese patients, for whom ventilation in the prone position is deemed high risk, the modified supine and lateral decubitus positions have been shown to be safe and effective.[61,62]

Lateral Decubitus: The lateral decubitus position provides significant relief of intra-abdominal pressure on the diaphragm and thus lowers airway pressures. However, nerve injury and rhabdomyolysis are commonly associated with the lateral decubitus position, obviating need for appropriate padding of pressure points.[63]

Dorsal Lithotomy: Obese patients in the lithotomy position have decreased lung volumes contributing to hypoxia and hypoventilation. Bariatric leg holders and adequate leg padding should be utilized to reduce pressure related injuries. High lithotomy position is associated with rhabdomyolysis in the obese patient.[64]

Intraoperative and Postoperative Considerations

In the obese urology patient intraoperative dilemmas are often encountered that require modifications in operative decision making or technique when compared to the non-obese patient. As a result of these decisions, the obese urology patient is at increased risk for perioperative complications. In this section we will highlight several of these dilemmas in both benign and oncologic urological surgery. Radical cystectomy. Both open and robotic approaches to cystectomy are available to the trained urologist with no difference in oncologic, quality of life or safety outcomes.[65,66] Robotic assisted intracorporeal radical cystectomy and urinary diversion may be associated with reduced perioperative morbidity, including decreased need for blood transfusions and hospital stay, although this has not been studied in obese populations.[67] In both robotic and open approaches intraoperative consideration must be made during conduit creation to account for distance from skin to peritoneum and avoidance of skin folds. This may contribute to the increased risk of parastomal hernias in obese patients postoperatively. Additionally obese patients undergoing radical cystectomy are at increased risk for acute kidney injury postoperatively. Obese patients undergoing radical cystectomy are at increased risk for thromboembolic events compared to non-obese peers and should continue venous thromboembolism prophylaxis in the extended postoperative setting.[68, 69]

Radical prostatectomy: With the transition to robotic surgery many of the obesity associated intraoperative concerns have been alleviated. However, obese patients may have worse non-oncologic postoperative outcomes. Obese men have worsening erectile dysfunction and urinary incontinence. In a national review of obese patients undergoing both robotic and open prostatectomy obesity was significantly associated with increased hospital costs and perioperative complications.[70]

Radical/partial nephrectomy: Minimally invasive partial and radical nephrectomy procedures in obese patients are associated with few changes in perioperative morbidity and mortality. In a NSQIP® review obese patients undergoing either radical or partial nephrectomy shared no difference in complications or 30-day readmission.[71]

Percutaneous nephrolithotomy: Endoscopic urology often avoids the many of the intraoperative considerations associated with increased body mass index. However, considerations must be made when performing PCNL to account for increased skin-to-kidney distance and prolonged operative time in the prone position. Despite these difficulties, PCNL in obese patients does not result in higher rates of complications or transfusions. However, obese patients do have greater length of stay and total hospital costs.[72] A 2017 metanalysis showed no significant difference in stone-free rates among non-obese, obese and morbidly obese patients.[73] However, in the perioperative window obese patients with metabolic syndrome undergoing PCNL are at increased risk for cardiac events including myocardial infarction. As advanced endourologists have become more comfortable with ultrasound guided access, it is also important to consider that ultrasound guided PCNL access is associated with a larger learning curve in patients with increased BMI, and may result in inferior access and prolonged operative times.[74]

Disease independent postoperative complications: Obesity is recognized as an independent risk factor for postoperative complications in both urological and non-urological

surgery. A review of NSQIP data allows for a better understanding of population based data regarding cardiovascular, pulmonary, thromboembolic, renal and surgical site complications. Based on the 2014 American Society of Anesthesiologists guidelines for perioperative cardiac evaluation in patients undergoing non-cardiac surgery, obesity is not individually associated with worse cardiac outcomes.[75] Functional status appears to be more associated with cardiac outcomes when compared to obesity. Similarly increased BMI alone is not associated with worse pulmonary outcomes, including reintubation, postoperative respiratory failure and pneumonia. However, obese patients have a higher prevalence of obstructive sleep apnea. Untreated obstructive sleep apnea is associated with increased cardiopulmonary complications when compared to those treated preoperatively with CPAP (continuous positive airway pressure). BMI greater than 40 is associated with acute renal failure and rhabdomyolysis in patients undergoing abdominopelvic surgery. With BMI above 55 American Society of Anesthesiologists guidelines recommend postoperative screening of creatinine kinase in high risk patients with prolonged operative time. Postprocedural surgical site infections have an incidence of 4.8% for those with a normal BMI (18.5 to 25), 11.0% for BMI 25 to 30 and 10.9% for BMI greater than 30 per recent NSQIP analysis. Despite increased morbidity, evidence surrounding mortality is unclear. At present, normal weight patients likely have a survival benefit compared to obese peers; however, there are likely underlying confounders.[76]

Conclusions

Obesity is a ubiquitous disease state that has myriad consequences for the practice of urology, and its impact will continue to grow. Nearly every facet of urological disease and practice is influenced in some way by obesity and its numerous anatomical and physiological consequences. In the case of benign urological pathologies there exists an opportunity for primary prevention and, in some cases, reversal or improvement of disease course. There is much room for further investigation on disease specific cancer outcomes of obese patients. The efficacy of various treatment modalities and screening therapies (e.g. ESWL and PSA screening) differ in obese patients. Future therapeutic targets specifically more effective in obese populations or derived from research into obesity mediated mechanisms of disease may be developed in the future.

Obesity treatment, counseling and prevention are commonly viewed as part of primary care practice; however, it is the responsibility of the consultant urologist to reinforce these efforts, particularly by providing context and specialist insight regarding the interplay between obesity related factors and the pathological conditions that we treat regularly. In the case of erectile dysfunction it would be prudent to recommend weight loss as a management strategy given the discussed evidence. For entities such as prostate cancer the urologist should be vigilant to make sure that patients are not pursuing lifestyle modification alone when evidence-based treatments are available. Keeping these issues in mind will allow practicing urologists to better prepare for the realities of modern practice and ultimately to provide better, more holistic care to our patients.

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