'Gleason 3 + 3 = 6 carcinoma.' They are told they have a tumour that is 6 on a scale from 2 to 10 in severity. This is surely taken by most patients to represent a medium-risk tumour, as they presume that the risk rises equally with the score, and that each score is well established and common. However, the moderate pathology equates with an excellent prognosis. The largest study of clinically localized conservatively treated prostate cancer was published recently [10]. No cases of Gleason grade 1 were diagnosed, and patients with a Gleason 6 (3 + 3) tumour and a PSA level of <4 ng/mL had only a 10% risk of dying from prostate cancer within 10 years.

Despite reassurances from the urologist, it is not surprising that some might opt for radical treatment and refuse conservative treatment, thinking they have a 'moderate' cancer. Also, while Gleason grade 1 is still an entity, higher grades will be misdiagnosed as 2 (1 + 1), and patients will be given erroneous information on the risks of recurrence. The removal of the low-score lesions from the Gleason system would aid clinicians and patients in their interpretation of results, and lead to a grading system that would honestly reflect the current understanding of prostate carcinoma. The Gleason system would then remain robust and comprehensible to clinicians and patients.

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**CONFLICT OF INTEREST**

None declared.

**REFERENCES**


**IS OBESITY A RISK FACTOR FOR PROSTATE CANCER?**

Miles A. Goldstraw, Dler Besrani*, Peter Amoroso† and Roger S. Kirby†† — Departments of Urology, The Royal Marsden Hospital and *The London Clinic, and ††The Prostate Centre, London, UK

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**INTRODUCTION**

Obesity is reaching epidemic proportions, affecting >30% of the population in the USA [1] and becoming a growing problem worldwide. While obesity has recognized links with various chronic disease states, including diabetes, hypertension and cardiovascular disease, it might be a factor in the causes of prostate cancer. However, attempting to identify obesity as a risk factor from other related factors, e.g. dietary intake, socio-economic status and genetic susceptibility, is extremely difficult, necessitating multivariate analysis of large-scale epidemiological studies. Therefore, whether obesity is a causal factor or merely associated with prostate cancer is a matter of continued debate. Confirmation of a link could have enormous implications for prostate cancer management and quality of life issues.

The precise biological processes linking obesity and prostate cancer are unknown, but there are several possible mechanisms proposed. Obesity is associated with several hormonal alterations, including lower levels of sex hormone-binding globulin that might increase the fraction of biologically available testosterone. Certainly androgens have been implicated as a potential cause of prostate cancer and endocrine aberrations might have a role in progression to clinically significant disease. Obesity is associated with diabetes, the metabolic syndrome with insulin resistance and hyperinsulinaemia; exposure to elevated levels of insulin and circulating IGF-1 might facilitate the progression of prostate cancer. Increased levels of leptin and decreased levels of adiponectin may also be important. The mitogenic effects of leptin on cancer cells, combined with increased expression of growth factors, might be more likely to contribute to the progression of prostate cancer. Therefore, obesity associated with high leptin levels should be considered a risk factor in patients with prostate cancer [2]. Mistry et al. [3] suggested that adiponectin and its receptors might contribute to the molecular association between obesity
and prostate cancer through a complex interaction with other hormones and cytokines that are also important in the pathophysiology of obesity and prostate cancer. Any or all of these factors might have a part in the initiation and/or progression of prostate cancer.

There is accumulating evidence that high dietary fat intake might be associated with the risk of prostate cancer [4], with some studies suggesting a high intake of red meat might promote the development of a more aggressive disease. However, while higher fat intake and obesity are clearly linked, the same cannot be said for obesity and the incidence of prostate cancer. Large-scale epidemiological studies show conflicting results for any potential link. One recent case-controlled study from the USA [5] examined men aged 40–64 years and noted an inverse association between body mass index (BMI) and prostate cancer risk; they reported that men with a BMI of $\geq 29$ kg/m$^2$ had the lowest risk of prostate cancer, with an odds ratio of 0.77 (95% CI 0.56–1.06). Giovannucci et al. [6] agreed with this inverse association using a large prospective longitudinal study of $>50,000$ men aged 40–75 years, commenting that men aged $<60$ years and with a BMI of $\geq 27.5$ kg/m$^2$ were about half as likely to be diagnosed with prostate cancer. This latter study was unusual in that the BMI as a predictor for prostate cancer was mutually adjusted for confounding factors, e.g. height, history of diabetes, physical activity and dietary intake (including red meat and processed meat). In stark contrast, perhaps the largest study into BMI and prostate cancer incidence involved 950,000 Norwegian men followed for a mean of 21 years [7]; the results showed a modest positive correlation, with an increased relative risk of 1.09 (95% CI 1.29–1.94) for obese men (BMI $\geq 30$) compared with men of normal weight. A subgroup analysis identified that in those aged 50–59 years the relative risk increased to 1.58 (1.29–1.94), indicating that BMI might have a greater role in younger men. These results are somewhat confusing and at first glance appear to suggest no association between obesity and overall prostate cancer risk. Confounding factors include inherent problems with study design, and inability to stratify for other risk factors. Irani et al. [8] attempted to counter many of these confounding factors by comparing 194 men with prostate cancer with an equal number of those with BPH; the results showed that BMI was not significantly associated with prostate cancer when compared with BPH, but in general, obese men had 2.5 times the risk of having prostate cancer. Another study by Scales et al. [9] examined a representative sample of 57,827 men aged $\geq 40$ years and concluded that obese men were more likely than men of normal weight to be screened for prostate cancer. However, by contrast, it might be the case that obese men have lower levels of PSA, which could mask biologically significant prostate cancer [10].

Perhaps more convincing is the association between obesity and the risk of advanced prostate cancer and death from prostate cancer. One comprehensive analysis retrospectively studied 135,066 Swedish construction workers [11] with a mean 18-year follow-up; the results showed a significant positive association between BMI and prostate cancer incidence, but more importantly a strong association between mortality and BMI, with a greater relative risk of 1.4 (1.09–1.81) for a BMI of $>26.2$ kg/m$^2$ than for a normal BMI ($<22.1$ kg/m$^2$). This suggests that obese men with prostate cancer might have biologically more aggressive disease. Support for this theory is provided by recent data on men having a radical prostatectomy for early-stage prostate cancer [12,13]. Amling et al. [12] evaluated the effect of BMI on such men, the results showing that BMI was an independent predictor of higher Gleason score and biochemical recurrence. The apparent contradiction that obesity affects prostate cancer mortality while not affecting prostate cancer incidence suggests that obesity might differentially regulate prostate cancer progression rather than tumour initiation. Freedland et al. [14] argued the point quite convincingly that obesity might affect the development of unaggressive vs aggressive prostate cancer differently.

In conclusion, the precise association between obesity and prostate cancer is unclear; large-scale epidemiological studies have failed to find conclusive evidence of an associated increased incidental risk. More recent data might suggest a role in tumour progression, with the development of a more aggressive phenotype. Significantly, a recent study by Rodríguez et al. [15] suggested that men who lose weight might reduce the risk of death from prostate cancer. It is important that health professionals encourage individuals to participate in practical and simple dietary changes, with fitness education, as these changes improve overall longevity and quality of life. The profound adverse effect of obesity on general health is dramatic. Dietary modification, matched with recommendations for preventing cardiovascular and other chronic diseases, is desirable.

CONFLICT OF INTEREST

None declared.

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Correspondence: Miles Goldstraw, The Royal Marsden Hospital, Fulham Road, London SW3 6JJ, UK.
e-mail: miles.goldstraw@gmail.com

Abbreviation: BMI, body mass index.


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INTRODUCTION

An unshakeable principle of the surgical treatment of cancer is to dissect through normal tissue and to remove the tumour with a negative margin. Conventional wire-loop transurethral resection of bladder tumour (TURBT) does not achieve this. The tumour is deliberately incised and removed piecemeal, scattering millions of tumour cells throughout the bladder. In any other tumour type this would be considered oncological madness; in the bladder it is the norm. Perhaps unsurprisingly, recurrence rates for superficial bladder cancer are astronomically high, at up to 64% at 5 years. In other tumour types this rate of recurrence would be unacceptable: local recurrence after partial nephrectomy for renal cancer is 5–10% at 5 years; after breast conservation therapy it is 5–22%. Moreover, in rectal cancer surgery, operative technique has been shown to be a very important factor of local recurrence rates: after total mesorectal excision there is recurrence in 4–9%, compared with 32–35% with conventional surgery [1].

The question inevitably arises as to whether the technique of wire-loop TURBT is outdated. In particular, might a technique that attempts to remove a bladder cancer en bloc by dissecting through normal tissue be more oncologically appropriate? Could urologists take their cue from golfers; the perfect bunker shot is made by swinging the sand wedge through the sand under the ball with no contact between the club and the ball. The ball emerges from the bunker on a cushion of sand, to float gently onto the green (Fig. 1). Should we be looking to execute a ‘sand wedge resection’ of bladder tumours?

Bladder cancer recurrence due to implantation of floating neoplastic cells was first discussed in 1903 by Albarran and Imbert. In one clinical study in 32 patients the vault of the bladder was rarely the site of primary tumour (6.3%) but commonly the site of recurrence (90.6%); might the recurrences be caused by implantation of tumour cells floating on the air bubble after tumour resection [2]? Molecular studies which demonstrate multifocal bladder tumours to be monoclonal also support theories of implantation [3].

Urological surgeons have not been complacent about recurrence. Intravesical chemotherapy in the first few hours after surgery works in some patients, reducing the risk of recurrence from 38% to 26%. In a sense though, the use of intravesical chemotherapy is in itself an admission of failure of surgical technique. Moreover, a treatment benefit of 12% from an adjuvant ‘single dose’ of chemotherapy means that for each patient who benefits, seven patients will not, but will be exposed to the potential side-effects of the drug.

Surgical technique does affect the volume of viable tumour cells released during tumour resection in animals: conventional TURBT released 620% more tumour cells than neodymium laser irradiation of the tumour [4].

The first principles of surgical oncology dictate that the ideal local resection of bladder tumour would be a deeper dissection of the wall of the bladder through essentially normal tissue, i.e. an excision biopsy with a margin of normal tissue, the ‘sand wedge resection’. En bloc resection of bladder tumour has been reported to be feasible by various techniques, including a flat-loop electrode [5], a knife electrode [6], a J-shaped needle electrode [7,8], and the holmium:YAG laser [9]. The intact tumour specimen is removed whole by vacuum evacuation.

In 1997, a new technique of TURBT was reported using a bespoke J-needle electrode that allowed en bloc resection of a 25 mm papillary tumour with muscle layer [7]. Another Japanese group used a similar technique to resect 108 stage pTa and pT1 tumours of up to 20 mm. An incision was made in normal urothelium with a 5-mm margin from the tumour base, and then incisions through muscle were made to ‘sculpt’ out the tumour en bloc [8]. Complications were few, with no uncontrollable bleeding and only one extraperitoneal bladder perforation.

The holmium : YAG resection of bladder tumour (HoLRBT) is an attractive alternative to wire-loop TURBT. Holmium lasers have a long wavelength, so that tissue penetration is only 0.4 mm, making them safer than neodymium : YAG lasers, which have a typical tissue penetration of 4–6 mm. There are now