high-technology simulators before moving on to real-life scenarios and live firing missions, with a similar acquisition of skills as used to train novice surgeons.

However, questions remain unanswered: When, for how long and what types of video games are best? If skills are best developed when younger, then would video gaming practice during surgical training be fruitless? Should we be advising more Chinese take-aways to enhance chopstick skills while doing surgical on-calls? More concerning are the studies showing that young people who played violent games tended to be more aggressive, less forgiving and believed violence to be normal, compared to those who played non-violent games. Also, those who played more entertainment games did less well in school and were at greater risk of obesity.

Does the evidence support a role for video gaming in laparoscopic training? There appears to be a positive relationship and it is tempting to encourage video gaming in laparoscopic departments as a relatively cheap, enjoyable and readily available adjunct to laparoscopic training. However, we need to avoid training methods that lead to violence, obesity and other, as yet undetermined, consequences. Ideally, the combined opinion of psychologists, medical educationalists and laparoscopists, alongside further larger studies, is needed before video gaming could be accepted as good practice, and before we can relax general concerns about video gaming amongst the younger generation.

CONFLICT OF INTEREST

None declared.

REFERENCES

1 **Keeley FX Jr, Eden CG, Tolley DA, Joyce AD.** The British Association of Urological Surgeons: guidelines for training in laparoscopy. *BJU Int* 2007; **100**: 379–81

2 **Grantcharov TP, Bardram L, Funch-Jensen P, Rosenberg J.** Impact of hand dominance, gender, and experience with computer games on performance in virtual reality laparoscopy. *Surg Endosc* 2003; **17**: 1082–5

3 **Rosser JC Jr, Paul J, Lynch PJ *et al.*** The impact of video games on training surgeons in the 21st century. *Arch Surg* 2007; **142**: 181–6

4 **Rosenberg BH, Landsittel D, Averch TD.** Can video games be used to predict or improve laparoscopic skills? *J Endourol* 2005; **19**: 372–6

5 **Madan AK, Frantzides CT, Park WC, Tebbit CL, Kumari NV, O'Lear PJ.** Predicting baseline laparoscopic surgery skills. *Surg Endosc* 2005; **19**: 101–4

6 **American Psychological Association Annual Convention 2008.** Upside to videogames? Meeting Highlight. Available at: http://www.apa.org/convention08. Accessed 31 August 2008

Correspondence: Manit Arya, Kings College Hospital, Denmark Hill, London, SE5 9RS, UK. e-mail: manit_arya@hotmail.com

LOOKING AT THE PROSTATES OF PATIENTS WITH BLADDER CANCER: A THOUGHTFUL EXERCISE

Riccardo Autorino, Giuseppe Di Lorenzo*, Gianluca Giannarini†, Luca Cindolo‡, Estevão Lima§, Marco De Sio, Maria Gaetana Lamendola¶ and Rocco Damiano†† – Clinica Urologica, ¶Istituto di Anatomia Patologica, Seconda Università degli Studi, *Dipartimento di Oncologia Molecolare e Clinica, Università Federico II, Napoli, †Dipartimento di Urologia, AOU Santa Chiara, Università di Pisa, Pisa, ‡UO di Urologia, Ospedale Civile, Vasto, ††UO di Urologia, Università Magna Graecia, Catanzaro, Italy, and §School of Health Sciences, University of Minho, Portugal

Accepted for publication 14 January 2009

INTRODUCTION

The coincidence of prostate and bladder cancer occurring together in the same individual is considered common. One factor to be considered is the likelihood of diagnostic bias when the presence of one genitourinary cancer leads to a more detailed clinical and pathological examination, resulting in the incidental diagnosis of another genitourinary cancer. Singh *et al.* [1] evaluated the risk of prostate cancer as a second malignancy in patients diagnosed with bladder cancer after adjusting for possible diagnostic and treatment biases. The standardized incidence ratio (actual number of cases in a population at a given time to the number that would be expected based on the cancer rates in the same area) of prostate cancer in patients with urothelial cancer was significantly increased. The same ratio was not increased for other malignancies.

The high coincidence of prostate and bladder cancers occurring together might be also explained by a common carcinogenic pathway. Tumour-suppressor genes might be crucial in the development of both [2]. Amara *et al.* [3] showed by immunohistochemical analysis that prostate stem-cell antigen is over-expressed in most TCCs. Despite these findings, the model for a common carcinogenic pathway remains to be confirmed.

ADENOCARCINOMA OF THE PROSTATE: ITS BURDEN IN CYSTOPROSTATECTOMY SPECIMENS

As recently addressed by Saad *et al.* [4], cystoprostatectomy specimens provide a unique chance to define the features of silent adenocarcinoma of the prostate. The variability of its frequency can be explained in the first instance by the sampling approach adopted to process the prostate. When slices are too thick, small foci of cancer might remain undetected because they remain 'buried'. The advantage of complete sampling over partial sampling is that small foci of cancer are seen more frequently and cancer features, such extraprostatic extension and positive margins, are more accurately evaluated. Using the technique of McNeal *et al.* [5], with slices taken every 2.5 mm from the base to the apex of the gland, a high incidence of prostate cancer can found. Ruffion *et al.* [6] detected an incidental prostate cancer in 51% of their samples. Similar results were obtained by others with serial step-sections taken at 2–3 mm intervals [7,8]. Winkler *et al.* [9] reported the highest detection rate so far (60%) by using 2 mm sections. Nevertheless, although using the same technique, Cindolo *et al.* [10] reported much lower rates (12.6%), as also did Saad *et al.* [4]. However, there is a similar wide variability when using a pathological protocol

© 2009 THE AUTHORS
JOURNAL COMPILATION © 2009 BJU INTERNATIONAL

with 5-mm sections. The detection rate increased to 42% in the study by Montironi *et al.* [8], whereas it was surprisingly low (4%) in a recent report from a Taiwanese group [11]. This latter result might be influenced by the lower incidence of prostate cancer in Asian countries. Some studies do not include a description of the applied histopathological evaluation [12].

CLINICAL SIGNIFICANCE OF AN INCIDENTALLY DISCOVERED PROSTATE CANCER

Stamey *et al.* [13] discovered unsuspected prostate cancer in 40% of a group of cystoprostatectomy specimens. Reasoning that according to epidemiological data only 8% of prostate cancers are clinically apparent, and that these must be the largest, they took 8% of the largest tumours identified in their series (0.5–6.1 mL) and concluded that any tumour of >0.5 mL must be clinically significant. With the additional inclusion of any poorly differentiated Gleason 4 or 5 cancer, the 0.5 mL size criteria for a 'clinically significant' tumour has gained wide recognition.

Authors attempted to incorporate PSA levels into predictive models of tumour significance. However, Winkler *et al.* [9] found a weak correlation between PSA levels and tumour volume, and no difference between median PSA values for patients with and without prostate cancer.

Revelo *et al.* [7] reported a 41% rate of unsuspected prostate adenocarcinoma, only 48% of these being considered clinically significant. The presence of clinically significant prostate cancer in the study by Barbisan *et al.* [14] was much higher (81%) than previously reported.

A few non-morphological studies have indicated that incidental cancer is different from clinical cancer in terms of marker expression. In particular, it has cell features of less aggressiveness than clinically detected cancers [15].

PATIENTS WITH CONCOMITANT PROSTATE AND BLADDER CANCER, AND THEIR FATE

Androulakakis *et al.* [16] initially suggested that the prognosis in these patients appears to be related to the characteristics of each tumour, separately. Konski *et al.* [17] reported that most of the patients presented with an early stage of one malignancy and an advanced stage of the other. In their experience, patients presenting with prostate cancer had a better 5-year survival rate (50%) than those presenting with bladder cancer (32%). The most significant prognostic factor was the stage of the bladder cancer.

More recently, Delongchamps *et al.* [18] reported on 141 patients with invasive bladder cancer, mostly of an advanced tumour stage; 20 (14%) had incidental prostate cancer. Ten patients died from bladder cancer after a median interval of 13 months. The poor survival rate was due to the advanced stage of the bladder tumours seen in the most patients.

Despite a limited amount and profile of available data, it can be concluded that the outcome of patients with incidentally discovered prostate cancer after cystoprostatectomy depends on the prognosis of the bladder tumour.

HOW DOES PSA WORK IN THESE CASES?

Winkler *et al.* [9] found a statistically significantly higher PSA level in those with incidental prostate cancer, but in the study by Ruffion *et al.* [6] the mean PSA level in the prostate cancer group was 2.84 ng/mL, which was similar to that in the group without prostate cancer (2.19 ng/mL). The authors could not find a plasma PSA threshold beneath which there was a <5% association with prostate cancer. More recently, Rocco *et al.* [19] concluded that PSA levels in their series did not correlate either with the overall risk of prostate cancer or with the risk of clinically significant disease. Saad *et al.* [4] found no significant correlation between preoperative PSA levels and the presence of adenocarcinoma, the Gleason score or prostatic tumour stage.

Based on the available data, for those who are candidates for prostate-sparing surgery, it seems reasonable to include a routine prostate biopsy in the standard preoperative evaluation, even in men with a normal DRE and PSA levels.

UROTHELIAL PROSTATE CANCER: ITS INCIDENCE AND PROGNOSTIC SIGNIFICANCE

Reports of prostatic urethral involvement at the time of radical cystectomy are mostly retrospective and lack careful pathological assessment of the prostate. Thus, it is likely that the true incidence of involvement with urothelial carcinoma is under-reported. However, the incidence of prostatic urethral involvement approaches 50% in series in which there is a detailed pathological assessment of the prostate [20].

In a prospective pathological assessment of 121 consecutive cystoprostatectomy specimens analysed by whole mounts, Revelo *et al.* [7] found urothelial carcinoma involving the prostatic urethra in 48% of cases, 33% of them having apical involvement. All prostates with prostatic apical involvement through urothelial carcinoma uniformly had involvement of more proximal portions of the prostate. These results support the concept of standard cystoprostatectomy.

Retrospective studies have suggested that multifocal bladder tumours, carcinoma *in situ* (CIS) in the bladder and bladder tumour location in the bladder neck are independent risk factors for prostatic urothelial carcinoma in men undergoing radical cystectomy [20].

Interestingly, Pettus *et al.* [21] found that bladder tumours at or below the trigone and CIS in the bladder were associated with prostatic involvement. However, the absence of one or both of these factors was not adequate to identify the entire population of patients without prostatic urothelial tumour.

In this respect, limited biopsies of the prostate urothelium are not adequate to identify prostatic urothelial cancer. Donat *et al.* [22] took a transurethral biopsy of the prostatic urethra in 246 men undergoing radical cystectomy. The sensitivity of transurethral biopsy for prostatic stromal invasion was 53% and the specificity was 77%, for a positive predictive value of 45% and a negative predictive value of 82%.

Prostatic involvement in urothelial bladder cancer is considered to be an advanced disease. The TNM classification categorises prostate involvement as stage pT4a. This classification does not differentiate contiguous (transmural invasion of the bladder tumour) and non-contiguous (tumour arising in the prostatic urethra) involvement, which are distinct clinicopathological entities with a dissimilar prognosis.

© 2009 THE AUTHORS
JOURNAL COMPILATION © 2009 BJU INTERNATIONAL

In the report by Ayyathurai *et al.* [23] there was no statistically significant survival difference between those with contiguous and non-contiguous stromal involvement. This emphasizes that the depth of invasion in the prostate, rather than the mode of invasion, affects the outcome. Prostatic stromal involvement, which reflects the depth of invasion, is the most important prognostic factor and the international consensus committee on bladder cancer concluded that the TNM classification of urothelial bladder cancer defines pT4a as prostatic stromal invasion [24].

CONCLUSIONS

Incidental prostate adenocarcinoma has a variable incidence in cystectomy specimens. Its clinical significance remains questionable, as the outcome of patients depends on the prognosis of the bladder tumour. For those candidates for prostate-sparing surgery, it seems reasonable to include a routine prostate biopsy in the standard preoperative evaluation. Even if it is likely that its true incidence is under-reported, urothelial involvement of the prostate in cystoprostatectomy specimens is common. Multifocal bladder tumours, CIS in the bladder and bladder tumour in the bladder neck are independent risk factors for prostatic urothelial carcinoma. The most important finding in predicting prognosis is the depth of invasion, as reflected by stromal involvement, and not the route of invasion.

CONFLICT OF INTEREST

None declared.

REFERENCES

1 **Singh A, Kinoshita Y, Rovito PM *et al.*** Higher than expected association of clinical prostate and bladder cancer. *J Urol* 2005; **173**: 1526–9

2 **Singh A, Jones RF, Friedman H *et al.*** Expression of p53 and pRb in bladder and prostate cancer in patients having both cancers. *Anticancer Res* 1999; **19**: 5415–7

3 **Amara N, Palapattu GC, Schrage M *et al.*** Prostate stem cell antigen is overexpressed on human transitional cell carcinoma. *Cancer Res* 2001; **61**: 4660–5

4 **Saad M, Abdel-Rahim M, Abol-Enein H, Ghoneim MA.** Concomitant pathology in the prostate in cystoprostatectomy specimens: a prospective study and review. *BJU Int* 2008; **102**: 1544–50

5 **McNeal JE, Redwine EA, Freiha FS *et al.*** Zonal distribution of prostatic adenocarcinoma: correlation with histologic pattern and direction of spread. *Am J Surg Pathol* 1988; **12**: 897–906

6 **Ruffion A, Manel A, Massoud W *et al.*** Preservation of prostate during radical cystectomy: evaluation of prevalence of prostate cancer associated with bladder cancer. *Urology* 2005; **65**: 703–7

7 **Revelo MP, Cookson MS, Chang SS, Shook MF, Smith JA Jr, Shappell SB.** Incidence and location of prostate and urothelial carcinoma in prostates from cystoprostatectomies: implications for possible apical sparing surgery. *J Urol* 2004; **171**: 646–51

8 **Montironi R, Mazzucchelli R, Santinelli A, Scarpelli M, Lopez-Beltran A, Bostwick DG.** Incidentally detected prostate cancer in cystoprostatectomies: pathological and morphometric comparison with clinically detected cancer in totally embedded specimens. *Hum Pathol* 2005; **36**: 646–54

9 **Winkler MH, Livni N, Mannion EM, Hrouda D, Christmas T.** Characteristics of incidental prostatic adenocarcinoma in contemporary radical cystoprostatectomy specimens. *BJU Int* 2007; **99**: 554–8

10 **Cindolo L, Benincasa G, Autorino R *et al.*** Prevalence of silent prostatic adenocarcinoma in 165 patients undergone cystoprostatectomy: a retrospective study. *Oncol Rep* 2001; **8**: 269–71

11 **Lee SH, Chang PL, Chen SM *et al.*** Synchronous primary carcinomas of the bladder and prostate. *Asian J Androl* 2006; **8**: 357–9

12 **Damiano R, Di Lorenzo G, Cantiello F *et al.*** Clinicopathologic features of prostate adenocarcinoma incidentally discovered at the time of radical cystectomy: an evidence-based analysis. *Eur Urol* 2007; **52**: 648–57

13 **Stamey TA, Freiha FS, McNeal JE, Redwine EA, Whittemore AS, Schmid HP.** Localized prostate cancer. Relationship of tumor volume to clinical significance for treatment of prostate cancer. *Cancer* 1993; **71** (Suppl. 3): 933–8

14 **Barbisan F, Mazzucchelli R, Scarpelli M *et al.*** Urothelial and incidental prostate carcinoma in prostates from cystoprostatectomies for bladder cancer: is there a relationship between urothelial and prostate cancer? *BJU Int* 2009 (in press)

15 **Santinelli A, Mazzucchelli R, Barbisan F *et al.*** alpha-Methylacyl coenzyme A racemase, Ki-67, and topoisomerase II alpha in cystoprostatectomies with incidental prostate cancer. *Am J Clin Pathol* 2007; **128**: 657–66

16 **Androulakakis PA, Schneider HM, Jacobi GH, Hohenfellner R.** Coincident vesical transitional cell carcinoma and prostatic carcinoma: clinical features and treatment. *Br J Urol* 1986; **58**: 153–6

17 **Konski A, Rubin P, Disantagnese PA, Mayer E, Keys H.** Simultaneous presentation of adenocarcinoma of prostate and transitional cell carcinoma of bladder. *Urology* 1991; **37**: 202–6

18 **Delongchamps NB, Mao K, Theng H *et al.*** Outcome of patients with fortuitous prostate cancer after radical cystoprostatectomy for bladder cancer. *Eur Urol* 2005; **48**: 946–50

19 **Rocco B, de Cobelli O, Leon ME *et al.*** Sensitivity and detection rate of a 12-core trans-perineal prostate biopsy: preliminary report. *Eur Urol* 2006; **49**: 827–33

20 **Autorino R, Di Lorenzo G, Damiano R *et al.*** Pathology of the prostate in radical cystectomy specimens: a critical review. *Surg Oncol* 2008; **18**: 73–84. Epub 2008 Aug 29

21 **Pettus JA, Al-Ahmadie H, Barocas DA *et al.*** Risk assessment of prostatic pathology in patients undergoing radical cystoprostatectomy. *Eur Urol* 2008; **53**: 370–5

22 **Donat SM, Wei DC, McGuire MS, Herr HW.** The efficacy of transurethral biopsy for predicting the long-term clinical impact of prostatic invasive bladder cancer. *J Urol* 2001; **165**: 1580–4

23 **Ayyathurai R, Gomez P, Luongo T, Soloway MS, Manoharan M.** Prostatic involvement by urothelial carcinoma of the bladder: clinicopathological features and outcome after radical cystectomy. *BJU Int* 2007; **100**: 1021–5

24 **Palou J, Baniel J, Klotz L *et al.*** Urothelial carcinoma of the prostate. *Urology* 2007; **69** (Suppl.): 50–61

Correspondence: Riccardo Autorino, Clinica Urologica, Policlinico SUN, Piazza Miraglia 2, 80138, Napoli, Italy.
e-mail: ricautor@tin.it

Abbreviation: **CIS**, carcinoma *in situ*.

© 2009 THE AUTHORS
JOURNAL COMPILATION © 2009 BJU INTERNATIONAL