

coordinating, and performing large trials in recent years. There are many reasons for these difficulties: insufficient funding, complicated bureaucracy (European and international), challenges in recruiting patients and in retrieving follow-up data, and problems identifying centres that are willing to work hard in huge trials that will never compensate the efforts of the majority of uro-oncologists. Even if we were able to overcome these difficulties, we would have to wait at least 5–10 yr before we have the answers to our questions.

In the meantime, which therapeutic strategy should we follow? We should very critically evaluate the data that are already available and select the most relevant clinical, pathologic, and biomolecular characteristics of each bladder tumour patient. Urologists and oncologists should use neoadjuvant chemotherapy and stratify their bladder cancer patients according to known prognostic factors. Biomolecular markers are not yet ready for current use; proven negative prognostic factors for progression are stage higher than T2, young age, the presence of concomitant carcinoma in situ, and/or lymph vascular invasion in the transurethral resection specimens. When present, these factors should suggest the use of neoadjuvant chemotherapy before cystectomy.

In summary, while waiting for the outcome of new studies, “adequate” surgery preceded by neoadjuvant

chemotherapy in selected patients with negative prognostic factors should be considered the new standard for patients with invasive bladder cancer.

*Conflicts of interest:* The author has nothing to disclose.

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## Re: Comparative Effectiveness of Minimally Invasive vs Open Radical Prostatectomy

Hu JC, Gu X, Lipsitz SR, et al

*JAMA* 2009;302:1557–64

### Expert's summary:

This group of outstanding investigators presented a paper on the comparative effectiveness of minimally invasive radical prostatectomy (MIRP) versus open retropubic radical prostatectomy (RRP). The data source was the Surveillance, Epidemiology, and End Results (SEER) Medicare database. The authors identified 137 217 men aged  $\geq 65$  yr who were diagnosed with carcinoma of the prostate between 2002 and 2005. Of those, 8837 (6%) make up the study cohort. Much detailed information regarding methods and statistical analysis is provided. The authors found that patients who underwent MIRP “experienced more urinary complications, incontinence and erectile dysfunction.”

### Expert's comments:

There is currently a flourish of activity around comparative effectiveness research (CER). This activity is based on the belief that CER will discern the most effective therapies for different diseases, with localized prostate cancer at the top of the list. Consequently, this paper is most timely. CER can only be as good as the data on which it is based and the interpretation of that data. Failure at either point could have far-reaching deleterious effects.

My impression after reading this paper was that MIRP had inferior outcomes to RRP. Was that true or was my impression shaped by the way the data were presented? I believe the latter. The authors' conclusion, quoted above, left me with a negative impression of MIRP. The tone throughout the paper bolstered that negative feeling.

The authors correctly state and reference that both MIRP and RRP have long learning curves of 150–250 cases and that surgical volume drives outcomes [1–3]. These two variables are included in their analysis, but when the authors report on these two important variables, it seems no difference was observed. The authors never discuss the departure from previous publications. Why not? If these two important validated measures of outcome are not met in this paper, how reliable are the other conclusions? What is striking is that if you had an RRP, you had a 20% chance of receiving a blood transfusion, whereas if you had an MIRP, that chance was 3%. This information is not presented in the conclusion.

If CER is going to be used to direct care, it must be based on sound data and must be accompanied by reports that are impartial.

*Conflicts of interest:* The author has nothing to disclose.

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**Re: Reducing Laparoscopic Radical Prostatectomy False-positive Margin Rates Using Cyanoacrylate Tissue Glue**  
 Kumar M, Mansour P, Vesey SG

*Eur Urol* 2009;56:651–8

**Expert's summary:**

The authors tested the use of cyanoacrylate glue to repair prostate surface trauma during laparoscopic radical prostatectomy (RP). The feasibility of the glue application and its eventual impact on histologic processing and analysis were first evaluated by using a porcine renal model. The authors subsequently compared the rate of positive surgical margins (PSMs) in 80 consecutive RP specimens with and without glue repair.

The authors found that glue repair did not affect renal tissue processing or histologic analysis. In the group of 40 RP specimens without glue repair, PSMs were identified in 35% of cases and biochemical relapse occurred in 7.5% of patients after a mean follow-up of 40 mo. In the group with glue repair, PSMs were identified in 10% of cases and biochemical relapse occurred in 2.5% of patients after a mean follow-up of 7 mo.

**Expert's comments:**

The authors' honesty should be acknowledged in their reporting of the technical difficulties encountered during laparoscopic RP; however, the methodology of their study is surprising. Why did they use kidneys to validate the feasibility of glue repair on prostates? The reproducibility of the technique may be irrelevant. Furthermore, the very substance of their study is misleading. If inadvertent prostate trauma occurs perioperatively, why should we not consider this a reality? Before artificially modifying any RP specimen, clinicians should know what data they expect from pathologists and how to deal with that data. The presence of tumor cells on the inked surface of the prostate may be interpreted differently when balanced with perioperative events, with macroscopic examination of the gland, and with pathologic features, including cancer

distance from the capsule. If gland trauma has occurred, its precise location and distance from cancer may be of major interest. The ostrichlike approach of burying one's head in the sand may interfere with further medical management.

Capsular incision through organ-confined cancer was reported to have worse prognosis than focal extraprostatic disease with negative margins [1]. Repairing these capsular incisions would thus lead to inappropriate follow-up. Macroscopically, it is impossible to distinguish capsular incisions within benign versus malignant tissue. Consequently, any attempt at selective repair would be misleading.

In its early development, laparoscopic RP has shown higher rates of PSMs when compared with open surgery [2]. Capsular incision is associated with neurovascular bundle preservation, particularly in cases of intrafascial dissection [3]. Care should be taken to limit perioperative prostate injuries rather than to repair them postoperatively.

**Conflicts of interest:** The author has nothing to disclose.

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**Re: Anti-androgens and Androgen-depleting Therapies in Prostate Cancer: New Agents for an Established Target**  
 Chen Y, Clegg NJ, Scher HI

*Lancet Oncol* 2009;10:981–91

**Expert's summary:**

Strong preclinical evidence shows that castration-resistant prostate cancer (CRPC) presents androgen receptor

overexpression and overexpresses enzymes involved in androgen biosynthesis [1]. Based on these data, new antiandrogens such as MDV3100 and androgen-depleting agents such as abiraterone acetate have been developed and evaluated in clinical trials. The impressive results obtained in phase 2 trials for these two agents have confirmed the presence of a hormone-dependent CRPC phenotype. Phase 3 trials are ongoing.