Robotic radical prostatectomy as the initial step in multimodal therapy for men with high-risk localised prostate cancer: initial experience of 160 men


*Department of Urology, Royal Melbourne Hospital, †Australian Prostate Cancer Research Centre, Epworth Richmond Hospital, and ‡Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Australia

Accepted for publication 21 April 2011

What’s known on the subject? and What does the study add?
The choice of therapy with high-risk localised prostate cancer is difficult and, in the stark absence of any randomised trials, comparative retrospective analyses of case series continue to be necessary. Radical surgery has been considered by many to be inferior to a combination of radiotherapy (RT) and androgen deprivation therapy (ADT), but this changing perhaps coincidentally with the widespread acceptance of robot-assisted laparoscopic prostatectomy surgery (RALP). Further evidence has now described the long-term toxicities related to ADT, and this has strengthened a desire amongst many to at least defer, if not avoid, ADT unless absolutely necessary.

This article presents a single-centre experience of RALP in the setting of high-risk localised disease, and concludes that RALP incorporating the use of post-operative RT represents a strong perhaps optimum management strategy.

OBJECTIVES

• To report the outcome of robotic-assisted laparoscopic radical prostatectomy (RALP) for men with localised high-risk prostate cancer at diagnosis.
• Although commonly managed by radiotherapy (RT) with prolonged androgen-deprivation therapy (ADT), we hypothesize that initiation of multimodal therapy with RALP is oncologically efficacious and may allow many men to avoid ADT.

PATIENTS AND METHODS

• Between December 2003 and September 2010, 1480 men underwent RALP of whom 160 fulfilled the National Comprehensive Control Network criteria for high-risk disease (prostate-specific antigen (PSA) >20 ng/mL and/or clinical stage, cT ≥ 3 and/or biopsy Gleason score ≥8).
• Biochemical recurrence (postoperative PSA ≥ 0.2) was used to assess outcome after RALP monotherapy.
• Treatment failure was defined as either a rising PSA level after salvage RT or the initiation of ADT.

RESULTS

• The mean age ± standard deviation was 63.1 ± 6.3 years. Median PSA level was 9.95 ng/mL (interquartile range 6.0–21.4).
• Analysis of prostatectomy specimen showed Gleason 8–10 cancers in 65 (41%), and extracapsular disease, pT ≥ 3, in 96 (60%) of which seminal vesicle invasion was evident in 36 (23%). Downgrading by prostatectomy occurred in 64 (40% of total group) and five (3%) were downstaged to pT2 disease. By contrast, any upgrading occurred in 29 (18% of total group) and upstaging occurred in 68 (43%). The overall positive surgical margin rate was 38%, correlating with stage pT2 (15%) or pT3 (53%).
• With median follow-up of 26.2 months (interquartile range 5.5–37.3), two non-cancer-related deaths have occurred (overall survival 98.8%; cancer-specific survival 100%), and biochemical recurrence has occurred in 53 men (33%). RALP surgery has served as monotherapy (n = 117, 73%), or has been followed by salvage RT (n = 24, 15%) and/or ADT (n = 43, 27%). Overall 2-year and 3-year treatment failure was 31 and 41%, respectively.
• Serum PSA level was the only independent predictor of overall treatment failure (hazard ratio [HR] 1.02, P = 0.001) although a strong trend was observed for both clinical stage (HR 1.22, P = 0.058) and the number of positive biopsy cores on transrectal biopsy (HR 1.06, P = 0.057).

CONCLUSIONS

• RALP incorporating the use of postoperative RT is a good multimodal management strategy for men with this aggressive variant of prostate cancer.
• At median follow-up in excess of 2 years, we found low rates of treatment failure enabling a high proportion of men to remain free of ADT.

KEYWORDS

high-risk, robotic, prostatectomy, prostate cancer
INTRODUCTION

Originally described as a means of predicting outcome for men undergoing localised therapy, the concept of risk stratification for men with non-metastatic prostate cancer is increasingly identified as crucial [1]. Such a strategy allows for therapy to be targeted to those with higher-risk disease in whom the disease is likely to impact on their life expectancy while allowing men with lower-risk disease to escape the toxicity of treatment [2,3]. Risk stratification for men with prostate cancer can be performed at diagnosis (using serum PSA levels, clinical T-stage and biopsy Gleason (bGS) score), and revised or reaffirmed after surgical removal of the prostate (pathological variables such as T-stage, prostatectomy Gleason score, surgical margin status and lymph node status), and again after primary therapy by monitoring biochemical (PSA doubling time) and clinical progression of disease. Stratification at diagnosis facilitates the choice of primary therapy, whereas later stratification can guide the scrupulous use of adjuvant or salvage therapy. Numerous refinements of each stratification process have been proposed, all essentially with minor variation and associated with minimal differences in biochemical relapse-free survival, suggesting that those defined as high risk universally represent a population at increased risk of disease-related mortality [4].

Management of high-risk localised prostate cancer has been dominated in the last decade by radiotherapy (RT) administered in combination with androgen deprivation therapy (ADT) [5]. Good evidence underscores the necessity of adjuvant ADT to supplement external beam RT for men with high-risk disease (locally advanced or unfavourable histology) [6–8]. Radical surgery in this setting has been avoided by many because of concerns over poor oncological outcome (failure to cure) and increased morbidity (particularly incontinence), despite considerable evidence now casting doubt on both these assertions. But, like surgery, neither RT nor ADT come without toxicity. Dose escalation of RT enhances efficacy in the high-risk setting, but has been associated with increased toxicity particularly to the rectum [8,9]. Severe rectal complications of RT for prostate cancer are rare but devastating when they do occur [10,11]. The toxicity of the newer regimens of intensity-modulated RT for high-risk disease have been described, and although severe long-term toxicity is confined to a few men treated in this way, acute toxicity to urinary tract and bowel of lower severity occurs in most [12,13].

While both surgery and RT may be associated with difficult complications in a minority, increasing attention is now focused on ADT as potentially the most morbid component of prostate cancer therapy, even when used for only a short period [14]. Systematic review of hormonal manipulation for prostate cancer has shown an increased risk of cardiovascular disease, diabetes and skeletal problems, independent of the risk conferred by the disease process itself [15]. Further review has found the deleterious metabolic and systemic effects to occur within months and noted that the adverse effects could persist long after discontinuation of therapy [16]. Adverse effects on endurance, upper extremity strength and physical components of quality of life have been documented within 3 months [17]. ADT rapidly accelerates bone loss, contributing to increased risk of fractures, made worse by the further effects of muscle weakness, impaired balance and postural hypotension [18]. In a survey of sexual, urinary and general health, others have reported that in addition to reduced general wellbeing, patients who had received ADT were more bothered by urinary and sexual function than men undergoing other treatments (surgery or RT), except surveillance [14].

Advocates of robotic-assisted laparoscopic prostatectomy (RALP) surgery now believe the low general morbidity of the robotic technique, as evidenced by the trend towards single-day hospitalization, has resulted in the morbidity of surgery for most men being comparable to that of RT [19]. Previously this group has reported functional outcome for the initial 400 cases of our learning curve with RALP (now exceeding 1400 cases) and showed 91.4% continence and 62% potency at 12 months after radical surgery [20]. Others have shown previously that complications and continence rates of surgery in men with high-risk disease mirrors those of men with organ-confined disease [21].

The senior authors of this study have hypothesized since the introduction of RALP that this technique offers an oncologically efficacious initial step in treating men with high-risk localised prostate cancer, and will allow many men to avoid or at least defer ADT. It is appreciated that for many men, satisfactory oncological outcome after surgery will require external-beam RT as part of what we now recognize as multimodal therapy [22–24]. This study examines this hypothesis by analysis of the oncological outcome of robotic prostatectomy, with or without use of salvage external-beam RT, in a series of 180 consecutive men with National Comprehensive Control Network-defined high-risk disease at time of diagnosis with localised prostate cancer.

PATIENTS AND METHODS

Between December 2003 and September 2010, 1480 men underwent RALP by two different surgeons performing surgery at the Australian Institute for Robotic Surgery in Melbourne, Australia. A prospective database was convened before the initiation of the robotic service. Following ethical board review, approval was given to search the database to identify outcomes of patients undergoing RALP for high-risk prostate cancer. For the purpose of this study we accepted the definition of high-risk prostate cancer proposed by the National Comprehensive Control Network (PSA > 20 ng/ml or clinical stage ≥ T3 or bGS ≥ 8) [25]. No case of ‘salvage’ prostatectomy was included in this series. Neoadjuvant hormonal manipulation was not considered a contraindication to RALP but was confined to a few men (5%), all of whom had this therapy stopped at the time of the decision to undertake surgery.

All men were evaluated radiologically before surgery using CT of the abdomen and pelvis together with whole-body bone radionuclide scintigraphy. Any evidence of metastasis was a contraindication to surgery. MRI of the pelvis was not undertaken in all cases. Surgical technique was performed using a standard six-port, transperitoneal technique employing the DaVinci surgical robotic system (Intuitive Surgery, Sunnyvale, Sacramento, CA). Selection for nerve-sparing technique was based upon ipsilateral disease burden including introoperative assessment, and preoperative sexual function with patient preferences. Pelvic lymph node
dissection was not routinely performed in all patients, but each case was considered at the discretion of the operating surgeon. When performed, node dissection included any overt enlarged nodes, but alternatively was confined to each obturator fossa.

The prospective-acquired dataset was supplemented where necessary by review of the medical records. Follow-up interval was defined as interval from surgery to time of last review or correspondence. Postoperative radiation as part of a multimodal approach was given in a salvage, as opposed to an adjuvant manner with initiation of postoperative RT being at the discretion of the treating physician. However, in general, RT was commenced after biochemical failure (PSA > 0.2 ng/mL) in men who had experienced a post-surgical PSA level nadir of <0.2 ng/mL. It was the aim of the treating physician to refer the patient for RT when the serum PSA level was 0.5 ng/mL or less. Patients with a positive surgical margin after surgery did not routinely undergo RT. Instead a period of PSA monitoring was performed with RT reserved for those patients with biochemical failure. Androgen deprivation was routinely initiated in patients not achieving a post-surgery PSA nadir of 0.2 ng/mL or less.

The primary outcome measure was treatment failure after a multimodal treatment approach. Overall treatment failure was considered to have occurred in those receiving salvage RT if the patients PSA rose above that recorded immediately before starting salvage RT or if the patient was commenced on salvage hormone therapy after RT. In those patients not receiving salvage therapy, failure after multimodal therapy was considered to have occurred when the postoperative PSA level was >0.2 ng/mL. Four secondary outcome measures were included. First, the proportion of men experiencing biochemical failure (BCF) – defined as a postoperative PSA measurement >0.2 ng/mL. Second, the proportion of men receiving salvage RT after surgery. Third, the proportion of men receiving adjuvant hormone therapy – irrespective of whether salvage RT was performed and finally, the proportion of men being downgraded after surgery.

The Kaplan–Meier method was used to report BCF after surgery, uptake of adjuvant therapy as well as overall treatment failure after multimodal therapy. All patients were censored on the date of their last follow-up appointment or at the time of death. Univariate and multivariate Cox Proportional Hazard models were developed to identify independent determinants of both BCF, need for adjuvant therapy and overall treatment failure after multimodal therapy. Univariate and multivariate logistic regression models were developed to report determinants of downgrading after surgery. Statistical significance was determined by a $P \leq 0.05$. All statistical analyses were performed using STATA version 8 software (STATA Inc., College Station, TX, USA).

### RESULTS

In total, 160 (11%) of the 1480 men within the database fulfilled the National Comprehensive Control Network criteria for high-risk disease. Risk stratification was derived from PSA level >20 ng/mL, cT ≥ 3 or bGS ≥ 8 in 43, 32 and 120 men respectively, of whom 34 had more than one risk factor and five fulfilled all three criteria. The preoperative demographics of this cohort of men are summarized in Table 1, and may be compared with the pathological analysis of prostatectomy specimen presented in Table 2. Overall, mean follow-up for men

**Table 1:** Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>160</td>
</tr>
<tr>
<td>Serum PSA, mean (median)</td>
<td>15.3 (9.9)</td>
</tr>
<tr>
<td>Gleason Score, mean (median)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>No. of TRUS biopsy cores, mean (median)</td>
<td>12.1 (12)</td>
</tr>
<tr>
<td>No. of positive cores, mean (median)</td>
<td>5.4 (4)</td>
</tr>
<tr>
<td>Max core involvement, mean (median)</td>
<td>61 (68)</td>
</tr>
<tr>
<td>Peri-neural invasion, mean (median)</td>
<td>37 (23)</td>
</tr>
<tr>
<td>No. receiving neoadjuvant hormones, n (%)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Clinical stage, n (%)</td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>58 (36)</td>
</tr>
<tr>
<td>T2a</td>
<td>26 (16)</td>
</tr>
<tr>
<td>T2b</td>
<td>38 (24)</td>
</tr>
<tr>
<td>T2c</td>
<td>6 (4)</td>
</tr>
<tr>
<td>T3a</td>
<td>28 (18)</td>
</tr>
<tr>
<td>T3b</td>
<td>4 (3)</td>
</tr>
<tr>
<td>No. with PSA &gt; 20, n (%)</td>
<td>48 (30)</td>
</tr>
<tr>
<td>No. with Gleason 8 or greater disease, n (%)</td>
<td>120 (75)</td>
</tr>
<tr>
<td>Mean follow-up, days (months)</td>
<td>786 (26.2)</td>
</tr>
</tbody>
</table>

**Table 2:** Postoperative pathology

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological stage, n (%)</td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>9 (6)</td>
</tr>
<tr>
<td>T2b</td>
<td>5 (3)</td>
</tr>
<tr>
<td>T2c</td>
<td>49 (40)</td>
</tr>
<tr>
<td>T3a</td>
<td>58 (37)</td>
</tr>
<tr>
<td>T3b</td>
<td>36 (23)</td>
</tr>
<tr>
<td>T4</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>No. up-staged to T3 disease, n (%)</td>
<td>70 (55)</td>
</tr>
<tr>
<td>No. down-staged to organ-confined disease, n (%)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Pathological Gleason score, mean (median)</td>
<td>7.7 (7)</td>
</tr>
<tr>
<td>No. up-graded, n (%)</td>
<td>29 (18)</td>
</tr>
<tr>
<td>No. down-graded, n (%)</td>
<td>64 (40)</td>
</tr>
<tr>
<td>No. with PSM, n (%)</td>
<td>60 (38)</td>
</tr>
<tr>
<td>PSM organ-confined disease</td>
<td>9 (15)</td>
</tr>
<tr>
<td>PSM with T3 disease</td>
<td>51 (53)</td>
</tr>
<tr>
<td>Positive lymph nodes (total node dissections; %)</td>
<td>4 (27; 14.8)</td>
</tr>
<tr>
<td>Tumour volume (mL), mean (median)</td>
<td>6.3 (4.4)</td>
</tr>
<tr>
<td>Tumour density, mean (median)</td>
<td>0.13 (0.08)</td>
</tr>
</tbody>
</table>
Discordance in stage and grade between preoperative and prostatectomy evaluation was substantial. Of 128 men with cT ≤ 2 (clinically organ-confined) by preoperative assessment, 68 (53%) were upstaged to pT ≥ 3 (pathologically locally advanced), whereas of 32 men with cT3 (clinical locally advanced), five men (16%) were downstaged to pT2 (pathologically organ-confined). Similarly for grade change, of 40 men with bGS < 8, six (15%) were upgraded to pathological GS ≥ 8, whereas of the 120 men with bGS ≥ 8 61 (51%) were downgraded to pathological bGS < 8 by analysis of prostatectomy specimen.

Overall treatment failure after a multimodal approach was 31% and 41% at 2 and 3 years (Fig. 1; Table 3). Serum PSA level was the only independent predictor of overall treatment failure (hazard ratio [HR] 1.02, P = 0.001). However, there was a strong trend for both clinical stage (HR 1.22, P = 0.058) and the number of positive prostate biopsy cores at initial transrectal biopsy (HR 1.06, P = 0.057). Stage was the only pathological variable to predict outcome after multimodal therapy (HR 1.9, P = 0.01). However, a trend was also found for tumour volume (HR 1.08, P = 0.06). Two-year and 3-year BCF after RALP monotherapy was 44% and 55% (Fig. 2).

Both clinical and pathological determinants of outcome are presented in Table 4. Increasing serum PSA levels and more...
advanced clinical stage were both found to correlate with increasing risk of BCF after RALP monotherapy in multivariate analyses. Interestingly, neither the number of positive prostate biopsies nor the biopsy Gleason grade were found to predict BCF. In contrast, when pathological parameters were evaluated, pathological grade was the only factor that independently predicted BCF after RALP.

Within the current cohort, 16% underwent salvage RT within 2 years of RALP whereas 31% underwent salvage RT by year 3. Both preoperative serum PSA level (HR 1.04, \( P < 0.001 \)) and clinical stage (HR 1.3, \( P = 0.03 \)) were found to independently predict use of salvage RT. However, although pathological Gleason grade, pathological stage, margin status and tumour volume all predicted salvage RT use in univariable analyses, no postoperative pathological variable was found to independently predict salvage RT use in multivariable analyses.

Adjuvant hormone therapy was slightly more common after RALP in our patient cohort than salvage RT with 2- and 3-year uptake of adjuvant hormone therapy being 30% and 40% respectively. In multivariate analyses, both preoperative serum PSA (HR 1.03, \( P = 0.002 \)) and clinical stage (HR 1.35, \( P = 0.006 \)) predicted adjuvant hormone therapy use after RALP. In contrast, pathological Gleason score was the only pathological determinant that predicted adjuvant hormone therapy use (HR 1.48, \( P = 0.044 \)).

Downgrading from the bGS assigned by median 12-core transrectal ultrasound-guided biopsy was a very common occurrence after RALP, constituting 40% of this total series and 53% of those men with bGS \( \geq 8 \). Determinants of downgrading are presented in Table 5. Serum PSA, Biopsy Gleason score and clinical stage along with pathological Gleason score and tumour volume were all found to independently predict risk of downgrading in multivariate analyses.

### DISCUSSION

In the absence of the highest quality evidence, the debate regarding the merits of surgery for this patient group remains important. As an alternative to high-dose RT and prolonged ADT for all men with this diagnosis, this series clearly shows surgery to be an oncologically efficacious initial step in management. Albeit with a relatively short period of follow-up, it is clear that RALP surgery frequently suffices as monotherapy, and allows many men to avoid RT and also avoid, or at least defer, the toxicities implicit with ADT. Reports of surgery in the setting of high-risk disease are not new but are almost universally confined currently to open surgery. Spannh et al. [26], in reporting a multicentre experience of 712 men undergoing RP with PSA level \( > 20 \) ng/mL, found that outcome was heavily influenced by the number of high-risk parameters fulfilled, with 10-year cancer-specific mortality of 5% if one criteria was fulfilled, increasing to 35% if all three are fulfilled. Similarly, we found that men fulfilling multiple risk factors had worse outcome and represented the subgroup at highest risk of treatment failure. Ward et al. [21] have the largest published experience of surgery for clinical T3 disease, reporting down-staging to organ-confined disease in 27% of 842 men. Analysis of our series shows less downstaging (16%), albeit from a much reduced patient number with cT3 disease, but importantly we found upstaging in 53%. Our positive surgical margin rate (overall 38%) was influenced by the local stage of disease, 15% for organ-confined disease vs 53% for extracapsular disease, but the manner of this relationship closely mimics that found in open series, such as the 60% reported by Van Poppel et al. [27] when describing the outcome of 158 patients with locally advanced disease. This finding is clearly important given that some have argued that the lack of haptic feedback inherent in robotic surgery risks impairing the oncological outcome.

Many believe Gleason grade to be the strongest single predictor of progression and mortality after surgery in this group of patients [28], and notably 75% of our patients were bGS \( \geq 8 \). Bastian et al. [29] examined the outcome of surgery for biopsy Gleason score \( \geq 8 \) and showed 10-year biochemical-free survival of 27%. Manoharan et al. [30] analysed a similar group and reported a biochemical failure rate at 5 years of 38%, but with downgrading evident in 31%. Downgrading has been shown to have a marked impact on biochemical failure after surgery. Donohue et al. [31] reported downgrading in 45% of a series of 238 men with high-risk disease defined by bGS \( \geq 8 \) and showed a 10-year biochemical recurrence-free probability of 56% compared with 27% in...
those with a final Gleason score that remained ≥8. These findings are perhaps even more marked in our current study where we found significant downgrading in 51% of the 120 men with bGS ≥8, and patients being downgraded had a 3-year BCF rate of 35% vs 77% for those not being downgraded. We found that men with more advanced clinical stage and those with higher serum PSA before surgery were less likely to be downgraded. Manoharan et al. [30] showed that PSA, clinical stage and positive surgical margin status each independently predicted biochemical failure in multivariate analysis. Multivariate analysis of preoperative parameters in our series found PSA and clinical stage, but not biopsy Gleason grade or number of positive cores, predictive of BCF after RALP monotherapy. By contrast, when pathological parameters were evaluated, we found that pathological grade was the only factor that independently predicted BCF after RALP.

Reports of open surgery in the high-risk setting, supported by our findings, consistently reinforce the concept of an overt lack of reliability in predicting (by preoperative parameters) the pathological risk stratification after prostatectomy, particularly for those men defined as high risk by a single preoperative criterion. This is important because in the current era where men tend to undergo extensive TRUS biopsy regimens before undergoing surgery (mean and median of 12 biopsy cores in our series is in keeping with international recommendations), many men continue to be misclassified as high-risk when in truth they really have a lower risk cancer.

Yet no prospective randomized trial currently provides high-level evidence comparing radical surgery with RT for any risk stratification of prostate cancer, and the best retrospective evidence currently available cautiously suggests comparative outcomes for men with high-risk disease [32]. Do et al. [33] suggested in 2001 that what we now perceive to be multimodal therapy (surgery with adjuvant postoperative RT) furnished better biochemical progression-free survival than either surgery or RT alone (70% biochemical failure, BCF, with surgery alone vs 35% for men undergoing surgery plus salvage RT). This figure of 35% is not dissimilar to our 5-year BCF after multimodal therapy of 43%. In a more recent report of high-dose intensity-modulated RT, Alicikus et al. [34] reported 10-year biochemical relapse-free survival of 62% for men with high-risk disease not defined by any single risk factor. By comparison Loeb et al. [28] recently reported 10-year biochemical relapse-free survival of 68% in a single-centre series of 175 men undergoing surgery. In a more direct retrospective comparison of therapy initiated by intensity-modulated external-beam RT (minimum 81 Gy) in a single specialized cancer centre, Zelefsky et al. [35] reported substantial reduction in the risk of metastasis for men treated with radical prostatectomy, with the most overt difference existing for men with unfavourable-risk disease. Also recently, Cooperberg et al. [36], using CaPSURE data on 7538 men and therefore not based on a randomized population, showed significant reduction in mortality associated with therapy initiated by radical prostatectomy, again most evident in men with high-risk disease at the outset. Using a propensity-based approach analysis of 453 men with Gleason score ≥8, Tewari et al. [37] reported substantial benefit from either RT or surgery when compared with observation, and found the lowest long-term risk of cancer-related death in those treated with surgery. In perhaps the largest analysis, based on SEER registry data, Abdullah et al. [38] reported cancer-specific and other-cause mortality to be most favourable in men treated initially with radical prostatectomy, with the exception of octogenarian men. Furthermore, for men with high-risk parameters at the outset, Abdullah et al. found that surgery was better than RT for men under the age of 70 years.

Few data are currently available reporting outcome specific to robotic surgery for men with high-risk disease. Lavery et al. [39] recently reported the outcome of 123 men undergoing RALP for high-risk disease from the USA, finding positive surgical margins of 31% (comparable to our rate of 38%), and biochemical failure of 20% at median follow-up of 13 months (comparable with 41% treatment failure rate at 3 years in our series). A further excellent recent study by Wambi et al. [40] addressed the outcome of 368 men with high-risk stratification derived from the analysis of robot-assisted prostatectomy specimens. Although not the same as the preoperative stratification that we report, they found a positive surgical margin rate of 56% in non-organ-confined disease (compared with 53% in this series), and further reported a 52% biochemical failure at 5 years for Gleason 8 cancers that were non-organ-confined.

This study has several methodological limitations that must be discussed. First it was a retrospective study, which is subject to bias and confounding because of difficulty accessing historical data. This is unlikely to have had a major impact on the findings of this report because we mainly report ‘hard’ outcome measures such as death and use of adjuvant therapies, which are normally clearly documented within the medical notes. Furthermore, a large proportion of the data presented in this report, for example clinical stage, pathological data and serial PSA measurements, were collected prospectively within the institutions’ prospective database. The second methodological limitation of this study is the lack of data concerning functional and quality of life outcomes after therapy. These are clearly very important as the toxicity of treatment has contributed to the limited use of surgery in men with high-risk prostate cancer. However, we have previously reported continence rates for our first 400 cases (91% at 12 months) and although most of these patients did not have high-risk disease, the functional outcomes, certainly with regard to continence, are likely to be similar given that the dissection of the prostate is similar, albeit that nerve sparing was performed less frequently in the high-risk population [20]. Importantly Ward et al. [21] previously showed that complications and continence rates of men with clinical locally advanced disease mirrored those of men with cT2 disease. The third and final limitation of this study is that there was no specified predetermined protocol for provision of multimodal therapy after surgery, either for RT or the institution of ADT. The administration of post-prostatectomy RT in this series was exclusively in a salvage rather than adjuvant manner. Level one evidence now supports the use of adjuvant RT with unfavourable pathological parameters obtained from prostatectomy, such as pT3 disease and also perhaps positive surgical margins [41,42]. The practice reported in this series largely reflects an ongoing concern regarding morbidity incurred by high-dose RT to the prostate bed, a patient preference to avoid early adjuvant intervention, and also the
fact that our series extends back to 2003 [43]. Although clear protocols for the administration of multimodal therapy would have been ideal in the trial setting, the results from this study may be more reflective of current diversity in management given that the results from this report are more likely to reflect everyday practice.

In conclusion, this report shows that many men (41%) with clinical high-risk prostate cancer can be re-stratified to a lower risk category for disease recurrence after radical surgery. RALP produces satisfactory oncological results, similar to the largest open surgical series in the high-risk setting. When employed as part of a multimodal approach, this series shows that RALP can achieve low rates of treatment failure, and many men (73%) at just over a median 2 years of follow-up will avoid use of ADT. Risk of biochemical failure as well as the need for adjuvant post-surgery therapy can be predicted by serum PSA and clinical stage, but importantly not biopsy Gleason grade.

CONFLICT OF INTEREST

None declared.

REFERENCES

21 Ward JF, Slezak JM, Blute ML, Bergstrahl EJ, Zincke H. Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate-specific antigen testing: 15-year outcome. BJU Int 2005; 95: 751–6
22 Cremers RG, van Lin EN, Gerrits WL et al. Efficacy and tolerance of salvage radiotherapy after radical prostatectomy, with emphasis on high-risk patients suited for adjuvant radiotherapy. Radiother Oncol 2010; 97: 467–73


28 Loeb S, Schaeffer EM, Trock BJ, Epstein JI, Humphreys EB, Walsh PC. What are the outcomes of radical prostatectomy for high-risk prostate cancer? *Urology* 2010; 76: 710–4


39 Lavery HJ, Nabizada–Pace F, Carlucci JR, Braitbord JS, Samadi DB. Nerve-sparing robotic prostatectomy in preoperatively high-risk patients is safe and efficacious. *Urol Oncol* 2010; [Epub ahead of print]


42 Thompson IM, Tangen CM, Paradelo J et al. Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term followup of a randomized clinical trial. *J Urol* 2009; 181: 956–62

43 McVey GP, Parker C. Adjuvant vs. salvage radiotherapy for pathologically advanced prostate cancer. *Curr Opin Urol* 2010; 20: 229–33

Correspondence: Stephen S. Connolly, Department of Urology, Royal Melbourne Hospital, Grattan Street, VIC 3050, Australia.

e-mail: stephensconnolly@gmail.com

Abbreviations: RT, radiotherapy; ADT, androgen deprivation therapy; RALP, robotic-assisted laparoscopic prostatectomy; BCF, biochemical failure; HR, hazard ratio.