Austin Journal of Urology

Austin Publishing Group

Open Access Full Text Article

Review Article

# Expanding Role of Surgery in Management of High Risk Prostate Cancer

**Turker P[1] and Turkeri LN[2]***

[1]Department of Urology, Namik Kemal University, Turkey

[2]Department of Urology, Marmara University, Turkey

***Corresponding author:** Turkeri LN, Department of Urology, Marmara University, Turkey

**Received:** August 11, 201 4; **Accepted:** September 06, 2014; **Published:** September 11, 2014

## Abstract

Patients with high risk prostate cancer (PCa) have an increased risk of PSA failure, need for secondary therapy, metastatic progression and death from their disease. Although, definition of high risk PCa is not uniform and associated with a variable prognosis, there is an increased interest in surgery for the treatment of high risk PCa. Reported clinical series have shown that radical prostatectomy (RP) has excellent long-term outcomes for the treatment of the high risk patients and 50% of them can be spared of secondary treatments like androgen deprivation therapy. Surgery is also effective in selected patients with lymph node positive disease as part of a multi-modality management. Also, accurate pathologic staging after surgery ensures the application of proper secondary treatments in a timely fashion. At present, the lack of randomized trials comparing the long-term outcomes of RP and radiotherapy in high risk PCa precludes a certain conclusion if surgery-based management strategy is better or not.

**Keywords:** Prostate cancer; Radical prostatectomy; High risk prostate cancer; Outcomes; Adjuvant

## Introduction

Today most of the men with prostate cancer (PCa) are diagnosed with clinically localized disease [1]. However, high-risk disease still accounts for 15-35% of all prostate cancer diagnoses [2,3]. Radical prostatectomy (RP) has an established role in first line treatment of localized PCa. But its role in high risk PCa is still controversial. Current classification systems of PCa yield a heterogeneous group of high risk patients. An important portion of patients in this group will benefit from surgery and achieve excellent survival outcomes by surgery alone. In this article the place of surgery in the management of high risk PCa will be reviewed based on the current available literature.

### Definition of high risk prostate cancer

Definition of high grade prostate cancer available today based on clinicopathological findings. Although they are easy to use and have similarities, unfortunately they yield a heterogeneous group in terms of prognosis. The definition of D'Amico et al. for high-risk PCa was a PSA value >20 ng/ml or biopsy GS 8–10, or clinical stage ≥ T2c [4]. This definition is accepted by the American Urological Association (AUA). The definition accepted by European Association of Urology (EAU) [5] and the National Comprehensive Cancer Network [6], is PSA value >20 ng/ml or biopsy GS 8–10, or clinical stage ≥ T3a. They appear to be the commonest definitions used in the studies evaluating high risk disease. However, using these definitions, a man presenting with a , Gleason score of 7, PSA 21ng/ml, tumor in 3 cores may be placed in the same category as a man with a PSA level of 42 ng/ml, Gleason score 9 and tumor in all cores which makes it difficult to counsel based on risk grouping alone. A patient in this group with a single risk factor may have a totally different prognosis from a patient with all three risk factors.

Spahn et al. at their multi-institutional study evaluated 712 patients with PSA >20 ng/dl at diagnosis [7]. In this report 27% of patients with only one risk factor (PSA >20 ng/dl) were more likely to had a favorable histology at radical prostatectomy in comparison to 0% of patients with three risk factors (PSA >20 ng/ml, cT3–4, and Gleason score 8). Almost a third of the study population had specimen-confined disease, potentially curable by surgery alone. Following RP, prostate specific survival at 10 years for locally advanced disease was 91% for patients with PSA >20 ng/dl and 65% in those patients with a PSA >20 ng/ml and Gleason ≥ 8.

Yossepowitch et al. compared eight different definitions of 'high risk PCa' and showed that high risk patients did not have a uniformly poor prognosis. Depending on the definition used 10-year PCa specific mortality in high risk patients ranged from 3% to 11% when treated with radical prostatectomy [8].

Interestingly, Nguyen et al. showed that biochemical recurrence-free survival following radiotherapy did not vary significantly based on six different definitions [9].

### Overstaging/Overgrading problem

The rate of downgrading between the biopsy and the radical prostatectomy Gleason score is also not low. Several studies demonstrated that one third of patients with a preoperative Gleason score 8 are downgraded to Gleason ≤ 7 at surgery [10,11]. This group in particular may benefit most from surgery. Another study also reported that among patients presenting with cT3b or cT4 PCa approximately one-third of them have either organ-confined disease (7.8%) or capsular perforation only (29.4%) [12]. Overstaged patients were often cured by surgery alone and 35.3% of the whole group did not receive any form of neoadjuvant/adjuvant treatment and 21.6% remained free of additional therapies at a median follow-up of 108 months.


Turkeri et al. © All rights are reserved

**Citation:** Turker P and Turkeri LN. Expanding Role of Surgery in Management of High Risk Prostate Cancer. Austin J Urol. 2014;1(2): 5.

To identify which high-risk prostate cancer (PCa) patients might have favorable pathologic outcomes when surgically treated Briganti et al. proposed a nomogram [13]. They evaluated 1366 high risk patients who had RP and lymph node dissection at 8 European centers between 1987 and 2009. A favorable pathologic outcome was defined as specimen-confined (SC) disease (pT2–pT3a, node negative PCa with negative surgical margins). SC disease was detected 37% of the patients and these patients had better 10 year biochemical recurrence free and case specific survivals when compared to patients who had non-SC disease (66% vs 47% and 98 vs 88%, respectively; all $p < 0.001$). Forty-eight percent of the patients received adjuvant therapy (ADT and/or RT). All preoperative variables were found to be independent predictors of SC disease. They built up a nomogram for identifying SC disease patients preoperatively using age, PSA, Gleason score and clinical stage with 72% accuracy.

## Age Factor

Older men with high-grade disease, even those diagnosed in their 80s, face a substantial risk of cancer-specific mortality in the absence of local therapy [14]. Although elderly men are more likely to have high-risk disease, they are less likely to receive definitive therapy [15]. Instead they are more likely to get ADT as monotherapy. Controlling for age, comorbidity and risk, older men with high-risk tumors receiving local therapy had a 46% reduction in mortality compared with those treated conservatively.

### Non-curative intervention vs curative treatment

In the past, patients in the high risk PCa category were considered as non-curable and managed conservatively, Albertsen et al. reported the outcomes following conservative management (observation or ADT) of clinically localized PCa and showed that the estimated risk of dying from PCa was 60–90%, at 20 years [16].

A Swedish population based study assessed the mortality of PCa treated with non-curative intent [17]. The number of high risk PCa patients in the database was 30.159 and high risk disease was defined as stage T3 or prostate specific antigen (PSA) level 20 to less than 50 ng/ml or Gleason score ≥ 8. The 10 and 15-year PCa mortality rates of the high-risk PCa group were 28.8% and 35.5%, respectively. In the same study the number of patients with regionally metastatic disease was 10,315 which was defined as stage N1 or T4 or PSA level 50–100 ng/ml. PCa mortality at 10 and 15-year reported as 41.3% and 49.1% in this patient population, respectively.

Another study from Sweden with a cohort of over eleven thousand PCa patients has shown that, after adjusting for age, comorbidity, Gleason score, T category and PSA level at the time of diagnosis, any curative treatment appears to be of benefit in high-risk patients (PSA 20-100 ng/mL and no distant metastasis) compared with any palliative therapy, with a dramatic reduction in cause-specific death [18].

Although there is no consensus yet about the optimal treatment of high risk disease it has been shown clearly that at least part of these patients may benefit from some kind of curative intervention. Treatment of the primary tumor is essential not only for local control but also to prevent subsequent spreading to distant metastatic sites.

### Role of surgery in the treatment of high risk prostate cancer

There is no consensus about the optimal treatment of high risk disease. Although both surgery and radiotherapy are equally recommended as the first line treatment options in guidelines [5], traditionally androgen-deprivation therapy (ADT) plus external-beam radiation therapy (EBRT) is more often recommended. Only about 36% of high-risk cases are initially treated with radical prostatectomy despite the absence of any sound evidence to support the superiority of any particular treatment option [19].

When compared with low and intermediate risk PCa, high risk disease is associated with increased risk of microscopic metastases surgical margin positivity and the need for additional treatments after surgery. Because of the risk of suboptimal cancer control by surgery alone, traditionally most of the urologists were discouraged about performing RP in this high risk group.

Recently, several large retrospective studies have clearly demonstrated favorable long-term prostate cancer-specific survival rates with radical prostatectomy and pelvic lymph node dissection with or without adjuvant therapies in this group of patients [7,20-25].

Stephenson et al. reported long-term outcomes after RP in a multicenter study [21]. Out of 12,677 patients treated with RP between 1987 and 2005, 1,962 had high risk disease (%17). The 10 and 15 year prostate cancer-specific survival rates were excellent, 92% and 81% respectively. Authors also developed a preoperative nomogram predicting the risk of disease specific mortality at 10 and 15 years. On the basis of Gleason score, clinical stage and PSA, the externally validated concordance index of the nomogram was 0.82.

Tewari et al. reported long-term survival outcomes in patients with PCa with Gleason score 8 or greater who were treated with conservative therapy, radiation therapy and radical prostatectomy [22]. The cohort comprised of 453 patients. Median overall survival for conservative therapy, radiation and radical prostatectomy was 5.2, 6.7 and 9.7 years, respectively. Median cancer specific survival was 7.8 years for conservative therapy and more than 14 years for radiation therapy and radical prostatectomy. The risk of cancer specific death following radical prostatectomy was 68% lower than for conservative treatment and 49% lower than for radiation therapy ($p<0.001$ and 0.053, respectively).

In another study Ploussard et al. tried to estimate the effect of predictive factors for oncologic outcomes after RP for high risk PCa [26]. In a series of 813 patients, organ confined disease was reported in 36.5%. Each preoperative criteria of high risk PCa (PSA level >20 ng/mL, Gleason score 8-10, or clinical Stage T2c-T4 disease) found to be an independent predictor for PSA failure. Additionally the PSA failure risk was increased by 1.5- and 2.8-fold in men with 2 and 3 criteria, respectively. They reported that 75% of the high risk patients remained disease free at 5 years after surgery.

## Comparison of Radiotherapy versus Surgery

Although RP has been shown to be effective for high risk PCa, there is not a single completed randomized trial comparing the efficacy of RP and EBRT yet. The available studies comparing the survival outcomes of RP vs RT for high risk disease in the literature are all retrospective.

Abdollah et al. retrospectively compared the mortality outcomes

of RP and EBRT for patients with localized prostate cancer in a cohort of 68,665 patients from SEER database [23]. According their results, patients treated with surgery fared better in all categories but especially patients with high risk disease benefited the most from surgery compared to those treated with EBRT. For patients treated with radical prostatectomy versus radiotherapy, the 10-year cancer-specific mortality rates were 6.8 versus 11.5% in high-risk prostate cancer, respectively. Stratification based on Charlson Comorbidity Index and age resulted in similar finding, approximately twice the mortality rate with radiotherapy. At multivariable analyses, radiotherapy was associated with less favorable cancer-specific mortality in all categories, suggesting radical prostatectomy as a more effective form of therapy.

In another study Boorjian et al. evaluated long-term survival of RP, EBRT plus ADT and EBRT alone, in high risk PCa patients [24]. Overall, 1,238 patients underwent RP, and 344 received EBRT plus ADT, and 265 received EBRT alone. The 10-year cancer-specific survival rate with RP vs EBRT plus ADT was 92% and 92%, respectively. EBRT alone resulted in a lower survival of 88%.

Petrelli et al. also compared the results of RP and EBRT for localized high risk prostate cancer in a systematic review including 17 studies [20]. Overall and cancer-specific mortality rates appear to be better with RP compared with EBRT in localized, high-risk PCa. Interestingly, surgery was also associated with a 50% decreased risk of non-PCa specific mortality compared to EBRT.

Several randomized trials have shown that EBRT requires ADT to achieve better results compared to EBRT alone for the treatment of high risk PCa. The duration of the ADT appears to be at least 2 years to get the maximal benefit [27,28]. The need for this combination resulted in adverse consequences of ADT and negative impact on quality of life have also been reported [29,30]. High risk patients who were treated with radiation therapy were 3,5 times more likely to receive ADT when compared to RP [31]. Thus, surgery provides additional advantages since RP for high risk PCa avoids the use of ADT in approximately 50-70% of these patients [25,32].

Also, up to 57% of patients classified as having high risk PCa are found to have organ confined tumors at surgery and thus may be spared the cost and potential side effects of secondary treatment [33,34]. Other institutions reported similar results with excellent disease control and prevention of secondary hormonal therapy by the use of RP. Investigators from John Hopkins reported long-term outcomes of RP for high risk PCa, performed by a single surgeon [25]. Among 175 high-risk patients, 63 (36%) had organ-confined disease in the RP specimen. At 10 years, biochemical recurrence-free survival was 68%, metastasis-free survival was 84%, and disease specific survival was 92%. A substantial proportion of these patients remained free of additional therapy and 10-year rate of freedom from any hormonal therapy was 71%.

In another study from Cleveland Clinic 267 high risk patients treated by RP was examined for the ability of surgery as initial management in avoiding ADT [32]. Overall, 8-year probabilities of freedom from biochemical recurrence, distant metastasis and prostate cancer specific mortality (PCSM), were 46% (95% CI, 38-54), 87% (95% CI, 84-90), 93% (95% CI, 91-95), and 71% (95% CI, 65-77), respectively. Also 71% of these patients were spared from ADT.

Thus, results from clinical series suggests that at least 50-70% of the patients with high risk prostate cancer can be spared from additional hormonal therapy whereas the great majority will require a combination with ADT if radiotherapy will be the mode of local treatment.

## Multimodality Therapy

Nevertheless, a major concern in high risk patients is the possibility of a need for additional therapy after surgery in order to ensure a better disease control. Published literature that about half of the patients treated with RP for high risk disease will need some form of adjuvant therapy (RT and/or ADT) [35].

Another important issue is the effect of various sequences in therapy on quality of life which was explored for patients who required a multimodal treatment approach. Patients were less likely to wear pads and experience erectile dysfunction when the treatment sequence was RP and then salvage RT compared to patients treated with RT and then salvage RP [36].

### Surgical technique

The surgery for high risk disease needs expertise. The boundaries during RP are extended; wide local excision of the neurovascular bundles, en bloc removal of both layers of Denonvillier's fascia with an en bloc excision of seminal vesicles may be needed [37]. Extended pelvic lymph node dissection (ePLND) should be performed which has shown to be effective in both more accurate staging and the potential cure of micro-metastatic disease [28]. Knowing that one third of the population has organ confined disease nerve sparing procedure can also be carried out in a very select group of patients.

Robotic prostatectomy has shown comparable results with open technique although open RP still the choice in most of the centers for treatment of high risk PCa [38]. A recent multicenter retrospective study compared 5,556 robot-assisted radical prostatectomy (RARP) and 7,878 open radical prostatectomy cases from 2004 to 2009 [39]. In this series better surgical outcomes with RARP were reported in intermediate and high risk patients compared to open technique. Fewer positive margins and better early cancer control, less use of additional androgen deprivation and radiation therapy within 2 yr of surgery were reported after RARP. However, the superiority of either surgical approach is still debatable.

Functional outcomes are a major concern in patients with high risk disease undergoing RP, since a wide resection is usually applied potentially involving the neurovascular bundle and may injure the sphincteric mechanism.

### Surgery for LN (+) disease

Extended pelvic lymph node dissection (ePLND) should be performed in all high-risk PCa cases, due to estimated risk for positive lymph nodes of 15-40% [35]. Also, ePLND is the most accurate method for accurate staging of microscopic lymph node metastasis which may guide the application of secondary therapies and may delay or avoid the need for ADT [40].

Traditionally, involvement of lymph nodes in prostate cancer was considered as an adverse prognostic factor associated with limited long-term survival regardless of treatment. However, new clinical data suggests the oncological benefit of local treatment even

in metastatic PCa [41]. Engel et al. compared the survival rates of LN(+) patients with or without RP [42]. This study revealed two-fold increased risk of death if RP was abandoned because of LN(+) disease , compared to patients who had completed RP. Similarly, Stueber et al. reported a 10 year disease specific survival of 93% versus %56 for patients with and without RP, respectively [43]. Therefore, currently it is recommended to complete the radical prostatectomy and ePLND regardless of the intraoperative lymph node status.

In addition, even in the case of lymph node positive disease at diagnosis it has been shown that surgery may have a role as part of a multimodality management. Improved survival was reported for patients who are treated with RP plus ADT compared to ADT alone [44]. At a median follow-up of 11.9 years, patients assigned immediate ADT had a significant improvement in overall survival (HR 1.84, p=0.04), prostate-cancer-specific survival (HR 4.09, p=0.0004), and progression-free survival (HR 3.42, p<0.0001).

The outcomes are even better when the number of positive lymph nodes is few or there is micro-metastatic disease. Schumacher et al analyzed 122 consecutive LN(+) PCa patients with negative preoperative staging examinations and no neoadjuvant ADT or RT who underwent ePLND (minimum 10 lymph nodes in the surgical specimen) followed by RP [45]. They reported median cancer-specific survival at 5 and 10 yr as 84.5% and 60.1%, respectively. In patients with ≤ 2 or ≥ 3 positive nodes, median cancer-specific survival at 10 yr was 78.6% and 33.4%, respectively ($p < 0.001$) suggesting that there may be a curative potential of surgical resection in the presence of a limited nodal involvement.

In an effort to better define prognostic stratification of these patients Briganti et al., included 703 LN(+) patients from two institutions treated with ePLND and RP [46]. They showed that 2 positive nodes represent a significant cut-off value for cancer specific survival in patients with node positive prostate cancer. Patients with 2 or less positive nodes had significantly better disease specific survival at 15 year follow-up compared to patients with more than 2 positive nodes (84% vs 62%; p<0.001).

Prognostic implications of microscopic LN involvement at final specimen are still undetermined and, the role of immediate ADT is questionable. EAU guidelines recommend a follow-up by PSA and delaying the initiation of HT until biochemical recurrence is observed in patients with less than 2 microscopically involved lymph nodes discovered through extended nodal dissection [28]. Further studies are required to determine if multimodality treatment may result in a better outcome.

## Future Directions

The optimal treatment strategy in high risk prostate cancer is not determined yet. A number of clinical research is underway in an attempt to improve the effectiveness of surgery including the use of neoadjuvant (e.g. chemotherapy-NCT01530295, NCT01530295; chemotherapy and ADT-NCT01250717; bevacizumab and chemotherapy-NCT00321646; downstream target inhibition of PI3K-NCT01695473; temsirolimus-NCT00071968) and adjuvant therapies (e.g. ADT-NCT01753297; chemotherapy and hormonal therapy-NCT00193271, NCT00283062).

## Conclusion

High grade prostate cancer managed with non-curative intent is associated with a reduced survival. Therefore, patients with a certain life expectancy who are diagnosed with high risk PCa should receive some form of curative treatment. RP with ePLND offers good long-term results in selected patients, either alone or as a part of a multimodality therapy. In this context there is definitely a need for better classification of high risk PCa in order not to 'over-' or 'under-treat' these patients.

## References

1. Makarov DV, Trock BJ, Humphreys EB, Mangold LA, Walsh PC, Epstein JI, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. Urology. 2007; 69: 1095-1101.
2. Cooperberg MR, Broering JM, Carroll PR. Time trends and local variation in primary treatment of localized prostate cancer. J Clin Oncol. 2010; 28: 1117-1123.
3. Shao YH, Demissie K, Shih W, Mehta AR, Stein MN, Roberts CB, et al. Contemporary risk profile of prostate cancer in the United States. J Natl Cancer Inst. 2009; 101: 1280-1283.
4. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998; 280: 969-974.
5. Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. Eur Urol. 2011; 59: 61-71.
6. Site CCNW. NCCN guidelines: prostate cancer. 2011.
7. Spahn M, Joniau S, Gontero P, Fieuws S, Marchioro G, Tombal B, et al. Outcome predictors of radical prostatectomy in patients with prostate-specific antigen greater than 20 ng/ml: a European multi-institutional study of 712 patients. Eur Urol. 2010; 58: 1-7.
8. Yossepowitch O, Eggener SE, Serio AM, Carver BS, Bianco FJ Jr, Scardino PT, et al. Secondary therapy, metastatic progression, and cancer-specific mortality in men with clinically high-risk prostate cancer treated with radical prostatectomy. Eur Urol. 2008; 53: 950-959.
9. Nguyen CT, Reuther AM, Stephenson AJ, Klein EA, Jones JS. The specific definition of high risk prostate cancer has minimal impact on biochemical relapse-free survival. J Urol. 2009; 181: 75-80.
10. Bastian PJ, Gonzalgo ML, Aronson WJ, Terris MK, Kane CJ, Amling CL, et al. Clinical and pathologic outcome after radical prostatectomy for prostate cancer patients with a preoperative Gleason sum of 8 to 10. Cancer. 2006; 107: 1265-1272.
11. Manoharan M, Bird VG, Kim SS, Civantos F, Soloway MS. Outcome after radical prostatectomy with a pretreatment prostate biopsy Gleason score of >/=8. BJU Int. 2003; 92: 539-544.
12. Joniau S, Hsu CY, Gontero P, Spahn M, Van Poppel H. Radical prostatectomy in very high-risk localized prostate cancer: long-term outcomes and outcome predictors. Scand J Urol Nephrol. 2012; 46: 164-171.
13. Briganti A, Joniau S, Gontero P, Abdollah F, Passoni NM, Tombal B, et al. Identifying the best candidate for radical prostatectomy among patients with high-risk prostate cancer. Eur Urol. 2012; 61: 584-592.
14. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, et al. Outcomes of localized prostate cancer following conservative management. JAMA. 2009; 302: 1202-1209.
15. Bechis SK, Carroll PR, Cooperberg MR. Impact of age at diagnosis on prostate cancer treatment and survival. J Clin Oncol. 2011; 29: 235-241.
16. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative

management of clinically localized prostate cancer. JAMA. 2005; 293: 2095-2101.

17. Rider JR, Sandin F, Andrén O, Wiklund P, Hugosson J, Stattin P, et al. Long-term outcomes among noncuratively treated men according to prostate cancer risk category in a nationwide, population-based study. Eur Urol. 2013; 63: 88-96.

18. Ladjevardi S, Berglund A, Varenhorst E, Bratt O, Widmark A, Sandblom G. Treatment with curative intent and survival in men with high-risk prostate cancer. A population-based study of 11 380 men with serum PSA level 20-100 ng/mL. BJU Int. 2013; 111: 381-388.

19. Inman BA, Davies JD, Rangel LJ, Bergstralh EJ, Kwon ED, Blute ML, et al. Long-term outcomes of radical prostatectomy with multimodal adjuvant therapy in men with a preoperative serum prostate-specific antigen level > or =50 ng/mL. Cancer. 2008; 113: 1544-1551.

20. Petrelli F, Vavassori I, Coinu A, Borgonovo K, Sarti E, Barni S, et al. Radical prostatectomy or radiotherapy in high-risk prostate cancer: a systematic review and metaanalysis. Clin Genitourin Cancer. 2014; 12: 215-224.

21. Stephenson AJ, Kattan MW, Eastham JA, Bianco FJ Jr, Yossepowitch O, Vickers AJ, et al. Prostate cancer-specific mortality after radical prostatectomy for patients treated in the prostate-specific antigen era. J Clin Oncol. 2009; 27: 4300-4305.

22. Tewari A, Divine G, Chang P, Shemtov MM, Milowsky M, Nanus D. Long-term survival in men with high grade prostate cancer: a comparison between conservative treatment, radiation therapy and radical prostatectomy--a propensity scoring approach. J Urol. 2007; 177: 911-915.

23. Abdollah F, Schmitges J, Sun M, Jeldres C, Tian Z, Briganti A, et al. Comparison of mortality outcomes after radical prostatectomy versus radiotherapy in patients with localized prostate cancer: a population-based analysis. Int J Urol. 2012; 19: 836-844.

24. Boorjian SA, Karnes RJ, Viterbo R, Rangel LJ, Bergstralh EJ, Horwitz EM, et al. Long-term survival after radical prostatectomy versus external-beam radiotherapy for patients with high-risk prostate cancer. Cancer. 2011; 117: 2883-2891.

25. Loeb S, Schaeffer EM, Trock BJ, Epstein JI, Humphreys EB, Walsh PC, et al. What are the outcomes of radical prostatectomy for high-risk prostate cancer? Urology. 2010; 76: 710-714.

26. Ploussard G, Masson-Lecomte A, Beauval JB, Ouzzane A, Bonniol R, Buge F, et al. Radical prostatectomy for high-risk prostate cancer defined by preoperative criteria: oncologic follow-up in national multicenter study in 813 patients and assessment of easy-to-use prognostic substratification. Urology. 2011; 78: 607-613.

27. Bolla M, de Reijke TM, Van Tienhoven G, Van den Bergh AC, Oddens J, Poortmans PM, et al. Duration of androgen suppression in the treatment of prostate cancer. N Engl J Med. 2009; 360: 2516-2527.

28. European Association of Urology Guidelines. 2014.

29. Potosky AL, Knopf K, Clegg LX, Albertsen PC, Stanford JL, Hamilton AS. Quality-of-life outcomes after primary androgen deprivation therapy: results from the Prostate Cancer Outcomes Study. J Clin Oncol. 2001; 19: 3750-3757.

30. Sanda MG, Dunn RL, Michalski J, Sandler HM, Northouse L, Hembroff L, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med. 2008; 358: 1250-1261.

31. Meng MV, Elkin EP, Latini DM, Duchane J, Carroll PR. Treatment of patients with high risk localized prostate cancer: results from cancer of the prostate strategic urological research endeavor (CaPSURE). J Urol. 2005; 173: 1557-1561.

32. Miocinovic R, Berglund RK, Stephenson AJ, Jones JS, Fergany A, Kaouk J, et al. Avoiding androgen deprivation therapy in men with high-risk prostate cancer: the role of radical prostatectomy as initial treatment. Urology. 2011; 77: 946-950.

33. Boorjian SA, Karnes RJ, Rangel LJ, Bergstralh EJ, Blute ML. Mayo Clinic validation of the D'amico risk group classification for predicting survival following radical prostatectomy. J Urol. 2008; 179: 1354-1360.

34. Hull GW, Rabbani F, Abbas F, Wheeler TM, Kattan MW, Scardino PT, et al. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. J Urol. 2002; 167: 528-534.

35. Briganti A, Larcher A, Abdollah F, Capitanio U, Gallina A, Suardi N, et al. Updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection: the essential importance of percentage of positive cores. Eur Urol. 2012; 61: 480-487.

36. Van Der Poel HG, Moonen L, Horenblas S. Sequential treatment for recurrent localized prostate cancer. J Surg Oncol. 2008; 97: 377-382.

37. Ischia J, Gleave M. Radical prostatectomy in high-risk prostate cancer. Int J Urol. 2013; 20: 290-300.

38. Lee EK, Baack J, Duchene DA. Survey of practicing urologists: robotic versus open radical prostatectomy. Can J Urol. 2010; 17: 5094-5098.

39. Hu JC, Gandaglia G, Karakiewicz PI, Nguyen PL, Trinh QD, Shih YC, et al. Comparative Effectiveness of Robot-assisted Versus Open Radical Prostatectomy Cancer Control. Eur Urol. 2014.

40. Kane CJ, Presti JC Jr, Amling CL, Aronson WJ, Terris MK, Freedland SJ; SEARCH Database Study Group. Changing nature of high risk patients undergoing radical prostatectomy. J Urol. 2007; 177: 113-117.

41. Ghadjar P, Briganti A, De Visschere PJ, Fütterer JJ, Giannarini G, Isbarn H, et al. The oncologic role of local treatment in primary metastatic prostate cancer. World J Urol. 2014.

42. Engel J, Bastian PJ, Baur H, Beer V, Chaussy C, Gschwend JE, et al. Survival benefit of radical prostatectomy in lymph node-positive patients with prostate cancer. Eur Urol. 2010; 57: 754-761.

43. Steuber T, Budaus L, Walz J, Zorn KC, Schlomm T, Chun F, et al. Radical prostatectomy improves progression-free and cancer-specific survival in men with lymph node positive prostate cancer in the prostate-specific antigen era: a confirmatory study. BJU Int. 2011; 107: 1755-1761.

44. Messing EM, Manola J, Yao J, Kiernan M, Crawford D, Wilding G, et al. Immediate versus deferred androgen deprivation treatment in patients with node-positive prostate cancer after radical prostatectomy and pelvic lymphadenectomy. Lancet Oncol. 2006; 7: 472-479.

45. Schumacher MC, Burkhard FC, Thalmann GN, Fleischmann A, Studer UE. Good outcome for patients with few lymph node metastases after radical retropubic prostatectomy. Eur Urol. 2008; 54: 344-352.

46. Briganti A, Karnes JR, Da Pozzo LF, Cozzarini C, Gallina A, Suardi N, et al. Two positive nodes represent a significant cut-off value for cancer specific survival in patients with node positive prostate cancer. A new proposal based on a two-institution experience on 703 consecutive N+ patients treated with radical prostatectomy, extended pelvic lymph node dissection and adjuvant therapy. Eur Urol. 2009; 55: 261-270.

Austin J Urol - Volume 1 Issue 2 - 2014
**ISSN: 2472-3606** | www.austinpublishinggroup.com
Turkeri et al. © All rights are reserved

**Citation:** Turker P and Turkeri LN. Expanding Role of Surgery in Management of High Risk Prostate Cancer. Austin J Urol. 2014;1(2): 5.