Significance and management of positive surgical margins at the time of radical prostatectomy

Jonathan L. Silberstein, James A. Eastham

Department of Urology, Tulane University School of Medicine, New Orleans, LA, USA, 1Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

ABSTRACT

Positive surgical margins (PSM) at the time of radical prostatectomy (RP) result in an increased risk of biochemical recurrence (BCR) and secondary treatment. We review current literature with a focus on stratifying the characteristics of the PSM that may define its significance, the impact of modern imaging and surgical approaches in avoidance of PSM, and management strategies when PSM do occur. We performed a review of the available literature to identify factors associated with PSM and their management. PSM have been repeatedly demonstrated to be associated with an increased risk of BCR following RP. The specific characteristics (size, number, location, Gleason score at the margin) of the PSM may influence the risk of recurrence. Novel imaging and surgical approaches are being investigated and may allow for reductions of PSM in the future. The use of adjuvant treatment for a PSM remains controversial and should be decided on an individual basis after a discussion about the risks and benefits. The goal of RP is complete resection of the tumor. PSM are associated with increased risk of BCR and secondary treatments. Of the risk factors associated with BCR after RP, a PSM is directly influenced by surgical technique.

Key words: Biochemical recurrence, prostate cancer, radical prostatectomy, robotic, surgical margin

INTRODUCTION

Wide variations in the incidence of positive surgical margins (11–48%) have been reported at the time of radical prostatectomy (RP).[1-8] Centers of excellence tend to report PSM in the lower end of this range[2] while population-based studies demonstrate results on the upper end which may be more reflective of most clinicians experience.[1] Cancer registries such as Surveillance, Epidemiology and End Results Program (SEER) have been shown to grossly underreport PSM and may be inaccurate.[5] Regardless, the incidence of PSM depends on both the characteristics of the cancer and the technique of the surgeon. Achieving a negative surgical margin may be the most significant opportunity the surgeon has to influence the natural history of the disease, as patients with PSM have been repeatedly demonstrated to have greater rates of biochemical recurrence (BCR).[2,4,6-8] Additionally, some clinicians view PSM as a trigger for adjuvant radiation therapy.

Attaining a negative surgical margin at the time of RP is the primary goal of the surgeon, but it is not an isolated goal. Preserving the neurovascular tissue and maintaining maximal urethral length are crucial for erectile functional and continence outcomes. Balancing oncologic and functional goals which are at odds with one another is fundamental to successfully performing RP regardless of surgical approach.

When a PSM is encountered, the specific characteristics of the PSM may influence the risk of BCR and subsequent disease progression. The specific pathologic characteristics of the PSM (length, number, location and Gleason score at the PSM) may all influence the risk of BCR. Because of the increased risk of BCR with PSM, some advocate immediate adjuvant treatment; however this may result in deterioration in quality of life and over treatment for many patients. In this review we will consider the definition and significance of a PSM, the pathologic
characteristics that influence the significance of the margin, recent surgical and imaging techniques that may reduce the rates of PSM and management of PSM when they are encountered.

DEFINITION OF A SURGICAL MARGIN

In theory, the definition of a PSM is clear; “tumor that extends to the surface of the prostate wherein the surgeon has cut across the tissue plane.” However, because the prostate lacks a true histologic capsule, in practice the definition can become confusing. In order to facilitate defining surgical margins (SM) status upon receipt by the pathologist, the entire surgical specimen should be inked and fixed. A positive margin is simply identified as “cancer cells extending to the inked surface of the specimen”. Margin status is negative if tumor cells are microscopically close to (<0.1 mm), but not actually in contact with the inked surface or when they are at the surface of the tissue lacking any ink. Even with proper handling of the specimen by the pathologist, SM assessment may be complicated by crush, thermal, or electrocautery artifact, partial tearing of the extraprostatic soft tissue during processing or tissue banking and incomplete or irregular tracking of ink. Such findings may contribute to interobserver variation with reported kappa values of 0.45 (moderate agreement) between local pathologists and expert pathologists and values of 0.74 between expert pathologists.

Surgical margins in the presence of extra-prostatic extension (EPE) may represent an over enthusiastic effort on the part of the surgeon to preserve the neurovascular bundle (NVB) or tumor that invades into vital structures and could not be completely resected [Figure 1a]. PSM in the absence of EPE, usually represent a capsular incision into tumor, an iatrogenic positive margin, due to an improper dissection plane with incision into the prostate and into the tumor [Figure 1b]. Importantly this scenario, pT2+, has prognostic significance. Such patients have greater rates of biochemical recurrence than patients with either pT2 cancers with negative SM or cancers with EPE and negative SM (pT3a, SM negative).

PATHOLOGIC CHARACTERISTICS OF SURGICAL MARGINS

Patients with PSM have increased risk of BCR. For example in a multi-institutional study of more than 7000 patients the 5 and 10 year BCR rate for PSM were 0.53 (95% CI 0.494, 0.566) and 0.36 (95% CI 0.28, 0.45), [Figure 2], a Kaplan-Meier curve adapted from this publication demonstrating BCR stratified according to margin status. This figure also demonstrates that many patients, despite the presence of PSM will not develop BCR even with 10 years of follow. Many investigators have attempted to better define the pathologic characteristics of PSM in order to better risk stratify patients and potentially offer adjuvant intervention for those at high risk of progression while sparing over treatment for others.

“Amount” of positive margin

Multiple investigators have sought to quantify the “amount” of PSM either by counting the number of positive margins in a given specimen, or the extent of the positive margin quantified as binary variable such as focal versus extensive often seen in older studies or as a more reproducible linear extent. The rationale behind these attempts assumes that a greater amount of PSM is associated with greater quantity of tumor left behind and a greater potential for growth, biochemical recurrence, and metastases. Multiple analyses from our institution and others have demonstrated that multiple PSM confer increased risk of BCR when compared with a solitary margin. Although the number of positive margins may be an independent predictor in multivariable analysis for BCR, the number of positive margins may not significantly impact the predictive accuracy of nomogram predictions compared to a PSM modeled more simply as positive or negative.

Multiple investigators have attempted to determine if the extent of the positive margin has prognostic significance. Examining our data as focal compared to extensive as...
Anatomic location of positive surgical margin

Efforts to reduce PSM have lead surgeons and pathologists to define their anatomic location and determine if the site-specific location impacts rates of recurrence. Repeatedly studies have demonstrated that the two most likely locations for PSM are the apex of the prostate and the posterolateral margins. Together these sites make up the majority of PSM accounting for 60–75% of PSM in most reported series of either open retropubic or robotic approaches. The apex of the prostate has less supporting tissue than the rest of the gland, it contains the least amount of capsule, and even benign glands can become adjoined with skeletal muscle at this location. This coupled with the increased traction placed on the apex during various parts of the procedure and efforts to maintain urethral length may explain the increased rates of PSM in this location. The posterolateral margin of the prostate is the second most common location of PSMs and this is likely due to attempts to preserve as much of the neurovascular bundle as possible which run in this location.

Gleason score at positive surgical margin

Recently, investigators have begun to investigate the importance of the Gleason score at the PSM. Theoretically when a higher Gleason score is found at the PSM, a more aggressive tumor remains in the patient with potentially higher rates of BCR. Several studies have demonstrated that grade of cancer at the PSM is associated with greater rates of BCR. Gleason score in the primary tumor is highly correlated with Gleason score at the margin for Gleason 6 tumors but this concordance rate diminishes rapidly as the primary tumor Gleason score increases. At MSKCC, Udo and colleagues noted that Gleason grade was associated with increased risk of BCR in a univariate analysis but it did not significantly enhance the concordance index of a model incorporating specimen Gleason Score and overall SM status. While ISUP currently recommends that reporting Gleason score at PSM remain at the discretion of the reporting pathologist, it may remain an important discriminator for determining the importance of a positive margin, particularly for those with Gleason 7 or greater disease, further study will be needed to verify the importance of these findings.

All together these data suggest that length of the PSM, the number of PSMs, the Gleason score at the PSM, and potentially even the location of the PSM may each play important roles in defining the risk of BCR following RP. Inter-institution variability in reporting makes comparisons or collaborations difficult. Potentially one could envision a scenario in which the characteristics (length, location, number, Gleason score) of a margin would have value in determining who should receive adjuvant therapy; however, this has yet to be demonstrated convincingly. Furthermore, while each of these factors may have significance on their own they have not demonstrated benefit in predicting outcomes when added to existing models.

BLADDER NECK MARGIN

Extraprostatic extension with microscopic invasion of the bladder neck—previously designated as T4 according to the American joint commission on cancer (AJCC)—has recently been revised to be included in T3a category. This reclassification is based on the work of several retrospective series which have demonstrated that patients with isolated positive bladder neck margins have outcomes that more closely approximate T3 lesions. Typically, direct extension of cancer from the organ of origin into surrounding structures is designated as T4; however, at the bladder neck, the interwoven nature of the outer layers of the bladder with the smooth muscle of the prostate obscure distinct tissue boundaries. It is unclear if a PSM at the bladder neck is associated with a worse prognosis than PSM in other locations, as isolated bladder neck margins are rare and often associated with multiple high-risk features. Further investigation is needed to more clearly define whether isolated bladder neck margin truly does have a worse prognosis than margins in other locations, if confirmed, clarification of the AJCC might be to define bladder neck invasion as T3b and seminal vesicle invasion as T3c as suggested by some groups.

SURGICAL APPROACH

With the huge shift towards robotics and away from open RP that has occurred over the last decade, invariable the question is asked does the surgical approach influence SM status. Currently, there are no large prospective randomized surgical trials designed to answer this question and even if there were, a larger problem might still remain. Large heterogeneity in PSM exists between individual surgeons performing RP through the same approach even after adjusting for case mix, surgery date, and surgery volume. In a review of the SMS of 44 different surgeons at two large urban centers PSM ranged, for each surgeon, from 10% to 48%. Substantial variation in outcomes remained even when analyses are limited to high or very high volume surgeons and are likely to dwarf differences between surgical approaches limiting the utility of comparative studies.
Despite these limitations various investigators have compared margin rates, location, and length for one surgical approach with another. Because of the increased use of robotic-assisted laparoscopic prostatectomy investigators have been interested in the impact that this novel surgical approach has on SM status. In a recently published meta-analysis with propensity adjustment for patient, surgeon, and hospital factors, the authors found no difference in PSM for open and robotic surgery. A prior meta-analysis that limited its analysis to comparative studies only demonstrated that PSM rates were similar between approaches. Administrative care datasets have not been able to directly compare PSM for differing surgical approaches but have demonstrated similar rates in the use of secondary therapies between different surgical approaches as a surrogate. At our institution we have found no significant difference in PSM or BCR for one surgical approach compared with another, but again individual surgeon variation is likely to be of greater importance than surgical approach.

**IMAGING TOOLS PREDICT OR PREVENT POSITIVE MARGINS**

Partial preservation of the neurovascular bundle (NVB) is likely the best compromise between oncologic and erectile functional outcomes in men at risk for EPE in the area of the NVB. Key to this approach is identification of the specific location of the cancer in relation to the NVB. Pre-operative MRI has been demonstrated to alter surgical plan prior to RP in approximately 40% of patients; however, MRI is reader dependent with significant interobserver variability. Another strategy has been the use of a real-time transrectal ultrasound during RP to help outline the suspected area of EPE. Using this technology, one group demonstrated a reduction in their PSM rates from 29% to 9%. More recently urologists have begun to incorporate the use of the TilePro to display the ultrasound images on the da Vinci surgical system console. Mounting interest in MR-US fusion technology is likely to result in utilizing this technology in a similar fashion to attempt to minimize PSM and maximize preservation of the NVB.

Near-infrared fluorescence imaging has been used for the identification of renal tumors and sentinel lymph nodes for prostate cancer. In the future similar types of technology may assist in the identification of the NVB or the location of the prostate tumor in order to reduce the rates of PSM.

**MANAGEMENT OF POSITIVE MARGINS**

Large multi-institutional studies have demonstrated that patients with PSM are more than twice as likely to experience BCR as patients without, even after adjusting for age, PSA, pathologic Gleason score, pathologic stage, and year of surgery. This leaves clinicians and patients in the challenging position of considering the role for additional treatment in the absence of any detectable disease. Unfortunately, adjuvant radiotherapy comes at the cost of increased risk of urinary incontinence, urinary stricture disease, proctitis, and rectal bleeding. Furthermore, although patients with PSM are at an increased risk of developing BCR many never do and are exposed to the potential harms of adjuvant radiotherapy without benefit.

Three randomized trials have examined the role of adjuvant radiotherapy in men with ‘adverse’ pathologic features in the RP specimen. Eligible patients were randomized to either adjuvant radiotherapy or “wait and see”. All three trials documented improvement in BCR free-survival with adjuvant radiotherapy compared to a “wait and see” approach. Two of these trials also demonstrated a reduction in clinical locoregional failure with adjuvant radiotherapy.

In all three studies the group gaining the most benefit from adjuvant radiotherapy was men with PSM. Based largely on the results of these three trials the American Urological Association (AUA) and the American Society for Therapeutic Radiology Organization (ASTRO) released joint guidelines stating that patients with adverse pathologic features (including but not limited to a PSM) should be offered ART. The guidelines continue on to state that the decision of whether to receive adjuvant radiotherapy should be based on a shared decision making process by a multidisciplinary team and the patient with consideration of the “patient’s history, functional status, values, preferences, and tolerance for potential toxicities and QoL effects of radiotherapy.”

A remaining and important limitation of the existing data is that none of these randomized trials have compared adjuvant radiotherapy to early salvage radiotherapy. It has been demonstrated that salvage therapy administered at lower PSA levels is associated with greatest effectiveness. The ability to detect PSA at very low levels has led many to conclude that a preferable strategy would be to offer early salvage treatment when patients have low but detectable PSA rather than adjuvant radiotherapy. Such a strategy may reduce the over treatment of patients who are never destined to develop BCR while maintaining the potential advantage of radiotherapy. Two ongoing randomized clinical trials, RADICALS (Radiotherapy and Androgen Deprivation In Combination After Local Surgery, NCT # 00541047) and RAVES (Radiotherapy Adjuvant vs. Early Salvage, NCT # 00860652), are evaluating whether progression-free and/or prostate cancer specific and overall survival are significantly prolonged by the use adjuvant radiotherapy compared to early salvage radiotherapy at the time of PSA failure.

Lastly, some practitioners use androgen deprivation therapy (ADT) alone for patients with adverse pathologic...
characteristics including a PSM. In one small randomized trial, whose results have not been confirmed, ADT following prostatectomy for patients with lymph node positive disease was demonstrated to result in overall survival benefit but for node negative patients ADT has never been demonstrated to have similar benefit. ADT has the potential for significant harm, reduces QoL, and should only be considered for patients with a positive lymph node or those undergoing adjuvant or salvage radiotherapy.

CONCLUSIONS

PSM are associated with an increased risk of BCR. The presence of a PSM may be more influenced by the individual surgeon than the surgical approach used to perform RP. Longer PSM (>3 mm), multiple PSM, and higher Gleason score at the PSM are associated with an increased risk of BCR. The presence of a PSM may be more influenced by the individual oncologic factors as well as those of the PSM—withe a tendency toward ART for multiple high risk features and toward early salvage for those with few—may be the most rational approach.

REFERENCES

1. Jayachandran J, Bañez LI, Levy DE, Aronson WJ, Terris MK, Presti JC Jr, et al. Risk stratification for biochemical recurrence in men with positive surgical margins or extracapsular disease after radical prostatectomy: Results from the SEARCH database. J Urol 2008;179:1791-6.
2. Eastham JA, Kuroiwa K, Ohori M, Serio AM, Gorbonos A, Maru N, et al. Prognostic significance of location of positive margins in radical prostatectomy specimens. Urology 2007;70:965-9.
3. Eastham JA, Kattan MW, Riedel E, Begg CB, Wheeler TM, Gerigk C, et al. Variations among individual surgeons in the rate of positive surgical margins in radical prostatectomy specimens. J Urol 2003;170:2292-5.
4. Karakiewicz PI, Eastham JA, Graefen M, Cagianos I, Stricker PD, Klein E, et al. Prognostic impact of positive surgical margins in surgically treated prostate cancer: Multi-institutional assessment of 5831 patients. Urology 2005;66:1245-50.
5. Shah SK, Fleet TM, Williams V, Smith AY, Skipper B, Wiggins C. SEER coding standards result in underestimation of positive surgical margin incidence at radical prostatectomy: Results of a systematic audit. The Journal of urology 2011;186:855-9.
6. Blute ML, Bostwick DG, Birkmeyer NH, Slezak JM, Martin SK, Amling CL, Zincke H. Anatomic site-specific positive margins in organ-confined prostate cancer and its impact on outcome after radical prostatectomy. Urology 1997;50:733-9.
7. Stephenson AJ, Wood DP, Kattan MW, Klein EA, Scardino PT, Eastham JA, et al. Location, extent and number of positive surgical margins do not improve accuracy of predicting prostate cancer recurrence after radical prostatectomy. J Urol 2009;182:1357-63.
8. Sofer M, Hamilton-Nelson KL, Vivantes F, Soloway MS. Positive surgical margins after radical retropubic prostatectomy: The influence of site and number on progression. J Urol 2002;167:2453-6.
9. Tan PH, Cheng L, Sigle JR, Griffeth D, Humphrey PA, van der Kwast TH, et al. International society of urological pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 5: Surgical margins. Mod Pathol 2011;24:48-57.
10. Emerson RE, Koch MO, Dagg J, Cheng L. Closest distance between tumor and resection margin in radical prostatectomy specimens: Lack of prognostic significance. Am J Surg Pathol 2005;29:225-9.
11. Evans AJ, Henry PC, Van der Kwast TH, Tkachuk DC, Watson K, Lockwood GA, et al. Interobserver variability between expert urologic pathologists for extraprostatic extension and surgical margin status in radical prostatectomy specimens. Am J Surg Pathol 2008;32:1503-12.
12. van der Kwast TH, Collette L, Van Poppel H, Van Cangh P, Vekemans K, Del Pozzo L, et al. Impact of pathology review of stage and margin status of radical prostatectomy specimens (EORTC trial 22911). Virchows Arch 2006;449:428-34.
13. Meeks JJ, Eastham JA. Radical prostatectomy: Positive surgical margins matter. Urol Oncol 2013;31:974-9.
14. Preston MA, Carrière M, Raju G, Morash C, Doccuette S, Gerritzen RG, et al. The prognostic significance of capsular incision into tumor during radical prostatectomy. Eur Urol 2011;59:613-8.
15. Udo K, Cronin AM, Carlino LJ, Savage CJ, Maschino AC, Al-Ahmadi HA, et al. Prognostic impact of subclassification of radical prostatectomy positive margins by linear extent and Gleason grade. J Urol 2013;189:1302-7.
16. Brimo F, Partin AW and Epstein JI. Tumor grade at margins of resection in radical prostatectomy specimens is an independent predictor of prognosis. Urology 2010;76:1206-9.
17. Smith JA Jr, Chan RC, Chang SS, Herrell SD, Clark PE, Baumgartner R, et al. A comparison of the incidence and location of positive surgical margins in robotic assisted laparoscopic radical prostatectomy and open retropubic radical prostatectomy. J Urol 2007;178:2385-9.
18. Vokes GE, McNeal JE, Redwine EA, Freiha FS, Stamey TA. Morphologic analysis of surgical margins with positive findings in prostatectomy for adenocarcinoma of the prostate. Cancer 1992;69:520-6.
19. Pettus JA, Weight CJ, Thompson CJ, Middleton RG, Stephenson RA. Biochemical failure in men following radical retropubic prostatectomy: Impact of surgical margin status and location. J Urol 2004;172:129-32.
20. Cao D, Kibel AS, Gao F, Tao Y, Humphrey PA. The Gleason score of tumor at the margin in radical prostatectomy is predictive of biochemical recurrence. Urology 2011;77:1409-14.
21. Smith JA Jr, Chan RC, Chang SS, Herrell SD, Clark PE, Baumgartner R, et al. A comparison of the incidence and location of positive surgical margins in robotic assisted laparoscopic radical prostatectomy and open retropubic radical prostatectomy. J Urol 2010;184:1399-1001.
22. Yossepowitch O, Sircar K, Scardino PT, Ohori M, Kattan MW, Wheeler TM, Reuter VE. Bladder neck involvement in pathological stage pT4 radical prostatectomy specimens is not an independent prognostic factor. J Urol 2002;168:119-21.
23. Pierorazio PM, Epstein JI, Humphreys E, Han M, Walsh PC, Partin AW. The significance of a positive bladder neck margin after radical prostatectomy: The American Joint Committee on Cancer Pathological Stage T4 designation is not warranted. J Urol 2004;172:129-32.
24. Cao D, Kibel AS, Gao F, Tao Y, Humphrey PA. The Gleason score of tumor at the margin in radical prostatectomy is predictive of biochemical recurrence. Am J Surg Pathol 2010;34:994-1001.
25. Illingworth P, Donohue JP, Eastham JA, Thompson DJ, Ko E, Han M, Walsh PC, Partin AW. The significance of a positive bladder neck margin after radical prostatectomy: The American Joint Committee on Cancer Pathological Stage T4 designation is not warranted. J Urol 2004;172:129-32.
26. Buschmeyer WC 3rd, Hamilton RJ, Aronson WJ, Presti JC Jr, Terris MK, Kane CJ, et al. Is a positive bladder neck margin truly a T4 lesion in the prostate specific antigen era? Results from the SEARCH Database. J Urol 2008;179:124-9.
27. Lowrance WT, Eastham JA, Savage C, Maschino AC, Laudone VP, Dechert CB, et al. Contemporary open and robotic radical prostatectomy practice patterns among urologists in the United States. J Urol 2012;187:2085-9.
26. Tewari A, Sooriakumaran P, Bloch DA, Seshadri-Kreaden U, Hebert AE, Wiklund P. Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: A systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. Eur Urol 2012;62:1-15.

27. Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: A systematic review and cumulative analysis of comparative studies. Eur Urol 2009;55:1037-63.

28. Hu JC, Gu X, Lipsitz SR, Barry MJ, D'Amico AV, Weinberg AC, et al. Comparative effectiveness of minimally invasive vs. open radical prostatectomy. JAMA 2009;302:1557-64.

29. Touijer K, Eastham JA, Secin FP, Romero Otero J, Serio A, Stasi J, et al. Comprehensive prospective comparative analysis of outcomes between open and laparoscopic radical prostatectomy conducted in 2003 to 2005. J Urol 2008;179:1811-7.

30. Silberstein JL, Su D, Glickman L, Kent M, Keren-Paz G, Vickers AJ, et al. A case-mix-adjusted comparison of early oncological outcomes of open and robotic prostatectomy performed by experienced high volume surgeons. Br J Urol Int 2013;111:206-12.

31. Hricak H, Wang L, Wei DC, Coakley FV, Akin O, Reuter VE, et al. The role of preoperative endorectal magnetic resonance imaging in the decision regarding whether to preserve or resect neurovascular bundles during radical retropubic prostatectomy. Cancer 2004;100:2655-63.

32. Labanaris AP, Zugor V, Takriti S, Smiszek R, Engelhard K, Nutzel R, et al. The role of conventional and functional endorectal magnetic resonance imaging in the decision of whether to preserve or resect the neurovascular bundles during radical retropubic prostatectomy. Scand J Urol Nephrol 2009;43:2-31.

33. Ukimura O, Magi-Galluzzi C, Gill IS. Real-time transrectal ultrasound guidance during laparoscopic radical prostatectomy: Impact on surgical margins. J Urol 2006;175:1304-10.

34. Long JA, Lee BH, Guillotreau J, Autorino R, Laydner H, Yakoubi R, et al. Real-time robotic transrectal ultrasound navigation during robotic radical prostatectomy: Initial clinical experience. Urology 2012;80:608-13.

35. Tobis S, Knopf J, Silvers C, Yao J, Rashid H, Wu G, et al. Near infrared fluorescence imaging with robotic assisted laparoscopic partial nephrectomy: Initial clinical experience for renal cortical tumors. J Urol 2011;186:47-52.

36. van der Poel HG, Buckle T, Brouwer OR, Valdés Olmos RA, van Leeuwen FW. Intraoperative laparoscopic fluorescence guidance to the sentinel lymph node in prostate cancer patients: Clinical proof of concept of an integrated functional imaging approach using a multimodal tracer. Eur Urol 2011;60:826-33.

37. Bolla M, van Poppel H, Collette L, van Cangh P, Vekemans K, Da Pozzo L, et al. Postoperative radiotherapy after radical prostatectomy: A randomised controlled trial (EORTC trial 22911). Lancet 2005;366:572-8.

38. Thompson IM, Tangen CM, Paradejo J, Lucia MS, Miller G, Troyer D, 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.

39. Wiegel T, Botke D, Steiner U, Siegmann A, Golz R, Störkel S, et al. Phase III postoperative adjuvant radiotherapy after radical prostatectomy compared with radical prostatectomy alone in pT3 prostate cancer with postoperative undetectable prostate-specific antigen: ARO 96-02/AUO AP 09/95. J Clin Oncol 2009;27:2924-30.

40. Thompson IM, Valicenti RK, Albertsen P, Davis BJ, Goldenberg SL, Hahn C, et al. Adjuvant and Salvage Radiotherapy After Prostatectomy: AJA/ASTRO Guideline. J Urol 2013;190:441-9.

41. 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;7:472-9.

How to cite this article: Silberstein JL, Eastham JA. Significance and management of positive surgical margins at the time of radical prostatectomy. Indian J Urol 2014;30:423-8.

Source of Support: Nil. Conflict of Interest: None declared.