Journal of Surgery: Open Access
ISSN 2470-0991 | Open Access

RESEARCH ARTICLE Volume 6 - Issue 5

Initial Experience and Assessment of Surgical Margins after Robotic Assisted Radical Prostatectomy at a Mexican University General Hospital

Reyna-Blanco Irving*, Navarro-Ruesga Iñigo, Chávez-Pedraya Rocío, Santa María Orozco Francisco Javier, Aguilar Méndez Marco Antonio, Marquina Cruz Manuel Arturo, Rodenas Gil Erick Alejandro, Ramírez González Andrey, Jiménez-García Aldo Daniel, Martínez-Salas Alan de Jesús, Muruato-Araiza Jesús Sebastián, Morales-Montor Jorge Gustavo, Martínez-Arroyo Carlos, Fernández-Noyola Gerardo, Cantellano-Orozco Mauricio, and Pacheco-Gahbler Carlos

Department of Urology, Hospital General "Dr. Manuel Gea González", Mexico City, Mexico

***Corresponding author:** Reyna-Blanco Irving, Department of Urology, Hospital General "Dr. Manuel Gea González", Calz. de Tlalpan 4800, Belisario Domínguez, Section 16, CP. 14080 Mexico City, Mexico, E-mail: irvingrblnco@gmail.com

Received: 28 Apr, 2020 | **Accepted:** 12 May, 2020 | **Published:** 18 May, 2020

Citation: Reyna-Blanco I, Navarro-Ruesga I, Chávez-Pedraya R, Javier SMOF, Antonio AMM, et al. (2020) Initial Experience and Assessment of Surgical Margins after Robotic Assisted Radical Prostatectomy at a Mexican University General Hospital. J Surg Open Access 6(5): dx.doi.org/10.16966/2470-0991.218

Abstract

Background: Prostate Cancer (PC) is the most common malignant neoplasm in men and it's the second cause of cancer specific mortality. The finding of Positive Surgical Margins (PSMs) after Radical Prostatectomy (RP) is an important predictive variable for Biochemical Recurrence (BR). Predictive variables are necessary to discriminate those prone to develop BR and therefore would benefit from adjuvant therapy from those that can safely be surveilled.

Objective: To identify patients with PSMs after Robotic-Assisted Radical Prostatectomy (RARP) at our urology department.

Materials and Methods: Observational, descriptive, transversal and retrospective study. Between December 2014 and December 2017, 68 patients with PC underwent RARP by a single surgeon. We assessed multiple variables to identify the ones associated with increased PSMs. Variables included: age, Prostate Specific Antigen (PSA), T clinical stage, biopsy's Gleason score, and number of positive fragments, perineural invasion, lymphovascular invasion, surgical specimen's Gleason score, and pathologic stage. For statistical analysis we used SPSS v23.0.

Results: 40/68 (58.8%) patients had PSMs, of them: 19/40 (47.5%) had a Gleason score 3+3=6, 7/40 (17.5%) had lymphovascular invasion, the region with greater PSMs was the prostate apex (70%), mean age was 64.2 years (SD 7.03 years), and mean PSA12.59 ng/mL (SD 12.12 ng/mL). Pathologic stage (p=0.04), PSA (p=0.021), and perineural invasion (p=0.0003) were statistically significant. 22 patients underwent surveillance, 2 Androgen Deprivation Therapy (ADT), 9 radiotherapy, and 7 radiotherapy+ADT.

Conclusion: It is of utmost importance to consider preoperative PSA as a predictive factor for PSMs and to correlate it with RARP's pathology report. These factors should guide treatment election and the need for closer postoperative follow-up.

Background

Prostate Cancer (PC) is the most common malign neoplasm in elderly men. Radical Prostatectomy (RP) has been able to provide favorable oncologic control and a prolonged survival for localized PC by reducing the risk of metastasis and local tumor progression [1].

Robotic-assisted surgery continues moving forward and promises to play a major role in the field of urology.

Advantages of this resource

Low blood loss, low postoperative pain, short hospital stay, and speedy patient recovery, have made Robotic-Assisted Radical Prostatectomy (RARP) more common in the treatment armamentarium for PC [2].

After RP, pathologic assessment of tumor's cellular differentiation (Gleason score) and pathologic stage, with preoperative PSA, can be used for staging patients in risk groups, predict outcomes (such as Biochemical Recurrence (BR) risk) and guide immediate treatment [3].

Avoiding Positive Surgical Margins (PSMs) after RP depicts the most important oncologic factor associated with the surgical procedure of RP for PC. Despite the debate of the influence of PSMs on long-term outcome, patients with PSMs have an increased risk for BR when compared to patients with Negative Surgical Margins (NSMs) [4].

Only a few studies (multi-institutional or meta-analysis) have shown a benefit of RARP *versus* Open Radical Prostatectomy (ORP) in reducing the rate of PSMs [5].

A series of patients without adjuvant treatment showed that those with PSMs have a 57.5% disease-free survival at 5 years [6]. However, disease-free survival at 10 years for those with focal

PSMs and extensive PSMs varies significantly between 64% to 38%, respectively [7].

Materials and Methods

An observational, descriptive, transversal, retrospective study was carried out. A review of clinical records from patients with diagnosis of PC that underwent RARP between December 2014 to December 2017 at our urology department was performed. The following variables were analyzed: age, PSA value, T clinical stage, biopsy's Gleason score, perineural invasion, lymphovascular invasion, surgical specimen's Gleason score, pathologic stage, and biochemical recurrence, with the aim of identifying the variables associated with PSMs. Continuous variables with normal distribution are expressed as mean and Standard Deviation (SD), otherwise they are expressed as median and range. Categorical variables are expressed as an absolute value and percentages. For the statistical analysis we used the Chi-squared test and SPSS v.23.0. Results were considered statistically significant if p value was <0.05.

Results

Patient demographics are shown in table 1 and 2. On statistical analysis, PSA level in patients with PSMs was higher than in patients with NSMs, having a significant correlation (p=0.021). When assessing the most frequent regions of PSMs, it was found that the most common site was the apex, followed by the posterior part of the prostate (Graph 1).

Table 1: Association between individual categorical variables with PSMs: univariate analysis.

	NSM	PSM	P value
Clinical Stage (cT)			
T1c	8	10	0.29
T2a	13	15	
T2b	1	6	
T2c	5	6	
T3a	0	3	
T3b	1	0	
Gleason score (biopsy)			
3+3=6	14	19	0.59
3+4=7	4	5	
4+3=7	4	10	
4+4=8	4	5	
4+5=9	1	0	
5+4=9	0	1	
5+5=10	1	0	
Gleason score after RARP			
3+3=6	8	19	0.57
3+4=7	7	5	
4+3=7	8	10	
4+4=8	1	5	
4+5=9	2	1	
5+4=9	2	0	
5+5=10	0	0	
Lymphovascular invasion			
Yes	3	7	0.5
No	25	33	

Table 2: Patient demographics.

Mean PSA(SD)	12.59 (12.13)
Mean age (SD)	64.2 (7.03)
Clinical stage (cT) (%)	
T1c	18 (26.4)
T2a	28 (41,1)
T2b	7 (10.2)
T2c	11 (16.1)
T3a	3 (4.4)
T3b	1 (1.4)
Gleason score (biopsy) (%)	
3+3=6	33 (48.5)
3+4=7	9 (13.2)
4+3=7	14 (20.5)
4+4=8	9 (13.2)
4+5=9	1 (1.4)
5+4=9	1 (1.4)
5+5=10	1 (1.4)
NCCN Risk group (%)	
Very low	3 (4.4)
Low	20 (29.4)
Favorable intermediate	17 (25)
Unfavorable intermediate	18 (26.4)
High	10 (14.7)
Gleason score after RARP (%)	
3+3=6	27 (39.7)
3+4=7	12 (17.6)
4+3=7	18 (26.4)
4+4=8	6 (8.8)
4+5=9	3 (4.4)
5+4=9	1 (1.4)
5+5=10	1 (1.4)
Pathologic stage (pT) (%)	
T2a	3 (4.4)
T2b	1 (1.4)
T2c	34 (50)
T3a	19 (27.9)
T3b	11 (16.1)
Surgical margins (%)	
Positive	40 (58.8)
Negative	28 (41.2)
PSMs site	
Prostate apex	28
Posterior	17
Anterior	7
Lateral	5
Prostate base	11

Biopsy's Gleason score underestimated the patients, since an increase in the Gleason score of the surgical specimens was found. However, the most frequent Gleason score in patients with PSMs was 3+3=6 (27.9%). No association was found when correlating surgical specimen's Gleason score and PSMs (P 0.57) (Graph 2).

The rate of PSMs for pT2a, pT2c, pT3a, pT3b was of 2/3 (66%), 19/34(55.8%), 9/19 (47.3%), and 10/11 (90.9%), respectively. PSMs rate had a significant association with pathologic stage (p=0.04) (Graph 3).

PSA had a significantly association in patients with PSMs compared to patients with NSMs (p=0.021) (Table 3). We also identified, the association between PSMs and perineural invasion, (p=0.04), however we did not found an association between PSMs and lymphovascular invasion (p=0.50) (Table 4).

40 patients had PSMs, of those: 22 underwent surveillance, 2 androgen deprivation therapy (ADT), 9 radiotherapy, and 7 trimodal therapy (surgery+radiotherapy+ADT). PSA persistence was found in 7 patients (10.2%), all of them with PSMs, considering the pathologic stage, 3 were pT3a, 3 pT3b, and 1 pT2c, assessing Gleason score, 5 had a score of 3+4=7, one 3+3=6, and another 4+4=8.Biochemical recurrence was found in 2 patients 9 months after RARP, both had PSMs and a pT2c pathologic stage.

Discussion

PSMs after RP in prostate cancer patients are considered a significantly predictive factor for BR and local recurrence, as well as for the necessity for adjuvant treatment.

In our study, the rate of PSMs is comparable with other reports. PSMs rate was significantly associated with tumor pathologic stage, as reported globally [8]. Other series report PSMs rates that oscillate between 11% to 37% after ORP, 11% to 30% after Laparoscopic Radical Prostatectomy (LRP), and 9.6% to 26% after RARP [9]. Coelho RF, et al. [10] remarked that clinical stage was the only preoperative independent variable associated with PSMs after RARP.

Liss M, et al. [11] informed that PSA (p=0.012) and PSA density (p=0.005) were predictive preoperative variables for PSMs after RARP.

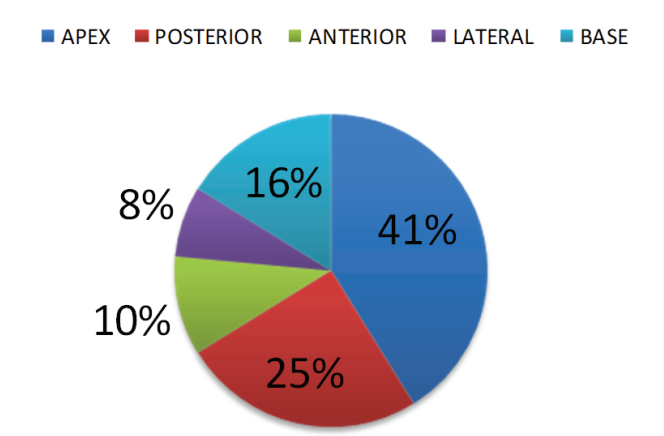
While most studies report similar PSMs rates for both surgical procedures, recent data has found that patients who undergo RARP are, in fact, more likely to have PSMs than those who undergo ORP [12].

In this study, pathologic stage, PSA and perineural invasion were significantly associated with PSMs rate.

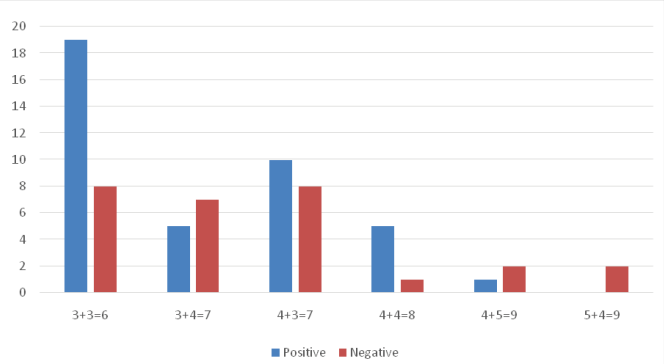
Tewari A, et al. [13] concluded in an extensive systematic review that PSMs rates are equivalent for both ORP and RARP. Despite discussion about the true incidence of PSMs in these surgical procedures, it is not known whether the finding of PSMs predicts a greater or lesser risk depending on whether ORP or RARP are performed.

No consensus has been reached on the most frequent PSMs region after ORP, LRP, and RARP, and which of these regions are associated with BR. According to multiple studies, the most common PSMs site after RARP is the prostate apex [14]. In our series, the most frequent region was the prostate apex (>40%), followed by the posterior region (25%), the finding of increased PSMs at the prostatic apex can be explained by at least 3 important surgical aspects: 1) there is no obvious anatomical boundary between the prostatic apex and the external urinary sphincter, therefore, to maximize urethral length, apical surgical margins are often compromised by the surgeon [15], 2) there is a low content of periprostatic fat in these region, making it easier to get PSMs, and 3) surgical manipulation may cause ink to reach the tumor, leading to a false PSMs [16]. On the contrary, it has also been reported that the posterior or postero-lateral region is the most common PSMs site after RARP [16]. Some series suggest that biochemical recurrence was independent of PSMs location [17,18]. Furthermore, it has been reported that PSMs located in the postero-lateral region are associated with worse prognosis [19].

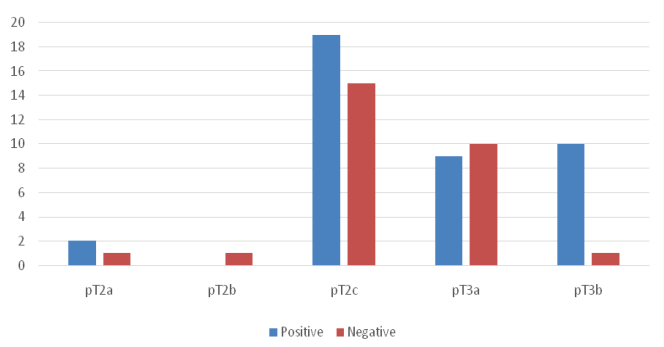
One study found a biochemical recurrence-free survival of 93.8% and 79.9% in patients with NSMs and PSMs, respectively [20]. In our study, only 2 patients developed BR within 9 months of follow-up, not



Graph 1: Positive surgical margins regions.



Graph 2: Patient's distribution according to Gleason score and surgical margins.



Graph 3: Relationship between pathologic stage and surgical margins.

Table 3: Association between PSA value and positive surgical margins (P=0.021).

		Surgical Margins		Total
		Negative	Positive	
PSA Value	<10 ng/mL	16	24	40
	>10<20 ng/mL	11	13	24
	>20 ng/mL	1	3	4
Total		28	40	68

Table 4: Association between perineural invasion and positive surgical margins (P=0.04).

		Margins		Total
		Negative	Positive	
Perineural Invasion	No	14	2	16
	Yes	14	38	52
Total		28	40	68

being able to establish an association with PSMs, we will have to do a long-term follow-up to assess the behavior of BR in these patients.

Studies that directly compare the effect of PSMs with metastasis-free survival and mortality are less conclusive. One of the largest studies, out of a registry of 65,633 patients, demonstrated a significant effect of PSMs on cancer-specific mortality (OR: 1,70, [1.32-2.18]) [21].

It seems that experience and careful attention to the surgical procedure also play an important role in decreasing the incidence of PSMs. Sooriakumaran P, et al. [22] reported a significant correlation between surgeon's experience and PSMs rate [22]. Ahlering TE, et al. [23] also reported a significant improvement in the PSMs rate associated with extensive surgical experience [23].

Limitations of the present study include its retrospective nature and the relatively small sample size. Furthermore, clinical examinations and surgical samples assessment were not performed by the same clinicians or pathologists. However, the initial experience of our urology department is reported.

Conclusions

It is important to consider preoperative PSA as a predictive factor for PSMs and correlate it with the pathologic result of the surgical specimen, these should guide treatment election and the necessity for closer postoperative follow-up.

Prospective studies with larger sample size should be encouraged. Furthermore, because the RARP learning curve may differ by surgeon, studies involving multiple surgeons are still necessary.

Conflict of Interest

None declared

References

1. Bivalacqua TJ, Pierorazio PM, Su LM (2009) Open, laparoscopic and robotic radical prostatectomy: optimizing the surgical approach. Surg Oncol 18: 233-241.
2. Rassweiler J, Hruza M, Teber D, Su LM (2006) Laparoscopic and robotic assisted radical prostatectomy--critical analysis of the results. Eur Urol 49: 612-624.
3. Graham J, Kirkbride P, Cann K, Hasler E, Prettyjohns M (2014) Prostate cancer: Summary of updated NICE guidance. BMJ 348: f7524.
4. Pfitzenmaier J, Pahernik S, Tremmel T, Haferkamp A, Buse S, et al. (2008) Positive surgical margins after radical prostatectomy: do they have an impact on biochemical or clinical progression? BJU Int 102: 1413-1418.
5. Di Pierro GB, Baumeister P, Stucki P, Beatrice J, Danuser H, et al. (2011) A prospective trial comparing consecutive series of open retropubic and robot-assisted laparoscopic radical prostatectomy in a centre with a limited case load. Eur Urol 59: 1-6.
6. Ploussard G, Agamy MA, Alenda O (2011) Impact of positive surgical margins on prostate-specific antigen failure after radical prostatectomy in adjuvant treatment-naïve patients. BJU Int 107: 1748-1754.
7. Lake AM, He C, Wood DP Jr (2010) Focal positive surgical margins decrease disease-free survival after radical prostatectomy even in organ-confined disease. Urology 76: 1212-1217.
8. Yossepowitch O, Briganti A, Eastham JA, Epstein J, Graefen M, et al. (2014) Positive surgical margins after radical prostatectomy: a systematic review and contemporary update. Eur Urol 65: 303-313.
9. Park JW, Won Lee H, Kim W, Jeong BC, Jeon SS, et al. (2011) Comparative assessment of a single surgeon's series of laparoscopic radical prostatectomy: conventional *versus* robot-assisted. J Endourol 25: 597-602.
10. Coelho RF, Chauhan S, Orvieto MA, Palmer KJ, Rocco B, et al. (2010) Predictive factors for positive surgical margins and their locations after robot-assisted laparoscopic radical prostatectomy. Eur Urol 57: 1022-1029.
11. Liss M, Osann K, Ornstein D (2008) Positive surgical margins during robotic radical prostatectomy: a contemporary analysis of risk factors. BJU Int 102: 603-608.
12. Williams SB, Chen MH, D'Amico AV, Weinberg AC, Kacker R, et al. (2010). Radical retropubic prostatectomy and robotic-assisted laparoscopic prostatectomy: Likelihood of positive surgical margin(s). Urology 76: 1097-1101.
13. Tewari A, Sooriakumaran P, Bloch DA, Seshadri-Kreaden U, Hebert AE, et al. (2012) 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 62: 1-15.
14. Patel VR, Coelho RF, Rocco B, Orvieto M, Sivaraman A, et al. (2011) Positive surgical margins after robotic assisted radical prostatectomy: a multi-institutional study. J Urol 186: 511-516.
15. Borin JF, Skarecky DW, Narula N, Ahlering TE (2007) Impact of urethral stump length on continence and positive surgical margins in robot-assisted laparoscopic prostatectomy. Urology 70: 173-177.
16. Kasraeian A, Barret E, Chan J, Sanchez-Salas R, Validire P, et al. (2011) Comparison of the rate, location and size of positive surgical margins after laparoscopic and robot-assisted laparoscopic radical prostatectomy. BJU Int 108: 1174-1178.
17. Sofer M, Hamilton-Nelson KL, Civantos F, Soloway MS (2002) Positive surgical margins after radical retropubic prostatectomy: the influence of site and number on progression. J Urol 167: 2453-2456.
18. Van den Ouden D, Bentvelsen FM, Boevé ER, Schröder FH (1993) Positive margins after radical prostatectomy: correlation with local recurrence and distant progression. Br J Urol 72: 489-494.

19. Hashine K, Ueno Y, Shinomori K, Ninomiya I, Teramoto N, et al. (2012) Correlation between cancer location and oncological outcome after radical prostatectomy. Int J Urol 19: 855-860.

20. Alkhateeb S, Alibhai S, Fleshner N, Finelli A, Jewett M, et al. (2010) Impact of positive surgical margins after radical prostatectomy differs by disease risk group. J Urol 183: 145-150.

21. Wright JL, Dalkin BL, True LD, Ellis WJ, Stanford JL, et al. (2010) Positive surgical margins at radical prostatectomy predict prostate cancer specific mortality. J Urol 183: 2213-2218.

22. Sooriakumaran P, John M, Wiklund P, Lee D, Nilsson A, et al. (2011) Learning curve for robotic assisted laparoscopic prostatectomy: a multi-institutional study of 3794 patients. Minerva Urol Nefrol 63: 191-198.

23. Ahlering TE, Eichel L, Edwards RA, Lee DI, Skarecky DW (2004) Robotic radical prostatectomy: a technique to reduce pT2 positive margins. Urology 64: 1224-1228.