Randomized trial comparing an anterograde versus a retrograde approach to open radical prostatectomy: results in terms of positive margin rate

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Abstract

Objectives: Surgical technique, patient characteristics and method of pathological review may influence surgical margin (SM) status. Positive surgical margin (SM+) rates of 14% to 46% have been reported in different radical retropubic prostatectomy (RRP) series. We evaluated the effect of an anterograde versus retrograde approach to RRP and specifically focused on the incidence of SM+.

Methods: From January 2003 to November 2007, we randomly assigned 200 patients with clinically localized prostate adenocarcinomas to undergo a retrograde (Group A) versus an anterograde (Group B) open RRP. All RRPs were performed at our institution by 2 surgeons. For all 200 patients, we evaluated a panel of clinical and pathological variables relating to their association with SM status.

Results: In Group A, 22% of cases after RRP showed a pT3 tumour and 39% of cases with a Gleason score ≥7 (4+3); in Group B, 20% of cases showed a pT3 tumour and 37% of cases with a Gleason score ≥7 (4+3) ($p > 0.10$). The incidence of SM+ was 18% in Group A and 14% in Group B ($p = 0.0320$). In Group A, 22.2% of cases with SM+ had multiple positive margins, whereas no cases in Group B showed multiple SM+. Regarding the localization of SM+, no difference was found between the 2 groups. In the multivariate analysis, only prostate-specific antigen ($p = 0.0090$ and $p = 0.0020$, respectively in the 2 groups) and pathological stage ($p < 0.0001$ in both groups) were significant and independently associated with SM+ occurrence.

Conclusion: In our experience, the anterograde approach to open RRP is associated with lower SM+ rates and no risk of multiple SM+ when compared with the retrograde approach.

Résumé

Objectifs : La technique chirurgicale, les caractéristiques du patient et la méthode d'examen pathologique peuvent tous avoir un impact sur le statut des marges chirurgicales. Des taux de marges chirurgicales positives de 14 à 46 % ont été notés lors de différentes séries de prostatectomies radicales rétropubiennes (PRR). Nous avons évalué l'effet d'un abord antérograde ou rétrograde, plus précisément sur l'incidence des marges chirurgicales positives.

Méthodologie : Entre janvier 2003 et novembre 2007, nous avons choisi au hasard 200 patients porteurs d'un adénocarcinome prostatique cliniquement localisé pour qu'ils subissent une PRR ouverte rétrograde (groupe A) ou antérograde (groupe B). Toutes les PRR ont été réalisées à notre établissement par deux chirurgiens. Pour chacun des 200 patients, nous avons évalué un ensemble de variables cliniques et pathologiques quant à leur lien avec le statut des marges chirurgicales.

Résultats : Dans le groupe A, 22 % des patients présentaient une tumeur pT3 et 39 %, un score de Gleason ≥ 7 (4+3) après la PRR; dans le groupe B, 20 % des patients présentaient une tumeur pT3 et 37 %, un score de Gleason ≥ 7 (4+3) ($p > 0,10$). L'incidence des marges chirurgicales positives était de 18 % dans le groupe A et de 14 % dans le groupe B ($p = 0,0320$). Dans le groupe A, 22,2 % des cas de marges chirurgicales positives étaient des cas multiples, tandis qu'aucun des patients du groupe B n'avaient de marges chirurgicales positives multiples. Aucune différence n'a été notée entre les deux groupes concernant l'emplacement des marges positives. Dans l'analyse multivariée, seuls l'antigène prostatique spécifique ($p = 0,0090$ et $p = 0,0020$, respectivement, dans les deux groupes) et le stade pathologique ($p < 0,0001$ dans les deux groupes) étaient significatifs et liés de façon indépendante à la présence de marges chirurgicales positives.

Conclusion: Selon nos observations, l'abord antérograde est lié à des taux inférieurs de marges chirurgicales positives et à un risque nul de charges chirurgicales positives multiples, en comparaison avec l'abord rétrograde.

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Introduction

Despite the widespread use of prostate-specific antigen (PSA) based tumour detection methods and improvements in surgical techniques, positive surgical margins (SM+) are frequently observed after radical retropubic prostatectomy (RRP). Positive surgical margin rates of 14% to 46% have been reported in RRP series.[1] Several studies demonstrate that SM+ are significantly associated with the risk of biochemical, local and systemic disease progression.[2,3] Certainly, surgical technique can affect margin status; therefore, surgical refinement to reduce SM+ may be important in improving oncological outcome.[4] Stephenson and colleagues[5] and Klein and colleagues[6] reported a reduction in SM+ rate associated with a modification of the surgical extirpative procedure. Many other surgeons have emphasized the importance of the surgical technique in reducing the incidence of SM+.[5,6,7] From 1995, we developed and used an antero-

grade approach to open RRP (from the original method described by Campbell[8]) with modifications based on more recent knowledge of pelvic anatomy.[9] A similar approach was also described by Serni and colleagues.[10]

The purpose of the present study was to evaluate the direct effect of an anterograde versus retrograde approach to open RRP, specifically on the incidence of SM+, in patients with clinically localized prostate adenocarcinoma considered for RRP. Although results in terms of biochemical failure or population survival are important, we did not address these results in this paper.

Methods

This study is a prospective single centre (2 surgeons) one directly comparing SM+ rate and location between an anterograde versus retrograde approach to open RRP. Between January 2003 and November 2007, 200 patients, diagnosed with clinically localized (Tlc-T2, NOMO) prostate adenocarcinoma, were considered eligible for RRP and included in this study. Using a computer-generated randomized table, we assigned 100 patients to undergo a retrograde open RRP (Group A) and 100 patients to undergo an anterograde open RRP (Group B) at our institution. To reduce the possibility of selection bias, we consecutively enrolled only patients who came to the clinic of the 2 surgeons (AS and CC). All patients undergoing RRP by these 2 surgeons during the study period were offered this protocol.

Their clinical and pathological data were entered into the institutional prostate cancer database. Patients who received neoadjuvant hormonal treatment were excluded from the study. No cases received radiation therapy preoperatively. The inclusion criteria for this study were patients with histologically proven clinically localized (Tlc-T2, NOMO) prostate adenocarcinoma considered for RRP who did not receive neoadjuvant hormonal or radiation treatments.

All 200 cases met the inclusion criteria. We also tallied their profile based on patient age, pre-treatment PSA, prostate volume, clinical stage, pathological Gleason grade and stage, surgical margin status, nerve-sparing (NS) procedure and lymph-node status. Tumour volume was not evaluated.

Preoperatively, all cases were evaluated with digital rectal examination, transrectal ultrasonography (TRUS), computed tomography scan and bone scan. In all men, serum was obtained for PSA testing before prostate manipulation. Prostate volume was preoperatively evaluated at TRUS using the ellipsoid method. Patient characteristics are reported in Table 1. All patients signed an informed consent form.

Pathological workup

Prostatectomy tissue block examinations were routinely performed. After the prostate was removed, we inked the surface of the specimen and the entire prostatectomy specimen was analysed at our institution. In brief, prostatectomy specimens were fixed in 10% buffered formalin for 2 to 3 days and were cut by the whole organ step-section technique at 2-mm intervals in a plane perpendicular to the tip of seminal vesicles. Cancer was considered organ-confined as long as the capsule was not penetrated, and a surgical margin was considered positive when neoplastic cells reached the inked surface.[11-13] As in previous studies[12] the location of SM+ was classified in the apex, the lateral and in other locations (anterior, posterior, bladder neck). We also subdivided margin status into negative (-), solitary positive (+) and multiple positive (++), as is performed in previous studies.[11] The pathological evaluation for all cases was performed by a single pathologist at our institution, with an expertise in prostate cancer.

Surgical technique

All 200 cases were submitted to open RRP at our institution by 2 surgeons (AS and CC). To reduce the potential of surgeon-bias on our results, both surgeons had similar, long-term experience either with the retrograde or with the anterograde approach. Both surgeons performed either the retrograde or the anterograde RRP. The RRP was performed in all patients under general anesthesia. For the retrograde approach to RRP, the surgeons applied the anatomic technique described by Walsh and colleagues[14] with more recent modifications. For the anterograde approach to RRP, they used the technique previously described.[9]

In all 200 cases, after a midline incision, a limited bilateral external iliac-obturator lymphadenectomy was performed before proceeding with RRP. In all cases, RRP was performed either with or without nerve sparing (NS) (mono or bilateral). The neurovascular bundle was transected when intraoperatively examination revealed palpable induration that was believed to encroach on the ipsilateral bundle. In both groups (retrograde and anterograde), the bladder neck was not conserved and the urethra-vesical anastomosis was performed with 5 2-0 Vicryl (Johnson & Johnson, Somerville, NJ) interrupted sutures, with a 5/8 needle, around a Foley 18 Ch catheter.

Follow-up

Our follow-up database included PSA measurements at 2-month intervals, starting from 30 days from RRP. Outcomes regarding urinary and sexual function were evaluated at the 1-month mark, during the follow-up visit. In cases with the NS technique who did not postoperatively receive radiation or hormone therapies, we evaluated erectile function at 12-month interval from RRP to estimate potency rates. All these cases were homogeneously rehabilitated after RRP using phosphodiesterase type-5 inhibitors. We evaluated the return of

Table 1. Preoperative and postoperative characteristics of cases in Group A (retrograde) and Group B (anterograde)

Variable	Group A	Group B	*p* value
No. cases (%)	100	100	
Age, yrs Mean ± SD (median) (range)	65.94±4.78 (66.50) (50.0–72.0)	64.10±5.25 (64.50) (50.0–72.0)	0.1732
PSA, ng/mL Mean ± SD (median) (range)	12.52±5.38 (12.0) (2.0–25.0)	13.36±5.61 (12.0) (4.0–25.0)	0.4331
Prostate volume, mL Mean ± SD (median) (range)	39.10±8.29 (40.0) (30.0–60.0)	38.50±6.87 (40.0) (30.0–60.0)	0.7688
Pathological stage (%) pT2 pT3	 78 (78.0) 22 (22.0)	 80 (80.0) 20 (20.0)	0.4354
Gleason score (%) ≤7 (3+4) ≥7 (4+3)	 61 (61.0) 39 (39.0)	 63 (63.0) 37 (37.0)	0.3220
Nerve sparing (%) No nerve sparing Unilateral Bilateral	 35 (35.0) 34 (34.0) 31 (31.0)	 35 (35.0) 32 (32.0) 33 (33.0)	0.7835
Lymph node status (%) N- N+	 97 (97.0) 3 (3.0)	 98 (98.0) 2 (2.0)	0.6320
Seminal vesicle invasion (%) Negative Positive	 95 (95.0) 5 (5.0)	 97 (97.0) 3 (2.0)	0.4450
SM+ (%) Apical (% of SM+) Lateral (% of SM+) Other (% of SM+) Multiple (%)	18 (18.0) 5 (27.8) 12 (66.7) 1 (5.5) 4 (22.2)	14 (14.0) 4 (28.6) 9 (64.3) 1 (7.1) 0 (0)	0.0320 0.570 0.5520 0.2430 0.0001

PSA = prostate-specific antigen; SM = surgical margin. Note: These results are employing the Mann-Whitney test.

urinary continence at the 6-month interval; continence was defined as needing no pads or other protection.

Statistical analysis

The 200 cases considered for RRP were randomized to Group A (retrograde approach) and Group B (anterograde approach). For all 200 patients, we evaluated a panel of clinical and pathological variables concerning their association with SM status. Parameters were age, prostate volume, preoperative PSA, NS procedure, pathological stage (pT2 vs. pT3, seminal vesicle and lymph-node involvement), Gleason score at surgery (≤7 [3+4] vs. ≥7 [4+3]) and SM. In particular, margin status was stratified as negative (SM-) and positive (SM+). Positive surgical margins were then subdivided as apical (ASM+), lateral (LSM+), other (OSM+) and multiple positive margins (MSM+). This model was calculated by either combining all positive margin subgroups into 1 variable or considering each of them separately. The mean differences between the groups were analysed with the Mann-Whitney test. Probability values at <0.05 were considered to be statistically significant. Spearman coefficients and logistic univariate analysis were used to determine association of the different clinical and pathological parameters with SM status. All variables were also included in logistic multivariate models. Odds ratio (OR), with a 95% confidential interval (CI) of SM+, was evaluated. GraphPad InStat (GraphPad Software Inc., La Jolla, CA) statistical software was used.

Results

Group A (retrograde) and Group B (anterograde) were comparable in terms of age, preoperative total serum PSA, prostate volume, pathological stage and Gleason score distribution (Table 1). In particular after RRP, 22% in Group A and 20% of cases in Group B showed a pT3 tumour. The positive lymph node (N+) rate was very low in both groups (3% in

Table 2. Preoperative and postoperative characteristics in our population stratified according to margin status

	Margins status stratification					
	Group A (retrograde)			Group B (anterograde)		
Parameter	**SM-**	**SM+**	***p* value**	**SM-**	**SM+**	***p* value**
No. cases (%)	82 (82.0)	18 (18.0)		86 (86.0)	14 (14.0)	
Age, yr Mean ± SD (median) (range)	66.31±4.84 (67.0) (50.0-72.0)	64.50±4.81 (65.0) (55.0–72.0)	0.0750	64.22±5.04 (64.50) (50.0–72.0)	63.35±6.60 (64.0) (52.0–72.0)	0.3220
PSA, ng/mL Mean ± SD (median) (range)	11.91±5.10 (11.70) (2.0-20.0)	15.43±5.88 (15.0) (5.8–25.0)	0.001	12.63±5.25 (12.0) (4.0–20.0)	15.80±5.86 (15.85) (5.71–25.0)	0.001
Prostate volume, mL Mean ± SD (median) (range)	37.31±7.37 (40.0) (30.0-50.0)	47.22±7.51 (50.0) (40.0–60.0)	0.001	38.37±7.0 (40.0) (30.0–60.0)	39.28±6.15 (40.0) (30.0–50.0)	0.3530
Pathological stage (%) pT2 pT3	 69 (84.1) 13 (15.9)	 9 (50.0) 9 (50.0)	0.001	 77 (89.5) 9 (10.5)	 3 (21.4) 11 (78.6)	0.0001
Gleason score (%) ≤7(3+4) ≥7(4+3)	 51 (62.2) 31 (37.8)	 10 (55.6) 8 (44.4)	0.4732	 54 (62.8) 32 (37.2)	 9 (64.3) 5 (35.7)	0.6840
Nerve sparing (%) No nerve sparing Unilateral Bilateral	 31 (37.8 25 (30.5) 26 (31.7)	 4 (22.2) 9 (50.0) 5 (27.8)	0.1230	 33 (38.4) 23 (26.7) 30 (34.9)	 2 (14.3) 9 (64.3) 3 (21.4)	0.0940
Lymphnode status (%) N- N+	 80(97.6) 2 (2.4)	 17 (94.4) 1 (5.6)	0.4260	 85 (98.8) 1 (1.2)	 13 (92.9) 1 (7.1)	0.6438
Seminal vesicle invasion (%) Negative Positive	 80 (97.6) 2 (2.4)	 15 (83.3) 3 (16.7)	0.0345	 85(98.8) 1(1.2)	 12(85.7) 2(14.3)	0.0372

SM = surgical margin; SD = standard deviation. Note: These results are employing the Mann-Whitney test.

Group A and 2% in Group B). A NS procedure was performed in 65% of cases in both groups (Table 1). The positive surgical margin rate was significantly lower in Group B (14%) than in Group A (18%) ($p = 0.0320$). This difference, in favour of Group B, was particularly evident in pT2 cases (Group A: 11.5% SM+ = 9 cases; Group B: 3.7% SM+ = 3 cases), whereas it was not present for pT3 cases (Group A: 40.9% SM+ = 9 cases; Group B: 55.0% SM+ = 11 cases). Regarding the location of SM+, no statistically significant difference ($p > 0.20$) between the two groups was found; in both groups, the most common location of SM+ was lateral (Group A 66.7%; Group B 64.3%) followed by the apex (Group A 27.8%; Group B 28.6%). No case of multiple SM+ was reported in the anterograde (Group B) group, whereas in the retrograde (Group A) group a 22.2% rate of multiple SM+ was described ($p = 0.0001$).

Table 2 shows preoperative and postoperative characteristics in our population stratified according to margin status. Preoperatively, in both groups, PSA was significantly higher ($p = 0.001$) in SM+ than in SM- cases. Postoperatively, in both groups, the distribution of pathological stage and seminal vesicles invasion were significantly different between SM+ and SM- cases ($p = 0.001$ and $p < 0.040$, respectively) (Table 2). Only in Group A (retrograde), did we find the prostate volume to be significantly ($p = 0.001$) higher in the SM+ (median 50.0 mL) than in the SM- (median 40.0 mL) cases.

Table 3 shows the results of univariate logistic analysis of factors predicting SM+. In the univariate analysis, in both groups, the preoperative PSA, pathological stage, seminal vesicle invasion, NS involvement and Gleason score were found to be significantly associated with and to be significant predictors of SM+; it is worth noting that age was not significantly associated with SM+. In Group A, prostate volume was also significantly associated with SM+ status, whereas in Group B, no significant association was found (Table 3). Regarding the NS procedure, we found that the

Table 3. Association of parameters with positive surgical margin status

	Retrograde				Anterograde			
Parameter	**r**	**OR**	**95% CI**	***p* value**	**r**	**OR**	**95% CI**	***p* value**
Age	-0.0330	--	-0.2377/0.1744	0.7490	0.0300	--	-0.2307/0.1731	0.7668
PSA	0.2575	--	0.1025/0.4040	0.0036	0.3121	--	0.1163/0.4845	0.0017
Prostate volume	0.2015	--	0.1052/0.3174	0.0108	0.0636	--	-0.1403/0.2623	0.5296
Pathological stage	0.3167	--	0.1224/0.4876	0.0013	0.5703		0.4161/0.6926	<0.0001
pT2		1.0				1.0		
pT3		1.40	1.10- 2.25	0.0010		1.80	1.30-2.60	0.0001
Gleason score	0.0523		-0.1514/0.2518	0.6053	-0.0107		-0.2124/0.1918	0.7155
≤ 7 (3+4)		1.0				1.0		
≥ 7 (4+3)		1.05	0.93- 1.12	0.6140		1.02	0.92-1.10	0.6530
Seminal vesicles	0.2508		0.0512/0.4311	0.0118	0.2219		0.0313/0.3615	0.0272
Negative		1.0				1.0		
Positive		1.45	1.10- 2.35	0.0120		1.36	1.05- 2.15	0.0254
Lymphonode status	-0.0824		-0.2799/0.1217	0.4151	-0.0709		-0.2692/0.1331	0.4830
N-		1.0				1.0		
N+		1.04	0.92- 1.09	0.5050		1.04	0.93-1.11	0.5130
Nerve sparing	0.0293		-0.1738/0.2301	0.5722	0.0471		-0.1565/0.2469	0.5415
No nerve sparing		1.0				1.0		
Unilateral		1.20	1.0-1.300.92-	0.0430		1.25	1.0-1.38	0.0390
Bilateral		1.02	1.10	0.6830		1.04	0.94-1.15	0.6513

r = Spearman coefficient; OR = odds ratio; 95% CI = 95% confidence interval; PSA = prostate-specific antigen.
Note: These results are employing the Spearman coefficients, logistic and univariate analysis).

OR for SM+ significantly increased for the unilateral and not for the bilateral NS procedure in both groups (Table 3). In particular, in 9 of the 34 cases in Group A (26.5%) and 9 out of the 32 cases in Group B (28.1%) who had unilateral NS showed SM+. Of these SM+ cases, only 2 (5.9%) in Group A and 1 (3.1%) in Group B showed a LSM+ on the same side as the NS. In the multivariate analysis, in both groups, only PSA ($p = 0.0090$ and $p = 0.0020$, respectively) and pathological stage ($p < 0.0001$ in both groups) were significantly and independently associated with SM+ occurrence.

Total operative time was significantly ($p < 0.0001$) lower in Group A (mean 98.5±9.4 mins; median 100 min; range 80-140 mins) than in Group B (119.8±13.1 mins; median 120 mins; range 100-150 mins). Similarly blood loss was significantly ($p < 0.0001$) lower in Group A (means 702.0±206.4 mL; median 700 mL; range 400-1400 mL) than in Group B (mean 813.0±206.8 mL; median 800 mL; range 400-1400 mL). No major intraoperative and perioperative complications were reported in both groups. There was no perioperative mortality. Anastomotic strictures were similarly ($p > 0.05$) reported in both groups (Group A 4.0%; Group B 3.0%). At the 6-month interval from RRP, a similar ($p > 0.05$) recovery in urinary continence (no pads) was obtained in the 2 groups (Group A 94%; Group B 96%). In both groups, recovery of continence was not significantly associated with the performance of NS surgery, PSA, Gleason score, pT stage and margin status ($p > 0.05$), but significantly associated with patient age and prostate volume ($p < 0.01$). At the 12-month interval from RRP, a similar ($p > 0.05$) rate of return of erections was found in both groups (Group A bilateral NS 74.2%, unilateral NS 52.9%; Group B bilateral NS 78.8%, unilateral NS 53.1%). In both groups, the return of erections was significantly associated with patient age ($p < 0.001$), but not with the other clinical and pathological parameters ($p > 0.05$).

Discussion

This is the first single centre randomized study directly comparing a retrograde versus an anterograde open technique for RRP, in terms of surgical margins. We reported a significantly lower ($p = 0.0320$) incidence of SM+ using the anterograde (SM+ = 14%) compared with the retrograde (SM+ = 18%) access to RRP. In major RRP series, SM+ rates of 14% to 46% were found.[1,2] The discrepancies among these studies are probably multifactorial. Specimen processing, patient selection and surgical technique vary among institutions. Regarding specimen processing, some groups use whole mount histological preparations, while others advocate routine sectioning. In the present study, all our pathological evaluations were done by a single pathologist

with a special expertise in prostate cancer. As defined by different groups.[11-13,15] We used a whole organ step-section technique at 2-mm intervals; a SM was considered positive when neoplastic cells contacted the inked surface.

For some time, patient selection had been deemed the most important factor in RRP outcome. The selection criteria have become more stringent over the last decade and some series of RRP are being confined to patients with T1c disease, moderate-grade disease and PSA <10 ng/mL.[16] Our experience, however, reflects a less selected patient population. In particular, the only selection was based on a clinically localized prostate cancer and no neoadjuvant hormonal or radiation treatments. In fact, 22% in the retrograde RRP group and 20% in the anterograde RRP group of our cases showed a pT3 disease; a Gleason score ≥7 (4+3) was found in 39% and 37%, respectively in the 2 groups; in both groups, the median PSA was 12 ng/mL. Moreover, cases randomized to retrograde versus anterograde RRP were comparable in terms of clinical and pathological parameters.

Some publications have described surgical technique modifications to reduce the incidence of SM+, in particular at the apical level.[7,17-19] All these studies suggest that the surgical technique can significantly affect SM status, particularly when the technique improves dissection at the apex and the posterolateral pedicles. In our study, we did not propose a specific single technique arrangement, but we analysed 2 different approaches to RRP. To reduce the possibility that other surgical factors may influence our results, all RRPs were performed at the same institution by only 2 surgeons for both groups, using a similar surgical procedure (i.e., no bladder neck conservation, section of puboprostatic ligaments, same lymph node dissection).

On the basis of the accurate pathological method used to determine SM positivity and despite the percentage of cases with adverse prognostic factors, we underline that an anatomical anterograde dissection of the prostate at RRP is associated with lower SM+ rate (14%) when compared with the retrograde technique (18%). This difference was particularly significant in pT2 cases, where only a 3.7% rate of SM+ was reported using the anterograde approach (11.5% SM+ in the retrograde group). On the contrary, in pT3 cases SM+ rate was higher in the anterograde (55.0%, 11 cases) than in the retrograde (40.9%, 9 cases) group. It is also important to underline that the anterograde RRP was not associated with multiple SM+ (0%), whereas a 22.2% rate of multiple SM+ was described using the retrograde RRP. No difference regarding the site of SM+ was found between the 2 groups.

As in previous experiences,[10,18,19] the most commonly reported sites for SM+ were the lateral surface and the apex. In a population of 84 cases (no comparison with retrograde RRP), similar data with a similar anterograde RRP were reported by Serni and colleagues,[10] showing a SM+ rate of 13%. We suggest that, during RRP, the anterograde point of view allows a better visual and digital determination of the points most at risk for SM+. Starting the procedure at the vesical-prostatic junction (after the dissection of vas deferens, seminal vesicles and Denonvillier's fascia), we found that the blunt dissection of the posterior wall of the prostate can be better controlled until the apex of the prostate is reached. Following the upward traction of the prostate allows complete visualization and digital exploration of the lateral boundaries of the gland and the prostatic pedicles, always from a large field related to the anterograde point of view. Also in a NS procedure, the plane between neurovascular boundles and the prostate is better defined towards the base of the gland, where the bundles begin to lateralize. The early posterior and lateral dissection facilitate the apical dissection. In fact, with the anterograde technique, the apex is approached at the end of the procedure, when the prostate remains attached at the anterior only, and the mobility of the prostate facilitates visual inspection and palpation of the apex. These surgical steps on the anterograde RRP technique requires more attention than retrograde technique and this aspect can explain the difference between the 2 groups in terms of total operative time ($p < 0.0001$), but the benefits obtained from these technical points of the anterograde RRP could be translated in the lower incidence of SM+ in all these sites. These same surgical steps, from an anterograde point of view, can explain the difference between the 2 groups in terms of bleeding ($p < 0.0001$). In the anterograde approach, starting the procedure at the vesical-prostatic junction, an additional risk of bleeding is represented by this initial step. After the dissection of vas deferens, seminal vesicles and Denonvillier's fascia, the blunt dissection of the posterior wall of the prostate is obtained. In these anatomical areas, if some vessels, such as anterior prostatic arteries, were approached at the beginning of the surgery, as in anterograde technique, it may explain the increased bleeding in group B; in group A, these same steps were approached at the end of the surgery and were more controllable.

We also analysed the influence of different adverse prognostic factors on SM+ status. Stratifying both groups according to SM, as with the univariate analysis independently to the surgical approach, preoperative PSA, pathological stage and seminal vesicle invasion were significantly associated with, and were significant predictors of SM+. In particular the OR of SM+ significantly increased in pT3 compared with pT2, in the positive versus negative seminal vesicle cases. We underline that, only using the retrograde approach, prostate volume significantly and positively influenced SM+ rate. On the contrary, the anterograde technique to RRP, starting at the vesical-prostatic junction and approaching the apex only at the end when the prostate is mobilized, maintains a low SM+ rate independent of prostate volume.

Different studies analysed the impact of NS procedure on SM+ rates.[12] In the recent study of Palisaar and colleagues,[12] in pT2 cancers, the incidence of SM+ did not differ significantly in NS versus no NS cases, whereas in pT3 cases SM+ rate was higher in NS than in no NS procedures. Therefore, Palisaar and colleagues[12] reported that the NS technique is associated with SM+ results, dependent on the pathological stage of the tumour. In our experience, the anterograde or retrograde approach did not modify the impact of NS technique on SM status. In particular, in both groups, distinguishing unilateral and bilateral NS procedures, at the univariate analysis the OR for SM+ significantly increased only for unilateral and not for bilateral NS. However, in unilateral NS groups, only 2 cases in Group A and 1 case in Group B showed a SM+ on the same side as the NS. As in the study of Palisaar and colleagues,[12] at the multivariate analysis and including the pathological stage, the NS procedure did not influence SM status.

Conclusion

The present work has been specifically focused on the impact of an anterograde versus retrograde approach to RRP on SM status. In our experience, we showed that an anatomical anterograde technique for RRP is associated with a lower incidence of SM+ and with no incidence of multiple SM+. However, a locally advanced pathological stage remains a significant factor in the determination of SM+ rate independent of the surgical anterograde or retrograde approach. On the contrary, only the anterograde RRP maintains a low SM+ rate independent of prostate volume.

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References

1. Pettus JA, Weight JC, Clinton JT, et al. Biochimical failure in men following radical retropubic prostatectomy: Impact of surgical margin status and location. *J Urol* 2004;172:129-32.
2. Epstein JI. Incidence and significance of positive margins in radical prostatectomy specimens. *Urol Clin North Am* 1996;23:651-8.
3. Chang SS, Cookson MS. Impact of positive surgical margins after radical prostatectomy. *Urology* 2006;68:249-56.
4. Eastham JA, Kattan MW, Riedel E. Variations among individual surgeons in the rate of positive surgical margins in radical prostatectomy specimens. *J Urol* 2003;170:2292-5.
5. Stephenson RA, Middleton RG, Abbott TM. Wide excision (non nerve sparing) radical retropubic prostatectomy using an initial perirectal dissection. *J Urol* 1997;157:251-5.
6. Klein EA, Kupelian PA, Tuason L, et al. Initial dissection of the lateral fascia reduces the positive margin rate in radical prostatectomy. *Urology* 1998;159:1281-5.
7. Soulie M, Seguin P, Benoit JM. Impact of a modified apical dissection during radical retropubic prostatectomy on the occurrence of positive surgical margins: a comparative study in 212 patients. *Urology* 2001;58:217-21.
8. Campbell EW: Total prostatectomy with preliminary ligation of the vascular pedicles. *J Urol* 1959;81:464-7.
9. Sciarra A, Gentile V, De Matteis A, et al. Long-term experience with an anatomical anterograde approach to radical prostatectomy: results in terms of positive margin rate. *Urol Int* 2008;80:151-6.
10. Serni S, Masieri L, Lapini A, et al. A low incidence of positive surgical margins in prostate cancer at high risk of extracapsular extension after a modified anterograde radical prostatectomy. *BJU Int* 2004;93:279-83.
11. Matsui Y, Utosonomiya N, Ichioka LK, et al. Risk stratification after radical prostatectomy in men with pathologically organ-confined prostate cancer using volume weighted mean nuclear volume. *Prostate* 2005;64:217-23.
12. Palisaar RJ, Noldus J, Graefen M, et al. Influence of Nerve Sparing procedure during radical prostatectomy on margin status and biochemical failure. *Eur Urol* 2005;47:176-84.
13. Watson RB, Civantos F, Soloway MS. Positive surgical margins with radical prostatectomy:detailed pathological analysis and prognosis. *Urology* 1996;48:80-8.
14. Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function:anatomical and pathological considerations. *Prostate* 1983;4:473-85.
15. Epstein JI, Sauvageot J. Do close but negative margins in radical prostatectomy specimens increase the risk of postoperative progression? *J Urol* 1997;157:241-9.
16. Connolly SS, O'Toole GC, O'Malley KJ, et al. Positive apical surgical margins after radical retropubic prostatectomy, truth or artefact? *Scand J Urol Nephrol* 2004;38:26-31.
17. Shah O, Melamed J, Lepor H: Analysis of apical soft tissue margins during radical retropubic prostatectomy. *J Urol* 2001;165:1943-9.
18. Laven BA, Alsikafi NF, Yang XJ, et al. Minor modifications in apical dissection of radical retropubic prostatectomy in patients with clinical stage T2 prostate cancer reduce positive surgical margin incidence. *Urology* 2004;63:95-8.
19. Richman M, McLaughlin S, Maygarden S, et al. Initial incision of lateral pelvic fascia and early ligation of vascular pedicles during radical prostatectomy: potential to reduce positive margin rates. *BJU Int* 2005:95:40-5.

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