The effect of local compression and topical epinephrine on perioperative bleeding and degree of urinary extravasation on postoperative cystogram following radical retropubic prostatectomy

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Objective: *To evaluate the efficacy of local compression and topical epinephrine in controlling perioperative bleeding during open radical retropubic prostatectomy (ORRP) and its impact on the degree of urinary extravasation on initial postoperative cystogram.*

Methods: *Between September 2005 to March 2009, 476 men underwent ORRP performed by a single surgeon. Group 1 (n = 200) underwent ORRP between September 2005 and November 2006 without pelvic compression; Group 2 (n = 76) underwent ORRP between November 2006 and May 2007 and a dry laparotomy pad was positioned in the pelvis immediately prior to abdominal wound closure; Group 3 (n = 200) underwent ORRP between May 2007 and March 2009 with a epinephrine soaked laparotomy pad positioned in the pelvis prior to abdominal wound closure. Hematocrit values were obtained prior to anesthesia induction, upon arrival in the recovery room and at hospital discharge in order to estimate intraoperative and postoperative bleeding. The number of allogenic and autologous units transfused was recorded. The utility of compressing the pelvis with a pad was examined by comparing estimated postoperative bleeding between Group 1 versus Groups 2 and 3 and the hemostatic utility of soaking the pad in epinephrine was examined by comparing Group 2 versus 3. Systolic and diastolic blood pressure and pulse measurements were obtained at baseline and 5 and 10 minutes after introducing the epinephrine pad. The relationship between estimated blood loss and degree of extravasation on initial postoperative cystogram was investigated.*

Results: *Estimated intraoperative, postoperative and total blood loss (mean change in Hct) was 12.2, 2.3, 14.2, in Group 1, 10.0, 1.5, 11.1 in Group 2, and 10.8, 2.1, and 12.6 in Group 3. Estimated intraoperative and total blood loss was significantly less in the men treated with a compression pad (Groups 2 and 3) versus no pad (Group 1). There were no significant differences in number of patients transfused, the number of units transfused or the degree of extravasation on postoperative cystograms between Group 1 versus Group 2 and 3 or Group 2 versus 3. However, postoperative bleeding was significantly less in Group 2 compared to Group 3. Mean systolic and diastolic blood pressure and pulse values were unchanged from baseline after epinephrine use.*

Conclusions: *Local compression of the pelvis with or without epinephrine prior to abdominal wound closure does not appear to have beneficial effects on reducing postoperative bleeding and decreasing the degree of urinary extravasation on cystogram following ORRP. While the use of topical epinephrine appears to be safe and relatively inexpensive, at the concentrations used in our study it does not appear to facilitate postoperative hemostasis.*

Key Words: prostate cancer, radical prostatectomy, epinephrine, hemostasis

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Introduction

Historically, significant blood loss was associated with open radical retropubic prostatectomy (ORRP) with reported transfusion rates up to 89%.[1] The anatomic

description of the dorsal venous complex along with a surgical technique for early control of this structure greatly diminished blood loss during ORRP.[2-4] In the modern era, transfusion rates following ORRP are typically less than 4%.[5,6] Blood loss may occur during the surgical procedure or following wound closure. The volume of total blood loss influences requirement for allogenic blood transfusion. Since the hematocrit level at the time of hospital discharge has been shown to be a primary factor influencing time to return to work and physical activities,[7] total blood loss also impacts convalescence. Postoperative bleeding accounts for approximately 20% of total blood loss attributable to ORRP.[7,8] Therefore reducing postoperative blood in selected cases would likely decrease both the incidence of re-operation for control of life threatening hemorrhage[8] and the requirement for allogenic blood transfusion while facilitating the pace of recovery. Another consequence of postoperative bleeding is the delayed healing of the vesicourethral anastomosis mediated via distractive forces of the pelvic hematoma.[9] Therefore minimizing postoperative bleeding following ORRP would likely yield beneficial clinical advantages.

In some cases, postoperative bleeding occurs despite meticulous efforts to secure hemostasis at the time of wound closure. The objective of the present study was to determine if compressing the operative field with or without an epinephrine soaked laparotomy pad immediately prior to wound closure diminishes postoperative bleeding and its consequences.

Methods

Between September 12, 2005 to March 23, 2009, 476 men underwent an ORRP by a single surgeon using a previously described technique.[10] All men signed informed consent to participate in our IRB approved NYU Radical Prostatectomy Longitudinal Outcomes Study. All outcomes captured in this retrospective review were exported for the database. Following tying of the anastomotic sutures and prior to abdominal wound closure, a meticulous attempt was made to secure hemostasis in all cases. Group 1 represents the 200 consecutive cases performed between September 2005 and November 2006 where the abdominal wound was closed without prior positioning of laparotomy pads in the pelvis. Group 2 represents the 76 consecutive cases performed between November 2006 and May 2007 where a dry laparotomy pad was positioned in the pelvis immediately prior to abdominal wound closure. Group 3 represents the 200 consecutive

TABLE 1. **Baseline characteristics of study population**

Characteristics	**Group 1 (n = 200)**	**Group 2 (n = 76)**	**Group 3 (n = 200)**	**p value**	
				Group 1 vs 2+3	**Group 2 vs 3**
Mean age (yrs) ± SE	58.23 ± 0.484	57.86 ± 0.774	59.82 ± 0.554	0.122	0.053
Mean body mass index (kg/m^2) ± SE	27.08 ± 0.249	26.52 ± 0.656	26.67 ± 0.371	0.305	0.832
Mean serum PSA (ng/mL) ± SE	5.71 ± .306	6.97 ± 0.936	5.66 ± 0.344	0.525	0.103
No. PSA (ng/mL) (96)					
≤ 4.0	62 (31.0)	19 (24.7)	66 (33.2)	0.850	0.275
4.1-10.0	120 (60.0)	50 (64.9)	120 (60.3)		
> 10	18 (9.0)	8 (10.4)	13 (6.5)		
No. Gleason score (96)					
≤ 6	90 (45.5)	27 (35.1)	70 (35.4)	0.007	0.999
7	102 (51.5)	43 (55.8)	110 (55.6)		
≥ 8	6 (3.0)	7 (9.1)	18 (9.1)		
No. pathologic stage (96)					
< Pt2	1 (0.5)	0	0	0.164	0.216
pT2	151 (76.6)	58 (76.3)	134 (68.7)		
pT3	45 (22.8)	18 (23.7)	61 (31.3)		

cases performed between May 2007 and March 2009 where a laparotomy pad soaked in an epinephrine solution was positioned in the pelvis immediately prior to wound closure. The epinephrine solution was made by diluting 1 cc of 1:1000 epinephrine into 100 milliliters of normal saline. In all cases, the laparotomy pad was tightly packed into the pelvis and left in place for 10 minutes.

Immediately prior to placement of the epinephrine soaked lap pad (t0), as well as 5 minutes (t5) and 10 minutes (t10) after placement of the epinephrine soaked pad, the systolic and diastolic blood pressures and pulse rates were measured and recorded by the anesthesiologist.

The hematocrit was measured immediately prior to anesthesia induction, upon arrival into the recovery room and at hospital discharge. The numbers of autologous and allogenic whole blood units transfused were recorded. The intraoperative, postoperative and total blood loss were estimated as previously described.[11] The intraoperative blood loss was calculated by determining the change in hematocrit between anesthesia induction and arrival into the recovery room. The postoperative blood loss was estimated by determining the change in hematocrit between arrival into the recovery room and hospital discharge. The total blood loss was estimated by determining the change in hematocrit between anesthesia induction and hospital discharge. A total of three hematocrit points was added to the blood loss calculation for any unit of blood transfused intraoperatively or postoperatively.

Cystography was performed on all men as previously described using fluoroscopy or ultrasound[11,12] on postoperative day 8. The degree of extravasation was categorized as none, slight, moderate and severe.

TABLE 2. **Blood loss and transfusion rates**

	Group 1	Group 2	Group 3	p value	
				Group 1 vs 2+3	Group 2 vs 3
Mean HCT at induction ± SE	47.596 ± 0.368	46.307 ± 1.05	47.49 ± 0.373	0.440	0.183
Mean HCT in recovery room ± SE	35.767 ± 0.314	35.155 ± 0.537	36.141 ± 0.288	0.810	0.085
Mean HCT at discharge ± SE	34.105 ± 0.302	34.279 ± 0.439	34.321 ± 0.294	0.603	0.941
Intraoperative blood loss ΔHCT ± SE	12.248 ± 0.467	9.980 ± 1.307	10.828 ± 0.435	0.014	0.346
Postoperative blood loss ΔHCT ± SE	2.26 ± 0.323	1.47 ± 0.536	2.06 ± 1.61	0.334	0.031
Total blood loss ΔHCT ± SE	14.209 ± 0.536	11.114 ± 1.386	12.603 ± 0.4631	0.008	0.711
No. total/units transfused (96)					
1 unit	5 (2.4)	2 (2.6)	10 (5.0)	0.364	0.673
2 units	4 (2.0)	2 (2.6)	8 (4.0)		
3 units	2 (1.0)	0 (0)	1 (0.5)		
4 units	1 (0.5)	0	0		
No. allogenic units transfused (96)					
1 unit	4 (2.0)	2 (2.7)	6 (3.1)	0.594	0.851
2 units	3 (1.5)	1 (1.4)	5 (2.6)		
3 units	2 (1.0)	0	1 (0.5)		
4 units	1 (0.5)	0			
No. autologous units tranfused (96)					
1 unit	3 (1.5)	0	4 (2.1)	0.230	0.457
2 units	0	1 (1.4)	3 (1.5)		
3 units	0	0	0		
4 units	0	0	0		

The mean differences between Group 1 (no compression pad) versus the combined Groups 2 and 3 (compression pad) and Groups 2 versus 3 (compression pad without versus with epinephrine) were determined using a students t-test and Kruskal Wallis non parametric analysis of variance. The baseline categorical parameters were compared for these groups using a chi-square analysis. A p value < 0.05 was required to achieve statistical significance. The differences between Groups 2 versus 3 were similarly ascertained in order to determine the hemostatic benefit soaking the laparotomy pad with epinephrine. The above statistical analyses were performed using SPSS v.14 software (SPSS, Chicago, Illinois).

Results

The baseline characteristics of the three groups are summarized in Table 1. At baseline, both Groups 2 and 3 had significantly more patients with Gleason scores ≥ 7, while Group 1 had significantly less patients with Gleason scores ≤ 6.

The mean induction, recovery room and discharge hematocrit levels, and the mean intraoperative, postoperative and total blood loss volumes are shown in Table 2 for the three groups. There were no significant differences between calculated postoperative blood loss between Group 1 versus 2 and 3. Group 2 was noted to have significantly less estimated postoperative blood loss in comparison to Group 3. Total blood loss and intraoperative blood loss was significantly greater in Group 1 versus 2 and 3.

The safety of packing the pelvis with an epinephrine soaked lap pad was examined by measuring systolic and diastolic blood pressures and pulse immediately prior to and after introducing the epinephrine soaked laparotomy pad into the pelvis, Table 3. There were no significant changes in any of these mean values relative to baseline.

TABLE 3. **Effect of intraoperative epinephrine on vital signs**

	Group 3
Systolic blood pressure (mmHG) ± SE	
Baseline	113.69 ± 1.06
5 minutes	114.78 ± 1.11
10 minutes	116.65 ± 1.17
Diastolic blood pressure (mmHG) ± SE	
Baseline	68.59 ± 0.99
5 minutes	69.80 ± 0.81
10 minutes	70.12 ± 0.88
Pulse (BPM) ± SE	
Baseline	70.25 ± 1.16
5 minutes	69.13 ± 1.09
10 minutes	69.67 ± 1.10

The findings on the postoperative day 8 cystogram are shown for the three groups in Table 4. Since the urinary catheters were routinely removed in the presence of none or slight extravasation, these groups were collapsed together; as was moderate and severe extravasation. The difference in degree of extravasation was not significantly different between Group 1 versus 2 and 3 or Group 2 versus 3.

Discussion

Blood loss associated with ORRP may occur during the surgical procedure and following would closure. The ability to control the dorsal venous plexus at the beginning of the surgical procedure has greatly diminished the extent of intraoperative bleeding.[3,4] It is our policy to achieve meticulous hemostasis prior to wound closure. Nevertheless, approximately 20% of total blood loss occurs after would closure[7,8] The theoretical advantages of preventing postoperative

TABLE 4. **Extent of extravasation on initial cystography**

Extent of extravasation	**Group 1 No. (96)**	**Group 2 No. (96)**	**Group 3 No. (96)**	**p value**	
				Group 1 vs 2+3	**Group 2 vs 3**
None	158 (81.4)	58 (78.4)	160 (84.2)	0.064	0.325
Slight	10 (5.2)	8 (10.8)	17 (8.9)		
Moderate	26 (13.4)	7 (9.5)	13 (6.8)		
Marked	0	1 (1.4)	0		
None/slight	168 (86.5)	66 (89.2)	177 (93.2)	0.058	0.284
Moderate/marked	26 (13.5)	8 (10.8)	13 (16.8)		

bleeding is lower rates of both re-operation to control life-threatening hemorrhage and autologous transfusions, faster recovery[7] and earlier removal of the urinary catheter.[11] The only proven advantage of robotic assisted laparoscopic radical prostatectomy (RALRP) over ORRP is less overall bleeding.[6] Decreasing blood loss using pelvic compression is feasible only during ORRP. Any technique that decreases blood loss associated with ORRP minimizes the blood loss advantage of RALRP.

Epinephrine is a potent vasoconstrictor. Epinephrine can elicit a local tissue vasoconstrictive effect which provides the rational for using epinephrine soaked gauze to facilitate hemostasis during hypospadius repair.[13] Topical epinephrine has also been used effectively in tonsilar surgery.[14] The role of topical epinephrine has not been explored as a measure to reduce pelvic bleeding. Previously, intraprostatic infiltrations of epinephrine prior to transurethral resection of the prostate have been studied and found to be effective in reduction of perioperative bleeding.[15]

In most cases requiring surgical intervention to control life threatening hemorrhage following ORRP, a specific bleeding site is not encountered suggesting the absence of a major site of bleeding.[8,16] Therefore, we speculated that compressing the pelvis with a laparotomy pad would facilitate hemostasis and minimize postoperative bleeding. After an initial experience in 76 cases, we elected to soak the laparotomy pad in epinephrine as a theoretical strategy to further reduce postoperative bleeding.

The transfusion requirements and amount of postoperative bleeding were not significantly different amongst the group of men without vs. with pelvic compression prior to wound closure (Group 1 versus Group 2 and 3). These observations suggest that pelvic compression in general prior to wound closure did not diminish postoperative bleeding.

In order to determine the hemostatic effect of soaking the laparotomy pad in a solution of epinephrine, we compared postoperative blood loss between Groups 2 versus 3. We are unable to explain why soaking the pad in epinephrine had a deleterious effect on estimated postoperative bleeding. The fact that pelvic compression with or without epinephrine did not impact the degree of extravasation on routine cystogram performed on postoperative day 8 suggests the modest observed decrease in estimated postoperative bleeding in Group 2 versus Group 3 was not clinically significant.

We did not observe any effect of topical epinephrine on blood pressure or pulse rate. It is possible that the concentration of the epinephrine was too low to achieve a physiologic effect. Higher concentrations of epinephrine may have yielded the clinical benefit recognized in other surgical procedures where the drug is delivered in a topical manner to diminish blood loss. The lack of any effect on cardiovascular parameters suggests that higher concentrations of epinephrine can safely be investigated.

There are some limitations to our study which include its retrospective design however all the data was collected prospectively as part of our longitudinal outcomes study. It is possible that our methodology for calculating postoperative blood loss based on differences between the hematocrits in the recovery room and upon discharge did not accurately capture true postoperative blood loss. The fact that utilizing a laparotomy pad with or without epinephrine did not impact findings on postoperative cystogram findings suggests that one of the ultimate clinical objectives of diminishing postoperative bleeding was not achieved.

Conclusions

Life threatening hemorrhage during or following ORRP is rare. We have identified several potential benefits associated with decreasing postoperative bleeding that will yield significant clinical benefits other than decreasing life-threatening hemorrhage. Our protocol for pelvic compression with or without epinephrine does not appear to reduce postoperative bleeding or impact the degree of urinary extravasation on a postoperative cystogram. Further studies using higher concentrations of epinephrine may show clinical benefit. □

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