Radical prostatectomy: size of the prostate gland and its relationship with acute perioperative complications

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Objective: *To determine if there is correlation between the size of radical prostatectomy specimens and perioperative complications including intraoperative blood loss.*

Methods: *One hundred twenty consecutive retropubic radical prostatectomy cases were retrospectively reviewed. Perioperative complications, intraoperative blood loss, pathologic stage, and size of the prostatectomy specimen were recorded. Logistic regression was used to determine whether variables such as age, PSA, and prostate weight are significant predictors of perioperative complications and intraoperative blood loss.*

Results: *The final analysis included a total of 117 cases. Significant complications were seen in 10 patients (8.5%). The median weight of the prostatectomy specimen in the group with major complications was 44.5 g (range 24 – 219) which was significantly higher than the median weight of 39.9 g (range 13 – 124) for the group without any complications (p = 0.034). The size of the prostate gland predicted the likelihood of a perioperative complication better than chance. A prostate size greater than 37 g was 10 times more likely to encounter major complications. Our analysis also indicated a statistically significant positive correlation between the weight of the prostatectomy specimen and intraoperative blood loss (p = 0.046).*

Conclusions: *Prostate size correlates with a higher risk of major perioperative complications and higher intraoperative blood loss.*

Key Words: prostate cancer, perioperative complications, blood loss, organ size

Introduction

Radical prostatectomy remains an important modality in the treatment of patients with localized prostate cancer. However, despite advances in both surgical technique and perioperative management, there continues to be significant morbidity and mortality associated with this procedure. In a recent study, major complications were identified in 9.8 % and minor complications in greater than 20% of radical prostatectomies.[1] Some of the common early complications of radical prostatectomy include deep venous thrombosis, pulmonary embolism, wound infection, myocardial infarction, and rectal injury.[1-3] The overall mortality of radical prostatectomy has generally been reported to be less than 1% in most recent series.[1-3]

Radical prostatectomy continues to be associated with a relatively high blood loss with a significant

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number of patients requiring transfusions intra and/or postoperatively.[4,5] Although age and co-morbidity has been shown to be a risk factor for perioperative complications,[1,6] other risk factors for increased blood loss and perioperative complications are lacking. Many urologic surgeons describe relative difficulty performing radical prostatectomy for both very small and very large specimens. We retrospectively studied the impact of prostate size on perioperative complications and intraoperative blood loss.

Materials and methods

Data collection

A retrospective review of patient hospital charts was performed. The records of 120 consecutive radical retropubic prostatectomies performed at our institution by staff urologists were examined. Of these, three were excluded from the study because of incomplete medical records. One hundred seventeen cases were included in the final analysis. Detailed information about the hospital course was gathered from the daily progress notes. Anesthesia logs were used to assess the duration of the procedure, intraoperative blood loss and intraoperative blood transfusions. Pathology reports were used to obtain the stage and grade of the disease along with the weight of the radical prostatectomy specimen. Pathologic staging was assigned according to the 1997 TNM classification: stage T2 disease localized to the prostatic capsule; stage T3 disease extending beyond the capsule.

Preoperative evaluation

All patients underwent a comprehensive history and physical exam that included a digital rectal exam. Diagnostic evaluation included measurement of serum prostate specific antigen and transrectal ultrasound guided prostate biopsies. Where indicated, a bone scan was also performed preoperatively.

Staff urologists

A total of 17 different urologists performed these surgeries. The individual number of cases performed by each urologist was variable and is listed in Table 1. Two surgeons performed greater than 10 cases each while the remaining 15 surgeons performed less than 10 cases each. The surgery was performed with the assistance of either the chief and/or the senior resident in urology.

Standard retropubic radical prostatectomy

Fifty one patients underwent bilateral pelvic lymph node dissection at the time of radical prostatectomy while 66 patients with low Gleason score and PSA did not undergo a lymph node dissection. The standard retropubic approach was used for all radical prostatectomies. A nerve sparing procedure was performed at the surgeon's discretion. An indwelling Foley catheter and JP drain(s) were left in place at the conclusion of the procedure.

TABLE 1. **Distribution of cases by individual surgeons**

Number of cases	Number of surgeons
1 - 5	10
6 – 10	5
11 – 15	0
16 – 20	1
>20	1

Assessment of morbidity

Inpatient charts were thoroughly examined to document any adverse events that occurred in the perioperative period. Patient progress was followed until hospital discharge. Any medical event that was considered to be a deviation from the standard postoperative course of a patient undergoing retropubic radical prostatectomy was recorded. A major complication was defined as any medical event occurring in the immediate postoperative period that significantly altered and/or prolonged the patient's hospital course. Examples of such an event would be postoperative ileus requiring the placement of nasogastric tube, acute renal failure requiring hemodialysis, infection requiring an added course of antibiotics, etc. An adverse event that was noted to be short lasting without any significant impact on patient's postoperative course was not considered to be a major complication. Examples of these minor events would be nausea/vomiting or fever from atelectasis, which resolves spontaneously with conservative care. The major complications were included in the final analysis and their relationships with a variety of parameters were statistically examined.

Statistical analysis

Univariate comparisons of patients with and without complications were done using either the student's t-test in the case of normally distributed variables (e.g., age) and with the Mann-Whitney test in the case of skewed variables (e.g., prostate weight). For major

TABLE 2. **Characteristics of the study sample**

	Age[a]	PSA[b]	Prostate weight (g)[b]	Blood loss (ml)[b]	Duration of operation[b]	Complications[c]	Hospital stay (days)[b]
Overall group (n=117)	59.8±6.2	7 (2-65)	37 (13-219)	1000 (200-6000)	240 (120-420)	10 (8.5)	3.86 (2-20)
T2 disease (n=74)	59.3±6.0	6.5 (2-29)	38 (20-219)	1000 (200-5000)	240 (125-420)	5 (6.8)	3.58 (2-8)
T3 disease (n=41)	60.4±6.5	8.6 (3.5-65)	37 (13-217)	800 (200-6000)	240 (120-420)	5 (12.2)	4.41 (2-20)
PIN (n=2)	63.5±4.9	4.8 (2-6.7)	48 (43-53)	1200 (1000-1400)	213 (211-215)	0	3.0 (3-3)

T2: organ confined disease; T3: margin positive disease; PIN: prostatic intraepithelial neoplasia
[a]Mean±SD
[b]Median (minimum-maximum)
[c]Frequency (percent)

complication as an outcome, logistic regression was used to test for any significant association with patient characteristics. Correlation and multiple regression were used for continuous outcomes (e.g., blood loss). An alpha of 0.05 was used for all comparisons.

Results

Table 2 shows the characteristics of the study sample separated by stage of the disease. Table 3 lists the major complications that occurred in the perioperative period along with the respective prostatectomy specimen size and intraoperative blood loss. The distribution of the prostatectomy specimen weight was quite large ranging from 13 g to 219 g. There were a total of four patients with prostate size greater than 100 g in this study. Three of these four patients encountered postoperative complications and large intraoperative blood losses. There were a total of 10 major complications in our study group which made

TABLE 3. **Major complications encountered during the perioperative period**

#	Age	Prostate size (g)	Case duration (min)	Blood loss (ml)	Complications
1	55	41	255	850	fever and ileus
2	70	48	280	1600	ileus
3	65	24	215	1000	ileus
4	65	190	200	600	pneumonia
5	62	38	275	300	pulmonary embolism
6	68	38	150	800	acute renal failure
7	67	217	420	6000	acute renal failure requiring hemodialysis
8	70	40	320	3000	postop bleeding requiring transfusions
9	54	51	420	2800	postop bleeding requiring transfusions
10	65	219	360	3000	urinary extravasation
Mean	64.1	90.6	289.5	1995	

TABLE 4. **Characteristics of patients with and without major complications**

Characteristics	Major complications[a] (n=10)	No major complication (n=107)	P value
Age	64.1±5.62	59.4±6.1	0.02
PSA	7.6 (4.1-34)	7.0 (2.0-65)	0.20
Prostate weight (g)	44.5 (24-219)	37.0 (13-124)	0.034
Blood loss (ml)	1300 (300-6000)	1000 (200-5000)	0.18
Overall transfusion rate	4.5 units (0-9)	1 units (0-7)	0.01
Pathologic staging	T2=5/T3=5	T2=69/T3=36	0.55
Duration of operation (minutes)	277 (150-420)	230 (120-400)	0.049
Hospital stay (days)	8.0 (5-20)	3.0 (2-5)	<0.001

[a]Median (minimum-maximum)

our complication rate 8.5%. There was no operative or perioperative mortality.

Table 4 compares the characteristics of the patients with and without major complications. The median weight of the prostatectomy specimen in the major complication group was 44.5 g which was significantly higher than the median weight of 37 g for the group without major complications (p = 0.034 by the Mann Whitney test). Significant differences between the groups were also found for age (p=0.02), duration of the operation (p=0.049), transfusion rate (p=0.01) and length of hospitalization (p< 0.001). While the intraoperative blood loss was greater in the complication group, this difference did not reach statistical significance (p=0.18).

Logistic regression was used to determine whether age, PSA, prostate weight and case duration were significant predictors of major complications. Since PSA and prostate weight were positively skewed, the natural log of these variables were used in order to normalize these data; ln(PSA) and ln(prostate weight) respectively. Table 5 shows the results of the univariate logistic regression (unadjusted results). These results replicate what is demonstrated in Table 4. Age and ln(prostate weight) are significant univariate predictors of major complications, whereas ln(PSA) is not. When age and ln(prostate weight) are combined together in one logistic regression model, only ln(prostate weight) is significant.

A Receiver Operator Characteristic (ROC) analysis was used to determine an optimal cut off in terms of prostate weight. The area under the ROC curve was 0.70 with a p-value = 0.03 which indicated that the discrimination between patients with or without major complications was significantly better than chance based on ln(prostate weight). An optimal cutoff point was found at in ln(prostate weight) = 3.62 which gave a sensitivity value equal to 90% and a specificity value equal to 54%. Taking larger values of ln(prostate weight) resulted in a large decrease in sensitivity without any marked increase in specificity. The anti-log of 3.62 yielded 37.5 g as a cut off point for prostate weight in real units. A univariate logistic regression using this cutoff as a predictor of major complications found that patients with prostates weighing 37.5 g or more were 10.65 times more likely to encounter major complications, p = < 0.001, 95% CI = (1.30,87.05).

TABLE 5. **Results of logistic regression for major complications**

Predictor	Unadjusted OR	Unadjusted p-value	Adjusted OR	Adjusted p-value
Age	1.17	0.025	1.12	0.12
ln(PSA)	2.11	0.16	na	na
ln(prostate weight)	8.02	0.002	5.84	0.009

Correlational and regression analyses were used to examine relationships with three outcomes: blood loss, duration of operation, and length of hospitalization. Table 6 shows the Pearson correlations between the natural log values of these outcomes and age, ln(PSA), and ln(prostate weight). Based on the univariate results, Ln(prostate weight) is correlated with ln(blood loss), while age and ln(PSA) are not. Ln(duration of surgery) is related to both ln(PSA) and ln(prostate weight). When these are both included in a stepwise multiple regression model, only ln(prostate weight) is included in the linear model ($p = 0.038$), indicating that it is the stronger predictor. Finally, ln(length of hospitalization) is significantly correlated with all three predictors. When these are included in a stepwise multiple regression model, only ln(PSA) and ln(prostate weight) are significant, $p = 0.02$ and $p < 0.001$ respectively.

Discussion

Radical prostatectomy has been the treatment of choice for localized prostate cancer. However, this procedure continues to be associated with significant morbidity. Most contemporary series on radical prostatectomies show a perioperative complication rate ranging from 6% to 10%.[1,3] Our major complication rate of 8.5% is consistent with these reports. The incidence of T3 disease was 35%, which also falls within the range reported in several recent studies.[7] The blood loss during radical prostatectomy is quite variable. Most recent series on radical prostatectomies have reported blood loss ranging from approximately 600 ml to 1500 ml.[4,5,8] Again, our average blood loss of 1240 ml is within this spectrum.

The goal of our study was to determine if the size of the radical prostate specimen has any correlation with perioperative complications including intraoperative blood loss. Long term complications of radical prostatectomy were not included in this study, and therefore patient information after hospital discharge was not collected.

A significant finding of this study was the association between prostate size and perioperative complications. Men with larger glands had a greater frequency of complications as compared to men with smaller glands. There were a total of four patients with prostate glands larger than 100 g in this study. Of these, three patients encountered perioperative complications and suffered relatively large intraoperative blood losses. This study also shows that the median age, case duration, and transfusion requirements were significantly greater in the group of patients with major complications than the group without major complications. Perhaps a larger sized prostate, by virtue of its size and anatomy, leads to greater operative duration and blood loss, and thereby leads to a higher rate of complications. Even though pelvic lymph node dissection adds to the overall duration of the case, it was not found to be a significant predictor of complications.

There are few studies that have focused on examining the relationship that we explored in our study. Shir, et al[4] examined the difference in blood loss between epidural and general anesthesia during radical retropubic prostatectomies. As part of their analysis, they also examined the relationship between intraoperative blood loss and prostate size. They found a significant correlation between these two parameters in the overall group (Epidural + General + Epidural/General). However, they failed to detect a correlation in the general anesthesia or Epidural and general anesthesia sub-groups of patients.

A clinical application of this finding lies in deciding which patients might require perioperative blood transfusions. Unfortunately, the issue of transfusion is somewhat subjective and there remains a large degree of variability in the transfusion threshold from one surgeon to another. Also, the presence of co-morbidities such as heart disease would require that different patients be transfused at different levels of acute blood loss. A detailed assessment of the transfusion criteria was not possible in this study. Consequently, this study focused more on

TABLE 6. **Correlations with blood loss, duration of surgery and length of hospitalization**

	In(blood loss)[a]	**Ln(Duration of surgery)**	**In(length of hospitalization)**
Age	0.01 (0.96)	0.02 (0.86)	0.25 (0.006)
In(PSA)	0.01 (0.92)	0.19 (0.038)	0.27 (0.004)
In(prostate weight)	0.19 (0.046)	0.18 (0.046)	0.36 (<0.001)

[a]Results reported as pearson r (p-value)

intraoperative blood loss than on perioperative blood transfusions. Our study showed that patients with large prostate glands are expected to have greater blood loss. Such patients may benefit from autologous blood donations, erythropoeitin treatment preoperatively, or perhaps intraoperative cell saver. Patients with smaller prostate glands might be spared these costly and cumbersome requirements. Obviously, further studies are required to better understand these relationships before such guidelines can be established.

Additionally, several studies have shown that preoperative hormone ablation therapy can shrink the size of the prostate gland. Macfarlane et al[9] showed a 33% decrease in the size of the prostate gland in men with locally advanced prostate cancer who were treated with 3 months of combined androgen blockade. While preoperative androgen blockade has been shown to decrease the rate of positive surgical margins in prostatectomy specimens,[10] the overall survival benefits are still questionable. However, this study suggests that perhaps preoperative hormonal therapy can be used to downsize large prostates prior to radical prostatectomy and reduce some of the complications associated with larger glands.

Unlike many recently published series on radical prostatectomies, this study does not represent the experience of a single surgeon. Table 1 shows the distribution of cases performed by different attending urologists. A total of 17 different urologists performed these cases with the assistance of the urology chief and/or senior resident. Two of the attendings performed greater than 10 cases each, while the remaining surgeons performed less than 10 cases each. It might be erroneous to assume that the attendings with fewer cases in this study were less experienced than those who performed a greater number of cases. Surgeons often have operating privileges in several hospitals. While some may choose to operate exclusively in one hospital, others tend to spread their cases among several hospitals. Hence, tallying up cases in one hospital may not reveal the full operative experience of each surgeon.

Although an overview of the data did not review any obvious differences among surgeons in terms of perioperative complications and intraoperative blood loss, the large number of different surgeons did not allow an analysis categorized by surgeon. While a variety of surgeons may make the results more applicable to all urologists, it would be very interesting to see if these results apply to large, single surgeon series as well.

Conclusions

Our study indicates that the size of the prostate gland removed during radical retropubic prostatectomy is related to complications seen during the perioperative period. Larger gland sizes were associated with greater number of complications as well as larger intraoperative blood losses. Specifically, a prostate gland weighing more than 37 g was 10 times more likely to encounter perioperative complications. Further studies are required to better understand these correlations. These correlations may make preoperative prostate size useful in determining average hospital stays, the need for preoperative autologous blood donation or erythropoetin treatment, or perhaps the need for intraoperative cell saver. Patients with relatively prostate glands might also benefit from preoperative treatments that help reduce the size of the prostate gland such as androgen deprivation therapy. □

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