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SUBJECTIVE AND OBJECTIVE ANALYSIS OF THE URINARY BLADDER MORBIDITY IN TERMS OF VOIDING DYSFUNCTION FOLLOWING TYPE III RADICAL HYSTERECTOMY FOR CARCINOMA UTERINE CERVIX – A PROSPECTIVE STUDY.

Oncology

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ABSTRACT

Introduction: Voiding dysfunction after pelvic plexus injury occurs most commonly after radical hysterectomy in females. The true incidence of neurogenic vesicourethral dysfunction after various types of pelvic surgery is unknown, because there are few prospectively studied series of patients with preoperative and postoperative urodynamic evaluation. The incidence has been estimated to range from 16 % to 80 % after radical hysterectomy [1]. These are estimates drawn from past literature and the current incidence is most likely significantly lower, owing to the use of nerve-sparing techniques during these types of pelvic surgery.

Aim: The aim of this study was to analyze subjectively and objectively the urinary bladder morbidity in terms of voiding dysfunction following type III radical hysterectomy for carcinoma uterine cervix.

Materials and methods: This was a single-institute prospective study.51 patients diagnosed with carcinoma cervix without any voiding dysfunction underwent radical hysterectomy along with uroflowmetry preoperatively and at 1st, 3rd, and 6th months after surgery. Standard statistical tests Fischer exact test for categorical values and Wilcoxon signed rank test for sequential continuous variable were used for analysis. All the data were expressed as mean ± SD or in percentage as needed. The differences were considered to be significant if p value < 0.05.

Results: The voiding dysfunction symptoms presented by patients after radical hysterectomy were straining, urinary incontinence, urgency, and dysuria. The overall voiding dysfunction rate at 1st, 3rd, and 6th month after surgery were 35.3 %, 13.8 %, and 3.9% respectively. The most common voiding dysfunction symptom was straining at 1st, 3rd, and 6th month which manifested in 18 (35.3 %), 7 (13.8 %), and 2 (3.9%) patients respectively. Incontinence manifested in 12 (23.5 %), 6 (11.8 %), and 1(2.0%) patients at 1st, 3rd and 6th month after radical hysterectomy. Urgency manifested in 7 (13.7 %), and 4 (7.8 %) patients at 1st, and 3rd month respectively. 5 (9.8%) patients needed catheterization at 1st month only. No patient needed catheterization at 3rd and 6th month. In 51 patients who underwent radical hysterectomy, the preoperative voided volume, maximal flow rate, average flow rate and post-void residual urine were 281±22, 21.7±1.9, 10.3±0.4, and 21.9±16.0 respectively. At 1st month, 3rd month and 6th month after radical hysterectomy these parameters were 266 ± 32, 20.6 ± 2.1, 9.9 ± 0.7, &35.2 ± 32.6; 271 ± 33, 21.1 ± 2.1, 10.0 ± 0.4, & 26.7 ± 22.3; and 278 ± 26, 21.4 ± 2.1, 10.1 ± 0.4, & 22.8 ± 19.3 respectively. In comparison of preoperative data with 1st, 3rd, and 6th month data, the mean value of voided volume, maximum flow rate and average flow rate decreased; and post-void residual urine increased. In comparison of preoperative data with 1st, 3rd and 6th month data, only maximal flow rate revealed a statistically significant difference ($p < 0.05$).

Conclusion – In conclusion, type III radical hysterectomy gives rise to transient alteration in the neurophysiology of the lower urinary tract which may be the cause for voiding dysfunction.

KEYWORDS

voiding dysfunction , radical hysterectomy , carcinoma cervix , uroflowmetry

INTRODUCTION

Voiding dysfunction after pelvic plexus injury occurs most commonly after radical hysterectomy in females. The true incidence voiding dysfunction after radical hysterectomy is unknown, because there are few prospectively studied series of patients with preoperative and postoperative urodynamic evaluation .

The incidence has been estimated to range from 16 % to 80 % after radical hysterectomy [1]. These are estimates drawn from past literature and the current incidence is most likely significantly lower, owing to the use of nerve-sparing techniques during these types of pelvic surgery. A few studies have suggested that the bladder dysfunction after radical hysterectomy may be transient and that bladder function may recover to baseline within 6 to 12 months [2].

It has been estimated that in 15 % to 20 % of affected individuals, the voiding dysfunction is permanent [3]. The injury may occur as a consequent to denervation or neurologic decentralization, tethering of the nerves or encasement in scar, direct bladder or urethral trauma, or bladder de-vascularization. Neoadjuvant and/or adjuvant therapy, such as irradiation, may play a role as well. The type of voiding dysfunction that occurs is dependent on the specific nerves involved, degree of injury and any pattern of re-innervation or altered innervation those results over time.

AIM

The aim of this study is to analyze subjectively and objectively the urinary bladder morbidity in terms of voiding dysfunction following type III radical hysterectomy for carcinoma uterine cervix.

METHODS AND MATERIAL

This prospective study was conducted at Royapettah Government Hospital, Chennai between January 2013 and January 2015 after obtaining permission from the Institutional Ethics Committee, and it was in accordance with the Declaration of Helsinki & Good Clinical Practice (GCP) guidelines. 51 patients who fulfilled the inclusion and exclusion criteria were enrolled in this study.

Inclusion Criteria: (1)Age: 18 to 70 years, (2) Patients with Carcinoma cervix, (3) patients who underwent open type III radical hysterectomy with curative indent Exclusion Criteria:(1)Patients with preoperative urinary symptomatology (urgency, straining, urinary incontinence, dysuria), (2)Abnormalities in preoperative uroflowmetry, (3) Patients with previous lower urinary tract surgery, (4)Patients not willing to give informed consent, (5) Patients not willing to do uroflowmetry in 1, 3, and 6 month

Study procedure:

A baseline screening for urinary bladder function was done at the

diagnosis of disease prior to start of preoperative treatment, if any before radical hysterectomy followed by postoperative evaluation of bladder function was done at 1st month, 3rd month and 6th month with urinary symptomatology (urinary bladder sensation, urgency, straining, urinary incontinence, and dysuria) and uroflowmetry (voided volume, maximum flow rate & average flow rate) and post-voided residual volume with ultra-sonogram.

The patients who presented with incontinence in the first visit were educated about and encouraged to perform pelvic floor exercises. Patients were followed up for subsequent management of urinary problems, if any.

Statistical Analysis:

The variables investigated included age, body mass index, urinary symptomatology (straining, incontinence, urgency, dysuria), parameters of uroflowmetry (voided volume, maximum flow rate, average flow rate), and post-void residual urine and needed catheterization. Standard statistical tests Fischer exact test for categorical values and Wilcoxon signed rank test for sequential continuous variable were used for analysis using SPSS 16. All the data were expressed as mean ± SD or in percentage as needed. The differences were considered to be significant if p value < 0.05.

Results

Out of 51 patients who underwent radical hysterectomy, there were no operative mortality and none of the patients had urinary bladder injury, ureteric injury, or postoperative urinary fistula. The mean age was 52.7 years and the mean body mass index was 23.8. All patients who underwent radical hysterectomy had negative vaginal margin and none had microscopic/macroscopic parametrial involvement in definitive histopathology. Only two patients had pelvic node positive disease. Only one patient had vault recurrence at 6 month despite adjuvant therapy.

Subjective Analysis - Symptoms

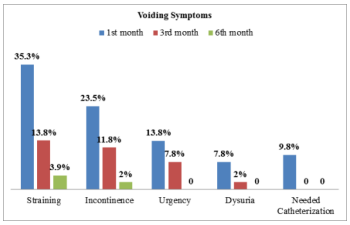
Table 1 - Voiding Dysfunction Symptoms in 51 patients

Symptoms	1st month	3rd month	6th month
Straining	18 (35.3 %)	7 (13.8 %)	2 (3.9 %)
Incontinence	12 (23.5 %)	6 (11.8 %)	1 (2.0 %)
Urgency	7 (13.8 %)	4 (7.8 %)	0
Dysuria	4 (7.8 %)	1(2.0%)	0
Needed Catheterization	5 (9.8 %)	0	0
Overall symptoms	18 (35.3%)	7 (13.8%)	2 (3.9 %)

The voiding dysfunction symptoms presented by patients after radical hysterectomy were straining, urinary incontinence, urgency, and dysuria. The overall voiding dysfunction rate at 1st, 3rd, and 6th month after surgery were 35.3 %, 13.8 %, and 3.9% respectively. The most common voiding dysfunction symptom was straining at 1st, 3rd, and 6th month which manifested in 18 (35.3 %), 7 (13.8 %), and 2 (3.9%) patients respectively.

Incontinence manifested in 12 (23.5 %), 6 (11.8 %), and 1(2.0%) patients at 1st, 3rd and 6th month after radical hysterectomy. Urgency manifested in 7 (13.7 %), and 4 (7.8 %) patients at 1st, and 3rd month respectively. Dysuria manifested in 4 (7.8%) and 1 (2.0 %) patients 1st, and 3rd month respectively. None had urgency and dysuria at 6 month after radical hysterectomy. 5 (9.8%) patients needed catheterization at 1st month only. No patient needed catheterization at 3rd and 6th month [Table 1].The rates of all the voiding dysfunction symptoms decreased at 6 months when compared to 1st and 3rd month after radical hysterectomy [Table 1].

Figure 1 – voiding symptoms



Objective analysis- Uroflowmetry parameters

Table 2 – Uroflowmetry Parameters after Radical Hysterectomy in 51 Patients

Parameters	Preoperative	1st month(p value)	3rdmonth(p value)	6th month(p value)
VV	281±22	266±32(0.110)	271±33(0.188)	278±26(0.520)
Q Max	21.7±1.9	20.6±2.1(0.011)	21.1±2.1(0.016)	21.4±2.1(0.045)
Q Avg	10.3±0.4	9.9±0.7(0.171)	10.0±0.4(0.101)	10.1±0.4(0.082)
PVR	21.9±16.0	35.2±32.6(0.058)	26.7±22.3(0.171)	22.8±19.3(0.936)

All data expressed as mean ± standard deviation; p value – Wilcoxon signed rank test VV= Voided volume (mL); Q Max=Maximum flow rate (mL/sec); QAvg=Average flow rate (mL/sec); PVR=Post-void residual urine (mL).

In 51 patients who underwent radical hysterectomy, the preoperative voided volume, maximal flow rate, average flow rate and post-void residual urine were 281±22, 21.7±1.9, 10.3±0.4, and 21.9±16.0 respectively. At 1st month, 3rd month and 6th month after radical hysterectomy these parameters were 266 ± 32, 20.6 ± 2.1, 9.9 ± 0.7, &35.2 ± 32.6; 271 ± 33, 21.1 ± 2.1, 10.0 ± 0.4, & 26.7 ± 22.3; and 278 ± 26, 21.4 ± 2.1, 10.1 ± 0.4, & 22.8 ± 19.3 respectively [Table 2].

Figure 2.a – uroflowmetry parameters

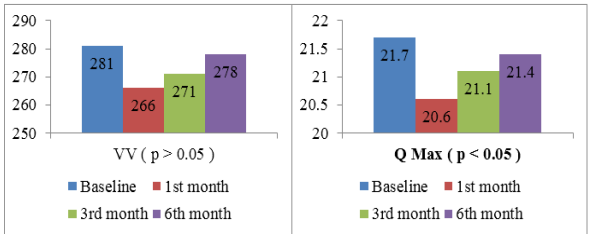
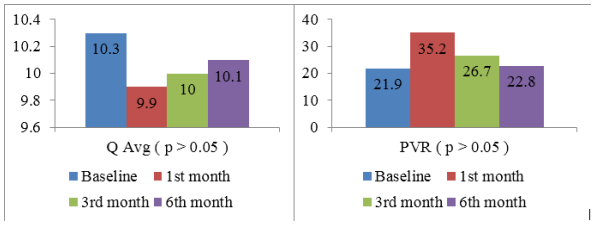


Figure 2.b – uroflowmetry parameters



In comparison of preoperative data with 1st, 3rd, and 6th month data, the mean value of voided volume, maximum flow rate and average flow rate decreased; and post-void residual urine increased [Table 2]. In comparison of preoperative data with 1st, 3rd and 6th month data, only maximal flow rate revealed a statistically significant difference ($p < 0.05$). Other parameters voided volume, average flow rate and post-void residual urine were not significant at 1st, 3rd, and 6th month when compared with preoperative data [Table 2].

Comparison of subjective and objective analysis of urinary bladder morbidity The association of straining and uroflow curve was considered to be statistically significant at 1st, 3rd, and 6th month [Table 3]. The association between maximum flow rate and straining was not statistically significant at 1st, 3rd, and 6th month [Table 4]. The association between post-void residual urine and voiding symptom straining was statistically significant at 1st month (p value 0.0022), and 3rd month (p value 0.0342) but was not statistically significant at 6th month (p value 0.3572) [Table 5]. The association between post-void residual urine and catheterization was statistically significant at 1st month (p value 0.0195), but not statistically significant at 3rd and 6th month [Table 6].

Table 3 - Comparison of Straining and Uroflow Curve

Straining	Uroflow curve		Total
	Abnormal	Normal	
1st month (p value= 0.0001)			
Present	12	6	18

Absent	4	29	33
Total	16	35	51
3rd month (p value = 0.0042)			
Present	4	3	7
Absent	3	41	44
Total	7	44	51
6thmonth (p value =0.0047)			
Present	2	0	2
Absent	2	47	49
Total	4	47	51

Table 4 - Comparison of Straining and Maximum Flow Rate

Straining	Maximum Flow Rate		Total
	Abnormal	Normal	
1st Month (p value =1)			
Present	0	18	18
Absent	0	33	33
Total	0	51	51
3rd Month (p value =1)			
Present	0	7	7
Absent	0	44	44
Total	0	51	51
6th Month (p value =1)			
Present	0	2	2
Absent	0	49	49
Total	0	51	51

Table 5 - Comparison of Straining and Post void-residual urine

Straining	Post-void Residual Urine		Total
	Abnormal	Normal	
1st Month (p value 0.0002)			
Present	11	7	18
Absent	5	28	33
Total	16	35	51
3rd Month (p value 0.0276)			
Present	3	4	7
Absent	3	41	44
Total	6	45	51
6th Month (p value 0.1493)			
Present	1	1	2
Absent	3	46	49
Total	4	47	51

Table 6 - Comparison of Post void residual urine with Catheterization

Catheterization	Post-Void Residual Urine		Total
	Abnormal	Normal	
1st month (p value= 0.0195)			
Needed	5	0	5
Not Needed	16	30	46
Total	21	30	51

Table 7 - Comparison of straining, post-void residual urine and catheterization

Comparison	Straining Present n = 18		Straining Absent n = 33		Total
Catheterization	Post-Void Residual Urine		Post-Void Residual Urine		
	Abnormal	Normal	Abnormal	Normal	
1st Month					
Needed	5	0	0	0	5
Not Needed	6	7	5	28	46
Total	11	7	5	28	51

In patients who had voiding dysfunction symptom straining, the association between post-void residual urine and catheterization was not statistically significant at 1st month (p value = 0.1013). In patients who did not have voiding dysfunction symptom straining, the association between post-void residual urine and catheterization was not statistically significant at 1st month (p value = 1) [Table 7].

DISCUSSION

The incidence rate of urinary bladder dysfunction after radical hysterectomy for uterine cervical cancer is known to be between 16 % and 85 % [1]. A few studies have suggested that the bladder dysfunction after radical hysterectomy may be transient and that bladder function may recover to baseline within 6 to 12 months [2]. In this study the rate of voiding dysfunction symptom was 35.3% at 1st month which decreased to 13.8% at 3rd month and 3.9% at 6th month. This showed improved voiding with time up to 6th month. In this study, the most voiding dysfunction symptom was straining, followed by incontinence, urgency and dysuria at 1st, 3rd, and at 6th month. However, Sekido et al. reported postoperative urinary tract dysfunction that was sustained for more than 10 years [4].

In general, bladder dysfunction after radical hysterectomy is known to be related to denervation of the autonomic nerve during surgical procedures. Chen et al. suggested that post-hysterectomy changes in urinary tract function may be related to the partial decentralization of the pelvic autonomic nerves [5]. It has also been suggested by Zullo et al. that the most important factor for postoperative bladder dysfunction was the resection of vaginal and paravaginal tissue which supports the urinary bladder [6].

In this study, the decrease in maximum flow rate following radical hysterectomy showed a statistical significance at 1st, 3rd, and 6th month when compared with preoperative data, even though the actual mean value was not abnormal. Other parameters voided volume, average flow rate, and post-void residual urine were not statistically different at 1st, 3rd, and 6th month when compared with preoperative data.

Even though there was no correlation between uroflow parameter maximum flow rate and straining symptom, uroflow curve was found be abnormal in symptomatic patients who had straining with statistical significance at 1st, 3rd, and 6th month.

In this study, post-void residual urine after type III radical hysterectomy at 1st, 3rd, and 6th month was not significant when compared with preoperative data. However the association of post-void residual urine with voiding symptom straining showed statistical significance at 1st and 3rd month but not at 6th month. The association of post-void residual urine and the need of catheterization showed statistical significance at 1st month. But in patients with straining the association of post-void residual urine and the need of catheterization was not found to be statistically significant.

LIMITATIONS OF THE STUDY

(1)The artificial situation of the urodynamic laboratory might produce a non-physiologic result.(2)The absence of a specific abnormality during urodynamic testing does not exclude its existence.(3)Only non-invasive uroflowmetry and measured of post-void residual urine by transabdominal ultrasound was used in this study, invasive urodynamic study such as cystometry and pressure flow studies were not used and measurement of post-void residual urine was not measured by catheterization.(4)Wide range of physiologic values in uroflowmetry in normal, asymptomatic patients.

CONCLUSION

In conclusion, type III radical hysterectomy gives rise to transient alteration in the neurophysiology of the lower urinary tract. Although most of these changes return to normal within a certain period of time (6-12 months), it is suggested to pay attention to voiding symptom of straining, and the uroflow parameter of maximum flow rate. The uroflow curve and post-void residual urine in also require note in patients with voiding symptom straining.

This study shows that it may not always be necessary to use uroflowmetry values to evaluate the voiding dysfunction following radical hysterectomy, as there is wide range of physiologic values in asymptomatic patients and not all abnormalities in uroflowmetry are clinically significant. Post-void residual urine measured with non-invasive method of ultrasound may be sufficient to identify patients who will not need intermittent catheterization. Further studies with a

larger number of patients and long-term follow-up are required to explore this.

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