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Clinical prognosis of hydronephrosis treated with urological intervention after radical hysterectomy for uterine cervical cancer: clinical study

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Summary

Purpose: To review the clinical prognosis of hydronephrosis treated with urological intervention (HTUI) after radical hysterectomy (RH) for uterine cervical cancer. *Materials and Methods:* Thirty-six of 270 patients who underwent RH between January 2010 and December 2015 were included. The authors compared the prognostic factors for the resolution of hydronephrosis between resolution (n= 17) and non-resolution groups (n=19) after HTUI. *Results:* There were no significant differences in valuables between the two groups. Combined percutaneous nephrostomy and intraureteric stent was most frequently used as the first procedure (n=23). Age > 55.5 years and onset time of hydronephrosis after RH > 2.75 months showed poor prognosis for HTUI on receiver operating characteristic (ROC) curve. The rates of HTUI varied depending on each institution (0−14.4%). *Conclusions:* Old age and later onset of hydronephrosis could be the important prognostic factors for HTUI. The rate of HTUI depended on each institution and its surgical techniques.

Key words: Hydronephrosis; Cervical cancer; Radical hysterectomy; Intervention.

Introduction

Treatment for uterine cervical cancer consists in surgery, radiation therapy, chemotherapy or chemoradiation, which are used alone or in combination [1]. These methods have post-procedural complications. In particular, the urinary tract is vulnerable to injury from radical pelvic surgery and radiation. Radical pelvic surgery, such as radical hysterectomy (RH), and radiation therapy can cause direct injury or unrecognized damage to the urinary tract. Dissection of the ureter from the peritoneum and vesicouterine ligament can injure the ureteric adventitia and induce ureteric stricture that is followed by renal hydronephrosis [2]. Radiation therapy can cause chronic urinary tract complications in 1–5% of patients, depending on the dose of radiation [1].

Renal hydronephrosis after treatment is a complication of surgery, radiation therapy or cancer recurrence. Hazewinkel e*t al.* reported that the incidence of hydronephrosis after RH for uterine cervical cancer was 12% and only 1% in patients were invasively treated for hydronephrosis [3]. Many studies have reported the incidence and treatment of renal hydronephrosis after RH, with various results [2-8]. However, few studies have reported the prognosis, clinical course, or factors that affect the clinical prognosis of hydronephrosis treated with urological intervention (HTUI) after RH. Therefore, in the current study the authors retrospectively reviewed the clinical prognosis of HTUI after RH.

Materials and Methods

The authors used images in Picture Archiving and Communication System (PACS) and registries from the Departments of Gynecology and Urology, Kyungpook National University Medical Center, Daegu, Korea, to retrospectively review 270 patients who underwent RH for uterine cervical cancer between January 2010 and December 2015. They included patients who met the following criteria: (1) cervical cancer, International Federation of Gynecology and Obstetrics (FIGO) Stage Ia2–IIA; (2) treated with RH with pelvic lymphadenectomy, and with/without para-aortic lymphadenectomy; (3) renal hydronephrosis detected by ultrasonography or computed tomography after RH; (4) treated with urological intervention for renal hydronephrosis; (5) no recurrent lesions near the urinary tract; (6) no known preoperative hydronephrosis or no known perioperative ureteral injury; (7) hydronephrosis grade II (moderate dilatation and wide separation of renal pelvis) or grade III (marked dilatation and calyceal clubbing with renal parenchymal thinning). Patients with grade I hydronephrosis (mild dilatation and urinary stasis) were excluded [9]. The medical records were reviewed to extract patient age;

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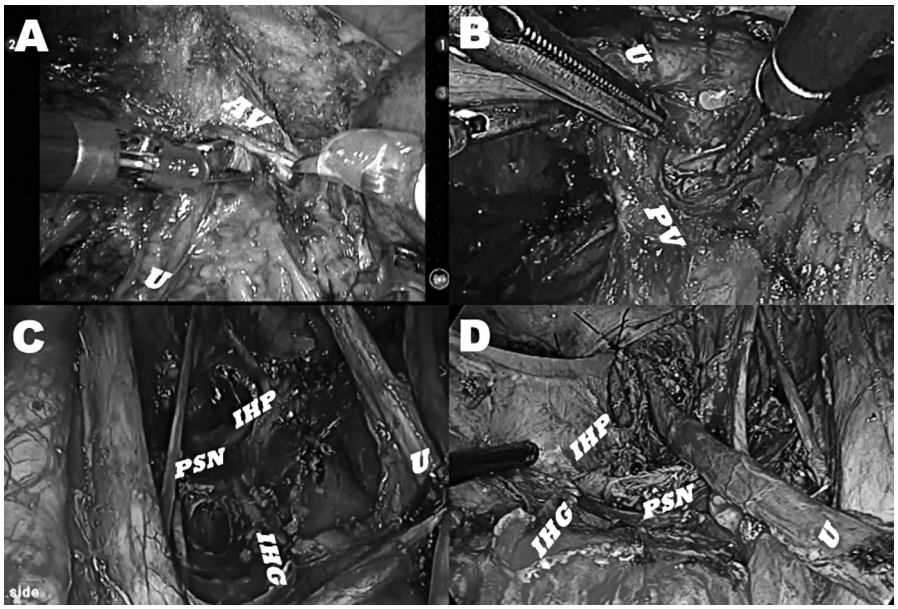

Figure 1. — (A) Dissection of anterior vesicouterine ligament. (B) Dissection of posterior vesicouterine ligament. (C) Postoperative view of deep pelvic cavity. (D) Postoperative view of skeletonized ureter. U: ureter; AV: anterior vesicouterine ligament; PV: posterior vesicouterine ligament; IHG: inferior hypogastric nerve; PSN: pelvic splanchnic nerve; IHP: inferior pelvic plexus.

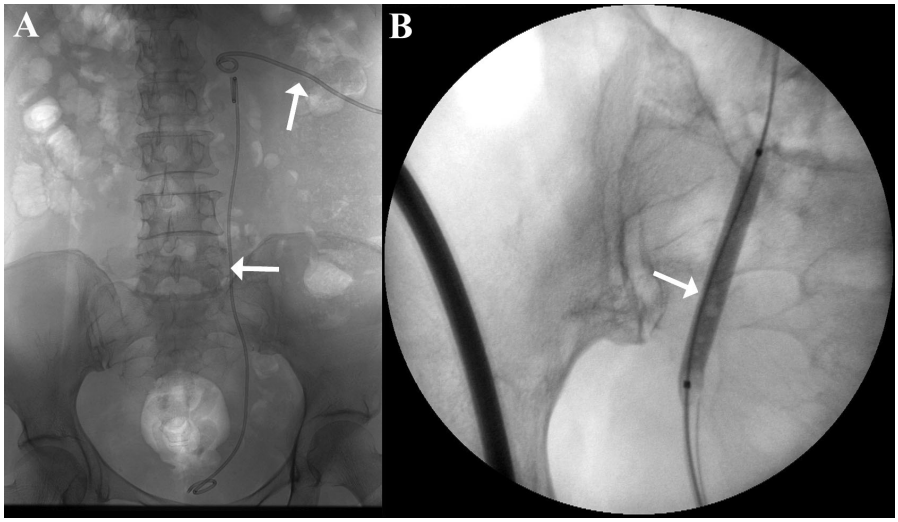

Figure 2. (A) Upper white arrow indicates percutaneous nephrostomy. Lower white arrow indicates intraureteric double J stent. (B) White arrow indicates intraureteric balloon dilatation.

body mass index, FIGO Stage, type of RH, surgeons' proficiency, surgical methods, such as laparotomy, laparoscopic, and robotic surgery, adjuvant therapy including radiation therapy or chemoradiation, number of harvested pelvic lymph nodes, site of hydronephrosis, onset time, and time from onset to resolution.

All the patients underwent RH with pelvic lymphadenectomy based on Piver–Rutledge classification [10]. The authors' institute also applies the method of Okabayashi with nerve sparing and total mesometrial resection to minimize bladder dysfunction and tumor recurrence [11-14]. Although RH was performed by laparotomy, laparoscopic or robotic surgery, all surgeons attempted to preserve the nerves and dissect the parametrium meticulously. In particular, to reduce harmful effects on the ureter which passes between anterior and posterior vesicouterine ligaments, vesicouterine ligaments, and its including veins were carefully separated and skeletonized (Figure 1) [15]. The patients received adjuvant radiation therapy or chemoradiation depending on the presence of risk factors. Renal ultrasonography was performed at seven days and four weeks after RH. This was followed by alternate abdominopelvic computed tomography and renal ultrasonography for regular check-up, which revealed the status of the kidneys every three months for five years. Primary management consisted of observation or urological intervention for hydronephrosis after RH. When there was non-symptomatic mild hydronephrosis, invasive urological intervention was not performed. If symptoms or no less than moderate hydronephrosis developed, active urological interventions such as intraureteric double J stent, percutaneous nephrostomy (PCN), and intraureteric ballooning dilatation were performed (Figure 2). The double J stent or PCN drainage was removed during follow-up if there was significant improvement of hydronephrosis. If there were no changes, aggravation or waxing and waning of hydronephrosis. The stents or drains were changed regularly.

Statistical analyses were performed using SPSS Statistics version 20. The patients' characteristics were compared between the non-resolution and resolution groups using the two-sample *t*-test and χ^2 test. The relationship between patients' characteris-

Table 1. — *Patient characteristics in both groups.*

		Non-resolution n=19	Resolution N=17	*p*-value
Age (years)		57.78 ± 8.60	54.23 ± 7.63	0.201*
BMI (kg/m^2)		24.89 ± 3.50	24.06 ± 3.71	0.520*
Stage (FIGO) (n)				0.812†
	Ia2	1	1	
	Ib1	14	11	
	Ib2	1	3	
	IIa1	3	2	
Type (n)				0.892†
	II	6	5	
	III	13	12	
Surgeon (n)				0.817†
	Non-expert	8	7	
	Expert	11	10	
Method (n)				0.682†
	Laparotomy	8	8	
	Laparoscopy	4	4	
	Robotic	7	5	
Adjuvant therapy (n)				0.163†
	None	8	11	
	Radiation	0	1	
	Chemoradiation	11	5	
Right pelvic LN (n)		12.82 ± 6.33	11.46 ± 4.22	0.488*
Left pelvic LN (n)		12.00 ± 5.25	10.60 ± 5.48	0.467*
Site (n)				0.201†
	Right	8	3	
	Left	7	10	
	Both	4	4	
Onset time (months)		6.21 ± 8.53	4.47 ± 6.34	0.498*
Resolution time (months)			4.30 ± 3.24	

Data are mean ± SD or number. Values of $p < 0.05$ were considered statistically significant.

**Two-sample t-test ; †χ^2 test. BMI: body mass index; FIGO: International Federation of Gynecology and Obstetrics; Type: Piver–Rutledge classification; Non-expert: < 50 cases of radical hysterectomy.*

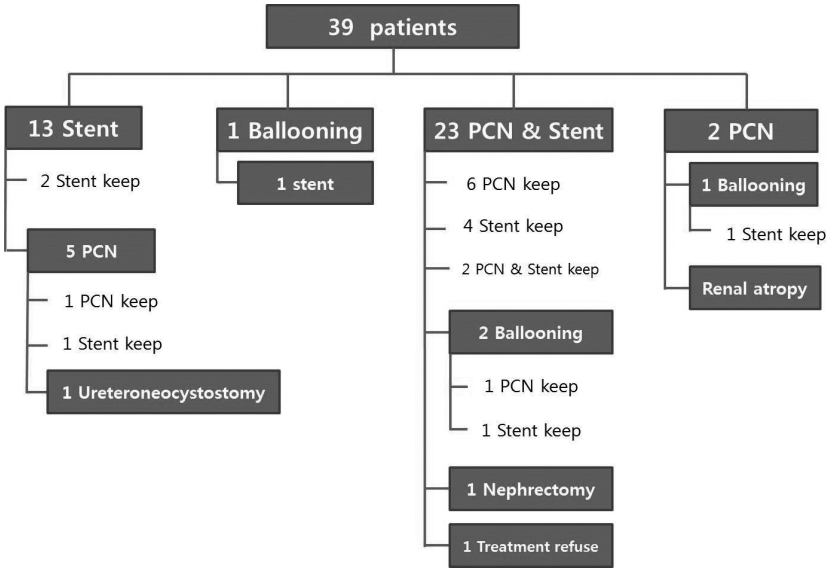

Figure 3. Urological inventions and final results of hydronephrosis after radical hysterectomy. Blue boxes indicate next urological interventions after previous intervention fails.

tics and resolution of hydronephrosis was analyzed using Pearson's correlation analysis. A receiver operating characteristic (ROC) curve was used to determine the cutoff age and onset time. A value of $p < 0.05$ was considered statistically significant.

Kyungpook National University Medical Center does not require institutional review board approval for retrospective chart reviews. Therefore, this study was exempt from the approval process.

Table 2. — *Intervention for hydronephrosis after radical hysterectomy for cervical cancer.*

Status	Interventions for hydronephrosis (n)
Resolution (n = 17)	
	Stent (6)
	PCN & stent (6)
	Stent → PCN (2)
	Stent → PCN → ureteroneocystostomy (1)
	PCN & stent →stent (1)
	Ballooning → stent (1)
Non-resolution (n = 19)	
	Stent kept (2)
	Stent → PCN kept (1)
	Stent → PCN → stent kept (1)
	PCN & stent → ballooning → PCN kept (1)
	PCN & stent → PCN kept (6)
	PCN → ballooning → stent kept (1)
	PCN & stent → stent kept (4)
	PCN & stent → PCN & stent kept (2)
	PCN & stent → ballooning → stent kept (1)
Others (n = 3)	
	PCN → atrophy (1)
	PCN & stent → treatment refuse (1)
	PCN & stent → nephrectomy (1)

PCN: percutaneous nephrostomy.

Results

There were no significant differences in variables such as age, body mass index, FIGO Stage, type of RH, surgeons' proficiency, surgical methods, adjuvant therapy, number of harvested pelvic lymph nodes, site of hydronephrosis, and onset time of hydronephrosis between two groups. The onset time varied from two weeks to 40 months after RH. The mean resolution time from onset to disappearance was 4.30 ± 3.24 months (Table 1). In the resolution group, nine cases were initially treated with double J stent, seven with combination of stent and PCN, and one with intraureteric ballooning. In the non-resolution group, four cases were treated with double J stent, one with PCN, and 14 with combination of stent and PCN. There were three cases that were not included in either of the two groups. In one case, there was renal atrophy that eventually led to loss of renal function; one patient refused treatment; and another underwent eventual one-sided nephrectomy. In both groups, 13 patients were treated initially with stent, and in five of these, hydronephrosis failed to resolve. One patient was treated with ureteroneocystostomy. Twenty-three patients were treated with a combination of PCN and stent, and in 16 of these, hydronephrosis failed to resolve. One patient underwent one-sided nephrectomy. The other three patients were treated initially with balloon dilatation or PCN, and in all of them, hydronephrosis failed to resolve (Table 2; Figure 3). The authors used a ROC curve to determine the specific age and onset time for prediction of prognosis of HTUI. Age > 55.5 years was associated with poor prognosis, and had a sensitivity of 0.737 and specificity of 0.647 in differentiating better and worse prognosis of HTUI. The area under the curve (AUC) was 0.638. The authors also showed that an onset time of 2.75 months after RH had a sensitivity of 0.737 and specificity of 0.647 in differentiating better and worse prognosis. The AUC was 0.681 (Figure 4). When the authors divided the age and onset time using the ROC curve, there were significant differences between two groups (age: $p = 0.020$; onset time: $p = 0.007$) (Table 3). Left-side stricture showed better prognosis than right or both-side, although there was not significant difference ($p = 0.106$).

Discussion

There are many studies regarding the incidence of hydronephrosis after RH for uterine cervical cancer. Gynecological oncologists can expect the risk and explain to patients the possibility of urinary complications after RH using the results of those studies. However, only a few studies have reported the prognosis of HTUI. Therefore, it is

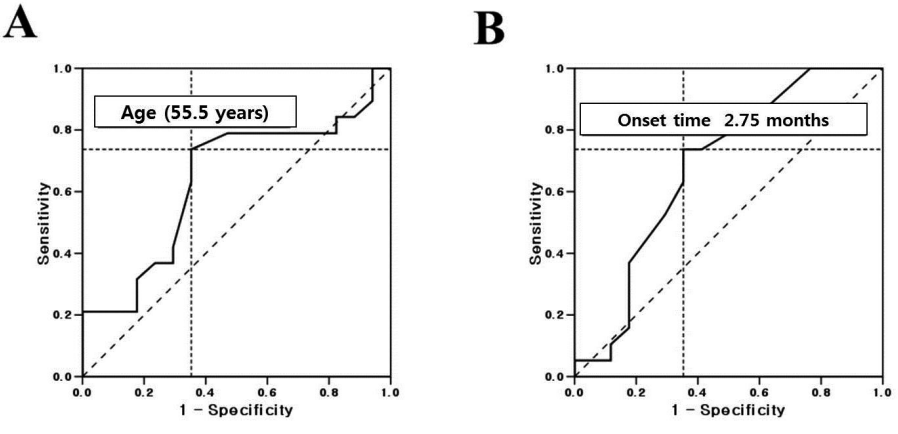

Figure 4. Receiver operating characteristic (ROC) curve for the age and onset time predictive of non-resolution of HTUI. (A) ROC for age, area under curve (AUC) = 0.638. (B) ROC for onset time, AUC = 0.681.

Table 3. — *Correlation between patient characteristics and status of resolution.*

		Non-resolution	Resolution	CE	*p*-value
Onset time (months)				-0.386	0.020*
	3<	6	12		
	≤ 3	13	5		
Age (years)				-0.442	0.007*
	56 <	6	14		
	≤ 56	13	3		
Site				-0.274	0.106
	Left	7	10		
	Right or both	12	7		

*CE: correlation coefficient. * $p < 0.05$ is considered statistically significant.*

Table 4. — *Summary of reported hydronephrosis after radical hysterectomy for cervical cancer.*

	Hazewinkel *et al.* [3]	Paick *et al.* [8]	Tsurusaki *et al.* [6]	Ulmsten *et al.* [4]	Hwang *et al.* [16]	Suprasert *et al.* [2]	Kim *et al.* [7]	Current study
No. of patients	281	34	47	100	120	55	34	270
Hydronephrosis	34 (12.1%)	7 (20.6%)	32 (68.1%)	21 (21.0%)†	1 (0.8%)	7 (12.7%)‡	7 (20.6%)	NA
Urological intervention	4 (1.4%)	0	10 (21.2%)	14 (14.0%)	1 (0.8%)	2 (3.6%)	0	39 (14.4%)
Non-resolution	NA	0	4 (8.5%)*	NA	NA	NA	0	21 (8.1%)

**Among patients who were not treated with urological intervention; †four recurrent patients were included; ‡persistent hydronephrosis three months after surgery. NA: none available*.

difficult to give patients sufficient information about the incidence of persistent hydronephrosis after RH, with no ovious, or unrecognized injuries to the ureter [2, 4-8]. Paick *et al.* reported that most cases of hydronephrosis after RH improved spontaneously and needed no ureteric stent or surgical intervention [8]. However, another study reported that 46% of patients treated with both surgery and radiotherapy had hydronephrosis. Among those patients, 46% developed persistent hydronephrosis, and two-thirds of them were treated surgically to preserve renal function [4].

In the current study, the rate of HTUI was higher compared with previous studies. Although Tsurusaki *et al.* reported that the rate of intervention was 21.2%, the current study might present a higher rate because the Tsurusaki *et al.* study included four recurrent cases. Among the studies which reported the incidences of HTUI, there were clear differences among the studies [2-4, 6-8, 16] (Table 4). Three studies including current study reported higher rates from 14% to 21.2% [4, 6] and the other five studies reported lower rates from 0% to 3.6% [2, 3, 7, 8, 16].

The main reason for the difference was supposed that there were different surgical techniques in each institution. The present authors' surgical techniques are based on those of Okabayashi [11], with nerve-sparing procedures and total mesometrial resection, which are among the most invasive and radical procedures performed worldwide. These surgical techniques increase the radicality of the operation but enhance the possibility of injuries to the lower urinary tract or near the base of the bladder. These surgical techniques require radical, deep, and meticulous dissection near the vesicouterine ligaments and parametrial area through which the ureter and supplying blood vessels pass. There have been a few randomized studies of nerve-sparing RH. Although these studies showed favorable improvement of bladder dysfunction, they did not investigate the effect on hydronephrosis that developed secondary to bladder dysfunction [17-19]. Some studies have suggested that urinary complications of RH depend directly on the length of resected parametrial tissue [20, 21]. Although many RH procedures are currently performed with nerve-sparing techniques, the main reason for the high rate of urinary complications is supposed to be the invasiveness of the operation, which might not be compensated by nerve sparing.

Radiation therapy has been considered a major factor in the development of hydronephrosis, regardless of combination with RH [22]. In the current study the effect of radiation for the HTUI was not large. The results for the effect of radiation in the current study require validation in larger, long-term follow-up studies.

In the resolution group, more cases of hydronephrosis were resolved using retrograde ureteric stent (n=6). However, Tsurusaki *et al.* reported no significant differences between stent and PCN [6]. In the present authors' institute they initially attempted retrograde stent due to its less invasiveness. When it failed or did not function, PCN with anterograde stent or ballooning were attempted.

In this study, though the AUC of age and onset time were insufficient to demonstrate better discriminatory abilities due to the low values [23], the authors recommend careful follow-up for the patients with old age or late onset of hydronephrosis after RH. The recommendation accords with previous reports [8, 22]. Early onset of hydronephrosis after RH is usually caused by transient reduction of peristaltic movements or peri-ureteric inflammation, which return to

normal after restoration of normal function [3]. Late-onset hydronephrosis develops with progressive peri-ureteric fibrosis and lack of vascularity, which are related to irreversible tissue damage.

Although there was no significant difference, left hydronephrosis improved more frequently, which has been reported previously [8]. The difference in pathophysiology between right and left hydronephrosis has not been studied.

The limitations of this study were as follows. First, the number of patients was too small to allow generalization of the results. Second, this was a non-randomized, unmatched, and retrospective study. Third, because data were collected only for patients with HTUI and not for all patients who experienced hydronephrosis after RH, the present results cannot be compared with other studies for the incidence of hydronephrosis after RH. However, this is one of only a few studies to study the clinical course of HTUI after RH.

Conclusion

In this study, the most important prognostic factors for the HTUI are old age and the late onset of hydronephrosis after RH. Careful follow-up is needed for the patients with old age or late onset of hydronephrosis after RH. The rate of HTUI might vary depending on each institution and its surgical techniques.

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