

COMPARISON OF SURGICAL OUTCOME AND THE SYSTEMIC INFLAMMATORY RESPONSE SYNDROME SCORE BETWEEN RETROPERITONEOSCOPIC HAND-ASSISTED NEPHROURETERECTOMY AND OPEN NEPHROURETERECTOMY

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The goal of this study is to compare surgical and oncological outcomes of laparoscopic nephroureterectomy and the open surgery using the concept of systemic inflammatory response syndrome (SIRS) in addition to common variables. Thirty-six and 23 patients having upper urinary tract urothelial cancer who were operated on with retroperitoneoscopic hand-assisted nephroureterectomy (RHANU) or standard open nephroureterectomy (ONU) retrospectively, were analyzed. Median operation time was 140 (range 70–200) and 60 (range 45–85) minutes, respectively in the RHANU group and the ONU group. The median days to ambulation and hospital stay of the RHANU group were significantly shorter than those of the ONU group. There was no significant difference in the incidence of SIRS and other surgical results between the two groups. In oncological outcome, no significant difference was found in the bladder recurrence rate (RHANU vs. ONU ; 52% vs. 45%), local recurrence (0% vs. 0%), distant metastasis (11% vs. 13%) or survival rate (94% vs. 91%) between the RHANU group and the ONU group at 2-year follow-up. There was no port site recurrence in the RHANU group.

Although the RHANU may have an advantage in terms of earlier recovery, there were no significant differences in the incidence of SIRS and oncological outcomes between the RHANU group and the ONU group.

(Hinyokika Kiyo 52 : 903–909, 2006)

Key words : Retroperitoneoscopic nephroureterectomy, Hand assistance, Open nephroureterectomy, SIRS

INTRODUCTION

Laparoscopic surgery changed the surgical treatment strategy for upper urinary tract urothelial carcinoma^{1–4)}. It is well established that laparoscopic nephroureterectomy is minimally invasive, with less pain, earlier recovery and full ambulation without impairing oncological outcomes^{2–6)}. On the other hand, open nephroureterectomy (ONU) is still the standard procedure for upper urinary tract urothelial carcinoma^{1,2,7)}.

However, we still have some questions about the surgical invasiveness of both approaches. First, we would like to clarify whether laparoscopic nephroureterectomy is less invasive than open surgeries performed with a short operation time (OT) because, in our hospital, open nephroureterectomy (ONU) is performed in about 1 hour.

Second, systemic effects of surgery should be evaluated for comprehensive analysis of surgical invasiveness in addition to common parameters. A few studies analyzed this issue through measurement of acute phase reactants^{8,9)}. Recently, systemic inflammatory re-

sponse syndrome (SIRS) is used as a parameter of surgical invasiveness^{10–13)}. The concept of SIRS may supplement the common parameters such as blood loss, pain and recovery from biological aspects of post surgical conditions to estimate surgical invasiveness, although this parameter was originally provided to evaluate the prognosis of severe sepsis or injury in a critical setting¹⁴⁾.

The goals of this study were to compare our RHANU and 1-hour ONU from the aspect of surgical invasiveness using the concepts of SIRS and oncological outcome retrospectively.

PATIENTS AND METHODS

1. Patients

Thirty-six and 23 patients having upper urinary tract urothelial cancer who were operated on with retroperitoneoscopic hand assisted nephroureterectomy (RHANU) and standard open nephroureterectomy (ONU), respectively, were analyzed. RHANU was performed from April 2002 to December 2004. After starting laparoscopic surgery, only 6 cases were operated by the ONU. These patients who received the ONU had relatively advanced conditions compared to those

Table 1. Patient demographics

Variables	RHANU group	ONU group	P value
Patients (n)	36	23	
Sex (n)			NS
Male	24	14	
Female	12	9	
Median age (y.o)	72 (46–81)	70 (51–80)	NS
Median BMI	22.9 (17.7–30.5)	23.8 (17.7–30.4)	NS
Location of tumor (n)			p=0.035
Pelvis	20	6	
Ureter	16	17	
Laterality of tumor (n)			NS
Right	18	11	
Left	18	12	

NS=not statistically significant. Data in parentheses are range, unless otherwise noted. Sex of patients, location of tumor and laterality of tumor were analyzed by χ^2 test. Patients' age and BMI were analyzed by Mann-Whitney U test.

operated by the RHANU. Thus, we compared patients operated by the ONU from January 1999 to December 2001 before starting laparoscopic operation in our institution. The demographics of both groups are described in Table 1. There were no significant differences in patients' characteristics except tumor site between both groups.

2. Analysis of surgical and oncological outcomes

Operation time (OT), estimated blood loss (EBL), and other surgical results and complications during and after surgery were analyzed as parameters of surgical outcomes. Incidence of "SIRS" was calculated in both groups as one of a parameter of surgical invasiveness. The definition of SIRS was taken from the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference¹⁴⁾: Patients were considered to have SIRS when they have two or more following conditions. Body temperature of 38°C or greater or less than 36°C, heart rate greater than 90 beats/minute; respiratory rate greater than 20 breaths/minute or partial pressure of carbon dioxide in arterial gas less than 32 mmHg; or white blood cell count greater than 12,000 cells/mm³ or less than 4,000 cells/mm³, or 10% immature band cell forms. The duration of SIRS was calculated in days.

For analysis of oncological outcomes, bladder and local recurrences, distant metastasis and cause-specific survival of both surgical groups were compared. Post operative follow-up consisted of cystoscopy and urinary cytology every three months, CT scan and IVP were performed every six to twelve months.

3. Operative procedures

The patients of both surgical groups consumed only clear liquid and received a mechanical bowel preparation on the day before surgery. On the day of surgery, they received broad-spectrum parenteral antibiotics. The patients of both operation groups were placed in the lateral position. The patient position was

not changed during the operative procedures in the two groups. In the RHANU, nephrectomy was performed by the retroperitoneoscopic hand-assisted method. The surgical details were described in our previous report¹⁵⁾. The 7 cm-pararectal incision was made at the umbilical level before port placement. The retroperitoneal space was developed with hand assistance. The dissection of renal hilum was performed by a "pure" laparoscopic procedure and hand assistance was applied again for the mobilization of the kidney. Managements of distal ureter and bladder cuff resection were performed by open procedure from the pararectal incision that was used for hand assistance. The incision was extended caudally by 2–3 cm if necessary. Bladder cuff resection was performed by an extravesical approach. Intravesical dissection was applied when a tumor involved in the intramural ureter. The intact en-block specimen was removed from the incision. The ONU was performed in the standard fashion. Bladder cuff resection was managed by the same principle to the RHANU. Subcostal and suprapubic incisions were made for the ONU in most cases. OT was defined as time from skin incision to wound closure. After surgery the patients received analgesics (Bupivacaine or Ropivacaine) through the epidural tube for one day. The regional lymph node dissection were performed when lymph node involvement were suspected by pre-operative examination and findings during the operations.

4. Statistics

The variables were expressed as the median value. The patients' demographics and their clinical outcomes were analyzed by Fisher's exact probability test or χ^2 test or Mann-Whitney U test. Kaplan-Meier curves were used for bladder recurrence-free survival and cancer-specific survival. They were statistically analyzed by using the log rank test according to operation method. Statistical significance was defined as $p < 0.05$.

Table 2. Surgical parameters

Variables	RHANU group (n=36)	ONU group (n=23)	p value
Median operation time (min)	140 (70-200)	60 (45-85)	p<0.0001
Median estimated blood loss (ml)	76 (10-519)	140 (46-350)	NS
Median weight of specimen (g)	275 (140-830)	260 (120-830)	NS
Transfusion (n)	4 (11%)	2 (9%)	NS
Analgesia			
Median days of epidural tubing (days)	1(1-2)	1(1-2)	NS
Median dose of NSAID (mg)	75(0-500)	50 (0-300)	NS
Median dose of pentazocine (mg)	30 (0-60)	15 (0-90)	NS
Median days to oral intake (days)	1 (1)	1 (1)	NS
Median days to ambulation (days)	1 (1-3)	2 (1-4)	p=0.0091
Major complication (n)	1 (3%)	None (0%)	NS
Open conversion (n)	1	—	
Median days of hospital stay (days)	16 (10-24)	21 (14-25)	p=0.0004

NS=not statistically significant; Data in parentheses are range, unless otherwise noted. Transfusion and major complication were analyzed Fisher's exact probability test. Other parameters were analyzed by Mann-Whitney U test.

Table 3. Incidence and duration of systemic inflammatory response syndrome

Variables	RHANU group (n=36)	ONU group (n=23)	p value
Patients with SIRS (n)	5 (14%)	4 (17%)	NS
Median duration of SIRS (days)	1 (1-2)	1 (1-3)	NS

NS=not statistically significant; Data in parentheses of patients with SIRS and median duration of SIRS are % and range, respectively. SIRS = systemic inflammatory response syndrome. Patients with SIRS and its duration were analyzed by Fisher's exact probability test and Mann-Whitney U test, respectively.

Table 4. Histopathological and follow-up data

Variables	RHANU group (n=36)	ONU group (n=23)	p value
Pathology (n)			NS
UC	33	22	
UC>SCC	3	1	
Pathologic T stage (n)			NS
pT $\leq$ 1/CIS	20	10	
pT2	4	6*	
pT3	11	7	
pT4	1*	0	
Grade (n)			NS
1	6	5	
2	24	14	
3	6	4	
Bladder recurrence (n)			NS
Superficial tumor	12	10	
Invasive tumor	0	3	
Location of bladder recurrence (n)			NS
Ipsilateral ureteral scar	3	4	
Other area	9	9	
Local recurrence (n)	0	0	
Distant metastasis (n)	4	3	NS
Cancer specific survival at 2 years (%)	94	91	
Mean follow up (month)	25 (2-46)	60 (1-82)	p<0.0001

NS=not statistically significant; Data in parentheses are range. Pathology, pathologic T stage and Grade were analyzed by χ^2 test. Bladder recurrences, location of bladder recurrence, local recurrence, and distant metastasis were analyzed by Fisher's exact probability test. Mean follow up- month was compared by Mann-Whitney U test. *=One case had lymph node metastasis.

RESULTS

1. Surgical outcome

OT of the ONU group was significantly shorter than that of the RHANU group (Table 2). There was no significant difference in EBL between the two groups. There were no significant differences in dose of NSAID (diclofenac sodium) and pentazosin between the two groups. Days to ambulation and hospital stay of the RHANU group were significantly shorter than those of the ONU group (Table 2).

The incidences of SIRS of the RHANU group and the ONU group were 14% (5/36) and 17% (4/23), respectively (Table 3). There were no significant differences in the incidence and duration of SIRS between the two groups.

One major complication occurred in the RHANU group on day 4 after the surgery (thrombus of the mesenteric artery).

2. Oncological outcomes

There was no significant difference in the distribution of histopathological (T stage and grade) and follow-up data between the two groups (Table 4). Lymph node involvements were found in one case in each group. No port site metastasis was found in the RHANU group. The bladder recurrence rate in the RHANU group and the ONU group was 52% and 45%, respectively at the 2-year follow-up. There was no significant difference in the bladder recurrence-free survival rates between the two group ($p = 0.67$ by log rank test, Fig. 1). The cause-specific survival rate in the RHANU group and the ONU group at 2 years was 94% and 91%, respectively (Table 4). There was no significant difference in the cause-specific survival rate between the two groups ($p = 0.83$ by log rank test, Fig. 1).

DISCUSSION

Many well-organized studies have demonstrated that laparoscopic nephroureterectomy achieves minimal invasiveness and oncological outcomes compatible to the standard open surgery in long-term follow-up^{2,3)}.

Our current study showed that the RHANU might have an advantage for earlier recovery and that there were no significant differences in the incidence of SIRS, other surgical results and oncological outcomes between the RHANU group and the one-hour ONU group. Although this study was retrospective, non-randomized and had small patient cohorts and short-term follow-up, this study provides some important findings.

In the current study, the days to ambulation and hospital stay in the RHANU group were significantly shorter than those in the ONU group, although the differences were minimal. The subcostal incision of the ONU may be associated with a delay of ambulation and recovery of normal activity compared to the RHANU. The RHANU also requires a 7–10 cm pararectal

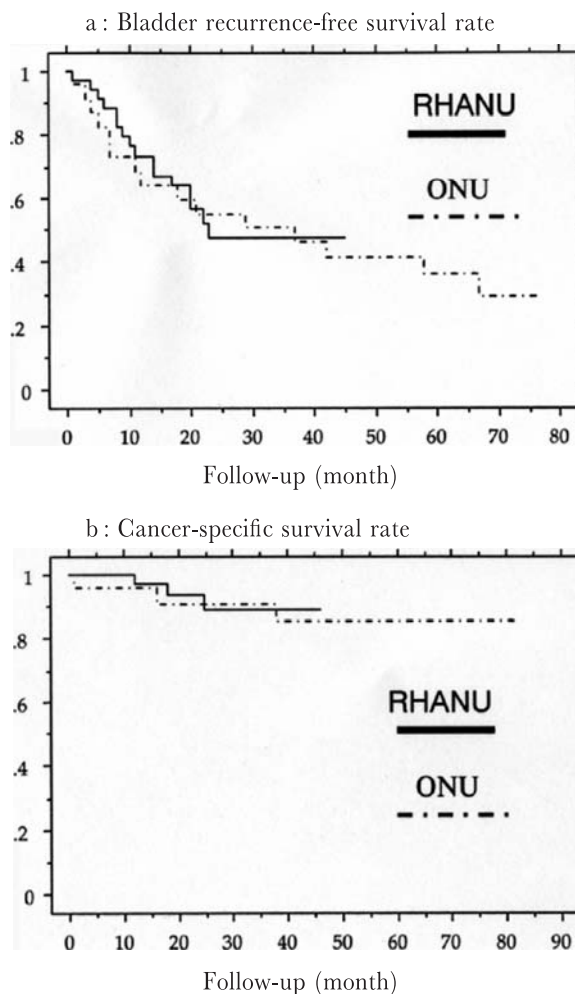


Fig. 1. a: bladder recurrence-free survival rate. There was no significant difference between the RHANU group and the ONU group ($p = 0.67$ by log rank test). b: Cancer-specific survival rate. There was no significant difference between the RHANU group and the ONU group ($p = 0.83$ by log rank test).

incision, and the wound pain is minimal because there is no muscle dissection in this incision. Thus our RHANU may provide attractive benefits of laparoscopic nephroureterectomy (nephrectomy) for patients through early recovery and a smaller operative wound compared to one-hour ONU. Long-term effects of both incisions of the RHANU and ONU on patients' quality of life also should be evaluated in the future.

On the other hand, we could not find any significant differences in the incidence and duration of SIRS and surgical parameters except operation time between the two groups. Previous studies suggested that laparoscopic surgery had fewer systemic effects as there were lower levels of acute phase reactants than for open surgery^{8,9)}. In contrast to these reports, our results suggested that both types of surgery may have similar systemic impacts on the patients. The application of SIRS for surgical invasiveness has not been validated fully; it has the potential to be a useful and reliable tool

to assess adverse biological impacts of various types of surgery including laparoscopic one¹⁰⁻¹³). In addition, the incidence of SIRS in both groups was lower than that of laparoscopic adrenalectomy¹⁰). OT and EBL, conventional parameters, of both groups were relatively short and low, respectively, compared to those of previous LNU and ONU series^{2,3,5,6,16-18}).

Our follow-up periods, in particular, that of the RHANU group was short, we could not reach conclusive results in oncological outcomes. There were no significant differences between the oncological outcomes of the two groups at present point. Laparoscopic procedures did not interfere with oncological safety as described in previous reports. Bladder recurrence, local recurrence, distant metastasis and cancer-specific survival rates in both groups were compatible with previous series^{2-4,20}). Specifically, the bladder recurrence rates in previous LNU and ONU series were 9 to 54 and 13 to 64%, respectively, although a recent report showed that laparoscopic surgery had a significant impact on bladder recurrence¹⁹). The bladder recurrence rate in our RHANU and ONU groups was 52% and 45% at two years. The bladder recurrence rates in the ipsilateral ureteral scar area in our RHANU and ONU groups were 25 (3/12) % and 31 (4/13) %, respectively. These rates were also compatible with previous findings³). Distant metastasis rates were reported to be from 0 to 28% in LNU and from 0 to 29% for ONU²⁻⁴). In the current study, distant metastasis rates in the RHANU group and the ONU group were 11% and 13%, respectively. Those rates were also comparable to previous series. We did not encounter port-site metastasis, although port-site metastasis is rare according to previous reports²⁻⁴). Cancer-specific survival at two years in our series was similar to those of previous reports. The open bladder cuff resection using a supra inguinal incision simultaneously for intact retrieval of the specimen seems to be a trend in laparoscopic nephroureterectomy, although this method does not always guarantee complete resection of the "cuff", and various endoscopic approaches have achieved satisfactory outcomes^{2,3}). Thus, both our RHANU and ONU that were performed with relatively short OT did not cause oncological outcomes to be deteriorated.

The RHANU and ONU performed with shorter OT may have similar surgical invasiveness in some parameters and can be considered to be low invasive surgical procedures without detrimental oncological outcomes. The RHANU provided earlier recovery and a smaller incision. Further studies are required to evaluate long-term adverse medical effects of both surgical procedures and patients' quality of life. At this point, we chose the RHANU as a first line surgical therapy. However, we prefer the ONU for patients with risk for laparoscopic surgery. Specifically, in patients with obesity, adhesion of surgical area due to

inflammation and fibrosis, re-operation, medical comorbidities necessitate rapid procedure and locally advanced tumor^{2,21}). The benefits and risks of laparoscopic and open surgery for individual patients should be considered carefully for selection of operation methods.

CONCLUSIONS

The RHANU may have an advantage for earlier recovery. The RHANU and ONU groups exhibited similar incidences of SIRS and other surgical results. They are considered to be low-invasive surgical procedures without deleterious oncological outcomes. According to the current results, we prefer ONU in patient who may have risk for laparoscopic surgery. Operative methods should be chosen carefully, taking into consideration for the patient's the benefit.

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(Received on April 24, 2006)
(Accepted on August 9, 2006)

和文抄録

後腹膜鏡下ハンドアシスト法および開放腎尿管全摘除術の比較検討

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腎盂尿管腫瘍に対する体腔鏡下および開放腎尿管全摘除術につき手術成績, 術後経過を比較検討する. 全身的侵襲性の指標として systemic inflammatory response syndrome (SIRS) の発症頻度に関しても比較検討を行う.

腎盂尿管腫瘍に対して腎尿管全摘除術を施行した体腔鏡下手術36例 (2002年4月~2004年12月) 開放手術 (ONU) 23例 (1999年1月~2001年12月) を対象とした. 体腔鏡下手術は後腹膜鏡下ハンドアシスト法 (RHANU) を用いた.

手術時間 (中央値) は RHANU 群140分, ONU 群60分と ONU 群で有意に短かった. 出血量は両群とも平

均約 150 ml であった. RHANU 群において歩行開始日が有意に短縮していた. SIRS の頻度は RHANU 群17%, ONU 群26%と有意差を認めなかった. 膀胱再発率は52, 45% (以下 RHANU 群 vs ONU 群), 遠隔転移11, 13%, 局所再発は両群とも認めず2年での生存率は94, 91%であった.

体腔鏡下手術では, 歩行開始日が有意に短く早期の回復が示唆された. SIRS の頻度, 再発・転移・生存率に有意な差を認めなかった. 体腔鏡下手術のリスク, 術式の患者への利点を充分考慮した手術方法の選択が重要と思われた.

(泌尿紀要 52: 903-909, 2006)