

A CLINICAL STUDY OF TOTAL CYSTECTOMY FOR TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER

Masafumi Waki, Hidetoshi Fukatsu, Hitoshi Nonomura,
Yoshimasa Miyagawa, Yukio Hatano, Shinsuke Hiraiwa,
Tadashi Muramatsu, Yoshiaki Yamada
and Akio Segawa

From the Department of Urology, Aichi Medical University

Norimitsu Hirata

From the Department of Urology, Asai Hospital

Fifty six patients with transitional cell carcinoma of the urinary bladder were treated by total cystectomy from January, 1979 through December, 1988. A retrospective study was conducted on 52 patients on whom prognosis could be followed up. There were 40 men and 12 women (male to female ratio: 3.3: 1), between 32 and 79 years old (mean age, 64.1 years old).

The overall 1-, 3- and 5-year survival rates were 65.8%, 54.1% and 43.0%, respectively. The 5-year survival rates for patients with low grade (G. I, II) and high grade (G. III) were 41.9% and 42.7%, respectively: with no significant difference in the survival curves between the two groups. The 5-year survival rates according to histopathological stage were 78.9% for patients in low stage, 24.7% in high stage, and the difference in the survival curves between the two groups was statistically significant ($P<0.001$). The mortality in the 21 cases of the 33 high stage cases in which cisplatin was used was 42.9%, with 3- and 5-year survival rates were 53.1% and 36.8%, respectively. In the remaining 12 cases in which cisplatin was not used for post-operative chemotherapy, the mortality in the 12 cases was 83.3%, with 3- and 5-year survival rates of 25.1% and 12.3%, respectively.

Thus, the patients who received post-operative chemotherapy showed a better survival rate than those who did not with a significant difference ($P<0.05$). The results of the present study suggest the usefulness of post-operative adjuvant chemotherapy in the high stage case.

Key words: Transitional cell carcinoma, Total cystectomy, Prognosis

INTRODUCTION

Bladder cancer has the highest incidence of the malignant tumors in the urinary tract. It shows multiform histopathological findings and various treatments are performed for it. Total cystectomy is widely practiced as the optimum treatment of multiple superficial bladder cancer and infiltrating bladder cancer. However, since a total cystectomy alone often results in poor prognosis in cases of infiltrating bladder cancer, additional treatments such as radiation therapy and chemotherapy are tried for improvement of the prognosis¹⁻⁵).

In the present study, we investigated retrospectively 56 patients with transitional cell carcinoma of the urinary bladder treated by total cystectomy and evaluated prognosis in relation to histopathological grade, stage and post-operative adjuvant chemotherapy.

MATERIALS AND METHOD

During the 10-year period from January 1979 to December 1988, 56 patients with transitional cell carcinoma of the urinary bladder were treated by total cystectomy at urological clinics associated with the Aichi Medical University. 52 of the 56 patients were able to be traced. Forty

males and 12 females (sex ratio of 3.3:1) ranging in age from 32 to 79 years old (mean age : 64.1 years) were used as subjects.

Histopathological grade and stage of tumors were classified in grades I, II, and III, and stages 1 through 4 according to criteria established for urinary bladder cancers by the Japanese Urological Association⁶⁾. In this classification, grades I and II were low grade, grade III was high grade, stage pT₁ was low stage, and stages pT₂ through pT₄ were high stage. We started giving cisplatin to the high stage cases as chemotherapy 2 or 3 weeks postoperatively and compared the prognosis with that of untreated subjects. The medication was the same as CAP therapy (cyclophosphamide, doxorubicin, cisplatin) or M-VAC therapy (methotrexate, vinblastine, doxorubicin, cisplatin). We considered the case of chemotherapy when the total dose of cisplatin was not less than 100 mg.

Survival rates were illustrated by the Kaplan-Meier method. A significant difference was calculated by the generalized Wilcoxon method.

RESULTS

Table 1 shows the grade and stages for all 52 subjects.

The 1-year survival rate for the 52 subjects was 65.8%, the 3-year survival rate was 54.1%, and the 5-year survival rate was 43.0% (Fig. 1).

1. Histopathological grade and prognosis

Among the 52 subjects, none were grade I, 17 were grade II, and 35 were grade III; 17 subjects had low grade (32.7%)

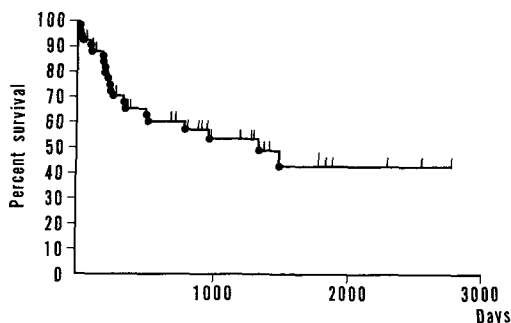


Fig. 1. Survival rate of 52 cases

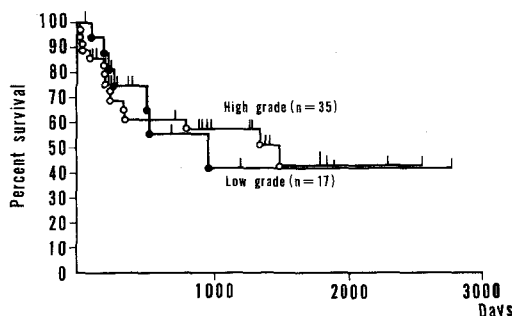


Fig. 2. Survival rate according to grade

and 35 subjects had high grade (67.3%). The low grade 5-year survival rate was 41.9% and the high grade 5-year survival rate was 42.7%; no significant difference was observed between the survival curves of these groups (Fig. 2).

2. Histopathological stage and prognosis

Among the 52 subjects, 19 were classified as pT₁, 10 as pT₂, 14 as pT₃, and 9 as pT₄; a total of 19 subjects (36.5%) were classified as low stage, and 33 (63.5%) as high stage. The 5-year survival rate was 78.9% for the low stage group and 24.7% for the high stage group. A significant difference ($P < 0.001$) was seen between the survival curves of these two groups (Fig. 3).

3. Post-operative adjuvant chemotherapy and prognosis

Twenty one of 33 subjects classified as high stage were treated with adjuvant chemotherapy. The 5-year survival rate for the 21 subjects treated with adjuvant chemotherapy was 36.8%, and 12.3% for the 12 untreated subjects. A significant difference ($P < 0.05$) was noted between

Table 1. Grade and stage of total cystectomy cases

Stage	Grade			Total
	I	II	III	
PT ₁		9	10	19
PT ₂		3	7	10
PT ₃		3	13	16
PT ₄		2	5	7
Total		17	35	52

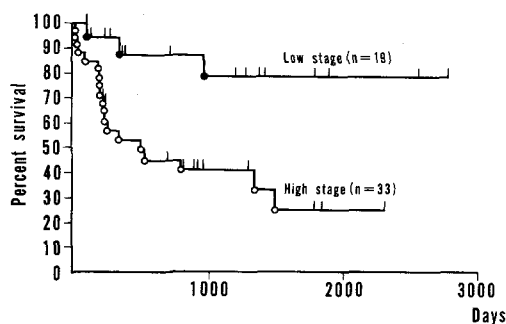


Fig. 3. Survival rate according to stage

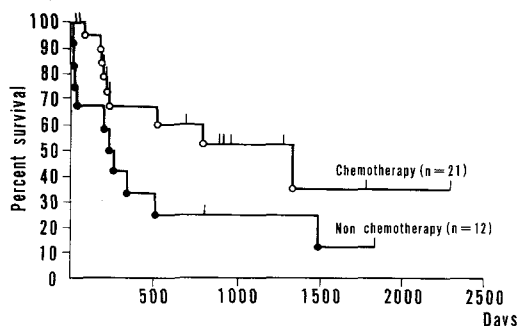


Fig. 4. Survival rate according to post-operative chemotherapy

the survival curves for the two groups (Fig. 4).

DISCUSSION

Tanaka et al.⁷⁾ reported a 5-year survival rate of 58.2% after the treatment of total cystectomy for the patients with transitional cell carcinoma of the urinary bladder, Sumiyoshi et al.⁸⁾ reported that of 52.6% and Kobayashi⁹⁾ reported 42.0%. We obtained a 3-year survival rate of 54.1% and the 5-year survival rate of 43.0%.

It is clear from works already published that the histopathological grade and stage are important as factors affecting the prognosis in cases of transitional cell carcinoma of the urinary bladder. In general, high grade and high stage cases have a poor prognosis.

There are many reports that the higher the grade becomes, the lower the survival rate becomes, in correlation with the survival rate and grade of cases of total cystectomy as treatment of transitional

cell carcinoma of the urinary bladder. Kobayashi⁹⁾ reported that the 5-year survival rate was 47.0% in grade II cases and 41.0% in grade III cases, while no significant difference was observed between the two. We obtained a 5-year survival rate of 41.9% in low grade cases and 42.7% in high grade cases, with no significant difference between the two survival curves.

According to many reports, the survival rate becomes lower the higher the stage becomes. Kobayashi⁹⁾ reported a 5-year survival rate of 76.0% in low stage cases (pT_a and pT₁) and 24.0% in high stage cases (pT₂ through pT₄), and observed a significant difference between the two. We also found that at the 5-year survival rate was 78.9% in low stage cases and 24.7% in high stage cases, with a significant difference between the two. The above findings suggest that as the factors affecting the prognosis, stage is of greater importance than grade.

There are many reports on the clinical efficacy of radical total cystectomy as a means to purify the pelvic lymph nodes. However, in high stage cases, the prognosis is extremely poor^{10,11)}. To improve the prognosis, the importance of post-operative adjuvant chemotherapy is strongly emphasized. In recent years, chemotherapy using cisplatin has been reported to be very effective in cases of progressive transitional cell carcinoma of the urinary tract. Schwartz et al.¹²⁾ have observed 57.0% efficacy on CAP therapy, and Sternberg et al.¹³⁾ have observed 71.0% efficacy on M-VAC therapy. There are also reports on efficiency of post-operative adjuvant chemotherapy using cisplatin. Uekado et al.¹⁴⁾ have reported that 17 cases of high stage treated with adjuvant chemotherapy using cisplatin after total cystectomy showed good results with a 33-month survival rate of 84.0%.

Numazawa et al.¹⁵⁾ observed improvement of the 3-year survival rate using cisplatin adjuvant chemotherapy following total or partial cystectomy in cases of infiltrating vesical transitional cell

carcinoma with vascular invasions. Logothetis et al.¹⁶⁾ also have observed improved survival rates using CAP adjuvant chemotherapy following total cystectomy in cases of infiltrating vesical transitional cell carcinoma. We also used cisplatin on 21 subjects with high stage cases as post-operative adjuvant chemotherapy and compared the prognosis with that of 12 untreated subjects, and found a significantly higher survival rate as compared with the untreated cases. We believe that these findings suggest the efficacy of post-operative adjuvant chemotherapy using cisplatin, and expect more improvement of the prognoses.

REFERENCES

- 1) Skinner DG, Tift JP and Keufman JJ: High dose, short course preoperative radiation therapy and immediates single stage radical cystectomy with pelvic node dissection in the management of bladder cancer. *J Urol* **127**: 671-674, 1982
- 2) Hall RR and Heath AB: Radiotherapy and cystectomy for T3 bladder carcinoma. *Br J Urol* **53**: 598-601, 1981
- 3) Uekado Y, Ogawa T, Yoshida T, Yamamoto S, Hirono A, Watanabe T, Shinka T and Ohkawa T: Chemotherapy for advanced bladder cancer: clinical evaluation of chemotherapy for advanced or metastatic bladder cancer and adjuvant chemotherapy for deeply invasive bladder cancer following radical cystectomy. *Acta Urol Jpn* **31**: 1365-1370, 1985
- 4) Hasui Y, Osada Y, Uehara K, Koriyama K and Saito Y: Clinicopathological evaluation of preoperative combined therapy with total cystectomy for bladder cancer. *Nishinohon J Urol* **51**: 1127-1133, 1989
- 5) Oda H, Fujita K, Yoshioka S, Seike H, Wakatsuki A, Yokoyama M, Iwata H, Matsumoto A and Takeuchi M: Evaluation of adjuvant therapy combined with total cystectomy for high stage bladder cancer. *Nishinohon J Urol* **50**: 109-112, 1988
- 6) Japanese Urological Association and The Japanese Pathological Society: General rule for clinical and pathological studies on bladder cancer. 1st ed., pp. 62-86, Kanahara publication, Tokyo, 1980
- 7) Tanaka S, Hara Y, Ishikawa S, Morita T, Moriguchi H, Kobayashi Y, Tozuka K, Ohba S, Tokue A and Yonese Y: Clinical study of total cystectomy on the patients with bladder transitional cell cancer. *Acta Urol Jpn* **31**: 1939-1943, 1985
- 8) Sumiyoshi Y, Kagawa S, Takigawa H and Kurokawa K: Clinical study of total cystectomy: 1. simple cystectomy for transitional cell carcinoma of the bladder. *Nishinohon J Urol* **49**: 797-802, 1987
- 9) Kobayashi H: The study of cell surface antigens in bladder tumors: ABH-isoantigen and Thomsen friedreich antigen. *Acta Urol Jpn* **33**: 535-544, 1987
- 10) Nishio Y, Matsumoto K, Ohtani M and Kakizoe T: Radical cystectomy for transitional cell carcinoma of the bladder. *Jpn J Urol* **77**: 79-86, 1986
- 11) Miyakawa M, Oishi K, Okada Y, Takeuchi H, Okada K and Yoshida O: Results with multidisciplinary treatment for invasive bladder cancer. *Acta Urol Jpn* **32**: 1931-1939, 1986
- 12) Schwartz S, Yogoda A, Natale PB, Watson RC, Whitmore WF and Lesser M: Phase II trial of sequentially administered cisplatin, cyclophosphamide and doxorubicin for urothelial tract tumors. *J Urol* **130**: 681-684, 1983
- 13) Sternberg CN, Yagoda A, Scher HI, Watson RC, Ahmed T, Weisberg LR, Geller N, Hollander PS, Herr HW, Sogani PC, Morse MJ and Whitmore WF: Preliminary results of M-VAC (methotrexate, vinblastine, doxorubicin and cisplatin) for transitional cell carcinoma of the urothelium. *J Urol* **133**: 403-407, 1985
- 14) Uekado Y, Shinke T, Kumeda K, Hirano A, Yoshida M, Yamamoto S, Watanabe T and Ohkawa T: Adjuvant chemotherapy for high stage and/or high grade bladder cancer following radical cystectomy: a preliminary report. *Jpn J Urol* **77**: 466-473, 1986
- 15) Numasawa K, Suzuki H, Kakizaki H, Hirano K, Takamizawa A, Kubota Y and Suzuki K: Postoperative adjuvant chemotherapy for bladder cancer. The effects of cisplatin administration positive cases of vascular invasion. *Jpn J Urol* **78**: 489-495, 1987
- 16) Logothetis CJ, Johnson DE, Chong C, Dexeus FH, Ogden S, von Eschenbach A and Ayala A: Adjuvant chemotherapy of bladder cancer: a preliminary report. *J Urol* **139**: 1207-1211, 1988

(Received on November 14, 1989)
(Accepted on March 8, 1990)

(迅速掲載)

和文抄録

膀胱移行上皮癌に対する膀胱全摘除術の治療成績

愛知医科大学泌尿器科学教室（主任：瀬川昭夫教授）

和気 正史，深津 英捷，野々村仁志

宮川 嘉真，羽田野幸夫，平岩 親輔

村松 直，山田 芳彰，瀬川 昭夫

浅井病院泌尿器科

平 田 紀 光

1979年1月1日より1988年12月31日までの10年間に、愛知医科大学付属病院泌尿器科にて、膀胱移行上皮癌56例に対して膀胱全摘除術を施行した。

追跡可能であった52例において、その予後と病理組織学的異型度、深達度および術後化学療法との関係について検討した。

性別は男性40例，女性12例でその比は3.3：1であった。年齢は最少32歳，最長79歳で平均64.1歳であった。

52例の1年，3年および5年生存率はそれぞれ65.8%，54.1%，43.0%であった。

病理組織学的異型度では，5年生存率で low grade (G. I, II) 41.9%，high grade (G. III) 42.7%であり，両生存曲線間には有意差はなかった。

病理組織学的深達度では，5年生存率で low stage

(pT₁) 78.9%，high stage (pT₂~pT₄) 24.7%であり，両生存曲線間には有意差が認められた ($P < 0.001$)。

術後 cisplatin を中心とした化学療法を，high stage 症例33例中21例に施行した。施行21例中死亡9例 (42.9%) で，3年および5年生存率はそれぞれ53.1%，36.8%であった。一方，非施行12例中死亡10例 (83.3%) で，3年および5年生存率はそれぞれ25.1%，12.3%であった。術後化学療法施行例は非施行例に比べて生存率は高く，両生存曲線には有意差が認められた ($P < 0.05$)。

以上のことは，high stage 症例に対する術後の補助的化学療法の有効性を示唆しているものと考えられる。

(泌尿紀要 36：649-653, 1990)