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# Guideline Adherence of Immediate Post-Transurethral Resection Intravesical Chemotherapy for Patients with Nonmuscle Invasive Bladder Cancer

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## Abstract

**Introduction:** Immediate postoperative instillation of chemotherapy to prevent intravesical recurrence of nonmuscle invasive bladder cancer is supported by level 1 evidence and recommended by contemporary guidelines. However, there have been a few reports on the feasibility and adherence of immediate postoperative chemotherapy instillation after transurethral resection. We retrospectively assessed the adherence rate of this treatment in patients with nonmuscle invasive bladder cancer.

**Methods:** We identified 438 patients with clinically Ta/T1 bladder cancer who underwent transurethral resection with curative intent between 2008 and 2013. We investigated the implementation of immediate postoperative instillation of chemotherapy. For those who did not receive this treatment we tried to identify the reasons for nonadministration from the clinical record and categorized them into technical, patient or other factors. We further interrogated clinicopathological characteristics associated with nonadministration.

**Results:** Overall 193 of the 438 study patients (44.1%) did not receive immediate postoperative instillation of chemotherapy. The noninstillation rate constantly decreased with time from 58.8% to 28.0% between the study periods. Deep resection was the most common reason for nonadministration. There was a statistically significant decreasing time trend for nonadministration. Multivariate analysis revealed that clinical stage T1 tumor, negative cytology and larger tumor size were independently associated with nonadministration.

**Conclusions:** Guideline adherence improved with time, suggesting that better education and better understanding of the guideline contributed to achieve high adherence. Deep resection was the most common reason for nonadministration, which was associated with clinically infiltrating cancer and larger tumor size.

*Key Words:* urinary bladder neoplasms; drug therapy; neoplasm recurrence, local; guideline adherence; practice patterns, physicians'

**Abbreviations and Acronyms**

IPIOC = immediate postoperative instillation of chemotherapy

NMIBC = nonmuscle invasive bladder cancer

TUR = transurethral resection

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The natural history of NMIBC is characterized by frequent intravesical recurrence at a rate of up to 75%.[1] IPIOC is supported by level 1 evidence showing an approximately 30% decrease in the intravesical recurrence rate and 40% prolongation of recurrence-free survival.[2,3] Guidelines also support IPIOC,[4–7] although the level of recommendation varies from standard to optional, reflecting the unresolved controversy about uniform application to all Ta/T1 tumors without exception.[8]

Indeed, a national practice survey in the United States revealed that IPIOC was used in only about 4% of potential patients.[9] Even after the publication and dissemination of guidelines the utilization rate of IPIOC was still as low as 30%.[10] The low guideline adherence could be attributable to insufficient dissemination of the guideline and to heterogeneous study populations in terms of patient preferences and physician practice patterns.

In this regard a practice based collaborative group in the United States reported a higher utilization rate of approximately 80% for IPIOC.[11] This suggests that the relatively low administration rates in the previous national surveys were due in part to the study design based on administrative data collection.[9,10] Additionally, another report from the same collaborative group suggested that the IPIOC utilization rate could be improved to some degree with better education and understanding of indications and treatments.[12] However, the report also showed the so-called ceiling effect, which makes it difficult to improve practice beyond a certain degree of high quality care at baseline.

Thus, it is still unclear how well the guideline recommendation for IPIOC is feasible and can be adhered to after it has been adopted and disseminated into real world clinical practice. We report the use of IPIOC for NMIBC with regard to the rate of instillation, reasons for nonadministration and clinical characteristics associated with nonadherence at a single academic institution.

## Patients and Methods

We adopted IPIOC into our clinical practice protocol in 2008. Since then, NMIBC treated with TUR with curative intent has been considered the indication for IPIOC with epirubicin (50 mg/50 ml saline for 1 hour) in principle irrespective of tumor size, appearance, number, clinical stage and suspicion of carcinoma in situ. To investigate the adherence and the feasibility of the treatment strategy, we retrospectively reviewed the records of our patients with NMIBC.

We identified 438 patients with clinically Ta/1N0M0 bladder cancer who underwent TUR with curative intent between 2008 and 2013 (table 1). Those undergoing diagnostic transurethral biopsy of the bladder or repeat TUR following initial TUR for pT1 bladder cancer were excluded from study. We reviewed clinical records with regard to whether the patient received an immediate intravesical instillation postoperatively as well as other clinicopathological characteristics. Class 4 or 5 urine cytology results were considered positive. If intravesical chemotherapy was

**Table 1.**
Patient characteristics

| | Overall | | Instillation | | | | p Value | |
|---|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | | |
| No. pts (%) | 438 | (100) | 245 | (100) | 193 | (100) | – | |
| Median age (range) | 73 (29–96) | | 72 (35–96) | | 75 (29–94) | | 0.036 | (Mann-Whitney U test) |
| No. clinical stage (%): | | | | | | | <0.0001 | (Fisher exact test) |
| Ta | 353 | (81) | 217 | (89) | 136 | (70) | | |
| T1 | 85 | (19) | 28 | (11) | 57 | (30) | | |
| No. cytology (%): | | | | | | | 0.0002 | (chi-square test) |
| Pos | 283 | (65) | 178 | (73) | 105 | (54) | | |
| Neg | 147 | (34) | 65 | (27) | 82 | (42) | | |
| Not done | 8 | (2) | 2 | (1) | 6 | (3) | | |
| No. multiplicity (%): | | | | | | | 0.492 | (Fisher exact test) |
| Single | 175 | (40) | 94 | (38) | 81 | (46) | | |
| Multiple | 263 | (60) | 151 | (62) | 112 | (54) | | |
| No. recurrence history (%): | | | | | | | 0.442 | (Fisher exact test) |
| Primary | 217 | (50) | 117 | (48) | 100 | (52) | | |
| Recurrence | 221 | (50) | 128 | (52) | 93 | (48) | | |
| No. tumor size (%): | | | | | | | <0.0001 | (chi-square test) |
| 3 cm or Less | 386 | (88) | 230 | (94) | 156 | (81) | | |
| Greater than 3 cm | 41 | (9) | 10 | (4) | 31 | (16) | | |
| Not assessable | 11 | (3) | 5 | (2) | 6 | (3) | | |
| No. TUR yr (%): | | | | | | | <0.0001 | (Fisher exact test) |
| 2008–2010 | 243 | (55) | 111 | (45) | 132 | (68) | | |
| 2011–2013 | 195 | (45) | 134 | (55) | 61 | (32) | | |