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Intraoperative hypothermia is a significant prognostic predictor of radical cystectomy especially for stage II muscle-invasive bladder cancer

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Abstract

The objective of this study was to evaluate intraoperative hypothermia as a predictor of complication and prognosis in patients with muscle-invasive bladder cancer treated with radical cystectomy.

The data of 124 patients treated with radical cystectomy for muscle-invasive bladder cancer in our department, from 2003 to 2016, were retrospectively collected. The patients were divided into 2 groups according to the lowest intraoperative deep body temperature, that is, the hypothermia group (<96.8°F) and the normothermia group (≥96.8°F). Preoperative and intraoperative variables were compared among the 2 groups, and factors associated with complications, recurrences, and survivals were analyzed.

Sixty-eight (54.8%) of the 124 patients presented intraoperative hypothermia. There was no significant difference in the patient's characteristics between the 2 groups. Postoperative complications (Clavien–Dindo ≤III) of any types occurred in 15 patients (22.1%) in the hypothermia group, as compared with 8 patients (14.3%) in the normothermia group ($P = .27$). The hypothermia group had a higher pathologic stage ($P = .029$) and a higher recurrence rate within 12 months ($P = .013$), as compared with the normothermia group. Intraoperative hypothermia was an independent prognostic factor for overall survival in all patients (hazard ratio [HR] 2.47; 95% confidence interval [CI], 1.01–2.85; $P = .047$). When stratified by disease stage, stage II intraoperative hypothermia was an independent prognostic factor for disease-free survival (HR 3.35; 95% CI, 1.27–8.83; $P = .015$) and overall survival (HR 4.24; 95% CI, 1.38–12.9; $P = .011$).

This study suggests that intraoperative hypothermia could be a significant predictor for recurrence and survival in muscle-invasive bladder cancer treated with radical cystectomy.

Abbreviations: ASA = American Society of Anesthesiologist, BCa = bladder cancer, CI = confidence interval, DFS = disease-free survival, HR = hazard ratio, MIBC = muscle-invasive bladder cancer, OR = odds ratio, OS = overall survival, PS = performance status, RC = radical cystectomy, SSI = surgical-site infection, UTI = urinary tract infection.

Keywords: complication, intraoperative hypothermia, muscle-invasive bladder cancer, prognosis, recurrence

1. Introduction

Bladder cancer (BCa) is the 4th and 5th most commonly diagnosed malignancy in the United States and Europe, respectively, and approximately 25% of BCa are muscle-invasive bladder cancer (MIBC).[1] Radical cystectomy (RC) with urinary diversion and neoadjuvant chemotherapy is the gold standard treatment for MIBC.[2] However, it sometimes causes severe complications like urinary tract infection (UTI), surgical-site infection (SSI), and bowel obstruction, and the recurrence of diseases after RC is not uncommon.[3] In fact, several previous studies reported that rate of complications after RC was 25% to 67%,[3,4] and that rate of local recurrence and distant metastasis after RC was 4% to 29% and 22% to 38%, respectively.[5]

Factors associated with complications and prognosis after RC have been well studied. Age, sex, American Society of Anesthesiologist performance status (ASA-PS) classification, preoperative sepsis, chronic obstructive pulmonary disease, low serum albumin concentration, preoperative radiotherapy, preoperative transfusion >4 units, or operative time >6 hours, were associated with complications after RC.[4,6] On the contrary, PS, preoperative hydronephrosis, pathologic results, molecular markers such as p53, p21, pRB, and p16, and preoperative hematologic biomarkers such as hemoglobin, lymphocyte, and C-reactive protein are reported to be associated with prognosis after RC.[1,7–10] While a lot of factors predicting complications or prognosis after RC have been reported, other factors like genetic alterations, health conditions, or unknown factors might also be associated with complications or prognosis.[8,10]

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Recently, intraoperative hypothermia has been reported to be associated with complications in several kinds of cancer surgeries.[11–15] Hypothermia increases blood loss and the need for transfusion during surgery, delays healing, and increases SSI.[11,12] Moreover, hypothermia can induce lymphopenia.[16] Lymphopenia may be related to the suppression of the immune system for cancer, and could be an independent predictor for prognosis in several cancers.[17–19] These changes indicate that intraoperative hypothermia itself could be related to poor prognosis.

There have been no reports which studied intraoperative hypothermia in patients treated with RC. Therefore, we examined relationship between intraoperative hypothermia and complications or prognosis in these patients.

2. Methods

The data of 124 patients treated with RC for MIBC in our department from 2003 to 2016 were retrospectively collected. RCs were performed in open fashion with minimal standard template pelvic lymph node dissection including all potential lymph node-bearing tissue with the lateral limit of the genitofemoral nerve, distal Cooper ligament to include Cloquet node, proximal crossing of the ureter over the common ileac vessels, the medial bladder including tissue medial to the hypogastric artery, the posterior floor of the obturator fossa with circumferential mobilization of the external iliac artery, and vein off the pelvic side wall. Regarding urinary diversion, ureterocutaneostomy, ileal conduit, or neobladder was chosen depending on the patient status and preference.

Clinical information included sex, age, PS, smoking, neoadjuvant, or adjuvant chemotherapy, epidural anesthesia, amount of bleeding, operative duration, postoperative courses, complications, histologic findings, recurrence, cancer-specific deaths, and any deaths. Complications were classified according to the Clavien–Dindo classification.[20] Tumor stages were classified according to the 2009 TNM-UICC stage classification system. Recurrences and deaths were determined by review of the medical records.

Esophageal temperatures were measured by the transesophageal approach at every 5 minutes intervals, as intraoperative deep body temperature. A warm-air unit (Bair Hugger) was used as the warming device. Intraoperative hypothermia was defined as the lowest intraoperative deep body temperature below 96.8°F (36.0°C) in accordance with the guideline of ASA.[15] The patients were divided into 2 separate groups according to their lowest intraoperative body temperature, that is, the hypothermia group (<96.8°F) and the normothermia group (≥96.8°F). Preoperative and intraoperative variables were compared among the 2 groups, and factors associated with complications, recurrences, and survivals were statistically analyzed.

A Chi-squared test and the Mann–Whitney *U* test were used to evaluate associations between intraoperative hypothermia and clinicopathologic parameters. Survival curves were plotted using the Kaplan–Meier method and statistical significance was assessed using the log rank test. The Cox proportional hazards regression analysis was used to evaluate factors predicting intraoperative hypothermia, recurrence, and overall death. A predictor of intraoperative hypothermia was evaluated by logistic regression analysis. A *P*-value of .05 or less was considered statistically significant. Statistical analyses were performed using the Bell Curve for Excel, version 2.13, for Windows.

3. Results

3.1. Comparison of clinical and pathologic variables according to intraoperative body temperature

Table 1 lists the patient characteristics and clinicopathologic findings of the 2 intraoperative body temperature groups. Sixty-eight (54.8%) of the 124 patients treated with RC had intraoperative hypothermia. There was no significant difference between the 2 groups, with regard to sex, mean age, PS, smoking, epidural anesthesia, and surgery. In the clinicopathologic findings, the hypothermia group had a higher pathologic stage ($P=.029$) and had a significant recurrence within 12 months ($P=.013$). The hypothermia group was likely to have a poor PS ($P=.063$), LN metastasis ($P=.13$), and total recurrence ($P=.16$) with no significant difference.

A logistic regression analysis showed no independent indicators of intraoperative hypothermia (Table 2). Age and PS appeared to be associated with intraoperative hypothermia, but the difference was not statistically significant.

Postoperative complications (Clavien–Dindo ≤III) of any type occurred in 15 patients (22.1%) in the hypothermia group, as compared with 8 patients (14.3%) in the normothermia group ($P=.27$). When comparing each grade 3 or greater complications including death within the first 30 postoperative days, bowel obstruction, UTI, SSI, anastomotic event of the urinary tract, cardiovascular event, respiratory event, and gastrointestinal hemorrhage, there was no significantly different association between the 2 groups (Table 3).

3.2. Survival analysis of MIBC

Median follow-up durations from RC in the hypothermia and normothermia groups were 21.5 months (4–174 months) and 37.5 months (2–163 months), respectively. Median overall survival (OS) duration from RC in the hypothermia and normothermia groups were 29 months (4–174 months) and 109 months (2–163 months), respectively ($P=.078$; Fig. 1A). Median disease-free survival (DFS) durations from RC in the hypothermia and normothermia groups were 29 months (4–174 months) and 109 months (1–163 months), respectively ($P=.083$; Fig. 1B). The Cox proportional hazards regression analysis showed stages III and IV, urinary diversion by ureterocutaneostomy, and the presence of lymphovascular invasion as independent indicators of DFS (Table 4). Intraoperative hypothermia appeared to be associated with DFS, but the difference was not statistically significant (hazard ratio [HR] 1.42; 95% confidence interval [CI], 0.88–2.29; $P=.15$). Regarding OS, intraoperative hypothermia was an independent prognostic factor (HR 2.47; 95% CI, 1.01–2.85; $P=.047$). Neoadjuvant or adjuvant chemotherapy, urinary diversion by ureterocutaneostomy, and lymphovascular invasion were also identified as the other independent predictors for OS (Table 5). There was no significant difference, compared by duration of intraoperative hypothermia (data not shown).

3.3. Survival analysis, according to disease stage

When subgrouped by pathologic stages, there was no significant difference in both OS and DFS among stages III and IV patients (data not shown). However, in stage II, both OS and DFS were significantly shorter in the hypothermia group than in the normothermia group. In stage II, median OS duration from RC in the hypothermia and normothermia groups were 34 months

Table 1

Distributions of patient characteristics and clinicopathologic findings according to intraoperative body temperature.

Characteristic	Normothermia	Hypothermia	*P*-value
Patients, n	56	68	
Mean follow-up, mo (range)	37.5 (2–163)	21.5 (4–174)	NS (.07)
Sex, n (%)			
Male	41 (73.2)	52 (76.5)	
Female	15 (26.8)	16 (23.5)	NS (.68)
Mean age, yr (range)	69 (49–83)	72 (48–90)	NS (.23)
PS, n (%)			
0–1	50 (89.3)	52 (76.5)	
2–4	6 (10.7)	16 (23.5)	NS (.063)
Smoking, n (%)	26 (46.4)	30 (44.1)	NS (.80)
Chemotherapy, n (%)	26 (46.4)	23 (33.8)	NS (.15)
Epidural anesthesia, n (%)	46 (82.1)	53 (77.9)	NS (.66)
Urinary diversion, n (%) (ileal conduit or neobladder)	35 (62.5)	39 (57.4)	NS (.56)
Mean amount of bleeding, mL (range)	1395.5 (304–4720)	1281.5 (249–5223)	NS (.28)
Mean duration of surgery, min (range)	397 (160–774)	367.5 (160–720)	NS (.36)
Transfusion, n (%)	23 (41.0)	33 (48.5)	NS (.41)
Complications (Clavien–Dindo), n (%)			
≤II	48 (85.7)	53 (77.9)	
≥III	8 (14.3)	15 (22.1)	NS (.27)
Stage, n (%)			
II	24 (42.9)	26 (38.2)	
III	18 (32.1)	11 (16.2)	.029
IV	14 (25.0)	31 (45.6)	
LN metastasis, n (%)	12 (21.4)	23 (33.8)	NS (.13)
Lymphovascular invasion, n (%)	29 (51.8)	33 (48.5)	NS (.72)
Recurrence, n (%)	25 (44.6)	39 (57.4)	NS (.16)
Recurrence within 12 months, n (%)	10 (17.9)	26 (38.2)	.013

NS = not significant, PS = performance status.

(4–169 months) and not reached (2–163 months), respectively ($P = .017$; Fig. 2A). Median DFS durations from RC in the hypothermia and normothermia groups were 24 months (1–169 months) and not reached (2–163 months), respectively ($P = .0047$; Fig. 2B). The Cox proportional hazards regression analysis revealed that intraoperative hypothermia for stage II was an independent prognostic factor for DFS (HR 3.35; 95% CI, 1.27–8.83; $P = .015$) and OS (HR 4.24; 95% CI, 1.38–12.9; $P = .011$). Lymphovascular invasion was also identified as an independent predictor for DFS and OS (Tables 6 and 7).

Table 2

A predictor of intraoperative hypothermia in 124 patients with muscle-invasive bladder cancer.

	P-value Univariate analysis
Variable	
Sex (male vs female)	0.68 (OR, 1.19; 95% CI 0.53–2.69)
Age, yr (70≤ vs <70)	0.09 (OR, 1.85; 95% CI 0.90–3.79)
PS (2–4 vs 0–1)	0.08 (OR, 2.41; 95% CI 0.86–6.68)
BMI (≤20 vs 20<)	0.24 (OR, 1.73; 95% CI 0.68–4.44)
Smoking	0.72 (OR, 0.88; 95% CI 0.43–1.78)
Neoadjuvant chemotherapy	0.31 (OR, 0.70; 95% CI 0.35–1.40)
Urinary diversion	0.80 (OR, 0.91; 95% CI 0.45–1.86)
Ileal conduit or neobladder vs ureterocutaneostomy	
Transfusion	0.36 (OR, 1.39; 95% CI 0.68–2.84)
Stage (III, IV, vs II)	0.66 (OR, 1.17; 95% CI 0.57–2.41)

BMI = body mass index, CI = confidence interval, OR = odds ratio, PS = performance status.

4. Discussion

Intraoperative hypothermia is caused by distribution of body heat by vasodilation after induction of anesthesia.[21] Several previous studies revealed that hypothermia induces vasoconstriction, lymphopenia, and inhibition of platelet aggregation, resulting in increase of blood loss, cardiovascular events, and infectious complications such as SSI.[11–13,16]

This is the 1st report which discusses the association between intraoperative hypothermia and RC. The rate of hypothermia in patients treated with RC was 54.8%. The rates of intraoperative hypothermia varied depending on the surgeries. Multicenter retrospective study in Japan reported

Table 3

Association between intraoperative hypothermia and perioperative complications according to Clavien–Dindo classification.

Complications	Normothermia	Hypothermia	*P*-value
Any grade	32 (57.1%)	42 (61.8%)	NS (.60)
Grade III≤	8 (14.3%)	15 (22.1%)	NS (.27)
Death within 30 d	0 (0%)	2 (2.9%)	NS (.20)
Bowel obstruction	4 (7.2%)	2 (2.9%)	NS (.28)
Urinary tract infection	2 (3.6%)	3 (4.4%)	NS (.81)
Surgical site infection	1 (1.8%)	4 (5.9%)	NS (.25)
Anastomotic event of urinary tract	1 (1.8%)	1 (1.5%)	NS (.89)
Cardiovascular event	1 (1.8%)	1 (1.5%)	NS (.89)
Respiratory event	1 (1.8%)	1 (1.5%)	NS (.89)
Gastrointestinal hemorrhage	1 (1.8%)	1 (1.5%)	NS (.89)

NS = not significant.

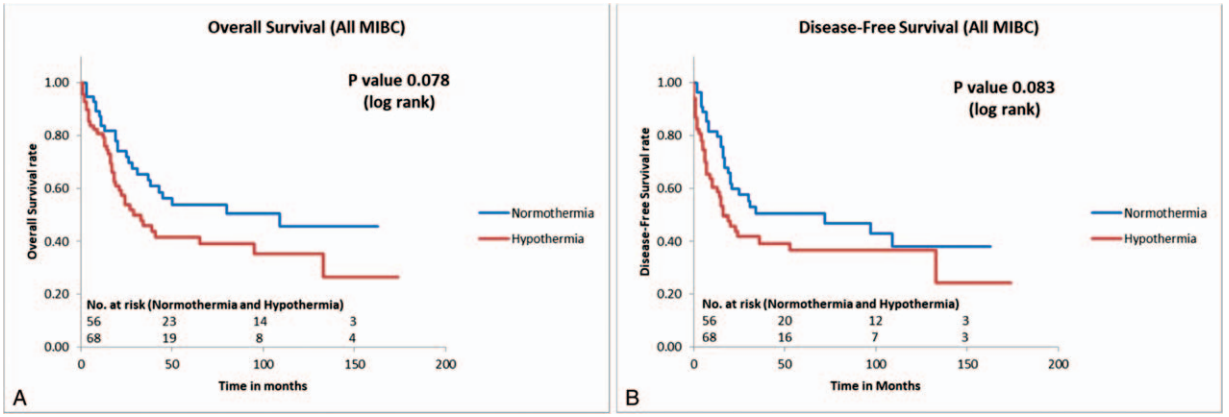

Figure 1. Kaplan–Meier analysis of overall survival ($P = .078$, A) and disease-free survival ($P = .083$, B), according to intraoperative body temperature for all muscle-invasive bladder cancer.

that the rate of intraoperative hypothermia was 40.0% in gastric surgery, 43.7% in colon surgery, 82.1% in rectal surgery, and 41.9% in hepatobiliarypancreatic surgery.[22] Long et al reported that 73.7% of the patients treated with primary cytoreductive surgery for advanced ovarian cancer presented intraoperative hypothermia.[23]

In this study, the rate of grade III or greater postoperative complications was likely to be higher in the hypothermia group than in the normothermia group. However, there was no statistically significant difference (22.1% vs 14.3%, $P = .27$). Types of complications did not differ among the groups, but it is too difficult to draw any conclusions because of small sample size in this study. In fact, several previous studies showed that intraoperative hypothermia increased postoperative complications. Melling et al reported that intraoperative hypothermia was associated with the increased incidence of

Table 4

Prognostic factors for disease-free survival in 124 patients with muscle-invasive bladder cancer.

	P-value	
	Univariate analysis	**Multivariate analysis**
Variable		
Sex (male vs female)	0.38 (HR, 0.79; 95% CI 0.47–1.33)	
Age, yr (70≤ vs <70)	0.61 (HR, 1.13; 95% CI 0.70–1.83)	
PS (2–4 vs 0–1)	0.11 (HR, 1.60; 95% CI 0.88–2.89)	
Smoking	0.39 (HR, 0.81; 95% CI 0.50–1.31)	
Chemotherapy	0.14 (HR, 1.43; 95% CI 0.89–2.31)	
Urinary diversion (ileal conduit or neobladder vs ureterocutaneostomy)	0.0033 (HR, 0.49; 95% CI 0.30–0.79)	0.0041 (HR, 0.49; 95% CI 0.30–0.80)
Clavien–Dindo (III≤ vs ≤II)	0.62 (HR, 0.89; 95% CI 0.55–1.43)	
Stage (III, IV, vs II)	0.018 (HR, 1.61; 95% CI 0.91–2.87)	0.029 (HR, 1.72; 95% CI 1.02–2.91)
Presence of lymphovascular invasion	0.002 (HR, 2.30; 95% CI 1.36–3.88)	0.043 (HR, 1.87; 95% CI 1.07–3.28)
Presence of intraoperative hypothermia	0.15 (HR, 1.42; 95% CI 0.88–2.29)	

CI = confidence interval, HR = hazard ratio, PS = performance status.

Table 5

Prognostic factors for overall survival in 124 patients with muscle-invasive bladder cancer.

	P–value	
	Univariate analysis	**Multivariate analysis**
Variable		
Sex (male vs female)	0.95 (HR, 0.98; 95% CI 0.56–1.72)	
Age, yr (70 ≤ vs <70)	0.40 (HR, 1.24; 95% CI 0.75–2.06)	
PS (2–4 vs 0–1)	0.073 (HR, 1.76; 95% CI 0.95–3.25)	
Smoking	0.60 (HR, 0.87; 95% CI 0.53–1.45)	
Chemotherapy	0.038 (HR, 1.70; 95% CI 1.03–2.80)	0.0064 (HR, 2.13; 95% CI 1.24–3.69)
Urinary diversion (ileal conduit or neobladder vs ureterocutaneostomy)	0.002 (HR, 0.45; 95% CI 0.27–0.75)	<0.001 (HR, 0.36; 95% CI 0.21–0.61)
Clavien–Dindo (III ≤ vs ≤ II)	0.96 (HR, 0.87; 95% CI 0.61–1.66)	
Stage (III, IV, vs II)	0.0072 (HR, 2.13; 95% CI 1.23–3.68)	0.32 (HR, 1.36; 95% CI 0.74–2.50)
Presence of lymphovascular invasion	<0.001 (HR, 2.58; 95% CI 1.53–4.38)	0.0019 (HR, 2.14; 95% CI 1.24–3.69)
Presence of intraoperative hypothermia	0.048 (HR, 1.52; 95% CI 1.01–2.53)	0.047 (HR, 2.47; 95% CI 1.01–2.85)

CI = confidence interval, HR = hazard ratio, PS = performance status.

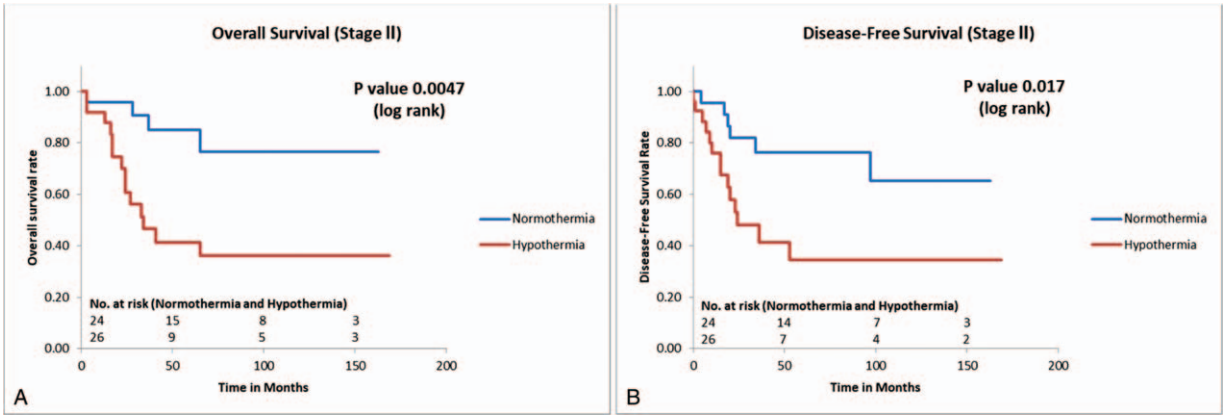

Figure 2. Kaplan–Meier analysis of overall survival ($P = .0047$, A) and disease-free survival ($P = .017$, B), according to intraoperative body temperature for stage II.

SSI in 421 patients undergoing clean surgery.[24] Yamasaki et al reported that intraoperative hypothermia was an independent risk factor for early postoperative complications following esophagectomy.[25] Other studies demonstrated that intraoperative hypothermia significantly increased SSI in colon surgery, and deep vein thrombosis and infection in cytoreductive surgery for advanced ovarian cancer.[15,22,23] Further analyses with large a sample size would be needed to make clear which kinds of complications are likely to be developed by intraoperative hypothermia.

This study showed that intraoperative hypothermia was an independent prognostic factor for OS and appeared to be associated with DFS in MIBC patients treated with RC. The exact reasons for an association between intraoperative hypothermia and prognosis in patients treated with RC are unknown, but the hypothermia group had poor PS or advanced stages, as compared with the normothermia group in this study. Frank et al revealed that poor PS, older age, and thinness were an independent predictor for intraoperative hypothermia,[26] which may indicate that patients with unfavorable prognostic factors before surgery are likely to present intraoperative

Table 6

Prognostic factors for disease-free survival in 50 patients with stage II bladder cancer.

	P-value	
	Univariate analysis	**Multivariate analysis**
Variable		
Sex (male vs female)	0.39 (HR, 0.68; 95% CI 0.28–1.66)	
Age, yr (70 ≤ vs < 70)	0.32 (HR, 1.58; 95% CI 0.64–3.90)	
PS (2–4 vs 0–1)	0.54 (HR, 1.41; 95% CI 0.47–4.24)	
Smoking	0.86 (HR, 0.92; 95% CI 0.38–2.25)	
Chemotherapy	0.70 (HR, 0.82; 95% CI 0.30–2.26)	
Urinary diversion (ileal conduit or neobladder vs ureterocutaneostomy)	0.07 (HR, 0.44; 95% CI 0.18–1.06)	
Clavien–Dindo (III ≤ vs ≤ II)	0.19 (HR, 0.55; 95% CI 0.23–1.33)	
Presence of lymphovascular invasion	0.041 (HR, 2.51; 95% CI 1.04–6.07)	0.021 (HR, 2.85; 95% CI 1.17–6.95)
Presence of intraoperative hypothermia	0.024 (HR, 3.02; 95% CI 1.15–7.90)	0.015 (HR, 3.35; 95% CI 1.27–8.83)

CI = confidence interval, HR = hazard ratio, PS = performance status.

Table 7

Prognostic factors for overall survival in 50 patients with stage II bladder cancer.

	P-value	
	Univariate analysis	**Multivariate analysis**
Variable		
Sex (male vs female)	0.57 (HR, 1.35; 95% CI 0.48–3.79)	
Age, yr (70 ≤ vs < 70)	0.73 (HR, 1.18; 95% CI 0.46–2.99)	
PS (2–4 vs 0–1)	0.41 (HR, 1.60; 95% CI 0.53–4.87)	
Smoking	0.74 (HR, 0.92; 95% CI 0.46–2.97)	
Chemotherapy	0.81 (HR, 1.14; 95% CI 0.40–3.19)	
Urinary diversion (ileal conduit or neobladder vs ureterocutaneostomy)	0.32 (HR, 0.63; 95% CI 0.25–1.58)	
Clavien–Dindo (III≤ vs ≤II)	0.39 (HR, 0.67; 95% CI 0.26–1.69)	
Presence of lymphovascular invasion	0.040 (HR, 2.46; 95% CI 1.06–6.26)	0.047 (HR, 1.76; 95% CI 1.30–2.94)
Presence of intraoperative hypothermia	0.0097 (HR, 4.35; 95% CI 1.43–13.3)	0.011 (HR, 4.24; 95% CI 1.38–12.9)

CI = confidence interval, HR = hazard ratio, PS = performance status.

hypothermia, resulting in shorter survivals after RC compared to those without hypothermia.

Moreover, intraoperative hypothermia especially resulted in poor DFS and OS for stage II MIBC. The exact reasons for the stronger association between intraoperative hypothermia and prognosis in patients treated with stage II are also unknown. However, some explanations for the possibility of hypothermia inducing poor prognosis in stage II MIBC might be possible. Sejima et al reported that patients undergoing RC with stage T3, T4, and node positive BCa were more likely to have micrometastases which are not detected by standard staging procedures, and had a 50% or greater recurrence rate.[1] As the cancer progression itself affected the prognosis in patients treated with stages III and IV, intraoperative hypothermia might not be significant as a prognosis predictor. On the contrary, as the frequency of preoperative metastases seemed to be low in stage II, intraoperative hypothermia might have been identified as an independent prognostic factor for DFS and OS. From this point, this study showed that intraoperative hypothermia as a prognostic predictor could be more effective predictor in patients with localized cancer.

The 2nd explanation is immune suppression due to hypothermia. Several previous studies reported that surgical stress, such as massive blood loss or lengthy operative time, was associated with hypothermia, which induced lymphocyte dysfunction.[14–16] Lymphocyte dysfunction may cause suppression of the cancer immune system and may lead to an increase in risk of disease recurrence. [17–19,27–29] In fact, Tai et al reported that perioperative lymphocyte dysfunction increased metastatic recurrence and resulted in poor OS in surgical cancer patients.[30] These findings indicate that lymphocyte dysfunction, due to intraoperative hypothermia, might affect the prognosis in patients with MIBC treated with RC in this study.

Influence of preventing intraoperative hypothermia on complications was studied by Kurz et al in 1996. They conducted a randomized controlled trial in which 200 patients undergoing colorectal surgery were randomly assigned to routine intraoperative thermal care or additional warming, and showed that preventing intraoperative hypothermia reduced the rate of SSI and the duration of hospitalization.[11] Frank et al also performed a randomized controlled trial in patients with cardiac risk factors who were scheduled to undergo noncardiac surgery and demonstrated that preventing intraoperative hypothermia reduced incidence of morbid cardiac events and ventricular tachycardia.[13] Unlike complications, influence of preventing intraoperative hypothermia on recurrence and survival has never been studied before. Future study would be necessary to examine whether preventing intraoperative hypothermia could lead to a decrease in incidence of complications or improve survivals.

We acknowledge the limitations of this study. This study was a retrospective study with a small sample size and a relatively short follow-up period in a single institution. Our patients had heterogeneous backgrounds. For example, standard management of MIBC was neoadjuvant chemotherapy followed by RC, but chemotherapy was performed after RC for some patients and never performed in other patients. We do not have information regarding nutritional condition, hydronephrosis, and surgeon volume which have been reported to be associated with complications or oncologic outcomes. Despite these limitations, this study has revealed the rate of intraoperative hypothermia in patients treated with RC and showed the possibility of intraoperative hypothermia on predicting recurrence and survival. These data may be helpful for urologists, because careful management or close follow-up after RC for patients who presented intraoperative hypothermia may improve prognosis.

The data presented in this study suggest the usefulness of intraoperative hypothermia as a predictive factor for DFS and OS in patients with MIBC treated with RC. This is believed to be the 1st study showing the significance of intraoperative hypothermia as an independent prognostic predictor for patients undergoing RC.

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