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Original Article

Impact of immediate intravesical therapy on non-muscle invasive bladder cancer with risk factors analysis for recurrence

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Abstract: Objective: To evaluate the impact of immediate intravesical therapy (IIT) on recurrence rates in non-muscle invasive bladder cancer (NMIBC) patients and to explore the potential protective role of vitamin supplementation. Methods: A retrospective analysis was conducted on 216 NMIBC patients treated between April 2019 and March 2023. Patients were categorized into two groups: IIT group (n = 154) and no-IIT group (n = 62). Inclusion criteria included pathologically confirmed NMIBC, initial transurethral resection of bladder tumor (TURBT), and a minimum follow-up of one year. Patients who underwent radical cystectomy, had other malignancies, or suffered from severe comorbid conditions were excluded. Recurrence within one year post-treatment was used to stratify patients into recurrence and non-recurrence groups. Statistical analyses were performed to identify factors significantly associated with recurrence. Logistic regression and receiver operating characteristic curve analyses were employed to evaluate predictive performance. Results: The recurrence rate was significantly lower in the IIT group (33.12%) compared to the no-IIT group (95.16%, $P < 0.001$). IIT significantly reduced the risk of recurrence ($P < 0.001$). Among vitamin supplements, only vitamin K3 demonstrated a significant association with recurrence ($P = 0.010$). Logistic regression confirmed IIT as an independent protective factor (OR = 0.026, $P < 0.001$). The area under the curve (AUC) for individual predictors ranged from 0.587 to 0.754, while the combined model achieved an AUC of 0.877, indicating strong predictive performance. Conclusion: IIT and self-supplementation with vitamin K3 are associated with a reduced risk of NMIBC recurrence. These findings suggest that adjunctive strategies alongside standard transurethral resection of bladder tumor may enhance patient outcomes. Further prospective studies are warranted to confirm these associations and support their integration into clinical practice.

Keywords: Non-muscle invasive bladder cancer, recurrence, immediate intravesical therapy, vitamin self-supplementation, risk factors

Introduction

Bladder cancer is one of the most commonly diagnosed malignancies of the urinary tract and presents significant challenges in clinical management, primarily due to its high recurrence rate [1]. Non-muscle invasive bladder cancer (NMIBC), which comprises approximately 70-80% of all bladder cancer cases, is characterized by tumors confined to the mucosa and submucosa without muscular invasion [2]. Despite its generally favorable prognosis, NMIBC exhibits recurrence rates as high as 50-70% within five years of initial treatment, necessitating intensive surveillance and effective therapeutic strategies to prevent progression and optimize patient outcomes [3]. The recurrent nature of NMIBC places a substantial financial burden on healthcare systems globally, primarily due to the need for frequent cystoscopic follow-up and repeated interventions [4]. Beyond physical implications, recurrence also significantly impacts patients' psychological well-being [5]. Given its public health relevance and economic consequences, NMIBC remains a critical area of focus. Identifying risk factors for recurrence and exploring potential interventions to mitigate these risks are essential for improving both clinical outcomes and quality of life in affected patients [6].

The conventional management of NMIBC involves transurethral resection of bladder tumor (TURBT), followed by adjuvant intravesi-

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cal therapy using agents such as Bacillus Calmette-Guérin (BCG) or chemotherapeutic drugs. Among these, gemcitabine has emerged as a promising alternative due to its favorable safety and efficacy profiles [7]. Intravesical therapy has been shown to significantly reduce tumor recurrence and progression by exerting localized cytotoxic and immunostimulatory effects [8]. However, heterogeneous treatment responses and recurrence rates across patient populations highlight the multifactorial nature of NMIBC prognosis, influenced by both intrinsic and extrinsic variables [8, 9]. Recent research has increasingly emphasized the need to identify modifiable biological targets and adjunctive treatment options that may further reduce recurrence risk [10].

In this context, the role of diet, nutrition, and micronutrient intake in cancer prevention and treatment has garnered growing attention over the past decade [11]. Diets rich in fruits, vegetables, and whole grains are associated with lower cancer incidence and improved survival. Micronutrients, including vitamins and minerals, support numerous physiological functions and may influence carcinogenic and tumor-suppressive pathways. For example, antioxidants such as vitamins C and E help neutralize free radicals, potentially minimizing DNA damage and cancer risk. Similarly, B vitamins are essential for DNA methylation and repair-key processes in maintaining genomic stability. Vitamin K3 (menadione) has been shown to selectively induce oxidative stress and apoptosis in tumor cells while sparing normal tissues [12], a property that may translate into reduced recurrence in cancer patients taking this supplement [13]. Integrating such nutritional strategies into NMIBC management could offer adjunctive benefits, meriting further investigation. Nevertheless, the efficacy of vitamin supplementation in altering NMIBC outcomes remains inconclusive, warranting additional empirical validation.

The concept of "vitamin self-supplementation" refers to the independent use of vitamins by individuals without medical supervision. In NMIBC, this practice may hold particular significance. Owing to the chronic and recurrent nature of the disease, patients are often motivated to adopt proactive health behaviors, including self-directed nutritional strategies. Vitamin supplementation may represent an accessible and cost-effective means of supporting treatment, particularly in resource-limited settings. Moreover, given the individual variability in treatment response, personalized approaches that account for nutritional status and lifestyle factors are increasingly viewed as essential components of precision medicine. Tailored vitamin use may enhance therapeutic efficacy and improve long-term outcomes.

To address existing knowledge gaps and explore new avenues for reducing NMIBC recurrence, this study aims to investigate key risk factors for recurrence, with a specific focus on the potential protective role of vitamin self-supplementation. The rationale for this focus lies in the biological relevance of vitamins in cellular health and metabolic regulation, as well as emerging evidence supporting their anticancer properties. Vitamins are known to affect pathways involved in cell proliferation, apoptosis, and inflammation-central mechanisms in tumor development and recurrence. By examining the association between vitamin use, particularly Vitamin K3, and recurrence outcomes, this study seeks to determine whether such supplements can serve as effective adjuncts to standard therapies. In addition to assessing immediate post-operative interventions such as intravesical therapy, this research also considers long-term lifestyle modifications, including dietary habits and supplement use, to provide a comprehensive understanding of factors influencing recurrence in NMIBC patients.

Materials and methods

Study design

This retrospective study included 216 patients diagnosed with NMIBC at Taihe Hospital between April 2019 and March 2023. Patients were categorized into two groups based on whether they received immediate intravesical therapy (IIT) following diagnosis: the IIT group (n = 154) and the non-IIT group (n = 62). After a one-year follow-up, patients were further stratified according to recurrence status: the recurrence group (n = 110) and the non-recurrence group (n = 106). The study protocol was approved by the Ethics Committee and Institutional Review Board of Taihe Hospital.

Inclusion and exclusion criteria

Inclusion criteria: 1) Pathologically confirmed NMIBC with no evidence of distant metastasis; 2) Initial treatment with TURBT; 3) Minimum follow-up period of one year; 4) Age ≥ 18 years;

5) Karnofsky Performance Status score > 70; 6) TNM stage Ta-T1; 7) Tumor grade G1-G2.

Exclusion criteria: 1) Undergoing radical cystectomy before recurrence; 2) History of other malignancies; 3) Incomplete clinical data; 4) Severe comorbidities (e.g., significant heart, lung, liver, or kidney; disease); 5) Muscle-invasive bladder cancer; 6) Coagulation disorders; 7) Uremia.

Patients who underwent radical cystectomy were excluded to ensure a homogenous study population and to focus specifically on NMIBC-related recurrence risk factors. Radical cystectomy, typically reserved for more advanced disease, introduces significant heterogeneity in prognosis and treatment response. Unlike TURBT and intravesical therapies, cystectomy alters recurrence patterns by shifting the risk toward distant rather than local recurrence, potentially confounding outcome analyses.

Treatment protocol

All patients underwent TURBT as their initial treatment. Under general or spinal anesthesia, patients were placed in the lithotomy position, followed by standard disinfection and sterile draping. A 26F resectoscope was inserted to assess the ureteral orifices, tumor size, location, number, and mucosal abnormalities. Tumor tissue, along with a 1 cm margin of surrounding normal mucosa, was completely excised down to the muscle layer and submitted for pathological examination. Residual fragments were removed using an Ellick evacuator, and electrocautery was applied to the tumor bed for hemostasis. An 18F three-way Foley catheter was inserted postoperatively.

Patients in the IIT group received immediate intravesical instillation of gemcitabine (Eli Lilly, approval number H20160759, 1 g/vial) either in the operating or recovery room. A dose of 1.0 g gemcitabine was dissolved in 50 mL of normal saline and retained in the bladder for one hour. Instillations were administered weekly for eight weeks, followed by monthly instillations. Patients were instructed to avoid excessive fluid intake, intravenous fluids, or diuretics within two hours before treatment and to empty their bladder prior to instillation. The drug was administered via disposable catheter, and patients were asked to change position every 10 minutes (supine, left lateral, prone, and right lateral) to ensure even distribution.

Follow-up Protocol: During the first year, patients underwent cystoscopy and renal ultrasonography every three months. Monthly assessments of liver and kidney function, along with routine blood and urine tests, were conducted. Contrast-enhanced CT scans were performed when clinically indicated.

Data collection

Demographic and clinical data were extracted from patient medical records, including gender, age, body mass index (BMI), family history of cancer, smoking history, secondary resections, tumor stage and grade, tumor multiplicity and size, and whether intravesical therapy was administered (both immediate and maintenance phases).

Data on vitamin supplementation were collected via a structured questionnaire administered one year post-treatment. The questionnaire assessed self-supplementation with vitamins A, B, C, D, E, and K3 during follow-up. It included both closed-ended (yes/no) and open-ended questions for capturing dosage, frequency, and specific vitamin types. To enhance data reliability, patient responses were cross-referenced with clinical records whenever possible, reducing recall bias and improving validity.

Patients' motivations for vitamin supplementation were grounded in the established biological functions of vitamins: their antioxidant properties, capacity to induce apoptosis in cancer cells, potential to enhance radiosensitivity, and anti-inflammatory effects. These benefits may contribute to reduced recurrence in NMIBC patients [14-17]. Recognizing this potential, our institution incorporated documentation of vitamin self-supplementation into standard follow-up procedures for NMIBC patients.

Statistical methods

Sample size estimation was performed using G*Power software (version 3.1.9.7) to ensure adequate statistical power to detect clinically meaningful effects. Assuming a medium effect size ($d = 0.5$) and a two-tailed α of 0.05, a minimum of 61 participants per group was required to achieve 78% power using a two-sample equal-variance t-test.

Statistical analysis was conducted using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). Ca-

Table 1. Comparison of baseline characteristics between IIT and non-IIT groups

	IIT (n = 154)	Non-IIT (n = 62)	t/χ^2	P
Gender (Male/Female)	115 (74.68%)/39 (25.32%)	47 (75.81%)/15 (24.19%)	0.030	0.862
Age	64.87 ± 6.12	64.32 ± 6.45	0.590	0.556
BMI	23.09 ± 2.35	22.98 ± 2.21	0.318	0.751
Family history of tumor (Yes/No)	69 (44.81%)/85 (55.19%)	33 (53.23%)/29 (46.77%)	1.258	0.262
Smoking history (Yes/No)	95 (61.69%)/59 (38.31%)	38 (61.29%)/24 (38.71%)	0.003	0.957
Tumor stage			0.187	0.666
T1	82 (53.25%)	31 (50%)		
Ta	72 (46.75%)	31 (50%)		
Tumor grade			0.418	0.518
G1	72 (46.75%)	32 (51.61%)		
G2	82 (53.25%)	30 (48.39%)		
Multiple tumor (Yes/No)	81 (52.6%)/73 (47.4%)	30 (48.39%)/32 (51.61%)	0.314	0.575
Tumor size/cm			0.844	0.358
≥ 5	6 (3.9%)	5 (8.06%)		
< 5	148 (96.1%)	57 (91.94%)		

IIT: immediate intravesical therapy; BMI: Body Mass Index.

tegorical variables were presented as frequencies and percentages [n (%)]. The chi-square test was used for categorical comparisons.

Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with normal distribution were expressed as mean ± standard deviation (SD), and group comparisons were performed using independent samples t-test. For variables that did not meet the criteria for normal distribution, the Mann-Whitney U test was selected. A two-sided *p*-value < 0.05 was considered statistically significant.

Variables that were statistically significant in univariate analyses-including immediate intravesical therapy and vitamin K3 self-supplementation - were entered into a logistic regression model. The combined predictive performance of these variables for NMIBC recurrence was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC).

Results

Comparison of baseline characteristics between IIT and non-IIT groups

All baseline characteristics, including gender, age, BMI, family history of cancer, smoking history, tumor stage, tumor grade, multiplicity, and tumor size, showed no statistically significant differences between the IIT and the non-IIT groups (all P > 0.05), suggesting well-balanced demographic and clinical profiles (**Table 1**).

Comparison of efficacy outcomes between IIT and non-IIT groups

The efficacy outcomes of patients in the IIT and non-IIT groups are presented in **Table 2**. The recurrence rate was significantly lower in the IIT group (33.12%) compared to the non-IIT group (95.16%) (χ^2 = 68.088, P < 0.001). Additionally, the rate of secondary resection was also significantly lower in the IIT group (43.51%) than in the non-IIT group (64.52%) (χ^2 = 7.805, P = 0.005).

Comparison of baseline characteristics between recurrence and non-recurrence groups

To identify risk factors for recurrence in NMIBC, baseline characteristics were compared between patients with and without recurrence (**Table 3**). There were no significant differences in gender (P = 0.875), age (P = 0.279), BMI, smoking history, or family history of cancer (all P > 0.05). Although the proportion of patients undergoing secondary resection was higher in the recurrence group, this difference was not statistically significant (P = 0.220). Similarly, tumor stage, grade, multiplicity, and tumor size showed no significant differences (all P > 0.05). Notably, IIT was significantly more common in

Table 2. Comparison of efficacy outcomes between IIT and non-IIT groups

	IIT (n = 154)	Non-IIT (n = 62)	t/χ^2	P
Recurrence Rate	51 (33.12%)	59 (95.16%)	68.088	< 0.001
Secondary Resection Rate	67 (43.51%)	40 (64.52%)	7.805	0.005

IIT: immediate intravesical therapy.

Table 3. Comparison of baseline characteristics between recurrence and non-recurrence groups

	Non recurrence (n = 106)	Recurrence (n = 110)	t/χ^2	P
Gender (Male/Female)	79 (74.53%)/27 (25.47%)	83 (75.45%)/27 (24.55%)	0.025	0.875
Age	65.29 ± 5.97	64.38 ± 6.31	1.086	0.279
BMI	23.17 ± 2.42	22.86 ± 2.17	0.999	0.319
Family history of tumor (Yes/No)	46 (43.4%)/60 (56.6%)	56 (50.91%)/54 (49.09%)	1.223	0.269
Smoking history (Yes/No)	65 (61.32%)/41 (38.68%)	70 (63.64%)/40 (36.36%)	0.123	0.725
Secondary resection (Yes/No)	48 (45.28%)/58 (54.72%)	59 (53.64%)/51 (46.36%)	1.507	0.220
Tumor stage			2.616	0.106
T1	51 (48.11%)	65 (59.09%)		
Ta	55 (51.89%)	45 (40.91%)		
Tumor grade			2.616	0.106
G1	55 (51.89%)	45 (40.91%)		
G2	51 (48.11%)	65 (59.09%)		
Multiple tumor (Yes/No)	54 (50.94%)/52 (49.06%)	67 (60.91%)/43 (39.09%)	2.176	0.140
Tumor size/cm			2.204	0.138
≥ 5	3 (2.83%)	8 (7.27%)		
< 5	103 (97.17%)	102 (92.73%)		
IIT (Yes/No)	103 (97.17%)/3 (2.83%)	51 (46.36%)/59 (53.64%)	68.088	< 0.001
Accomplish subsequent intravesical therapy (Yes/No)	87 (82.08%)/19 (17.92%)	85 (77.27%)/25 (22.73%)	0.768	0.381

IIT: immediate intravesical therapy; BMI: Body Mass Index.

the non-recurrence group (P < 0.001). Although more patients in the non-recurrence group completed subsequent intravesical therapy, the difference was not statistically significant (P = 0.381).

Comparison of vitamin supplement usage between recurrence and non-recurrence groups

The use of self-administered vitamin supplements was analyzed to assess its association with NMIBC recurrence (**Table 4**). Vitamin K3 use was significantly higher in the non-recurrence group (53.77%) compared to the recurrence group (36.36%) (χ^2 = 68.088, P = 0.014). In contrast, the usage of other vitamins, including C, D, A, B, and E, did not differ significantly between the two groups (P = 0.146-0.886).

Logistic regression analysis of recurrence risk factors

Logistic regression analysis was conducted to identify independent risk factors for NMIBC recurrence (**Table 5**). Two variables were included: IIT and Vitamin K3 self-supplementation. IIT was significantly associated with a reduced recurrence risk (Coefficient = -3.642, SE = 0.618, Wald = 5.897, P < 0.001, OR = 0.026, 95% CI: 0.008-0.088). Vitamin K3 supplementation also showed a protective trend (Coefficient = -0.565, SE = 0.334, Wald = 1.694, P = 0.090, OR = 0.568, 95% CI: 0.296-1.093), though it did not reach statistical significance.

ROC analysis for predicting NMIBC recurrence

A predictive model for NMIBC recurrence was constructed based on logistic regression results (**Figure 1**). ROC curve analysis demonstrated that the area under the curve (AUC) for IIT and Vitamin K3 self-supplementation were 0.754 and 0.587, respectively. IIT showed high specificity (0.972) but moderate sensitivity (0.536), while Vitamin K3 had a sensitivity of 0.636 but lower specificity (0.538). A combined predictive model incorporating both variables achieved an AUC of 0.877 (**Figure 2**).

Table 4. Comparison of vitamin supplement usage between recurrence and non-recurrence groups

	Non-recurrence (n = 106)	Recurrence (n = 110)	χ^2	P
Vitamin C	51 (48.11%)	54 (49.09%)	0.021	0.886
Vitamin K3	57 (53.77%)	40 (36.36%)	6.613	0.010
Vitamin D	38 (35.85%)	35 (31.82%)	0.392	0.531
Vitamin A	29 (27.36%)	38 (34.55%)	1.303	0.254
Vitamin B	38 (35.85%)	32 (29.09%)	1.126	0.289
Vitamin E	27 (25.47%)	38 (34.55%)	2.113	0.146

Table 5. Logistic regression analysis of factors affecting recurrence in NMIBC

	Coefficient	Std Error	Wald	P	OR	OR_CI_Lower	OR_CI_Upper
IIT (Yes/No)	-3.642	0.618	-5.897	< 0.001	0.026	0.008	0.088
Vitamin K3	-0.565	0.334	-1.694	0.090	0.568	0.296	1.093

NMIBC: Non-muscle invasive bladder cancer; IIT: immediate intravesical therapy; OR: Odds Ratio; CI: Confidence Interval.

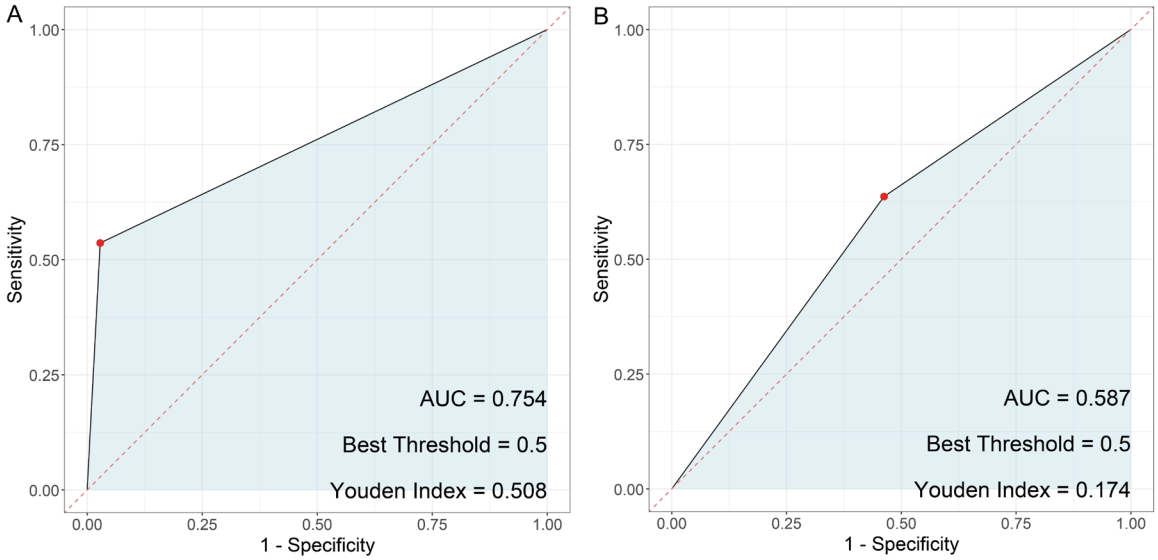

Figure 1. Predictive value of various indicators for recurrence in NMIBC. Note: A. IIT; B. Vitamin K3. NMIBC: Non-muscle invasive bladder cancer; IIT: immediate intravesical therapy; AUC: area under the curve.

Discussion

This retrospective analysis evaluated the impact of multiple factors on NMIBC recurrence, with a particular focus on IIT and vitamin supplementation. The findings underscore IIT as a key component in the management strategy for NMIBC, given its strong association with reduced recurrence rates and decreased need for secondary resections.

One of the most notable findings is the significant protective effect of IIT on recurrence in NMIBC patients. This observation aligns with prior studies [18] demonstrating the efficacy of intravesical therapies, such as BCG, in reducing recurrence. The proposed mechanism involves both direct cytotoxic effects and the activation of local immune responses, which help eliminate residual tumor cells post-resection [19]. Initiating IIT immediately after transurethral resection is thought to take advantage of a critical therapeutic window, targeting microscopic residual disease before it can proliferate [20].

While previous studies have confirmed the benefits of IIT in reducing recurrence, our study provides novel insights by concurrently evaluating the role of vitamin supplementation-specifically

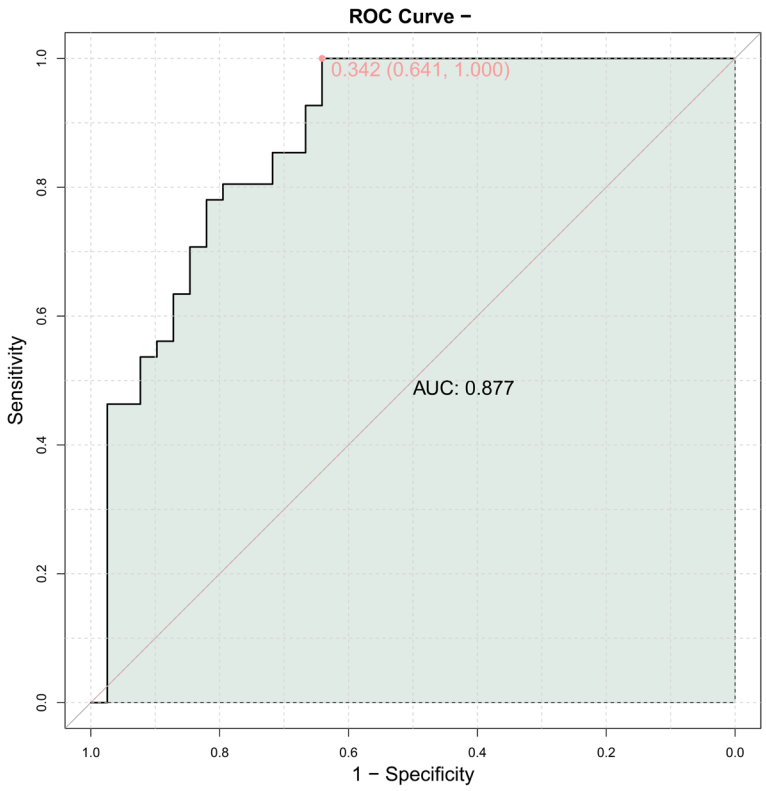

Figure 2. Combined predictive model for the recurrence of NMIBC. NMIBC: Non-muscle invasive bladder cancer; ROC: receiver operator characteristic; AUC: area under the curve.

Vitamin K3-alongside conventional treatments. This dual focus offers a broader perspective on both established and emerging therapeutic strategies. Moreover, by incorporating patient-reported data on vitamin intake, we explore potential synergistic effects between IIT and vitamin supplementation, an area that remains underexplored in current literature [21-23].

The potential role of Vitamin K3 (menadione) in reducing recurrence adds another compelling dimension to our findings. Experimental evidence suggests that Vitamin K3 may inhibit tumor growth by disrupting cell proliferation and inducing apoptosis [24]. Its ability to generate reactive oxygen species selectively in malignant cells could lead to oxidative stress-induced cytotoxicity, sparing healthy tissues [25]. This selective mechanism presents a promising therapeutic avenue with potentially fewer adverse effects.

Vitamin supplementation is increasingly recognized as a potential adjunct in NMIBC therapy [22, 26, 27]. Our findings highlight the anti-cancer potential of Vitamin K3, which has demonstrated tumor-specific cytotoxicity through pro-apoptotic and tumor-suppressive pathways [14, 15, 28]. This line of investigation opens the door for complementary therapies that enhance traditional treatment approaches. Furthermore, the growing interest in personalized medicine emphasizes the importance of tailoring interventions-including vitamin use-based on individual nutritional profiles and treatment responses. Such strategies may improve clinical outcomes and are particularly relevant for resource-limited settings due to the affordability and accessibility of vitamins [29-33].

The lack of observed benefit from other vitamins (A, C, D, and E) may reflect their differing biological roles. These vitamins contribute to immune modulation and oxidative balance but may require specific conditions or dosages to exert measurable anti-tumor effects [13].

From a mechanistic perspective, the observed protective effects of Vitamin K3 may involve complex interactions within the tumor microenvironment and systemic immune responses [34]. Modulation of inflammation, oxidative stress, and immune surveillance are key pathways through which such agents exert their effects [35]. This study proposes a synergistic model in which IIT and an optimal vitamin status together create an unfavorable environment for tumor recurrence. While IIT acts directly on residual tumor cells to prevent reimplantation, Vitamin K3 may improve the integrity of the bladder mucosa and surrounding tissue. The combined outcomes-reduced inflammation, lower oxidative stress, and enhanced immune surveillance-form a comprehensive approach that not only mitigates immediate post-treatment risks but also supports long-term disease control. Elucidating these mechanisms may facilitate the development of per-

sonalized interventions. For instance, patients with elevated inflammatory markers or oxidative stress may benefit from targeted vitamin supplementation, while those with compromised immunity could receive adjunctive immunomodulatory therapies.

Importantly, these findings have significant implications for NMIBC clinical management. Incorporating IIT into standard care may enhance therapeutic precision and effectiveness. However, this integration requires robust monitoring to assess patient responses and dynamically adjust treatment plans. Routine evaluations of recurrence, adherence, and clinical outcomes are essential for tailoring regimens and addressing issues proactively. This patient-centered model may improve long-term outcomes in NMIBC, which is characterized by chronicity and recurrence. Additionally, our findings underscore the potential of individualized nutritional interventions. Tailoring vitamin regimens to correct specific deficiencies or optimize micronutrient status could support systemic health and potentially improve oncologic outcomes. In summary, this study affirms the protective role of IIT and suggests that personalized strategies-incorporating both medical and nutritional elements-could advance NMIBC treatment and long-term patient care. A deeper understanding of the interplay between nutrition and therapy may foster innovative, patient-centered approaches that enhance both quality and efficacy of care.

Despite these promising insights, several limitations must be acknowledged. First, the retrospective design carries inherent risks of selection bias and limits the ability to infer causality between interventions and recurrence. Data were extracted from medical records, which may contain inconsistencies or omissions, particularly regarding dietary and supplementation behaviors. The relatively small sample size also restricts the generalizability of the findings. Furthermore, the study did not account for key confounding factors such as baseline nutritional status, lifestyle behaviors, or genetic predispositions. The follow-up duration may have been insufficient to capture late recurrences, and the absence of blinded assessments introduces the potential for observer bias.

To address these limitations, future research should employ larger, prospective cohorts and include more rigorous controls and longer follow-up periods. Ideally, randomized controlled trials (RCTs) should be conducted to confirm these preliminary findings and establish causality. RCTs would enable better control of confounders, ensure balanced treatment allocation, and generate higher-quality evidence regarding the efficacy of IIT and Vitamin K3 in preventing NMIBC recurrence.

In conclusion, this study contributes to the growing body of research on non-conventional adjunctive therapies in cancer management by providing evidence for the potential roles of IIT and vitamin self-supplementation in reducing NMIBC recurrence. Future investigations should aim to clarify the underlying biological mechanisms of these interventions, potentially leading to novel preventive or adjuvant treatment strategies. Large-scale randomized trials are essential to validate these findings and ensure safety and efficacy in broader patient populations. Furthermore, examining the interactions between dietary habits, genetic susceptibility, and micronutrient supplementation may reveal additional insights that enhance the precision and effectiveness of recurrence prevention strategies in NMIBC.

Disclosure of conflict of interest

None.

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