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ARTICLE

Overweight status predicts improved overall survival after radical nephroureterectomy for upper tract urothelial carcinoma

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Introduction: Upper urinary tract urothelial carcinoma (UTUC) is a rare malignancy, particularly in the ureter, and is associated with high rates of recurrence and metastasis. Although body mass index (BMI) has been associated with prognosis in multiple cancer types, its role as a predictive factor in UTUC is still debated. This study aimed to investigate how BMI influences survival outcomes in patients with UTUC treated with radical nephroureterectomy (RNU). **Methods:** This multi-center retrospective analysis by the Taiwan UTUC Collaboration Group involved 2503 patients who underwent treatment across 19 hospitals from 1988 to 2022. Patients were categorized into normal ($18.5 \leq \text{BMI} < 24$), overweight ($24 \leq \text{BMI} < 27$), and obese ($\text{BMI} \geq 27$) groups. Demographic, clinical, and pathological data were analyzed. Overall survival

(OS), cancer-specific survival (CSS), disease-free survival (DFS), and intravesical recurrence-free survival (IVRFS) were assessed using Kaplan–Meier analysis and Cox proportional hazards models.

Results: The median follow-up period was 44.2 months. In multivariable analysis, overweight patients demonstrated significantly better OS compared with normal-weight patients ($p = 0.033$), and the obesity group showed a favorable, though not statistically significant, trend toward better OS. However, BMI was not an independent predictor of CSS, DFS, or IVRFS. Independent predictors of worse outcomes included older age, end-stage renal disease, ureteral tumor location, tumor size ≥ 3 cm, and high-grade urothelial carcinoma. Tumor stage and grade were comparable across BMI groups.

Conclusions: Overweight status was associated with better OS in patients with UTUC treated with RNU, while BMI had no significant impact on CSS, DFS, or IVRFS. These findings suggest a potential protective effect of higher BMI on OS, warranting further investigation in prospective studies. However, BMI alone should not guide clinical decisions and may instead reflect broader patient health characteristics.

Key Words: Urothelial cancer, body mass index, upper urinary tract urothelial carcinoma, oncological outcomes, radical nephroureterectomy

Introduction

Urothelial carcinoma (UC) can occur in any site on the urinary tract lined with urothelium. Upper urinary tract urothelial carcinoma (UTUC) is uncommon, representing about 5% of all urothelial cancers and approximately 5–10% of renal malignancies.¹ UTUC occurs less commonly in the ureter than in the renal pelvis.^{2,3} An unusually high incidence of UC and

a high prevalence of UTUC have been reported in Taiwan.⁴

At present, radical nephroureterectomy (RNU) combined with bladder cuff excision is the standard treatment for UTUC. However, disease recurrence and metastasis are high.^{5,6} Recent genomic profiling studies have highlighted the distinct molecular characteristics of UCs originating in the upper urinary tract versus the bladder, revealing notable differences

in mutational landscapes and therapeutic vulnerabilities.⁷ These findings underscore the importance of considering tumor biology, in addition to clinical features, when evaluating prognostic indicators such as body mass index (BMI).

Traditionally, the commonly reported prognostic factors of UTUC are pathological primary tumor stages, lymphovascular invasion (LVI), positive lymph nodes, presence of high-grade tumor, and distant metastasis.^{8–11} Chang et al.¹² reported a higher mortality rate of UTUC among individuals residing in areas with arsenic contamination of water, such as south Taiwan. BMI serves as a prognostic indicator in numerous benign and malignant conditions, with several urological cancers—such as urothelial carcinoma, renal cell carcinoma, and prostate cancer—showing associations with BMI.^{13–15}

However, the prognostic outcomes of UTUC with BMI are controversial. A Western study reported that higher BMI (BMI ≥ 30 kg/m²) was associated with worse cancer-specific outcomes.¹⁶ Another study reported that preoperative underweight status (BMI <18.5 kg/m²) is an independent predictor of lower recurrence-free survival and cancer-specific survival (CSS) in Chinese patients with UTUC, and obesity was associated with superior recurrence-free survival and CSS.¹⁷ Furthermore, Yeh et al.¹⁸ reported that higher BMI (overweight and obese) was associated with improved outcomes than those with normal weight in Asian patients with UTUC.

BMI may influence cancer prognosis through several mechanisms. Higher BMI is often associated with greater metabolic and nutritional reserves, which may help patients tolerate aggressive cancer treatments and recover more effectively. Adipose tissue also secretes adipokines and cytokines that can modulate tumor biology and immune responses, potentially affecting tumor progression. Conversely, obesity is linked to chronic low-grade inflammation and metabolic dysregulation, which may promote tumor growth in certain contexts. These complex and sometimes opposing effects may partly explain the variability in reported associations between BMI and oncological outcomes.¹⁹ This study was designed to assess how elevated BMI or obesity influences clinical outcomes in patients with UTUC.

Materials and Methods

Study design

This multicenter study, conducted by the Taiwan UTUC Collaboration Group across 19 hospitals in Taiwan, enrolled 5295 patients between July 1988

and May 2022. All personally identifiable information was removed prior to analysis. The study protocol was approved by the Ethics Committee of Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (Approval Number: 06-X34-105). In addition, the requirement for informed consent was waived because of the study's retrospective design. All participating hospitals are certified cancer treatment centers in Taiwan and adhere to national clinical guidelines. Indications for RNU and follow-up protocols were generally consistent across centers.

Clinical data were primarily extracted from institutional electronic medical records and standardized according to the 2010 TNM staging system. When electronic records were incomplete, corresponding paper records were reviewed to ensure data completeness. Patients without complete records of BMI and oncological outcomes, as well as those classified as underweight (excluded due to the very small sample size), were omitted from the analysis. Finally, we included 2503 patients (Figure 1) who were divided into three groups based on their BMI, as defined by the Health Promotion Administration, Ministry of Health and Welfare, Taiwan: normal ($18.5 \leq \text{BMI} < 24$), overweight ($24 \leq \text{BMI} < 27$), and obese ($27 \leq \text{BMI}$).

Data collection

The database included the following data: sex, age, BMI, end-stage renal disease (ESRD), and smoking status. Tumor-specific parameters and treatments were also recorded as tumor size, tumor location, tumor grade, tumor stage, LVI, histological variants, and surgical margin. Tumor stage was determined according to the 2010 American Joint Committee on Cancer TNM classification, and tumor grade was assigned based on the 2004 World Health Organization (WHO) criteria. All patients received standard treatment according to the guidelines. Following treatment, patients underwent routine follow-up assessments—including physical examinations, laboratory tests, and imaging studies—in line with standard guidelines. UTUC recurrence was defined as tumor regrowth at the primary site, involvement of regional lymph nodes, or metastasis to distant organs. Information on patient survival was obtained through linkage with the National Health Insurance Research Database. For those who had died, the underlying cause was identified from official death records and, when applicable, from the final hospital discharge summary.

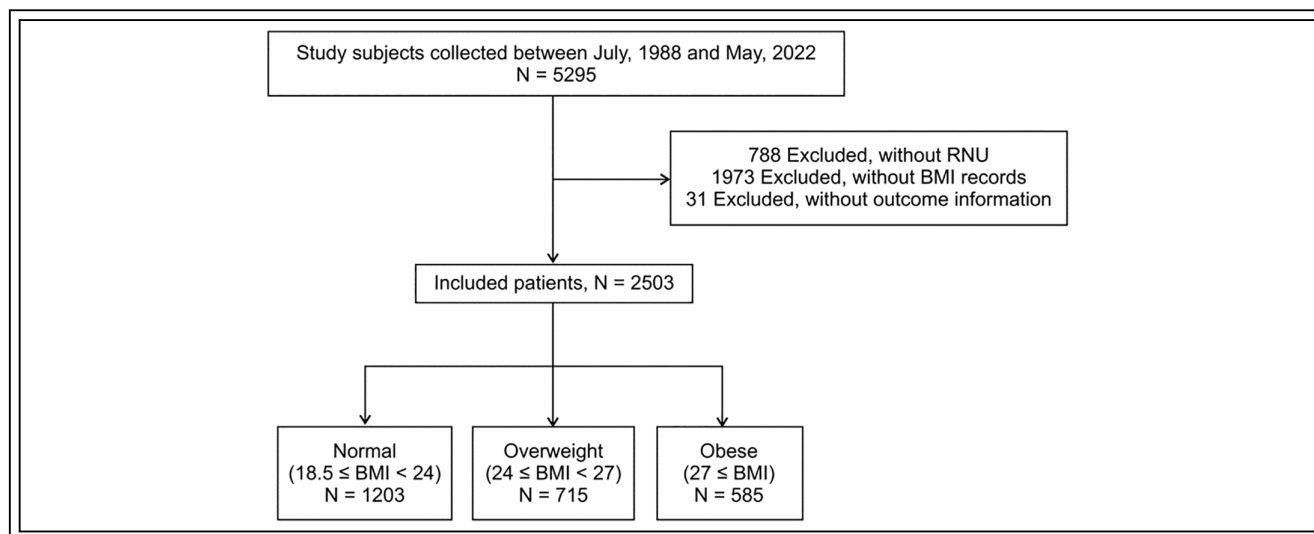


FIGURE 1. Flow diagram showing the case recruitment process

Data analysis

Group comparisons were carried out using one-way ANOVA for continuous data and Pearson's chi-square test for categorical data. The normality of continuous variables was assessed with the Kolmogorov–Smirnov test. Prognostic outcome rates were analyzed using Kaplan–Meier survival curves, including overall survival (OS), CSS, disease-free survival (DFS), and intravesical recurrence-free survival (IVRFS). The stratified log-rank test was used to compare the survival curves. Cox proportional hazards regression was applied to evaluate the association between surgical approach and prognostic outcomes, both in unadjusted analyses and after controlling for relevant confounding factors. All tests were two-sided, with p -values < 0.05 considered statistically significant. Data analyses were conducted using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA).

Results

Of the total 5295 patients, BMI information was available for 2503 individuals (47.3%). The median age of these patients was 69.0 years (interquartile range [IQR] 61.4–75.9), with a median follow-up of 44.2 months (IQR 22.8–77.4). [Table 1](#) summarizes their demographic, clinical, and pathological characteristics by BMI category. The overall median BMI in this cohort was 24.2 (IQR 21.9–26.8) kg/m^2 . The normal weight, overweight, and obese groups had a median BMI of 21.8 (IQR, 20.6–23.0), 25.4 (IQR,

24.7–26.1), and 28.9 (IQR, 27.7–30.9) kg/m^2 , consisting of 1203 (48.1%), 715 (28.6%), and 585 (23.4%) patients, respectively.

The major differences between the three groups were due to patient profile rather than oncological characteristics. Patients with obesity tended to be younger than the other groups ($p = 0.011$). The normal-weight category included a smaller percentage of male patients ($p < 0.001$). Obese individuals had a higher prevalence of smoking compared to those of normal weight ($p = 0.001$). End-stage renal disease was more frequently observed in the normal-weight group than in the other BMI groups ($p = 0.001$). However, tumor size was the only tumor-specific parameter statistically different between the BMI groups. Those with obesity tended to have larger tumors compared with the other groups ($p = 0.043$). There were no statistically significant differences among BMI groups in terms of tumor location, pathological stage, histological type, tumor grade, lymphovascular invasion, or surgical margin status. ([Table 1](#)).

For oncologic outcomes, the median OS, CSS, DFS, and IVRFS did not differ significantly among BMI groups in unadjusted comparisons ($p > 0.4$ for all). In univariate analysis, predictors of worse outcomes included older age, ESRD, ureteral involvement, tumor size ≥ 3 cm, advanced stage, variant histology, and high-grade UC. After adjustment in multivariable analysis, overweight patients showed significantly better OS compared with normal-weight patients ($p = 0.033$), whereas BMI did not independently predict cancer-specific survival, disease-free

TABLE 1. Patient characteristics and tumor-specific parameters of different BMI groups

Characteristic/Parameter	BMI category			p-value
	BMI < 24	24 ≤ BMI < 27	27 ≤ BMI	
Number	1203	715	585	
Age				0.012
Years (mean, SD)	68.4 ± 10.6	68.9 ± 10.1	67.2 ± 10.3	0.011
<70 (N, %)	628 (52.6%)	353 (49.8%)	339 (58.0%)	
≥70 (N, %)	567 (47.4%)	356 (50.2%)	245 (42.0%)	
Sex				<0.001
Male (N, %)	481 (40.0%)	347 (49%)	277 (47.4%)	
Female (N, %)	722 (60.0%)	368 (51.5%)	308 (52.6%)	
Smoking				0.001
No (N, %)	1017 (84.5%)	582 (81.4%)	454 (77.5%)	
Yes (N, %)	186 (15.5%)	133 (18.6%)	132 (22.5%)	
ESRD				0.001
No (N, %)	448 (37.2%)	299 (41.8%)	272 (46.4%)	
Yes (N, %)	755 (62.8%)	416 (58.2%)	314 (53.6%)	
History of bladder cancer				0.831
No (N, %)	899 (74.9%)	544 (76.5%)	438 (74.9%)	
Yes (N, %)	301 (25.1%)	167 (23.5%)	147 (25.1%)	
Tumor location				0.386
Renal pelvis (N, %)	516 (42.9%)	304 (42.5%)	261 (44.5%)	
Ureter (N, %)	454 (37.7%)	258 (36.1%)	228 (38.9%)	
Both (N, %)	230 (19.1%)	152 (21.3%)	97 (16.6%)	
Not available (N, %)	3 (0.2%)	1 (0.1%)	0 (0.0%)	
Tumor size				0.043
Non-visible (N, %)	36 (3.0%)	21 (2.9%)	13 (2.2%)	
<1 cm (N, %)	88 (7.3%)	41 (5.7%)	31 (5.3%)	
≥1 and <2 cm (N, %)	230 (19.1%)	152 (21.3%)	87 (14.8%)	
≥2 and <3 cm (N, %)	269 (22.4%)	160 (22.4%)	132 (22.5%)	
≥3 cm (N, %)	580 (48.2%)	341 (47.7%)	323 (55.1%)	
Tumor stage				0.471
pT0/pTis/pTa	204 (17.2%)	124 (17.6%)	89 (15.3%)	
pT1	302 (25.5%)	173 (24.6%)	161 (27.7%)	
pT2	225 (19.0%)	153 (21.7%)	118 (20.3%)	
pT3	391 (33.1%)	225 (32.0%)	194 (33.4%)	
pT4	61 (5.2%)	29 (4.1%)	19 (3.3%)	
Unknown				
Cell type				0.879
Urothelial (N, %)	1122 (93.3%)	666 (93.1%)	548 (93.5%)	
Squamous (N, %)	1 (0.1%)	0 (0.0%)	0 (0.0%)	
Small cell (N, %)	4 (0.3%)	3 (0.4%)	0 (0.0%)	
Adenocarcinoma (N, %)	1 (0.1%)	0 (0.0%)	1 (0.2%)	
UC with variants (N, %)	67 (5.6%)	39 (5.5%)	33 (5.6%)	
Others (N, %)	8 (0.7%)	7 (1.0%)	4 (0.7%)	

(Continued)

TABLE 1. (Continued)

Characteristic/Parameter	BMI category			p-value
	BMI < 24	24 ≤ BMI < 27	27 ≤ BMI	
Grade				0.761
Papillary urothelial neoplasm of low malignant potential (N, %)	2 (0.2%)	0 (0.0%)	0 (0.0%)	
Low grade (N, %)	150 (12.7%)	95 (13.6%)	84 (14.5%)	
High grade (N, %)	1006 (85.0%)	586 (83.8%)	484 (83.7%)	
Gx (N, %)	9 (0.8%)	6 (0.9%)	4 (0.7%)	
G2 (N, %)	16 (1.4%)	11 (1.6%)	6 (1.0%)	
Well-differentiated (N, %)	0 (0.0%)	1 (0.1%)	0 (0.0%)	
LVI				0.219
No (N, %)	920 (78.1%)	520 (74.6%)	436 (76.4%)	
Yes (N, %)	258 (21.9%)	177 (25.4%)	135 (23.6%)	
Surgical margin				0.738
Free (N, %)	1019 (95.3%)	609 (95.6%)	503 (96.2%)	
Positive (N, %)	50 (4.7%)	28 (4.4%)	20 (3.8%)	
Mortality				0.062
No (N, %)	657 (54.7%)	419 (58.8%)	365 (62.4%)	
UTUC-related (N, %)	200 (16.7%)	109 (15.3%)	91 (15.6%)	
non-UTUC-related (N, %)	211 (17.6%)	107 (15.0%)	79 (13.5%)	
Unknown (N, %)	133 (11.1%)	77 (10.8%)	50 (8.5%)	

Note: BMI, body mass index; ESRD, end-stage renal disease; UC, urothelial carcinoma; UTUC, upper urinary tract urothelial carcinoma; LVI, lymphovascular invasion.

survival, or intravesical recurrence-free survival. Factors independently associated with worse prognosis were older age, presence of ESRD, tumor located in the ureter, tumor size ≥ 3 cm, high pathological grade, and non-urothelial carcinoma histology. Table 2 summarizes the statistical findings for each endpoint, while Figure 2 illustrates the relationship between BMI and survival outcomes.

Discussion

The present study examined the impact of BMI during RNU on the survival outcomes of Taiwanese patients with UTUC. Among the 2503 patients who received RNU for UTUC, being overweight was associated with improved OS compared with those of normal weight. In contrast, BMI showed no independent association with cancer-specific, disease-free, or intravesical recurrence-free survival. Our study showed that obese patients with UTUC tended to be younger, male, with a large tumor (>3 cm), non-smokers, and without ESRD.

Previous studies have attempted to determine the predictors of UTUC, with tumor size, stage, and

cell type being the commonly reported predictors.²⁰ However, UTUC cannot be controlled, other than through early diagnosis and early intervention, but preventing the occurrence of UTUC is difficult in the real world. The limited resources available should be used correctly. Moreover, patients' clinical baseline characteristics could be useful predictors in further cancer care when they are clinically relevant.

In our study, BMI was associated with post-RNU prognosis only in terms of OS; overweight patients had better OS than those with normal BMI. In contrast, CSS, DFS, and IVRFS were comparable across normal-weight, overweight, and obese groups, as were clinical and tumor-specific characteristics.

BMI classification varies globally, with different thresholds adopted by the WHO, the U.S. Centers for Disease Control and Prevention, and Taiwan's health authorities. Notably, the 2004 WHO Expert Consultation²¹ recommended lower BMI cutoffs for Asian populations due to their increased risk of metabolic complications at lower BMI levels compared to European populations. This supports our use of Taiwan-specific BMI categories (normal: 18.5–24, overweight: 24–27, obese: ≥ 27) in this analysis.

TABLE 2. (Continued)

Characteristic/ Parameter	Overall survival		Cancer-specific survival		Disease-free survival		Intravesical recurrence-free survival	
	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)
Tumor stage								
pT0/pTis/pT1a	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
pT1	1.220 (0.938– 1.586)	0.137 <0.001	1.650 (0.904– 3.014)	0.103 <0.001	1.662 (1.078– 2.562)	0.021 <0.001	1.535 (0.928– 2.538)	0.095 <0.001
pT2	1.597 (1.227– 2.079)	<0.001	3.534 (2.001– 6.241)	<0.001	3.488 (2.312– 5.260)	<0.001	3.590 (2.243– 5.744)	<0.001
pT3	2.924 (2.306– 3.708)	<0.001	10.945 (6.483– 18.479)	<0.001	7.918 (5.407– 11.595)	<0.001	8.812 (5.698– 13.627)	<0.001
pT4	8.368 (6.149– 11.388)	<0.001	35.722 (20.274– 62.942)	<0.001	24.475 (15.932– 37.599)	<0.001	26.810 (16.537– 43.463)	<0.001
Cell type								
Urothelial	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Non-urothelial	1.885 (1.110– 3.199)	0.019	3.395 (1.910– 6.034)	<0.001	3.529 (2.178– 5.719)	<0.001	3.143 (1.847– 5.349)	<0.001
Grade								
Low grade	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High grade	1.606 (1.296– 1.989)	<0.001	4.271 (2.658– 6.863)	<0.001	3.579 (2.492– 5.141)	<0.001	6.626 (3.892– 11.280)	<0.001
Gx	1.117 (0.613– 2.034)	0.718	1.550 (0.457– 5.264)	0.482	1.389 (0.540– 3.574)	0.496	3.033 (1.091– 8.428)	0.033
G2	1.174 (0.477– 2.885)	0.727	1.109 (0.148– 8.308)	0.920	1.219 (0.292– 5.093)	0.786	2.633 (0.598– 11.588)	0.200

Note: BMI, body mass index; ESRD, end-stage renal disease; HR, hazard ratio. HR > 1 indicates increased risk; HR < 1 indicates reduced risk. Statistical significance was defined as $p < 0.05$.

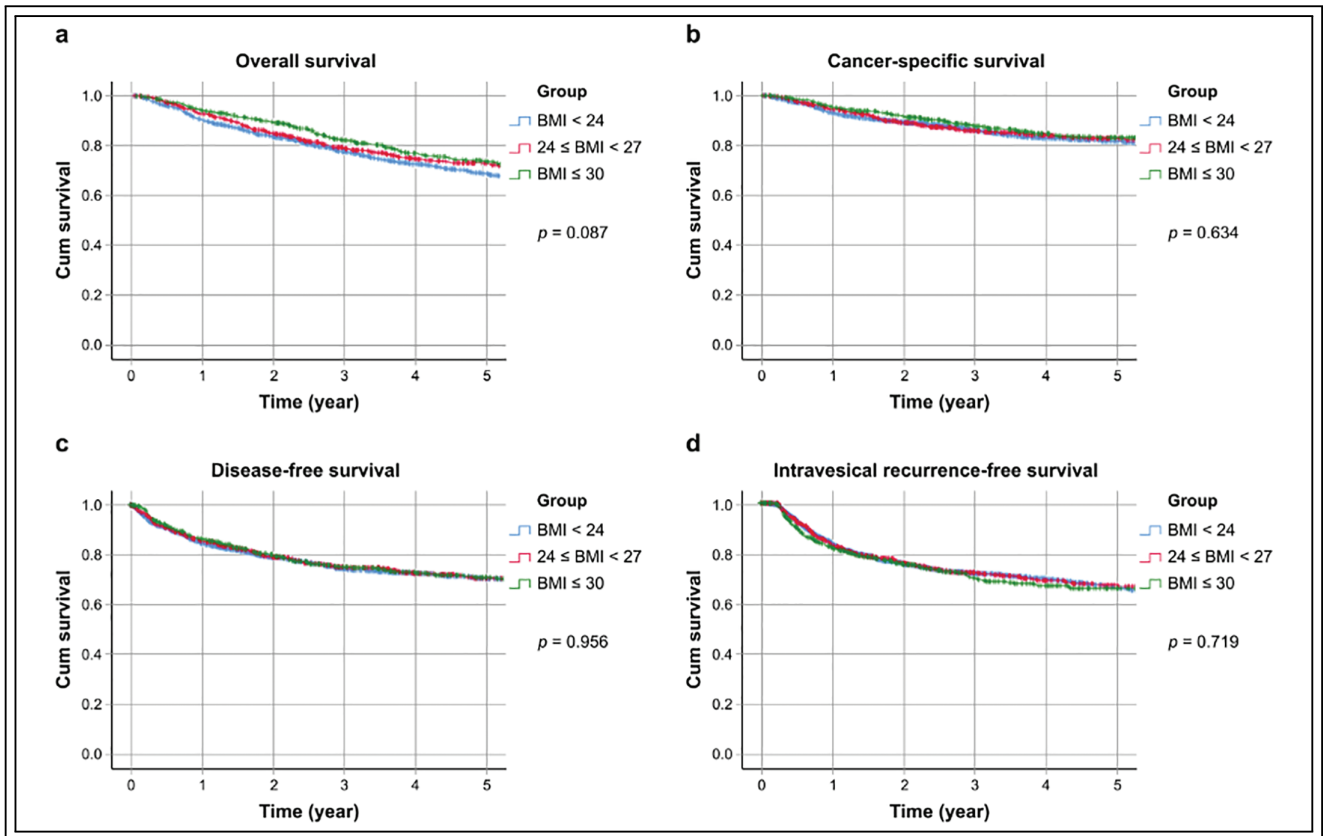


FIGURE 2. Association between BMI and cancer survival outcomes. Kaplan-Meier estimates of (a) overall survival, (b) cancer-specific survival, (c) disease-free survival, and (d) intravesical recurrence-free survival

These thresholds differ from the WHO classification, which defines overweight as $BMI \geq 25$ and obesity as $BMI \geq 30$. Such differences reflect variations in body composition and associated health risks among populations. Importantly, the primary rationale for using BMI is to stratify individuals according to disease risk. While the exact cutoffs may differ across regions, the relative classification into underweight, normal weight, overweight, and obese remains consistent in its ability to identify prognostic trends, thereby preserving the clinical relevance of our findings across populations.

BMI is widely acknowledged as an important determinant in the risk profile of numerous health conditions. Ehdaie et al.¹⁶ found that, among 520 Western patients with UTUC, obesity correlated with poorer overall survival, cancer-specific survival, and recurrence-free survival. However, the WHO also emphasized that the link between BMI, body fat percentage, and health risk differs significantly between Asian and European populations. Supporting this, a Japanese study even identified increased BMI as an independent predictor of favorable OS and CSS.²² Our

study, which includes the largest cohort of Taiwanese UTUC patients to date, provides additional evidence on this association. To the best of our knowledge, this is the first comprehensive study in which data were collected from hospitals across Taiwan to examine the association between BMI and UTUC. Compared to the recent single-center study by Yeh et al.,¹⁸ our multicenter design enhances generalizability and minimizes the risk of selection bias.

Although a previous Taiwanese study reported significantly lower recurrence rates in overweight and obese patients compared with those of normal weight, and identified obesity as an independent prognostic factor for favorable CSS and OS, our study did not replicate these findings.¹⁸ Several factors may account for this discrepancy. First, differences in patient selection, follow-up duration, and inclusion criteria between the two studies may have influenced the outcomes. Second, variations in the definition of BMI categories and potential residual confounding from unmeasured clinical variables—such as comorbidities, tumor characteristics, and perioperative management—may have contributed

to the differences. Lastly, our study's multicenter design and broader inclusion criteria could have introduced heterogeneity that diluted the strength of associations observed in more homogeneous single-center cohorts.

Several explanations have been suggested for the varying relationship between BMI and UTUC, with obesity widely recognized as a contributing factor to numerous diseases, including cancers. The International Agency for Research into Cancer and the World Cancer Research Fund reported substantial evidence supporting the association between obesity and endometrial, esophageal, colorectal, postmenopausal breast, prostate, and renal cancers. Thus, the link between elevated BMI and unfavorable outcomes in UTUC appears evident. However, this situation is only seen in the West and might be explained by genetic factors, diet, or body composition. However, direct evidence confirming this hypothesis is still lacking. A comparative study in Asian patients with UTUC found that higher BMI correlated with better clinical outcomes.¹⁸ In Asian populations, individuals classified as overweight or obese experienced markedly lower UTUC recurrence rates compared to those of normal weight, with obesity emerging as an independent predictor of improved CSS and OS. In contrast, the outcomes were not significantly different between normal, overweight, and obese Caucasians.

The mechanisms underlying these findings are not fully understood. One possibility is that BMI serves as a proxy for body fat composition, reflecting both visceral adiposity and overall nutritional status. Furthermore, in obese individuals, the greater perirenal fat between the kidney and Gerota's fascia may provide a physical barrier that limits tumor spread. This hypothesis was derived from the observation that thick renal parenchyma acts as a protective barrier against tumor spread in clinical pT3 UTUC.^{23,24} Moreover, an appropriate nutritional reserve may improve survival.²⁵ Residual microinvasions of different cancers are less likely to be undetected in obese patients, supporting this hypothesis.²⁴⁻²⁷ Nevertheless, analysis of our cohort's pathology reports revealed no significant variation in LVI among the different BMI categories.

One possible explanation is that excess adipose tissue in obese individuals secretes various cytokines and other bioactive molecules that can promote a state of persistent, low-grade inflammation within the tumor environment, which may contribute to cancer progression. In addition, research on urinary bladder transitional cell carcinoma has indicated that systemic inflammatory responses—reflected by markers such as C-reactive protein—can have a

stronger impact on survival than certain tumor-specific features, including histologic grade, COX-2 expression, or the degree of T-lymphocyte infiltration.²⁸ Santoni et al.²⁹ linked obesity and cancer, and insulin resistance in obese patients was associated with the activation of many complex pathways, such as PI3K/AKT/mTOR, MARK, and Ras pathways, which can stimulate tumor growth. Metabolic dysregulation in obese patients might affect the hormonal, endocrine, or nutritional factors that contribute to UTUC. However, the basic biological evidence is still lacking.^{17,18} In the case of underweight patients (not included here); previous studies have suggested that lower body weight may reflect sarcopenia or cancer-related cachexia, characterized by the depletion of muscle and fat stores, which is linked to poorer clinical outcomes.³⁰

Notably, the survival advantage for overweight patients was observed only in the multivariable analysis and not in the univariate analysis. This discrepancy may be explained by the confounding effects of other prognostic factors, including patient age, tumor dimensions, and accompanying medical conditions, which were adjusted for in the multivariable model. Overweight patients in our cohort tended to be younger and have fewer cases of ESRD, which could have contributed to the improved OS after adjustment. Although this finding reached statistical significance ($p = 0.033$), its clinical relevance should be interpreted with caution. The magnitude of benefit was modest, and BMI was not associated with improved CSS, DFS, or IVRFS. Therefore, we believe that BMI alone should not influence clinical decision-making but may reflect underlying patient characteristics rather than a direct protective effect of excess weight. Future studies with larger samples and detailed nutritional and metabolic assessments are warranted to clarify this association.

This study has several limitations. First, due to its retrospective design and reliance on a multicenter database, detailed individual-level clinical information was not available. In particular, data on whether lymph node dissection was performed during RNU—which may influence oncological outcomes—were lacking. Information regarding adjuvant chemotherapy regimens, timing, and duration after recurrence was also unavailable. These missing data may limit the ability to fully assess the impact of perioperative and post-recurrence treatments on survival outcomes. Second, conducting a unified central pathological review was not possible due to the participation of numerous institutions. Nevertheless, our initial multicenter pathology assessment revealed a moderate level of agreement

on key cancer-related parameters, including tumor grade and stage of UTUC.³¹ Third, BMI data were missing for a substantial number of patients, which may introduce selection bias. Additionally, clinical practices and surgical approaches may have varied across centers and evolved over the study period, although general treatment principles were followed. Despite these constraints, our research offers important perspectives on the relationship between BMI and cancer outcomes in UTUC, specifically within this unique population. Although data were collected from multiple institutions, adherence to national treatment guidelines and standardized staging criteria helped ensure a degree of consistency. Nevertheless, the possibility of unmeasured inter-institutional variability cannot be excluded.

Conclusions

In this extensive, multi-center cohort of patients with UTUC, BMI did not emerge as an independent determinant of CSS, DFS, or IVRFS, and its association with OS was observed only after adjustment for confounders. These results suggest that BMI alone should not guide clinical decisions but may reflect broader patient health characteristics, such as comorbid conditions and functional status. In clinical practice, prognostic counseling and treatment planning should continue to focus primarily on tumor stage, grade, and comorbidities, rather than BMI. Further studies exploring the role of body composition and nutritional status may help clarify whether these factors can meaningfully influence outcomes.

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Author Contributions

Conceptualization, Yao-Chou Tsai; methodology, Yao-Chou Tsai; data collection, analysis and interpretation, Shu-Yu Wu, Ching-Chia Li, Wen-Jeng Wu, Kuan-Hua Huang, Chien-Liang Liu, Shian-Shiang Wang, Jian-Ri Li, Han-Yu Weng, Ta-Yao Tai, Pi-Che Chen, Ian-Seng Cheong, Chung-You Tsai, Pai-Yu Cheng, Jian-Hua Hong, Chung-Hsin Chen, Jen-Shu Tseng, Wun-Rong Lin, Yuan-Hong Jiang, Yu-Khun Lee, Po-Hung Lin, See-Tong Pang, Yung-Tai Chen, Wei-Chieh Chen, Chia-Chang Wu, Thomas Y. Hsueh, Hsu-Che Huang, Wei-Yu Lin, Chia-Cheng Yu, Jen-Kai Fang, Chih-Chin Yu and Yao-Chou Tsai; writing—original draft, Shu-Yu Wu; writing—review and editing, Chia-Cheng Yu and Yao-Chou Tsai. All authors reviewed and approved the final version of the manuscript.

Availability of data and Materials

All data are available upon request from the corresponding author.

Ethics Approval

This study was approved by the Ethics Committee of Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (Approval Number: 06-X34-105). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Informed Consent

Patient consent was waived due to the retrospective nature of this study.

Conflicts of Interest

The authors declare no conflicts of interest to report.

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