The Impact of Body Mass Index on Survival Endpoints among Patients with Metastatic Urothelial Carcinoma Undergoing Treatment with Immune Checkpoint Inhibitors: A Real-World Multicenter Analysis

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BACKGROUND

- Studies on the correlation between high **body mass index (BMI)** and extended survival among patients receiving immune checkpoint inhibitors (ICIs) have been made, although findings have shown variability.
- Our research explored the phenomenon of the "obesity paradox" in patients with metastatic urothelial carcinoma (mUC) undergoing treatment with ICIs.

METHODS

Patients and treatments

- Histopathologic confirmed mUC
- All patients received at least one cycle of ICI treatment.
- BMI was calculated by dividing the weight (in kilograms) by the square of the height (in meters), and patients were classified based on the Asian-Pacific classification.
- Clinical characteristics of the patients were recorded including sex, age, ECOG performance status, body weight, body height, line of ICI treatment, primary tumor location, metastatic site, PD-L1 expression by combined positivity score (CPS), and survival.

Statistic Analyses

- Study endpoints: Overall survival (OS) and progression-free survival (PFS).
- Kaplan-Meier analysis was used to estimate OS.
- Uni- and multivariate analyses for survival were performed using the Cox proportional hazards model.
- \blacksquare P < 0.05 was considered statistically significance.

RESULTS

Patient characteristics

- From September 2015 through January 2023, 215 patients with mUC were enrolled in this study, including 128 males (59.5%) and 87 females (40.5%).
- The median age is 70 years.
- The median follow-up time was 31.3 months.

Table 1. Clinicopathologic characteristics of all patients

	BMI category (kg/m²)						
	All (n, %)	Underweight (< 18.5)	Normal (18.5-23)	Overweight (23-25)	Obese (≥ 25)	p value	
Age (year)						0.33	
< 65	68 (31.6)	2 (16.7)	34 (37.8)	11 (26.8)	21 (29.2)		
≥ 65	147 (68.4)	10 (83.3)	56 (62.2)	30 (73.2)	51 (70.8)		
Sex						< 0.0001	
Female	87 (40.5)	11 (91.7)	40 (44.4)	13 (31.7)	23 (31.9)		
Male	128 (59.5)	1 (8.3)	50 (55.6)	28 (68.3)	49 (68.1)		
ECOG PS						0.15	
0-1	178 (82.8)	8 (66.7)	74 (82.2)	38 (92.7)	58 (80.6)		
≥ 2	37 (17.2)	4 (33.3)	16 (17.8)	3 (7.3)	14 (19.4)		
Primary site						0.96	
Bladder	99 (46.0)	5 (41.7)	39 (43.3)	21 (51.2)	34 (47.2)		
UTUC	114 (53.0)	7 (58.3)	50 (55.6)	20 (48.8)	37 (51.4)		
Multifocal	2 (1.0)	0	1 (1.1)	0	1 (1.4)		
Visceral mets						0.34	
No	103 (47.9)	8 (52.6)	39 (43.3)	18 (43.9)	38 (52.8)		
Yes	112 (52.1)	4 (47.4)	51 (56.7)	23 (56.1)	34 (47.2)		
LN mets						0.55	
No	57 (26.5)	2 (16.7)	24 (26.7)	14 (34.1)	17 (23.6)		
Yes	158 (73.5)	10 (83.3)	66 (73.3)	27 (65.9)	55 (76.4)		
Treatment						0.30	
1 st line	130 (60.5)	10 (83.3)	56 (62.2)	22 (53.7)	42 (58.3)		
≥ 2 nd line	85 (39.5)	2 (16.7)	34 (37.8)	19 (46.3)	30 (41.7)		
Bajorin risk						0.62	
0	87 (40.5)	5 (41.7)	35 (38.9)	16 (39.0)	31 (43.1)		
1	107 (49.8)	6 (50.0)	43 (47.8)	24 (58.5)	34 (47.2)		
2	21 (9.8)	1 (8.3)	12 (13.3)	1 (2.4)	7 (9.7)		
PD-L1 CPS (%)		- ·		·		0.49	
< 10	84 (39.1)	6 (50.0)	38 (42.2)	17 (41.5)	23 (31.9)		
≥ 10	58 (27.0)	1 (8.3)	21 (23.3)	11 (26.8)	25 (34.7)		
Missing	73 (34.0)	5 (41.7)	31 (34.4)	13 (31.7)	24 (33.3)		

Abbreviation: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; PS, performance status; PD-L1, programmed cell death ligand-1; CPS, combined positive score

Table 2. Efficacy of immune checkpoint inhibitor stratified by BMI groups

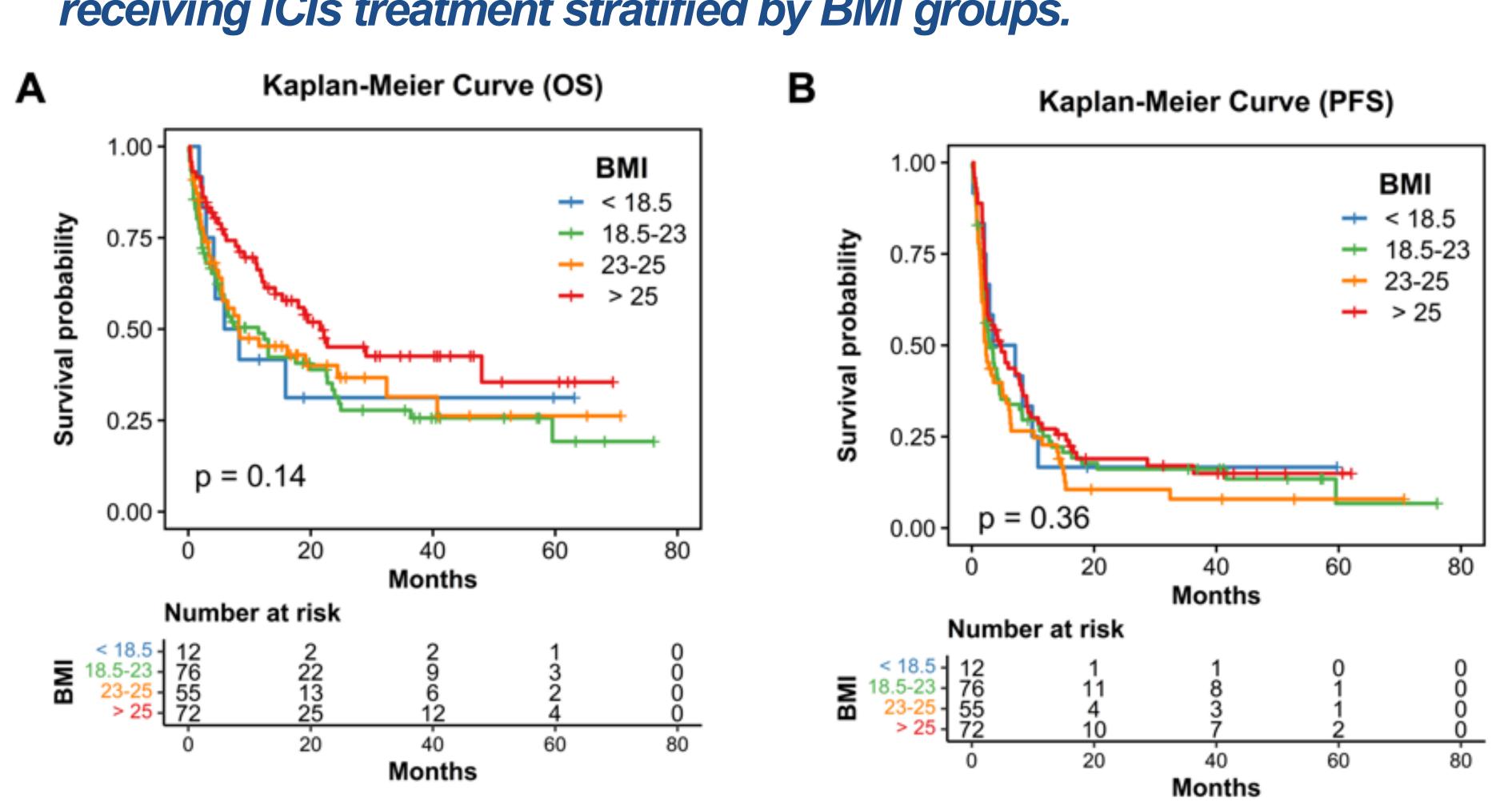
	Underweight (< 18.5 kg/m²)	Normal (18.5-23 kg/m²)	Overweight (23-25 kg/m²)	Obese (≥ 25 kg/m²)	p value
CR	1 (9.1)	9 (11.5)	3 (8.1)	11 (16.2)	0.44
PR	3 (27.3)	15 (19.2)	7 (18.9)	11 (16.2)	
SD	2 (18.2)	8 (10.3)	6 (16.2)	17 (25.0)	
PD	5 (45.5)	46 (59.5)	21 (56.8)	29 (42.6)	
ORR	4 (36.4)	24 (30.8)	10 (27.0)	22 (32.4)	0.92
DCR	6 (54.5)	32 (41.0)	16 (43.2)	39 (57.4)	0.22

Abbreviation: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate.

BMI and overall survival

- The median OS of the 4 groups were 5.9 (underweight), 8.2 (normal), 8.4 (overweight) and 21.9 (obese) months, respectively (log rank p = 0.14; Fig 1A).
- The median PFS of the 4 groups were 3.5 (underweight), 2.8 (normal), 2.5 (overweight) and 4.7 (obese) months, respectively (log rank p = 0.36; Fig 1B).

Figure 1. Kaplan–Meier curves of OS (A) and PFS (B) for mUC patients receiving ICIs treatment stratified by BMI groups.



- Patients in BMI-high group had a significant better OS than patients in the BMI-low group (21.9 vs 8.3 months; p = 0.021; Fig 2A).
- The median PFS showed no significant difference between the BMI-high and BMI-low groups (4.7 vs. 2.8 months; p = 0.16; Fig 2B).

Figure 2. Kaplan–Meier curves of OS (A) and PFS (B) for mUC patients receiving ICIs treatment divided by BMI-high or BMI-low groups.

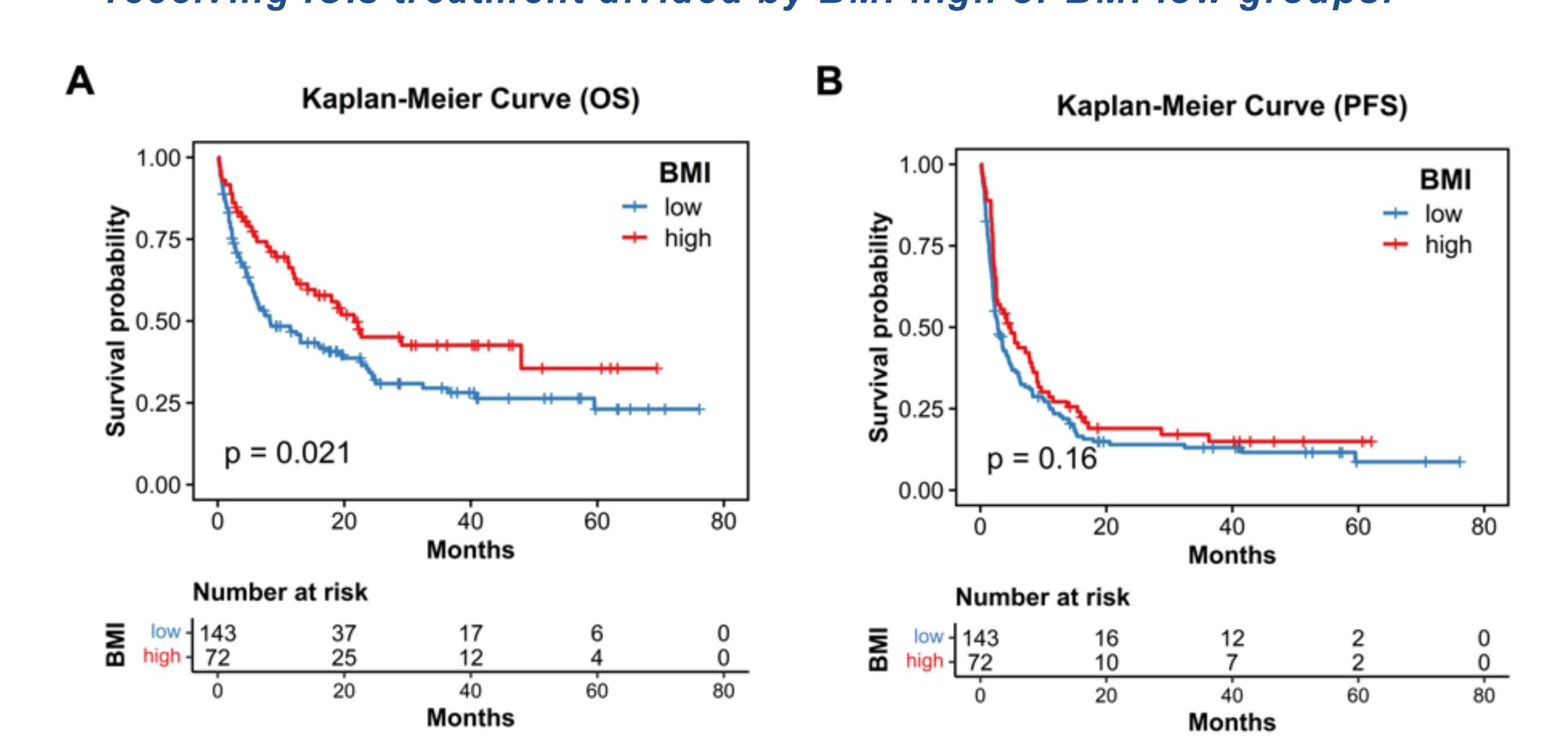
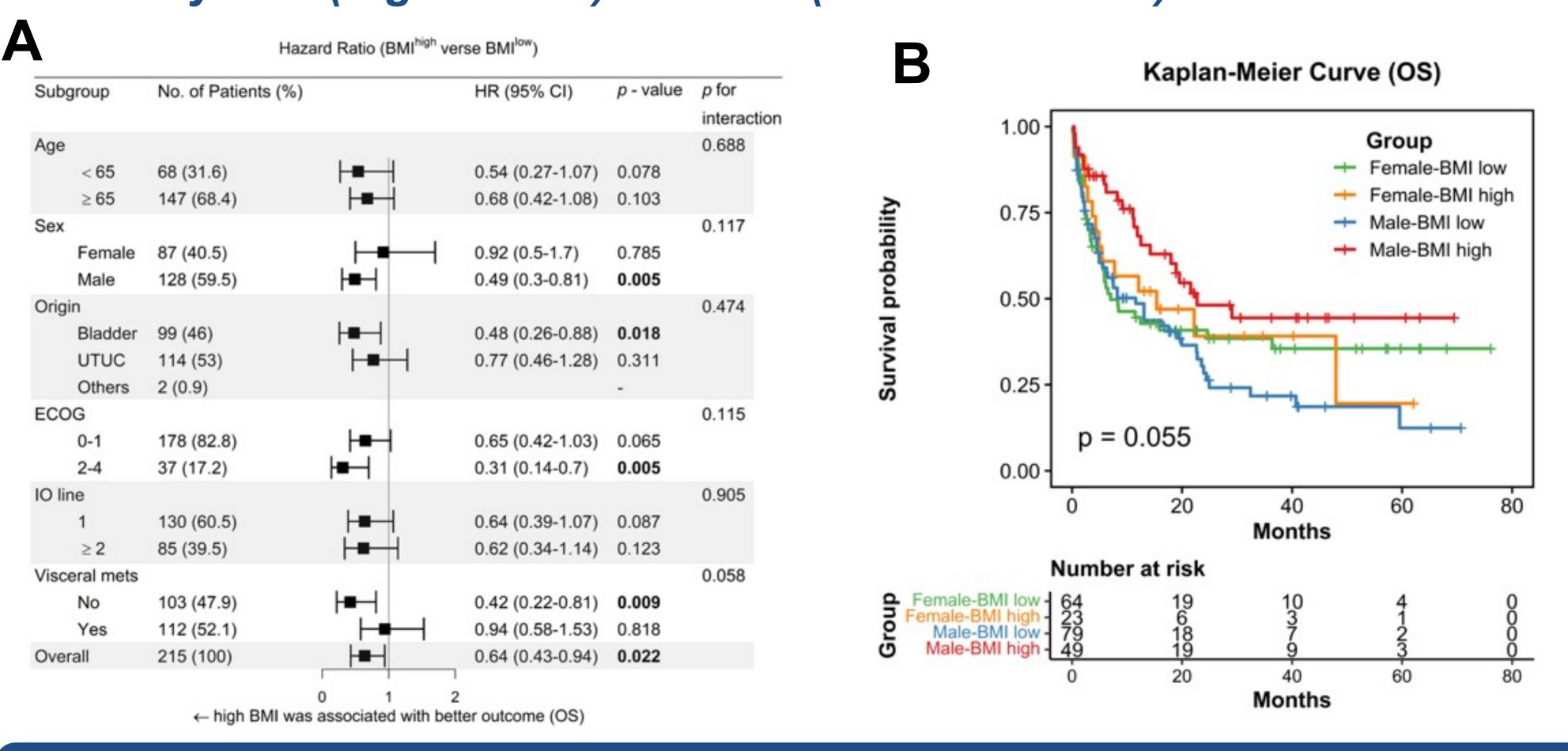


Table 3. Univariate and multivariate analysis of OS

Characteristics	Median OS	Univariate		Multivariate	
		HR (95% CI)	р	HR (95% CI)	р
Age (year)			0.76		0.65
< 65	16.2	1		1	
≥ 65	12.5	1.06 (0.73-1.53)		1.09 (0.75-1.60)	
Sex			0.91		0.46
Female	8.4	1		1	
Male	17.6	0.98 (0.69-1.39)		1.16 (0.78-1.72)	
ECOG status			<0.0 001		<0.0 001
0-1	19.5	1		1	
≥2	4.3	2.58 (1.70-3.90)		2.94 (1.86-4.62)	
Origin			0.45		0.94
Bladder	18.9	1		1	
UTUC	8.4	1.15 (0.81-1.63)		1.02 (0.68-1.52)	
LN metastasis			0.02		0.07
No	36.4	1		1	
Yes	11.5	1.64 (1.07-2.52)		1.49 (0.96-2.29)	
Visceral mets			<0.0 001		0.00 1
No	29.1	1		1	
Yes	6.2	2.07 (1.45-2.96)		1.93 (1.31-2.83)	
Treatment		· · · · · · · · · · · · · · · · · · ·	0.68	· · · · · · · · · · · · · · · · · · ·	0.49
1 st line	15.9	1		1	
≥ 2 nd line	12.1	1.08 (0.76-1.53)		1.14 (0.78-1.66)	
BMI (kg/m²)			0.02		0.00
< 25	8.3	1		1	
≥ 25	21.6	0.64 (0.43-0.94)		0.54 (0.35-0.81)	

Figure 3. (A) Forest plots of hazard ratios (HRs) for patients with high BMI versus low BMI by clinicopathologic factors; (B) KM analysis of OS divided by BMI (high or low) and sex (male or female).



Conclusion

Based on real-world data from the Asia-Pacific region, there appears to be a correlation between high BMI and prolonged OS in patients receiving ICI treatment for mUC.

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