

Roberto Borea^{1,2}, Carlos Ayala¹, Francesco Drago¹, Diego Enrico^{1,2} Eswar Shankar¹, Giovanni Nigita^{1,3,4,*}, Christian Rolfo^{1*}

¹Department of Internal Medicine, Division of Medical Oncology, The Arthur G. James Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio, USA., ² Department of Internal Medicine and Medical Sciences (DIMI), School of Medicine, University of Genova, Genova, Italy. ³ Pelotonia Institute for Immuno-Oncology, The Arthur G. James Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio, USA., ⁴ Center for RNA Biology, The Ohio State University, Columbus, Ohio, USA. * These authors equally contributed to the work.

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Introduction

Current evidence indicates that obesity is associated with improved overall survival (OS) in non-small cell lung cancer (NSCLC), a phenomenon called obesity paradox. However, its clinical validity, particularly in oncogene-driven disease, remains incompletely characterized. This study aimed to evaluate the prognostic value of Body Mass Index (BMI) in a broad NSCLC cohort and, specifically, to interrogate the BMI-treatment interaction in patients (pts) receiving Tyrosine Kinase Inhibitors (TKIs) to determine whether metabolic status impacts outcome.

Methods

We conducted a retrospective analysis of 310 pts with NSCLC included in the ORIEN/Avatar data at The Ohio State University, collected between 2009 and 2024. Pts were categorized by BMI into: Normal Weight (NW; 18.5≤BMI<25; n=126), Overweight (OW; 25≤BMI<30; n=95), and Obese (Ob; BMI≥30; n=89). OS was evaluated in the total population and in pts affected by NSCLC treated with TKIs. Survival distributions were estimated using Kaplan-Meier methods with log-rank tests, and hazard ratios (HR) were calculated using Cox proportional hazards regression models.

Patient characteristics

Median age	65,6
Sex	
Male	54,0%
Female	46,0%
Race	
White	90,8%
Black or African American	8,8%
Others	0,4%
Smoking status	
Current	16,9%
Former	65,4%
Never	10,7%
Unknown/Not Applicable	7,0%
Alcohol use	
Current	29,8%
Former	20,8%
Never	42,3%
Unknown/Not Applicable	7,4%
BMI	
LowUnderweight (<18,5)	3,7%
Normal (18,5-24,9)	32,0%
Overweight (25-29,9)	30,1%
Obese (≥30)	34,2%
Stage	
I (I-IA-IB)	59,9%
II (II-IIA- IIB)	7,0%
III (III-IIIA- IIIB)	12,9%
IV	2,6%
Unknown/Not Reported	8,1%
Histology	
Adenocarcinoma	52,2%
Squamous	36,8%
Others	11,4%
Vital Status	
Dead	52,2%
Alive	47,8%

Results

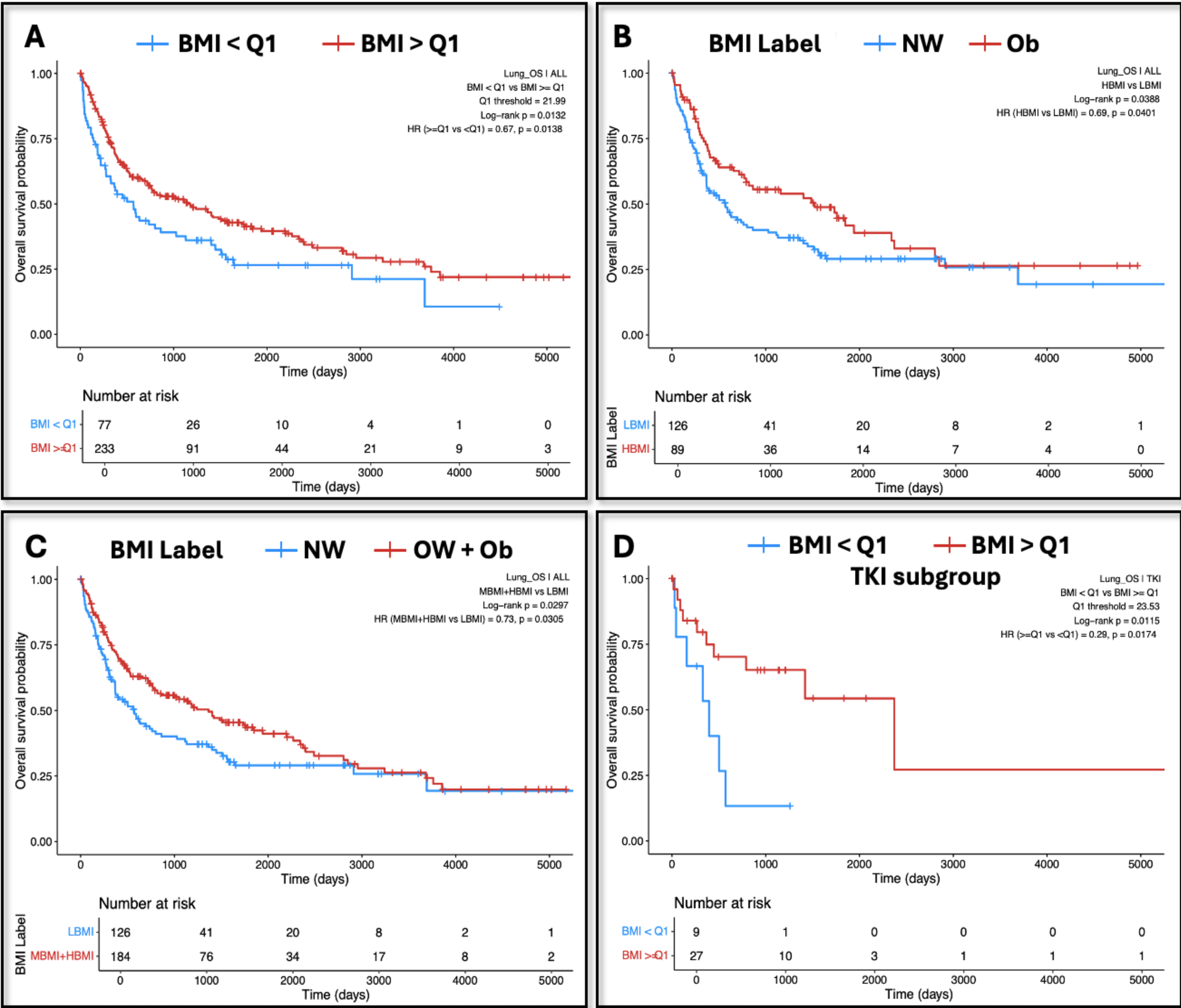
Higher BMI was associated with longer OS in the overall NSCLC cohort (N=310). Pts at or above the lowest-quartile threshold (BMI ≥21.99 kg/m²; n=233) had significantly longer OS than those in the lowest quartile (n=77) (HR=0.67, p=0.014; log-rank p=0.013; Figure 1A). The extreme-quartile comparison (Q1 vs. Q4, ≥30.94 kg/m²) was consistent (HR=0.61; log-rank p=0.016).

Conventional WHO categories captured the same trend in the overall cohort. Ob pts had longer OS than NW pts (n=89 vs. 126; HR=0.69, p=0.040; Figure 1B), as did the pooled OW/Ob group (n=184 vs. 126; HR=0.73, p=0.031; Figure 1C).

The association was strongest in pts treated with TKIs (N=36). Within this subgroup, quartile-based stratification identified a threshold of 23.53 kg/m²: pts at or above Q1 (n=27) had markedly longer OS than those below it (n=9) (HR=0.29, p=0.017; log-rank p=0.012; Figure 1D), corresponding to a 71% reduction in the hazard of death. The extreme-quartile comparison pointed in the same direction (HR=0.27, p=0.063; log-rank p=0.048).

In the TKI subgroup, the prognostic cutoff lies within the WHO normal-weight range (18.5–24.9 kg/m²). The at-risk pts are therefore subsumed within the NW category, and conventional BMI classes (NW, OW, Ob) did not show a significant OS difference in TKI-treated pts, whereas the data-driven threshold did.

The BMI effect was more than two-fold larger in TKI-treated pts than in the overall cohort (HR=0.29 vs. 0.67, i.e., 71% vs. 33% hazard reduction), suggesting that the BMI-associated survival advantage may be amplified in the context of TKI therapy.



Conclusions

These findings support the obesity paradox in NSCLC, with higher BMI associated with prolonged OS across the full cohort. In pts treated with TKIs, low BMI marked poorer outcomes, with a larger effect than in the unselected population. Standard WHO-based categories failed to reach significance in this subgroup, while a data-driven threshold (23.53 kg/m²) did, likely reflecting both the limited sample size and a prognostic cut-off falling below the normal-weight boundary.



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No Disclosure to declare

roberto.borea@osumc.edu
christian.rolfo@osumc.edu



RobertoBoreaMD



RolfoLab

