



Obesity and immune-checkpoint inhibitors in advanced melanoma: a meta-analysis of survival outcomes from clinical studies

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Introduction

The role of obesity in melanoma incidence, progression, and response to immune-checkpoint-inhibitors (ICI) is still controversial. On the one hand, increased levels of lipids/adipokines can promote tumor proliferation and several genes associated with fatty acid metabolism have been found to be upregulated in melanomas. On the other hand, immunotherapy seems to be more effective in obese animal models, presumably due to an increase in CD8+ and subsequent decrease in PD-1+ T-cells in the tumor microenvironment.

Materials and methods

The aim of this research has been to systematically review the scientific literature on studies evaluating the relationship between increased BMI and survival outcomes (i.e., OS-PFS) in melanoma patients treated with ICI and to perform a meta-analysis on those sharing common characteristics. A sensitivity analysis using the "leave-one-out" method was performed. Heterogeneity among studies was measured through the I^2 statistic.

Results

After screening 1070 records, 18 articles assessing the role of BMI-related exposure in relation to survival outcomes in ICI-treated melanoma patients were included in our qualitative synthesis analysis (PRISMA flowchart, fig.1). Overall, eleven studies (61.1%) found a protective role of the BMI and/or BMI-related parameter on the survival outcome in study, whilst seven studies (38.9%) did not find any significant association. In the meta-analysis of the association between overweight (defined as BMI>25 or BMI 25–30), overall survival (OS), and progression free survival (PFS), 7 studies were included, yielding a summary HR of 0.87 (95% CI: 0.74–1.03) and 0.96 (95% CI: 0.86–1.08), respectively (FOREST PLOTS, Fig.2, Fig.3).

Fig.1

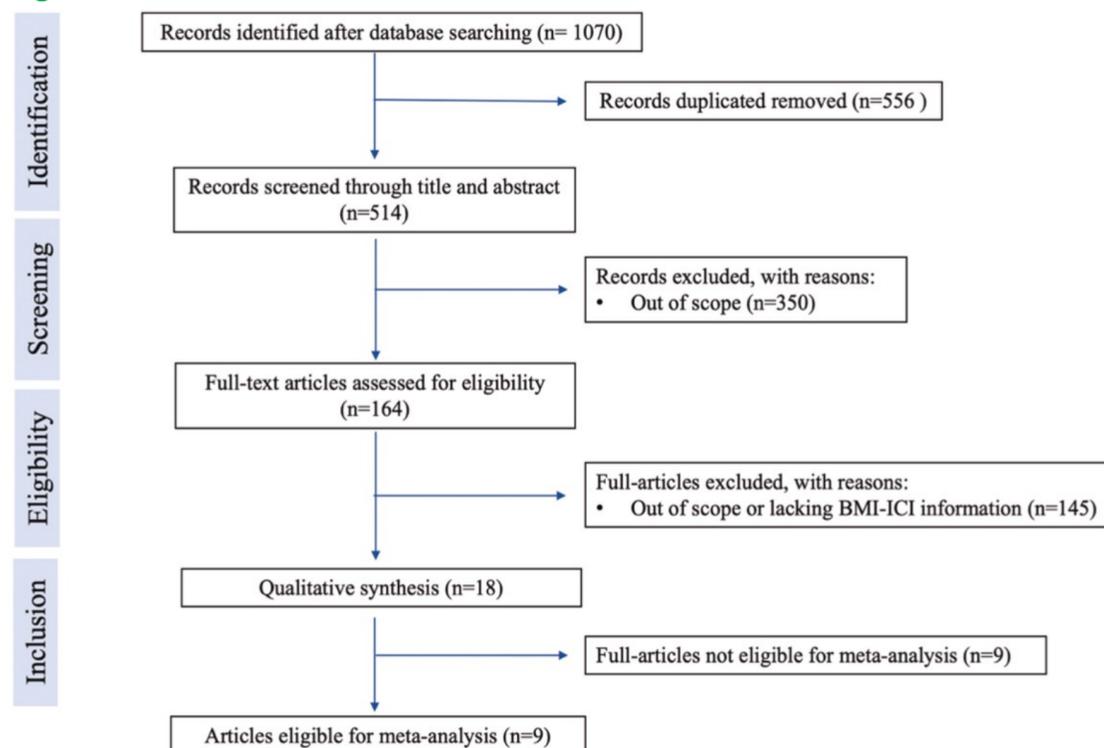


Fig.2

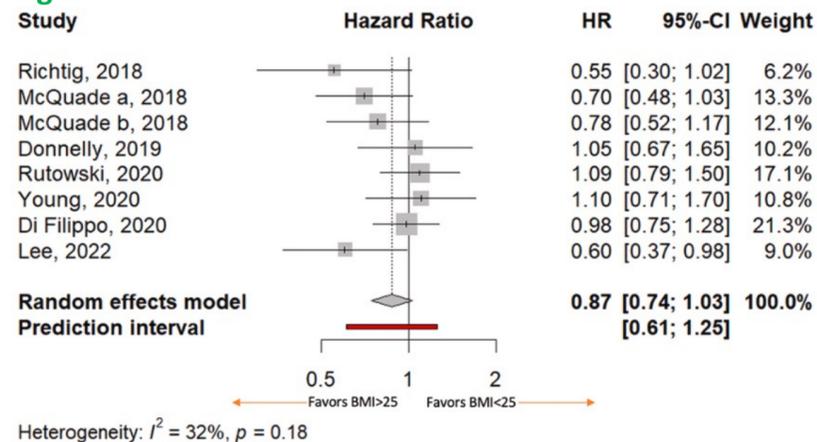
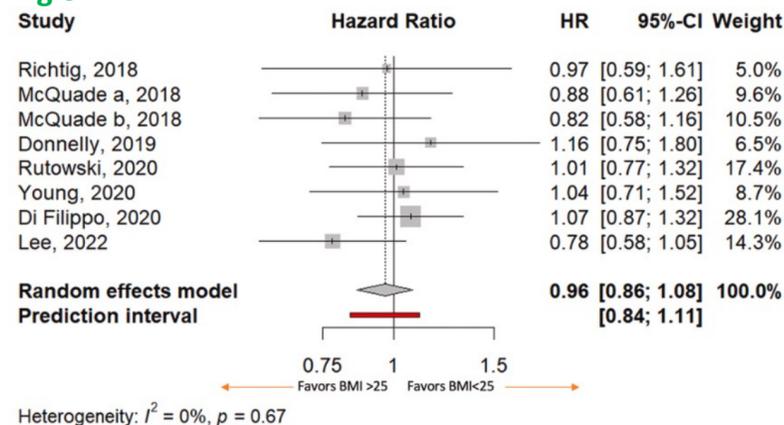


Fig.3



Discussion

The potential protective role of BMI> 25 at first suggested by McQuade *et al.* has not been replicated by the following studies, except for Lee *et al.*, with meta-analytic estimates close to the null (HR: 1.00) in terms of both OS and PFS. Our results show that, despite few suggestive findings, the use of BMI as a valuable predictor of melanoma patients' survival in terms of PFS and OS should not be currently recommended, due to the limited evidence available.

References

Full references can be found in the original draft: Rocuzzo G, Moirano G, Fava P, Maule M, Ribero S, Quaglino P. Obesity and immune-checkpoint inhibitors in advanced melanoma: A meta-analysis of survival outcomes from clinical studies. *Semin Cancer Biol.* 2023;91:27-34. doi:10.1016/j.semcancer.2023.02.010