



Letter to the Editor

Comments on: Sarcopenia and sarcopenic obesity are significantly associated with poorer overall survival in patients with pancreatic cancer: Systematic review and meta-analysis


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Dear Sir/Madam,

We read your published article on “Sarcopenia and sarcopenic obesity are significantly associated with poorer overall survival in patients with pancreatic cancer: Systematic review and meta-analysis” with great interest and commend the authors for a great review of the topic of sarcopenia which is reported to impact outcomes in oesophagogastric cancers from recent reviews [1,2]. However, little is known on the impact of sarcopenia in patients with pancreatic cancer, specifically pancreatic ductal adenocarcinoma (PDAC) since no meta-analysis is available. We have several comments on the paper for which we would like to address.

Firstly, this review included studies reporting on outcomes of pancreatic cancers of mixed underlying histologies such as cholangiocarcinoma, duodenal and ampullary carcinoma, although only PDAC's was planned to be reported as described in the abstracts and methods. It is well reported that outcomes of these different subtypes are variable with PDAC having the poorest long-term survival, followed by distal cholangiocarcinoma, duodenal and ampullary [3]. An analysis of a large American cancer database demonstrated the median survival for ampullary carcinoma were significantly longer than duodenal, distal cholangiocarcinoma and PDAC (median 41 vs 37 vs 24 vs 19 months, $p < 0.001$) and corresponding 5-year survival were 47, 42, 32 and 19%, respectively. Hence, exclusion of these studies with mixed pancreatic and non-pancreatic cancer subtypes will allow a better characterisation on the impact of sarcopenia on short-term and long-term outcomes of patients with pancreatic ductal adenocarcinoma.

Secondly, this review included studies reporting on sarcopenia in both resectable and unresectable cohorts in the same meta-analysis. Understandably, unresectable pancreatic cancers will have poorer survival than patients undergoing surgical resection for several reasons including advanced disease stage at presentation and higher rates of sarcopenia likely to reflect more on aggressive tumour biology. Hence, inclusion of studies reporting on outcomes of the unresectable cohort into the meta-analysis together will most certainly deflate the survival, further overestimating the impact of sarcopenia in patients undergoing surgical resection.

Furthermore, this study does not address methods of assessment of sarcopenia which may include computer tomography (CT), dual-energy

X-ray absorptiometry (DXA) and bioelectrical impedance (BIA). CT scans form a regular part of the standard management of pancreatic cancer patients and hence offers an opportune method for assessment of body composition at specific and relevant time-points in the patient treatment pathway. This avoids exposing the patient to repeated imaging and high radiation doses; and it is the authors' recommended method for body composition analysis. A recent study has found excellent correlation between results obtained from DXA and analysis of CT scans [4]. The definition of sarcopenia, a state of severe depletion of skeletal muscle mass (and function), have been largely established using CT measures and is associated with an increased risk of mortality in many malignant conditions.

Finally, the right statistical methods should be used in meta-analyses to allow accurate reporting of effect sizes. Normally, a fixed effects model is used when we assume that the true effect of any variable, such as sarcopenia, is the same across all studies i.e the study is on a single population. However, as the studies combined in this meta-analysis are drawn from heterogeneous populations with differing disease factors and biology, it is unlikely that this assumption will hold true. Indeed, most meta-analyses of interventions or risk factors utilise random effects models, as this is considered a more statistically consistent approach when combining medical literature. Additionally, as fixed effects models tend to underestimate heterogeneity, the statistical analysis used in this study is likely to overestimate the precision of the impact of sarcopenia in pancreatic cancers [5].

In summary, we welcome the authors to address the points above with a view of generating discussions surrounding the impact of sarcopenia and sarcopenic obesity on long-term outcomes in pancreatic cancers.

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