Unified definition of relapse-free survival should be used for evaluating survival benefit in oesophageal adenocarcinoma

With great interest, I read the report[1] by Turkington *et al* and applaud their proposed DNA damage immune response (DDIR) assay, which could predict survival benefit from DNA-damaging neoadjuvant chemotherapy following surgical resection in oesophageal adenocarcinoma (OAC). However, the definition of relapse-free survival (RFS) in their study was not widely accepted, leading to poor comparability among studies.

In the present study, RFS was defined as "the time from surgical resection to relapse of disease" in the statistical analysis section. Actually, the definition previously mentioned is generally considered as the meaning of time to recurrence (TTR).[2 3] And the RFS is always defined as "time to any event, irrespective of cause, except for any second primary cancers".[3] The confusion about the concept of RFS and TTR will lead to different results. For example, one patient with OAC died of coronary heart disease at the 50th month after surgery and neoadjuvant chemotherapy, with no evidence of recurrence before death. For the death of this patient, the TTR should be regarded as a censored event, whereas the RFS should be regarded as an endpoint event. The duration of RFS and TTR is the same (ie, 50 months), but its final event is different. In this situation, Turkington *et al* may have overestimated the RFS rate and thus produced biased predictive power of DDIR assay.

For evaluating the validity of the DDIR assay for predicting RFS, further external validation studies need to be carried out. I would recommend that future research on this topic report their result using the unified generally recognised definition of RFS.

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