Editorial

What is the real value of predictive models?

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Identification of image-based phenotypes that can be combined with clinical data and emerging biomarkers has the potential for great clinical impact. The development of these predictive models will not only improve evaluation, risk stratification, diagnosis and treatment of non-small cell lung cancer (NSCLC) patients, but also, make clinicians work easier, allowing for an integrated and practical analysis of all patients' characteristics (1).

However, regardless of the increasing amount of data obtained from each patient, clinical utility and implementation of these models remain controversial and more challenging than initially expected.

Hannequin *et al.* (2) present the results of their retrospective study where positron emission tomography/computed tomography (PET/CT) and CT scan radiomic features fail to predict overall survival (OS) and progression-free survival (PFS) when compared to other traditionally used clinical variables, as gender and stage.

In this issue of *Translational Lung Cancer Research*, Hannequin *et al.* describe the results of different predictive models including clinical characteristics, as gender and tumor stage, radiomic features obtained from CT scan and PET-CT images and histological features as PD-L1 expression. Despite the intrinsic power author's observe in CT and PET-CT radiomic features to predict survival, the truth is their models are not able to predict OS and PFS better than traditional models based in clinical data.

As the authors describe, among the main limitations of their study are its retrospective nature, the low number of events included in their stepwise models, that could have affected the results, the low number of patients studied and the lack of consideration of other important histopathological characteristics, as response to immune checkpoint inhibitors (ICI) or neutrophils to leukocyte ratios.

Furthermore, although predictive models trying to correlate radiomic features to clinical and histopathological responses to treatment continue to proliferate, the role of radiomics in real clinical practice remains still indeterminate.

Predictive models based in clinical, radiologic and genomic features, will hopefully improve patients' data processing and help in multidisciplinary teams' decision making, taking into account specific patients' characteristics (1).

Unfortunately, despite multiple studies trying to correlate radiological findings with tumor characteristics, OS and PFS, they still face some challenges and potentially difficult to overcome limitations, as radiomic workflow lack of repeatability or reproducibility under particular circumstances (3). In addition, although the field of radiogenomics aims to combine radiomic features with genetic biomarkers (4), the major challenge it faces is the difficulty to obtain comprehensive information regarding tumor biology and responses to treatment. Whether this challenge could be overcome using artificial intelligence to

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analyze large imaging and pathological datasets would be determined by costs, time and data analysis limitations.

In the present study, authors have tried to correlate CT and PET-CT findings with PD-L1 expression, and, although other investigators have tried to find a relationship between CT and PET-CT characteristics with EGFR, KRAS mutations and ALK translocations (5-7), their results remain difficult to translate into clinical practice. Other attempts to try to predict OS and PFS in early stage NSCLC, as the model designed and validated by Vaidya *et al.* (8) have shown promising results, even in predicting the benefit of adjuvant chemotherapy following surgical resection.

The number of predictive models developed in the recent years focused in both improvement of diagnosis and prediction of survival in NSCLC, has increased exponentially, but their clinical applications and their usefulness in a real word scenario is yet to be defined. Similarly, the number of variables and features included in these models does not correlate to their ability to discriminate different outcomes, and the simpler the model, the more likely it would be implemented in daily clinical practice.

To overcome the current challenges, it is of utmost importance to have prospective, independent and properly audited databases able to capture clinical, radiologic, surgical and genetic information in a standardized, reproducible manner. Furthermore, the problem that entails the processing of the massive amount of data generated will be solved, or at least improved, by the correct application of these models (1,9).

In a near future where machine-learning processes will be part of the healthcare workforce, the correct development and integration of these predictive models in the daily clinical practice will not only facilitate all clinicians' work but also improve considerably patient care, from diagnosis to treatment and follow-up, avoiding unneeded invasive procedures and derived complications.

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