Editorial Commentary

Not all that glitters is gold

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Lung cancer (LC) is the leading cause of cancer-related death worldwide with an overall 5-year survival of 15–20%, mostly due to a delayed diagnosis encountering an elevated percentage of advanced stages (1). For this reason, in the last years, huge and onerous efforts have been made in different countries to develop computed tomography (CT) screening programs aiming at improving the detection of early-stage LC. A complementary result of this policy has been the identification of a higher number of potential cancers presenting as different forms of ground-glass opacities (GGOs) (2). They are radiologically defined as focal areas of slightly increased CT attenuation through which the normal lung parenchyma structures, airways, and vessels are visually preserved. According to several papers (3,4), the lung nodules can be simply classified using the consolidation-to-tumor ratio (CTR) obtaining three groups: pure GGOs (non-solid tumors) with CTR =0, part-solid nodules with CTR between 0 and 1, and solid nodules with CTR =1. This radiological classification has been proven to have an impact on prognosis showing a strong correlation between an increased CTR and poorer survival (5). Pure GGOs are a subset of lesions ranging from benign findings to adenocarcinoma *in situ* or minimally invasive adenocarcinoma (MIA) up to, in some circumstances, invasive adenocarcinoma. These findings imply that a correct timing and an appropriate management of these lung nodules are crucial to achieve satisfactory long-term results. The paper by Li *et al.* (6) published in August 2023 in the *Annals of Thoracic Surgery* highlights these aspects showing excellent results about long-term follow-up in a "subgroup of 308 patients with pure GGOs". In particular, the 10-year recurrence-free survival was 100% and the 10-year overall survival of 96.9%; furthermore, more than 60% of operative procedures were sublobar resections, with a higher prevalence of wedge resections and a quarter of patients were affected by invasive cancers. At the first glance, the strength of the numbers (308 patients with pure GGOs), a long-term follow-up (10 years), and the impressive survival rates could persuade us that this paper represents a milestone in the management of GGOs. However, not all that glitters is gold...

In fact, the paper reveals some criticisms suggesting further analysis. First, the taxonomy is crucial: "pure GGO" is well defined as a nodule with CTR =0 meaning that no solid part must be present in the nodule. Travis *et al.* (7) in 2016 showed in a table the comparison between clinical and pathological features of small lung adenocarcinoma (<3 cm) with ground glass and lepidic component. In this table, it is clearly reported that in lepidic predominant adenocarcinomas (LPAs) the solid part is constantly present as like as in case of acinar predominant adenocarcinomas (APAs) or papillary predominant adenocarcinomas (PPAs). Thus, this population (21.6%) might be excluded from the analysis because it has not a "pure GGO" lesion.

Furthermore, we should focus also on MIAs because in these lesions a solid component is radiologically often present as reported by Travis; sometimes, it is related to zones of organizing pneumonia, but in other circumstances it could be the sign of the cancer progression and in this study more the 40% of patients had a MIA.

The second point is related to the window time of surgery. As reported by authors, at first detection of a pure GGO nodule their policy is to follow it and to operate only in case of slowly and progressive growth. This could be an acceptable strategy, but it is not clear the timing of this follow-up or if some radiological guidelines are considered. Also, it is not clear which is the diameter cut-off that makes to prefer a sublobar resection respect to a lobectomy. Furthermore, no mention is dedicated to lymph node management; it is true that some recent studies (8,9) have shown that in GGO lesions a systematic lymph node dissection could have no impact on prognosis, but (I) the study population of this paper is antecedent [2007–2013] of these trials and, thus, it is not justified an absence of any form of lymph node assessment and (II) when frozen section is not performed (as in this study), the risk of an invasive adenocarcinoma must be considered and a correct intraoperative staging must be always obtained (10).

Finally, as noted by the authors the population study represents a subgroup of patients with already known favorable prognosis (high percentage of female gender and never smokers). This could make difficult to compare these results with less homogenous and selected patients worldwide and to attend same survival rates in other countries.

Although in clinical studies the number of the population and a long-term follow-up are two powerful factors, we have always to keep in mind that other parameters as methodology, accuracy of the data, correct classification, and management are crucial to leave an adequate take-home message.

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