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An Inspirational All-Around Survey on Ground Glass Opacities

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Short Communication

In the last decade, with the advent of computed tomography screening for lung cancer, the number of Ground-Glass Opacity (GGO) nodules detected and referred for diagnosis and management has been increased. In particular their incidence has been reported with a range from 6% to 12% of all pulmonary nodules founded in usual Computed Tomography (CT) screening programs [1]. Indeed, GGO is a radiologic definition indicating a "lesions showing hazy increased attenuation without obliteration of the underlying bronchial or vascular structures on high-resolution CT" [2].

Unfortunately, a mere GGO finding is not "per se" diagnostic, in fact "GGO" is a rather unspecific radiologic feature common in several clinical conditions ranging from benign to malignant pathologic diseases.

For instance, lung infections, lung edema or interstitial diseases may present with GGO features. But often GGOs are also expression of primary lung cancer, therefore correct and early diagnosis and management are mandatory, since 75% of persistent GGO nodules are attributable to adenocarcinoma [3].

It has been showed that lung adenocarcinoma carcinogenesis follows a straight-line multistep progression and Atypical Adenomatous Hyperplasia (AAH) evolves into Adenocarcinoma in Situ (AIS), which in turn become invasive adenocarcinoma [4]. GGOs, in case of malignancy, correlates with different histologic patterns usually in accordance with specified radiologic features. First of all, it has been showed that risk of malignancy is significantly increased for GGOs with a large diameter, high mean CT value and maximum CT value [5]. More specifically, distinction between pure and partial GGOs, and the ratio between solid and non solid components are a main issues when evaluating the oncologic outcomes of these radiologic findings [6,7]. Matsunaga and colleagues have brilliantly described this topic [8], showing that part-solid tumors can be categorized by invasiveness and prognosis, based on a cutoff consolidation-to-tumor ratio of 0.5 (consolidation-to-tumor ratio less than 0.5 equivalent to non solid-predominant part solid lesion; consolidation-to-tumor ratio greater than 0.5 equivalent to solid-predominant lesion).

In the last decade several papers have been published on GGOs radiologic features, methods for diagnosis and surgical treatment. However, to this day, many surgeons find it difficult to manage patients with these asymptomatic and occasionally detected nodules [9]. In our opinion the possible main causes of this lack of confidence, as opposed to solid nodules, may be summarized as follows:

1. GGOS clinical behavior is generally indolent [10]; Fukui in 2017 [11] presented a retrospective study to state differences in the pathological invasiveness between GGO with and without changes over time and found that the pathological results of part-solid GGO with changes were similar to those without changes. Moreover, also results of pure GGO with changes were corresponding to those of part-solid GGO. They concluded that surgery can be deferred until part-solid GGO lesions demonstrate changes and, even for pure GGO, follow up is mandatory.

2. Their preoperative diagnosis is quite difficult, as even fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) often fails to distinguish benign from malignant GGO nodules [12]; moreover, its role in tumor is staging is dubious or even unuseful as showed by Cho et al. in their study on 164 patients who underwent surgical resection for adenocarcinoma with pure GGO features.

3. It is technically challenging to perform both Endobronchial Ultrasonography (EBUS) and percutaneous biopsy because nodule size is usually small and specimen obtained is often not proper for diagnosis, especially in pure GGOs. However, when EBUS is combined with Virtual

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Bronchoscopic Navigation (VBN) results are encouraging as showed by Ikezawa et al. who reported a diagnostic yield according to lesion size summarized as follows: diagnostic yield of 40% for lesions less than 15 mm, 66% for lesions 15 mm to 19 mm, 74% for lesions 20 mm to 24 mm, 65% for lesions 25 mm to 29 mm, and 88% for lesions greater than 30 mm [13]. Few data are reported as concerning percutaneous biopsy utility;

4. Surgical resection is often required to obtain actual diagnosis [14];

5. Radiological pathological concordance is non-specific, therefore is very challenging to distinguish between diagnosis of malignancy, such as adenocarcinoma, non-malignant or non-invasive lesions, such as those of Atypical Adenomatous Hyperplasia (AAH) and Adenocarcinoma In Situ (AIS), or other non-neoplastic diseases;

6. Prognosis is very heterogeneous also among neoplastic GGOs supporting the possibility of different surgical approaches [15]. The debate is still open on the best parenchyma resection (lobectomy, segmentectomy or wedge resection) and utility of nodal dissection according to radiological features.

7. In our personal experience, indeed, these points give arise to the most frequent dissenting views when cases are discussed during interdisciplinary meeting.

8. As has been said, many studies have been started concerning GGOs prognosis and surgical approach and some meaningful guidelines have been released. However, despite many data have been collected, GGOs are still one of the most controversial issues among thoracic surgeons.

In view of this scenario, we have read a very recent paper by Lococo and Co-workers from the PNR Group [16]. This is a survey submitted from the SICT (Italian Society of Thoracic Surgeons) to its members with the aim to obtain a snapshot on current practices in the management of GGOs. Firstly, in our opinion, Lococo and Co-workers paper is a particularly relevant initiative; as they correctly underline, indeed, one of the most important role for a surgical society is to promote research and education, but most of all, to create a network between specialists to bring out their current practice during clinical activity. So, we congratulate with to Authors for their job, particularly since we did not find similar surveys in literature among other thoracic surgeons societies.

Second, in more detail, some data surprised us. To start, percentage of questionnaire completed slightly exceed the half of members enrolled, showing a good but improvable adhesion. Then, many controversies emerged regarding main topics such as terminology, the use of PET/CT for pure GGOs, surgical timing during follow-up, extension of pulmonary resection and use of frozen section. Lastly, as the Authors underlined, some practices seems to be unfortunately dictated by defensive medical practice.

Data leads to conclude that Authors results confirm survey utility and strongly encourage a list of recommendations regarding GGOs management. Despite many indications have been already reported in literature, it is likely that a recommendations list edited by the belonging surgical society could further impact clinical practice.

We think that single or multi-center studies on GGOs management may still be meaningful but the next main goal should be to obtain a homogeneous approach among thoracic surgeons. Moreover, this is a necessary condition for organizing proper study without significant original bias. Therefore similar survey administration should be promoted by every thoracic surgeon's society, just like SICT did. Awareness of our diversity is the first and most difficult step to a future consensus.

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