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Editorial

New Bronchoscopic Treatments for Lung Peripheral Lesions

Nuevos tratamientos endoscópicos de lesiones pulmonares periféricas

The finding of pulmonary nodules in thoracic imaging tests or even in tests performed for other purposes is one of the most frequent realities in the routine practice of respiratory medicine. It is well known from the lung cancer screening programs that have been developed in recent years, especially after the publication of the results of the National Lung Screening Trial (NLST)[1] that most of these findings are usually benign in nature.

However, it is not uncommon for either studies of high-risk populations or other imaging tests to incidentally discover what later turns out to be lung neoplasms. The management of these findings represents both a diagnostic challenge and a problem in managing the uncertainties or fears of affected patients.

In recent years, there are numerous minimally invasive techniques that allow the diagnosis of these pulmonary alterations. From the bronchoscopic point of view, the development of radial ultrasound probes (rEBUS) and endobronchial electromagnetic navigation systems allow locating these lesions through bronchial divisions that cannot be reached with conventional bronchoscopic vision.

Other alternatives for the diagnosis of this pathology are percutaneous approaches both with thick needle and fine needle puncture (FNA) especially for lesions of subpleural location with variable safety profiles.

Focusing on the bronchial tree, the addition of imaging techniques such as conventional fluoroscopy and cone beam CT to the above-mentioned technologies improve the accuracy and provides real time view affecting to both diagnostic yield and safety outcomes.

At present, curative treatments for stage I and II non-small cell lung cancer include surgery and treatment with stereotactic ablative radiotherapy, also known as SBRT. The choice of one alternative over the other is usually conditioned by the patient's functional pulmonary status and comorbidity. These treatment alternatives are also available for the local treatment of oligometastases of certain tumors such as colon, melanoma, sarcomas or the lung itself, among others. Another alternative in these lesions with a transthoracic approach such as percutaneous thermal ablation could be considered in selected cases.

Although empirical treatment may be considered in selected cases, the need for histological sampling is necessary, especially with the promising results of targeted therapies and immunotherapy in early stages.[2]

It has been an ambition of interventional pulmonology for years to achieve the possibility of local treatment of these neoformative lung lesions. This approach has been evaluated in the same anesthetic act, turning bronchoscopy into a both diagnostic and therapeutic approach.

Until a few years ago it was only possible to apply endoscopic treatments on neoplasms located in the trachea and accessible bronchi with traditional bronchoscopes (mainly palliative), such as laser therapy, endobronchial brachytherapy, cryotherapy or photodynamic therapy. At present there are several alternatives proposed for this purpose and the following lines will detail the most relevant ones and the scientific evidence available on them.[3]

Radiofrequency ablation

This technique has the most evidence available up to date. Radiofrequency is considered a low frequency technology within the electromagnetic spectrum. Waves with a wavelength between 350 and 500 kHz are generated by means of an electrode and a grounding. This energy, through changes in the electron layers of the molecules, generates a heat that results in tissue necrosis at 60 °C and above. One of the main limiting factors of this technique is the low impedance and the dissipation (heat-sink) of heat produced by the blood vessels.

The current evidence is based on case series, including those published by Koizumi et al.[4] where radiofrequency was applied through the bronchoscope channel and controlled with real-time CT to patients with pulmonary neoformations with good results (20 patients were treated with a local control of 82.6%, without serious complications) and with a 5-year survival rate of 60%.

Microwave ablation

With respect to radiofrequency, microwaves are waves with a higher frequency reaching up to 2.5 GHz. The energy is applied through a needle inserted in the tissue that causes a movement in the charges of the water molecules which generates an increase in temperature through the effect known as dielectric hysteresis.[5] The area of effect of the treatment is highly variable, being subject to the physical properties of the tissue and the type of probe through which the energy is applied.

In the study published by Lau et al.,[6] 3 patients with metastatic lesions of tumors of other location were treated, combining

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electromagnetic navigation (superdimension-Medtronic, Minneapolis, MN, U.S.A.) and cone beam CT (Phillips, Eindhoven) with follow-up 30 days after the procedure. No remarkable adverse effects were reported.

Bronchoscopic thermal vapour ablation

Steam thermoablation therapy has been consistently tested for the treatment of lung volume reduction in carefully selected patients with pulmonary emphysema. The treatment consists of the application of steam to limited areas of the lung parenchyma with an application of heat adjusted to the density of the targeted lobe. This heat generates an inflammatory response that consequently generates a cicatricial response with a consequent reduction in lung volume.

Its application for malignant lung lesions has been published in feasibility studies[7] where 6 patients were treated, and surgical resection was completed in 5 of them. The analysis of the post intervention samples showed a uniform ablation in the areas treated with doses higher than 3 calories/ml. The validation of this treatment and the effective dose are still pending despite the promising results.

Irreversible electroporation

Electroporation treatment aims the formation of pores in the cell membrane through the application of a high energy pulsed electric field, which in some cases causes irreversible cell death.[8] This technology has been applied in liver or prostate tumors and in the case of transient electroporation it is estimated that it can have a "sensitizing" role as a complement to chemotherapy treatment. Other studies show that electroporation treatment can increase immune cells in the treated areas by preserving blood vessels and releasing extracellular matrix proteins, which may play an adjuvant role in immunotherapy treatment.[9] There are no human studies available for endobronchial treatment and there are some publications on its percutaneous application that do not allow its generalization to date.

Cryotherapy

The use of intense cold to freeze and destroy tissue have been used for central tumors and some articles have been published with a percutaneous approach in peripheral lung lesions,[10] but there is not current evidence by endobronchial approach treatments.

There are other proposed technologies with promising research but their use is far from widespread in the field of thoracic oncology.

In conclusion, with the development of early detection programs for lung cancer, the detection of neoplastic lesions allows the approach of curative treatments. For those cases that cannot benefit from surgical approaches, treatment with radiotherapy is the main alternative but complications should always be considered especially in patients with pulmonary comorbidities.

Endoscopic lung nodule treatment approaches are one of the greatest ambitions of interventional pulmonologists, allowing treatment to be applied at the same time as diagnosis and staging. There are several techniques and technologies proposed for this purpose and although none of them is currently within the usual treatment standards, the technological development and the growing evidence allow us to contemplate a potential role for the future. Endobronchial treatments cannot only be considered as a lonely local control of pulmonary neoplasm, its inclusion in the framework of a multimodal treatment with the support of a multidisciplinary committee may represent a major growth area for interventional pulmonology.

We are in a time of great changes in bronchoscopy due to technological advances and it is foreseeable that soon we will be able to perform the diagnosis and treatment in the same procedure with the consequent benefit for the patient. Exciting years lie ahead of us.

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