

Editorial

The New Ice Age: Cold Applications in Pulmonology

La nueva edad de hielo: aplicaciones del frío en neumología



While climate change drives global temperatures upward, pulmonology has found in cold a powerful ally. The cryoprobe now stands as an essential instrument for diagnostic and therapeutic bronchoscopy. The process is based on the Joule–Thomson effect, whereby the adiabatic expansion of a compressed gas generates rapid cooling. This drop in temperature cools the tip of the cryoprobe, which adheres to the tissue by crystallizing water molecules at the interface, facilitating its removal.¹

Diagnostic applications

Diagnostic bronchoscopy and its related techniques (biopsy, puncture, brushing, etc.) are widely used to detect central endobronchial neoplasia, but its failure rate requires frequent repetition of the procedure. Hetzel et al. described that endobronchial cryobiopsy offers a higher diagnostic yield (95%) than conventional biopsy (85.1%), even when used in conjunction with other procedures (88%). This diagnostic superiority over forceps biopsy is due to a larger sample size, less tissue damage, and the ability to sample in tangential positions thanks to the concentric expansion of freezing.²

Cold sampling has also been shown to play a role in the study of mediastinal lymphadenopathy. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is the preferred method for the study of hilar and mediastinal lesions. However, sometimes the sample is insufficient, especially in lymphoproliferative or benign pathologies, and requires a surgical approach with a higher risk of complications.³

Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy (EBUS-TMC) is emerging as a novel technique that allows for larger, better-preserved samples to be obtained for analysis. After performing EBUS-TBNA, a channel is created into the lymph node, which can be made with the needle itself or by using devices like the high-frequency hybrid needle knife. Through this channel, the cryoprobe, usually 1.1 mm, is introduced to obtain the sample by freezing. Mathew et al. described that the incorporation of EBUS-TMC significantly improves the diagnostic yield compared to EBUS-TBNA alone (91% vs. 81%), mainly in benign pathologies (91% vs. 58%) and lymphomas (87.5% vs. 29%). No significant differences were observed in lung cancer or other malignancies, although an advantage was evident in molecular studies (95–97% vs. 74–79%). This all comes with a safety profile comparable to that of EBUS-TBNA.⁴

For lymphadenopathy not addressable by conventional EBUS, performing lymph node cryobiopsy via the esophageal route has reported similar results, also with a good safety profile.⁵

The diagnosis of interstitial lung diseases (ILD) is generally achieved by integrating clinical, laboratory, and radiological data in a multidisciplinary discussion; however, in some patients these elements are insufficient, making lung histological evaluation necessary. Transbronchial forceps biopsy is safe, but it has a low yield in complex patterns such as usual interstitial pneumonia (UIP), while surgical biopsy, considered the gold standard, offers high diagnostic yield (~90%) and improved diagnostic confidence, though it is limited by its morbidity and mortality. Transbronchial lung cryobiopsy (TBLC) has been investigated as a less invasive alternative to surgical biopsy, allowing for larger and better-quality samples than conventional transbronchial biopsy. TBLC offers a good diagnostic yield (73–83%) and increases diagnostic confidence, with lower mortality, complications, hospital stay duration, and costs when compared to surgical biopsy, as described by Korevaar et al.⁶

Furthermore, cryobiopsy is an emerging modality in the diagnosis of peripheral lung lesions (PLLs). Giri et al. described that it allows for larger sample sizes and provides a higher diagnostic yield compared to forceps biopsy (76.5% vs. 65.3%), with a similar safety profile.⁷

In lung transplantation, cryobiopsy also offers a higher diagnostic yield for both acute and chronic rejection, without significantly increasing complications.⁸

Pleural biopsy is a common procedure in the diagnosis of various pleural pathologies and can be performed percutaneously or endoscopically, the latter offering the highest diagnostic yield. Pleural cryobiopsy allows for the collection of larger and better-preserved tissue fragments than those obtained with flexible forceps, with a similar safety profile. However, no significant differences in diagnostic yield were observed between the two techniques (96.5% vs. 93.1%), as described by Shafiq et al.⁹

Therapeutic applications

Cryorecanalization must be distinguished from cryotherapy. The former involves the immediate removal of exophytic tumor tissue using cryoprobes,¹⁰ thus providing immediate relief. The procedure and freezing time were described in the early 2000s, and its use subsequently became widespread in the treatment of central airway obstructions (CAO) as monotherapy or in combination with

other techniques. An example of this is the French national registry of patients with CAO of malignant etiology – where cryorecanalization was used in 2.7% of cases – or the removal of endobronchial clots.¹² Cryotherapy, on the other hand, involves the therapeutic application of extreme local cold to destroy living tissue. In 1996, Mathur et al.¹³ described the successful application (>80%) of cryotherapy in obstructive endobronchial lesions in 1–3 cycles lasting at least 1 min, with extraction in a second endoscopic procedure 10 days later. Similarly, according to Bertoletti et al. and Deygas et al., low-grade endobronchial malignancies – such as non-invasive carcinoma and/or typical carcinoid tumors – can be treated endoscopically with cryotherapy, with response rates of 91% and 100%, respectively.^{14,15}

Without a doubt, we are experiencing a new ice age in pulmonology. But the cold does not paralyze us; it leads us to more precise diagnoses, safer therapies, and opens up a rapidly expanding research horizon. The current challenge is to consolidate the evidence, standardize protocols, democratize access to cryotechnology, and assess its cost-effectiveness compared with conventional techniques.

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Conflicts of interest

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Eduardo Solís García^{a,b,c,*}, Blanca de Vega Sánchez^d

^a Interventional Pulmonology Unit, Pulmonology Department, Hospital Universitario Rey Juan Carlos, Móstoles, Spain

^b Grupo Emergente de Broncoscopia y Neumología Intervencionista (GEBRYN) de la Sociedad Española de Neumología y Cirugía Torácica (SEPAR), Spain

^c Instituto de Investigación Sanitaria Fundación Jiménez Díaz (IIS-FJD, UAM), Madrid, Spain

^d Interventional Pulmonology Unit, Pulmonology Department, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

* Corresponding author.

E-mail address: solisariego@gmail.com (E. Solís García).