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Reviewer A

This paper is a narrative review that analyzes the published literature to evaluate the diagnostic accuracy and safety of endobronchial ultrasound guided transbronchial mediastinal cryobiopsy (EBUS-TMC).

EBUS-TMC is a relatively new technique of sampling mediastinal lymph nodes/lesions, performed with the aim of obtaining a greater amount of tissue to improve histological diagnosis and biomolecular investigations.

The topic is interesting and of current utility in clinical practice.

Comment

The review is well written and the evaluation of the literature is complete and up-to-date. I have just few comments.

Comment:

the Authors describe the technique used for EBUS-TMC, underlining the need to create a hole in the bronchial wall (with needle, or electrocautery knife or laser) to facilitate the insertion of the cryoprobe. This is true, but the hole is also necessary to allow the passage of the biopsy specimen when the bronchoscope with the attached cryoprobe is retracted. This concept should be reported.

Reply:

Your comment is much appreciated, and you have raised a valid point. The tract that has been established will indeed aid in the smooth retrieval of the cryobiopsy specimen.

Changes in the text:

In some instances, tools such as an electrocautery knife or laser are used to widen the tract, facilitating insertion of the cryoprobe. Furthermore, this tract facilitates passage of the biopsy specimen during retrieval of the cryoprobe and bronchoscope post EBUS-TMC. (revised manuscript, page 9 lines 23-26)

Comment:

While a table on the narrative review checklist is not necessary, I think it could be useful for the reader to include a Table which summarizes the results reported in the different mentioned studies. This Table should report Authors, year, number of patients, kind of study (randomized, retrospective, observational), and a short note on the results.

Reply:

Thank you for the suggestion.

Changes in the text: I have included a table.

Reviewer B

In this paper the authors review the published data about the use of cryoprobes to sample the mediastinal lymph nodes.

The article is interesting, well written and provide a good summary of available data.

Recommend minor revisions in two areas:

Comment:

Page6 -line31 "This was specifically done in cases where the cryoprobe's insertion was unsuccessful post TBNA" It is unclear what additional meaning this phrase add to the previous line. Recommend removing it.

Reply: Apologies that this sentence was not clear. In Gershmann et al. (13), when encountering difficulties introducing the cryoprobe through the orifice created by the Procore TBNA needles (8 out of 24 patients), they used an N YAG Laser (Medialis Fiberton 8100 Dornier MedTech) to enlarge the orifice. In these cases, they opted to use the 1.7 mm cryoprobe to perform the EBUS-TMC. This choice was likely to have been made because the laser-enlarged tract provided the necessary space for the 1.7 mm cryoprobe to pass through.

Changes in the text

When faced with challenges inserting the cryoprobe through the tract created by the TBNA needles (8 out of 24 patients), Gershmann et al. (13) used an N YAG laser (Medialis Fiberton 8100, Dornier MedTech) to enlarge the tract. In these instances, a 1.7 mm cryoprobe was used to perform EBUS-TMC procedures. (revised manuscript, page 10 lines 19-23)

Comment:

Page 7 line 1-6; the reported procedural time needed for EBUS cryobiopsy compared to EBUS alone is unclear- Please revise the whole paragraph.

Reply:

The inclusion of EBUS-TMC alongside EBUS-TBNA typically extends the total procedure duration compared to performing EBUS-TBNA alone. The reasons for this are mentioned in the Discussion. I will change the original text to make this clearer.

Changes in the text:

Most studies (12–15) did not report the time it took to perform EBUS-TMC in addition to the standard EBUS-TBNA procedure. Among those that did, the time to perform EBUS-TBNA versus EBUS-TMC differed, with the cryobiopsy generally being lengthier than TBNA. Zhang et al. (9) noted a mean time of 31.9±9.1 min for EBUS examination, with cryobiopsy taking slightly longer than TBNA (11.7±5.3 versus 9.4±2.6 min, p<0.001). Fan et al. (10) reported a mean time of 22.3 min for combined EBUS-TBNA and EBUS-TMC, slightly exceeding EBUS-TBNA alone (17.0 min; p<0.0001). The final study to report procedure duration (11) did not compare the procedure time between EBUS TBNA and EBUS TMC, but reported an average time of 33.96±5.86 min for the total procedure (EBUS TBNA and EBUS TMC), with EBUS-TMC taking 9.54±2.10 min. (revised manuscript, page 11 lines 6-15)