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Original Research Paper

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DIAGNOSTIC ALTERNATIVES TO ENDOCOSPIC ULTRASOUND IN SUBEPITHELIAL LESIONS: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Subepithelial lesions are a challenge in clinical practice, often requiring a biopsy for a proper diagnosis. Currently, the gold standard is an endocospic ultrasound, which is rarely available.

Objectives: Use a systematic review to check the effectiveness of the mucosal incision-assisted biopsy and assess whether it can be an alternative to endocospic ultrasound.

Methods: The most relevant studies in the MedLine and SciELO databases were reviewed, and only randomized controlled clinical trials (RCT) and meta-analyses were considered. The search strategy used the following combinations of keywords: subepithelial lesion mucosal incision biopsy. The following terms were used to identify the study designs: clinical trials.

Results: Seven articles that demonstrated the usefulness of the study technique and diagnostic efficacy were included in the scope of this review. This technique seems safe for biopsies. However, it is controversial for the resection of lesions. It has limitations, such as being more time-consuming.

Conclusion: Mucosal incision-assisted biopsy can be considered useful in clinical practice and is still an effective technique and an alternative to endocospic ultrasound

KEYWORDS : Gastric Subepithelial Lesions, Endocospic Ultrasound, Diagnosis.

INTRODUCTION

Subepithelial lesions are a challenge to clinical practice, demanding complex and costly tests, which delay diagnosis and treatment. Currently, the gold standard is the ultrasound-guided biopsy[1].

Endoscopic ultrasound, also called echo-endoscopy, is noteworthy, since it can identify the location, echogenicity, size, and vascularization, as well as assess the involvement of adjacent organs and be used for analysis and biopsy[1,2].

Subepithelial tumors are usually of a benign origin. However, some lesions may be malignant. Gastrointestinal stromal tumors (GIST), which are the most common mesenchymal neoplasms originated in the muscularis propria layer of the stomach, are malignant in 10-30% of the cases. Resection is suggested where GIST > 2 cm; when < 2 cm, it may be accompanied by imaging[3,4].

Subepithelial lesions > 10 mm should be biopsied. Smaller lesions should only be followed up. Since there is no consensus as to the timing, a simple endoscopy follow-up is suggested in the first six months, then annually. However, in the case of suspected intramural metastases, lymphomas, neuroendocrine tumors or GIST (with indication of a neoadjuvant chemotherapy), biopsies should be performed, regardless of size. An adequate diagnosis can improve the clinical management decisions in these patients. Lesions with an increase in size or changes in their characteristics should also be biopsied[1,2].

However, this test is still rare and expensive for clinical practice. In addition, such biopsies require costly materials. There are several types of needles for this procedure. However, there are no formal recommendations on what type of needle is suitable for each tissue and no detailed information about the architecture of a tissue based on higher sample yields[5-7].

Because of the low availability of the endocospic ultrasound in the clinical practice, other techniques are considered. Therefore, the objective of this study is to use a systematic review to assess the safety of the mucosal incision-assisted biopsy technique, as well as its efficacy and complications.

METHODS

The most relevant studies originally published in English over the last five years were reviewed, using the National Library of Medicine and National Institutes of Health (MedLine) and Scientific Electronic Library Online (SciELO) databases as references. In order to select studies with greater scientific evidence, only clinical trials and descriptive studies were considered.

The search strategy used the following keywords: subepithelial lesion mucosal incision biopsy. The following terms were used to identify the study designs: clinical trials and observational study. Inclusion and exclusion criteria were applied based on the types of studies, language, type of therapy and date of publication considering each item listed in Table 1. The inclusion and exclusion criteria shown in Table 1 were applied in selecting the studies.

TABLE – 1
INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria	
Design	• Clinical trials and observational studies

Patients	• Patients with upper gastrointestinal tract subepithelial lesions
Intervention	• Mucosal incision-assisted biopsy
Language	• English and Portuguese
Exclusion criteria	
Design	• Case reports and case series
Intervention	• Performed on animal models • Performed outside the upper gastrointestinal tract
Method of administration	• In abstract only
Main clinical outcomes	
• Mucosal incision-assisted biopsy effectiveness and complications.	

RESULTS

Twenty-four studies involving the mucosal incision-assisted biopsy technique were initially identified. However, after applying the Clinical Trials and Observational Study filter, twelve studies were found. After reading the articles and excluding by the abstracts, seven articles were selected involving the subject of analysis and included in the scope of this review. Figure 1 illustrates the study selection flowchart and Table 1 shows a summary of the studies selected and reviewed for this study.

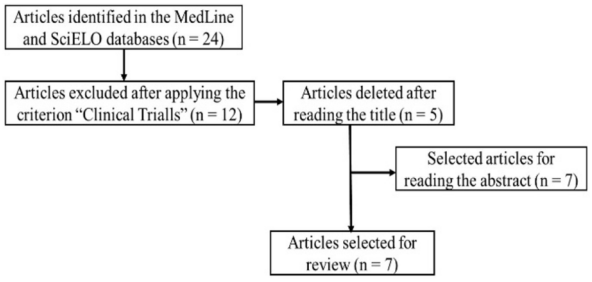

Figure 1: Study Selection Process Flowchart.

TABLE – 1 Summary Of The Studies And Their Main Results Involving The Mucosal Incision-assisted Biopsy Technique

Author	Sample	Method/ Intervention	Results
Minoda et al.[8]	177 patients with gastric subepithelial lesions submitted to EUS-FNA or MIAB in 5 hospitals in Japan.	Retrospective review of medical records. Diagnostic yield, procedure time and adverse event rates for both procedures before and after propensity score matching.	No procedure-related adverse events. They produced highly accurate diagnoses. For lesions > 20 mm in diameter, there was no difference in the diagnostic quality. However, the mucosal incision-assisted biopsy required more time to be performed.
Osoegawa et al.[9]	47 patients with gastric subepithelial lesions with suspected GIST.	A prospective, randomized, cross-over multicenter study. Sample divided into a mucosal incision-assisted biopsy group MIAB (n = 23) and a EUS-FNA group (n = 24).	There was no significant difference in the diagnostic yield for MIAB and EUS-FNA. The complication rates were similar, with no statistically significant difference. The time to perform the mucosal incision-assisted biopsy was significantly longer.
Jung et al.[10]	42 patients with gastric subepithelial tumors >10 mm were enrolled between May 2013 and October 2014.	Biopsies were performed using a forceps after a small endoscopic dissection of the submucosa. Cases were compared with retrospective data of 30 EUS-FNA cases.	There were no procedure-related adverse events in both groups. The diagnostic yield of forceps biopsies after a small endoscopic dissection of the submucosa was comparable to that of the EUS-FNA. The mean time for the biopsy procedure was shorter than that of the EUS-FNA.
Matsuzaki et al.[11]	10 patients (mean lesion size 16 mm, range 15-44 mm) submitted to endoscopic ultrasound-guided forceps biopsy.	This study was a series of prospective cases. Viability of the endoscopic ultrasound-guided forceps biopsy. Samples using hot biopsy forceps after mucosal sections under real-time ultrasound visualization and hemoclip closure.	The overall rate of histological diagnosis using the endoscopic ultrasound-guided forceps biopsy was 100%. Rate of diagnosable samples: 97.6%. Mean procedure time for endoscopic ultrasound-guided forceps biopsy and complete closure = 28.5 and 4.5 minutes. No adverse events occurred.
Ye et al.[12]	85 patients with subepithelial tumors of the gastrointestinal tract ≤ 3 cm originating from the muscularis propria layer (60 esophagus, 16 cardia, and 9 stomach).	Submucosal tunneling endoscopic resection followed by closing the mucosal incision with several clips.	Success rate: 100%. The mean tumor size was 19.2 mm. The mean procedure time was 57.2 min. During the procedure, 8 patients developed pneumothorax, subcutaneous emphysema or pneumoperitoneum; effective conservative treatment. Larger lesions originated in the deeper MP layer (70%) than in the superficial MP layer. No residual or recurrent tumor was seen.
Zhou et al.[13]	21 patients with submucosal tumors originated from the muscularis propria layer in the gastroesophageal junction.	Mucosal incision, submucosal tunneling and tumor resection under direct endoscopic view, hemostasis and hemoclip closure. The mean follow-up period after the procedure was 6 months.	Success rate: 100%. The mean size was 23 mm. The mean procedure time was 62.9 minutes. Events: mediastinal and subcutaneous emphysema in 9 patients; one required percutaneous drainage. There were no massive or delayed bleeding incidents.

Zhang et al.[14]	14 patients with gastric subepithelial tumors originated from the muscularis propria.	Ligation-assisted endoscopic submucosal resection with apical mucosal incision between December 2016 and May 2017. Patients were followed up for 2-6 months.	The total resection rate was 100%; the mean tumor size was 10.71 mm. Mean operative time was 18.5 min. Perforation occurred in 4 patients, all lesions being totally repaired by endoscopy. No bleeding or peritoneal signs were seen. No residual injury or recurrence was found during the follow-up period.

Key: EUS-FNA (endoscopic ultrasound-guided fine-needle aspiration); MIAB (mucosal incision-assisted biopsy); GIST (gastrointestinal stromal tumor): MP (muscularis propria).

DISCUSSION

Subepithelial lesions can be seen via endoscopy, but often require a biopsy for diagnostic evaluation and treatment. With the advent of technology, an endocospic ultrasound was chosen for evaluation. However, it is known that it is a high-cost test and often only available in large cities. In view of the low availability of this test in clinical practice, this study searched for alternatives to the endocospic ultrasound.

The selected studies demonstrate that the mucosal incision-assisted biopsy is effective for diagnosis. It is able to collect good fragments for anatomopathological analysis. However, it is a more time-consuming procedure. Complications were not observed in the studies under review.

In a study by Minoda et al.[8] in Japan, the diagnostic yield, procedure time and adverse events were evaluated retrospectively. By directly comparing the endoscopic ultrasound-guided fine-needle aspiration biopsy with the mucosal incision-assisted biopsy, the result was favorable in both techniques, signaling a superiority in the mucosal incision-assisted biopsy in lesions smaller than 20 mm. There were no differences between complications.

Osoegawa et al.[9] also made a direct comparison between both techniques. They observed that there was no significant difference in the diagnostic yield for the mucosal incision-assisted biopsy and the endoscopic ultrasound-guided fine-needle aspiration biopsy. The complication rates were similar, with no statistically significant difference. They only pointed out a significant time difference for the procedure, with the mucosal incision-assisted biopsy being more time-consuming.

Jung et al.[10] confronted the need for an ultrasound, comparing biopsies performed after a small dissection of an ultrasound-guided submucosa with a non-guided biopsy, showing efficacy in both techniques. No adverse events were seen in any of these types of procedures. In a study by Matsuzaki et al.[11], the endocospic ultrasound-guided submucosal resection was assessed, once again showing the superiority of the sample collected after submucosal resection, in addition to procedure safety. The mean procedure times for an endoscopic ultrasound-guided forceps biopsy and complete closure were 28.5 and 4.5 minutes, respectively. No adverse events occurred.

This and other studies demonstrated the efficacy of mucosal dissection as a lesion resection approach[12-14], in which the technique employed was similar to that used for biopsies, considering the lesion resection and showing therapeutic success. With the occurrence of events, Ye et al.[12] reported that eight (9.41%) patients developed pneumothorax, subcutaneous emphysema, or pneumoperitoneum, with an effective conservative treatment, and also showed that the complications were greater for lesions originated in the deeper muscularis propria (70%) than in the superficial muscularis propria. In a study by Zhou et al.[13], similar events were described in nine (42.8%) patients, and one (4.76%) patient required percutaneous drainage. There were no massive bleeding incidents. Zhang et al.[14] observed perforation in four (28.5%) patients, with all lesions completely repaired via endoscopy, and no delayed bleeding or signs of peritoneal irritation were observed.

This is in agreement with other articles in the literature as verified by Chung et al.[15], who demonstrated the safety of the procedure with a low perforation index accounting for 6.1% in fixed lesions; then, the patients were followed up by endocospic ultrasound. This was also reviewed in a large study carried out in China by He et al.[16] in a large sample of 144 patients, in which a low complication rate was observed: 14% perforations, and 4.83% bleeding, all of which were repaired in the intraoperative period, showing safety and efficacy for the mucosal dissection technique.

After a review of the studies included in the synthesis of this systematic review, it was found that the mucosal incision technique seems safe for biopsies and is also a great option for the collection of histopathological samples. However, the technique does not appear to be superior to the endoscopic ultrasound, since it is more time-consuming. Despite complications, as mentioned above, they are insignificant and are usually treated without the need for a new approach and are circumvented during the procedure.

CONCLUSION

Based on the reviewed articles, it is suggested that the endoscopic mucosal incision-assisted biopsy technique seems to be superior for small lesions and a histopathological diagnosis. This technique has its limitations such as the need for qualified technical training and length of the procedure. Therefore, learning this technique should be encouraged and even considered as an option for endocospic ultrasound. Despite complications, these are insignificant and are usually treated without the need for a new approach and are circumvented during the procedure. No differences were observed in adverse effects between the biopsy techniques. Therefore, it is considered a safe technique. However, well-designed clinical trials are necessary for a better evaluation.

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