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SYSTEMATIC REVIEWS

# Dental trauma in endoscopy: A systematic review and experience of a tertiary endoscopy centre

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## Abstract

### *BACKGROUND*
Dental injury is the leading cause of litigation in anaesthesia but an underrecognized preventable complication of endoscopy.

### *AIM*
To determine frequency and effects of dental injury in endoscopy, we present findings from an audit of outpatient endoscopy procedures conducted at a tertiary university hospital and a systematic review of literature.

### *METHODS*
Retrospective review of 11265 outpatient upper endoscopy procedures over the period of 1 June 2019 to 31 May 2021 identified dental related complications in 0.284% of procedures. Review of literature identified a similar rate of 0.33%.

### *RESULTS*
Pre-existing dental pathology or the presence of prostheses makes damage more likely but sound teeth may be affected. Pre-endoscopic history and tooth examination are key for risk stratification and may be conducted succinctly with limited time outlay. Tooth retrieval should be prioritized in the event of dental injury to minimize aspiration and be followed by prompt dental consultation for specific management.

*CONCLUSION*
Dental complications occur in approximately 1 in 300 of upper endoscopy cases. These are easily preventable by pre-endoscopy screening. Protocols to mitigate dental injury are also suggested.

**Key Words:** Teeth; Dental trauma; Endoscopy; Digestive system



**Core Tip:** Peri-intubation dental injury is a leading cause of litigation in endoscopy, and its complications are largely prevented with sufficient foreknowledge and counselling. We summarize findings from an audit of dental injury on endoscopy as well as review relevant literature to guide identification, mitigation and management of peri-endoscopic dental trauma.

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## INTRODUCTION

Peri-intubation dental injury is a leading cause of litigation in anaesthesia[1] with incidence of between 0.02%-0.07%[2-5]. Endoscopic procedures such as Oesophagogastroduodenoscopy (OGD), Endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP) and Bronchoscopy likewise involve per-oral intubation and face similar complications. This subject has been under-represented in the field of endoscopy and is a cause for concern[6]. Dental complications are largely prevented with sufficient foreknowledge and counselling. We hence aim to study the impact of dental injury on endoscopy in our centre as well as review relevant literature to guide identification, mitigation and management of peri-endoscopic dental trauma.

## MATERIALS AND METHODS

### *Dental audit*

We reviewed outpatient endoscopy records over a two-year period at the National University Hospital, Singapore. This was a large university hospital system that included community referrals and tertiary care centres across multiple specialties. According to centre protocol, dentition is reviewed once by the nursing team at triage and subsequently by the procedural team prior to endoscopy. Upper endoscopy is cancelled should dental concerns be identified. Cancelled endoscopies and serious reportable events due to dental reasons were compiled into a database for analysis.

### *Systematic review*

The review was conducted with reference to the Preferred Reporting Items for Systematic Reviews and Meta-analyses[7-11]. The PRISMA flowchart demonstrating the study selection process is presented in Figure 1. A systematic search was conducted on Medline using the following Medical Subject Headings (MeSH) terms: (("Tooth Injuries"[Mesh]) OR ("Mouth Protectors"[Mesh])) AND ((("Bronchoscopy"[Mesh]) OR "Endoscopy, Digestive System"[Mesh])) and EMBASE using the following EMTREE subject headings: ('digestive tract endoscopy'/exp OR 'bronchoscopy'/exp) AND ('tooth injury'/exp OR 'mouth protector'/exp). We additionally searched websites and conference abstracts for unpublished, updated reports on dental trauma in endoscopy and mitigation measures. Only English articles involving human subjects published prior to 1 November 2021 were considered for inclusion. Two independent reviewers (BT, CTQL) performed a systematic search, evaluated the titles and abstracts, and selected relevant studies with any discrepancies resolved by a third independent reviewer (LYWG). 46 articles were retrieved from the initial search strategy with 42 remaining after duplicate removal. A total of four publications involving dental trauma in relation to gastrointestinal and bronchial endoscopy were identified using this methodology (see Table 1). Major adverse events were characterized as cases of tooth fracture, tooth avulsion, tooth subluxation while minor adverse events encompassed all other complications including gum discomfort, masticatory pain, toothache, and cancellations due to dental reasons.

## RESULTS

From 1 June 2019 to 31 May 2021 a total of 16961 outpatients registered for endoscopy with 4643 patients undergoing

**Table 1 Summary of studies on dental trauma in endoscopy**

| Ref. | Type | Description | *n* | Dental events |
|---|---|---|---|---|
| Evers *et al*[8], 1967 | Cohort study | Adverse dental events in cohort of patients having orahesive applied prior to endoscopy or general anaesthesia | 110 | No adverse dental events reported |
| Ackerman *et al* [9], 1996 | Cohort study | Observational study on adverse dental events following upper endoscopy over 3 years | 5000 | Major adverse events[a]: 2; No minor adverse events[b] studied |
| Min *et al*[10], 2008 | RCT | Dental related complications following use of TPM and MB-142 mouth guards assessed *via* structured questionnaire 3-4 after index upper endoscopy | 865 | Major adverse events: 2; Minor adverse events: 19 |
| Mogrovejo *et al* [11], 2015 | Case series | Report on 3 cases of dental injury sustained after upper endoscopy | | |

[a]Major adverse event includes cases of tooth fracture, tooth avulsion, tooth subluxation.
[b]Minor adverse events includes gum discomfort, masticatory pain, toothache and cancellations due to dental reasons.
RCT: Randomized control trial; TPM: Teeth-protecting mouthpiece

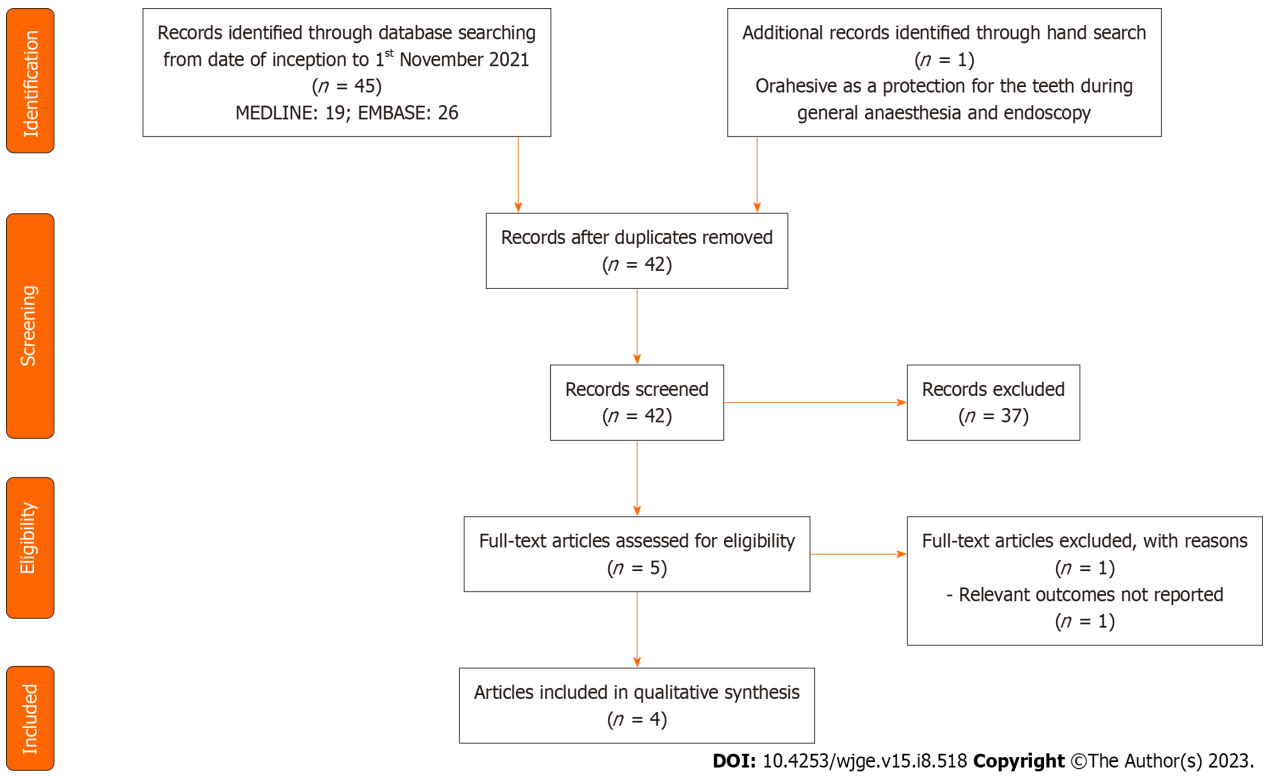


**Figure 1 Flow diagram on study selection process.**

multiple procedures in one setting for a total of 21539 procedures. Of which, 11265 involved upper endoscopies which was defined by any procedure involving insertion of a scope per-orally (see Table 2).

There was a total of 32 cancellations over the study period, 30 for Oesophagogastroduodenoscopy/antegrade enteroscopy and 2 for EUS (see Table 3). Of these cases, there were 6 patients requiring tooth extraction and the other 26 required dental specialist review. There was one major adverse event involving dislodgement of a glued incisor tooth chip lost during gastroscopy where judicial proceedings were avoided following prompt dental review and waiver of treatment fees. A photograph of a dislodged tooth extracted by endoscopy can be found below in Figure 2.

## DISCUSSION

### *Study findings*

Our study reported a total of 32 cancellations out of the 11265 upper endoscopy cases, giving an overall of 0.284% or 1 out of 352 patients. 1 to 2 cases had to be cancelled and rearranged per month resulting in substantial logistical burden over time. Of these cancellations, at least 6 may have resulted in tooth avulsion if allowed to proceed. Pooling our findings with results obtained from the systematic review, this identified an overall adverse event rate of 0.33% with major

**Table 2 Outpatient endoscopy cases during a two-year period**

| Type | No. |
|---|---|
| Oesophagogastroduodenoscopy/antegrade enteroscopy | 10142 |
| Colonoscopy/sigmoidoscopy | 10263 |
| Endoscopic ultrasound | 423 |
| Endoscopic retrograde cholangiopancreatography | 248 |
| Bronchoscopy | 452 |
| Others (*e.g.*, thoracoscopy) | 11 |
| Total number of upper endoscopy cases | 11265 |
| Total number of cases | 21539 |

**Table 3 Summary of dental related events**

| | |
|---|---|
| Cancellations | 32 |
| Oesophagogastroduodenoscopy | 30 |
| Endoscopic ultrasound | 2 |
| Dental injury | 1 |

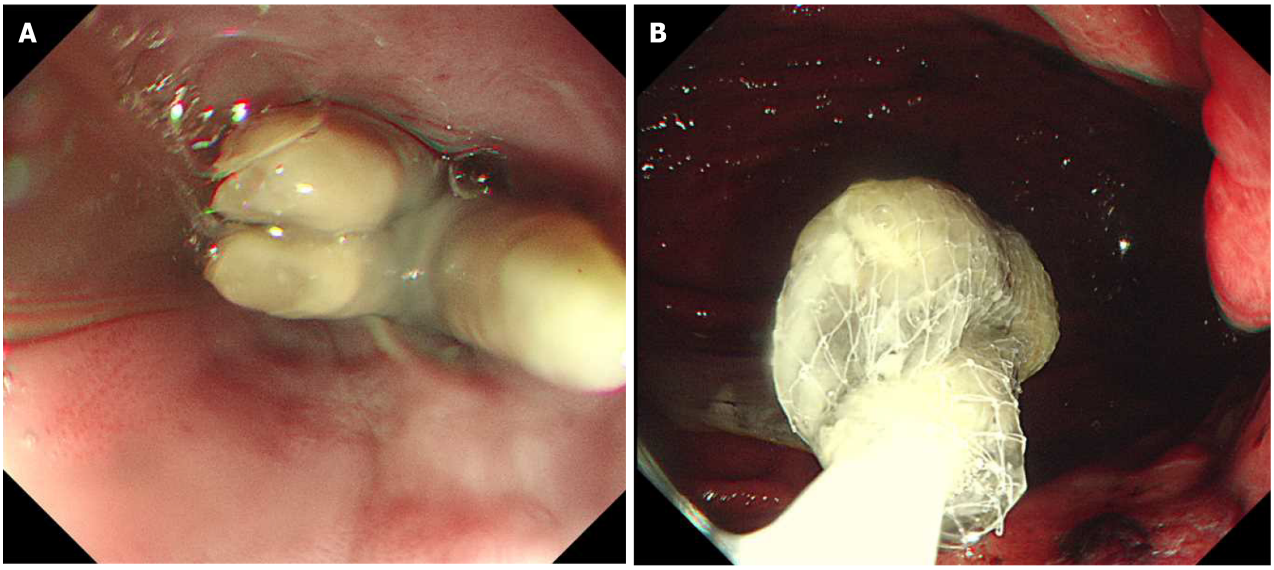


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**Figure 2 Endoscopic images of adverse events.** A: Periprocedural complication of avulsed tooth lodged in the distal oesophagus; event occurred prior to study period; B: Avulsed tooth being retrieved.

adverse events occurring in 0.03% of upper endoscopies (see Table 4). These figures are comparable to anaesthesia data and suggest need for greater awareness of dental trauma as a complication of upper endoscopy and consequent steps for mitigation and management[12].

### *Overview of dental injury*

Teeth are subjected to immense loads generated during mastication with forces exerted exceeding 800N during strenuous clenching[13]. Dental damage may occur during instrumentation, insertion of bite-block, due to inadequate pressure distribution or slippage of the bite-block during upper endoscopy[8,14]. There has been a report of dental implant dislodgement from reflexive jaw clenching upon retroflexion during colonoscopy[15]. Dental injury may further be contributed by involuntary grinding of teeth during sedation which exerts significant pressures. These factors may chip, break or avulse a tooth as well as damage brittle prosthetic devices.

**Table 4 Pooled adverse dental event rate**

| Ref. | *n* | Major events[a] | Minor events[b] |
|---|---|---|---|
| Evers *et al*[8],1967 | 110 | 0 | Not studied |
| Ackerman *et al*[9],1996 | 5000 | 2 | Not studied |
| Min *et al*[10],2008 | 865 | 2 | 19 |
| Our centre experience | 11265 | 1 | 32 |
| **Event rate** | | | |
| Rate of major events: 5/17240 = 0.029% | | | |
| Rate of minor events[c]: 51/12130 = 0.42% | | | |
| Overall event rate: 56/17240 = 0.33% | | | |

[a]Major Adverse Event includes cases of tooth fracture, tooth avulsion, tooth subluxation.

[b]Minor Adverse Events includes gum discomfort, masticatory pain, toothache and cancellations due to dental reasons.

[c]Only studies reporting minor adverse events were included in the calculation.

To our knowledge, there have been no studies identifying teeth most likely to be injured during endoscopy. Extrapolating from anaesthesia procedures which similarly require instrumentation within the oral cavity, the incisors are the most commonly injured representing 50% of cases[16]. They are particularly prone to fracture due to their anatomical position as well as being small-rooted and having a narrow cross-sectional area with a slight anterior axis. The most commonly reported dental injuries included enamel fractures, loosened or subluxated teeth, tooth avulsion and crown or root fractures[3].

The most significant risk factor for dental injury is pre-existing pathology such as caries, periodontitis and tooth restorations, the presence of which conveys a 3 to 12-fold increased risk[4,17,18]. Injury is most common in patients aged between 50 and 70 years who are more likely to have teeth weakened by periodontal disease while remaining dentulous [1]. Presence of restorative treatments raises the potential of damaged prosthesis and underlying periodontal disease. Removal of tooth matter during the process of restoration unavoidably weakens tooth structure and renders restored teeth prone to injury[19-21]. A non-exhaustive list of restorative and reconstructive dental treatments is included below in Table 5.

### *Pre-procedural evaluation*

Preventing dental trauma begins with recognizing risk factors. Patients with identified concerns should be advised for dental optimization prior to endoscopy which can minimize procedural trauma by restoring caries, replacing damaged restorations, and splinting or extraction of loose teeth[22]. History and examination are paramount in this regard, and should be routinely included prior to all upper endoscopies[16,23]. Assessment should include asking patients about loose or damaged teeth and history of past restorative dental treatments. Examination of dentition involves inspection for diseased dentition and palpation for loose teeth. Tooth mobility may be evaluated clinically by applying firm pressure with a gloved finger and is reliably graded according to the Millers Index (see Table 6)[24]. A Miller's grade of two and above suggests need for tooth extraction and warrants dental consultation[25].

Documentation of findings improves pre-procedural provision of information to patients and may reduce liability in the event of injury. Notation systems such as the Palmer and World Health Organization ISO system[26,27] may increase precision in documentation but may require more time and training for completion. Photo documentation is increasingly valuable for records of preprocedural tooth condition and may be considered with appropriate consent.

We propose the following framework for pre-endoscopy screening involving two questions followed by a physical examination. A screening form (Figures 3 and 4) may be conducted within five minutes and does not require specialist training.

### *Management of dental injury*

Dental injuries often require time-sensitive management to minimize irreversible dentition loss. In all cases, the nature of the injury and the circumstances in which it occurred must be clearly documented in the patient record and full disclosure should be provided to the patient[28,29].

When dental trauma is suspected, the first step would be review of preprocedural dental records to ensure the injury was not present to begin with[16]. Once iatrogenic trauma is confirmed, it is essential to localize avulsed and broken teeth, or prostheses to minimise risk of aspiration and obstruction of airway. Retrieval of avulsed teeth, prostheses, or teeth fragments using Magill's forceps may be attempted. If these measures are not successful, imaging in the form of cervical and thoracic radiography should be performed to identify aspiration into the lungs or oesophagus. Not all dental prostheses are radiopaque, and thus are difficult to visualize on a chest radiograph and may require direct visualisation in the form of urgent bronchoscopy or OGD[18]. Early consultation with thoracic surgical services is suggested in this event. A stepwise workflow to manage dental injury has been illustrated in Figure 5.

**Table 5 Restorative and reconstructive dental treatments[18,21]**

| Type of treatment | Description and related problems |
|---|---|
| **Direct restoration (filled in single procedure with material being placed, adapted and shaped by clinician)** | |
| Filling | May comprise amalgam, ceramic or precious metals. Susceptible to expansion or shrinkage when setting, which might cause tooth fracture or further decay |
| **Indirect restoration (filling created outside of mouth, either from impression or digital scan of tooth)** | |
| Inlays/onlays | An inlay is a filling made outside the mouth, then bonded to the teeth. This is less prone to expansion or shrinkage. An onlay refers to an inlay which covers a dental cusp |
| Crown | An onlay which fully covers the tooth which is required in the setting of marked tooth damage |
| Veneer | A thin layer bonded to the tooth surface to enhance appearance of fractured or discoloured teeth |
| **Prosthesis** | |
| Bridge | Fixed partial denture secured to adjacent teeth |
| Denture | Removable prosthesis which may be attached to remnant teeth *via* clasps |
| Implant | Permanent prosthesis integrated into alveolar bone *via* screws and cement. Eventual recession of gingiva may result in implant weakening |

**Table 6 Millers index of grading tooth mobility**

| Grade | Description |
|---|---|
| 0 | "Physiological" mobility measured at the crown level. The tooth is mobile within the alveolus to approximately 0.1-0.2mm in a horizontal direction |
| 1 | Increased mobility of the crown of the tooth to at the most 1 mm in a horizontal direction |
| 2 | Visually increased mobility of the crown of the tooth exceeding 1 mm in a horizontal direction |
| 3 | Severe mobility of the crown of the tooth in both horizontal and vertical directions impinging on the function of the tooth |

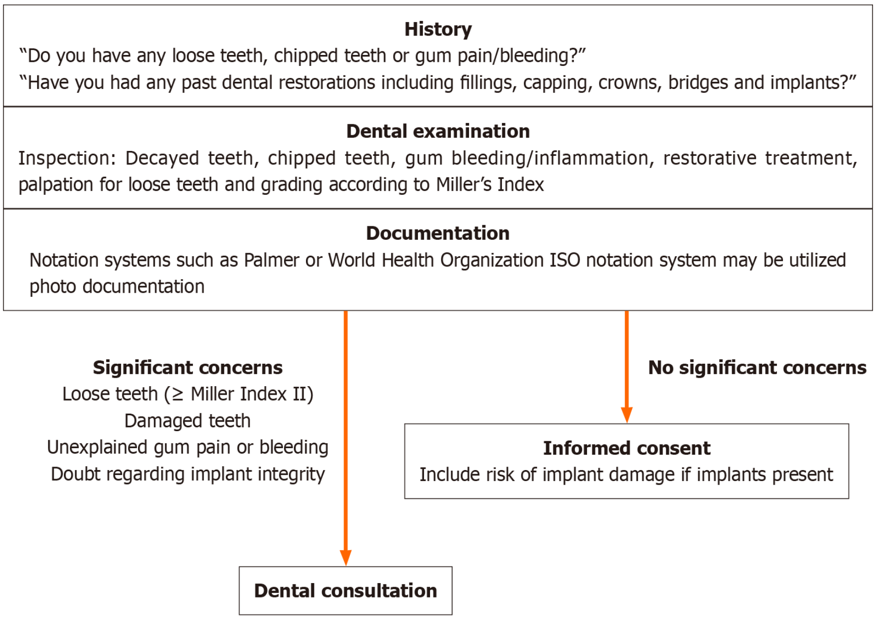


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**Figure 3 Pre-endoscopy screening.**

In most situations, replantation by pushing the tooth into its socket followed by firm pressure for several minutes is the immediate treatment of choice. This may not be appropriate in immunocompromised patients or those with severe periodontal disease due to the risk of bacterial seeding. If replantation is not possible, recovered teeth and teeth fragments should be placed in a suitable storage medium such as cold saline or milk and urgent dental review within 30 minutes

**For patient**

| Questions | Yes | No |
|---|---|---|
| Do you have any loose teeth? | | |
| Do you have any chipped or damaged teeth? | | |
| Do you have any gum pain? | | |
| Do you have any gum bleeding? | | |
| Have you had any past dental restorations including fillings, capping, crowns, bridges and implants?<br>If yes, please specify what type and when it was done. | | |

**For endoscopist**

| Examination | Yes | No |
|---|---|---|
| Presence of decayed teeth | | |
| Presence of chipped teeth | | |
| Presence of gum bleeding/inflammation | | |
| Presence of restorative treatment | | |
| Presence of loose teeth on palpation<br>If present, Miller's grade | | |

If concerns regarding dental trauma present, please refer for dental clearance and advice on use of dental protectors

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**Figure 4 Pre-endoscopy checklist.**

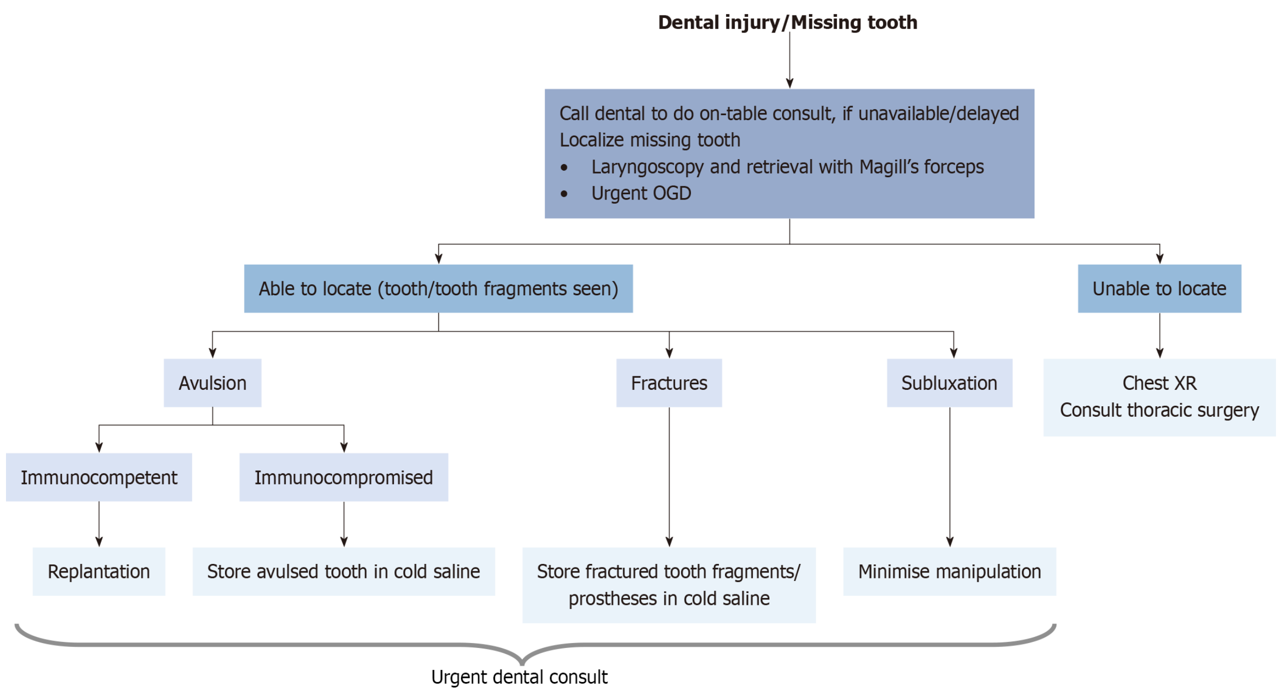


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**Figure 5 Management of dental injury.**

should be arranged[18,22].

### *Measures to minimize dental injury*

Use of tooth protectors and mouth guards have been proposed to minimize dental injuries[15,30-32]. These function by dispersing force applied among the teeth to minimize overloading a damaged tooth. Teeth protectors also serve to stabilise loose teeth and secure avulsed or broken dental fragments during trauma, thus minimising aspiration and facilitating retrieval. However, such guards often limit the amount of space for insertion of bite-blocks and instrumentation[33]. One randomized controlled trial suggested that a novel teeth-protecting mouth piece showed advantage over traditional devices in preventing endoscopy related complications of the teeth and temporomandibular joint, though this is not widely available[10]. More prospective well-designed trials supporting routine usage of dental protective devices are required prior to utilization.

In the event emergent endoscopy is required before dental consultation may be obtained, temporizing measures such as splinting loose teeth to adjacent healthy dentition or securing them *via* a chord affixed outside the oral cavity may be considered. All these measures should be accompanied by informed consent.

## LIMITATIONS

Nevertheless, several limitations need to be considered in the interpretation of our findings. Firstly, this was a retrospective audit with heterogeneity across study subjects, in terms of examination methods and baseline dental health of each patient. Secondly, there was limited availability of data with regards to pre-existing trismus which may potentially be a risk factor for dental trauma. Lastly, the adverse event rate was small, with only one instance of dental injury, suggesting need for further studies with larger sample size.

## CONCLUSION

Dental injury during endoscopy is an underreported complication with potential for significant litigious consequences. It is a preventable complication with adequate foreknowledge and precautionary measures. Prompt recognition and treatment in the event of trauma can potentially minimize irreversible loss of dentition.

## ARTICLE HIGHLIGHTS

### *Research background*

We present findings from an audit of outpatient endoscopy procedures conducted at a tertiary university hospital and a systematic review of literature.

### *Research motivation*

Dental injury is the leading cause of litigation in anaesthesia but an underrecognized preventable complication of endoscopy.

### *Research objectives*

We aim to study the impact of dental injury on endoscopy in our centre as well as review relevant literature to guide identification, mitigation and management of peri-endoscopic dental trauma.

### *Research methods*

We reviewed outpatient endoscopy records over a two-year period at the National University Hospital, Singapore. We also conducted a review with reference to the Preferred Reporting Items for Systematic Reviews and Meta-analyses.

### *Research results*

We identified overall adverse event rate of 0.33% with major adverse events occurring in 0.03% of upper endoscopies. These figures are comparable to anaesthesia data and suggest need for greater awareness of dental trauma as a complication of upper endoscopy and consequent steps for mitigation and management. We identified different risk factors for dental injury and proposed a framework for pre-endoscopy screening to prevent dental injury. We also discuss measures to manage and minimise dental injury.

### *Research conclusions*

Dental injury during endoscopy is an underreported complication with potential for significant litigious consequences. It is a preventable complication with adequate foreknowledge and precautionary measures. Prompt recognition and treatment in the event of trauma can potentially minimize irreversible loss of dentition.

### *Research perspectives*

Further research can be done with larger sample sizes, to compare different risk factors for dental trauma.

## FOOTNOTES

**Author contributions:** Tan CQL and Loh GYW contributed equally to this work; Tan CQL, Loh GYW, Tay WRB, Koh CJY, Mok JSR, Hartono JL, Chua KTC, Tan HH, Siah KTH conceived and designed the study; Tan CQL, Loh GYW, Tay WRB Chua KTC performed research and analyzed data; and Tan CQL, Loh GYW, Tay WRB, Koh CJY, Mok JSR, Hartono JL, Chua KTC, Tan HH, Siah KTH wrote the paper; all authors reviewed and approved the final manuscript.

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*META-ANALYSIS*

# Endoscopic ultrasound artificial intelligence-assisted for prediction of gastrointestinal stromal tumors diagnosis: A systematic review and meta-analysis

Rômulo Sérgio Araújo Gomes, Guilherme Henrique Peixoto de Oliveira, Diogo Turiani Hourneaux de Moura, Ana Paula Samy Tanaka Kotinda, Carolina Ogawa Matsubayashi, Bruno Salomão Hirsch, Matheus de Oliveira Veras, João Guilherme Ribeiro Jordão Sasso, Roberto Paolo Trasolini, Wanderley Marques Bernardo, Eduardo Guimarães Hourneaux de Moura

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## Abstract

*BACKGROUND*

Subepithelial lesions (SELs) are gastrointestinal tumors with heterogeneous malignant potential. Endoscopic ultrasonography (EUS) is the leading method for evaluation, but without histopathological analysis, precise differentiation of SEL risk is limited. Artificial intelligence (AI) is a promising aid for the diagnosis of gastrointestinal lesions in the absence of histopathology.

*AIM*

To determine the diagnostic accuracy of AI-assisted EUS in diagnosing SELs, especially lesions originating from the muscularis propria layer.

*METHODS*

Electronic databases including PubMed, EMBASE, and Cochrane Library were searched. Patients of any sex and > 18 years, with SELs assessed by EUS AI-assisted, with previous histopathological diagnosis, and presented sufficient data values which were extracted to construct a 2 × 2 table. The reference standard was histopathology. The primary outcome was the accuracy of AI for gastrointestinal stromal tumor (GIST). Secondary outcomes were AI-assisted EUS diagnosis for GIST *vs* gastrointestinal leiomyoma (GIL), the diagnostic performance of experienced endoscopists for GIST, and GIST *vs* GIL. Pooled sensitivity, specificity, positive, and negative predictive values were calculated. The corresponding summary receiver operating characteristic curve and post-test probability were also analyzed.

***RESULTS***

Eight retrospective studies with a total of 2355 patients and 44154 images were included in this meta-analysis. The AI-assisted EUS for GIST diagnosis showed a sensitivity of 92% [95% confidence interval (CI): 0.89-0.95; $P < 0.01$), specificity of 80% (95%CI: 0.75-0.85; $P < 0.01$), and area under the curve (AUC) of 0.949. For diagnosis of GIST *vs* GIL by AI-assisted EUS, specificity was 90% (95%CI: 0.88-0.95; $P = 0.02$) and AUC of 0.966. The experienced endoscopists' values were sensitivity of 72% (95%CI: 0.67-0.76; $P < 0.01$), specificity of 70% (95%CI: 0.64-0.76; $P < 0.01$), and AUC of 0.777 for GIST. Evaluating GIST *vs* GIL, the experts achieved a sensitivity of 73% (95%CI: 0.65-0.80; $P < 0.01$) and an AUC of 0.819.

***CONCLUSION***

AI-assisted EUS has high diagnostic accuracy for fourth-layer SELs, especially for GIST, demonstrating superiority compared to experienced endoscopists' and improving their diagnostic performance in the absence of invasive procedures.

**Key Words:** Subepithelial lesions; Ultrasound endoscopy; Artificial intelligence



**Core Tip:** Artificial intelligence (AI) has shown itself as a promising tool in diagnostic endoscopic ultrasound. This systematic review and meta-analysis analyze the diagnostic performance of endoscopy ultrasound with AI for subepithelial lesions and compare it with experienced endoscopists. Based on our meta-analysis, the endoscopy ultrasound assisted for AI has high diagnostic accuracy with superiority over experienced endoscopists.

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## INTRODUCTION

Gastrointestinal subepithelial lesions (SELs) are tumors that originate from the muscular mucosa, submucosa, or muscular propria, with the stomach being the most common location where they are identified[1]. Although most SELs are benign and asymptomatic at presentation, up to 15% present malignant potential and may cause symptoms such as bleeding and abdominal pain[1,2]. The most common histological types are gastrointestinal stromal tumor (GIST) and gastrointestinal leiomyoma (GIL), with GIST having malignant potential[3]. One major diagnostic challenge is differentiating between GIST and leiomyoma considering that both commonly originate from the muscular propria and have overlapping features on imaging evaluation[4]. The differentiation among them is imperative due to the difference in prognosis and therapeutic strategy[5,6]. Surgical resection is recommended after GISTs diagnosis due to the risk of malignancy and requires prior histological confirmation, even in small lesions[1].

Endoscopic ultrasonography (EUS) is a valuable tool for SELs because it can characterize them by size, vascularity, internal structure, location, echogenicity, shape, and the layer of origin[6,7]. However, the gold standard for diagnosis is histopathological evaluation, which is indicated in suspected GIST, size > 20 mm, high-risk malignancy, surgical indication, or oncological treatment[1]. In uncertain cases, auxiliary procedures such as fine needle aspiration or fine needle biopsy can be performed for tissue sampling acquisition and immunohistochemical analysis, leading to more accurate results, especially in lesions > 20 mm[8,9]. For lesions < 20 mm with malignancy risk, further analysis with a contrast-enhanced technique can stratify risk to help determine the need for and safety of biopsy[10,11].

Artificial intelligence (AI) has emerged as a powerful and exciting technology impacting many aspects of health care and promoting changes in daily clinical practice, especially for early, accurate, and real-time diagnosis[12]. Since the 1960s, AI systems have been applied in radiology for the recognition and interpretation of images and subsequently expanded to other areas including ophthalmology, cardiology, and neurology[13,14]. Between 2017 and 2018, the Food and Drug Administration approved more than 20 AI tools for medical use, including the endoscopy field[14]. In 2020, AI helped in the rational management of the coronavirus disease 2019 pandemic in various scenarios and countries, from predicting diagnostic imaging, manufacturing vaccines, and preventing viral spread[15].

The use of AI systems able to recognize specific patterns in EUS began in early 2000 and was initially applied to the evaluation of pancreatic disorders, especially differential diagnoses between chronic pancreatitis and pancreatic neoplasms[16]. Subsequently, the excellent results contributed to the development of studies that explored diagnosis and malignancy prediction for gastrointestinal SELs, particularly for GIST[17,18]. Although EUS AI-assisted has promising results, the real benefits, ethical implications, and clinical relevance need scientific evidence that supports the use in diverse clinical settings[19].

Considering the deficiency of research and the need for quality evidence to support the application of AI assistance in the subepithelial tumors EUS evaluation, this systematic review aims to perform an analysis of endoscopic ultrasound with AI assistance for GIST diagnosis. The main outcome was the diagnostic accuracy of AI-assisted EUS for GIST. Furthermore, we evaluated the AI capability that distinguishes between GIST and GIL and the experienced endoscopists' performance.

## MATERIALS AND METHODS

### *Protocol and registration*

This study was structured according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [20] and recent recommendations for diagnostic test accuracy reviews[21]. This study was registered in the International Prospective Register of Systematic Reviews under the file number CRD42023418987.

### *Literature search*

A comprehensive literature search was performed in the following databases up to December 2022: EMBASE, Cochrane Library, and MEDLINE. Two reviewers screened titles and abstracts of all the identified articles that evaluated the performance of AI for the diagnosis of SELs using EUS. Divergent opinions were resolved by a third reviewer. The MESH Terms for searches used were: ("endoscopic" OR "endoscopy") AND ("ultrasound" OR "endosonography" OR "echoendosonography") AND ("artificial intelligence" OR "neural network" OR "computer neural network" OR "deep learning") AND ("GIST" OR "subepithelial tumor" OR "subepithelial lesion" OR "stromal tumor" OR "gastrointestinal subepithelial tumor") present in titles, abstracts or full-text articles.

### *Inclusion and exclusion criteria*

The studies included were performed in adults patients (> 18 years) with SELs assessed by EUS AI-assisted, with histopathological diagnosis established, and presented true-negative, true-positive, false-negative, and false-positive values which were extracted to construct a 2 × 2 table. Case reports, systematic reviews, reviews, editorials, conference abstracts, articles with algorithms different from convolutional neural network (CNN), and articles with incomplete data were excluded.

### *Data extraction*

Using a standardized form, the relevant data from eligible studies were extracted and organized using the following main data: First author, year of publication, study type, geographical setting, number of patients, gender, number of GIST tumors, number of GIL tumors, number of other SELs, number images, tumor location, AI model, external validation, endoscopists comparison, and histopathologic analysis. All relevant texts, tables and figures were reviewed for data extraction.

### *Risk of bias assessment and quality of evidence*

The risk of bias and quality assessment were assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) too[22]. The quality of the studies was evaluated by two authors independently, and disagreement was resolved by consensus in consultation with the third author.

### *Measured outcomes*

The main outcomes evaluated were the pooled accuracy, sensitivity, positive likelihood, negative likelihood, and specificity of AI-assisted EUS for the diagnosis of GIST based on analysis of images obtained by EUS of gastrointestinal SELs. The positive post-test probability and negative post-test probability were calculated based on likelihood ratios and GIST mean prevalence values from each article. The accuracy was defined as the area under the summary receiver operating characteristic (SROC) curve. Secondary outcomes were performed to evaluate the diagnostic performance of AI for GIST *vs* GIL, the diagnostic performance of experienced endoscopists for GIST, and GIST *vs* GIL. Experienced endoscopists were those who performed more than 500 EUS examinations or had at least 5 years of experience evaluating gastrointestinal SELs.

### *Statistical analysis*

The pooled data of sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio, were meta-analyzed with a 95% confidence interval (CI) using the random effect model for the accuracy of EUS AI-assisted and experienced endoscopists. A SROC curve was drawn and the area under the curve (AUC) was calculated to estimate the accuracy.

Forest plots were made to show the point estimates in each study in relation to the summary pooled estimate. The width of the point estimates in the forest plots indicated the assigned weight for that study. For 0 values, 0.5 was added, as described by Cox and Snell[23]. The heterogeneity of likelihood ratios and diagnostic odds ratios were tested using Cochran's $Q$ test based on inverse variance weights. The heterogeneity of the sensitivities and specificities was tested using the likelihood ratio test. Heterogeneity among studies was also tested using SROC curves. Heterogeneity was assessed and data were analyzed using Meta-DiSc (Clinical Biostatistics HRC, Madrid, Spain)[24]. The Bayes model was used to calculate the post-test probability and elaborate Fagan's Nomogram[25] using estimated mean prevalence data from each article for GIST.

## RESULTS

### *Search results and characteristics of the included studies*

A total of 163 studies were extracted after the search strategy which was shown in Figure 1. After the exclusion of 150 titles, based on the selection criteria, 13 studies were eligible for full-text examination. Of those, 4 were removed for being review articles and one[26] for not using a CNN model. Thus, eight relevant articles were selected for the present meta-analysis (Table 1) with a total of 2355 patients and 44154 images[27-34]. All articles were retrospective studies. The characteristics of the included studies are summarized in Table 1. A total of 1436 patients were diagnosed with GIST, 725 were GIL, and 194 were non-GIST/non-GIL with a GIST prevalence of 68% and leiomyoma being 30% in the present study. The Asian continent has the largest number of publications, a total of 7 articles (4 Japanese, 2 Korean, and 1 Chinese), and Europe has one (Turkey). As for the AI model used, all 8 studies were developed with a CNN algorithm.

### *Risk of bias and quality*

The quality of the included studies was evaluated according to the QUADAS-2 tool. The risk of bias of the 8 studies is shown in Figure 2, where 7 were categorized as high risk or uncertain risk for one or more fundamental elements due to their retrospective designs (Figure 2).

### *Diagnostic accuracy of AI-assisted EUS for GIST*

The diagnostic accuracy of GIST for AI-assisted EUS presented summary sensitivity values of 92% (95%CI: 0.89-0.95; $P$ < 0.01), specificity of 80% (95%CI: 0.75-0.75; $P$ < 0.01) (Figure 3), with substantial heterogeneity for both ($I^2$ = 75.2% and $I^2$ = 71%, respectively). A positive likelihood ratio of 4.26 (95%CI: 2.7-6.7; $P$ = 0.01), negative likelihood ratio of 0.09 (95%CI: 0.04-0.18; $P$ < 0.01), and diagnostic odds ratio of 71.74 (95%CI: 22.43-229.46; $P$ < 0.01) was achieved. Figure 4 shows the SROC curve, with an AUC of 0.949 ($P$ = 0.03) indicating high diagnostic accuracy (Table 2). The positive post-test probability was 90% (95%CI: 0.88-0.92), and the negative post-test probability was 16% (95%CI: 0.11-0.22), as shown in Fagan's nomogram (Figure 5A).

### *Subgroup analysis*

**Diagnostic accuracy of AI-assisted EUS for GIST *vs* GIL:** For differentiation between GIST and GIL, the AI-assisted EUS presented a combined sensitivity of 93% (95%CI: 0.88-0.97; $P$ = 0.08) and combined specificity of 90% (95%CI: 0.88-0.95; $P$ = 0.02), positive likelihood ratio of 6.48 (95%CI: 2.14-19.6; $P$ = 0.01), negative likelihood ratio of 0.06 (95%CI: 0.02-0.21; $P$ = 0.05) and diagnostic odds ratio of 128.18 (95%CI: 18.6-883.25; $P$ = 0.03). The heterogeneity was $I^2$ = 55% for sensibility and $I^2$ = 68.6% for specificity. The area under SROC curve expressed high diagnostic accuracy, with values of 0.966 (AUC).

**Diagnostic performance of experts for GIST:** Seven studies included in this meta-analysis evaluated the diagnostic performance of experienced echo-endoscopists. The combined general values of sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and the area under the summary ROC curve were, respectively, 72% (95%CI: 0.67-0.76; $P$ < 0.01), 70% (95%CI: 0.64-0.76; $P$ < 0.01), 2.51 (95%CI: 1.75-3.61; $P$ = 0.08), 0.42 (95%CI: 0.33-0.52; $P$ = 0.16), 6.88 (95%CI: 3.95-11.99; $P$ = 0.14) and 0.777 (AUC). The heterogeneity was $I^2$ = 77.3% for sensibility and $I^2$ = 73.8% for specificity.

**Diagnostic performance of experienced endoscopists' for GIST *vs* GIL:** Considering only the differentiation of GIST and GIL, the combined sensitivity was 73% (95%CI: 0.65-0.80; $P$ < 0.01), specificity 75% (95%CI: 0.65-0.84; $P$ = 0.91), positive likelihood ratio 2.61 (95%CI: 1.75-3.88; $P$ = 0.70), negative likelihood ratio 0.37 (95%CI: 0.22-0.64; $P$ = 0.02), diagnostic odds ratio of 7.21 (95%CI: 2.95-17.59; $P$ = 0.16) and area under the SROC curve of 0.819 (AUC). The heterogeneity was $I^2$ = 77.3% for sensibility and $I^2$ = 0.0% for specificity. The post- and pre-test probability were, respectively, 84% (95%CI: 0.80-0.86) and 46% (95%CI: 0.42-0.50), as shown in Figure 5B.

## DISCUSSION

AI has the world's attention for the impacts generated after its implementation in the most diverse fields, especially in diagnostic medicine. The utilization of AI technology in the field of medical imaging enhances the diagnostic process, leading to improved accuracy and the early detection of diseases, thus ensuring enhanced disease management and clinical outcomes[31]. In the present systematic review and meta-analysis, we analyze the application of appropriately

**Table 1 Summary of all studies investigating the development of machine learning algorithms for the endoscopic ultrasound diagnosis of subepithelial lesions**

| Ref. | Geographical setting | Study type | Patients | Sex (male/female) | GIST | GIL | Other SELs | Images | Tumor location | AI model | External validation | Endoscopists comparison | Histopathology |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Minoda *et al* [29], 2022[1] | Eastern | Retrospective | 52 | 33/19 | 36 | 14 | 2 | 2718 | Esophagus, duodenum, and colon | CNN | Yes | Yes | Yes |
| Hirai *et al*[33], 2022 | Eastern | Retrospective | 664 | 231/188 | 435 | 97 | 100 | 16110 | Esophagus, stomach, and duodenum | CNN | Yes | Yes | Yes |
| Tanaka *et al* [34], 2022 | Eastern | Retrospective | 53 | 28/25 | 42 | 11 | - | 10600 | Stomach | CNN | No | Yes | Yes |
| Yang *et al*[32], 2022 | Eastern | Retrospective | 752 | 337/415 | 348 | 404 | - | 10439 | Esophagus, stomach, duodenum, colon, and rectum | CNN | Yes | Yes | Yes |
| Oh *et al*[30], 2021 | Eastern | Retrospective | 168 | NI | 125 | 43 | - | 546 | Stomach | CNN | Yes | Yes | Yes |
| Seven *et al*[31], 2022 | Eastern | Retrospective | 145 | 72/73 | 109 | 36 | - | 1362 | Esophagus, stomach, and duodenum | CNN | Yes | Yes | Yes |
| Kim *et al*[27], 2020 | Eastern | Retrospective | 248 | 111/137 | 157 | 55 | 35 | 1117 | Stomach | CNN | Yes | Yes | Yes |
| Minoda *et al* [28], 2020 | Eastern | Retrospective | 273 | 138/135 | 184 | 65 | 24 | 3980 | Stomach | CNN | Yes | Yes | Yes |

[1]The author utilized the same software developed in the previous study (2020), however evaluating non-gastric subepithelial lesions.

NI: Non-information; GIST: Gastrointestinal stromal tumor; AI: Artificial intelligence; CNN: Convolutional neural network; GIL: Gastrointestinal leiomyoma.

trained software on EUS AI-assisted diagnosis of fourth-layer SELs, mainly for GIST, representing the largest pooled data including eight studies with more than 2300 patients and 44154 images. Through the evaluation of AI performance in this review, we achieved a combined sensitivity of 92%, a combined specificity of 80%, a positive post-test probability of 90%, and a negative post-test probability of 16% when distinguishing between GIST and non-GIST SELs based on EUS images.

The imaging modality frequently used to evaluate SELs is the EUS because of its ability to characterize the size, echogenicity, originating layer, shape, vascularity, and location[1,3,35]. Regarding conventional EUS findings for GIST, just stronger echogenicity in comparison with the surrounding muscle echo is an associated independent diagnostic factor[31]. A previous study reported that echogenicity, the presence of hyperechogenic spots and anechoic spaces, tumor shape, and marginal regularity in the EUS were not helpful in differentiating GIST from non-GIST tumors, being homogeneity was the only predictive factor[35]. Thus, the differentiation between GIST from other SELs without histological evaluation is difficult using EUS images only because the interpretation of the features is subjective and dependent on the experience of the endoscopist with a heterogeneous inter-observer agreement[28,31]. Although the gold standard diagnostic is histological evaluation, someone’s SELs can only be monitored with follow-up exams in the absence of risk stigmata and resection indications[9,10].

**Table 2 Artificial intelligence and experienced endoscopists' diagnostic performance for gastrointestinal stromal tumor and differentiation of leiomyoma**

| | Prevalence (mean) | Sensitivity | Specificity | LR+ | LR- | AUC | PTP+ | PTP- |
|---|---|---|---|---|---|---|---|---|
| AI | | | | | | | | |
| GIST | 68% | 92% | 80% | 4.26 | 0.09 | 0.949 | 90% | 16% |
| GIST *vs* GIL | 70%[1] | 93% | 90% | 6.48 | 0.06 | 0.966 | 94% | 12% |
| Endoscopists | | | | | | | | |
| GIST | 67% | 72% | 70% | 2.51 | 0.42 | 0.777 | 84% | 46% |
| GIST *vs* GIL | 67%[1] | 73% | 75% | 2.61 | 0.37 | 0.819 | 84% | 43% |

[1]Gastrointestinal stromal tumor prevalence.

GIST: Gastrointestinal stromal tumor; GIL: Gastrointestinal leiomyoma; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative; PTP+: Post-test probability positive; PTP-: Post-test probability negative; AUC: Area under the curve; AI: Artificial intelligence.

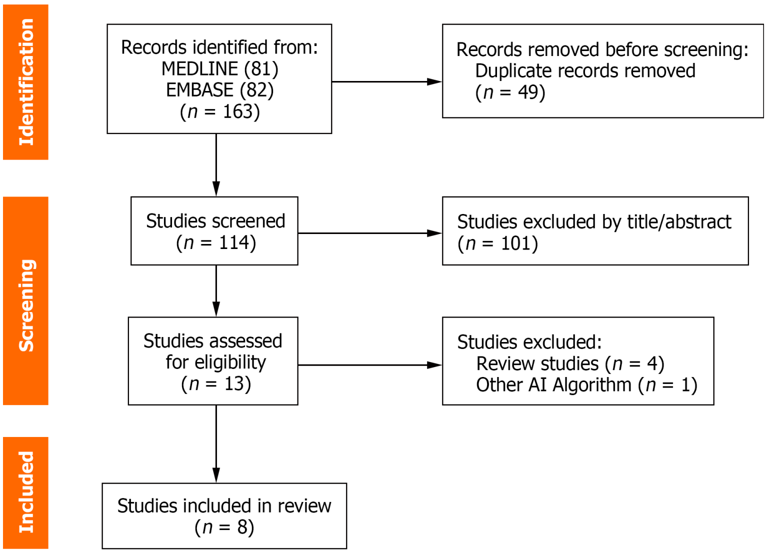


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**Figure 1 Flow diagram showing the study selection process for meta-analysis.** AI: Artificial intelligence.

The implementation of AI technology to improve the EUS diagnostic performance compensates limitations and disagreements discussed previously. Our results for overall GIST diagnosis by AI were superior to the EUS doctors' performance earlier reported[36], showing the ability to improve differential diagnosis with efficiency, quick evaluation, and reduce unnecessary procedures and surgical interventions. AI can evaluate specific patterns in the pixel-level characteristics of a tumor, making it more accurate than the naked eye in its analysis, and was observed that the size of the lesion increases, diagnostic accuracy increases in parallel, being more expressive from > 20 mm[28,34]. Considering the risks of invasive procedures, the misdiagnosis rate of GIST, the requirement of pathologic specimens for determining malignancy potential, and eligibility for neo-adjuvant therapy, the application of AI has significant improvements in the safety clinical management of SELs[28]. Recently, software developed and trained with gastric GIST images for EUS AI-assisted diagnosis has been used in other gastrointestinal sites with excellent results[29]. Furthermore, EUS assisted by AI developed to diagnose and prediction of the malignancy risk of GIST showed excellent performance[18], assisting in the decision for resection with or without neoadjuvant therapy. Using AI as an auxiliary tool in the diagnosis in endoscopy aims primarily to increase diagnostic accuracy and reduce the number of false negatives and positives.

In the evaluation of SELs originating from the muscular layer, the differentiation between GIST and leiomyoma is one of the most challenging, since they have very similar sonographic characteristics: Both are hypoechoic, usually homogeneous, have well-defined limits, and may originate from the second or fourth-layer. Diagnosis is a challenge, even in contrast to enhanced exams[34] yet it is extremely important since it determines the need for surgical resection. When evaluating the differentiation between GIST *vs* GIL by the AI-assisted EUS, combined sensitivity and specificity of 93% and 90% respectively were obtained with an AUC of 0.966, indicating excellent performance. The AI software increases the possibility of correct diagnosis avoiding unnecessary invasive procedures and excess risk with biopsies, without size limitation even for lesions < 20 mm[32]. The AI-assisted EUS performed even better for lesions larger than 20 mm, which is highly relevant considering, for example, that GIST > 2 cm has an indication for resection while asymptomatic

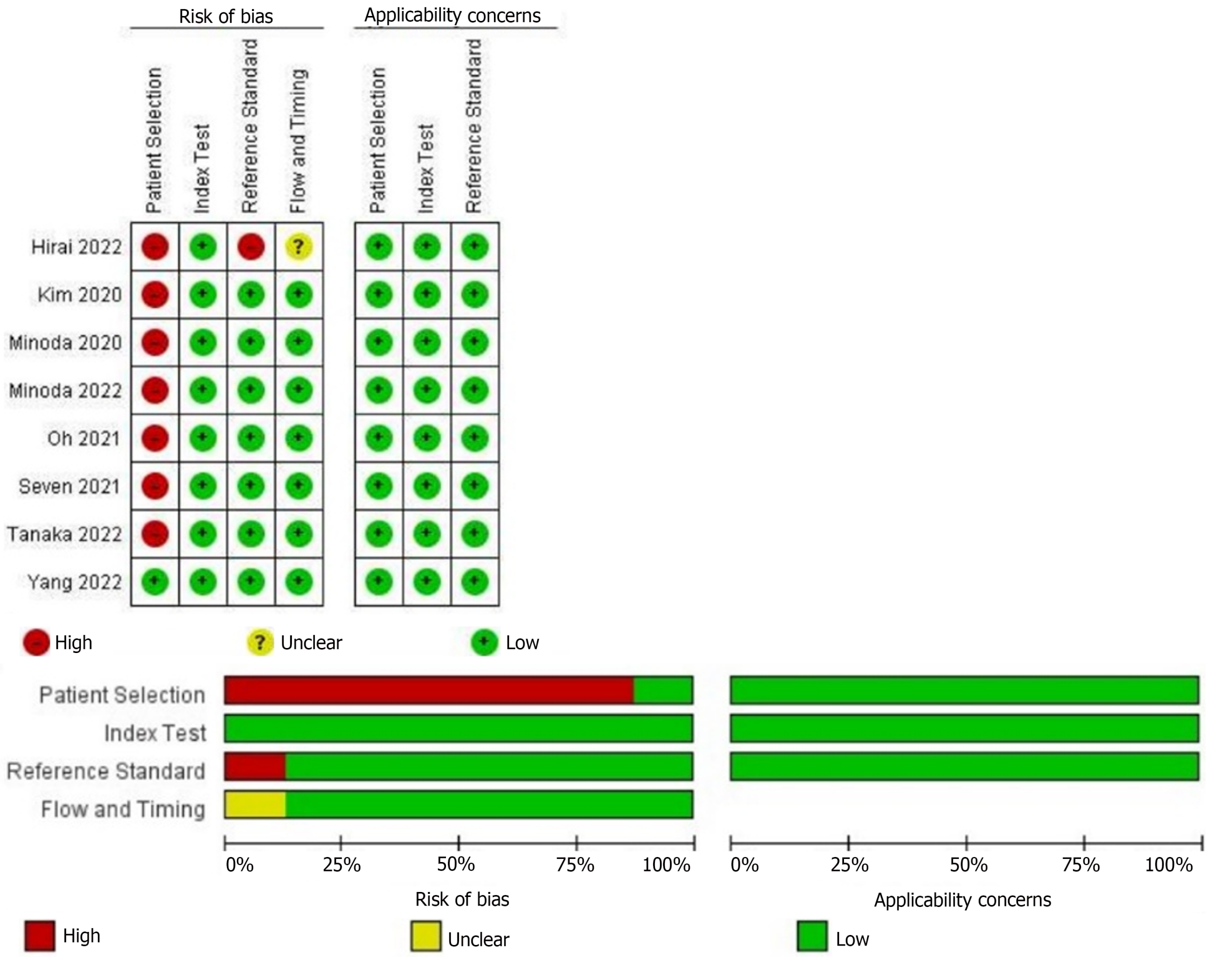


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**Figure 2 Risk of bias and applicability concerns of 8 included records using the Quality Assessment of Diagnostic Accuracy Studies tool.**

leiomyomas should not be removed.

The performance of AI was superior to EUS experts, even in cases where the expert was informed of the source layer and the location of the lesion[31], a fact that favors the expert because with some information certain diagnoses become obvious. For example, a soft, hyperechoic lesion of the submucosa, in the antrum, is highly suspicious for lipoma. With a sensitivity of 72% (*vs* 93% AI-assisted), experts can expect to have a miss rate of approximately 3 in every 10 cases of GIST. The diagnostic accuracy of the experts for GIST, although considered good, was much lower than that of the AI system (AUC 0.819 *vs* 0.966). A previous study reported an increase in accuracy, specificity, and positive predictive value after joint diagnosis of endoscopists with AI assistance to distinguish GIST from leiomyoma, demonstrating that AI has the potential to help enhance correct diagnosis even for experienced endoscopists. In addition, the rapid development of AI systems capable of performing fast and more specific analyses without increasing operating costs or equipment updates[32] makes it possible and attractively apply in diagnostic centers of lower volume and invariably assists inexperienced endoscopists' diagnoses.

Although these results are exciting, they should be evaluated with caution due to the dynamic nature of diagnostic examinations. In these studies, experts evaluated images of SEL without being able to perform their usual maneuvers. Moreover, most studies did not provide essential information commonly known in clinical practice, such as the patient's medical history, color at white light endoscopy, or lesion consistency[37]. Additionally, the expected performance of AI can be influenced by factors such as disease prevalence and severity, the expertise and training of endoscopists, and the interaction between AI and endoscopists[19]. It is crucial to emphasize that the use of machine learning models in the medical field should not be seen as a direct competition to endoscopists. Instead, they should be regarded as auxiliary diagnostic tools and even training aids for less experienced endoscopists.

Despite the number of studies, patients, and reviewed images, this meta-analysis has certain limitations. Firstly, although we included several studies with a large number of patients, all of them were retrospective, thereby reducing the quality of evidence. However, given the scarcity of data, this meta-analysis is crucial in improving our understanding of the current level of evidence for AI-assisted EUS. Secondly, this meta-analysis exhibited significant heterogeneity, likely due to the variability in the populations included in the studies. For instance, two studies evaluated the AI's performance by categorizing the SELs based on a 20 mm cut-off for size[28,34], which limits the performance evaluation to SELs < 20 mm. Thirdly, the varying quality of EUS devices and images used in the trials limits their applicability in

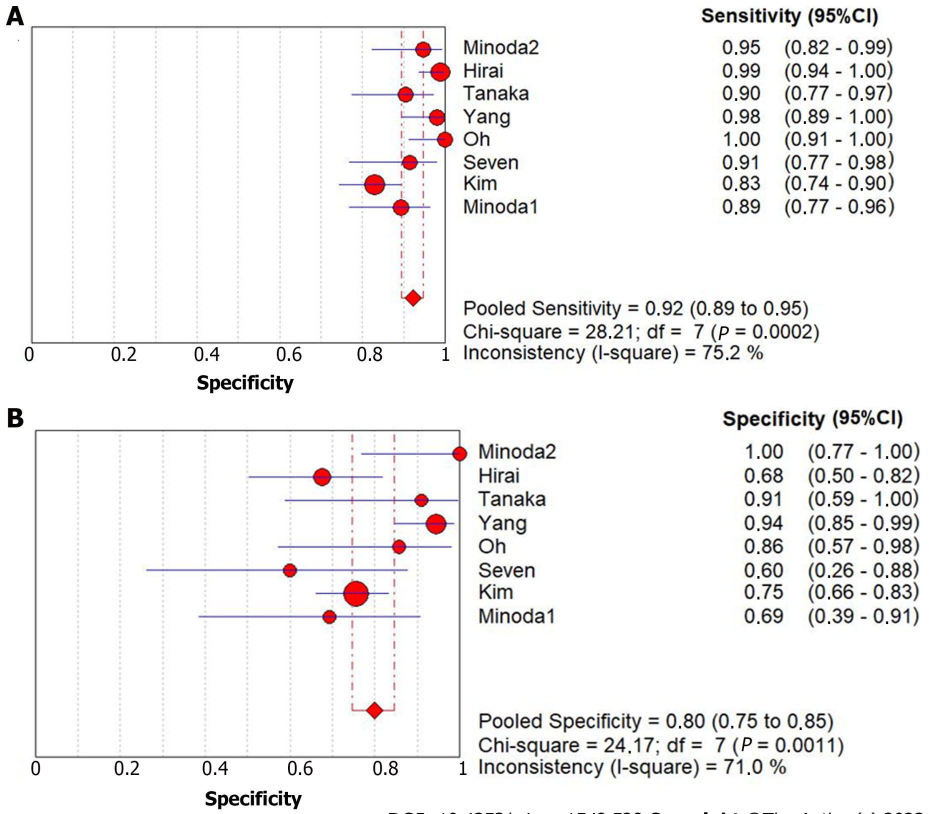


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**Figure 3 Sensibility and specificity of endoscopic ultrasound with Artificial Intelligence for overall diagnosis of gastrointestinal stromal tumor.** A: Sensibility; B: Specificity. CI: Confidence interval.

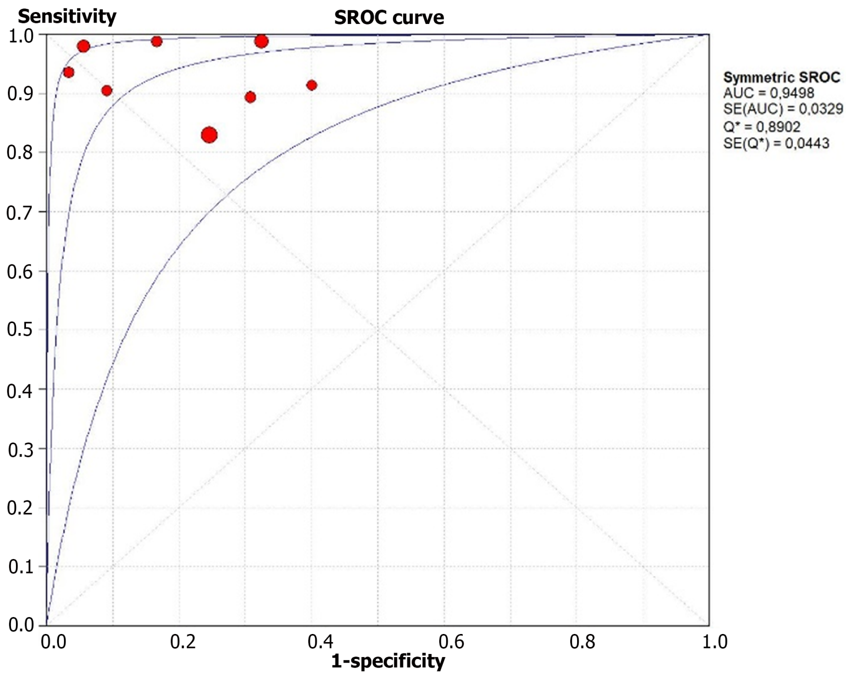


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**Figure 4 Summary receiver operating characteristic curve of endoscopic ultrasound with artificial intelligence for gastrointestinal stromal tumor diagnostic. Each circle represent an individual study.** SROC: Summary receiver operating characteristic; AUC: Area under curve.

real-world scenarios. Many of these studies only employed internal validation datasets for training the algorithms, which may potentially result in an overestimation of the AI models' performance. This situation is indicative of overfitting[37], where a machine learning model becomes overly specialized to the training data and performs poorly on new.

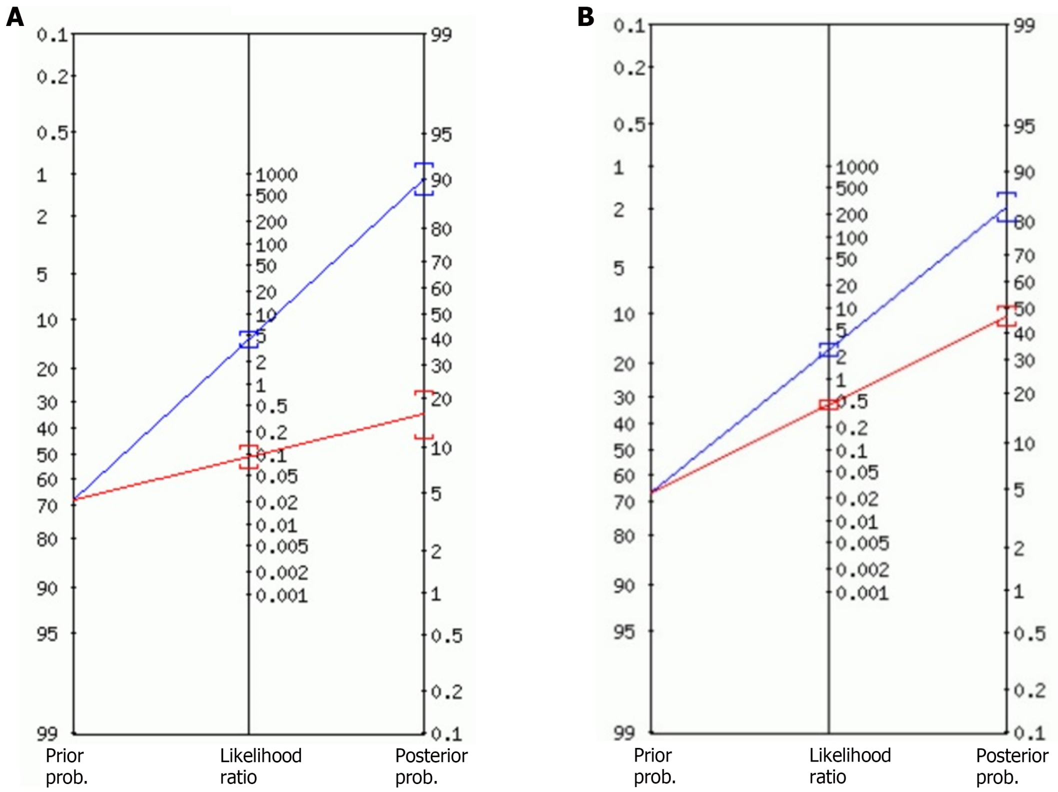


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**Figure 5 Fagan plot depicting the impact of a positive or negative result on pretest probabilities.** A: Fagan plot depicting the impact of a positive or negative result of artificial intelligence; B: Fagan plot depicting the impact of a positive or negative result of experienced endoscopists' (*i.e.*, the pooled prevalence of subepithelial lesions).

In summary, AI-supported EUS demonstrates notable diagnostic precision in retrospective investigations related to the detection of GIST. Furthermore, AI has shown superior accuracy compared to experienced endoscopists, indicating its potential as a significant diagnostic adjunct in this field. The advancement of AI algorithms and EUS devices, along with the increased accessibility of EUS and the availability of high-quality EUS images, creates a favorable environment for robust studies aiming to achieve enhanced diagnostic performance and develop valuable, clinically applicable tools. Consequently, AI technology has the potential to profoundly influence all aspects of healthcare, as indicated by current research findings.

## CONCLUSION

In conclusion, our systematic review and meta-analysis demonstrated the high diagnostic accuracy of EUS AI-assisted for the differentiation of SELs, especially GIST from other fourth-layer subepithelial tumors. AI revealed the potential to become help enhance endoscopists' diagnostic performance in the EUS evaluation of SELs and avoid unnecessary invasive procedures.

## ARTICLE HIGHLIGHTS

### *Research background*

Endoscopic ultrasonography (EUS) with artificial intelligence (AI) has shown high diagnostic accuracy for subepithelial lesions (SELs), particularly gastrointestinal stromal tumors (GISTs). The performance of AI systems has demonstrated superiority over experienced endoscopists and the ability to improve diagnostic power through collaborative diagnosis.

### *Research motivation*

This paper aims to investigate the diagnostic capabilities of AI-assisted EUS for SELs by analyzing images and comparing them with the expertise of experienced endoscopists.

### Research objectives

The research aims to assess the accuracy of AI-assisted EUS in diagnosing SELs, particularly those originating from the fourth layer. Additionally, the study analyzes the diagnostic performance of experienced endoscopists and compares it with AI systems.

### Research methods

Retrospective studies were selected of AI-assisted EUS for the diagnosis of SELs, using histopathology as the standard method. The included studies utilized EUS with AI for SELs diagnosis through image analysis. The risk of bias and quality of evidence were assessed, and the analysis was performed using Meta-Disc software.

### Research results

This meta-analysis included eight retrospective studies with a total of 2355 patients and 44154 images. The AI-assisted EUS for GIST diagnosis showed a sensitivity of 92% [95% confidence interval (CI): 0.89-0.95; $P < 0.01$], specificity of 80% (95%CI: 0.75-0.85; $P < 0.01$), and an AUC of 0.949. For the diagnosis of GIST *vs* gastrointestinal leiomyoma (GIL) by AI-assisted EUS, specificity was 90% (95%CI: 0.88-0.95; $P = 0.02$) and AUC 0.966. The experienced endoscopists achieved a sensitivity of 72% (95%CI: 0.67-0.76; $P < 0.01$), specificity of 70% (95%CI: 0.64-0.76; $P < 0.01$), and an AUC of 0.777 for GIST. Evaluating GIST *vs* GIL, the experts achieved a sensitivity of 73% (95%CI: 0.65-0.80; $P < 0.01$) and an AUC of 0.819.

### Research conclusions

This systematic review and meta-analysis demonstrate the high diagnostic accuracy of AI-assisted EUS in differentiating SELs, particularly GIST, from other fourth-layer subepithelial tumors.

### Research perspectives

This study demonstrated that by integrating machine learning techniques with EUS images, AI can aid in distinguishing benign from malignant lesions and guiding treatment decisions, with high accuracy. Additionally, through AI assistance image recognition can enhance real-time diagnosis during EUS evaluations, increasing the performance of even experienced endoscopists.

## FOOTNOTES

**Author contributions:** Gomes RSA contributed to the acquisition of data; Gomes RSA, de Oliveira GHP, Hirsch BS, Ribeiro Jordão Sasso JG, Matsubayashi CO, Kotinda APST, Veras MO, Moura DTH, Bernardo WM, and de Moura EGH contributed to the analysis of data; Gomes RSA, de Oliveira GHP, Hirsch BS, Ribeiro Jordão Sasso JG, Matsubayashi CO, Kotinda APST, Veras MO, Moura DTH, Bernardo WM, Trasolini RP, and de Moura EGH contributed to the interpretation of data; Gomes RSA, de Moura DTH, Trasolini RP, Bernardo WM, and de Moura EGH drafted the article; Gomes RSA, de Oliveira GHP, Hirsch BS, Ribeiro Jordão Sasso JG, Matsubayashi CO, Kotinda APST, Veras MO, de Moura DTH, Trasolini RP, Bernardo WM, and de Moura EGH revised the manuscript; Trasolini RP revised the English language; and all author approved the final manuscript.

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*CASE REPORT*

# Acute pancreatitis following endoscopic ampullary biopsy: A case report

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## Abstract

### *BACKGROUND*

Endoscopic biopsy is mandatory for the diagnosis of malignant and premalignant ampullary tumours. The commonly reported inadvertent complications following routine mucosal biopsy include perforation and haemorrhage. Acute pancreatitis is an extremely rare complication following this procedure.

### *CASE SUMMARY*

This report details the case of a 59-year-old man who underwent biopsy of the ampulla for a suspected periampullary tumour. Following the procedure, the patient presented with symptoms of acute pancreatitis which was substantiated by laboratory and radiological investigations. He was conservatively managed and discharged following complete resolution of symptoms.

### *CONCLUSION*

This case report serves to highlight the importance of this potential complication following routine endoscopic biopsy of the ampulla.

**Key Words:** Acute pancreatitis; Endoscopy; Ampullary biopsy; Ampullary lesions; Ampulla of Vater; Case report

**Core Tip:** Gastrointestinal endoscopic procedures are relatively safe and are being routinely performed with the advent of minimally invasive procedures. Acute pancreatitis is an extremely uncommon complication following endoscopic ampullary biopsy. It is important for endoscopists to be mindful of this untoward complication with appropriate post-procedure monitoring and support.

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## INTRODUCTION

Endoscopic biopsy is recommended for the evaluation of ampullary adenomas, ampullary tumours, and more recently, immunohistological staining for autoimmune pancreatitis[1,2]. The commonly encountered complications following this procedure include bleeding, infection, and perforation. Acute pancreatitis is an extremely uncommon complication with a high rate of morbidity and mortality. It can be attributed to the mucosal edema or intraductal hematoma caused by the ampullary biopsy[6]. Although rare, endoscopists are to be aware of this complication and patients need to be closely monitored following the procedure.

## CASE PRESENTATION

### *Chief complaints*

A 59-year-old man presented to our tertiary centre with symptoms of dyspepsia for which ultrasound of the abdomen was done and it showed dilatation of the common bile duct (10 mm). For further evaluation, liver function test was done, which was reported as normal. Contrast-enhanced computed tomography (CT) of the abdomen was then performed, which revealed dilatation of the common bile duct and pancreatic duct (3.5 mm). Side-viewing duodenoscopy (Olympus TJF-150 Video Duodenoscope; Olympus, Tokyo, Japan) was done, which revealed an ulcerated papilla from which a biopsy was taken (Figure 1). The sampling was done with Jumbo biopsy forceps without spike. Haemostasis was confirmed and the procedure was uneventful. Two hours later, the patient presented with acute onset upper abdominal pain and profuse sweating which developed 30 min following his meal.

### *History of present illness*

The pain was localised to the epigastrium and was severe in nature (8 on the Visual Analogue Scale) with radiation to the back. There was no history of vomiting.

### *History of past illness*

The patient was not a known diabetic or hypertensive.

### *Personal and family history*

The patient did not have any relevant family history. He was a non-alcoholic and non-smoker.

### *Physical examination*

At the Emergency Room, the patient's heart rate was 110 per minute and blood pressure was 140/80 mm of Hg. On examination of the abdomen, there was severe epigastric tenderness with guarding. The rest of the abdominal quadrants were non-tender with normal bowel sounds.

### *Laboratory examinations*

The patient's blood work-up pre- and post-procedure is shown in Table 1.

### *Imaging examinations*

Computed tomography of the abdomen showed features consistent with acute pancreatitis such as pancreatic enlargement and diffuse peri-pancreatic fat stranding (Figure 2).

## FINAL DIAGNOSIS

The patient was further evaluated to determine other attributing factors causing pancreatitis such as gallstone disease, alcohol, or any other precipitating drugs. After ruling these out, endoscopic biopsy of the ampulla was attributed as the

**Table 1 The patient's blood work-up pre- and post-procedure**

| Blood investigation | Pre-procedure | Post-procedure |
|---|---|---|
| WBC count | 7500/$mm^3$ | 13000/$mm^3$ |
| AST | 35 IU/L | 65 IU/L |
| ALT | 40 IU/L | 82 IU/L |
| Serum amylase | 50 IU/L | 1500 IU/L |
| Serum lipase | 110 IU/L | 800 IU/L |

AST: Aminotransferase; ALT: Alanine aminotransferase; WBC: White blood cell.

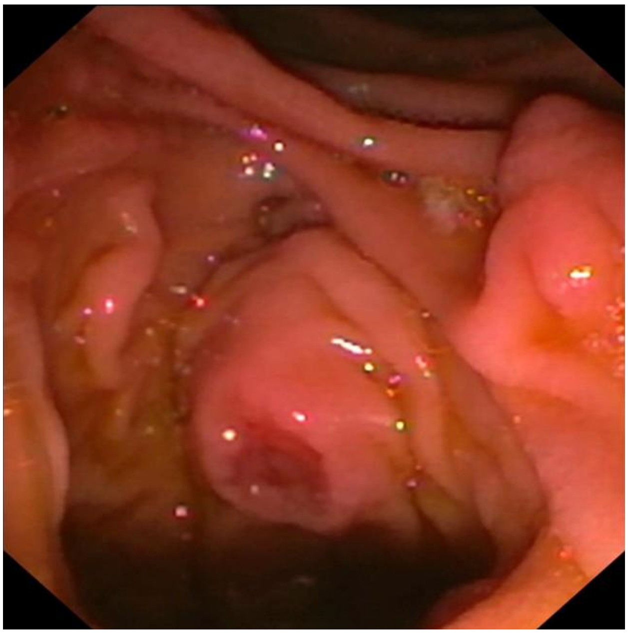



**Figure 1 Image as visualized through a side-viewing dudenoscope showing an ulcerated papilla from which a biopsy was taken.**



**Figure 2 Computed tomography of the abdomen showing features consistent with acute pancreatitis such as pancreatic enlargement and diffuse peri-pancreatic fat stranding.**

cause.

## TREATMENT

The patient was admitted and kept nil per oral. He was managed conservatively with intravenous fluids, antibiotics, and analgesics. His general condition improved and he was gradually initiated on diet. He achieved complete resolution of symptoms and was discharged 48 h later.

## OUTCOME AND FOLLOW-UP

Histopathological examination of the tissues samples showed an adenomatous polyp with moderate dysplasia. The patient remained asymptomatic over a follow-up period of 6 mo.

## DISCUSSION

Upper gastrointestinal endoscopy is central for the diagnosis of a wide array of tumours arising at the ampulla of Vater including neoplasms such as neuroendocrine tumours, adenomas, and adenocarcinomas as well as non-neoplastic lesions such as lipomas, lymphangiomas, fibromas, adenomyomas, and hamartomas[3-5]. Acute pancreatitis, a commonly encountered complication following endoscopic retrograde cholangiopancreatography, is extremely rare following non-thermal endoscopic biopsy of the ampulla of Vater without previous cannulation. Morales *et al*[6], who reported the first such case in 1994, propositioned mucosal edema or intraductal hematoma with a resultant increase in pressure in the pancreatic duct as the cause. Ishida *et al*[7] presented a similar case of acute pancreatitis following endoscopic biopsy of the ampulla of Vater in 2013, where the cause was ascribed to the small ampulla of the patient. Confirmation of hemostasis at the end of the procedure is important in order to prevent the inadvertent development of acute pancreatitis as a result of intramural hematoma. Another contributing factor is the ampullary edema as a result of the biopsy forceps. Ampullary biopsy with side-viewing endoscopy is pivotal for the diagnosis of periampullary carcinoma. However, the yield of ampullary surface biopsies is limited and there arises the need for deeper biopsies which can further contribute to ampullary edema. In a case of acute pancreatitis following endoscopic ampullary biopsy reported by Michopoulos *et al* [8], they directed the biopsies to the area around the orifice. It is recommended to avoid biopsying the normal ampulla and to biopsy some distance from the mouth of the pancreatic duct to prevent acute pancreatitis; however, bleeding and edema can obscure vision, proving this to be difficult. There are very limited reported cases of acute pancreatitis following endoscopic biopsies from the ampulla of Vater. Most of these patients have had an uneventful recovery. Skelton *et al*[9] reported a case of severe necrotising pancreatitis following ampullary biopsy where the patient required multiple necrosectomies and two CT-guided drains. In our case, the patient was discharged 48 h post-procedure without any untoward outcomes.

## CONCLUSION

This case reports serves to enlighten endoscopists regarding the potential complication of acute pancreatitis following endoscopic biopsy of the ampulla, to educate patients regarding this complication, and to closely monitor them following the procedure.

## FOOTNOTES

**Author contributions:** George NM, Rajesh NA, and Chitrambalam TG contributed equally to this work; George NM assisted in patient care and wrote the manuscript, Rajesh NA and Chitrambalam TG assisted in data collection and manuscript revision; all authors have read and approved the final manuscript.

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