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Risk Factors and Causes of Fever after Endoscopic Submucosal Dissection

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Abstract

Background: The aim of this study was to investigate the fever and related risk factors of gastrointestinal mucosa or submucosal lesions after endoscopic submucosal dissection (ESD).

Methods and Results: This retrospective study included 290 patients undergoing ESD. Patients were divided into two groups according to the presence or absence of post-ESD fever. Patient-related factors and lesion-related factors were counted in both groups. The incidence of post-ESD fever was 31.0% (90/290) after the operation. Among them, 87 patients developed fever within 24 hours after the operation.

Gender, smoking, hypertension, and infiltration depth of lesions were not risk factors for fever; age, diabetes, operation time, lesion size, and operation location were risk factors for post-ESD fever. Multivariate logistic stepwise regression was performed for the above statistically significant factors to control for confounding factors. The results showed that age above 60 (OR=1.045, 95% CI: 0.945-2.145, *P*=0.002), esophageal mucosal defect of more than 3/4 (OR=8.231, 95% CI: 6,745-11.342, *P*=0.033), and diabetes (OR=2.143, 95% CI: 1.345-4.236, *P*=0.034) were independent risk factors for esophageal stenosis after ESD.

Conclusion: This study indicated that patients who are older, whose operation site is in the esophagus, who have diabetes or large tumors, and long operation time were more likely to develop post-ESD fever, but there was a low probability that bacteremia was the cause of fever. Patients after ESD may show some manifestations of inflammatory reactions, but the possibility of bacteremia is small.(**International Journal of Biomedicine. 2025;15(1):155-161.**)

Keywords: endoscopic submucosal dissection • fever • complication

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Abbreviations

BT, body temperature; **CT**, computed tomography; **ESD**, endoscopic submucosal dissection.

Introduction

Endoscopic submucosal dissection (ESD) is a minimally invasive procedure that has revolutionized the treatment of early gastrointestinal neoplasms. It allows for precise en-bloc resection with minimal invasion and rapid recovery.[1] This technique has been particularly effective in managing larger or more complex lesions that previously were challenging with traditional endoscopic resection methods. Over the past five years, numerous studies have contributed to developing and refining ESD practices, addressing various aspects such as procedural efficacy, safety, and technical innovations.[2-5]

Endoscopic submucosal dissection has been used as a common endoscopic treatment method for early gastrointestinal cancer, precancerous lesions, and submucosal lesions in recent years. Safety and management of complications have also been central to ESD research. The most common complications of ESD include bleeding and perforation; post-ESD fever is also a common complication, but there are few systematic data about post-ESD fever. A study by Yongkang

Lai and colleagues[6] retrospectively reviewed patients who underwent ESD for gastric lesions and found that 23.1% of patients experienced post-ESD fever, with the highest fever temperature being 37.6±3.12°C and the number of days with fever being 1.48±0.85. The researchers identified age, procedure time, postoperative gastric tube placement, intraoperative hemorrhage, and perforation as independent risk factors for post-ESD fever. This suggests that patient age, the duration of the procedure, and the occurrence of intraoperative complications are significant predictors of post-ESD fever. Another study focusing on esophageal ESD and its derived technique reported a fever incidence of 30.3%, with factors such as age, lesion size, operation time, and nasogastric tube placement being associated with postoperative fever.[7]

By counting patient- and lesion-related factors, this retrospective study analyzed the risk factors and causes of post-ESD fever.

Materials and Methods

This retrospective study collected a total of 290 cases of ESD from the same senior endoscopy physician in Shandong Cancer Hospital, from July 1, 2018, to July 1, 2019. Before this study, the physician had performed ESD surgery in over 100 cases and was proficient in the operation. Post-ESD fever refers to the patient's body temperature (BT) after ESD ≥38.0°C. According to whether there was post-ESD fever, the patients were divided into two groups: Group A, BT ≥38.0 °C and Group B, BT <38.0 °C.

Preoperative Preparation

All patients signed the ethical informed consent form and underwent routine clinical examination after admission, including blood routine, coagulation function, electrocardiogram, and enhanced CT of the lesion site. Patients with hypertension and diabetes should be operated on when their condition is basically stable. Informed consent and surgical consent should be signed before the operation. The oral temperature of patients was measured 2 hours before the operation. For those whose BT was higher than 38.0°C, the operation was suspended to find out the cause of the fever.

Endoscopic Submucosal Dissection

Both esophageal and gastric ESD were performed using an Olympus Q260J electronic gastroscope; colorectal ESD was performed using an Olympus Q260JI electronic colonoscopy. Other equipment used included a high-frequency generator (VIO200D, ERBE, Elektromedizin, Germany), DualKnife (Olympus, Japan) for electrocoagulation, KD-650Q knife for esophageal lesions, KD-650L knife for gastric lesions, and KD-650U knife for colorectal lesions, hemostatic forceps (FD-411UR, Olympus, Japan) and hemostatic clips (ROCC-D-26-195, Micro-Tech Co, China).

The upper gastrointestinal ESD surgery was performed under general anesthesia with tracheal intubation, and the catheter was inserted before the operation. The lower gastrointestinal ESD surgery was performed with the patient awake, without a catheter. Blood oxygen saturation and electrocardiographic monitoring were performed in all patients during and 24 hours after the operation.

Narrow band imaging or chromoendoscopy staining was used to determine the lesion range: 1.2% compound iodine solution was sprayed for esophageal mucosal lesions, and 0.4% indigo carmine was sprayed for gastric and colorectal mucosal lesions. A DualKnife was used to electrocoagulate the lesion range at a distance of 5 mm from the peripheral edge of the lesion, with an interval of 5 mm between each marker point. A 4% methylene blue glycerin fructose mixture was used for multi-point submucosal injection outside the marked range to raise the lesion and separate it from the muscular lamina propria. The mucosa was cut with the DualKnife along the peripheral marks of the lesion, and then the submucosa was peeled off step by step. After the entire specimen was resected, the exposed vessels of the wound surface and wound margin were prevented from hemostasis by electric hemostatic forceps or clips. The postoperative resection specimens were fixed on the foam plate with pins, marked on the oral and anal sides, and immersed in 10% formalin solution. The operating time of ESD extended from the beginning of the peripheral markers to the end of preventive hemostasis after ESD.

Figure 1 illustrates three ESD procedures at our hospital, each targeting distinct gastrointestinal sites: esophageal, gastric, and colorectal.

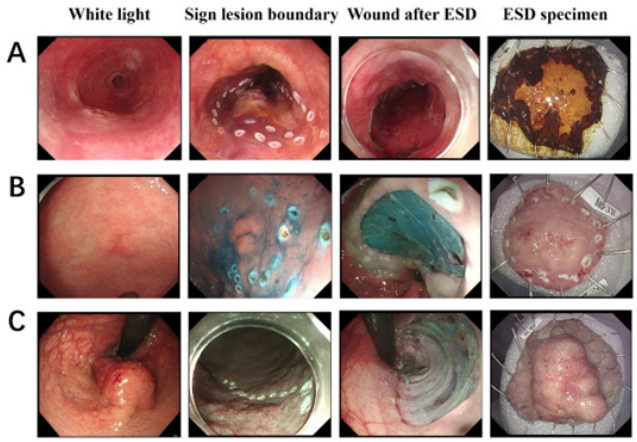

Fig. 1. *Images of ESD procedures. A: ESD images for esophageal lesions. B: ESD images for gastric lesions. C: ESD images for colorectal lesions.*

Complications

Common complications of ESD included bleeding and perforation, while pneumonia was referred to as the new pulmonary infiltration, consolidation, or pleural effusion found in the chest CT examination, compared to the preoperative examination.[8]

Pathology

The lesion size, site, histological type, depth of infiltration, degree of differentiation, horizontal and vertical margins, and presence or absence of vascular and lymphatic infiltration were recorded. The length of the lesion was measured on the specimen after ESD surgery, and the longest diameter of the lesion was taken as its length.

Postoperative Management

After upper gastrointestinal tract ESD, a gastrointestinal decompression tube was placed, food and water prohibited,

and acid suppression and gastric mucosal protection drugs were applied intravenously. If there was no perforation or massive bleeding, no matter whether or not there was a fever, patients began to drink water and eat soft food 3 days after ESD. Fasting and water deprivation were recommended on the first day after lower gastrointestinal ESD, with water and soft food intake allowed on the next day after surgery.

After surgery, all patients measured their BT at 8:00, 12:00, 16:00, and 20:00 for 72h. Blood leukocyte counts were checked on the second day after ESD to evaluate the inflammatory reaction. Blood culture and chest CT were carried out if the patient's BT increased.

Body temperature, peripheral blood analysis, lung breath sounds, blood culture results, and chest CT were analyzed to determine whether febrile patients had an infection and needed antibiotics.

If there was no evidence of infection, antibiotics were not given, and a physical cooling method or antipyresis would be given to patients with oral temperatures above 38.5℃. If there was evidence of infection, antibiotics were given according to the blood culture results and whether the patient had any other discomfort symptoms, such as pain, amount of drainage fluid, delayed bleeding, and delayed perforation.

Follow-up: Gastroscopy was performed 3, 6, and 12 months after surgery and once a year thereafter. A combination of outpatient and telephone follow-up was used.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). The measurement data were expressed as median (minimum, maximum) and were compared using the Mann-Whitney U test. Group comparisons with respect to categorical variables are performed using chi-square tests with Yates correction or Fisher's exact test. A multiple logistic regression analysis was conducted to calculate the odds ratios (OR) with 95% confidence intervals (95% CI). Cutoff points of continuous variables were detected by ROC curve analysis. The Jordan index was used to calculate the optimal cutoff value. A *P*-value of <0.05 was considered statistically significant.

The study was conducted in accordance with the ethical principles of the WMA Declaration of Helsinki (1964, ed. 2000) and approved by the ethics committee of the Shandong Cancer Hospital Affiliated with Shandong University (# SDTHEC201806067, June 2018). The informed consent was obtained from all patients.

Results

In Group A, the oral temperature was between 37.5℃ and 39.6℃, with an average of 38.3 ± 0.53℃, and the duration of fever was 1–7d, with an average of 2.82 ± 1.186 d. Seventy-seven patients had normal blood and urine tests, no urinary tract infection, cough and sputum, and negative blood culture. Eight patients had increased leukocyte (>10×10^9/L) and proportion of neutrophils (>70%), no urinary tract infection, cough and sputum, negative blood culture, normal chest CT, and urinalysis; no antibiotics were given, only physical cooling or antipyretic treatment when the oral temperature was over 38.5℃, all patients could drop to normal BT after 1–3 days. Five patients had normal urine routine tests and increased leukocyte (>10×10^9/L) and neutrophils (>70%); they had clinical symptoms of lung infection, such as cough and sputum; chest CT showed pneumonia, blood culture was positive in one case, and they were confirmed as pneumonia; all of them were elderly patients (≥70.6 years) with esophageal disease. The urine routine was normal in all patients with fever, and blood culture was positive in one case.

There were no significant differences between the two groups in terms of gender, history of hypertension, smoking, BMI, and depth of lesion infiltration (Table 1). In contrast, the patient's age, lesion location, history of diabetes, alcohol consumption, lesion size, and operation time were all found to influence the occurrence of post-ESD fever significantly.

Table 1.

Comparison of the study groups.

	Group A (n=90)	Group B (n=200)	P-value
Gender (M/F)	46/44	108/92	0.492
Age (years)	70.6 (36-83)	62 (35-84)	0.049
Lesion location esophagus/stomach/intestine)	38/48/4	34/144/22	0.000
BMI (kg/m^2)	22.40	21.87	0.570
History of hypertension	26 (28.9%)	54 (27.0%)	0.514
History of diabetes	7 (7.8%)	5 (2.5%)	0.000
Smoking	14 (15.6%)	44 (22%)	0.197
Alcohol consumption	31 (34.4%)	63 (31.5%)	0.018
Lesion size (cm)	6.3	3.27	0.000
Operation time (min)	195.8	106	0.000

The frequency of post-ESD fever was different for different surgery locations (*P*<0.001) (Figure 2). The incidence of esophageal post-ESD fever was 52.8%, gastric post-ESD fever was 25%, and colorectal post-ESD fever was 15.4%.

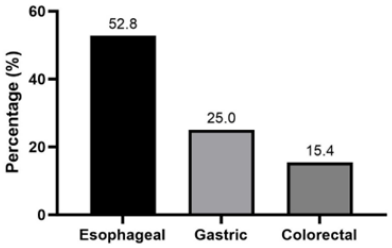

Fig. 2. *The frequency of post-ESD fever for different surgery locations.*

The average operation time in Group A was 195.8 minutes, significantly longer than in Group B (106 minutes) (*P*=0.000). The size of the lesions in Group A was 6.3 cm, significantly higher than Group B (3.27 cm) (*P*<0.001).

A logistic analysis of the risk factors of post-ESD fever is shown in Table 2. Gender, smoking, hypertension, and infiltration depth of lesions were not risk factors for fever; age, diabetes, operation time, lesion size, and operation location were risk factors for post-ESD fever. Multivariate logistic stepwise regression was performed for the above statistically significant factors to control for confounding factors. The results showed that age above 60, esophageal mucosal defect of more than 3/4, and diabetes were independent risk factors for esophageal stenosis after ESD.

Table 2.

Logistic analysis of the risk factors for post-ESD fever.

Index	Univariate analysis			Multivariate analysis		
	OR	95%CI	*P*	OR	95%CI	*P*
Gender	1.862	0.343-10.105	0.471			
Age	1.185	1.131-1.242	0.000	1.045	0.945-2.145	0.002
BMI	1.202	0.938-1.540	0.145			
Hypertension	1.679	0.319-8.843	0.541			
Diabetes	3.289	1.015-10.662	0.007	2.143	1.345-4.236	0.034
Smoking	0.405	0.039-4.248	0.451			
Drinking	0.763	0.155-3.768	0.740			
Lesion size	12.361	5.202-29.371	0.000	8.231	6.745-11.342	0.033
Operation time	1.022	1.003-1.042	0.022	1.015	0.894-1.223	0.154
Infiltration depth	1.494	0.385-5.795	0.562			
Pathology	1.211	0.417-3.517	0.725			

The lesion size >4cm was a predictor of post-ESD fever, with a sensitivity of 93.5% and specificity of 96.7%. For patients over 65, the sensitivity and specificity of post-ESD fever detection were 67.5% and 77.8%, respectively. For patients with a history of diabetes, the sensitivity and specificity of post-ESD fever detection were 72.0% and 72.2%, respectively (Table 3). By ROC curve analysis, the AUC of lesion size more than 4cm in post-ESD fever detection was 0.849 (Figure 3).

Table 3.

The sensitivity and specificity of risk factors for post-ESD fever.

Index	Sensitivity (200)		Specificity (90)	
	n	%	n	%
Age (65 years)	135	67.5	70	77.8
History of diabetes	144	72.0	65	72.2
Lesion size (4 cm)	187	93.5	87	96.7

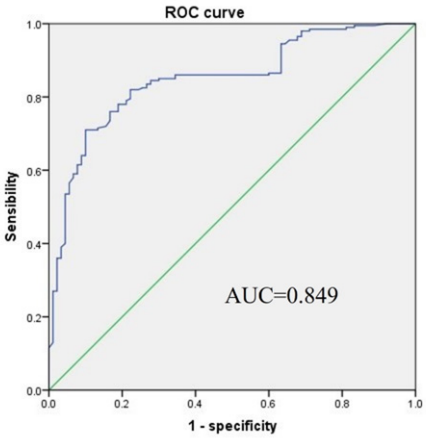

Fig. 3. *AUC (0.849) of lesion size more than 4 cm in post-ESD fever detection.*

Discussion

Surgical fever is prevalent after open surgery, which is one of the host responses to surgery.[10] Postoperative fever is most commonly attributed to noninfectious causes. It is associated with the normal thermoregulatory response without infection in vivo. It is most commonly caused by inflammatory changes from releasing pyrogenic cytokines (IL-1, IL-6, TNF-α, and IFN-γ).[11] The cytokines act directly on the anterior hypothalamus and cause a release of prostaglandins, which mediate the febrile response inflammation secondary to cytokine release.[12] Except for postoperative pain and discomfort, patients may have changes in blood routine, no abnormality in chest CT, and the possibility of fever caused by infection may be excluded. Compared with the conventional ulcer, the ulcer after ESD is formed in a short period of time, and the ulcer infiltrates deeper; it suffers from more invasive injury in a short period of time, such as electrocoagulation or electrotomy for cutting or hemostasis, which inevitably contact the muscularis propria, leading to inflammation or fever. Compared with open surgery, the wound surface of ESD patients is smaller, so the incidence of reaction heat after ESD is lower than that of open surgery. In this study, the incidence of post-ESD fever was 31.0%. The author considers that the cause of fever is surgical.

Another common hospital infection is urinary tract infection, associated with indwelling catheters in 80% to 90% of cases, mostly caused by long-term indwelling catheters or unsatisfactory aseptic operation during catheterization and improper perineal care.[13] Bacteria can retrograde along the urethra and develop cystitis and even nephritis. Our preventive measures are as follows: (1) Catheter insertion should be strictly sterile, and daily wiping and washing of the perineum should be done with 0.05% iodine solution. Colorectal ESD was performed carefully, and no catheter was placed. (2) Catheter removal should be done as soon as possible to shorten the indwelling time, generally not more than 24 hours. The results of the above measures were satisfactory; 290 patients had no urinary tract infection.

This study also found that the incidence of pneumonia in elderly patients increased significantly. The reason is that due to aging, changes in the anatomy and function of the respiratory system result in decreased defense and immune function of both the whole body and local respiratory tract, reduced cough reflex leads to abatement of the airway's ability to purify and clear itself; on the other hand, elderly patients may differ from younger patients in several ways, including the number and severity of comorbid conditions they have.[14] As the population ages, issues related to the surgical care of elderly patients are becoming increasingly common.[15] Understanding the perioperative factors associated with adverse outcomes can allow for the identification of at-risk patients to enable the development of tailored preventive strategies and resource planning to decrease the complications of elderly surgical patients.[16]

During the ESD, an injection needle catheter is passed through the contaminated endoscopic channel and may directly inoculate bacteria into the bloodstream during submucosal injection.[17] In addition, ESD can produce mucosal defects, which are open without closure, and submucosal and muscularis propria. And exposure to native bacterial flora in the gastrointestinal tract may lead to bacteremia and/or endotoxemia.[18-20] Although we performed a blood culture on each patient with post-ESD fever, only one patient with confirmed pneumonia had a positive blood culture. Kawata et al. observed a similar situation. They performed blood culture immediately on 101 post-ESD patients, seven of whom were positive, and only one was positive on the second day after the operation.[21] None of the 10 patients whose BT>38℃ showed positive blood culture. Combined with our research, we believe that the incidence of bacteremia after ESD is low, post-ESD fever is not related to bacteremia, and blood culture is not a sensitive indicator of clinical fever. The reasons were analyzed:[22] (1) the postoperative infection was limited, and bacteria did not enter the systemic circulation; (2) blood collection time was not during the time of bacteria entering the blood flow. On the contrary, it has been reported that prophylactic antibiotics before and after surgery can reduce the incidence of fever and pneumonia.[23,24] There is no clear guidance on whether to use antibiotics routinely after ESD. According to recent guidelines for gastroenteroscopy in the United States, antibiotics are unnecessary to prevent fever and pneumonia. American Society of Gastroenterology and British Society of Gastroenterology guidelines only recommend prophylactic antibiotics for ERCP, ileostomy, and variceal ligation in digestive endoscopy.[25-27] Endoscopic submucosal dissection ESD is a critical strategy to prevent infection of the mediastinum, retroperitoneum, or free peritoneum around the surgical site, as well as to mitigate the risk of postoperative systemic infection. This preventive measure is particularly crucial for patients who have undergone extensive procedures, have experienced long operation times, or have had repeated submucosal injections leading to peripheral inflammatory edema. Additionally, there is an elevated risk in cases where gastrointestinal perforation has occurred or is a possibility.[28] However, this claim lacks the support of evidence-based medicine. Therefore, more studies are needed to determine whether prophylactic antibiotic use is necessary and whether it can reduce the incidence of postoperative pneumonia and fever. Our study found that patients after ESD may show some inflammatory manifestations, but the possibility of bacteremia is small. The positive rate of blood culture in patients with post-ESD fever was low. However, not every patient in this study underwent blood culture and routine urine examination, so the infection status may be biased, and statistics on this aspect need to be improved in the next prospective study.[29]

The difficulty of ESD operation in different parts of the body is different, which is related to the operator's operation level and experience. This study was performed by the same surgeon, who was skilled in this kind of operation. We found that the probability of fever in different parts of the digestive tract was different. The probability of post-ESD fever in the esophagus and stomach was higher than in the colorectal area. The reasons are analyzed: the esophageal wall is relatively thin, the operation space is small, the surgery is more likely to cause perforation and then may cause pneumothorax and mediastinum infection; pump water may be needed to flush the wound surface during the operation due to the patient's intubation under general anesthesia, the possibility of mis-inhalation and aspiration pneumonia increased, may lead to fever. Our findings show that the probability of post-ESD fever in the colorectal area is lower than in the stomach, which differs from some previous studies.[30] The reasons are analyzed: (1) To reduce the chance of perforation, bleeding, and infection, most of the wounds after colorectal surgery are closed with metal clips unless the wounds are too large to cause intestinal stenosis if metal clips are closed. (2) In this study, colorectal ESD was performed in the conscious state; the recovery of the body state was faster after the operation, and aspiration under anesthesia was avoided. (3) The colorectal sample was small in this study.

By ROC curve analysis, we found that the lesion size >4 cm was a predictor of post-ESD fever, with a sensitivity of 93.5% and specificity of 96.7%.

In the cases of more complicated ESD, the duration of the operation tends to be longer. In addition, when the surgical region is relatively large, the operation requires a longer duration, the contact time between the electrosurgical knife and the submucosa is also extended, and mechanical injury to the tissue increases.[31] It is suggested that for patients with large specimens or complicated lesions, we should be alert to post-ESD fever, intervene, and prevent it early.

Patients with diabetes in this study had a higher incidence of post-ESD fever, which may be related to the deficiency of immune functions, cell chemotaxis and phagocytosis, depressed polymorphonuclear leukocyte function under acidosis, and other defense functions. Leukocyte adherence, chemotaxis, and phagocytosis may be affected, and antioxidant systems involved in bactericidal activity may also be impaired so that diabetic patients are prone to infection.[32] Changes such as surgical stress and significant changes in blood glucose can also make diabetes patients susceptible to infection and fever. There is evidence that improving glycemic control in patients can improve immune function, and the efficiency of intracellular killing of microorganisms may improve with

better glycemic control. It is suggested that the blood glucose level should be controlled well perioperative ESD, and the insulin dosage should be adjusted reasonably according to the patient's specific conditions.[33,34]

In conclusion, our study identified several risk factors for post-ESD fever, including the operation site in the esophagus, a history of diabetes, age above 70.6 years, resection diameter exceeding 4.25 mm, and operation time surpassing 196 minutes. Consequently, heightened vigilance is warranted for patients presenting with these risk factors. The ESD procedures in this study were conducted by a single senior physician at one research center, allowing us to control surgeon experience and skill level variability. However, the findings require validation through studies with larger sample sizes. Regarding the diagnosis of pneumonia, clinicians should consider the necessity of a CT scan based on the postoperative condition of patients. It is acknowledged that not all patients undergo postoperative examinations, which may cause missed diagnoses. Given that pneumonia is a primary cause of post-ESD fever and considering the potential influence of different anesthetic methods and drugs on the incidence of postoperative pneumonia, further investigation into the relationship between anesthesia and fever is warranted.

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Competing Interests

The authors declare that they have no competing interests.

References

1. Pimentel-Nunes P, Libânio D, Bastiaansen BAJ, Bhandari P, Bisschops R, Bourke MJ, Esposito G, Lemmers A, Maselli R, Messmann H, Pech O, Pioche M, Vieth M, Weusten BLAM, van Hooft JE, Deprez PH, Dinis-Ribeiro M. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. Endoscopy. 2022 Jun;54(6):591-622. doi: 10.1055/a-1811-7025. Epub 2022 May 6. PMID: 35523224.

2. Draganov PV, Wang AY, Othman MO, Fukami N. AGA Institute Clinical Practice Update: Endoscopic Submucosal Dissection in the United States. Clin Gastroenterol Hepatol. 2019 Jan;17(1):16-25.e1. doi: 10.1016/j.cgh.2018.07.041. Epub 2018 Aug 2. PMID: 30077787.

3. Shah RH, Amin S. Building the Toolbox of Devices to Optimize a Practice in Submucosal Endoscopy. Gastrointest Endosc Clin N Am. 2023 Jan;33(1):15-28. doi: 10.1016/j.giec.2022.09.001. PMID: 36375879.

4. Dobashi A, Storm AC, Wong Kee Song LM, Deters JL, Miller CA, Tholen CJ, Gostout CJ, Rajan E. An internal magnet traction device reduces procedure time for endoscopic submucosal dissection by expert and non-expert endoscopists: ex vivo study in a porcine colorectal model (with video). Surg Endosc. 2019 Aug;33(8):2696-2703. doi: 10.1007/s00464-019-06817-8. Epub 2019 May 8. PMID: 31069502.

5. Fleischmann C, Probst A, Ebigbo A, Faiss S, Schumacher B, Allgaier HP, Dumoulin FL, Steinbrueck I, Anzinger M, Marienhagen J, Muzalyova A, Messmann H. Endoscopic Submucosal Dissection in Europe: Results of 1000 Neoplastic Lesions From the German Endoscopic Submucosal Dissection Registry. Gastroenterology. 2021 Oct;161(4):1168-1178. doi: 10.1053/j.gastro.2021.06.049. Epub 2021 Jun 26. PMID: 34182002.

6. Lai Y, Zhang Q, Liao F, Pan X, Zhu Z, Long S, Zhou X, Li G, Zhu Y, Chen Y, Shu X. Incidence and risk factors for fever after endoscopic submucosal dissection and its derivative technology for gastric lesions. Heliyon. 2024 Feb 7;10(4):e25748. doi: 10.1016/j.heliyon.2024.e25748. PMID: 38384516; PMCID: PMC10878927.

7. Liao F, Zhu Z, Lai Y, Pan X, Long S, Zhou X, Li G, Zhu Y, Chen Y, Shu X. Risk Factors for Fever After Esophageal Endoscopic Submucosal Dissection and Its Derived Technique. Front Med (Lausanne). 2022 Feb 22;9:713211. doi: 10.3389/fmed.2022.713211. PMID: 35273969; PMCID: PMC8902360.

8. Gong EJ, Kim DH, Jung HY, Lim H, Ahn JY, Choi KS, Lee JH, Choi KD, Song HJ, Lee GH, Kim JH, Baek S. Pneumonia after endoscopic resection for gastric neoplasm. Dig Dis Sci. 2014 Nov;59(11):2742-8. doi: 10.1007/s10620-014-3223-2. Epub 2014 Jul 15. PMID: 25023226.

9. Feng F, Tian Y, Yang X, Sun L, Hong L, Yang J, Guo M, Lian X, Fan D, Zhang H. Postoperative fever predicts poor prognosis of gastric cancer. Oncotarget. 2017 Mar 7;8(37):62622-62629. doi: 10.18632/oncotarget.15979. PMID: 28977974; PMCID: PMC5617534.

10. Narayan M, Medinilla SP. Fever in the postoperative patient. Emerg Med Clin North Am. 2013 Nov;31(4):1045-58. doi: 10.1016/j.emc.2013.07.011. PMID: 24176478.

11. Prajitha N, Athira SS, Mohanan PV. Pyrogens, a polypeptide produces fever by metabolic changes in hypothalamus: Mechanisms and detections. Immunol Lett. 2018 Dec;204:38-46. doi: 10.1016/j.imlet.2018.10.006. Epub 2018 Oct 15. PMID: 30336182.

12. Chiumello D, Gotti M, Vergani G. Paracetamol in fever in critically ill patients-an update. J Crit Care. 2017 Apr;38:245-252. doi: 10.1016/j.jcrc.2016.10.021. Epub 2016 Nov 5. PMID: 27992852.

13. Nicolle LE. Urinary tract infection. Crit Care Clin. 2013 Jul;29(3):699-715. doi: 10.1016/j.ccc.2013.03.014. PMID: 23830659.

14. Davis P, Hayden J, Springer J, Bailey J, Molinari M, Johnson P. Prognostic factors for morbidity and mortality in elderly patients undergoing acute gastrointestinal surgery: a systematic review. Can J Surg. 2014 Apr;57(2):E44-52. doi: 10.1503/cjs.006413. PMID: 24666459; PMCID: PMC3968213.

15. Massarweh NN, Legner VJ, Symons RG, McCormick WC, Flum DR. Impact of advancing age on abdominal surgical outcomes. Arch Surg. 2009 Dec;144(12):1108-14. doi: 10.1001/archsurg.2009.204. PMID: 20026827.

16. Ingraham AM, Cohen ME, Raval MV, Ko CY, Nathens

AB. Variation in quality of care after emergency general surgery procedures in the elderly. J Am Coll Surg. 2011 Jun;212(6):1039-48. doi: 10.1016/j.jamcollsurg.2011.03.001. PMID: 21620289.
17. Lees MC, Merani S, Tauh K, Khadaroo RG. Perioperative factors predicting poor outcome in elderly patients following emergency general surgery: a multivariate regression analysis. Can J Surg. 2015 Oct;58(5):312-7. doi: 10.1503/cjs.011614. PMID: 26204143; PMCID: PMC4599992.
18. Aadam AA, Abe S. Endoscopic submucosal dissection for superficial esophageal cancer. Dis Esophagus. 2018 Jul 1;31(7). doi: 10.1093/dote/doy021. PMID: 29982386.
19. Itaba S, Iboshi Y, Nakamura K, Ogino H, Sumida Y, Aso A, Yoshinaga S, Akiho H, Igarashi H, Kato M, Kotoh K, Ito T, Takayanagi R. Low-frequency of bacteremia after endoscopic submucosal dissection of the stomach. Dig Endosc. 2011 Jan;23(1):69-72. doi: 10.1111/j.1443-1661.2010.01066.x. PMID: 21198920.
20. Kato M, Kaise M, Obata T, Yonezawa J, Toyoizumi H, Yoshimura N, Yoshida Y, Kawamura M, Tajiri H. Bacteremia and endotoxemia after endoscopic submucosal dissection for gastric neoplasia: pilot study. Gastric Cancer. 2012 Jan;15(1):15-20. doi: 10.1007/s10120-011-0050-4. Epub 2011 May 11. PMID: 21559862.
21. Kawata N, Tanaka M, Kakushima N, Takizawa K, Imai K, Hotta K, Matsubayashi H, Tsukahara M, Kawamura I, Kurai H, Ono H. The low incidence of bacteremia after esophageal endoscopic submucosal dissection (ESD) obviates the need for prophylactic antibiotics in esophageal ESD. Surg Endosc. 2016 Nov;30(11):5084-5090. doi: 10.1007/s00464-016-4857-2. Epub 2016 Mar 16. PMID: 26983438.
22. Nakanishi T, Araki H, Ozawa N, Takada J, Kubota M, Imai K, Onogi F, Ibuka T, Shiraki M, Shimizu M, Moriwaki H. Risk factors for pyrexia after endoscopic submucosal dissection of gastric lesions. Endosc Int Open. 2014 Sep;2(3):E141-7. doi: 10.1055/s-0034-1377274. Epub 2014 Jul 10. PMID: 26134960; PMCID: PMC4440359.
23. Zhang QS, Han B, Xu JH, Gao P, Shen YC. Antimicrobial prophylaxis in patients with colorectal lesions undergoing endoscopic resection. World J Gastroenterol. 2015 Apr 21;21(15):4715-21. doi: 10.3748/wjg.v21.i15.4715. PMID: 25914483; PMCID: PMC4402321.
24. Lee SP, Sung IK, Kim JH, Lee SY, Park HS, Shim CS, Ki HK. A randomized controlled trial of prophylactic antibiotics in the prevention of electrocoagulation syndrome after colorectal endoscopic submucosal dissection. Gastrointest Endosc. 2017 Aug;86(2):349-357.e2. doi: 10.1016/j.gie.2016.11.022. Epub 2016 Nov 27. PMID: 27899322.
25. Allison MC, Sandoe JA, Tighe R, Simpson IA, Hall RJ, Elliott TS; Endoscopy Committee of the British Society of Gastroenterology. Antibiotic prophylaxis in gastrointestinal endoscopy. Gut. 2009 Jun;58(6):869-80. doi: 10.1136/gut.2007.136580. PMID: 19433598.
26. ASGE Standards of Practice Committee; Khashab MA, Chithadi KV, Acosta RD, Bruining DH, Chandrasekhara V, Eloubeidi MA, Fanelli RD, Faulx AL, Fonkalsrud L, Lightdale JR, Muthusamy VR, Pasha SF, Saltzman JR, Shaukat A, Wang A, Cash BD. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc. 2015 Jan;81(1):81-9. doi: 10.1016/j.gie.2014.08.008. Epub 2014 Nov 11. PMID: 25442089.
27. Tang X, Gong W, Jiang B. Antibiotic prophylaxis for GI endoscopy. Gastrointest Endosc. 2015 Jun;81(6):1503-4. doi: 10.1016/j.gie.2015.01.021. PMID: 25986123.
28. Mendelson M, Lewnard JA, Sharland M, Cook A, Pouwels KB, Alimi Y, Mpundu M, Wesangula E, Weese JS, Røttingen JA, Laxminarayan R. Ensuring progress on sustainable access to effective antibiotics at the 2024 UN General Assembly: a target-based approach. Lancet. 2024 Jun 8;403(10443):2551-2564. doi: 10.1016/S0140-6736(24)01019-5. Epub 2024 May 23. PMID: 38797179.
29. Oh D, Lee SS, Song TJ, Choi JH, Park DH, Seo DW, Lee SK, Kim MH. Efficacy and safety of a partially covered duodenal stent for malignant gastroduodenal obstruction: a pilot study. Gastrointest Endosc. 2015 Jul;82(1):32-36.e1. doi: 10.1016/j.gie.2014.11.039. Epub 2015 Mar 11. PMID: 25771068.
30. Izumi K, Osada T, Sakamoto N, Kodani T, Higashihara Y, Ritsuno H, Shibuya T, Nagahara A, Ogihara T, Kikuchi K, Watanabe S. Frequent occurrence of fever in patients who have undergone endoscopic submucosal dissection for colorectal tumor, but bacteremia is not a significant cause. Surg Endosc. 2014 Oct;28(10):2899-904. doi: 10.1007/s00464-014-3551-5. Epub 2014 May 23. PMID: 24853844.
31. Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: A systematic review and meta-analysis. Int J Surg. 2020 Jan;73:28-41. doi: 10.1016/j.ijsu.2019.11.027. Epub 2019 Nov 26. PMID: 31783166.
32. Collins TJC, Morgan PK, Man K, Lancaster GI, Murphy AJ. The influence of metabolic disorders on adaptive immunity. Cell Mol Immunol. 2024 Oct;21(10):1109-1119. doi: 10.1038/s41423-024-01206-1. Epub 2024 Aug 12. PMID: 39134802; PMCID: PMC11442657.
33. Xu Z, Zhuang J, Zhu X, Yao J. A nomogram for predicting the risk of postoperative fever in elderly patients undergoing endoscopic submucosal dissection of the upper gastrointestinal tract. Medicine (Baltimore). 2023 Dec 15;102(50):e36438. doi: 10.1097/MD.0000000000036438. PMID: 38115330; PMCID: PMC10727573.
34. Jin X, Wang J, Ma Y, Li X, An P, Wang J, Mao W, Mu Y, Chen Y, Chen K. Association Between Perioperative Glycemic Control Strategy and Mortality in Patients With Diabetes Undergoing Cardiac Surgery: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2020 Dec 17;11:513073. doi: 10.3389/fendo.2020.513073. PMID: 33391180; PMCID: PMC7774648.

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