

Hybrid Knife Technology in Endoscopic Therapy

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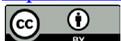
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Abstract

Hybrid knife as a multi-function endoscopic instrument provides an effective model for endoscopic diagnosis and treatment of diseases. Hybrid knife does not need exchange of instrument during endoscopic operation. It can effectively reduce the potential risk of perforation and hemorrhage so that improving quality of life for patients. The technology has been widely used in clinic, especially in the treatment of digestive internal medicine, and in the course of respiratory intervention. Researchers have started to use the hybrid knife technique and have obtained good surgical results. In this review, we introduced the advantages of hybrid knife and summarized the clinic application, including the tumor excision and the tissue collection for pathology. Furthermore, the application of hybrid knife has significant implication to gastrointestinal and urinary diseases, and airway tumors, and we also explored the possibility of application of hybrid knife system in more diseases. Hybrid knife system has important clinical significance and is worth further study and exploration.

Keywords

Hybrid Knife, Endoscopy, Clinical Application, Risk Management

1. Introduction

Endoscopic submucosal dissection (ESD) is an important therapy technology that removed en bloc lesion of gastrointestinal mucosal neoplasia. The normal ESD steps are followed: marking, elevation, incision, dissection and coagulation. In some cases, chromoendoscopy was also used to stain lesions by methylene blue or other stains before marking. The lesion was marked around in a circle, and the separation medium was injected in the mucous layer and selectively

generated a fluid cushion in the mucosa [1]. Lesion was shifted up by the fluid cushion and this elevation has benefits for incision and dissection. Incision was made from the marked line near the edge of fluid cushion. Endoscopic knife was applied to dissect the submucosa beneath the lesion and kept the lesion intact. If the fluid cushion was diminished or lost, the process was repeated among injection and dissection. Repeating the elevation provides a good presentation of the cut level (beneath the tumor) and contributes towards achieving the desired tumor resection. Vessels or seeping bleeding was avoided, if occurred, coagulation was necessary. At the beginning of ESD development, four steps were involved in the different endoscopic instruments. No-knife change is the aim of ESD improvement to decrease the operation time with the low risk of bleeding and perforation.

Multi-function probe of hybrid knife realized the same device for submucosal injection, circular cutting, focus dissection and electrocoagulation hemostasis [2] (Figure 1). Hybrid knife combined the waterjet system and electrosurgical tip together and carried out the marking, injection and incision in one probe. Waterjet system of hybrid knife was a sophisticated control fluid system which performed medium injection and lesion elevation.

Injection fluid was not limited to normal saline and other media were also used to keep the pad shape longer [3]. It is possible for hybrid knife to replenish fluid immediately during endoscopic surgery. Good fluid cushion boarded surgical sites, exposed lesions and compressed blood vessels.

The broad surgical site provided a window to cut and peel around the mucosa of the lesion more safely [4]. The hybrid knife can shorten ESD operation time and reduce the bleeding and perforation in clinic surgery [5].

Hybrid knife was used to en bloc resection of bladder tumors and other fields, because of the advantages of hybrid's cutting tool such as cutting-edge fluid injection and no-change instruments during operation. The application of hybrid knife to en bloc resection has extended from superficial gastrointestinal tumors to non-invasive bladder tumors [6] [7]. With the rapid development of endoscopic technologies and instruments, hybrid knife was also applied to treat achalasia [8]. Beside on this, hybrid knife was carried out in clinical detection and

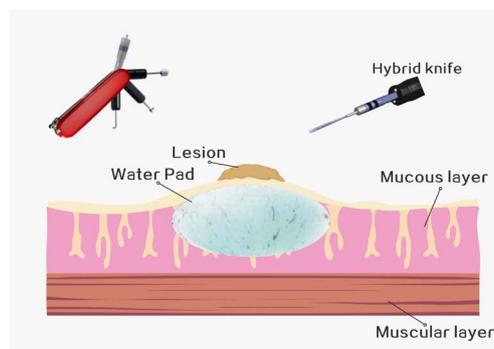


Figure 1. Comparison of cutting superficial tumor with traditional endoscopic knife and hybrid knife. Notes: According to the characteristics and functions of Hybrid knife, we draw this picture (Figure 1).

diagnosis, such as pathological tissue collection and pleural biopsy of early bladder cancer [9] [10].

In this article, we reviewed the application of hybrid knife system in endoscopic surgery. At first, we introduced the clinical research of the surgical treatment of bladder cancer, early gastric and cancer colorectal cancer by using hybrid knife under endoscope, and then discussed the application of hybrid knife in the collection of pathological tissues of early bladder cancer and the collection of biopsy specimens from pleural diseases. Finally, we introduced the research of Hybrid knife in related animal experiments, and discussed the feasibility of Hybrid knife in more clinical diseases in the future.

2. Traditional High-Frequency Electric Knife Used in Clinic

In endoscopic surgery, there are many traditional instruments, high-frequency electric knife is widely used in clinic. With the development of domestic medicine and the maturity of applied medical devices, domestic medical devices are becoming more mature. As early as 1995, the clinical doctors compared the domestic instruments with the imported instruments. The results showed that the performance of the domestic high-frequency electric knife could fully meet the requirements of the operation. The main performance of the domestic high-frequency electric knife system had reached the level of the same as imported product, and the price was lower than that of the foreign products [11] [12] (Table 1). Experts believed that domestic high-frequency electric knife is worth popularizing and suitable for clinic. However, due to the high current intensity of high-frequency electric knife, if it is used improperly, it is easy to cause serious harm to patients. Therefore, on the basis of these traditional instruments, combined with their advantages and disadvantages, new endoscopic instruments have been developed and used in clinic, and the hybrid knife is one of the new endoscopic treatment systems in nowadays.

3. The Application of Hybrid Knife in Endoscopic Surgery

3.1. Non-Muscle Invasive Bladder Cancer (NMIBC)

Among the 81,190 estimated newly diagnosed bladder cancer in the US in 2018,

Table 1. Comparison between domestic high-frequency electric knife and imported products.

Country	Model	Price	Power	Operation effectiveness
USA	Valleylab (SSE4)	expensive	1 - 300 w	100% success
USA	Force GSU	expensive	1 - 250 w	100% success
Germany	ERBE (T400)	expensive	1 - 400 w	100% success
China	GPD	1/5 of Valleylab (SSE4) products	1 - 350 w	100% success
China	ZARS	1/4 of Force GSU products	1 - 350 w	100% success

nearly 75% were non-muscle-invasive bladder cancer (NMIBC) [13]. 5-year survival rate of NMIBC reached 94% [14]. Transurethral resection of bladder tumor (TUEBRT) was the first choice of treatment NMIBC based on transurethral electroresection [14].

In 2013, Dr. Mundhenk *et al.* Firstly reported the use of Hybrid knife to perform TUEBRT on 16 NMIBC patients [15]. The average resection time was 27 minutes without significantly decrease of hemoglobin and other major complications [15]. Another study about the methods and postoperative effects of Hybrid knife in NMIBC surgery showed that the operation time was 35 minutes, without replacement of the surgical instrument in the four working stages: marking, elevation, incision/dissection and coagulation [7]. Therefore, four working stages were not disrupted by the instrument change and the operation time sharply decreased.

The researchers showed that Hybrid knife expanded the benefits of submucosal water cushion. Hybrid knife has been standard technique to keep the submucosal water pad intact during the dissection and focal resection and inject additional fluid according to the necessary [1] [2]. Animal research showed that the fluid cushion formed a selective edema in the submucosal to protect the mucosal layers. This protection was not limited to the separation mucosal layers from the focus, increased operation window but also included prevention of thermal damage. Meanwhile the fluid cushion increased the pressure of mucosal layers and compressed the blood vessels to decrease bleeding. So that Hybrid knife removed the en-block tumor without fragments and maximized the prognosis without bladder perforation or tumor implants [7]. Through the Hybrid knife technique, the tumor can be cut off by the whole piece, safe and effective postoperative results and curative effects can be obtained.

3.2. Early Gastric Cancer (EGC)

Endoscopic submucosal dissection (ESD) is a mature endoscopic technique for the treatment of early gastrointestinal epithelioma [16] [17]. ESD has become a treatment option for early EGC and is increasingly used in early esophagus and colorectal cancer. Many foreign researchers made a comparative study, it is about application of traditional knife and hybrid knife in endoscopic submucosal dissection, and compared the characteristics of hybrid knife and traditional incision knife in the treatment of gastric lesions. It shows that using hybrid knife technology can effectively shorten operation time and improve operation efficiency. Some researchers carried out a prospective study on 30 patients with early gastric cancer, the results show that ESD can obtain 100% complete resection rate and 90% overall resection rate of endoscope by using hybrid knife [6]. Research display [18], after the use of the hybrid knife, the performance of endoscopic submucosal stripping was increased by 28.9%, and the improvement was more significant in technically simpler parts, such as lesions under the stomach or less than 4 cm.

3.3. Colorectal Polyps and Superficial Tumors

The treatment strategy for colorectal polyps and superficial tumors has gradually turned from surgery to endoscopic resection. Compared with surgery, endoscopic resection was less invasive, which made patients recover faster and maintain normal intestinal function. ESD was a wide spread technique for the treatment of early superficial gastrointestinal tumors. ESD was operated in almost any location of the gastrointestinal tract [19] [20]. But whole resection of large superficial colorectal tumors was difficult by ESD because of the thin wall of the colon, the poor flexibility and elongation of the colon [21]. During endoscopic resection of lesions, colon circulation, intestinal motility, folding anatomy and surgical field of vision were major factors to impact the prognosis. In order to prevent complications such as perforation and uncontrollable bleeding, it was important to maintain a good image of the submucosal anatomical layer [21] [22]. Hybrid knife provided a good surgical exposure area to improve ESD safety and effectiveness. High-pressure injection liquid of Hybrid knife separates the focus from the muscular layer quickly and safely, and made the submucosal space visible. At the same time, the water pad remains the colon muscular layer intact and the water beam had little damage to it. Hybrid knife was very effective and safe in treating large superficial colorectal lesions that were not suitable for endoscopic mucosal resection (EMR) or endoscopic polypectomy [23]. There are clinical trials show that the combined use of water-jet hydrodissection, saline solution immersion, and the pocket-creation method to perform ESD can be an effective technique to remove colorectal polyps. The hybrid knife “probe mode” can be used safely and effectively in saline solution immersion. The resected specimen size was 120 × 80 mm, and the procedure time was 241 minutes. There was no perforation or bleeding either during or after the procedure [24].

3.4. Achalasia of Cardia (AC)

Achalasia is a primary esophageal dyskinesia functional disease. At present, the treatment methods included muscle relaxants, endoscopic botulinum toxin injection, balloon dilation and surgical myotomy [25]. Endoscopic esophageal sphincterotomy (POEM) is a new minimally invasive technique for the treatment of esophageal achalasia [26]. However, it is reported that gas-related complications after surgery, such as mediastinal emphysema and pneumothorax, with mucosal perforation up to 20%. At the same time, the average operation time was 68 - 114 minutes [27] [28].

Evidence from prospective randomized trials indicated that Hybrid knife technology significantly reduced the surgical processing time of POEM, also reduced the bleeding rate [8]. In this prospective randomized, 100 patients with achalasia were randomly divided into two groups: hybrid knife group, conventional group [8]. The experimental results showed that the average time of operation in the hybrid knife group was about 22.9 minutes, the operation time of the conventional group was 35.9 minutes, the hemostatic rate of the convention-

al group and the usage rate of the hemostatic clamp were higher than the hybrid knife group, and 96.5% of the patients had successful treatment. There are a lot of literature to describe conventional knife and hybrid knife used in clinical and animal experiments (Table 2), and the application of hybrid knife technology in some surgeries (Table 3).

3.5. Respiratory Diseases

Currently, more clinical workers begin to learn the hybrid knife technology, and apply it in clinical research. Hybrid knife is widely used in the treatment of digestive diseases. For example, it is used in early gastric cancer, achalasia of cardia, rectal polyps diseases [18] [25] [29] [30]. However, at present, some researchers have applied this technology to respiratory diseases, such as the diagnosis and treatment of bronchial mucosal tumors. Clinical workers have used hybrid knife to treat and diagnosis primary bronchial mucosa-associated lymphoid tissue (MALT) [33]. In this study, they applied a water-jet hybrid knife in biopsy excision of intracheal broad-based lesions. This is the first time that hybrid knife has used in bronchoscopy, and it has been successful. In addition, there were researchers used hybrid knife technology in the bronchial cyst and

Table 2. Comparison of the features of conventional knife and hybrid knife in surgeries.

Classification	Operation	Conventional knife				Hybrid knife				References
		Cases	Average time (min)	Hemorrhage (%)	Perforation (%)	cases	Average time (min)	Hemorrhage (%)	Perforation (%)	
Clinical trial	ESD	34	57.2	2.94	5.88	49	41.3	0	4.08	[29]
	ESD	59	35.0	4.85	3.39	58	27.5	1.64	1.72	[3]
	ESD	39	44.0	7.70	5.13	39	27.0	7.70	2.56	[18]
	STER	15	78.7	40.67	0	16	50.5	22.69	0	[30]
	POEM	50	35.9	0	0.02	50	22.9	0	0	[8]
Animal experiment	ESD	6	58.32	58.33	22.17	6	47.18	47.17	2.84	[31]
	ESD	20	68.7	20	10	30	44.6	13	13	[4]
	ESD	13	9.5	23.08	0	14	8.0	14.29	7.14	[32]

Notes: STER: submucosal tunnel endoscopic resection; ESD: Endoscopic submucosa dissection; POME: Peroral endoscopic myotomy.

Table 3. The application of hybrid knife technology in some surgeries.

Disease	Operation	Cases	Average time (min)	Perforation	References
NMIBC	TUR-BT	16	27	0	[15]
Giant rectal polyp	ESD	1	241	0	[24]
Achalasia of cardia	POEM	11	100.7	0	[27]
Achalasia of cardia	POEM	16	114	0	[8]

Notes: NMIBC: Non-muscle invasive bladder cancer; TUR-BT: Transurethral resection of bladder tumor; ESD: Endoscopic submucosa dissection; POME: Peroral endoscopic myotomy.

deep benign fibrous histiocytoma [34] [35]. They think the common complications in the treatment of tumors of the membranous trachea are bleeding and perforation. The combination of lelectrocautery and electrocoagulation may decrease the risk of bleeding. The hybrid knife can create an adequate submucosal cushion, and the direction of dissection can be targeted tangentially to the surface of the lesion at the submucosal layer to minimize the risk of perforation. At present, hybrid knife technology plays a key role in the clinic. The researchers have more in-depth study of it, and the field of application is become more extensive, and they have got good results in clinical diagnosis and treatment. In the future, hybrid knife technology is likely to be applied to radical surgery of airway tumor.

4. Disease Detection

4.1. Pathological Tissue Collection of Early Bladder Cancer

For early bladder cancer diagnosis, Hybrid knife technique also has a good function of tumor pathological tissue collection. Because of high 5-year survival rate of early bladder cancer, fine diagnosis completely improved the life quality of patients. Preservation ordered structure and prevention disordered deformation are the key of pathological tissue collection for early bladder cancer diagnosis. Some traditional methods may have disordered cutting directions, disorganized and broken tissues, which were not conducive to detection, leading to erroneous reports of anatomical and pathological detection, thus making uncertainty in the final diagnosis of patients and delaying in treatment [9]. Hybrid knife did not need to change the instrument or perform transverse tumor resection during the operation, so that Hybrid knife preserved the integrity of the tissue and made the accurate detection of histopathology. And the pathological examination department believed that the positive degree of tumor process, vascular invasion and bladder muscle invasion were easily determined both macroscopically and microscopically by using the Hybrid knife technique to obtain pathological tissues [7]. It was helpful to determine the depth of invasion, degree of differentiation, vascular and lymphatic invasion of the lesion and to evaluate the prognosis of the patient.

4.2. Biopsy Specimens Obtained from Pleural Diseases

Hybrid knife was applied to the definite diagnosis of pleural diseases and sufficient samples were obtained from the thickened pleura [10]. Yan Yin *et al.* described three patients with pleural effusion of unknown cause and performed pleural biopsy using high pressure water jet [36]. The cases showed that Hybrid knife was more effective in pleural biopsy when encountering malignant or benign fibrous thorax. Hybrid knife took biopsy in no more than 15 minutes, and its function of high-pressure water jet makes submucosal injection easier than conventional injection. The size of biopsy specimen obtained with Hybrid knife is significantly larger than that obtained with traditional methods, such as injec-

tion needle and triangular sharp knife [37]. Therefore, the Hybrid knife system is a time-saving, convenient, safe and effective technology in the application of video-assisted thoracoscopic biopsy specimens. The effectiveness and optimal indications of this technique need further research to explore and prove.

5. Conclusion and Prospect

As a new type of endoscopic treatment instrument, hybrid knife is widely used in clinic, especially in the treatment of gastrointestinal diseases and urinary diseases. The water jet hybrid knife performed endoscopic liver wedge resection through the natural opening of the pig model. This technique still has a long way to go to reach the same level as the commonly used segmental keratectomy [38]. Some researchers have performed transumbilical endoscopic cholecystectomy in a pig non-survival model using the water jet hybrid knife technique. The operation had achieved some results, they believed that this technique still need further research before it can be applied in clinic treatment [39]. Although these animal experimental research results are still in the preliminary exploration stage and have not been applied to clinical, these studies suggest a new direction for the application of hybrid knife technology and provide a new scheme for minimally invasive surgical treatment.

The hybrid knife system technology under endoscope can be applied to the treatment of various diseases, which has important clinical significance and was worth further study and exploration. In-depth study and discussion of hybrid knife technology, its diagnosis and treatment of diseases have theoretical significance and clinical value. At present, hybrid knife technology is mainly used in digestive system. To explore the application of hybrid knife system technology in other diseases or surgeries, it will be a new choice for ESD development to provide clinical diagnosis and treatment of diseases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviation Note List

Abbreviation	Full Name in English
ESD	Endoscopic Submucosal Dissection
NMIBC	Non-Muscle Invasive Bladder Cancer
TUEBRT	Transurethral Resection of Bladder Tumor
EGC	Early Gastric Cancer
EMR	Endoscopic Mucosal Resection
AC	Achalasia of Cardia
POEM	Endoscopic Esophageal Sphincterotomy
STER	Submucosal Tunnel Endoscopic Resection
TUR-BT	Transurethral Resection of Bladder Tumor
MALT	Mucosa-Associated Lymphoid Tissue