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The Usefulness of Capsule Endoscopy for Small Bowel Tumors

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Video capsule endoscopy (VCE) has expanded the range of endoscopic examination of the small bowel. The clinical application of VCE is mainly for obscure gastrointestinal bleeding (OGIB) and small bowel tumor is one of the clinically significant diagnoses of VCE, often requiring subsequent invasive interventions. Small bowel tumors are detected with a frequency of around 4% with VCE in indications of OGIB, iron deficiency anemia, unexplained abdominal pain, and others. Protruding mass with bleeding, mucosal disruption, irregular surface, discolored area, and white villi are suggested as the VCE findings of small bowel tumor. Device assisted enteroscopy (DAE), computed tomography enteroclysis/enterography and magnetic resonance enteroclysis/enterography also have clinical value in small bowel examination and tumor detection, and they can be used with VCE, sequentially or complementarily. Familial adenomatous polyposis, Peutz-Jeghers syndrome, melanoma, lymphoma, and neuroendocrine tumor with hepatic metastasis are the high risk groups for small bowel tumors, and surveillance programs for small bowel tumors are needed. VCE and radiological imaging have value in screening, and in selected cases, DAE can provide more accurate diagnosis and endoscopic treatment. This review describes the usefulness and clinical impact of VCE on small bowel tumors. **Clin Endosc 2016;49:21-25**

Key Words: Small bowel; Neoplasms; Capsule endoscopy

INTRODUCTION

The small intestine is the largest organ in the body and occupies over 90% of the surface of the gastrointestinal tract. However, diagnosis of small bowel tumor is rare in practice.[1] Rapid epithelial turnover with rapid intestinal transit, abundant lymphoid tissue and immunoglobulin A secretion, neutral pH, and lower bacterial load are responsible in explaining the extremely low tumorigenic property of the small intestine. Only 3% to 6% of all gastrointestinal neoplasms develop in the small intestine and over 40 different histological types of tumors are diagnosed. Adenoma and mesenchymal tumors are the most common ones. Malignant tumors include neuroendocrine tumor, adenocarcinoma, lymphoma, and sarcoma in order of frequency.[2] Skin melanoma, colorectal cancer, prostate cancer, and lung and breast cancers are the common origins of metastatic small bowel tumors.

Capsule endoscopy is a small capsule type digital camera which can be swallowed orally and takes images of the small bowel lumen. The major indications for small bowel video capsule endoscopy (VCE) are obscure gastrointestinal bleeding (OGIB), suspicious small bowel Crohn disease (CD), unexplained iron deficiency anemia (IDA), and unexplained abdominal pain. The diagnostic yield of VCE is any detectable lesion which can explain the clinical manifestation, and small bowel tumor is one of the significant diagnoses. The frequency of small bowel tumor in VCE for all indications ranges from 2.4% in European study[3] to 4.3% to 9.5% in a Korean study.[4,5] Guidelines for VCE in small bowel diseases are published in Korea and Europe.[6-8] The clinical value of VCE for small bowel tumors are reviewed here in comparison to other small bowel examination modalities.

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THE VAGUE CLINICAL PRESENTATION OF SMALL BOWEL TUMORS

There is no definite clinical manifestation suggestive of small bowel tumor. Most clinical presentations are vague and non-specific. Therefore, most cases of small bowel tumors are unexpectedly diagnosed in the course of a thorough diagnostic workup for patients with OGIB, unexplained IDA, and unexplained abdominal pain. Obscure or overt bleeding is the most common presentation and occurs due to ulceration of tumors. Patients presenting with OGIB are proven to have small bowel tumor in around 6% of cases.[9-12] Two out of 110 patients presenting with unexplained abdominal pain were revealed to have small bowel tumor.[13] Nausea and vomiting can occur when obstruction develops, especially in a form of intussusception. Weight loss is an alarming sign requiring a thorough investigation, especially in elderly patients, and presenting in 30% to 50% of small bowel tumors. However, small sized tumors are mostly asymptomatic. When the signs and symptoms of small bowel tumor become obvious, it can already be in an advanced stage, and have metastasis. The vagueness of presentation can delay the diagnosis and make the prognosis less favorable in malignant tumors. In short, small bowel tumors should be listed as a possible diagnosis when patients present with OGIB, unexplained abdominal pain, nausea, and vomiting and weight loss. Suspicious findings on radiological imaging are also a significant suggestion of small bowel tumors.

High-risk group of small bowel tumors should be borne in mind. Follicular lymphoma, metastatic neuroendocrine tumor, and malignant melanoma often have small bowel involvement.[14,15] The risk of small bowel adenocarcinoma is increased with long lasting small bowel CD and inherited polyposis syndromes including familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), and Lynch syndrome (hereditary non-polyposis colorectal cancer). Small bowel surveillance strategies are on the table for FAP and PJS. Celiac disease increases the risk of small bowel T cell lymphoma and adenocarcinoma in Western population.[16] Smoking and red meat intake are related to small bowel cancer as well as colorectal cancer.

THE VALUE AND PRIORITY OF VCE IN DIAGNOSIS OF SMALL BOWEL TUMORS

Small bowel investigation is now possible and new modalities include VCE, device assisted enteroscopy (DAE), computed tomography enteroclysis/enterography (CTE), and magnetic resonance enteroclysis/enterography (MRE). Push enteroscopy and sonde endoscopy were the sole endoscopic tools in the past, but now are scarcely used in clinical practice. Small bowel series, small bowel follow-through (SBFT), and enteroclysis are radiological imagings. In the past, enteroclysis was accepted as the most accurate diagnostic tool for small bowel disease, but caused high inconvenience both for physician and patient, preventing routine clinical usage.

When OGIB and IDA are not explained otherwise, and small bowel tumors are suspected, European guidelines recommend early use of VCE.[8] In OGIB, VCE yields better diagnostic outcomes than SBFT and enteroclysis, and the diagnostic yield was 50% to 75%.[17] VCE provided superior diagnostic yields to push enteroscopy, 50% to 67.2%, and 20% to 28%, respectively.[18-20] However, because the reach of push enteroscopy is reliable up to proximal jejunum, in case of the small bowel tumor detected on VCE, and located in proximal jejunum, push enteroscopy can be employed to obtain tissue biopsies. VCE and DAE showed comparable diagnostic yields. When DAE was performed with one sided approach, VCE provided better diagnostic yield than DAE.[21]

The findings of small bowel tumor in VCE are not always easily interpreted. An experimental proposal by Chinese researchers recently described a scoring system to interpret VCE findings in small bowel tumors. The proposed tumor score was composed of five components: bleeding, mucosal disruption, an irregular surface, color, and white villi. These can be scored for probability of mass lesions seen at capsule endoscopy.[22] This system is not perfect yet, but these factors have to be kept in mind. Contrarily, innocent bulging can be characterized as a mass with ill-defined boundaries, larger diameter than height, invisible lumen with a mass like contour, and mass image lasting less than 10 minutes.[23] MRE and CTE reported similar diagnostic yields to VCE. When MRE was performed in patients with suspicion of small bowel tumor, the overall sensitivity, specificity, and accuracy in identifying patients with small-bowel lesions were 86%, 98%, and 97%, respectively.[24] In a study of small bowel diseases, including small bowel tumor, CD, and others, the diagnostic specificity of MRE was higher than that of VCE (0.97 vs. 0.84, p=0.047), whereas sensitivity was similar (0.79 vs. 0.74, p=0.591).[25] In a small radiological study for OGIB, CTE demonstrated better diagnostic yield than VCE, in term of sensitivity (88% vs. 38%).[26] Authors reported that, CTE detected 9 of 9 tumors but VCE only 3 of 9 tumors. This is a kind of deviated result from others, and we can assume that the small bowel tumors with exophytic growth may possibly be overlooked by VCE. Study populations and properties of small bowel tumors also affect the study outcomes, and we cannot easily determine the superiority of a single examination to another. MRE and CTE can provide the intra- and

extra-luminal images combined with contrast enhancement and functional images. MRE and CTE may serve as the first-line diagnostic tool along with VCE for patients with OGIB and suspicion of small bowel tumors.

The detection of small bowel tumors with DAE was dependent on clinical suspicion, and was very seldom due to a general indication. In patients who were suspected of having small bowel tumors in other studies, there was a markedly high rate (47%) of tumor diagnosis with DBE.[27] In Korean studies, DAE for OGIB, detected small bowel tumors in 17.4% to 19.7% cases and small bowel tumors are common following small bowel ulcer and vascular lesion.[9,28] Benign polyps are the most common (33.9%), followed by mesenchymal tumors, lymphoma, adenocarcinoma, and metastatic cancers in sequence.[28] Diagnostic concordance was 78.3% for small bowel tumor between DAE and VCE.[28] while it was 7% to 20% in Japanese reports.[12,29] The higher small bowel tumor detection rate of DAE over VCE must result from the patient selection difference as well as the better maneuverability. The risk of false negative results should be always taken into account in VCE.[30] VCE may easily miss the tumors which are located in duodenum or proximal jejunum due to rapid transit. The subepithelial tumors with intact overlying mucosa also can be missed with VCE. Another critical advantage of DAE over VCE is the possibility of endoscopic treatment, mainly polypectomy. Patients with PJS and FAP are at high risk of small bowel polyps, and polypectomy using DBE can prevent the possibility of small bowel obstruction and the need of subsequent small bowel resections in PJS.[31-33] DBE is comparably effective but less invasive than intraoperative endoscopy in patients with PJS.[32] DAE, however, often fails to achieve complete small bowel examination, elicits significant discomfort, radiation exposure, and leads to complications in patients during examination. Therefore, DAE might be better employed in a highly selected group, while VCE is used initially to detect patients with possible small bowel tumors, from the larger group with OGIB. DAE should be considered in preference to VCE to confirm the diagnosis through visualization and histology, when small bowel tumors are suspected with prior imaging studies.[8]

The only procedure related complication of VCE is capsule retention. Capsule retention occurred in 2.5 % of all cases.[33] CD and intestinal tuberculosis often lead to luminal stenosis and capsule retention. Small bowel tumors are also one of the major diseases associated with capsule retention. However, on suspecting small bowel tumor, patency investigation before VCE is not needed.[8] Capsule retention occurs only at the point of pathology and can guide the surgery.

HIGH-RISK GROUP SURVEILLANCE FOR SMALL BOWEL TUMOR

Small bowel tumor surveillance in high-risk group can result in early detection of disease and make the prognosis better. VCE as well as CTE and MRE can help in surveillance. Inherited polyposis syndromes, melanoma, lymphoma, and neuroendocrine tumor with hepatic metastasis are well known high-risk groups of small bowel tumors. Inherited polyposis syndromes including FAP and PJS are at increased risk of small bowel adenocarcinoma as well as colorectal cancer.

In patients with FAP, duodenal adenomatosis commonly develops and increases the risk of cancer with age. The cumulative lifetime risk of duodenal adenomatosis is 88% and the cumulative incidence of cancer was 18% at 75 years of age.[34] Spigelman staging is a well known predictor system for malignant changes in duodenal adenomatosis, and consists of the number of polyps, size, histology, and degree of dysplasia.[35] Spigelman stage IV on esophagogastroduodenoscopy (EGD) predicts a cancer risk of 33% at 75 years of age. Surveillance of the proximal small bowel in FAP is properly performed using conventional forward viewing EGD and side-viewing duodenoscopy.[8] Up to 70% of patients with FAP have adenomatous polyps in jejunum and ileum; however, cancer has been rarely reported. VCE as well as CTE or MRE can be considered to detect polyps in the rest of the small bowel, but the clinical relevance is not established yet.

PJS is a hereditary polyposis syndrome and patients with PJS often present polyp related symptoms from an early age. Intussusceptions and anemia are common in childhood and need surgery. Later in life, polyps can progress to cancer, and the relative risk of small bowel cancer is about 520 (95% confidence interval, 220 to 1,306).[36] Increased risk of cancer is identified in small bowel as well as esophagus, stomach, colon, pancreas, breast, uterus, and ovary. The lifetime cumulative risk for all cancer was 93% at 64 years of age. Prophylactic polypectomy can reduce the development of polyp related complications. Screening EGD and colonoscopy are recommended, beginning at the age of 18, with 2- to 3-year intervals.[37] Small bowel surveillance is also needed to perform timely polypectomy and reduce polyp related complications and future risk of small bowel cancer. VCE is recommended as an adequate surveillance method as well as MRE in European guidelines.[8] VCE has a better sensitivity in detecting small bowel polyps than SBFT and MRE, especially for small polyps. VCE and MRE both equally detect larger polyps >1.0 cm.[38] MRE has an advantage in polyp localization and accurate size measurement. Polyps >1.5 cm is better defined with MRE, and false negative results may occur with VCE.[39] Small bowel screening using VCE is recommended to be preformed

every 3 years if polyps are found at the initial examination, from age of 8 years, or earlier if the patient is symptomatic.[40] If few or no polyps are found at the initial examination, screening should commence again at the age of 18 years.[40] DAE is more accurate in detecting small bowel polyps than VCE, but DAE may be better employed following VCE for the purpose of endoscopic treatment. Polyp size is the most important factor for polyp related complications. Polyps >1.5 cm often result in intussusception and are the indication for DAE polypectomy. However, when there is a concern about safe polypectomy for a larger polyp or which is in an unreachable position with DAE, intraoperative enteroscopy could be considered.

Lynch syndrome is another well-known condition associated with an increased risk of small bowel cancer. Lynch syndrome is caused by a germline mutation in one in the mismatch repair (MMR) genes MLH1, MSJ2/Epcam, MSH6, or PMS2. Asymptomatic mutation carriers are recommended to undergo surveillance colonoscopy every 1 to 2 years, starting from the age of 20 to 25 years. The estimated lifetime risk for small bowel cancer is 4.2%,[41] and is similar to that of colorectal cancer in the general population. Because the small bowel cancer localization is almost even in duodenum, jejunum, and ileum, screening with conventional EGD is recommended to detect both stomach and small bowel cancer since small bowel cancer localization is almost even in duodenum, jejunum and ileum, In a recent study with VCE, the prevalence of small-bowel tumor in an asymptomatic mutation carrier of Lynch syndrome was 1.5%. However, all tumors were located in the duodenum and within reach of conventional EGD.[42]

CONCLUSIONS

Small bowel tumors are diagnosed in about 4% of cases of OGIB, and other small bowel study indications. Clinical suspicion of small bowel tumor can raise the diagnostic yields in VCE and DAE. VCE and MRE/CTE can serve as proper screening tools for small bowel tumors in patients presenting with small bowel symptoms. DAE might be better employed for endoscopic treatment or biopsy after VCE or MRE/CTE with impression of small bowel tumor. High-risk group of small bowel tumors includes patients with FAP, PJS, Lynch syndrome, and lymphoma and skin melanoma. VCE as well as MRE/CTE are promising in small bowel surveillance.

Conflicts of Interest

The authors have no financial conflicts of interest.

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