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# The role of capsule endoscopy in the detection of small bowel disease

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**Rezumat**

***Rolul videocapsulei endoscopice în detecția afecțiunilor situate la nivelul intestinului subțire***

Videocapsula endoscopică (VCE) poate identifica leziuni ale intestinului subțire care ar fi greu de detectat prin alte metode. Am selectat un număr de 53 de pacienți cu simptome digestive, la care endoscopiile superioare și inferoare nu au identificat leziuni. Pacienții au fost clasificați în trei grupe, pe baza indicațiilor majore pentru explorarea VCE: grupul unu – sângerări obscure gastrointestinale: grupul doi – simptome abdominale nescpecifice, grupul trei – monitorizarea unei patologii preexistente. Am obținut valori mari pentru predictivitate, sensibiliate și specificitate în diagnosticul sângerărilor obscure gastrointestinale. VCE a fost de asemenea utilă în detectarea și evaluarea extensiei bolii Crohn și a bolii celiace. VCE este de asemenea capabilă de a detecta tumorile intestinului subțire cu suficientă acuratețe, putând fi folosită pentru monitorizarea pacienților cu afecțiuni ereditare premaligne, cum ar fi polipoza familială. Au existat câteva efecte adverse ușoare, fără complicații majore. În concluzie, VCE este o investigație sigură și eficace în detectarea leziunilor intestinului subțire.

**Cuvinte cheie:** videocapsula endoscopică, sângerare intestinală obscură, boală Crohn, boală celiacă, tumori ale intestinului subțire

**Abstract**

Videocapsule endoscopy (VCE) can identify lesions in the small bowel which would otherwise be hard to detect. We have selected 53 patients with digestive symptoms in which upper and lower endoscopy had provided no findings. Patients were classified into three groups, based on their main indication for VCE exploration: group one - obscure gastrointestinal bleeding (OGIB); group two - unspecific abdominal symptoms; group 3 - monitoring of a prior known pathology. We found that VCE has high predictive values, sensibility and specificity in the diagnosis of OGIB. VCE was also useful in the detection and extent evaluation of lesions in Crohn's and celiac disease. VCE is also able to detect tumors of the small bowel with sufficient accuracy, and can be used to monitor patients with hereditary pre-malignant diseases such as FAP. There were few light adverse effects and no major complications. We conclude that VCE is a safe and effective procedure for the detection of small bowel lesions.

**Key words:** videocapsule endoscopy, obscure gastrointestinal bleeding, Crohn's disease, celiac disease, small bowel tumors

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## Introduction

The small bowel is one segment of the digestive system that is hard to examine because of its particular location and

anatomy. The exploration of the jejunum and ileum presents great significance towards the detection of a number of diseases; however, until recently there were no techniques that could offer an examination both complete and diagnostically satisfactory (1).

Recently, technological progress has led to the development of new diagnostic methods. Video capsule endoscopy (VCE) allows for the non-invasive exploration of any segment of the digestive system. Presently it is used for the exploration of the small bowel, where it can identify lesions that were otherwise undetectable (1-5).

The number of uses for VCE is continually increasing. It has been used successfully for the diagnosis of obscure gastrointestinal bleeding (OGIB), Crohn's disease, celiac disease, vascular and tumoral lesions (6-21).

The main disadvantage of capsule endoscopy consists in its inability to carry out therapeutic maneuvers or to take biopsies. Therefore, it continues to represent a purely diagnostic technique. These shortcomings can be, however, counterbalanced by the use of enteroscopy (22).

## Patients and Methods

### *General characteristics of the study group*

Our retrospective study has included 53 patients from the Internal Medicine and Gastroenterology departments of Craiova Emergency Hospital admitted between June 2008 and August 2010.

Inclusion criteria were represented by suspected small bowel pathologies that were inaccessible to non-surgical investigative procedures. Clinical data consisted mainly of unspecific symptoms that would generally suggest an obscure gastrointestinal bleeding or the presence of inflammatory or tumoral lesions. All patients had undergone upper and lower endoscopies that had not provided any findings that could offer or at least suggest a diagnosis.

Exclusion criteria consisted of clear contraindications for VCE, and 10 patients were excluded from the group. All had antecedents of intestinal occlusion, six of them due to chronic mesenteric ischemia and four due to invagination or volvulus.

The remaining 43 patients (19 men and 24 women) underwent VCE investigation, followed by surgery, where necessary.

The patients were classified into three groups, based on their main indication for VCE exploration. The first group consisted of patients with either iron-deficiency anemia (IDA) of unknown origin or obscure gastrointestinal bleeding (OGIB) – 19 patients; the second group consisted of patients with unspecific abdominal symptoms (chronic diarrhea, diffuse abdominal pain) – 17 patients; the third group consisted of patients that needed evaluation or monitoring of a known prior pathology (surgically-removed intestinal tumor, known Crohn's disease, familial adenomatous polyposis (FAP), cancer of unknown origin) – 7 patients.

### *Method*

Preparation consisted of fasting for at least 12 hours before capsule ingestion. Two liters of polyethylene-glycol solution were administered orally, 16 to 12 hours before the exploration. Patients were allowed to drink clear liquids 2 hours after capsule ingestion and were given light meals after 5 hours.

The images taken by the capsule were recorded by a belt-mounted device connected to eight sensors placed on the abdomen of the patient. The recorder was worn for 8 hours (the lifetime of the battery) without impairing usual activities of the patient. The images taken were analyzed by a gastroenterologist.

All patients gave informed consent before the VCE examination, consisting of a detailed explanation of the procedure and both its diagnostic advantages and its risks.

### *Statistical analysis*

The results were analyzed using descriptive statistics. The statistical indicators included: standard deviation, variation coefficient, standard mean error, 95% confidence interval.

## Results

### *Group description*

A number of 43 remaining patients were included in our study, after the exclusion of 10 cases with clear contraindications for the ingestion of the videocapsule. Ages ranged from 15 to 82 years, with a mean age of 58.27 years, standard deviation of 15.08, CI 95% ±6.30. Sex distribution slightly favored women, with a ratio of 1.3 to 1. There were 19 men (44%) and 24 women (56%). Most patients came from an urban environment (28 patients – 65%).

### *Group distribution – indications for VCE exploration*

Based on the indication for VCE exploration, the patients were divided into three groups: IDA of unknown origin / OGIB, unspecific abdominal symptoms and monitoring and evaluation of a prior disease. Patient distribution based on unspecific signs and symptoms, manifestations of undetermined origin or prior known diseases are detailed in *Table 1*.

***Table 1.*** *Patient distribution based on inclusion criteria*

| Inclusion criteria | Number |
|---|---|
| Abdominal pain | 7 |
| Chronic diarrhea | 10 |
| IDA of unknown origin / OGIB | 19 |
| Lymph node metastasis of unknown origin | 1 |
| Surgically-removed intestinal tumor | 2 |
| FAP | 1 |
| Known Crohn's disease | 3 |
| Total | 43 |

*OGIB*

Obscure gastro-intestinal bleeding (OGIB) is defined as the absence of an identifiable source for a recurrent or persistent digestive bleeding. A total of 19 patients (44%) underwent VCE exploration after being subjected to standard upper and lower endoscopy that did not identify any source for a GIB. Clinically, the patients had manifesting intestinal bleeding (melena, hematochezia), positive tests for occult bleeding and / or IDA of unknown origin. VCE has visualized intestinal bleedings in 15 cases (79% of the group), including active bleeding, ulcerations, angiodysplasia and polyps.

Active bleeding (fresh blood) was identified in two cases. The first patient had presented with lower GIB and severe IDA. VCE has shown large angiectasias in the distal ileum and the caecum, with oozing hemorrhage. For the second patient, the source of the bleeding was shown to be Vater's papilla.

Possible sources of bleeding were detected in 13 other patients (69% of group), without any active bleeding at the moment of the investigation. The most common finding was angiodysplasia (*Fig. 1*) detected in seven patients, with locations in the proximal small bowel (four patients), in the distal small bowel (one patient), in both the proximal and distal small bowel (one patient) and in the caecum (one patient). In another patient VCE showed an ulcerated submucous tumoral formation in the proximal jejunum, which was suggestively the cause of the OGIB. In two other cases, typical ulcerations in the distal ileum were identified as Crohn's disease. Also, in three cases we found polyps to be the possible source of the OGIB (*Fig. 2*).

In one female patient where VCE had identified an angiodysplasia that could have been the cause for her IDA, the source of the bleeding was later proven to be gynecological, and in four patients VCE did not find any causes for the OGIB.

Consequently, the positive and negative predictive values (PPV and NPV) of VCE exploration in the case of OGIB / IDA were, in our study, 93.3% and 100%, respectively. Sensibility and specificity were 100% and 80%, respectively. (*Table 2*)

*Unspecific abdominal symptoms*

Our second group comprised 17 patients (39.5% of total) that presented with unspecific abdominal symptoms. Of

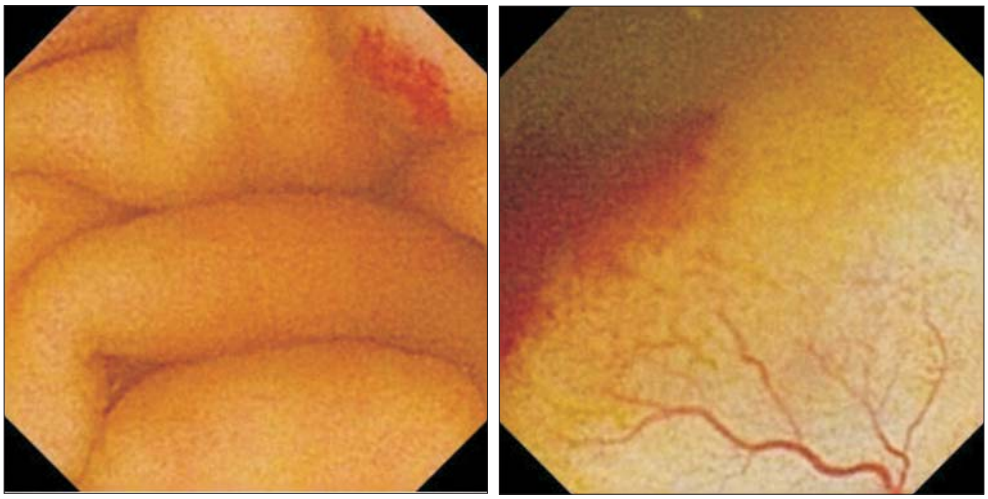

***Figure 1.*** *Telangiectasia and active bleeding as shown by VCE*

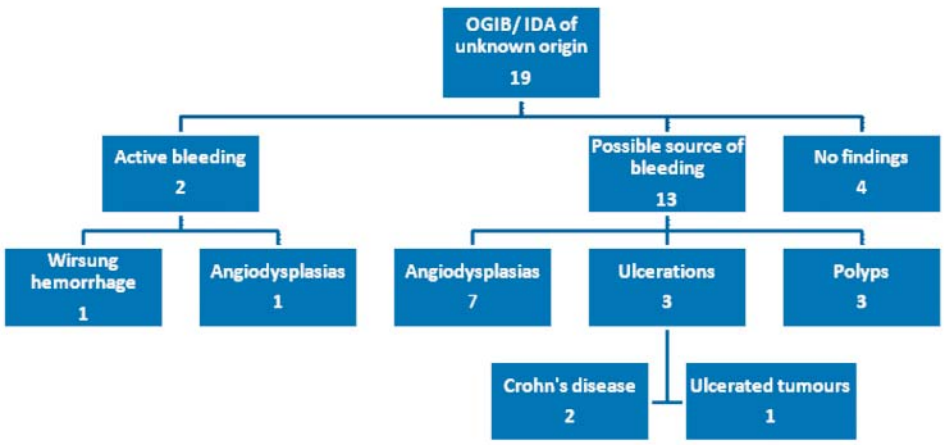


***Figure 2.*** *VCE results in OGIB / IDA of unknown origin*

***Table 2.*** *Diagnostic rates of VCE exploration for OGIB / IDA of unknown origin*

| | | monitoring | | |
|---|---|---|---|---|
| | | + | - | total |
| VCE | + (source) | 14 | 1 | 15 |
| | - (no source) | 0 | 4 | 4 |
| | total | 14 | 5 | 19 |

| | | |
|---|---|---|
| sensibility | = | 100.00% |
| specificity | = | 80.00% |
| PPV | = | 93.33% |
| NPV | = | 100.00% |

these, 10 patients (59% of group) had chronic diarrhea, and 7 patients (41% of group) had abdominal pain.

Of the 17 patients, VCE exploration found four with Crohn's disease, one with celiac disease and nine with intestinal tumors, of which five were malignant and four were benign. No lesions were found in three of these patients (*Fig. 3*).

In four of the cases the macroscopic aspect suggested the presence of Crohn's disease. In three of them VCE images showed diffuse mucosal ulcerations of variable diameters up to 1.5 cm, with the axis parallel to the length of the intestinal wall, while the other case they were suggestive for the chronic phase, showing an inflammatory tuberculoid granuloma.

In the case of one patient that was investigated because of chronic diarrhea, we could see modifications of the intestinal mucosa with nodularity, atrophy of the villosities, cobblestone images and scalloping folds – typical for celiac disease (*Fig. 4*). The mucosa progressively regained its normal aspect towards the distal ileum, with the reemergence of villi; therefore, we did not only diagnose celiac disease by VCE but also evaluate its extent. No tissue sampling was available from prior endoscopies.

In one patient with chronic abdominal pain and moderate anemia, VCE showed an irregular tumor, prominent in the intestinal lumen, images that were considered suggestive for adenocarcinoma. Surgical resection and histology showed it was an ulcero-vegetative and infiltrative tumor with moderately differentiated adenocarcinoma structure.

In one woman who had chronic pain in the left iliac fossa with loss of appetite and vomiting, VCE showed a prominent, slightly discolored tumor. Surgically it was a well delimitated tumor of 3 cm in diameter covered by a white-yellow ulcerated intestinal mucosa. Histologically, the aspect pleaded towards neuroendocrine carcinoma.

The two patients with malignant stromal tumors presented with abdominal pain that intensified after meals. Tumoral

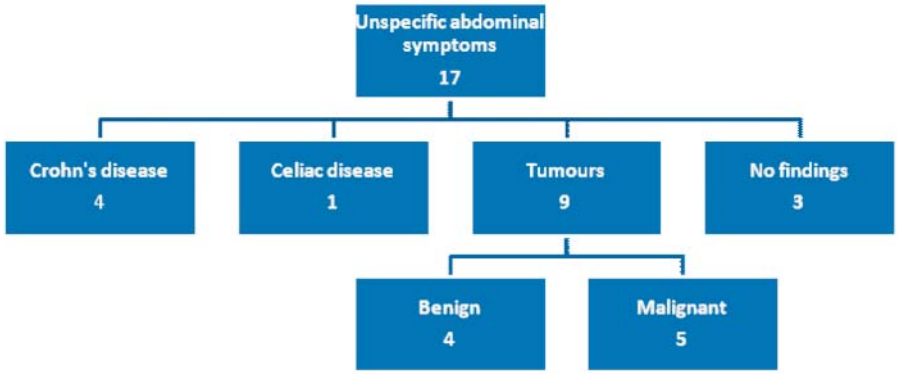


***Figure 3.*** *VCE results for patients with unspecific abdominal symptoms*

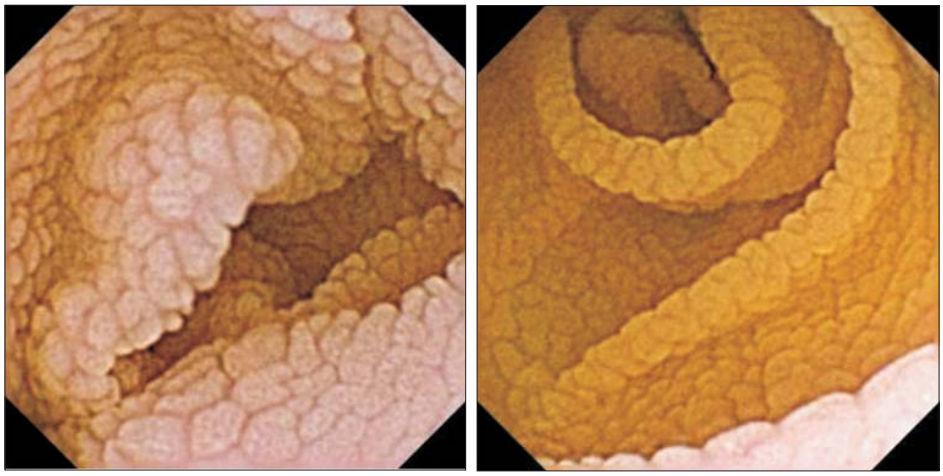

***Figure 4.*** *Characteristic aspects of celiac disease, as shown by VCE*

masses were identified by VCE as single, circumscribed tumors, oval or lobulated in shape, from 3 to 5 cm in diameter, with visibly raised mucosa (*Fig. 5*), which was ulcerated in one of the cases. Surgical resection was needed, and both cases showed degenerative modifications that are characteristic for malignant stromal tumors.

Two of the benign tumors were labeled as GISTs (one stromal mixoid tumor and one tumor with neural differentiation). Except for the lack of mucosal ulcerations, the aspect was similar to that of the malignant GIST tumors; therefore surgical resection was again recommended. There was no perfect delimitation between the muscular tissue and the tumoral cells, but there were no other histological criteria to suggest malignancy.

In two other patients that had short episodes of abdominal pain, loss of appetite and vomiting, VCE found small prominent masses with smooth surfaces and slightly discolored compared to surrounding mucosa. This was consistent with a diagnosis of sessile polyps (*Fig. 6*). Histological analysis after later endoscopic resection revealed them to have a tubular adenomatous structure.

In one woman that presented with abdominal pain, vomiting and loss of appetite, VCE revealed a deformed duodenal papilla, significantly different in color compared to surrounding mucosa. Endoscopic biopsies revealed it to be a papillary carcinoma. Final diagnosis was carcinoma of the duodenal papilla.

*Monitoring / evaluating prior pathology*

The third group consisted of seven patients (16% of total) who were admitted for either the evaluation or the monitoring of an already known disease. Two of them had undergone segmentary enterectomy for jejunal neurofibroma, three had Crohn's disease, one patient had FAP and one had lymph node metastases without a known point of origin (*Fig. 7*).

In one woman who had surgery for jejunal neurofibroma and a rectal highly dysplastic polyp that was removed endoscopically, the intestinal mucosa showed marked atrophy of the villi, with cobblestone aspect and scalloping folds, fissures, mosaic aspect, loss of circular folds and mucosal nodularity. This aspect was specific for celiac disease.

The second patient with prior surgically removed jejunal tumors, the VCE exploration did not show any macroscopic modifications.

The FAP patient had numerous polyps and, in the terminal ileum, one irregular, prominent tumor that was considered to likely be an adenocarcinoma, diagnosis that was confirmed by histology after the surgical intervention.

In one patient that presented with left supraclavicular adenopathy VCE exploration did not find any small bowel lesions.

Finally, three of the patients had known Crohn's disease, and were admitted for the evaluation of the extension of the disease. VCE did not show any lesions specific for extension in these patients. Prior endoscopies did not provide tissue samplings for these patients.

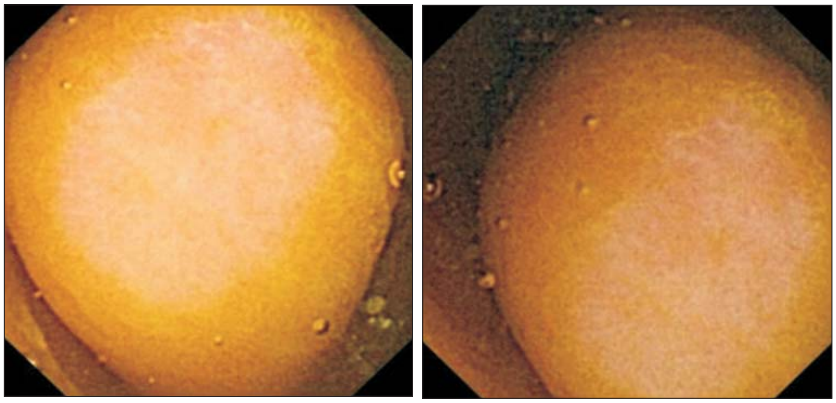

***Figure 5.*** *Stromal tumors – VCE aspect*

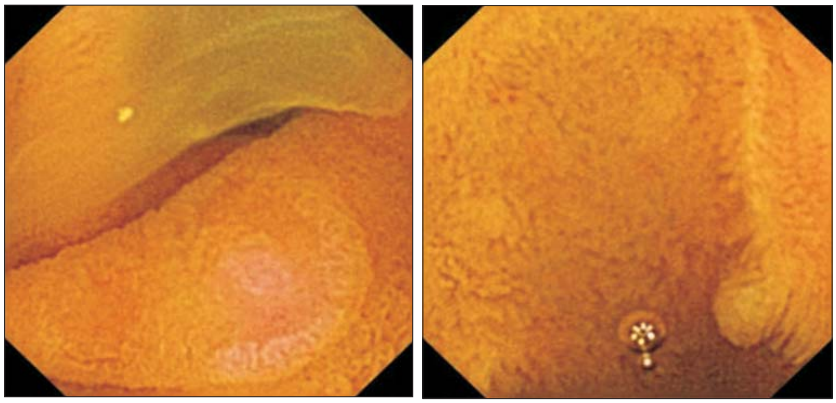

***Figure 6.*** *Small bowel polyps*

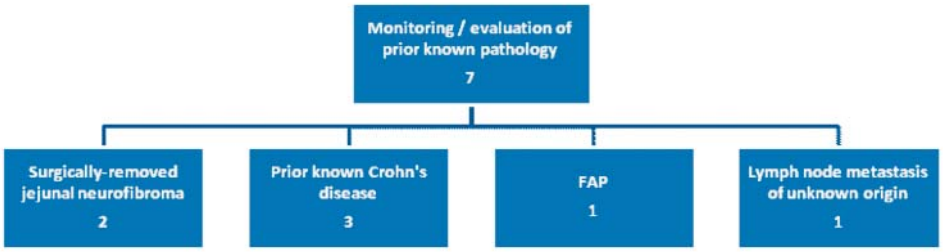


***Figure 7.*** *Distribution of VCE group with prior existing pathology*

### *Group distribution – VCE findings*

A clear diagnosis that explained the clinical symptoms was established in 18 patients (42%), suspect lesions were noted in 16 patients (37%) and in 9 cases (21%) VCE exploration yielded no results (*Fig. 8*). More detailed results can be found in *Table 3*.

### *Adverse effects and complications of the procedure*

Ingestion of the endoscopic videocapsule was followed by a slower intestinal transit in nine patients, seven of them having complete small bowel investigations. In a single patient the procedure had a gastric transit time of more than seven hours, the capsule being retained in the stomach, and later pushed downwards with an endoscope. In one other case the capsule was retained by an ileo-cecal stenosis, without leading to a complete obstruction or intestinal occlusion. In this region VCE revealed inflammatory lesions and fecal matter debris, while the later performed colonoscopy showed a pediculate polyp of 1cm in diameter and edematous mucosa of the distal ileum. In a single case there was an accelerated intestinal transit.

## Discussions

The small bowel was until recently considered to be "unknown territory" by the gastroenterologist, mostly because of its location and anatomy. The techniques for its exploration can be considered neither simple nor complete or diagnostically conclusive (1-4).

VCE seems to be one of the few investigations suited for small bowel pathology. Its diagnostic capabilities were mentioned in numerous studies (6-21), but detection rates vary within large limits, according to the number of patients in the study group (2,6,20,23,24,31-47).

### *Obscure gastro-intestinal bleeding*

The main indication of VCE is the diagnosis of OGIBs (25 - 30). They represent approximately 5% of the total number of gastrointestinal hemorrhages and are defined as the lack of an identifiable source for a recurrent or persistent digestive bleeding after the standard endoscopic exploration of the upper and lower GI tract. OGIB was the most frequent indication for VCE exploration in our study too (44%).

Global detection rates have been reported to be between 31–91% in different studies (2,6,20,31-47). One multicentric study yielded a diagnostic rate of 92.3% for active GIB and of only 44.4% for OGIB (33). In our study VCE exploration found the potential source of the bleeding in 79% of cases, of which 10.5% were active at the moment of the examination.

The most frequent lesions in published studies are gastrointestinal angiodysplasia and ulcerations, but it is considered that any illness that leads to the morphological alteration of the digestive mucosa may cause bleeding (48). In our study, the leading suspected source of the bleeding was angiodysplasia (53%), followed by ulcerations and polyps in 20% of OGIB cases each, and 7% other causes.


***Figure 8.*** *Diagnostic rates of VCE exploration*

***Table 3.*** *Diagnosis after VCE exploration*

| VCE diagnosis (presumptive) | total | men | women | also had IDA/OGIB |
|---|---|---|---|---|
| Wirsung bleeding | 1 | 1 | 0 | 1 |
| angiodysplasia | 8 | 3 | 5 | 8 |
| benign tumor | 7 | 3 | 4 | 3 |
| malignant tumor | 7 | 3 | 4 | 1 |
| Crohn's disease | 9 | 4 | 5 | 2 |
| celiac disease | 2 | 1 | 1 | 0 |
| no findings | 9 | 4 | 5 | 4 |
| total | 43 | 19 | 24 | 19 |

Our results yielded a PPV of 93.3%, NPV of 100%, sensibility of 100% and specificity of 80% in the diagnosis of OGIB. These results seem to be in accordance with published studies, which reported very high predictive values: 94% – 97% PPV and 82% – 100% NPV, with a sensibility and specificity between 79% – 95% and 75% – 100%, respectively (20, 31, 33).

### *Non-tumoral pathology*

*Crohn's disease*

Most imagistic explorations lack the necessary sensibility in order to identify early lesions of Crohn's disease, and enteroscopy does not allow for the complete examination of the intestine. VCE is capable of identifying mucosal modifications earlier than other techniques. Diagnostic rates vary between published studies, 43% to 71%, and are described to be better than those of barium follow-through, computer tomograph enterography, ileocolonoscopy and push-enteroscopy (24, 49, 50). In our study, we have found specific lesions in 45% of the patients with clinical suspicion of Crohn's disease.

*Celiac disease*

There are four main endoscopic markers of celiac disease atrophy of the villi: lack of mucosal folds, mosaic aspect, scalloping folds and mucosal nodularity.

In one study that evaluated 43 patients with signs and symptoms of celiac disease and positive serological markers, who also had both upper GI endoscopy and VCE, 65.11% of them showed suggestive modification at the VCE exploration. In 41.86% there were mucosal lesions that went beyond the duodenum, and in 6.97% the entire small bowel was affected (19).

In our study the 1/8 magnification system of the capsule easily spotted the specific lesions of the mucosa in one of the clinically suspected patients, as well as in a patient that was examined for a different pathology. Although chronic diarrhea was the second cause for VCE exploration, with 10 cases out of 43, the detection rate was sensibly smaller than the ones describes in published articles, which can be owed to the different criteria of patient selection: we did not perform serological tests, including patients only based on clinical reasons, and we did not include patients that already had specific mucosal lesions when upper GI endoscopy was performed.

VCE seems to also be the first investigation that can assess the extent of the villous atrophy (51). In our study, we could notice that the mucosa of the distal ileum progressively regained normal aspect with reemergence of the villi, VCE making therefore possible the evaluation of the extent of disease.

### *Tumoral pathology*

Although the small bowel represents 75% of the length and 90% of the absorption surface of the digestive system, malignancies here represent less than 5% of the total GI cancers (21). They represent less than 0.3% of all cancers and are often diagnosed badly or in late stages (52,53). Recently, studies have reported an incidence of small bowel tumors of 6-9% in VCE patients, leading to the idea that VCE has doubled the detection rate of small intestine tumors.

Present data suggests that tumoral lesions of the small bowel lead to OGIB in up to 10% of patients (54). In our study, bleeding was present in 28.5% of tumor patients. The most common clinical presentation for tumors is considered to be with abdominal pain, weight loss and intestinal transit disturbance, rather than OGIB (55), data that was verified by our study: 71.5% compared to 28.5%.

In most patients the endoscopic aspect is that of masses or polyps, and in a minority that of ulcers or stenosis. In our group a single tumor was ulcerated, the rest having a polypoid aspect.

Most tumors described in the literature were malignant (60%). In one recent retrospective study 65,843 patients were evaluated, of which 37.4% were diagnosed with carcinoid tumors, 36.9% with adenocarcinomas, 17.3% with lymphomas and 8.4% stromal tumors (56). In our group, tumoral lesions were divided equally between malignant and benign (seven cases each). The malignant ones were three adenocarcinomas, two malignant stromal tumors, one neuroendocrine tumor and one duodenal papilla cancer. The benign ones were mostly polyps (five cases), the rest being benign stromal tumors.

VCE could also be useful in the monitoring of patients with hereditary polyposic syndromes (FAP and Peutz-Jeghers syndrome), several studies showing that VCE is accurate in the detection of polyps (57 - 60). Our group included a patient with FAP, in which VCE showed numerous polyps as well as one distal ileum tumor that had an aspect which suggested an adenocarcinoma.

We must mention, though, that VCE is only able to offer a presumptive macroscopic diagnosis in the case of tumors, and that only histological and immunohistochemical techniques can lead to or exclude a clear diagnosis of malignancy (22).

The high diagnostic rates of VCE, coupled with the possibility for biopsies by enteroscopy make this combination of methods very effective in the assessment of small bowel tumoral pathology.

### *Adverse effects and complications of the procedure*

VCE represents a safe and well-tolerated method for the investigation of the small bowel in most patients. Contraindications include the presence of intestinal obstruction, fistulas and strictures. The major complication is represented by capsule retention, which must be differentiated from slow or incomplete transit and from regional transit anomalies. In the published literature the risk of retention is considered to be higher in patients with Crohn's disease, strictures and tumors (61-63). In our study we have met with one case of retention in a ileo-cecal stenosis and the impactation of the capsule in a ulcerated tumoral formation, retention rates amounting to

5% (two cases), while slow intestinal transit was registered in one patient. There were no cases where retention would lead to intestinal occlusion. Based on our data, we can say that VCE is a safe procedure.

## Conclusions

Videocapsule endoscopy opens new frontiers for the exploration of the small bowel.

The main indication for VCE is represented by the diagnosis of OGIB. Regarding Crohn's disease, the advantage that VCE presents over other techniques is the fact that it is capable of identifying early mucosal modifications. There are still numerous unknowns regarding false positives and false negatives, as not all ulcerations come from Crohn's disease. In the case of celiac disease, VCE can be used both as a diagnostic tool and for the evaluation of the lesions' extent and to screen for mucosal healing. Tumoral pathology of the small bowel is under-reported when compared to other segments of the digestive system. Being a non-invasive procedure with high patient acceptability, VCE can be used successfully in the screening of small bowel tumors, including the surveillance of patients with hereditary pre-neoplastic diseases.

More parallel studies on larger patient groups seem to be necessary in order to give a final verdict regarding the effectiveness of this method, but it is obvious that both the clinical assessment and the correct evaluation of the disease are positively influenced by the use of videocapsule endoscopy.

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