Hereditary & familial colorectal cancer
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CHAPTER 8

CAP-ASSISTED FORWARD-VIEWING ENDOSCOPY TO VISUALIZE THE AMPULLA OF VATER AND THE DUODENUM IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

F.G.J. Kallen, B.A.J. Bastiaansen, E. Dekker

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ABSTRACT

Background and study aims

Guidelines recommend surveillance endoscopy with both forward- and side-viewing endoscopes to identify duodenal and ampullary adenomas in patients with familial adenomatous polyposis (FAP). We hypothesized that both the duodenum and the ampulla of Vater can be completely visualized during cap-assisted forward-viewing endoscopy.

Patients and methods

A total of 40 patients with FAP underwent forward-viewing endoscopy with a short cap attached to the tip of the gastroscope, with the aim of visualizing both the duodenum and the ampulla of Vater. If unsuccessful, the procedure was followed by a side-viewing endoscopy. Adverse events were reported.

Results

The duodenum, including the ampulla of Vater, was completely visualized using the cap in 38/40 patients (95.0%). The ampulla could not be visualized using the cap in two patients, both of whom underwent additional side-viewing endoscopy, which was successful. No adverse events occurred.

Conclusions

This study showed that cap-assisted endoscopy can be used effectively and safely to visualize both the duodenum and the ampulla of Vater in patients with FAP. This practice might reduce burden, time, and costs of an additional side-viewing endoscopy.
INTRODUCTION

Familial adenomatous polyposis (FAP) is an autosomal dominant disorder, characterized by the presence of numerous colorectal adenomatous polyps. Several extracolonic manifestations are also common, of which duodenal and ampullary adenomas are the most frequent, with a lifetime risk approaching 100%. As a result, these patients have an increased risk for both duodenal and ampullary cancer.

Surveillance upper gastrointestinal (UGI) endoscopies are recommended to visualize the duodenum, including the periampullary region. Duodenal surveillance can be performed adequately using a forward-viewing gastroscope. However, visualization of the ampulla of Vater is usually insufficient using this type of endoscope owing to the position of the ampulla at a tangential angle. Therefore, international guidelines recommend that an additional side-viewing endoscopy is performed in patients with FAP.

Avoiding the need for an additional side-viewing endoscopy would be desirable. As UGI endoscopies can lead to discomfort, performing two UGI procedures might further increase this burden. In addition, not all endoscopists routinely perform this procedure, and proper disinfection processing of duodenoscopes results in additional healthcare costs. An alternative approach could be to attach a cap to the tip of a forward-viewing gastroscope, the so-called cap-assisted endoscopy (CAE), with the aim of visualizing the duodenum as well as the ampulla in one procedure. Using this technique, Choi et al. showed that CAE permitted complete visualization of the ampulla in 91.3% of healthy individuals in whom the ampulla could not be visualized when performing a regular forward-viewing endoscopy. The efficacy of duodenal surveillance was not evaluated. It thus remains unknown whether this procedure can also be performed successfully in patients with FAP, who tend to have multiple duodenal and ampullary adenomas. Therefore, the aim of the current study was to determine the efficacy and safety of cap-assisted forward-viewing UGI endoscopy in visualizing the ampulla and the duodenum in patients with FAP.

PATIENTS AND METHODS

Study population

This was a proof-of-concept study conducted at the Academic Medical Center in Amsterdam, The Netherlands. Between July 2015 and January 2016, we prospectively enrolled 40 consecutive patients with FAP who were scheduled to undergo surveillance UGI endoscopy. Only those patients who had undergone a previous duodenectomy were excluded from the study. The diagnosis of FAP was established clinically by the presence of >100 colorectal adenomas, and/or genetically by the presence of an APC gene mutation.
The study was approved by the institutional review board. As CAE was considered a part of standard health care by the institutional review board, additional approval or informed consent was not required according to Dutch law. The study was carried out in accordance with the Declaration of Helsinki.\textsuperscript{14}

**Endoscopic procedures**

All patients were requested to fast for 6 hours before the start of the endoscopy; oral intake of clear fluids was allowed up to 2 hours before the endoscopy. All procedures were performed with the patient in the left lateral position, and all patients received conscious sedation with either midazolam or propofol, or no sedation, depending on patient preference. Additional medications, such as fentanyl, butylscopolamine, and antifoaming agents, were used at the discretion of the endoscopist. All procedures were performed by one of two gastroenterologists who were specialized in the management of FAP.

All patients underwent a forward-viewing UGI endoscopy with a disposable short (4mm) transparent plastic cap (D-201-11304 or D-201-11804; Olympus Medical Systems, Corp., Tokyo, Japan) attached to the tip of a gastroscope (GIF-HQ 190 or GIF-180J; Olympus Optical Co., Ltd., Tokyo, Japan). Duodenal surveillance was conducted during insertion up to at least the third part of the duodenum and upon withdrawal. Inspection was considered complete if D1, D2, and D3 were assessable. If indicated, biopsies were taken and polypectomies were performed. During the same procedure, endoscopists also aimed to visualize the complete ampulla, including the orifice. If visualization of the ampulla was not successful, the procedure was followed by a side-viewing endoscopy (TJF-Q180 V or TJF-160 VR; Olympus Optical Co., Ltd.). Ampullary adenomas were not routinely biopsied. Complete visualization of the ampulla was photo documented by taking still images of the entire ampulla including the orifice. Other endoscopic data that were collected were endoscopic size of the ampulla, whether a previous endoscopic ampullectomy had been performed, and the ampullary aspect (adenomatous or nonadenomatous). Endoscopic signs of an ampullary adenoma were a size >10mm, a Kudo 3S/L or 4 pit pattern, or having at least one of the features of an adenoma according to the Narrow-band imaging International Colorectal Endoscopic classification. Finally, severity of duodenal polyposis, quantified according to the modified Spigelman staging system (Table 1), was reported.\textsuperscript{15}

**Adverse events**

Any adverse events that occurred during the endoscopic procedure were reported. Data on adverse events occurring within 30 days after endoscopy were collected by verifying medical files and by crosschecking with the Dutch national endoscopic complication registry.
Statistical analyses

The number of patients in whom CAE resulted in complete visualization of the ampulla and duodenum was reported as a proportion of all enrolled patients with the corresponding 95% confidence interval (CI). Quantitative variables were expressed as means (SD) or median and range when appropriate. All statistical analyses were performed using SPSS statistical software version 23 (IBM Corp., Armonk, New York, USA).

RESULTS

A total of 40 consecutive patients with FAP were enrolled. Patients had a median age of 42 years (range 21-75), and 18 (45.0%) were male. The duodenum, including the ampulla, was completely visualized using the cap in 38/40 patients (95%; 95%CI 83.5%-98.6%) (Table 2, Figure 1). Five patients received butylscopolamine.

In the 38 patients, median ampullary size was 6mm (range 0-20), 12 (31.6%) had endoscopic signs of an ampullary adenoma, and 5 (13.2%) had undergone a previous ampullectomy. Median Spigelman score was 7 (range 0-9), with a corresponding median Spigelman stage III (range 0-IV). Of note, multiple still images from different angles were occasionally needed to achieve and archive a complete visualization of the ampulla. All ampullary and duodenal biopsies were taken at the discretion of the endoscopist without any hindrance from the cap.

In two patients (5%; 95%CI 1.4%-16.5%), the ampulla could not be visualized using the cap, but a subsequent side-viewing endoscopy was successful for this purpose. In both cases,

<table>
<thead>
<tr>
<th>Factor</th>
<th>Score(^1)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1 point</td>
</tr>
<tr>
<td>No. of polyps</td>
<td>1–4</td>
</tr>
<tr>
<td>Polyp size, mm</td>
<td>1–4</td>
</tr>
<tr>
<td>Histology</td>
<td>Tubular</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>Low grade</td>
</tr>
</tbody>
</table>

\(^{1}\)Classification:
No polyps, stage 0
1–4 points, stage I
5–6 points, stage II
7–8 points, stage III
9–12 points, stage IV

Table 1. Modified Spigelman score and classification\(^{1,5}\)
the ampulla was hidden behind a duodenal fold and was not enlarged; one had undergone a previous ampullectomy (Table 2, Figure 1). Spigelman stages in these two patients were III and 0, respectively. In both patients, duodenal surveillance was otherwise complete when using the cap.

No adverse events occurred in any patient during endoscopy or during 30 days’ follow-up.

Table 2. Characteristics and endoscopic findings in patients with familial adenomatous polyposis, with and without a complete visualization of the ampulla of Vater when using a forward-viewing gastroscope with a cap.

<table>
<thead>
<tr>
<th>Ampulla completely visualized with cap n = 38 (95%)</th>
<th>Ampulla not completely visualized with cap n = 2 (5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Patient 2</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td>42 (21-75)</td>
</tr>
<tr>
<td><strong>Ampulla of Vater, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Ampullectomy performed previously</td>
<td>5 (13.2)</td>
</tr>
<tr>
<td>Ampullary adenoma</td>
<td>12 (31.6)</td>
</tr>
<tr>
<td>Endoscopic size of ampulla of Vater, mm</td>
<td>6 (0-20)</td>
</tr>
<tr>
<td><strong>Spigelman stage, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 (18.4)</td>
</tr>
<tr>
<td>I</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>II</td>
<td>7 (18.4)</td>
</tr>
<tr>
<td>III</td>
<td>18 (47.4)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td><strong>Complete duodenal surveillance with cap, n (%)</strong></td>
<td>38 (100)</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td></td>
</tr>
<tr>
<td>During endoscopy</td>
<td></td>
</tr>
<tr>
<td>At 30 days’ follow-up</td>
<td></td>
</tr>
</tbody>
</table>

*Reported numbers are median (range) for group with complete visualization.*
Figure 1. Endoscopic view of the ampulla of Vater using a forward-viewing gastroscope with a cap: A-D in a selection of four patients without an ampullary adenoma; E, F in two patients with an ampullary adenoma. G, H The ampulla of Vater using a side-viewing endoscope in two patients in whom cap-assisted endoscopy failed to visualize the ampulla of Vater.
DISCUSSION

In patients with FAP, duodenal and ampullary surveillance is important for the early detection of adenomatous polyps. Our study shows that performing a forward-viewing endoscopy with an attached short transparent plastic cap at the tip of the gastroscope results in complete visualization of the ampulla of Vater, as well as proper surveillance of the duodenum, in 95% of patients with FAP. In addition, as no adverse events occurred, CAE seems to be a safe procedure.

Only one previous study has evaluated the efficacy of CAE for the visualization of the ampulla, but not the duodenum, during routine gastroscopy, with a success rate of 91.3%. Though results were promising, the study included only 21 healthy individuals, who were unlikely to have had duodenal and ampullary adenomas. Moreover, CAE was only performed in those in whom a forward-viewing endoscopy without a cap failed to visualize the ampulla. This addresses the importance of our findings.

A potential factor that could influence the success rate of CAE is the experience of the endoscopist; an experienced ERCP endoscopist might be better at identifying the ampulla using CAE. In our study, one of the two endoscopists did not routinely perform ERCPs. The data are therefore more representative of the median experience of gastrointestinal endoscopists, unlike in the Choi study above, where all procedures were performed by an ERCP endoscopist. Interestingly, the endoscopists in the current study both performed an equal number of procedures, with success rates of more than 90%, indicating that most endoscopists should be capable of successfully performing CAE irrespective of their ERCP experience. Second, we did not perform side-viewing endoscopies to confirm the findings in patients for whom CAE was successful; the entire ampulla, including all of its borders and the orifice, had to be visualized to rate the CAE as successful. We believe that this justifies our decision to deviate from guidelines, in which expert opinion recommends a side-viewing endoscopy to inspect the ampulla. In addition, Vasen et al. previously reported that in some cases even a regular forward-viewing endoscopy might be appropriate for this purpose. Moreover, our definition of complete visualization of the ampulla makes it unlikely that we have mistaken another structure, such as a duodenal adenoma, for the ampulla. Finally, we noticed that the cap can obscure the field of visualization. However, we used a short cap. This involves only a small part of the field, making it very unlikely that a significant lesion will be missed. By making clockwise rotations upon withdrawal, we think that the risk of missing lesions was further minimized.

We chose to conduct a proof-of-concept study rather than a trial comparing CAE and side-viewing endoscopy. A forward-viewing endoscopy is indicated in all patients with FAP, and if the ampulla is successfully visualized then we can spare the patient an additional side-viewing endoscopy. With the reported success rate and the absence of adverse events, it seems
reasonable to consider that the costs of a cap outweigh the costs and burden of an additional side-viewing endoscopy, although a future cost-effectiveness study is needed to confirm this. In the meantime, we suggest to initiate all UGI surveillance endoscopies in patients with FAP using a gastroscope and a short plastic cap. In cases where the ampulla cannot be fully identified using this approach, a subsequent side-viewing endoscopy would need to be performed, but this should only be required in a minority of cases.

REFERENCES