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Efficacy of double-balloon enteroscopy for small-bowel polypectomy: clinical and economic evaluation

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Abstract

Background: We evaluated first the feasibility of endoscopic small-bowel polypectomy and second, the economic aspects, by comparing the cost of endoscopic and surgical polyp resection.

Methods: A prospective, observational, multicenter study included 494 patients with positive capsule endoscopy (CE) before double-balloon enteroscopy (DBE). We selected only CE with at least one polyp. The retrospective economic evaluation compared patients treated by DBE or surgery for small-bowel polypectomy. Hospital readmission because of repeat polyp resection or complication-related interventions was noted. The 1-year cost was estimated from the viewpoint of the healthcare system and included procedures, hospital admissions and follow up.

Results: CE indicated one or more polyps in 62 (12.5%) patients (32 males, 49 ± 5 years), all of whom underwent a successful DBE exploration. The DBE polyp diagnostic yield was 58%. There were no major complications. A total of 26 (42%) patients in the DBE group and 19 (39%) in the control group required hospital readmission. All readmissions in the DBE group were for repeat procedures to remove all polyps, and in the control group, for surgical complications. The total cost of the initial hospitalization (€4014 ± 2239 DBE *versus* €11,620 ± 7183 surgery, $p < 0.0001$) and the 1-year total cost (€8438 ± 9227 DBE *versus* €13,402 ± 7919 surgery, $p < 0.0001$) were lower in the DBE group.

Conclusions: Endoscopic polypectomy was efficient and safe. The total cost at 1 year was less for endoscopy than surgery. DBE should be proposed as the first-line treatment for small-bowel polyp resection.

Keywords: economic evaluation, enteroscopy, polypectomy, small-bowel polyps

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Introduction

Small-bowel exploration has been drastically revolutionized by capsule endoscopy (CE) and device-assisted enteroscopy (DAE). Double-balloon enteroscopy (DBE) is the most well studied DAE technique described in the literature.[1–3] In comparison with CE, which is a diagnostic-only technique, DBE allows both diagnostic and therapeutic management of small-bowel diseases. DBE is less invasive and more convenient for the patient than intraoperative small-bowel endoscopy.[4,5]

In this study, we focused on small-bowel tumors, which represent around 5% of all digestive tumors.[6] Most small-bowel tumors are benign, such as adenomatous polyps in Lynch syndrome or familial adenomatous polyposis (FAP), and hamartomatous polyps in Peutz-Jeghers syndrome (PJS).[7] Polyp resection is indicated for all

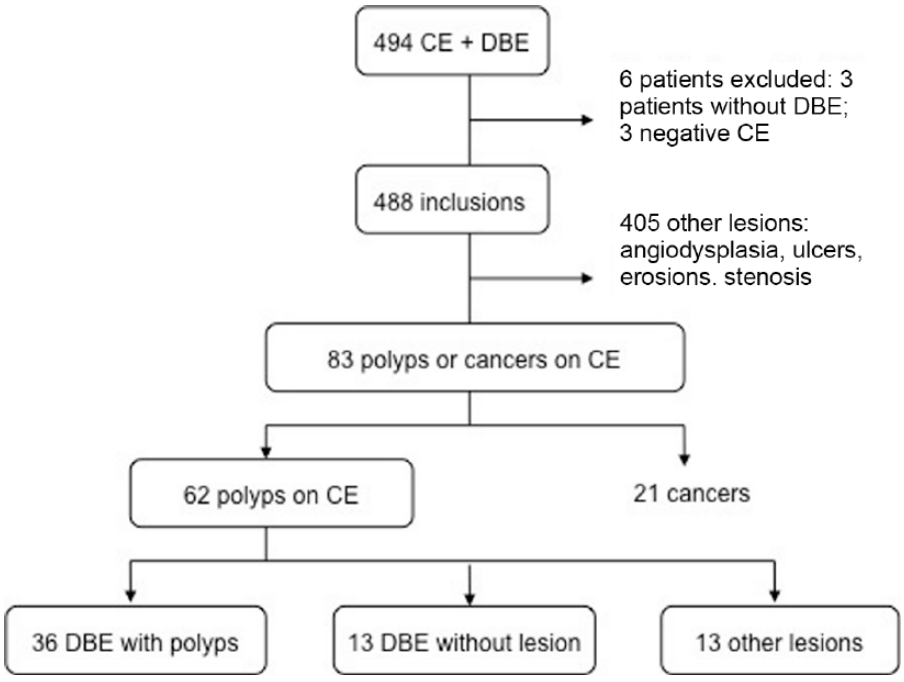

Figure 1. Patient selection for the study in the double-balloon enteroscopy group.
CE, capsule endoscopy; DBE, double-balloon enteroscopy.

adenomatous polyps and for large hamartomatous polyps (>15 mm in size).[8,9] Two therapeutic options exist: limited small-bowel surgical resection, which is the standard technique, or polypectomy during enteroscopy. The endoscopic solution is a mini-invasive strategy with the advantages of lower morbidity–mortality and a shorter hospital stay.[9,10] Moreover, repeated laparotomy with extensive small-bowel resection and eventual short-bowel syndrome is a major problem in patients with small-bowel polyposis.

A cost-effective approach for the treatment of patients with obscure gastrointestinal bleeding (OGIB) based on the comparison of different techniques of small-bowel exploration, push enteroscopy, intraoperative enteroscopy, angiography, DBE and CE, has already been described.[11] Capsule-directed DBE was associated with better long-term outcomes, with a low complication rate. However, limited data are available regarding first the efficacy of polypectomy during DBE and additionally the cost of DBE in comparison with surgery. To date, there has been little or no economic development of DBE in many countries.

Our principal objective was to evaluate the feasibility and efficacy of small-bowel polypectomy during the DBE procedure.

Until recently, the standard treatment for small-bowel polyps has been surgery. However, it is of interest to public healthcare systems, insurance companies and patients, to question whether an alternative procedure of polypectomy during DBE can be justified if this is shown to be more effective and less expensive? Hence, our secondary objective was to perform an economic evaluation and to compare the total estimated costs at 1 year of the endoscopic and surgical treatments during the same period.

Methods

Patients and inclusion criteria

We performed a prospective, multicenter study including 494 patients referred to 14 tertiary endoscopic centers in France for small-bowel examination by CE followed by DBE (CE-directed DBE) from February 2007 to December 2011. The main inclusion criterion was a positive CE for polyp(s) (Figure 1). DBE was performed after each positive CE in order to remove one or more polyps. Patients with lesions other than polyps were excluded. During the 1-year follow up, each patient had a clinical examination at 3 and 12 months. All patients provided written, informed consent for the study

and the research was approved by the 'Paris Ile de France II' Ethics Committee.

Small-bowel capsule endoscopy

All patients planned for DBE exploration had undergone a previous CE with the PillCam™ SB1 or SB2 device (Given imaging, Yoqneam, Israel). PillCam™ SB1 was used only at the beginning of the study, while PillCam™ SB2 was used for the majority of cases. To classify polyps using CE, we used a two-degree scale of likelihood of polyp, as described in previous published studies[12,13]: P1 for a doubtful image of a polyp and P2 for a typical image.

Double-balloon enteroscopy

DBE procedures were performed under general anesthesia, the recommended protocol in France, in most cases with endotracheal intubation. CO_2 insufflation was recommended in the study even if few DBE were performed with air insufflation at the beginning of the study. The required level of operator experience was >20 overtube-assisted enteroscopies. The enteroscope used (Fujinon Inc., EN-450T5) had a diameter of 9.3 mm, with an operating channel of 2.8 mm. The overtube (–13140) was 13.3 mm wide. The method used to determine the antegrade *versus* retrograde approach was based on capsule transit time index described by Gay *et al.*[14] A time index of >0.75 appears to reliably indicate an anal route. The depth of insertion was evaluated according to the method described by May *et al.*[15] Polypectomy was performed using an ERBE electrosurgical unit (Erbe, Elektromedizin, Tübingen) with endocut current and standard diathermic snare. To prevent post polypectomy bleeding, the patients were informed that antiplatelet agents or anticoagulation therapy should be discontinued before DBE.

Objectives of the study

Our primary objective was to assess the efficacy of polypectomy during DBE. Primary endpoints were the diagnostic yield, complication rate and hospital readmission rate. Limited progression because of technical difficulties was defined as the possibility to explore the small bowel by DBE less than 50 cm after the duodeno–jejunal junction for the oral route and less than 50 cm after the ileocecal valve for the anal route. The secondary objective was an economic evaluation of the endoscopic strategy for the treatment of small-bowel polyps.

Economic evaluation

We compared the group of patients treated by DBE for small-bowel polyps (new strategy) with a control group of patients treated by surgery (standard strategy) for the same indication. The control group of patients who underwent a surgical polypectomy was extracted from the national hospital discharge database, which records all acute-care hospital admissions using diagnosis-related groups (DRG) along with other variables, such as diagnoses (primary and secondary, using the 10th edition of the International Classification of Diseases, ICD-10), surgical procedures and length of stay. Record linkage is performed at the national level. We included patients aged 18–85 years, hospitalized during the study period for a primary diagnosis of benign small-bowel tumor that was treated by surgical resection and would have been eligible for endoscopic treatment. In this group, polyps were diagnosed using radiological techniques (small-bowel barium radiography, computed tomography with or without enteroclysis, and magnetic resonance).

For the economic evaluation, only hospital (acute) resources were considered. Procedure costs for DBE were obtained with a bottom-up microcosting approach that identified all relevant cost components of the procedure and valued each of those components for all of the individual patients using the following variables: duration of the procedure, staff present, medical devices used, and type of operating room. CE and other supplies for each patient were recorded in the case report form or retrieved from the surgical ward databases. Equipment, including video processors, light source and enteroscopes, were also accounted for. Hospitalization costs were estimated by adjusting the average national cost of each patient's DRG with their actual length of stay and resources used during their hospitalization. Repeat admissions within 1 year of the initial intervention were included. Additional tests during the 1-year follow up were also costed. The prices as of 2011 were used for the medical devices and additional tests used during the procedures.

The 'rate of readmission averted' was used as the efficacy endpoint in the cost-effectiveness

analysis. Hospital readmission was necessary in case of repeat polyp resection or complication-related interventions. We estimated the incremental cost per incremental event for DBE compared with surgery and quantified the uncertainty surrounding of ratio using a probabilistic sensitivity analysis.

Statistical analysis

Results are expressed as the mean ± one standard deviation (SD) or median (interquartile range, IQR). The diagnostic yield was defined as the proportion of patients with one or more polyps diagnosed on DBE. Because a single patient may have several polyps, each lesion was given a likelihood-of-bleeding score based on CE findings and the highest of these scores was recorded for that patient. In the univariate analysis, the log-rank test was used for qualitative variables. Significance was set at $p < 0.05$. Dichotomous variables were compared using the chi-square test or Fisher's exact test, while continuous variables, described by the mean and SD, were assessed with a Student's *t* test or Wilcoxon and Mann–Whitney tests. The bootstrap method was used to examine the distribution of the incremental cost and incremental effectiveness across the cost-effectiveness plane for hospital readmission averted. Analyses were performed using Excel (2010, Microsoft) and SAS (9.2, 9.3, SAS corp., NC) software.

Use of the national hospital-claims database with record linkage was approved by the French national data protection agency (CNIL 1165361).

Results

Patient characteristics

CE indicated the presence of one or more polyps in 62 (12.5%) of the 494 patients included in the study (32 males, 49 ± 5 years). Within this subset, the principal indication for CE was OGIB in 26 (42%) patients, seven of whom required a red blood cell transfusion. A personal or family history of polyposis was noted in 31 (50%) patients (PJS and Lynch syndromes in 26 and 5 patients, respectively). Other indications were digestive disorders, including abdominal pain and diarrhea in 6 (10%) patients; 17 patients (26%) had a history of digestive surgery and 31 (50%) patients had a previous small-bowel radiological exploration (abdominal CT scan and perhaps MRI with enteroclysis).

Endoscopic exploration of the small bowel

CE-directed DBE exploration was performed successfully in all 62 patients. The results are summarized in Table 1. The majority had a complete small-bowel exploration by CE (55 patients, 89%). Small-bowel preparation was excellent in 42 (68%) cases and acceptable in the other cases. Likelihood of polyps was weak (P1) in 24% and strong (P2) in 53% of cases.

The total procedure time for DBE was 80 ± 33 min. The diagnostic yield was 58% (one or more polyps were found in 36 cases). The mean insertion depth was greater by the oral route in comparison with the anal route (218 ± 99 cm *versus* 88 ± 59 cm, $p = 0.02$). Progression during the procedure was limited in 17 (27%) cases, and all of these patients had a history of previous digestive surgery. The polyp was located in the jejunum in 47 (76%) cases and the ileum in 16 (26%) cases. The mean number of polyps per patient was 2.1 ± 1.4. There was no lesion in 13 cases and a lesion other than a polyp (angiectasia with or without intestinal lymphangiectasia) was diagnosed in 13 other cases.

Polyp resection was possible in the majority of patients (97%), with no major complications. Surgical polyp resection was necessary in two patients because of technical failure, mainly due to the huge size of the polyp. The mean polyp size was 25 mm (12–50 mm) and 51 polyps were resected. Histological examination showed 37 hamartomas, 12 adenomas and 2 lipomas. Four (6.4%) patients had a longer hospital stay because of moderate post-procedure abdominal pain, with normal levels of plasmatic lipase, and were discharged after 3 days.

1-year follow up

By 1 year of follow up, 26 (42%) patients had undergone a repeat DBE for polyp resection because of additional polyps. For six patients, this was because the oral route had not reached the polyp and the patient was readmitted for a DBE by the anal route. No predictive factor was found for polyp-associated hospital readmission. However, 17 patients with a history of familial polyposis had multiple polyps at the first DBE

Table 1. Endoscopic exploration of the small bowel.

CE (n = 62)	
n (%) Complete small-bowel exploration	55 (89)
n (%) Degree of cleanliness	
Good	42 (68)
Moderate	7 (11)
Poor	1 (2)
Missing data	12 (19)
Likelihood (%)	
P1	24
P2	53
Mean duration of reading (min)	67 ± 28
DBE (n = 62)	
Length of small bowel explored (median, cm)	
Oral route	218 ± 99
Anal route	88 ± 59
Total duration of procedure (median, min)	80 ± 33
Total number of DBE positive for polyps (%)	36 (58)
Mean number of polyps per patient	2.2 ± 1.4
Polyp location, n (%)	
Jejunum	47 (76)
Ileum	16 (26)
Difficulty of insertion, n (%)	17 (27)

CE, capsule endoscopy; DBE, double-balloon enteroscopy.

and a second procedure was indicated to complete the first resection.

Economic evaluation

The hospital-claims database analysis identified 49 patients who had undergone surgery for small-bowel polypectomy during the study period. All patients in the DBE group (n = 62) and the 49 patients in the control group were included in the economic evaluation. The DBE and control groups were comparable in terms of age (49 ± 16 *versus* 53 ± 17 years, p = 0.18) and gender (52% *versus* 49% male, p = 0.8). The two groups were also comparable in terms of number of patients with hospital readmission for repeat polyp resection or repeat complication-related interventions (26 (42%) *versus* 19 (39%), p = 0.74). The initial length of stay was shorter in the DBE group compared with the control group (2.7 ± 1.9 *versus* 10.9 ± 6.8 days, $p < 0.0001$) (Table 2). The total cost of the initial stay was less in the DBE group (€4014 ± 2239 *versus* €11,620 ± 7183, $p < 0.0001$). A 1-year hospital readmission occurred for 26 patients (42%) in the DBE group and 19 patients in the control group (39%). Including the cost of readmissions (and additional tests), the 1-year follow-up costs were €4424 ± 8366 and €1782 ± 3214 in the DBE and control groups, respectively (p = 0.15). The 1-year total costs were lower in the DBE group than in the control group (€8438 ± 9227 *versus* €13,402 ± 7919, $p < 0.0001$) (Table 2, Figure 2).

The DBE strategy was decrementally cost effective, that is, cheaper, although requiring slightly more readmissions than controls. Figure 3 shows the uncertainty associated with DBE cost effectiveness as a scatter plot of mean cost-and-effect differences. The rate of patients without the need for hospital readmission was used to estimate the cost effectiveness. The majority of data points are on the left part of the graph, indicating that control patients experienced fewer readmissions than DBE patients. However, all data points are below the horizontal axis, indicating that DBE was always cheaper than surgery.

Discussion

CE-directed DBE for the diagnosis and resection of small-bowel polyps had a good diagnostic and therapeutic yield, with very few complications.[16,17] Our results were comparable with those already published in the literature in terms of feasibility and efficacy of small-bowel polypectomy.

Patients with PJS have small-bowel polyps that can cause intussusception and bleeding. In the majority of cases, more than one DBE procedure is necessary to remove all polyps.[18] In patients with PJS, it is recommended to remove all small-bowel polyps that are >10 mm in size.[19] Ohmiya *et al.* observed that polyps greater than 15 mm in size could have an adenomatous component and cause invagination.[20]

Small-bowel polyps in patients with FAP or Lynch syndrome are associated with an increased risk of small intestinal neoplasia.[21,22]

Table 2. Economic evaluation: initial and 1-year total costs.

	DBE	Surgery	*p*
Length of stay, mean ± SD	2.7 ± 1.9	10.9 ± 6.8	<0.0001
DBE cost, mean ± SD	784 ± 199	–	–
Initial stay total cost, mean ± SD (€)	4014 ± 2239	11,620 ± 7183	<0.0001
1-year follow-up cost, mean ± SD (€)	4424 ± 8366	1782 ± 3214	0.1508
Mean total cost ± SD (€)	8438 ± 9227	13,402 ± 7919	<0.0001

SD, standard deviation; DBE, double-balloon enteroscopy.

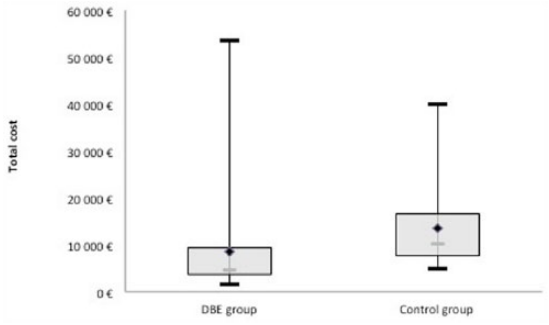

Figure 2. Distribution of 1-year median total costs in both groups.
DBE, double-balloon enteroscopy.

However, systematic CE is not recommended. Complete small-bowel exploration is usually performed only for patients with a family history of small-bowel adenocarcinoma or in cases of unexplained anemia.[23] Where small-bowel polyps are identified on CE, DBE allows a safe polypectomy.[24]

Even if this is already generally accepted to be the case, we have shown for the first time that an endoscopic strategy for small-bowel polypectomy is cheaper than the surgical strategy, without major complications. The overall cost per patient was €4964 cheaper in the DBE group than the surgical group, even if there was 3% additional hospital readmission in the DBE group. Decrementally cost-effective innovations are seldom reported, for reasons that are well described in the literature.[25] The results of the bootstrap analysis in our study oscillated between a dominant strategy and a strategy to discuss, given the reduced costs and small loss in efficacy. There is a 42% chance that the DBE strategy is dominant (more effective and less expensive) when the efficiency endpoint is the rate of patients without hospital readmission. Even though the endoscopic strategy was associated with a higher number of hospital readmissions for iterative polypectomies, there were no procedure-related complications. This option, in comparison with the surgical strategy, remains cheaper and may allow an efficient allocation of resources and ultimately be of benefit to the population in general.

Other authors have reported the cost effectiveness of CE-directed DBE, and DBE alone, compared with surgery, using cost inputs and medical efficacy endpoints reasonably similar to ours. Patients with OGIB, in most cases associated with angiectasia, were included. DBE alone and CE-directed DBE were cheaper than surgery. CE-directed DBE was less effective than surgery when bleeding cessation was the endpoint of interest.[11] The hierarchy of preferred strategies varied depending on the endpoint chosen: therapy, diagnosis or lesion identification.[11,26] Our real-life cost-effectiveness analysis confirmed that the results are sensitive to the endpoint evaluated and that CE-directed DBE is cheaper than surgical options.

Our study has limitations. First, because small-bowel polyps are not common, the study population was small. One or more polyps were identified in only 62 of 494 patients who underwent CE. This is, however, comparable with rates of small-bowel polyps reported in the literature. For the surgical control group, even fewer patients were included. The main reason for this was probably the evolution of changes in medical practices, with progressively more patients referred for endoscopic treatment instead of surgical resection. Second, we performed a retrospective economic comparison between endoscopic and surgical strategies for polyp resection. A

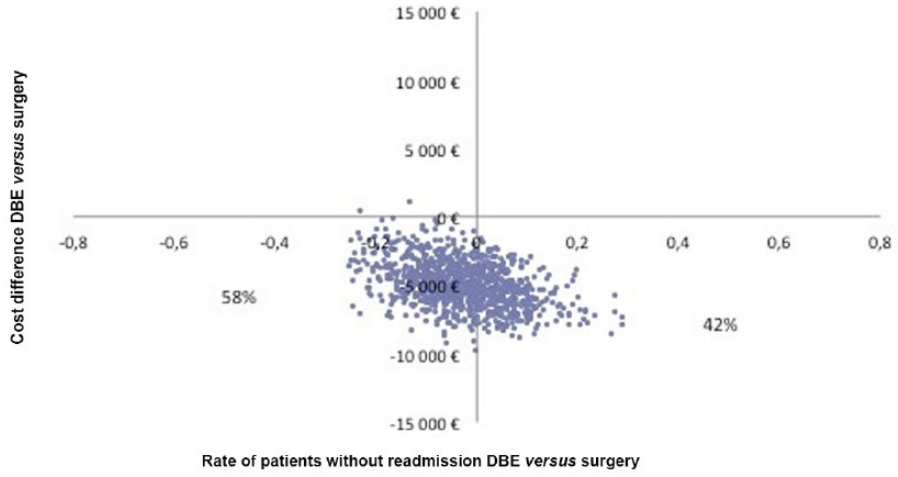

Figure 3. Cost-effectiveness planes depicting the results of the bootstrap analysis. The figure plots the first 1000 resamplings of the incremental cost-effectiveness ratio (ICER) comparing double-balloon enteroscopy *versus* the control group. Effectiveness is measured by the rate of patients without hospital readmission.
DBE, double-balloon enteroscopy.

randomized, comparative study would be optimal regarding the study methodology. However, all the patients with small-bowel polyps were referred for endoscopic resection because of the associated low morbidity. The control group was defined as patients who had a surgical polyp resection during the same study period and for whom data were available in a national hospital database (PMSI). All patients who had this type of surgery were recorded using well defined codes (10th edition of the International Classification of Diseases, ICD-10). The endoscopic and surgical groups were comparable in terms of gender, age and comorbidities. This a major point to minimize the bias of a retrospective analysis and to allow the comparison for hospital readmissions in patients after endoscopic or surgical treatment.

In conclusion, the study confirmed that DBE technique allowed efficient small-bowel polyp resection without major complications. A key advantage of the endoscopic strategy is the lower 1-year total cost. The only limitation in comparison with the surgical strategy was the frequent requirement for more than one DBE procedure to remove all polyps. However, DBE was less invasive than surgery and was associated was fewer complications.

We recommend the use of DBE as the first-line treatment for the resection of small-bowel polyps.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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