

Appropriateness of colonoscopy in Europe (EPAGE II)

Presentation of methodology, general results, and analysis of complications

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Institutions are listed at the end of article.

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Background and study aims: Appropriate use of colonoscopy is a key component of quality management in gastrointestinal endoscopy. In an update of a 1998 publication, the 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE II) defined appropriateness criteria for various colonoscopy indications. This introductory paper therefore deals with methodology, general appropriateness, and a review of colonoscopy complications.

Methods: The RAND/UCLA Appropriateness Method was used to evaluate the appropriateness of various diagnostic colonoscopy indications, with 14 multidisciplinary experts using a scale from 1 (extremely inappropriate) to 9 (extremely appropriate). Evidence reported in a comprehensive updated literature review was used for these decisions. Consolidation of the ratings into three appropriateness categories (appropriate, uncertain, inappropriate) was based on the median

and the heterogeneity of the votes. The experts then met to discuss areas of disagreement in the light of existing evidence, followed by a second rating round, with a subsequent third voting round on necessity criteria, using much more stringent criteria (i.e. colonoscopy is deemed mandatory).

Results: Overall, 463 indications were rated, with 55%, 16% and 29% of them being judged appropriate, uncertain and inappropriate, respectively. Perforation and hemorrhage rates, as reported in 39 studies, were in general <0.1% and <0.3%, respectively

Conclusions: The updated EPAGE II criteria constitute an aid to clinical decision-making but should in no way replace individual judgment. Detailed panel results are freely available on the internet (www.epage.ch) and will thus constitute a reference source of information for clinicians.

Background

Major progress in the accuracy and efficacy of diagnostic and therapeutic colonoscopy has been achieved over the last 30 years. Patient safety and comfort has increased with the advent of new endoscopic techniques [1,2] and methods of sedation [3–5]. The number of colonoscopic procedures performed is steadily increasing, as indicated by a recent survey in the USA that has shown a three- to fourfold increase in the number of colonoscopies between 1998 and 2004 [6]. Colonoscopy is currently the most frequently performed gastroenterological endoscopic procedure in the USA [7]. This rapid growth in colonoscopy services can be partly attributed to the growing prevalence of colorectal cancer (CRC) screening [8]. An increase in the number of endoscopies performed has also been observed in Europe [4,9]. Colonoscopy may, however, be challenged in the future by other technologies such as com-

puted tomography (CT) colonography (virtual colonoscopy) or wireless capsule endoscopy [10,11], and indeed many studies have already compared the performance of colonoscopy with CT colonography [12–17].

Maximizing the appropriateness of healthcare interventions is a key component of quality care. The indication for an intervention is deemed appropriate when the expected benefits are greater than the expected risks or inconvenience to the patient by a sufficiently large margin that the intervention is worth performing. Assessment of appropriateness should ideally be based on high-quality evidence; unfortunately, however, in many domains and for multiple clinical situations, the evidence base is poor or nonexistent. In such situations, an explicit multidisciplinary expert panel approach (the RAND/UCLA Appropriateness Method) has been used as a complement to evidence-based data [18,19]. This approach has previously been employed to establish

appropriateness criteria in various clinical fields, such as coronary angiography [20], Crohn's disease treatment [21], or surgery [22,23]. The 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy, EPAGE II, constitutes a necessary update of the first gastrointestinal endoscopy panel criteria established in 1998 (EPAGE I) [24–40]. The appropriateness criteria developed in 1998 were widely used to assess the appropriateness or the over- and underuse of colonoscopy [37,41–44], and could be used as a decision support tool for general practitioners [45]. In addition, because appropriateness implies a balance between the expected benefits and risks for the patient, the best available evidence on risks of colonoscopy complications should be examined. The aim of this project was thus to update the EPAGE appropriateness criteria, using the methods described in this report together with an executive overview of the risk of the procedure, while the benefits are reported by cluster of diagnostic indications in companion articles [46–50].

Methods

The RAND/UCLA Appropriateness Method

The same methodological approach as for the 1998 EPAGE I panel was used [18,38]. Briefly, a comprehensive literature review was undertaken (see below) to identify studies evaluating the benefits, effectiveness, safety, side effects, and possible complications of colonoscopy. A multidisciplinary panel of 14 European experts, who all have expertise in referral for or performance of colonoscopy was identified (Table e1): eight gastroenterologists, three primary care physicians and three surgeons. Four out of these 14 panelists were already familiar with the process as they had participated as panelists or organizers in EPAGE I.

A series of clinical indications was identified and categorized into 11 clinically relevant chapters corresponding to customary use of diagnostic colonoscopy. These chapters were: iron-deficiency anemia, hematochezia, nonspecific abdominal symptoms (uncomplicated lower abdominal pain and/or constipation and/or bloating), uncomplicated chronic diarrhea, evaluation of known inflammatory bowel disease (IBD), screening for colorectal cancer (CRC) in asymptomatic individuals and in IBD patients, surveillance after colonic polypectomy or after curative intent resection of CRC, and miscellaneous indications. A detailed description, including situations that were explicitly excluded from assessment, is shown in Table 2.

Literature review

An update of the literature review was established, covering from 1997 to February 2008 (the previous literature review covered publications up to 1997), based on a three-step search strategy. First, a systematic search of Medline (1997 to February 2008) and the Cochrane Database was conducted to identify selected published guidelines, systematic reviews and/or meta-analyses, as well as primary studies assessing the use of colonoscopy in adults in the various clinical categories. Details of these OVID searches using Mesh words, keywords and specific limits are available online (Table e3). A comprehensive search of clinical and medical scientific websites issuing guidelines and recommendations for endoscopy was also performed. Details of websites that contributed useful information are available in Table e4. Finally, a complementary manual search was carried out based on the reference lists of retrieved guidelines, reviews and articles.

Only articles in English, French or German, and dealing with adults, were considered for this literature review. One search strategy aimed to collect information about risks and complications of colonoscopy and the results are reported here.

Rating of clinical indications for appropriateness and necessity

About 3 months before the panel meeting, the panel experts received the list of clinical indications, the literature review, and detailed instructions on how to rate the level of appropriateness of each indication. Given the very low risk of complications related to the procedure, as shown below, and complementing the usual definition of appropriateness, as indicated above, a modification of the definition of appropriateness was used: an indication was considered appropriate if there is a reasonable likelihood of a significant finding, if such a finding would alter therapy or prognosis, and if therapy would be beneficial. In rating the appropriateness of colonoscopy, panelists were asked to imagine a “typical” patient with the described set of clinical features receiving care from a “typical” physician performing the procedure. Financial considerations were not included in the judgment process at this stage. Costs, social and other related health technology evaluation features may be introduced at a later stage, i.e. when developing guidelines from appropriateness criteria. The experts used a scale graded from 1 to 9 to rate the appropriateness of each of the several hundred indications for which colonoscopy could, in practice or in theory, be considered, using the following scores: 1 = extremely inappropriate, 5 = uncertain, 9 = extremely appropriate. The clinical indications were presented as a rating matrix which allowed a tabular presentation of the various scenarios by chapter. An indication for colonoscopy was considered appropriate if the median of the panelists' ratings was between 7 and 9, without disagreement, and inappropriate if the median was between 1 and 3, without disagreement. Scenarios with a median rating of 4 to 6, or those revealing disagreement among the panelists, were considered “uncertain” as to the appropriateness of colonoscopy in such cases. Disagreement was defined as occurring when at least four panelists rated an indication from 1 to 3 and four others from 7 to 9. Fig. 1 displays an example of the rating matrix which was used by the experts. The first round of individual ratings were analysed and a telephone interview took place with each panelist to review potential problems with the indications rated, and to receive their suggestions for changes in the list of indications and the literature review. The panel meeting took place in Montreux, Switzerland, over 2 days (April 17–19 2008). All chapters were discussed in the light of existing evidence that was summarized before the discussion and emphasized by the moderators, focusing on those indications for which there was disagreement between experts or uncertainty. A second round of ratings was then carried out during the panel meeting, followed by a third necessity rating round for those indications which were considered appropriate. An indication that the procedure was considered necessary fulfilled all of the following criteria [51]:

- ▶ The procedure is appropriate (that is, it must have a median rating of 7, 8 or 9 without disagreement at the second appropriateness rating round).
- ▶ It would be considered improper care or negligence not to provide this procedure.
- ▶ There is a reasonable chance that this procedure will benefit the patient. (A procedure could be deemed appropriate even if

Table 2 EPAGE II: main clinical categories (chapters).

Chapter	Title	Situations explicitly excluded from assessment	Number of clinical scenarios	
			Round 1	Round 2
1	Iron-deficiency anemia	Malabsorption syndrome Obvious cause of blood loss	57	48
2	Hematochezia	IBD Hemodynamic instability	24	54
3	Lower abdominal symptoms (chronic constipation/lower abdominal pain/bloating)	Duration < 3 months Known IBD FOBT-positive stools Unexplained iron-deficiency anemia Melena, hematochezia Weight loss Risk factors for CRC	24	12
4	Uncomplicated diarrhea	Acute diarrhea (< 4 weeks) Infectious origin Malabsorption syndrome Known IBD Anemia/ bleeding Laxative or sorbitol abuse Risk factors for CRC HIV/AIDS	22	6
5	Evaluation of ulcerative colitis	Prior colonoscopy Cancer surveillance colonoscopy	26	27
6	Evaluation of Crohn's disease	Prior colonoscopy Cancer surveillance colonoscopy	28	23
7	Screening for CRC in known IBD	Other specific colitides (or ileitis): Infectious Ischemic Radiation Microscopic colitis Urogenital ulcer Eosinophilic enteritis	27	43
8	Surveillance (follow-up colonoscopy) after colonic polypectomy	Symptomatic individuals FAP HNPCC (Lynch syndrome) Hyperplastic polyposis	84	77
9	Surveillance after curative-intent resection of colorectal cancer	Palliation	17	16
10	Screening for CRC	Symptomatic individuals Personal history of CRC Personal history of polyps	64	97
11	Miscellaneous indications (lesion detected at recent barium enema or sigmoidoscopy, preoperative colonoscopy, FOBT-positive stools, fulminant colitis, stenosis in IBD, acute diverticulitis, endometriosis, unexplained weight loss, melena, massive hematochezia, iron-deficiency without anemia, hyperplastic polyps at sigmoidoscopy)	All situations covered by other chapters	40	60
Total			413	463

EPAGE II, 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy; CRC, colorectal cancer; FAP, familial adenomatous polyposis; FOBT, fecal occult blood test; HNPCC, hereditary nonpolyposis colorectal cancer (Lynch syndrome); IBD, inflammatory bowel disease.

it had a low likelihood of benefit but there were few risks; such procedures should not be considered necessary.)

- ▶ The benefit to the patient is not small. (A procedure could be considered appropriate if it had a minor, but almost certain benefit to the patient, but would not, however, be considered necessary.)

A general description of the results of the second round of ratings, including the proportion of appropriate, uncertain and inappropriate ratings, globally and by chapter, is reported here. Additional information about the variation in agreement in panel ratings between the first and second round of ratings was established.

Panelist X – round 1/Chapter 1 – Page 1

Iron-deficiency anemia (malabsorption syndrome excluded)

	No current symptoms	Upper abdominal symptoms	Lower abdominal symptoms	Scenario Numbers
Age < 50, no risk factors for colorectal cancer				
Men, OR women with gynecological cause excluded				
No investigation done	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1–3
Previous lower GI investigation done (sigmoidoscopy, barium enema or both)				
Potential source of bleeding explaining IDA	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	4–6
Potential source of bleeding not identified	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	7–9
Previous upper GI endoscopy done				
Potential source of bleeding explaining IDA	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	10–12
Potential source of bleeding not identified	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	13–15
Women with gynecological cause NOT excluded				
No investigation done	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	16–18
Previous lower GI investigation done (sigmoidoscopy, barium enema or both)				
Potential source of bleeding explaining IDA	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	19–21
Potential source of bleeding not identified	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	22–24
Previous upper GI endoscopy done				
Potential source of bleeding explaining IDA	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	25–27
Potential source of bleeding not identified	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	28–30

Appropriateness scale: 1 = extremely inappropriate, 5 = uncertain, 9 = extremely appropriate

Fig. 1 Rating matrix for the first round (example). Example for iron-deficiency anemia (extract showing scenarios 1–30). The symptoms evaluated are represented in columns. The scenarios are further described in detail, with color coding for greater clarity. In each box, values are shown on a 9-point scale. Appropriateness scale: 1 = extremely inappropriate; 5 = uncertain; 9 = extremely appropriate.

Results

Appropriateness and necessity ratings

A total of 413 indications were submitted to the panelists for the first round of ratings. The analyses of the votes, experts' comments, and new evidence published during the process led to some slight modifications of the scenarios submitted for discussion by the panel and to the second round of ratings: 463 scenarios were rated by all experts, an increase of 11% on average. These indications were considered appropriate, uncertain, or inappropriate, in 255 (55%), 73 (16%), and 135 (29%) of the clinical indications, respectively. **Table 5** presents these results by chapter of indications.

There was an increase in the proportion of agreement between panelists between the first and second round of ratings. Disagreement between experts and the percentage of uncertain indications decreased between round 1 and round 2, from 15% to 9% and 23% to 16%, respectively. Detailed results by category of indication are presented in the companion articles. A total of 255 appropriate ratings were evaluated for necessity; in 160 (63%) a colonoscopy was considered necessary.

Risks and complications of colonoscopy

A total of 39 articles, published between 1997 and February 2008 and describing the complication rates of colonoscopy, were identified (**Table e6**) [1, 2, 52–88], including minor complications (i.e. abdominal pain or discomfort) or other negative outcomes (i.e.

work days lost). Few studies made a distinction between diagnostic and therapeutic procedures and/or accurately assessed severity of complications.

Perforation and hemorrhage rates were generally <0.1% and <0.3%, respectively. The highest rates reported were 0.25% for perforation [73] and 2.1% for bleeding [88]. Reported complication rates for therapeutic procedures were twice those of diagnostic colonoscopies, in particular for bleeding events.

Cardiovascular events were the most frequent complication occurring in between <0.001% and <2% of colonoscopies [64]. Mortality occurring during or after colonoscopy was assessed in 24 studies. In two-thirds of the studies, no death related to the endoscopic procedure was reported [54, 55, 60, 62, 63, 68, 74–78, 81, 84, 85, 88]. Authors who considered minor adverse events suggested that additional complications may occur subsequently outside the endoscopy suite setting [55, 62, 70, 74, 88]. As reported in three studies focusing on older patients undergoing colonoscopy [69, 78, 87], older patients do not seem to be at higher risk of complications than younger patients. Complication rates also seem to have decreased slightly since the mid-1990s [1], and screening colonoscopies seem to be associated with a lower rate of complications than therapeutic colonoscopies [5, 81, 89, 90].

Chapter*	Scenarios		Appropriateness, % of scenarios		
	Number	% of total	Appropriate	Uncertain	Inappropriate
1	48	10	58	27	15
2	54	11	83	13	4
3	12	3	42	25	33
4	6	1	67	0	33
5	27	6	41	4	55
6	23	5	30	30	40
7	43	9	47	19	35
8	77	17	56	7	38
9	16	4	63	25	12
10	97	21	51	20	29
11	60	13	53	10	37
Total	463	100.0	55	16	29

EPAGE II, 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy

* For complete chapter titles see [Table 2](#).

Table 5 EPAGE II appropriateness results by main clinical categories (chapters).

Conclusion

An update of the EPAGE appropriateness criteria for the use of colonoscopy was undertaken in the spring of 2008. The majority of the indications rated were considered appropriate, whereas about a third were considered inappropriate. The panel meeting led to enhanced agreement between panelists and, indeed, disagreement decreased to less than 10% and the proportion of uncertain indications was reduced by a third. For almost two-thirds of the indications rated as appropriate, the experts considered that colonoscopy was necessary. Given the large number of indications considered by the panel, tabular presentation is not feasible. A presentation by chapter, according to the constituent characteristics of the clinical indications, is, however, available in a convenient internet presentation. Answering a small number of questions allows the physician to determine, in a few simple steps, the degree of appropriateness of colonoscopy for any clinical indication (www.epage.ch).

It is difficult to assess complications of colonoscopy precisely, since there is no consensus on the definition of what constitutes a complication. While accurate data may be, and often are, obtained for severe and acute complications, the extent of delayed and/or minor complications is probably underestimated because of underreporting and the difficulties entailed in data collection. There are also minimal data for minor adverse events, and indirect negative outcomes such as work days lost secondary to colonoscopy, are rarely considered and recorded.

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Competing interests: None

Appendix: The EPAGE II Study Group

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The following tables are available online:
www.thieme-connect.com/media/endoscopy/200903/supmat/endo845.pdf

Table e1 EPAGE II experts.

Table e3 MeSH words/keywords for Medline searches and limits.

Table e4 Relevant websites.

Table e6 Complication rates of colonoscopy reported in 39 studies.