Colonoscopy appropriateness: Really needed or a waste of time?

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Abstract

Technical and quality improvements in colonoscopy along with the widespread implementation of population screening programs and the development of open-access units have resulted in an exponential increase in colonoscopy demands, forcing endoscopy units to bear an excessive burden of work. The American Society for Gastrointestinal Endoscopy appropriateness guideline and the European panel appropriateness of gastrointestinal endoscopy guideline have appeared as potential solutions to tackle this problem and to increase detection rates of relevant lesions. Inappropriate indications based on either guideline are as high as 30%. Strategies based on these clinical criteria or other systems may be used to reduce inappropriate indications, thus decreasing waiting lists for outpatient colonoscopy, saving costs, prioritizing colonoscopy referrals and subsequently decreasing interval times from diagnosis to treatment. Despite the potential role of appropriateness guidelines, they have not been widely adopted partly due to fear of missing significant lesions detected in inappropriate indications. We review the main appropriateness and prioritising systems, their usefulness for detecting relevant lesions, as well as interventions based on those systems and cost-effectiveness.

Key words: Colonoscopy appropriateness; European panel appropriateness of gastrointestinal endoscopy II; National Institute for Health and Clinical Excellence; Colonoscopy prioritisation; Open access endoscopy unit

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Core tip: There is increasing worldwide demand for colonoscopy referrals, overburdening endoscopy units. Controlling the appropriateness of colonoscopy referrals has been proposed to decrease the increased workload. The American Society for Gastrointestinal Endoscopy appropriateness and the European panel appropriateness of gastrointestinal endoscopy guidelines, and prioritisation criteria such as those of the National Institute for Health and Clinical Excellence and the Scottish Intercollegiate Guidelines Network are good candidates for this task. We review the available systems and interventions designed to rationalize colonoscopy demand.
INTRODUCTION
During the last decade we have witnessed a gradual increase of endoscopic procedures and a reduction of radiological techniques to examine the gastrointestinal tract such as esophagus-gastro-duodenal transit or barium enema. Some significant quality improvements have contributed to the widespread diffusion of endoscopic techniques, including conscious sedation[1], safety[2] and technological developments.

Furthermore, the implementation of screening programs for the early detection of colorectal cancer (CRC) and the development of open-access endoscopy units may further increase the demand for outpatient colonoscopy and the overall workload of endoscopy units. These factors are particularly worrisome in universal insurance health care systems.

In this setting, rationalization of the demand is mandatory to prevent overburdening endoscopy units, to improve efficiency in colonoscopy and to reduce costs and potential risks arising from inadequate colonoscopy referrals.

This review analyses, firstly, the causes of increasing workload of endoscopy units, with greater emphasis on especially focusing on population screening programs and open-access endoscopy units; secondly, strategies developed to control colonoscopy appropriateness and their results, including appropriateness criteria and adherence to guidelines, and finally criteria for prioritising referrals with higher risk of advanced colorectal neoplasms. Table 1 shows the highlights of this review.

INCREASING WORKLOAD OF ENDOscopy UNITS: SCREENING COLONOSCOPY AND OPEN ACCESS ENDOscopy UNITS
A recent survey carried out in the United States found that the number of colonoscopies performed had risen three to four times between 1998 and 2004[3], with colonoscopy being the most demanded endoscopic procedure. Similar patterns have been found in Europe[4]. Furthermore, the European Commission has recommended the implementation of programs for the detection of CRC in all countries of the Union[5]. A recent report assessed the amount of colonoscopies generated by a population screening program, depending on the screening strategy and uptake. Assuming a participation rate of 60%, screening might double the annual workload of endoscopy units[6]. Another source of additional referrals arising from screening programs are subsequent surveillance colonoscopies required after the resection of colorectal adenomas and CRC. Notably, surveillance colonoscopy after resection of colorectal adenomas is the most frequent indication in patients aged over 74 years in the United States, accounting for 28.9% in women and 37.9% in men[7]. Furthermore, according to a recent meta-analysis, more than 30% of the average-risk population may have colorectal adenomas[8]. Similar data have been reported in European studies[9-11]. Such a volume of colonoscopies represents a substantial burden.

A potential source of inappropriate referrals is open-access endoscopy units, increasingly frequent in both the United States and Europe. In open-access endoscopy units, any physician (not only a gastroenterologist) may request an endoscopic procedure[12]. These units emerged in an effort to save costs, preventing unnecessary office consultations with the gastroenterologist. Open-access endoscopy units may also be useful as a “shortcut”, decreasing waiting times between consultation and colonoscopy. In fact, time off work for appointments is a problem for patients and open-access endoscopy units may expedite the diagnosis of severe diseases, and decrease empirical treatments[13]. However, one wonders whether the ease of access would not also increase the workload of endoscopy units resulting from a higher rate of inappropriate referrals, further increasing waiting lists and total costs. Thus, rationalization of the indication is considered essential.

Open access endoscopy units can be roughly classified as simple or censored. While no control system is applied in the former, in the latter, referral appropriateness is continuously checked by trained staff[14].
Compared with ASGE criteria, EPAGE-Ⅰ criteria are usually considered “significant lesions”. To date, four studies have assessed the benefit of EPAGE-Ⅰ criteria for predicting appropriateness and diagnostic yield of significant lesions (Table 3) [9-10,16,33]. Only in the largest study was the design fully prospective [10]. Three studies were carried out in Spain [9-10,33] and one in Norway [10]. Although statistical performance with confidence intervals of EPAGE-Ⅰ studies were described in only two of the studies [10,16], enough information was available in the other two for
calculation\(^9,^{10}\). Taking into account the pooled results of the four studies, 75.4% of colonoscopy referrals were deemed appropriate, 13.9% inappropriate and 10.7% uncertain. A validation study of these criteria showed that significant lesions were more prevalent in appropriate colonoscopies than in those considered inappropriate (38.8% vs 24.5%; OR = 1.95, 95% CI: 1.22-3.13; \(P < 0.005\))\(^{10}\). This study also reported the performance for significant neoplastic lesions (advanced adenoma and CRC), showing sensitivity, specificity, positive and negative predictive values of 98% (95% CI: 95-100), 11.5% (95% CI: 9-14), 11.2 (95% CI: 9-13) and 98% (95% CI: 95-100) respectively. In accordance with other studies, an appropriate indication was more frequent in patients over 50 years compared with younger individuals (92.9% vs 76.7%; OR = 3.98, 95% CI: 2.60-6.09, \(P < 0.001\)). In fact, 50% of inappropriate referrals were found in patients younger than 50 years, despite constituting only 20% of referrals. In studies carried out in Spain, the indication with the highest rate of inappropriate was surveillance colonoscopy, ranging from 41% to 76%\(^{9,10,21,28}\), whilst in the Scandinavian study, this was lower abdominal symptoms (49%)\(^{10}\). In one study, inappropriateness in subjects younger than 50 years was separately analyzed. CRC screening at a younger age than usually recommended (33%) followed by surveillance colonoscopy at shorter intervals than recommended (20.8%) were the most frequent causes of colonoscopy overuse\(^{10}\).

Recent evidence has shown that the application of EPAGE-\(\text{\textregistered II}\) criteria decreases rates of inappropriate compared with EPAGE- I criteria and, more importantly, decreases the rate of missed significant lesions\(^9,^{16}\). In both studies, the specificity of EPAGE-\(\text{\textregistered II}\) criteria was lower than that of the first version, theoretically decreasing the impact of EPAGE-\(\text{\textregistered II}\) criteria on saving colonoscopies. Nevertheless, EPAGE- \(\text{\textregistered II}\) might be considered safer than EPAGE-I with respect to missed significant lesions. Some authors have suggested jointly calculating uncertain and inappropriate colonoscopies, as opposed to what is usually done (combining appropriate and uncertain together)\(^9,^{16}\). In fact, no significant differences in diagnostic yield were found in two studies that compared different combinations\(^9,^{16}\). However, some CRC might be missed with this approach. Of 109 CRC diagnosed in the 4 series, 2 were diagnosed in inappropriate referrals (1.83%) and 3 more in uncertain ones (2.75%). Therefore, it seems safer to consider uncertain and appropriate referrals together to prevent missing significant lesions. Recently, the combination of EPAGE criteria with blood or fecal biological markers was tested with the purpose of increasing appropriateness and improving diagnostic yield of significant lesions\(^{34}\). In one study, fecal calprotectin\(^{34}\), which has shown its capacity to distinguish organic diseases (\(i.e.,\) inflammatory bowel disease) from functional disorders, was tested with EPAGE criteria in 224 consecutive patients with abdominal discomfort. Diagnostic yield for significant lesions was significantly higher when the combined strategy was used (70.2%) compared with either EPAGE or calprotectin alone (diagnostic yield 23.6% and 57.4% respectively). The combined strategy also improved re-classification of patients with a higher rate of appropriateness.

In summary, the refined EPAGE-\(\text{\textregistered II}\) criteria are more sensitive than the old EPAGE-I, and may be an effective strategy to assist the clinician to decide whether a colonoscopy should be requested or not. They may also be a useful tool for decreasing colonoscopy overuse, as well as increasing diagnostic yield.

### INTERVENTIONS BASED ON APPROPRIATENESS CRITERIA

Several studies have suggested that the medical specialty of the referring physician may influence colonoscopy appropriateness\(^{9,10,21,28}\), with surveillance after polypectomy at shorter intervals than recommended being the most inappropriate indication. Therefore interventions based on audits and training of referring physicians are warranted to increase appropriateness.

Using EPAGE-\(\text{\textregistered II}\) criteria\(^{10}\), 91% of the inappropriate referrals corresponded to CRC screening, surveillance of neoplastic lesions (adenomas or CRC) or to subjects younger than 50 years. Subjects with any of these conditions had a lower rate of significant lesions and advanced neoplastic lesions than those who did not meet these conditions (31.2% vs 46.6%, \(P < 0.001\); OR = 1.9, 95% CI: 1.47 to 2.51 and 5.1% vs 18.1%, \(P < 0.001\); OR = 4.1, 95% CI: 2.60 to 6.41, respectively). In an interventional prospective study\(^{35}\), 451 patients with high probability for inap-

### Table 3  European panel appropriateness of gastrointestinal endoscopy \(\text{\textregistered II}\) studies addressing appropriateness and diagnostic yield

| Ref. | Design\(^\text{1}\) (referrals) | EPAGE-\(\text{\textregistered II}\) \(\%\) (appropriate) | \(S\) (95%CI) | \(Sp\) (95%CI) | PPV (95%CI)\(^*\) | NPV (95%CI)\(^*\) |
|------|----------------|-----------------|-------------|-------------|-----------------|-----------------|
| Carrion et al\(^8\)(2010) | R 655 | 82.0 | 80.3 (74.0-84.3) | 16.8 (14.9-18.5) | 24.8 (23.1-26.4) | 71.3 (63.1-78.6) |
| Arguello et al\(^8\)(2012) | R 619 | 82.6 | 78.3 (73.8-82.4) | 34.4 (31.3-37.3) | 45.2 (42.6-47.6) | 69.6 (63-75.4) |
| Gimeno García et al\(^8\)(2012) | P 968 | 89.5 | 93.1 (90.0-96.3) | 12.7 (10.0-15.0) | 38.8 (36.0-42.0) | 75.5 (67.0-84.0) |
| Eskeland et al\(^8\)(2014) | R 295 | 91.0 | 92.6 (84.8-96.6) | 22.9 (17.8-29.0) | 31.3 (25.3-37.3) | 89.1 (80.7-97.5) |

\(^\text{1}\)Study design: R (retrospective); P (prospective); \(^\text{2}\)Appropriate and uncertain referrals jointly analysed; \(^\text{3}\)S (sensitivity); Sp (specificity); \(^\text{4}\)PPV (positive predictive value); NPV (negative predictive value).
propriateness (age < 50 years, surveillance colonoscopy or screening colonoscopy) were attended in an appropriateness outpatient clinic. EPAGE II criteria along with current Spanish Association of Gastroenterology guidelines were applied and colonoscopy was finally requested when deemed appropriate. In patients with an inappropriate indication, a different approach was carried out; a more suitable examination was requested, (i.e., biochemical tests, abdominal ultrasonography) or treatment was prescribed when a functional disorder (intestinal bowel syndrome or functional dyspepsia) was suspected. Appropriateness was compared with a historical cohort of 968 patients who underwent colonoscopy and to whom EPAGE-II criteria were applied. The intervention achieved a significant reduction of appropriateness (5.2% vs 10.5%, OR = 0.46, 95%CI: 0.27-0.81) and, furthermore, increased the diagnostic yield of significant lesions (50.7% vs 37.3%, OR = 1.73; 95%CI: 1.33-2.25). However, these encouraging results of a censored open access unit should be taken with caution as the cost-effectiveness of this strategy has not been evaluated yet.

In another interventional study involving 133 GPs, a tailored educational program was assessed using ASGE/SIED appropriateness guidelines. Fifty GPs finally attended the course and completed a multiple choice test to assess the level of learning. The rest received a brief summary of the ASGE/SIED appropriateness criteria by regular mail. Colonoscopy appropriateness was compared before and after the intervention. In this study, appropriate referrals significantly increased from the first to the second period, resulting in a mere 7% of inappropriateness (23% vs 7% respectively; P < 0.001). Although the effect was more striking among attendants, appropriateness also increased in those GPs who did not attend the course but received the ASGE/SIED criteria by mail. Furthermore, the authors also reported long-term efficacy of the intervention, with the benefit being maintained 1 year later. Therefore, this study encourages greater diffusion of the current guidelines on the main colonoscopy indications and the usefulness of periodic educational programs in an open access unit setting.

ADHERENCE TO GUIDELINES
Several studies have addressed the impact of compliance with the current surveillance guidelines after adenoma or CRC resection on colonoscopy waiting lists. One study evaluated the effect of good compliance with the guidelines proposed by the American Gastroenterology Association (AGA) for surveillance after resection of colorectal adenomas on improving appropriateness and decreasing the waiting list. Compliance with guidelines not only improved appropriateness in this indication but also increased the interval between surveillance colonoscopies by 0.73 years, with a 14% reduction of annual colonoscopies for this indication. Another work assessed the impact of compliance with the guidelines of the British Society of Gastroenterology and the Association of Coloproctology of the United Kingdom and Ireland for screening and surveillance after endoscopic polypectomy. In this multicenter study, researchers from a tertiary care referral center applied these guidelines to the waiting list of several hospitals, recommending the exclusion of patients with an inappropriate referral. Overall, in 78% of cases the indication was inappropriate. The appointment was delayed in 27% on them, whilst the indication was deemed inappropriate in the remaining 51% and were cancelled. The authors therefore concluded that adherence to the guidelines could reduce waiting times for diagnostic colonoscopy, but might trigger ethical and moral debate.

CLINICAL IMPACT AND COST-EFFECTIVENESS OF APPROPRIATENESS GUIDELINES
The educational-based intervention study reported by Grassini et al., noted above, estimated a saving of 19500 euros per year in a low-volume endoscopy unit (1700 colonoscopies per year) and a 15% reduction on the waiting list for outpatient colonoscopy. A recent systematic review assessed the impact of ASGE and EPAGE-I criteria on the cost-effectiveness of colonoscopy based on the appropriateness of an indication in selecting patients who were referred for colonoscopy. Appropriateness studies reported until 2007 were considered for inclusion. In a decision-analysis model, a relatively high prevalence of CRC was found in inappropriate referrals (1.1%; 95%CI: 0.7%-1.4%) along with a significant reduction in survival because of CRC diagnostic delay. Therefore, the authors recommended refining the current criteria before using them in routine clinical practice. However, only the first version of EPAGE criteria was used in the studies included, but not the more recent EPAGE II criteria, which as previously mentioned are significantly more sensitive, especially for CRC.

STRATEGIES FOR PRIORITIZING PATIENTS
Some systems have been developed to prioritise patients with alarm signs or symptoms. The most well-known is the one developed in the United Kingdom by the National Institute for Health and Clinical Excellence (NICE), implemented in 2000 (Table 4). Based on this system, patients meeting certain clinical criteria are referred for consultation with the gastroenterologist within two weeks in order to decrease waiting times for CRC diagnosis. This guideline was updated in 2005, with the goal of reducing death...
rates by 20% in people under 75 years in 2010\(^{[42]}\). The United Kingdom National Health Service later developed the "straight to test" approach for suspected CRC, in order to delete time-wasting visits and therefore delays in the diagnosis phase\(^{[44]}\). The Scottish Intercollegiate Guidelines network (SIGN) has also developed referral criteria which are less strict than NICE criteria. They are also based on alarm signs and symptoms of CRC\(^{[45]}\) (Table 5).

Beggs et al\(^{[46]}\) compared the effect of the two week-referral pathway for colonoscopy with the traditional pathway (referring the patient firstly to the gastroenterologist) on colonoscopy waiting lists and direct costs (only consultation and colonoscopy). The former strategy was less costly (saving more than £26,000), and also significantly reduced colonoscopy waiting list numbers compared with the usual care process (by 166.6 d, \(P < 0.01\)). Another study assessed the time intervals between referral for colonoscopy, diagnosis and treatment in a fast referral group compared with the usual care process\(^{[47]}\). As expected, delay to endoscopic and histological diagnosis was significantly lower for the fast referral group (\(P < 0.0001\)), but also to treatment (\(P = 0.048\)). One study showed that the "straight to test" strategy was also an effective strategy for CRC detection at early stages compared with the standard of care\(^{[48]}\).

A recent Spanish multicenter study highlighted the limited accuracy of NICE criteria in a prospective cohort of 787 symptomatic patients referred for colonoscopy\(^{[49]}\). NICE and SIGN criteria were compared with the immunochemical fecal occult blood test (FIT) at 100 ng/ml threshold for CRC detection. FIT was significantly more sensitive than NICE criteria (87.6% vs 61.9% respectively; \(P < 0.001\)) but similar to SIGN criteria (82.5%, \(P = 0.4\)). However, the specificity of FIT was significantly higher than either NICE or SIGN criteria (77.4%, 65.2% and 42.7% respectively; \(P < 0.001\)). These data support the idea that, in isolation, NICE criteria lack sufficient diagnostic accuracy and should be used in combination with other markers. Studies using a combination of clinical, blood and fecal markers are currently ongoing in order to improve the accuracy of the clinical criteria\(^{[50]}\).

Recently, risk scores based on demographic and clinical information have been developed for either symptomatic or asymptomatic patients in order to prioritise outpatient colonoscopy\(^{[51,52]}\). Law et al\(^{[52]}\), with 1013 symptomatic Asian subjects, showed that a score higher than 17 predicted CRC with a specificity of 96%. The area under the curve of the risk score was 0.83, proving that the model had a good discrimination, leading the authors to conclude that this model might be useful to prioritise colonoscopy. Another recent study, carried out in asymptomatic Caucasian patients\(^{[51]}\), validated a model for detecting advanced colorectal neoplasia based on demographics and family history of CRC. The authors suggested that this model might help health care providers to make decisions about screening.

**CONCLUSION**

Although appropriateness criteria (ASGE and EPAGE II criteria) enable a better selection of colonoscopy referrals and increase the rate of significant lesions detected, further refinement is required since some relevant lesions are still missed even when the more sensitive EPAGE II criteria are used. Prioritising systems such NICE criteria seem to accelerate CRC diagnosis and treatment, without increasing the waiting list for outpatient colonoscopy, but they might not be sensitive enough for selecting patients with CRC. Educational programs on surveillance colonoscopy and adherence to the current guidelines are warranted to reduce inappropriate referrals. Finally, the combination of clinical criteria (appropriateness or prioritising criteria) with blood or fecal markers might be a better approach than isolated clinical criteria to increase the diagnostic yield of significant lesions.

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