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Screening for colorectal cancer: The role of CT colonography

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KEYWORDS
Colon; CT scan; Cancer; Organized screening programs

Abstract  Colorectal cancer, which is the third most frequent cancer and the cancer with the second highest mortality rate, frequently develops on a pre-existing adenomatous polyps whose slow growth and malignant degeneration can be identified and controlled by effective screening. Although most lesions can be detected and resected during optical colonoscopy (OC), the cost, risk and poor acceptance of this technique by the general population means that it is reserved for high-risk or very high-risk individuals. The fecal occult blood test (FOBT) (such as the Hemoccult®) is proposed for intermediate-risk individuals between 50 and 75 years old. However, despite the improvements that have been made in this method, sensitivity is low, and although it is simple, it is too rarely used. CT colonography (virtual colonoscopy) is proposed in case of failure, additional risk factors or refusal of optical colonoscopy in high-risk patients or in the presence of a positive FOBT. It should also be proposed as an alternative to the FOBT test to patients who accept the constraints of this technique.

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In 2012, colorectal cancer (CRC) was the third most frequent cancer, with 42,152 new cases in France, after prostate and breast cancer. It was the cause of 17,722 deaths, making it the cancer with the 2nd highest mortality after lung cancer. Although the global incidence has been stable for many years, mortality has decreased from nearly 20% in 1980 to less than 14% in 2010 in men and slightly less in women. The decrease has slowed since then. This decrease is due to more effective treatment, including of liver metastases as long as they are isolated and that a portion of the liver parenchyma is disease free. The development of an organized CRC screening program based on the fecal occult blood test (FOBT) has...
resulted in somewhat earlier detection of these cancers or
treatment of adenomatous polyps, which are precancerous
lesions. However this mass-screening program has two major
limitations:
• poor participation, approximately 33% of the French pop-
ulation;
• low sensitivity.

Indeed the sensitivity of this approach is approximately
50% for the diagnosis of cancer and approximately 10% for
the diagnosis of an adenoma larger than 10 mm. Of
course, the risk of mortality from CRC is reduced by 30%
in participants in the screening campaign, although the
test only provides earlier diagnosis of approximately half
of the cancers in this population, while it does not, like
colonoscopy in high-risk patients, effectively diagnose pre-
cancerous lesions.

CT colonography is an effective, very low risk technique
to explore the colon, which could play a role in cancer
screening: to determine its role, we must first understand
the basis of CRC screening.

The basis of screening

Adenoma-cancer sequence

More than 60% of CRC develop from adenomatous polyps,
initially benign lesions with a risk of malignant transforma-
tion. The risk of malignant degeneration increases with the
size of the polyp (above 1 cm, because below, the risk is less
than 0.3%), the presence of a villous component and the
degree of dysplasia. This “adenoma-cancer sequence” is
very slow and takes a mean 10—20 years except in the right
colon where serrated polyps, whose carcinogenesis is more
rapid, are located. Only an estimated 100/1000 (10%) ade-
nomas followed for 10 years will grow to 10 mm and 25 (2.5%) will
become malignant. It is therefore clear that colonoscopy and
removal of large polyps can significantly reduce the
development of colorectal cancer, except in the right colon.
However, it is not possible to propose this uncomfortable,
expensive test, associated with a certain risk (0.3% for per-
foration as well as the risks associated with anesthesia) to
the general population. It is only proposed to high risk or
very high risk patients.

Level of risk

The risk can be classified into three levels:
• average risk can be attributed to the general population over
the age of 50. The mean age of patients at diagnosis is
70 years old. The highest risk is at approximately 80 years
old. In France, diagnostic screening in this group is based
on the FOBT every two years;
• high risk is associated, in particular, with a history of CRC
or a polyp of more than one cm. A personal history of
CRC is not limited by age if it involves the patient or two
first-degree relatives. However, lesions detected before
the age of 65 are taken into account if only one mem-
ber of the family is concerned. In addition, patients with
extensive, chronic inflammatory disease of the intestine
for more than 10 years at diagnosis are also considered
high-risk. In this high-risk group, screening is based on reg-
ular colonoscopy after the age of 45, or earlier, five years
before the index case. Colonoscopy is repeated every five
years. This delay is shortened to three years if an ade-
noma of more than 1 cm or with a villous growth pattern
is detected. It is reduced to 5 years again after a normal
test;
• very high risk includes patients with genetic diseases such
as familial adenomatous polyposis with several hundred
polyps in the colon or the Lynch syndrome (or hereditary
non polyposis colorectal cancer [HNPCC]) with early onset
cancer, in particular colorectal cancer, but which may
involve other organs especially the endometrium. Regu-
lar colonoscopies should be performed after adolescence.
Prevention may even include preventive colectomy
during adolescence.

Besides this very specific context, it is clear that effec-
tive prevention must include early diagnosis of lesions larger
than a centimeter as of the age of 50 and especially between
65 and 75 or older depending on the patient’s physiological
condition.

Screening methods

An effective screening method should be easy to perform,
sensitive, inexpensive and accepted by the patient. There
are numerous screening methods [1]:
• the detection of FOBT is performed by the patient by six
fecal smears. This test is inexpensive and accepted by
patients (approximately 30%), but its efficacy in detecting
advanced adenomas is poor, approximately 10%; its advan-
tage is that it provides early diagnosis of half the cancers
in this population. The test must be performed every two
years to be effective. Marketing of an immunological test
(OC-Sensor® or Magstream®), which only requires a fecal
sample, is easier, simpler and slightly more specific. This
should improve results, but mainly in the detection of
cancers rather than pre-cancerous lesions;
• search for the presence of tumoral DNA in stools or blood
is also possible. This test is more sensitive but more expen-
sive and is only reimbursed by a few mutual insurance
policies;
• sigmoidoscopy is offered in numerous countries. It is
based on the fact that most (60%) lesions are located in
the sigmoid colon and that it can be performed without
general anesthesia. However, the colon must be cleansed
by an enema. This test is more difficult than a stool sample
for the patient, and the entire colon is not investigated;
• colonoscopy is considered to be the best method, because
polyps can be diagnosed and resected. Nevertheless it has
several limitations. Its results are not perfect, in particu-
lar in the right colon. It is incomplete in 5% of the cases,
but even if it is complete, colonoscopy does not identify
15—25% of adenomas less than 1 cm, 0—6% of adenomas
larger than 1 cm and 0.5—6% of CRC. It is associated with
a certain risk in addition to the risk of anesthesia, which
is very low except in frail patients, and especially per-
foration (0.1% for colonoscopy without polypectomy). It
generally requires hospitalization and sick leave the day
of the test and often the day before for the preparation. It is therefore expensive;
• finally CT colonography is an alternative to colonoscopy but only for detection. The use of this technique is still too limited in France.

CT colonography

This technique was introduced 20 years ago and it has gradually improved with optimization of bowel preparation, the quality of insufflation, sensitivity of CT scan sequences and improvements in visualization software, which also includes functions of automatic detection.

Colon preparation

It is generally based on a fiber-free diet, laxatives, increasingly replaced by a small quantity of polyethylene glycol (PEG). Fecal residue is tagged by ingestion of an iodated contrast medium the day before the examination. This preparation could be simplified to ingestion of the oral contrast medium alone to improve acceptance of this test for a mass-screening program.

If colonoscopy is unsuccessful, a complementary CT colonography performed before the end of the anesthesia in the prepared colon can be useful. Liquids should be tagged by having the patient drink 25CL of water containing 10% iodated contrast medium one hour before the test.

Colonic insufflation

It should be performed by insufflation of CO₂ using a rectal catheter and bulb. Insufflation should be gradual. Pressure is controlled by the device to prevent excess pressure, which could cause perforation. An average of three liters of air is insufflated, but this depends upon the size of the colon and is increased in case of leaks, in particular ileo-caecal valve incontinence with reflux into the small intestine. When the colon is fully distended, the patient has gas pains that may become intensely painful. Distension time may be limited by preparing the acquisition before full distension and by increasing pressure at the last minute. CO₂ reduces the patient’s discomfort in the immediate post-examination period because it is partially absorbed by the colonic mucosa.

Image acquisition

After at least one liter of insufflation, an adjusted scout-view is performed to position the slices so that the entire colon will be covered, leaving some leeway above to avoid cutting off a flexure. Infra-millimeter slices are not necessary because they often entail more radiation; the number of artefacts may be increased, as well as producing more images, limiting the fluidity of the 3D analysis. Radiation should be limited, for example by using 100 kV with a tube current of 35–70 mAs depending on the weight of the patient or automated with a high level of noise (for example 75 mAs for a general electric device). In this case, a dose-length product (DLP) of less than 300 mGy.cm is obtained for the entire test. Images should be obtained with the patient in two positions, supine and prone or in both decubitus lateral positions if the patient is overweight, to move remaining fecal residue or pendunculated polyps.

Interpretation and reading of results

2D interpretation

A primary 2D interpretation of images is performed with very large lung-size window widths to analyze the lumen of the colon. Any segments that are incomplete should be identified in this primary series of images, so that they can be obtained in the second series. If necessary, a third series should be obtained. Any lesions larger than a centimeter should be identified in this primary reading. The images should also be read in a narrower window width abdominal, for example, to identify extracolonic lesions (bladder, kidneys, aorta...)

3D interpretation

3D interpretation can be used to identify infracentimetric lesions that cannot be seen on 2D images. The first step is to define the central line. 3D interpretation can be performed using endoluminal navigation or "fly-through" views or by virtual dissection that "flattens" the colon. This latter method avoids antegrade and retrograde fly-throughs, by reversing the sense of the virtual camera. It requires specific training because it results in distortions, in particular of the sharp curves of the colon, as well as changes in the perception of reliefs. Computed aided detection (CAD) can facilitate lesion detection, especially if the colon is clean and relaxed. It reduces reading time and improves the results of less experienced radiologists [2].

Density measurement

When a polyp-type lesion is identified on 3D, its density must first be determined. The density of tumor tissue is similar to that of the wall of the colon while a lipoma or an inverted diverticulum is fatty and fecal residue is dense if it has been correctly tagged by contrast medium taken by patient the day before. If the lesion seems to have a soft tissue density it must be identified again in the same spot in an additional image to exclude non-tagged mobile residue (Fig. 1).

C-RADS Classification

The C-RADS [3] classification provides a standardized description of each lesion including:
• the segment of the colon as well as the side if the lesion is in a flexure;
• the shape of the lesion: sessile or pendunculated, flat with or without a depressed surface, irregular, or stenotic;
• the largest diameter of the head of the polyp (without taking into account a possible stalk…) while mentioning whether 2D or 3D visualization was used;
• the type of density of the lesion (cf. supra).

This classification proposes an approach (Table 1) that is not officially accepted in France, but which seems to be coherent with the level of risk of malignant degeneration in relation to the size of the lesion. "Diminutive" lesions of less than 6 mm can be left. On the other hand a follow-up colonoscopy is indicated in the presence of lesions that
Figure 1. Numerous polyps of the right colon in a patient who has already had several adenomas resected. CT colonography shows a sigmoid lesion (not shown) and small anomalies of the right colon, which illustrate the practical approach with this method: a: CT colonography view with flattening of the right colon from the series of images in the decubitus position. A grey band can be seen on top and on
are larger than 10 mm or more than three lesions larger than 5 mm. Other than these cases, follow-up by CT colonography or colonoscopy can be proposed.

Extracolonic lesions

Extra-colonic lesions can also be identified with CT colonography. Certain lesions have no practical impact, others require follow-up or even therapeutic management. The impact of these lesions is also classified by the C-RADS. Although their diagnosis usually provides additional benefit to the patient, there is also a risk of detecting lesions that do not have any impact.

Performance

The greatest difficulty of this technique is that it is complicated to learn to obtain adequate distension and especially reading and interpretation. Indeed, specific training including reading at least 50 cases is necessary to reach a minimum level of expertise as well as to avoid the main pitfalls of this technique. A highly experienced radiologist can reach a level of detection that is similar to that of colonoscopy, or approximately 90% of 8 mm lesions or lesions that are larger than 4–5 mm (Table 2) [4–7]. The differences observed in the multicenter French study were because certain teams had just begun to use this technique while others had more experience [7]. The final results of the readers were correlated to those obtained in the 50 training cases. The most experienced readers at the beginning of the study still obtained better results, despite training that should theoretically have been sufficient for all. The efficacy of CAD can partially compensate for these differences.

The role of CT colonography

In 2012, the French National Health Authorities (Haute Autorité de santé [HAS]) associated with expert medical societies defined the indications for CT colonography [8].

CT colonography is not indicated for screening in very high-risk patients.

In high or intermediate risk patients with a positive FOBT it should be proposed:

- as a complementary test in case of incomplete colonoscopy (Fig. 2);
- in case of co-morbidities that increase the risk of colonoscopy;
- or in case of refusal of colonoscopy.

The indication for CT colonography should be validated by the patient’s clinical physician and the radiologist who is

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### Table 1 Classification of colon lesions according to C-RADS guidelines from the Working Group on Virtual Coloscopy of American College of Radiology [3].

<table>
<thead>
<tr>
<th>C-RADS</th>
<th>Conclusion</th>
<th>Circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0</td>
<td>Technically incomplete test, non-contributory</td>
<td>Incomplete colon preparation, not possible to exclude the presence of a lesion larger than 10 mm; Insufficient colon distension with collapsus of one or more segments in the two series of images; Must be compared to an earlier test</td>
</tr>
<tr>
<td>C1</td>
<td>Normal results or a benign lesion: routine screening should continue in 5–10 years.</td>
<td>No polyp of 6 mm or more; Lipoma or inverted diverticulum; Non-tumoral lesion: diverticulum</td>
</tr>
<tr>
<td>C2</td>
<td>Intermediate lesion or undetermined diagnosis: follow-up in 3 years or colonoscopy recommended (American Cancer Society recommendations)</td>
<td>1 or 2 intermediate polyps 6–9 mm; Undetermined diagnosis: a polyp larger than 6 mm cannot be excluded because of a technically incomplete test</td>
</tr>
<tr>
<td>C3</td>
<td>Probable advanced adenoma: colonoscopy necessary</td>
<td>Polyp 10 mm or larger</td>
</tr>
<tr>
<td>C4</td>
<td>Colon mass, malignant unless proven otherwise: treatment necessary</td>
<td>More than 2 intermediate 6–9 mm polyps; Irregular mass or stenotic colon; Extracolonic extension</td>
</tr>
</tbody>
</table>
Table 2  Results obtained in the main studies comparing CT colonography to colonoscopy with a distinction by polyp size.

<table>
<thead>
<tr>
<th>References</th>
<th>Patients ( (n) )</th>
<th>CT colonography ( \geq 6 \text{ mm} )</th>
<th>CT colonography ( \geq 8 \text{ mm} )</th>
<th>CT colonography ( \geq 10 \text{ mm} )</th>
<th>Colonoscopy ( \geq 6 \text{ mm} )</th>
<th>Colonoscopy ( \geq 8 \text{ mm} )</th>
<th>Colonoscopy ( \geq 10 \text{ mm} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pickhardt et al. NEJM 2003 [4]</td>
<td>1233</td>
<td>88.7</td>
<td>93.9</td>
<td>93.8</td>
<td>92.3</td>
<td>91.5</td>
<td>87.5</td>
</tr>
<tr>
<td>Johnson et al. NEJM 2009 [5]</td>
<td>2531</td>
<td>78</td>
<td>87</td>
<td>90</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( \geq \): greater than or equal to.

performing the examination to adapt the bowel preparation and the technical protocol to the clinical context and any existing co-morbidities.

In France, CT colonography is not proposed for mass screening programs. From a medicoeconomic standpoint, CT colonography every 10 years should be less expensive and more effective than a Hemoccult® test every two years [9, 10]. However, it is obviously impossible to offer a CT scan to the general population because there are not enough machines and the rate of acceptance would be low, which would cancel the usefulness of screening. Colon preparation that does not require taking a laxative but an oral contrast medium for several days might improve acceptance slightly, but overall this technique has too many constraints to be widely accepted [11]. On the other hand, it should be recognized and covered by National Health Insurance in patients who accept the constraints of this test, which is not the case today in France [12].

Certain insurance policies in other countries such as the United States propose and even require screening for colon lesions by colonoscopy or increasingly frequently by CT colonography. In 2007, Kim compared the two strategies and analyzed two similar groups of more than 3000 patients [13]. One hundred twenty-one advanced adenomas or

Figure 2. Positive Fecal Occult Blood Test. Incomplete colonoscopy that does not reach the sigmoid which is deformed by severe chronic diverticulosis: a: axial slice showing diverticular lesion with thickening of the sigmoid wall resulting in stenosis which explains colonoscopy difficulties. Impacted diverticula (arrowheads); b: endoluminal view of a pedunculated polyp in the descending colon; c: endoluminal view of a sessile polyp in the transverse colon; d: coronal 2D reconstruction showing an irregular thickening of the medial wall of the caecum corresponding to an adenocarcinoma (arrow).
Cancers were discovered with seven perforations in the group that underwent colonoscopy as the first line screening test. In the group that underwent CT colonography as the first line screening test, 246 colonoscopies were performed based on C-RADS criteria or 7.8% of patients, resulting in a diagnosis of 123 advanced adenomas or cancers, and no perforations. The influence of mass screening by CT colonography on mortality will not be known for many years. In any case as long as screening tests are not required by mutual insurance companies, this should still be recognized as an acceptable test in France.

On the other hand from a medicoeconomic standpoint, individual patients who have understood what is at stake and who want an effective test for precancerous lesions and not just cancer, should certainly be proposed CT colonography performed by an experience team rather than colonoscopy which is more expensive, has a higher risk, and with very little difference in results.

**Conclusion**

Colon preparation for CT colonography is slightly less difficult than that for colonoscopy, and this technique is associated with fewer risks, is less expensive and does not necessarily require sick leave.

CT colonoscopy is an effective screening test for advanced colon tumors (cancers and adenomas of more than 10 mm)

The results of reading and interpretation vary considerably depending on the readers, but an experienced reader can obtain results similar to those obtained by colonoscopy.

In high-risk patients with clinical symptoms or with a positive fecal occult blood test, colonoscopy is the first line test, and CT colonoscopy is only proposed if colonoscopy is incomplete or cannot be performed because of patient refusal or additional risk factors.

In intermediate-risk patients, mass screening in France is based on the fecal occult blood test. This is moderately sensitive for cancers and has a very low sensitivity for adenomas.

In France, although CT colonography is not yet offered for mass screening in intermediate-risk populations, it is certainly preferable to colonoscopy for individual patients who would like more sensitive testing.

**Take-home messages**

- Colon cancer is one of the most frequent cancers (third most frequent).
- Mortality from colon cancer is high (second highest).
- It often develops on a pre-existing, slow growing, lesion (adenoma).
- Screening is based on:
  - the detection and resection of lesions by colonoscopy in high risk patients,
  - or the detection of asymptomatic cancers by the FOBT or its more sensitive replacement, for intermediate-risk patients.

- CT colonography is the best alternative to screening by colonoscopy.
- It is performed after colon preparation, tagging of fecal matter by ingestion of iodated contrast medium the day before the test, and colon insufflation, preferably automated and with CO2.
- Low dose radiation is sufficient.
- Two complementary views are obtained with the patient in two positions.
- 3D visualization with CAD and sufficient training results in an efficacy close to that of colonoscopy.
- CT colonoscopy is indicated in case of failure, additional risk factors or refusal of colonoscopy.
- It should also be offered to intermediate-risk patients who accept it as an alternative to the FOBT.
- Epidemiological data to support this proposal do not exist at present.

**Disclosure of interest**

The author declares that he has no conflicts of interest concerning this article.

**References**


