VIRTUAL COLONOSCOPY : THE NEW TOOL FOR SCREENING ! D. Bielen. Leuven, KUL.

Colorectal cancer is even today a major health issue, being third most frequent cancer worldwide ([1]). Fortunately, these tumors develop in 70-90% of the cases from pre-existing benign polyps over 5-10 years. Early screening for and removal of these polyps is therefore indicated ([2]). For persons at high risk (2- to 4-fold lifetime risk) the American Gastroenterological Association (AGA) recommends just conventional colonoscopy starting at age 40 or 10 years prior to the age of diagnosis in a first-degree relative ([3]). The population, with a lifetime risk of 4-6%, has a large choice : FOBT (fecal occult blood test), sigmoidoscopy, combination of FOBT and sigmoidoscopy, conventional colonoscopy and double contrast barium enema. Screening should start at age 50. Conventional colonoscopy is accepted being gold standard, although it has no 100% sensitivity ([4]). Large scale screening for colorectal cancer with conventional colonoscopy can lead to increased workload for gastroenterologists and even waiting lists for patients ! This opens perspectives for virtual colonoscopy as alternative or complementary tool for screening. This CT based technique, developed in the 90's, allows non-invasive visualization of the colonic wall for detection of polyps (5).
The 'Working Group on Virtual Colonoscopy' (Boston, October 2003) advices : bowel prep with Fleet Phosphosoda®), combined with fecal tagging ([6]) ; low dose ($\leq$ 50 mAs) thin slice ($\leq$ 3 mm) multi-slice CT ; retrograde filling of the colon with room air or carbon dioxide ; supine and prone acquisition ([7]).
Virtual colonoscopy can also be used for surveillance after polypectomy or surgery, to detect proximal lesions in case of an obstructing tumor, or when conventional colonoscopy is contra-indicated, incomplete or refused. Advantages are the non-invasiveness, the short examination time and the additional information of the extra colonic structures. Drawbacks are the need for bowel prep, time for interpretation (up to 60 minutes), the use of ionizing radiation and the inability to remove polyps. The problem of the ionizing radiation can be solved by using magnetic resonance colonography, a technique with promising results ([8]). The sensitivity for lesions $\geq$ 1 cm varies from 94% in 'good circumstances' ([4]) to just 55% in 'daily practice circumstances' ([9]).
The emergence of the virtual colonoscopy together with other new detection techniques (DNA mutations in stool, proteins in the blood, …) necessitate for cooperation between gastroenterologists and radiologists! The radiologist should offer diagnostic virtual colonoscopy, whereas the gastroenterologist can offer a-same-day therapeutic conventional colonoscopy in case of a positive virtual colonoscopy, without the necessitation for additional bowel prep. The threshold for referral depends on the size of the 'significant' polyp ! For polyps of 6 mm, 70,3% will not be referred, 86,5% for 8mm polyp size and up to 92,5% for 10mm polyp size ! How to elaborate this 'joint venture' in time and space is at the moment unclear, but for patient and public health reasons, it is worth paying attention to this opportunity !

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Computed tomographic colonography

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Abstract

Computed tomographic colonography, also called virtual colonoscopy, is an evolving technology under evaluation as a new method of screening for colorectal cancer. However, its performance as a test has varied widely across studies, and the reasons for these discrepancies are poorly defined. We provide an overview of some potential causes and discuss the available, often indirect, evidence. In addition, several other obstacles that may influence implementation are discussed. Future investigations should demonstrate the influence of these potential factors on sensitivity of computed tomographic colonography. Despite a growing body of evidence, it remains uncertain to what extent patient acceptance, radiation issues, flat lesions, and extracolonic findings will be a stumbling block to using computed tomographic colonography for colorectal cancer screening. (Acta gastroenterol. belg., **2005**, 68, **258-260**).

Key words : CT colonography, virtual colonoscopy, screening, colorectal cancer, virtual colonoscopy.

Introduction

Colorectal cancer (CRC) is an important leading cause of cancer death (1,2). Although death from colon cancer is largely preventable through routine screening of asymptomatic patients for early detection and removal of premalignant adenomatous polyp precursors, patient compliance remains poor, rarely exceeding 50% in population surveys. Of the currently recommended CRC screening tests, conventional colonoscopy is recognized as the gold standard. However, conventional colonoscopy has serious drawbacks as a screening test. It is invasive, with a small but definite risk of serious complications. It is expensive, and it requires intravenous sedation and a bowel prep, which discourages many patients from undergoing the test. Thus, there is a clear need for simpler screening methods that would allow conventional colonoscopy to be used more selectively and efficiently.

Computed tomographic colonography (CTC), also referred to as “virtual colonoscopy”, is rapidly evolving as a promising candidate for CRC screening. Several recent studies have reported sensitivities of more than 90% for detection of polyps greater than 10 mm, the size threshold for so-called “advanced adenomas”, which is the agreed principle target for colorectal cancer screening (14). In three recent studies in low-prevalence populations, however, these values vary from 55% to 94%. Many questions have been raised as to the cause of this remarkable variability, which hampers the implementation of CT colonography in colorectal cancer screening and surveillance. Sensitivity for smaller lesions 6-9 mm in size has generally been lower. Although detection (and exclusion) of all lesions is a desirable goal, the key screening parameter is the ability to detect patients with at least one clinically significant lesion (10 mm or larger), which would lead logically to therapeutic colonoscopy.

Prerequisites

Virtual colonoscopy is a rapidly involving, technique-intensive test for colorectal cancer screening that is being introduced into an environment with significant turf and economic implications. It is important to underscore that virtual colonoscopy is a sophisticated technologically advanced imaging procedure in which excellent results tend to be multifactorial. Adequate colon cleansing, bowel distension, state-of-the-art multislice CT equipment, and reader’s experience are the major determinants of quality of virtual colonoscopy. Radiologist CTC investigators believe that a minimum of 25 and preferably 50 proctored cases be studied before competence can be assumed. The nature of the reader software should also be state-of-the-art.

The “Working Group on Virtual Colonoscopy” (Boston, October 2003) advices : bowel prep with Fleet Phosphosoda®, combined with fecal tagging (3) ; low dose (< 50 mAs) thin slice (< 3 mm) multi-slice CT ; retrograde filling of the colon with room air or carbon dioxide ; supine and prone acquisition (4).

Advantages are the non-invasiveness, the short examination time and the additional information of the extra colonic structures. Drawbacks are the time for interpretation (up to 60 minutes) and the inability to remove polyps. Additional obstacles for implementation in prevention of colorectal cancer may be controversial results concerning patient acceptance, the large-scale use of ionising radiation, and difficulties in detecting flat adenomas (5). Use of primary three-dimensional review methods and endoscopic verification of false-positive results on CTC are speculated to have a positive influence on

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sensitivity. Future investigations should demonstrate the influence of these potential factors on sensitivity of CTC.

Indications of CTC

Despite a growing body of evidence, it remains uncertain to what extent patient acceptance, radiation issues, flat lesions, and extracolonic findings will be a stumbling block to using CT colonography for colorectal cancer screening. Virtual colonoscopy can also be used for surveillance after polypectomy or surgery, to detect proximal lesions in case of an obstructing tumour, or when conventional colonoscopy is contra-indicated, incomplete or refused.

Diagnostic yield

In a recent meta-analysis the results of 33 prospective studies of adults (6393 patients) undergoing CTC after full bowel preparation, with colonoscopy or surgery as the gold standard, were selected (6). Studies had to have used state-of-the-art technology, including at least a single-detector CT scanner with supine and prone positioning, insufflation of the colon with air or carbon dioxide, collimation smaller than 5mm, and both 2-dimentional and 3-dimentional views during scan interpretation. The evaluators of the colonogram had to be unaware of the findings from use of the gold standard test. Data on sensitivity and specificity overall and for detection of polyps less than 6mm, 6 to 9 mm, and greater than 9 mm in size were abstracted. Sensitivities and specificities weighted by sample size were calculated, and heterogeneity was explored by using stratified analyses and meta-regression. The sensitivity of CTC was heterogeneous but improved as polyp size increased (48% [CI, 25% to 70%] for detection of polyps < 6 mm, 70% [CI, 55% to 84%] for polyps 6 to 9 mm, and 85% [CI, 79% to 91%] for polyps > 9 mm). Characteristics of the CTC scanner, including width of collimation, type of detector, and mode of imaging, explained some of this heterogeneity. In contrast, specificity was homogenous (92% [CI, 89% to 96%] for detection of polyps < 6 mm, 93% [CI, 91% to 95%] for polyps 6 to 9 mm, and 97% [CI, 96% to 97%] for polyps > 9 mm). Limitations were that the studies differed widely, and the extractable variables explained only a small amount of the heterogeneity. In addition, only a few studies examined the newest CTC technology. They concluded that computed tomographic colonography is highly specific, but the range of reported sensitivities is wide. Patient or scanner characteristics do not fully account for this variability, but collimation, type of scanner, and mode of imaging explain some of the discrepancy. This heterogeneity raises concerns about consistency of performance and about technical variability. These issues must be resolved before CT colonography can be advocated for generalized screening for colorectal cancer.

It remains a fact that all major studies of CTC published by radiologists have shown far better performance than studies published by gastroenterologists (7-13). It is also unclear why CTC should be held to a higher performance standard than the other 3 approved CRC screening tests, i.e., FOBT, flexible sigmoidoscopy, or double contrast barium enema. None perform as well as colonoscopy, yet they remain standard tests. Assessment of CTC should be based on all the published evidence including comparison with all the existing approved CRC screening tests, not just colonoscopy.

Radiation exposure and risk of cancer from diagnostic CTC

The literature search revealed a median effective dose for a single CT colonography scan of 4.2 mSv (0.6 to 11 mSv). The median mAs was 88 (10 to 200 mAs), and the median collimation, 4.4 mm. But two-thirds of the scans were performed on a single-slice scanner. Introduction of multislice technology results in higher effective dose levels. A tube current modulation technique used for virtual colonoscopy reduces radiation exposure by one-third, and effective dose levels for the exam have remained constant despite the increased use of multislice technology, according to the findings of Dr. Anno Graser and colleagues at the Ludwig-Maximilians University Munich and Dr. Sebastiaan Jensch and colleagues from the Academic Medical Center in Amsterdam (presented at the 2004 Radiological Society of North America meeting).

The median effective dose for a single CT colonography at current protocol is 4.2 mSv (1.2 to 11.7 mSv). The present median mAs value is 70 (20 to 200 mAs), and the median collimation 2.5 mm.

If applied once to a population aged 50, CT colonography performed in supine and prone position will result in an estimated number of approximately one fatal cancer in 5000 individuals. It would become manifest after a long latent period, possibly decades.

Conclusions

The role of CT colonography in screening asymptomatic patients is controversial. Studies employing subjects with known neoplasms generally report higher accuracy, while studies employing surveillance subjects report lower accuracy. Technical factors that appear to be associated with higher accuracy include meticulous bowel preparation and inflation, multidetector CT, combined two- and three-dimentional visualization, and radiologist experience and proclivity. Interobserver variability and practice guidelines remain significant issues for this developing technique.

The imminent arrival of low prep laxative-free techniques for colon cleansing and the development of computer-aided detection techniques to provide consistent, confident automated computer marking of suspicious

lesions will likely add to both patient acceptance and the clinical performance in community practice. The prospects for CTC remain bright. Gastroenterologists, radiologists, and especially patients ultimately will all be winners.

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