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Chapter 12

Virtual Colonoscopy

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1. Introduction

Colorectal carcinoma ranks as the third most commonly diagnosed cancer and the second leading cause of death from cancer in the United States [1]. It is estimated that more than 150,000 new cases are diagnosed with more than 50,000 dying from the disease yearly in the U.S. alone [1]. Similar to other cancers, it is often diagnosed at advanced stage, after the patient has developed symptoms. Many colon cancer deaths can be avoided because mostly they arise from adenomatous polyps, which may be detectable years before malignant transformation.

Since the first report of a complete examination of the entire colon using a flexible endoscope, optical colonoscopy (OC) has evolved to be the current gold standard for evaluation of the colon [2]. OC has several limitations and drawbacks as a population-based screening tool. It is an invasive procedure requiring sedation. An escort is usually required to take the patient home, which increases the cost of the procedure from a societal perspective. OC also carries a small but significant risk of perforation and death. The risk of colonic perforation is about 1 per 1,000 cases and death is approximately 1 in 5,000 cases [3-5]. Failure to reach the cecum (5-10%) and missed polyps (10-20%) also are known limitations of the current gold standard test [6-9].

Computed tomographic colonography (CTC), also known as "virtual colonoscopy" was first described more than a decade ago [10]. In the early 1990's, several pilot studies evaluated the feasibility of (CTC) [11]. The advantages of developing a computerized-based screening tool includes: increased accessibility, non-invasiveness, and no sedation required [12]. These advantages of CTC may help to increase compliance with current screening recommendation guidelines [13].

2. Technique

As advancements in scanner technology and three-dimensional (3D) post-processing helped develop this method to mature into a potential option in screening for colorectal cancer, the fundamentals of the examination remained the same. It is a minimally invasive, CT-based procedure that simulates conventional colonoscopy using 2D and 3D computerized reconstructions [10]. CTC utilizes computer virtual-reality techniques to navigate inside a three-dimensionalz (3D) patient-specific colon model reconstructed from abdominal CT images, looking for polyps.

CTC examination starts by inflating a cleansed colon with room air or carbon dioxide (CO_2) introduced through rectal catheter [14]. With the patient in a prone position, air or CO_2 is insufflated under gentle pressure to ensure adequate distention of the bowel. The insufflation of gas is usually associated with a mild degree of patient discomfort or pain [15]. Although not common, vaso-vagal reactions can occur, especially if with small bowel distention occurs [16].

Then abdominal CT slice images are taken in seconds (during a single breath hold) with sub millimeter resolution in both axial and transverse directions resulting in excellent contrast between the colon wall and the lumen. The sliced images are stacked together as a volume image, from which the colon model is constructed. Image segmentation is necessary for the construction of an accurate colon model. Computer graphics are heavily involved to navigate or fly through inside the 3D colon model. The patient is scanned in both a prone and supine view [17]. Using a second view significantly improves the ability to identify patients with polyps 0.5 cm in diameter or larger [18].

CTC can be performed in patients with prior abdominoperineal resection and sigmoid colostomy, although increased difficulties with CO2 retention and adequate bowel distention exist [19]. The prevalence of transient bacterium after CTC is low therefore it follows that patients with at risk cardiac lesions should not require antibiotic prophylaxis beforehand [20].

Most commonly used bowel preparations include sodium phosphates, magnesium citrate and polyethylene glycol (PEG) [21]. Typical oral preparations used for bowel cleansing are: 4 L of PEG solution; 90 ml of phosphosoda; or 300 ml of magnesium citrate. Polyp detection is comparable for all three preparations, although phosphosoda has a significantly higher patient compliance and the least residual stool [22]. Residual fluid coverage negatively affects the quality of CTC [23].

The use of fecal tagging agents and intravenous contrast is not standardized. CTC experts were surveyed regarding their practice patterns [24]. Thirty-eight percent performed fecal tagging regularly and 81% [21/26] believed intravenous contrast was not necessary [24].

Non-operator dependent false positives and false negatives occur with CTC. For example, inadequately tagged stool can have the same density as a polyp, however the two can sometimes be distinguished by comparing prone and supine views, since stool is

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usually mobile and polyps are not. The rectal balloon is a potential blind spot for CTC, sometimes masking significant lesions [25, 26]. Also, poor colonic distention can result in a false negative reading [27].

3. Screening for colorectal cancer: CTC vs. OC

The primary aim of CTC is the detection of colorectal polyps and carcinomas, however; the precise role of CTC in screening asymptomatic patients is controversial [28]. Studies using patients with known adenomas generally report higher accuracy, while studies employing asymptomatic screening subjects report lower accuracy [28]. Two key areas have held back the widespread application of CTC as a screening test. These key areas are: [1] the variable sensitivity of CTC reported in mass screening programs (see Table) and [2], the expertise required to interpret the examination. These two areas are related [29]. Despite these drawbacks, the American College of Radiology, has endorsed the use of CTC as a screening tool for colo-rectal cancer stating that the sensitivity and specificity of CTC are high enough and comparable to those of OC [30]. In addition, CTC has received the endorsement of a multi-society task force that included the American Cancer Society and U. S. Multi-society Task Force on Colorectal Cancer [31].

Studies reveal a wide variation in performance measures (sensitivity and specificity) regarding polyp detection rates, especially for smaller polyps [10]. In an early feasibility study of 44 patients, CTC demonstrated reasonable sensitivity (83%) and specificity (100%) for polyps larger than 8 mm in size [32]. A second early study performed in 87 patients at high risk for colorectal neoplasia identified 49 patients with a total of 115 polyps and 3 carcinomas [33]. CTC identified all 3 cancers. The sensitivity was 91% for polyps that were 10 mm or more in diameter, 82% [33/40] that were 6 to 9 mm, and 55% [29/53] that were 5 mm or smaller [33]. There were 19 false positive findings of polyps and no false positive findings of cancer. In a larger study of 300 patients CTC demonstrated a sensitivity equal to 90% for polyps 10 mm or larger and 80.1% for polyps at least 5 mm in size [34]. The overall specificity for this study was 72.0% [34]. All 8 carcinomas in the study were detected by CTC.

Two later studies assessing the accuracy of CTC had varying results. Pickhardt et al. evaluated 1,233 asymptomatic patients with CTC and same-day OC [35]. The sensitivity of CTC for adenomatous polyps at least 10 mm in size was 93.8% and 88.7% for polyps at least 6 mm in size, which was comparable to OC. The specificity of CTC for adenomatous polyps at least 10 mm in size was 96.0% and 79.6% for polyps at least 6 mm in size. These encouraging results were followed a year later by less optimistic findings from a study by Cotton et al., that analyzed 600 participants undergoing both CTC and OC [36]. In the Cotton study, 104 of the participants (17.3%) had lesions sized at least 6 mm. The sensitivity of CTC for detecting 1 or more lesions sized at least 6 mm was only 39.0% and for lesions sized at least 10 mm, it was 55.0% (95% Cl, 39.9% - 70.0%) [36]. The specificity of CTC for detecting participants without any lesion sized at least 6 mm was 90.5% and without lesions sized at least 10 mm, 96.0% (95% Cl, 94.3% - 97.6%). CTC missed 2 of 8 cancers [36]. Lack of adequate radiologist training to read CTCs may have resulted in the low accuracy found in this study.

In a subsequent study of 2,531 asymptomatic patients, radiologists trained in CTC reported the accuracy of finding histologically confirmed adenomas [37]. The sensitivity for large adenomas [10 mm or larger) and medium-sized adenomas (6 – 9 mm) was 90% and 78% respectively [37]. CTC failed to detect a lesion measuring 10 mm or more in diameter in 10% of patients [37]. Pickhart et al. found that the positive predictive values (PPV) for polyps with threshold sizes 6 mm, 8 mm, and 10 mm are: 92.3%, 93.0%, and 93.1% respectively [38]. Others have also found that for significant adenomas, the PPV of CTC is high and ranges from 96 – 99% [37, 39].

Meta-analysis is a tool that attempts to summarize varying results across multiple studies. Meta-analysis of data suggests CTC has excellent per-patient average sensitivity and average specificity for detection of adenomatous polyps and cancer [40]. In one meta-analysis, 2,610 patients were included for study [41]. Large polyps (10 mm or greater) had a per-patient average sensitivity of 93% (95% CI,73% - 98%) and specificity of 97% 9(95% CI, 95% - 99%) [41]. The sensitivity and specificity decreased to 86% (95% CI: 75% - 93%) and 86% (95% CI, 76% - 93%), respectively, when the threshold was lowered to include medium sized polyps (6 mm to 9 mm). These findings are similar to another more recent meta-analysis using average risk patients that found a sensitivity of 87% and specificity of 97.6% for polyps at least 10 mm in size [42].

One of the problems of evaluating the test performance of CTC is the use of OC as the gold standard because OC has a miss-rate for polyps and cancer as well. In one study, Pickhardt et al. compared 1,233 asymptomatic adults who underwent same-day CTC and blinded segmental OC [43]. Polyps that were detected by CTC but initially missed by OC were considered missed polyps for OC. It was found that OC had a miss rate of 12% for adenomas 10 mm or greater. Of the missed polyps on OC, 14/15 (93.3%) non-rectal neoplasms were located on a fold. Five of 6 (83.3%) missed rectal lesions were located within 10 cm of the anal verge [43].

Another study analyzed 286 tandem colonoscopies [44]. The OC miss rates for adenomas 5 mm and larger and advanced adenomas (≥ 10 mm or high grade dysplasia) were: 11% and 9% respectively [44]. Therefore, OC does have a significant miss rate for adenomas 5 mm and larger and/or advanced adenomas. In fact, the OC miss-rate is similar to the CTC miss-rate for polyps 6-9 mm in size [27]. It should also be pointed out that in screening studies, CTC and OC have similar detection rates for advanced neoplastic polyps and cancer, 3.2% vs. 3.4% respectively [45]. OC detects significantly more adenomas less than 5 mm of size although the benefit of this remains to be seen [46]. In summary, CTC appears to have similar sensitivity to OC in detecting polyps 5 mm or greater when performed by readers with high experience [47].

The detection of flat adenomas are a major concern for colo-rectal cancer screening since these polyps are at a higher risk of harboring advanced pathology and are more difficult to detect by CTC as well as OC [48, 49]. In the general population, there is wide variation in the reported incidence of flat lesions, which may in part be due to the lack of a uniform definition of flat polyps. Various definitions of flat polyps have been used in CTC studies. For ex-

ample, in one study flat polyps were defined as those having a height less than one-half of their width [50]. In other studies, a definition of 3 mm or less in height is used [51].

The sensitivity for flat polyps appears to be lower than non-flat polyps, however, Pickhardt et al. found that the sensitivity of CTC for detecting flat adenomas measuring 6 mm or greater was similar to that of non-flat polypoid lesions [50]. Others have found lower sensitivities for flat polyps ranging from 15% to 65% [52]. Regardless of reader skills, truly flat or depressed adenomas will most likely pose a challenge for CTC. Also, flat carpet lesions of the colon can be difficult to detect by CTC [53].

CTC readers may not report polyps less than 5 mm in size [54]. The justification for this is that small polyps are usually benign and rarely harbor cancer or have much prognostic significance. In a large OC screening study, advanced histology was found in only 1.7% of polyps sized 5 mm or less indicating the lack of reporting of these small polyps by CTC may be justified [55]. On the other hand, 6.6% of polyps sized 6 to 9 mm, had an advanced histology implying polyps of this size if found on CTC should be followed up with OC in the near future [55]. This last point is somewhat contentious and some radiologic guidelines suggest surveillance with CTC after a shortened interval as an acceptable option for polyps 6 – 9 mm in size [56].

We feel a reasonable algorithm for CTC screening might be: 1. follow-up screening in 5 years if no polyps are found: 2. Follow-up CTC or OC in 5 years for polyps smaller than 5 mm: 3. OC if polyps measuring 6 mm or greater are found [57]. This algorithm is consistent with clinical sentiment since 71% of primary care physicians and 86% of gastroenterologists would send patients with polyps 5 mm in size or greater for a follow-up OC [58]. If this approach were adopted, a referral rate for OC of about 8% - 14% would be expected in the general population [45, 59]. Using a 6 mm threshold however may be very costly. A decision-analysis estimated that to prevent one colon cancer death would require over 9,000 OCs, resulting in 10 additional perforations at an incremental cost of $327,853 dollars [60].

4. Other uses of CTC

4.1. After incomplete colonoscopy

Sometimes OC can not be completed to the cecum due to technical factors such as prior abdominal surgery, colon length and number of flexures [61]. An important use of CTC is examination of the colon after incomplete OC [62]. In a retrospective study, 88/546 patients had lesions 6 mm or greater on CTC after incomplete OC. OC was repeated if findings on CTC were significant. The PPV of CTC for masses, large polyps, and medium polyps were 90.9% and 91.7%, and 64.7% respectively [63].

It may be valuable to perform a low-dose diagnostic CT before rectal tube insertion in patients referred for incomplete colonoscopy. In one study of 262 patients referred for incomplete OC, colon perforation was found on the low-dose CT scans of two of the 262 patients (0.8%; 95% CI, 0.1-2.7%) [64]. One of these patients had no symptoms; the other had mild

abdominal discomfort at the time of CTC. Therefore, the rate of occult colonic perforation after incomplete colonoscopy may warrant a spot CT prior to full examination.

4.2. For symptoms

CTC is being increasingly used for the radiological evaluation of colorectal symptoms. In symptomatic patients, CTC is equivalent to OC for diagnosing colon cancer and clinically significant polyps [65]. In a retrospective study of 1,177 older symptomatic patients, 59 invasive CRC were detected [66]. Three small colorectal cancers were missed by CTC. CTC has a high sensitivity (95%) and negative predictive value (99.7%) in excluding a CRC in patients with colorectal symptoms [66].

4.3. Inflammatory bowel disease and diverticulitis

CTC may be useful for diagnosing and managing patients with inflammatory bowel disease (IBD) [67]. CTC correctly identified acute and chronic IBD in 63.6%, and 100% of cases, respectively [68]. CTC was also helpful in assessing post-op strictures in Crohn's disease patients [69]. Perianastomotic narrowing or stenosis was detected by CTC in 11 of 15 patients. The sensitivity and specificity for perianastomatic narrowing were 73% and 100% respectively [69]. The risk of perforation, especially in patients with severe active colitis is a potential worry. Currently there is not enough data to measure the true risk in patients with severe active disease [70].

Examination of the colon is usually necessary after an adequate rest period for evaluation of patients with diverticulitis. CTC appears comparable to OC in the evaluation of these patients and is a reasonable alternative in follow-up of patients with symptomatic diverticular disease [71]. Diverticulosis may however, increase the chance of having a false positive test for polyps on CTC due to the appearance of inverted diverticula and fecoliths[72]. On the other hand, CTC may be helpful in diagnosing complications of diverticular disease and inflammatory bowel disease, such as colo-vesicular fistulae [73].

4.4. Detection of tumor for surgery

CTC is very useful in detecting colon cancer after incomplete colonoscopy and also for evaluating potential metastases [74-76]. CTC can help localize polyps or cancer prior to laparoscopic surgery and detect synchronous lesions beyond the reach of OC due to obstructing lesions [77, 78]. In fact, CTC is superior to OC in the localization of colonic tumors prior to surgery [79]. CTC is also a safe and useful method for preoperative examination of the proximal colon after metallic stent placement in patients with acute colon obstruction caused by cancer [80].

CTC is useful in surveillance after surgery for colo-rectal cancer, detecting local recurrence and metastasis [81-84]. In patients with ovarian cancer CTC may be helpful in detecting rectosigmoid wall involvement wall and predict the need for rectosigmoid resection [85]. The sensitivity, specificity, PPV and negative predictive value of CTC for the prediction of recto-

sigmoid resection in patients with ovarian cancer in one study were: 100%, 64.7%, 72.7% and 100%, respectively [85].

5. Reader experience and accuracy

Individual accuracy of reading polyps with CTC is highly variable among radiologists and depends largely on training and experience [86-88]. There is a significant learning curve involved in the interpretation of CTC studies, with performance improving with operator experience [89, 90]. Radiologists working in nonacademic centers may have less accurate results than would be expected from published data originating from experienced academic centers [91]. The steep learning curve involved with reading CTC has led some thought leaders to advise against widespread colorectal cancer screening programs with CTC outside of academic centers [29].

False negatives are a major concern, i.e. missing significant lesions. It appears that many false negatives are due to observer error and not due to the technical capabilities of CTC. For instance in one study, 53% of missed polyps (60 of 114) were attributed to observer-related errors, and 26% were attributed to errors classified as technical [92]. This implies that with improvements in reader skill the sensitivity of finding significant lesions would be acceptable and comparable to OC [90]. Technical factors that appear to be associated with higher accuracy include meticulous bowel preparation and inflation, multidetector CT, combined two and three-dimensional visualization [28, 93].

6. Radiation exposure

Radiation exposure at the time of CTC screening leads to a slight but increased risk of developing cancer at a future time [94]. Therefore, reducing radiation exposure is a major challenge for CTC screening.Currently, CTC scanning delivers a significant amount of X-ray radiation exposure to the patient [95]. In 2004, a survey of 28 institutions revealed the median effective dose of radiation was 5.1 mSv (range 1.2 mSv - 11.7 mSv) per position and the median mAs value was 67 mAs[96].

Given current CT technology, a simple and effective strategy to reduce radiation would be to lower the mAs level (i.e. deliver less X-ray photons to the body) during the data acquisition. This strategy would however, lead to a higher noise signal in the acquired data. Recent efforts on modeling a solution to avoid this noise artifact are aimed at minimizing the noise prior or during image reconstruction. Despite the great effort on this solution in the past decade, CTC still faces challenges at a mAs level lower than 50 [97].

A feasibility study examined low radiation doses from 10mAs to 40 mAs using adaptive statistical iterative reconstruction (ASIR) models [98]. Eighteen patients were scanned with a standard 50 mAs CTC dose in the supine position and a reduced dose of 25 mAs with 40%

ASIR in the prone position. No significant image quality differences were seen between standard-and low-dose images using 40% ASIR. The results of this pilot study show that the radiation dose during CTC can be reduced 50% below currently accepted low-dose techniques without significantly affecting image quality when ASIR is used [98]. Larger studies are needed to confirm this observation. Despite the increasing use of multi-slice scanners, which are slightly less dose-efficient, the median effective dose remained approximately constant between 1996 and 2004 [96]. Of 83 institutions, 62% used 64-detector row CT and 17 (50%) used dose modulation [99].

If the current CTC standards for radiation exposure are used for colorectal cancer screening, CTC is still be a viable screening tool, even after taking into account the increased risks of developing future cancers. Using a Monte Carlo simulation, it was found that for every 1 radiation-related cancer caused by CTC screening, 24 – 35 colorectal cancers would be prevented, implying a favorable risk to benefit ratio in favor of using CTC as a screening tool [100]. This model assumed using CTC every 5 years in patients aged 50 – 80 years old and using an estimated mean effective dose per CTC screening study of 8 mSv for women and 7 mSv for men.

An alternative solution to minimize the radiation is to use magnetic resonance imaging (MRI) instead of CT for virtual colonoscopy, i.e., MR colonography (MRC) [101]. However, this MRC alternative solution has several limitation compared to CTC. Currently it is more costly, more sensitive to motion and other artifacts, and has lower spatial resolution but with improvements with technology these disadvantages may be minimized.

7. Patient preferences

When asked if they would prefer CTC or OC, patients more often prefer CTC [102]. In one study, 696 asymptomatic patients at high risk for colorectal cancer screening underwent both CTC and OC [103]. Patients were asked using standardized forms about preparation inconvenience and discomfort, examination discomfort and examination preference. Overall, patients preferred CTC to OC (72.3% vs. 5.1%; $P < 0.001$). Reported discomfort however, was similar for CTC and OC ($P = 0.63$). In another study that evaluated patients with a history of diverticulitis, 74% preferred CTC preferred over OC [71]. Patients found colonoscopy more uncomfortable ($p < 0.03$), more painful ($p < 0.001$), and more difficult ($p < 0.01$) than CTC [71].

Other studies conflict with those mentioned above. Even though CTC is a less invasive alternative than OC, procedural pain is not uncommon. In several studies, the pain associated with CTC was higher than that associated with OC, albeit there is no sedation given for the former test [104]. Using a time-trade off technique, 295 patients reported statistically more pain and discomfort after CTC and showed preference for optical colonoscopy [105]. The pain during CTC however, is usually not so severe as to abort the test [33].

In a well-designed study, 111 patients underwent CTC followed immediately by OC [15]. The preference for either examination was evaluated after completion of both examina-

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tions. Of the 68 patients who favored one examination, 56 [82%) preferred CTC (P < 0.00001). CTC was regarded as "not painful" by 62 (57%) of 108 patients compared with 28 (26%) for colonoscopy [15].

Intuitively we may believe that CTC, being a noninvasive test, would be preferred to OC by most patients. However, when the risks of finding lesions that require follow-up and other factors are taken into account, patient preferences may change. In one study, OC was preferred over CTC as the need for a follow-up test increased, as the likelihood of missing cancers or polyps increased, and as the cost for CTC increased (the odds rato of preferring CTC to OC ranged from 0.65 to 0.80)[106]. Therefore, an informed decision regarding CTC vs. OC should include a discussion of the benefits, risks, costs and associated uncertainties of the tests. In summary, patients usually prefer CTC to OC but the preference is most likely dependent on a number of other factors such as insurance coverage, type of sedation used locally for OC, and the risk of finding a significant polyp on CTC thereby requiring a follow-up OC.

8. Extracolonic findings

Extracolonic findings are an important issue for CTC as they increase costs and patient risk by incurring addition tests. The frequency of extracolonic findings in the literature varies considerably as there are no standards for their reporting nor what constitutes a clinically significant extra-colonic finding. Some of the extracolonic lesions found are clinically important although most of them are incidental. In addition to increasing costs of CTC screening programs, they may cause undue worry and anxiety for the patient.

The prevalence of extracolonic findings can be as high as 40% - 75% and are increased with patient age [107-109]. Most extracolonic findings are incidental and not clinically important. The most common extracolonic findings causing further evaluation in one study were lung nodules and indeterminate kidney lesions adding a cost of $248 dollars per patient enrolled for CTC screening [110].

In general, significant extracolonic findings are found in about 10 - 23% of patients undergoing CTC [111-113]. Potentially important extracolonic findings were seen in 15.4% (89 of 577) of patients in one study, with a work-up rate of 7.8% (45 of 577)[114]. In another study only 4.4% - 6.0% of patients required follow-up radiologic testing for the extracolonic findings [109]. Another study showed that 10% of 681 patients screened for colon cancer had extracolonic findings of high clinical importance [115].

Although extracolonic finding add cost to CTC screening programs, they may benefit patients by diagnosing other potentially malignant lesions [112]. Unsuspected cancers (colonic and extra-colonic) are found in about 0.5% of screening cases [116]. In a large study, 36/10,286 patients (0.35%) undergoing a screening examination had an unsuspected extracolonic cancer which included renal cell carcinoma (n = 11), lung cancer (n = 8), non-Hodgkin lymphoma (n = 60, and a variety of other tumors (n = 11)[116). Other studies report a higher rate of 2.7% of extracolonic cancer detection [107].

9. Computer-Assisted Diagnosis (CAD)

An intensive area of research is the development of computer-assisted diagnosis (CAD) algorithms. CAD can assist radiologists as a second reader to improve accuracy [117, 118]. It has been shown that CAD can aid trained radiologists in the detection of significant polyps [119].CAD significantly improved polyp detection by 12% in one study, (from 48 to 60%) with only a moderate increase in interpretation time [120]. Another study demonstrated that using CAD in second-read mode increased accuracy in 13 of 19 readers 968%); CAD increased sensitivity of finding polyps but decreased specificity slightly [121]. In general, using CAD increases polyp detection but also increases false positives as well [122, 123].

Using CAD as a primary reader is feasible but early studies showed less sensitivity than human readers [124]. The sensitivity of CAD detected polyps 10 mm or greater was 64% (18/28) in one study [125]. In a later study of 1,186 patients undergoing both CTC and OC on the same day, CAD had a sensitivity of 89.3% (25/28; 95% CI: 71.8%-97.7%) for detecting adenomatous polyps at least 1 cm in size [126]. The false-positive rate was 2.1% (95% CI: 2.0% - 2.2%). CAD detected both of the carcinomas in the study group. In this study, CAD had a per-patient sensitivity comparable to that of OC for adenomas at least 8 mm in size [126]. Another study found a per-patient sensitivity of 96% was for CAD (in patients with a median polyp diameter of 6 mm) using external validation [127]. Several CAD polyp detection systems exist such as Polyp Enhanced Viewing (PEV) and the Summers computer-aided detection (CAD) system (National Institutes of Health (NIH)). These systems vary and have trade-offs in terms of sensitivity and specificity [128].

10. Safety

It is difficult to make a head-to-head comparison of the safety of CTC vs. OC since they are different technologies with varying risks. In one study, CTC screening was performed in 3,120 adults and compared to primary OC screening in 3,163 adults. There were seven colonic perforations in the OC group and none in the CTC group [45]. Colonic perforation has been reported with CTC but its occurrence is rare [129, 130]. Nine perforations out of 17,067 CTC examinations (0.052%) were reported in one study [131]. In another study of 11, 870 CTC studies, the perforation rate was 0.059% [132].

Possible factors that contribute to perforation are presence of an inguinal hernia containing colon (n = 4), severe diverticulosis (n = 3), and obstructive carcinoma (n = 1)[132, 133]. In cases of obstructing lesions, gas should be insufflated slowly [133]. Colonic pneumatosis is rarely seen (0.11%) in CTC studies and should not be confused with perforation [134, 135]. Overall, potentially serious adverse events related to CTC occur in less than 0.10% of patients [131].

11. Cost-effectiveness

With a 6-mm size threshold for polyps, the overall referral rate to optical colonoscopy is about 15% [114]. CTC is usually a less expensive test than OC, however the total costs may not be less if one considers all of the variables such as compliance rates and referral rates for OC after detecting lesions. Using a Markov model, screening by CTC costs $24,586 per life-year saved compared to $20,930 for OC screening [136]. CTC becomes a more cost-effective test as the compliance rate for screening increases or if the cost for CTC is 54% lower than OC. On the other hand in a recent analysis both CTC and OC were more costly and less effective than FOBT plus flexible sigmoidoscopy[137].

A Markov model was used to estimate the cost-effectiveness of CTC screening in an Italian population. In this study, colorectal cancer was reduced by 40.9% and 38.2%, with OC and CTC respectively. As compared to no screening, both CTC and OC were shown to be cost-saving with CTC being the less expensive option [138]. Since CTC can accurately detect and simultaneously screen for aortic aneurysms, cardiac atherosclerotic risk factors and osteoporosis, the benefits of CTC screening in an elderly population may be even more cost-effective than previously thought [139-141].

12. New directions – Noncathartic bowel preparations

One new hope for the future is for patients to undergo CTC without laxatives or the need for a purgative bowel preparation. Patients would only need to ingest fecal tagging agents such as Gastroview or barium, one to two days before the test [142]. A pilot study using a noncathartic bowel preparation (low fiber diet and fecal tagging) had disappointing results demonstrating that the lack of bowel cleansing made the examination subjectively harder to interpret and likely missed significant polyps [143]. A subsequent study however using a noncathartic bowel preparation was performed in a high risk population [144]. Subjects ingested 21.6 g of barium in nine divided doses. This study demonstrated that the sensitivity of CTC using a non-cathartic bowel preparation for polyps greater than 9 mm was over 90% [144].

Limited or non-cathartic bowel preparations may be especially useful in the frail or elderly patient. In a prospective study, 67 elderly patients with reduced functional status underwent CTC using a limited bowel preparation consisting of a low-residue diet for 3 days, 1 L of 2% oral diatrizoatemeglumine (Gastrografin) 24 hours before CTC, and 1 L of 2% oral Gastrografin over the 2 hours immediately before CTC [145]. No cathartic preparation was administered. All colonic segments were graded from 1 to 5 for image quality (1, unreadable; 2, poor; 3, equivocal; 4, good; 5, excellent). Overall image quality was rated good or excellent in 84% of the colonic segments. Colonic abnormalities were identified in 12 patients (18%), including four colonic tumors, two polyps, and seven colonic strictures [145].

Ref.	(%)Sensitivity	(%)Sensitivity	(%)Specificity	(N) Patients
	6 – 9 mm	1 cm or more		
33	82	91	79	87
34	80	90	72	300
35	89	94	79 – 96	1,233
36	39	55	91 – 96	600
37	78	90	90	2,531
41*	86	93	97	2,610
42*	76 – 83	83 – 88	91 – 98	4,086

* Meta-analysis

Table 1. Sensitivity and specificity of polyps detected by CTC.

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