Selected Summaries

Screening for colorectal cancer: Do we have a definitive answer?

Halligan S, Wooldrage K, Dadswell E, Kralj-Hans I, von Wagner C, Edwards R, Yao G, Kay C, Burling D, Faiz O, Teare J, Lilford RJ, Morton D, Wardle J, Atkin W, for the SIGGAR investigators. (Imperial College London, London; Queen Mary, University of London, London; University of Birmingham, Birmingham; Bradford Teaching Hospitals NHS Foundation Trust, Bradford; St Mark's Hospital, Harrow, Middlesex; and Imperial College Healthcare NHS Trust, United Kingdom.) Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): A multicentre randomised trial. *Lancet* 2013;**381:**1185–93.

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SUMMARY

These two pragmatic, multicentre, randomized trials were conducted on symptomatic patients with colorectal cancer. Research nurses at 21 UK National Health Service (NHS) teaching and general hospitals recruited patients aged ≥55 years who were fit to undergo full bowel preparation, had no known genetic predisposition to cancer, had no history of inflammatory bowel disease, had not had a whole-colon examination in the past 6 months and were not on active follow-up for previous colorectal cancer. Two parallel trials were created and, within which, patients were randomly assigned to either colonoscopy or computed tomographic colonography (CTC) in one study and barium enema or CTC in another. No patient was common in both the trials. The primary outcome was the detection of colorectal cancer or large polyps ≥10 mm.

In the barium enema trial, the detection rate of colorectal cancer or large polyps was significantly higher in patients assigned to CTC than in those assigned to barium enema (93 [7.3%] of 1277 *v.* 141 [5.6%] of 2527, relative risk [RR] 1.31, 95% CI 1.01–1.68; p=0.039). CTC missed 7% (3/45) colorectal cancers in contrast to barium enema which missed 14% (12/85). Though the rate of additional colonic investigation was higher after CTC than after barium enema (23.5% *v.* 18.3%, p=0.0003), this was predominantly due to a higher polyp detection rate by CTC.

In the colonoscopy trial, detection rates of colorectal cancer or large polyps in the trial cohort were similar (11%) for both the procedures. However, patients in the CTC group more often required additional colonic investigations compared with the colonoscopy group (RR 3.65, 95% CI 2.87–4.65, p<0.0001). Almost half the referrals for colonoscopy after CTC were for small (<10 mm) polyps or clinical uncertainty, with low predictive value for large polyps or cancer. CTC missed 1 of 29 colorectal cancers and colonoscopy missed none (of 55).

Serious adverse events were rare in both the trials.

COMMENT

CTC is a recent addition to the screening armamentarium of colorectal cancer. Since its development in the mid-1990s, it has developed into a sensitive technique to identify colorectal cancers and large polyps. The sensitivity of CTC for detecting colorectal cancer has been shown to be as high as 96%,[1] and in several studies to be as good as that of colonoscopy.[2] CTC has enjoyed considerable popularity among patients for being a less invasive alternative to colonoscopy for screening purposes. CTC can be of added value in patients with incomplete colonoscopy, as it not only reveals relevant additional lesions (both intra- and extracolonic) in 19.1% of patients, but is also useful in staging the tumour.[3]

The use of barium enema is waning in most of the developed world because of the availability of better options such as CTC and colonoscopy and lack of experienced radiologists to interpret the findings. Barium enema has significantly lower sensitivity and specificity than CTC in detecting polyps >6 mm.[4,5] It is also not preferred by patients because of more physical discomfort during and after the procedure.[6] Moreover, the radiation dose from a screening double-contrast barium enema is substantially higher than that from CTC.[7] The SIGGAR trial on barium enema vindicates the previously held notion about the superiority of CTC over barium enema for the screening of colorectal cancer.

Colonoscopy is the accepted gold standard investigation for detection of polyps or malignancies of the colon and rectum. Overall, the sensitivity of colonoscopy is better than CTC for detecting polyps <6 mm.[8] The National CT Colonography Trial showed that CTC had a sensitivity of 90% and specificity of 86% for detection of large colorectal adenomas and cancer.[9] Data from our institute showed that the sensitivity and specificity of CTC respectively were 65% and 77% for detection of lesions 1–5 mm; 97% and 83% for lesions 6–9 mm, and 100% and 100% for lesions ≥10 mm. Extracolonic findings were seen in 57% of patients.[10] Studies confirm higher patient acceptance rates for CTC than for colonoscopy, but interestingly, one study showed that although asymptomatic patients preferred CTC over colonoscopy, symptomatic patients did not show any preference. Moreover, studies published in radiology journals are more likely to report a preference for CTC over colonoscopy than gastroenterology or general medicine journals.[11] Patients who show positive findings on CTC are likely to eventually need a colonoscopy and biopsy for further evaluation. Colonoscopy may also be able to offer a therapeutic polypectomy in the same setting.

The SIGGAR trial is the first randomized study comparing CTC with colonoscopy in symptomatic patients and has shown that the sensitivity of CTC for detecting cancer is similar to that of colonoscopy. However, patients detected to have a lesion on CTC will require additional colonoscopy and biopsy for histological diagnosis. This makes CTC a less preferred investigation in symptomatic patients.

To conclude, these two randomized studies show the superiority of CTC over barium enema for detection of colon cancer and large polyps in symptomatic patients. The second trial shows equal efficacy of CTC compared with colonoscopy in detecting colorectal cancer but with a higher need for additional colonoscopy. Though CTC has been found equivalent to colonoscopy, the verdict is not still out whether CTC is to be recommended over colonoscopy in symptomatic patients.

The implications of this trial are not clear for India and other countries with a low prevalence of colorectal cancer and where screening programmes are not in place. In India, the ground reality is that CT scan machines are not accessible or affordable for most of the population. Moreover, colonoscopy costs half as much as CTC; it can detect, sample as well as allow therapy (polypectomy) in a single setting. Also, it obviates the need for a second investigation which may be required in patients who have undergone CTC as the first investigation. Moreover, the expertise to interpret CTC is still in the nascent stage and no standardized protocols have been developed. Thus, the sensitivity and specificity of CTC may be lower at most centres in India compared with the West. A standardized evaluation protocol as well as training of endoscopists are required to ensure the effective use of colonoscopy. In India, barium enema may still be a realistic diagnostic option for patients with symptoms suggestive of colorectal cancer due to the availability of equipment and expertise.

With advances in the field of colonoscopy in the form of water immersion technique to reduce patient discomfort, image enhancement with chromoendoscopy, narrow band imaging, confocal endomicroscopy, endocytoscopy for higher cancer detection rates at an earlier stage, colonoscopy will continue to challenge CTC despite it being a non-invasive procedure. CTC would be a useful option for those with incomplete colonoscopy. The emerging role of colon capsule endoscopy may change the way we look at this issue by the end of this decade.

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Tumour size and lymph node metastases as prognostic markers of pancreatic cancer: Old lessons revisited

Tummala P, Howard T, Agarwal B. (Division of Gastroenterology and Hepatology, St Louis University School of Medicine; and Missouri Baptist Medical Center, St Louis, Missouri, USA.) Dramatic survival benefit related to R0 resection of pancreatic adenocarcinoma in patients with tumor ≤25mm in size and ≤1 involved lymph nodes. *Clin Transl Gastroenterol* 2013;**4:**e33.

SUMMARY

This retrospective study by Tummala *et al*. aimed to analyse the impact of a complete (R0) resection, size of the tumour and peripancreatic lymph node metastases on survival in patients undergoing upfront surgery for pancreatic cancer. The authors divided their cohort of 154 patients treated over 10 years into those who underwent a complete curative or R0 resection (*n*=105 or 68%) and those in whom the pathological examination of the resection margin revealed the presence of cancer or R1 resections (*n*=49 or 32%).

While the overall median survival of the study subjects was 24.1 months, patients who underwent an R0 resection had a median overall survival of 26.8 months while those who underwent an R1 resection had a median overall survival of 17.7 months (p=0.01). On the other hand, patients who had no lymph node metastasis had a statistically significant benefit compared to patients with even a single lymph node metastasis (34.8 *v*. 19.9 months; p=0.014). Using Cox-proportional hazards regression analysis, the authors pin-pointed tumour size (>25 mm) and lymph node metastasis to two or more lymph nodes as the two most significant factors that negatively impact on survival despite an R0 resection. The authors indicate that their data regarding patients with tumours >25 mm and/or metastasis to two or more lymph nodes whom they suggest should be grouped under the 'borderline resectable cancers' raises a couple of questions: should this subset of patients be considered for neoadjuvant therapy or for no treatment at all?