Capsule Endoscopy For Colorectal Cancer (CRC) Screening
Executive Summary

[Adapted from the report by DR SYAQIRAH AKMAL]

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Background

Colorectal cancer (CRC) develops slowly from a growth of tissue or polyp on the inner lining of the colon or rectum over a period of 10 to 20 years. It is a largely preventable disease which requires community participation in the prevention process, such as life style modification and proper screening, early detection and removal of adenomatous polyps (precancerous polyps). The latest, updated Asia Pacific Consensus Recommendations for Colorectal Cancer Screening specifies the age range for CRC screening as 50 to 75 years. Low risk individuals are asymptomatic individuals who are below the age of 50 years while average risk individuals are asymptomatic individuals who aged 50 years and above. Individuals at increased risk of CRC include individuals with 1) history of adenomatous polyps or CRC; 2) family history of either CRC or colorectal adenomas diagnosed in a first degree relative 3) history of inflammatory bowel disease of significant duration; or 4) known or suspected presence of one of 2 hereditary syndromes (Lynch syndrome or familial adenomatous polyposis). Globally, colorectal cancer (CRC) is the third most commonly diagnosed cancer in males and the second in females, with over 1.2 million new cancer cases and 608,700 deaths estimated to have occurred in 2008. According to the latest report of the National Cancer Registry (NCR) in Malaysia 2007, colorectal cancer (CRC) is the commonest cancer among men and the second most common cancer among women. A total of 2,246 cases were diagnosed in 2007 and reported to NCR, representing 12.3 % of all cancer cases reported. The incidence of colorectal cancer in 2007 was slightly higher among males with age-standardised rate (ASR) of 13.4 per 100,000 population compared to females (ASR 10.2 per 100,000 population). The incidence was highest among Chinese where the ASR for males and females were 19.4 and 14.6 per 100,000 populations respectively.

Technical Features

The first generation colon capsule endoscopy (CCE-1) which was produced in Israel, uses a small, wireless camera contained in an easy-to-swallow and disposable capsule specifically designed to visualize the colon. The envelope of the capsule is made of biocompatible materials, sealed with biocompatible adhesives. The capsule measures 31 by 11 mm and has two imagers that enable it to acquire video images from both ends. The angle of view from each imager is 156º. It has a total operating time of 10 hours. At the beginning of the examination, CCE is turned on and transmits images for 3 min before it enters a “sleep” mode for 1 hour and 45 min to save battery energy. After this time, it automatically switches on and reactivates in the terminal ileum, allowing a complete colonic exploration.

The second generation colon capsule endoscopy (CCE-2) is similar to CCE-1 except it consists of a slightly bigger, ingestible video capsule. The CCE-2 has two imagers with a much wider angle of view that has been increased to 172 degrees per imager, allowing nearly 360 degrees coverage of the colon. The most unique feature of the CCE-2 is its adaptive frame rate (AFR). This new technology allows the CCE-2 to capture 35 images per second when in motion and 4 images per second when virtually stationary. CCE-2 has been provided with a new portable wireless data recorder able to automatically identify when the CCE enters into the small bowel. It also has a user-friendly interface, sending active, customised reminders to the patient, mainly in relation to the different laxative booster intake after capsule ingestion and when the procedure ended.

Policy Question

Should capsule endoscopy be used to screen adult population for colorectal cancer?

Objectives

i. To determine the diagnostic accuracy of capsule endoscopy for CRC screening in adult population compared with conventional colonoscopy.
ii. To assess the safety of capsule endoscopy compared with conventional colonoscopy in CRC screening.
iii. To determine the effectiveness of CRC screening using capsule endoscopy compared with conventional colonoscopy, with regards to patient outcomes such as detection rate, cancer mortality rate, survival rate, quality of life and quality adjusted life years (QALY) gained.
iv. To determine the economic evaluation of using capsule endoscopy compared with conventional colonoscopy for CRC screening.
v. To assess the ethical, legal, and organizational aspects related to CRC screening using capsule endoscopy.

Methods

Electronic databases such as MEDLINE, PubMed, EBM Reviews-Cochrane Database of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-Health Technology Assessment, EBM Reviews-Cochrane Methodology Register, EBM Reviews-NHS Economic Evaluation Database, Database of Abstracts of Reviews of Effects (DARE), Horizon Scanning database, INAHTA database, HTA database and FDA database were searched. No limits were applied to the search. Additional articles were identified from bibliographies of retrieved articles and hand-searching of journals. Studies were selected based on inclusion and exclusion criteria. All relevant literature was appraised using the Critical Appraisal Skills Programme (CASP) tool. All full text articles were graded based on guidelines from the U.S / Canadian Preventive Services Task Force.

Results and conclusions

A total of 1435 titles were identified through the Ovid interface and PubMed. The inclusion criteria included systematic review studies, randomised controlled trials (RCT), diagnostic accuracy studies, observational and economic evaluation studies on capsule endoscopy. The search was limited to adults aged 18 years and above. The exclusion criteria included animal study, narrative review and laboratory study as well as studies on hereditary colorectal cancer. Finally, eighteen full text articles were included in the review which comprised of three meta-analyses, one cost-effectiveness analysis and 14 observational studies.

Diagnostic accuracy and effectiveness

In the first generation capsule endoscopy (CCE-1), there was fair to good level of evidence that showed its accuracy in detecting polyps in patients with average risk (asymptomatic patients aged 50 years and above) and increased risk of CRC (individuals with personal and family history of adenomatous polyps or CRC, history of inflammatory bowel disease or those diagnosed with hereditary non-polyposis colon cancer or familial adenomatous polyposis). The sensitivity and specificity ranged from 68 to 84% and 62 to 92%, respectively. Its positive predictive value (PPV) ranged from 20 to 77% and negative predictive value (NPV) ranged from 71 to 93%. The diagnostic yield of the CCE-1 in detecting CRC ranged from 27 to 76%.

In second generation capsule endoscopy (CCE-2), there was also fair to good level of evidence that suggested its accuracy in detecting polyps and CRC among the average and increased risk patients. For the detection of polyps, CCE-2 showed sensitivity and specificity of 84 to 90% and 64 to 76%, respectively while its detection rate for CRC ranged from 90% to 93%.

The accuracy of CCE-1 was found to be suboptimal as compared to colonoscopy. There were wide variations in the sensitivity, specificity, positive predictive value

and negative predictive value of CCE-1 reported in the studies. The sensitivity of CCE-2 was found to be comparable to the sensitivity of colonoscopy although the specificity was slightly low. There was no retrievable evidence on mortality rate, survival rate and quality of life related to screening CRC using capsule endoscopy in the general population.

Safety

There was fair level of evidence to show that both CCE-1 and CCE-2 were safe to be used in the screening for colorectal cancer among the average and increased risk patients. Most of the adverse events were mild and related to bowel preparation. Both types of capsule endoscopy claimed to have received CE mark, with CCE-2 received US FDA approval to be used in cases of failed or incomplete colonoscopy.

Cost effectiveness

There was limited evidence on cost-effectiveness of CCE-1 in screening for CRC. In the Markov model, a hypothetical population of 100 000 individuals aged 50 years and over who underwent a 10 yearly screening procedure, the incremental cost−effectiveness (compared with no screening) of colonoscopy and capsule endoscopy was $16165 and $29244 per life−year saved, respectively. With 30% increase in compliance to screening, CCE-1 became more cost-effective than colonoscopy. However, there was no retrievable evidence on economic evaluation conducted on CCE-2. The cost per capsule was reported to be around RM 1688.25 (USD 500; 1 USD = RM 3.37).

Organizational

Level of accuracy of capsule endoscopy depends on the adequacy of bowel preparation and the experience of the readers. Spada et al. and Van Gossum et al. found that sensitivity of CCE was significantly higher in the patients with good or excellent cleanliness as compared with the patients with poor or fair cleanliness. Sidhu et al. found that the interpretation of CCE images was largely dependent on the expertise and experience of the gastroenterologist. Jang et al. also showed that the inter-observer differences were greatest for subtle lesions which were often missed by trainees and that experience with conventional endoscopy is important in reviewing CCE findings. Hence, proper and continuous training of staff is essential especially in reading and interpreting CCE images.

Good acceptability and higher uptake of capsule endoscopy was found among average and increased risk of CRC patients. Groth et al. found that offering capsule endoscopy led to a fourfold increase of screening uptake compared to standard colonoscopy while Pilz et al. found that patients preferred capsule endoscopy to colonoscopy. Capsule endoscopy was also found to be feasible and easily performed as an out-of-clinic procedure according to a study done by Adler et al.

Triantafyllou et. al and Pioche et al. found that capsule endoscopy performed after colonoscopy failure or in those contraindicated for colonoscopy is feasible and safe. Hence, in individuals at high risk and contraindicated for conventional colonoscopy, or those who are unwilling to undergo colonoscopy, capsule endoscopy could provide an alternative to conventional colonoscopy.

Recommendation

Based on this review, CCE-2 may be considered as a diagnostic tool to identify colonic polyps or CRC among patients with average or increased risk of CRC, particularly among those who are unwilling to undergo colonoscopy, have contraindication for colonoscopy and have history of incomplete colonoscopy. However, for general population screening for CRC, capsule endoscopy cannot be recommended yet until further quality evidence is available.