COMMENTARY

Issues in Colorectal Cancer Screening in the Asian Pacific Area

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Abstract

While the guaiac-based fecal occult blood test (FOBT) has been found to be effective for population screening for colorectal cancer, immunochemical FOBT (IFOBT) deserves attention as offering superior sensitivity, usually with no major loss of specificity. A great deal of interest has been concentrated on sigmoidoscopy or colonoscopy as alternatives but medical capacity is a major problem with these approaches, which have yet to be validated for general employment. Other major problems which have still to be overcome with regard to colorectal screening are physician and target population compliance with recommendations as well as ensuring that positives undergo appropriate diagnostic investigations. The APJCP/APOCP has an important role to play in their future solution.

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Key Words: screening methodology - efficacy - compliance

Introduction - FOBT and Sigmoidoscopy

There is a general concensus in the Western world that colorectal screening with the fecal occult blood test (FOBT) or sigmoidoscopy is a worthwhile approach to reduce the cancer burden (Bond, 1997. Thus three randomized control trials using guaiac-based FOBT, one in the USA and two in Europe have all found annual or biennial examinations to reduce colorectal cancer mortality by 15-33% (Hardcastle et al., 1996; Kronborg et al., 1996; Mandel et al., 1999))(see Table 1). Prevention of 18 % of colorectal cancers was described with early detection in one large series (Hristova and Hakama, 1997). Potentially higher effectiveness may be expeced from screening programs with immunochemical FOBT (IFOBT), that has a higher sensitivity and similar specificity to gauaic-FOBT, and the risk of tumor development within three years may in fact be halved (Saito et al., 1995). A 60% reduction was also observed in screen-detected cases as compared with routinely diagnosed cancers (Wada et al., 1996). Although the effectiveness of FOBT screening is generally established, it is considered to be relatively low for guaiac FOBT, especially in terms of cost-efficiency. Other than FOBT, sigmoidoscopy is the sole screening test for which there is reliable evidence of efficacy and reduction of mortality ((Selby et al., 1992).

FOBT, while itself leading to mortality reduction of 33% when conducted annually (Mandel, 1997), may give best results when followed by sigmoidoscopy (Manus et al., 1996), a comparison revealing costs of $1,436 for each polyp in the combined case, as opposed to $271 with endoscopy alone, but the number of cancers found was much greater. Sigmoidoscopy in one review was not considered recommendable for mass-screening of average-risk asymptomatic populations (Mandel, 1997) but may prevent 50% of cancers occurring after the age of 60 (Geul et al., 1997) with costs per year of life saved calculated as between $12,000 and $67,000 (Salkeld et al., 1996). One comparison pointed to decided benefit with signmoidoscopy in terms of costs (Sorrentino et al., 1999), and another in terms of lesions identified, one carcinoma and 30 adenomas thereby found not being detected with FOBT alone (Verne et al., 1998). Although sigmoidoscopy would be able to reduce mortality from cancers of the colon, there is no reported evidence of the feasibility of this approach for population screening, primarily due to the low compliance rate (Robinson, 1993). Moreover, sigmoidoscopy is unable to detect cancers of the proximal colon. Quite recently it has been emphasized that obstacles to screening with flexible sigmoidoscopy are surmountable, and that randomized trials should now be carried out (Verne et al., 1998). However, this appears premature and additional studies are necessary befor ethis can be recommended for the Asian Pacific region as a whole. While it must furthermore be borne in mind that FOBT can also detect cancers in the upper alimentary tract (Hsia and al-Kawas, 1992), these in fact accounting for

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Table 1. Reports on Evaluation of Colorectal Screening in Terms of Mortality Reduction

Country	Methods	Mortality Reduction	Study Design	Reference
USA	Sigmoidoscopy	70%	Case-control	Selby et al., 1992
USA	FOBT	31	Case-control	Selby et al., 1993
USA	FOBT	33	RCT	Mandel et al., 1993/1996
Japan	FOBT+IFOBT	76	Case-control	Hiwatashi et al., 1993
Japan	IFOBT	60	Case-control	Saito et al., 1995
Great Britain	FOBT	15	RCT	Hardcastle et al., 1996
Denmark	FOBT	18	RCT	Kronborg et al., 1996
Italy	FOBT+IFOBT	40	Case-control	Zappa et al., 1997
Finland	FOBT	18	Time trend	Hristova and Hakama, 1997

FOBT, guaiac-based fecal occult blood test; IFOBT, immunochemical FOBT; RCT, randomized controlled trial.

more positive results than colon cancers in one series (Rockey et al., 1998), this is not the case with IFOBT. This may therefore be regarded as more specific for colorectal screening. While alternatives have been proposed, for example using the marker galactose-N acetylgalactosamine, purported to have greater accuracy than FOBT, (Shamsuddin, 1996), molecular approaches (Jen et al., 1998) or virtual colonoscopy (Fenlon et al., 1998; Johnson et al., 1997), the most appropriate methods at the present time remain FOBT and sigmoidoscopy.

Colon Screening Strategy

It has been proposed that flexible sigmoidoscopy and double contrast barium enema are the most cost-effective strategies but they both require colonoscopy if a lesion is identified. Colonoscopy at 10-yearly intervals has in fact been shown to be possible at comparable cost to flexible sigmoidoscopy every 5 years and less costly than FSIG every 3 years (Khullar and DiSario, 1997). The precise relationships with combination strategies, using faecal occult blood testing with periodic flexible sigmoidoscopy or double contrast barium enema as compared to colonoscopy remain to be detailed. However, the choice of screening strategies needs to be tailored to the individual, and a process of community education and feedback is an essential prerequisite to the success of any programme (Bolin, 1996). It should be emphasized that there is not yet sufficient evidence that screening with diagnostic tests for colorectal cancer is actually effective after considering adverse effects and compliance rate. Further, it is essential to evaluate and take into account the capacity for the community to perform sigmoidoscopy or colonoscopy. In 1990, the capacity of Japan to carry out colonoscopy as a diagnostic investigation for screenees whose FOBT tested positive was calculated to be one million at most. From this figure the potential coverage rate of FOBT screening in the population aged 40 years or over was only 12.7% (Saito, 1995). Concerning flexible sigmoidoscopy, the corresponding value was 16.1%. While an increase in capacity has now been achieved, it is undoubtedly impossible to employ colonoscopy or sigmoidoscopy as a screening test for the entire population of Japan. Judging from the number of colonoscopies performed in the USA, less than 5 million per year (personal communication), colonoscopic screening is obviously also still not feasible for the entire population of America. This is particularly pertinent when considering the less economically developed countries of Asia.

As noted above, feasibility has been demonstrated for FOBT, but the problem is with the degree of effectiveness with the guaiac approach. IFOBT appears to have promising advantages in this respect. It has a much higher sensitivity than guaiac FOBT (St John et al., 1993; Allison et al., 1996; Saito, 1996). Thus sensitivities of 90% for one year, 83% for two and 71% for three have been reported, with a specificity of 95.6% (Nakama et al., 1996). A comparison revealed sensitivities of 70-90% for IFOBT as opposed to only 30% for guaiac FOBT (Saito, 1996). The efficacy of screening programs using IFOBT or guaiac FOBT and IFOBT has been shown by several studies (Hiwatashi et al., 1993; Saito et al, 1996; Zappa et al., 1997). Also in terms of cost-effectiveness, IFOBT has advantages over gaiaic FOBT. A screening strategy using IFOBT demonstrated a cost of $13,100 per year of life saved (Shimbo et al., 1994). The program with IFOBT has now been running for 10 years in Japan, with very positive evaluation for a national screening effort (Saito, 1996). Despite this fact, screening with guaiac FOBT is more prevalent in the other countries of the world. Clearly more stress is warranted on introduction of IFOBT.

With regard to target population for screening it is generally advised that all those aged above 50 undergo examinations at appropriate intervals, depending on the methodology adopted. In addition, the reported existence of genetic or other familial risk factors (Ahnen, 1996; Burt, 1996) means that individuals younger than 50 could also be advised to participate. Naturally, research is still needed

Table 2. Factors in Physician and Patient Compliance with Screening Recommendations

Target	Factor General	Factor Specific	Required measure
Physicians	Incentives	Financial	Appropriate recompense
		Professional/ Research	Participation in planning
	Training	Performance of Sigmoidoscopy	Onsite services
		Genetic counselling	Medical education
Patients	Incentives	Perceived benefit	General education
		Physical difficulty	Work-place scheduling
		Financial cost	Insurance coverage
	Belief status	Socioeconomic background	Group targeting
		Personal susceptibility	Group education

Table 3. Factors to be Considered in Colorectal Cancer Screening

Stage/Process	Measures in the Western World	Measures in the Asian Pacific
Methodology	Adopt FOBT Trials /Sigmoidoscopy	Introduce IFOBT
Target Population	Average Risk/Aged	Average Risk/Aged
Payment	National Health	?
Physician Compliance	Provide Training/Incentives	Provide Information
Paramedical Involvement	Allowed	Not Allowed
Population Compliance	Education	Education
Follow-up	Colonoscopy or Sigmoidoscopy + Barium Enema	Colonoscopy preferable

to identify the genes or their polymorphisms that cause common inherited susceptibility for colon cancer, and how they interact with environmental factors. One problem with family history, however, is that surgeons are generally not trained in either risk assessment of inherited colorectal cancer or genetic counselling, so that there may be wide variation in the practice of colorectal screening based on such criteria (Scolefield et al., 1998). Other high risk groups do exist, because of associated disease, including patients with primary sclerosing cholangitis and ulcerative colitis (Brentnall et al., 1996), as well as those with familial polyposis coli (FAP). Genotyping can substantially reduce the cost of FAP screening and, when possible, should start with the proband. (Cromwell et al., 1998). It has been argued that CRC surveillance of HNPCC gene carriers appears to be effective and considerably less costly than no CRC surveillance and therefore deserves to be supported by governmental agencies and health insurance organizations (Vasen et al., 1998).

Evidence-based guidelines have been published recommending combined annual FOBT with sigmoidoscopy every 5 years (Byers et al., 1997; Winawer et al., 1997). This is supported by cost-effectiveness analysis (Lieberman, 1995). While the choice of the least expensive and most effective screening strategy is still open to debate, depending on the cost of flexible sigmoidoscopy, patient age when screening starts, and target population size, the fact of US Preventive Services Task Force, American Cancer Society and Medicare endorsement provides strong evidence of the consensus reached (Bagley and McVearry , 1998 and cited in Levin 1999).

Compliance - Physicians and Patients

The cooperation of physicians is an absolute essential for success of colorectal screening efforts and therefore consideration must be given to their compliance in advising patients and performing the necessary tests (see Table 2). In one study, approximately half of primary care physicians trained in flexible sigmoidoscopy chose not to perform the procedure because of self-perceived deficiencies in ability to reliably perform the operation (Lewis et al., 1999). With Chinese-American physicians, it has been emphasized that there is a need to target barriers to screening (Lee et al., 1999). Financial incentives and feedback were not found to improve physician compliance with cancer screening guidelines in a Medicaid health maintenance organization (Hillman et al., 1998) but an outreach educational seminar combined with implementation of on-site sigmoidoscopy services is an effective strategy for increasing provider utilization

(Schroy et al., 1999). Age is obviously a determining factor and more emphasis must be placed on the, question of necessity before 50. Although increasing physician recommendation for CRC screening is important, primary care physicians report recommending earlier and more aggressive screening than that supported by national guidelines (Richards et al., 1998).

From the patient side, colorectal screening participation has been recently reviewed by Vernon (1997). Multivariate analyses showed that intention to screen was positively associated with employee past participation in screening, belief in the salience and coherence of screening, belief in screening efficacy, perceived self-efficacy, belief that polyp removal prevents colorectal cancer, perceived personal susceptibility to colorectal cancer or polyps, receptivity to family member support for screening, and workplace scheduling of screening examinations (Myers et al., 1998). Colorectal screening patterns and perceptions of risk among African-American users of a community health center.showed results suggest that: 1) educational efforts are needed to enhance knowledge and accuracy of risk perceptions for colorectal cancer; 2) further studies on attributions of risk are needed that may prove useful for developing intervention programs, and 3) studies need to interpret self-report data for colorectal cancer with caution. The existence of race, gender, and socioeconomic disparities in the use of colorectal technologies in a group of patients with near-universal insurance coverage demonstrates the necessity of understanding the reason(s) for these observed differences to improve access to appropriate technologies (McMahon et al., 1999). Social class is a powerful variable in young Americans, and there are racial disparities in older Blacks (Hoffman-Goetz, 1998). Significantly increased compliance may be achieved by provision of leaflets explaining the incidence of cancer and the rationale for screening (Hart et al., 1997). A pilot study is now being conducted in the UK to decide whether to introduce a nationwide screening program and this is being followed with great interest. The main purpose of the study is to determine compliance rtes for screenees after provision of full information about all advantages and disadvantages of the screening (National Screening Committee, UK, 1998).

Population-based interventions to increase screening will clearly benefit from targeting specific physician subgroups and attempting to improve patient acceptance of the procedure (Cooper et al., 1998). To accommodate the increased demand, many medical centers have trained paramedical personnel (i.e. physician assistants, nurses, and gastroenterology technicians) to perform FS. However, as a result of the paucity of research about this practice, only physicians receive a professional fee for performing screening FS. Many state Boards of Nursing explicitly prohibit registered nurses (RNs) from performing this procedure. A recent review outlined research about the effectiveness of paramedical endoscopists, medicolegal and reimbursement issues, and outlines a training program in FS for paramedical personnel (Schoenfeld, 1999). Nurses are allowed to perform flexible sigmoidoscopy in most states based on current state board of nursing guidelines and the employment of paramedical personnel to perform endoscopic procedures is increasing rapidly in the USA (Cash et al., 1999).

Clearly it is essential that appropriate measures be taken for those individuals who demonstrate positive results in screening tests. This may be a major problem, Lurie and Welch (1999) recently finding that only 34% of elderly people with fecal occult blood then undergoing the recommended evaluation with either colonoscopy or flexible sigmoidoscopy with an air-contrast barium enema. Similar results were also published for another study (Myers et al., 1993) although more optimal outcome was evident in two European series (Hardcastle et al., 1996; Kronborg et al., 1996) as well as community screening in Ohio and Texas (Morris et al., 1991; Levin et al., 1997). With regard to nationwide screening in Japan, the compliance rate for diagnostic investigation after positive FOBT was found to be only 70% and this figjure may now have decreased to 60%. Lack of knowledge about diagnostic tests may be one factor, but other influences remain to be clarified. This is a serious obstacle that will diminish screening efficacy.

For identification of lesions carrying risk of malignancy, high-resolution chromoendoscopy has been reported to provide morphological detail of diminutive colorectal polyps that correlates well with polyp histology. If incorporated into colon cancer screening, such techniques may limit the need for biopsy and/or subsequent colonoscopy and ultimately decrease costs (Axelrad et al., 1996). Computed tomographic colonography (Virtual colonoscopy) may also be useful for this purpose (Johnson et al., 1997).

Conclusions

In conclusion, there are a number of processes relevant to colorectal cancer screening which must be taken into account in optimizing efforts in this area within the Asian Pacific region (Table 3). As recently emphasized (Moore and Tsuda, 1999), education and provision of up-to-date information in a forum for debate is the key to success, with major roles for the Asian Pacific Organisation for Cancer Prevention (APOCP) and the Asian Pacific Journal for Cancer Prevention (APJCP) in this effort.

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