



Identification of subjects at risk of proximal advanced neoplasia for colorectal cancer screening [☆]



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Abstract Flexible sigmoidoscopy (FS) and colonoscopy are two commonly used screening tools for colorectal cancer (CRC), and FS mainly detects distal lesions. Colonoscopy resource is limited, yet there is no definite evidence on when flexible sigmoidoscopy is suitable as a screening alternative. This study evaluated the optimal cut-off score from a validated risk stratification system which best predicts proximal advanced neoplasia (PAN) by comparing the sensitivity, specificity and relative risk of PAN according to various cut-off scores. 5819 asymptomatic subjects aged between 50 and 70 years (average age 57.7 years, standard deviation (SD) 4.9) received colonoscopy between 2008 and 2014 in Hong Kong. Their prevalence of PAN was evaluated according to a prediction tool for colorectal neoplasia based on age, gender, smoking status, family history of CRC, body mass index (BMI) and diabetes (ranging from 0 to 6). One binary logistic regression model was performed with PAN as the outcome variable and the risk score as the variable tested for association. In multivariate regression analysis, risk score ≥ 3 was associated with significantly higher risk of PAN (3.4–9.1%; AOR = 3.18–8.09, $p < 0.001$) when compared with those scoring 0. Risk scores 0–2 were associated with either insignificant or lower risks of PAN compared to the overall risk. Applying FS for screening those who scored 0–2 and colonoscopy for those who scored ≥ 3 led to a very small proportion of PAN being missed (1.60%), whilst maintaining a high level of specificity

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(81.9%). Clinicians may use this scoring system to inform subjects and facilitate their choice between colonoscopy and FS.

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1. Introduction

Globally, colorectal cancer (CRC) is one of the most common malignancies. In 2012, it accounted for around 10% of all cancers and more than 8% of cancer-specific mortality worldwide [1]. In the past decades, many Asia Pacific countries were increasingly affected, gradually catching up the incidence figures of the Western countries [2]. It leads to a substantial public health burden in terms of morbidity and mortality.

CRC screening tests have been proven effective to reduce mortality by up to 33%, 40% and 56% using faecal occult blood tests, flexible sigmoidoscopy (FS) and colonoscopy, respectively [3,4]. Guidelines endorsed these three tests as suitable screening options [5,2]. In 2014, an updated Asia Pacific Consensus Recommendation for CRC screening proposed that colonoscopy is the preferred test of choice in high risk individuals [6]. Colonoscopy is also the predominant mode of screening in the US [7] among many other countries.

However, colonoscopy is a labour-intensive, invasive and expensive procedure relative to other screening modalities. Its demand is increasing, and endoscopic capacity constraints induce a prohibitive challenge to population-based CRC screening [8,9]. It also requires a high level of expertise – which implies that it might not be suitable as a first-line test in resource deprived regions.

On the other hand, FS represents an attractive option as it is an office-based procedure requiring minimal bowel preparation and no sedation. The reach of the FS endoscope allows examination of a portion of the descending colon. To deal with the increasing demand for colonoscopy, subjects at lower risks of proximal lesions – and hence more suited for FS – will need to be identified. Our research team has previously developed and validated a scoring system predicting the presence of colorectal neoplasia [10]. We have also evaluated the risk factors associated with advanced neoplasia [11], and also the association between distal hyperplastic polyps and proximal lesions. However, whether this scoring system could effectively predict the presence of proximal advanced neoplasia (PAN) remains unknown.

The objective of this study is to evaluate the optimal cut-off score from this risk stratification system which best predicts PAN by comparing the sensitivity, specificity and relative risk of PAN according to various cut-off scores. The primary purpose is to evaluate whether this existing validated scoring system for any colorectal advanced neoplasia [10] can also be used to stratify

screening participants according to their risk of proximal neoplasia. If so, the same scoring system can be used by primary care professionals to risk stratify subjects according to their overall risk of colorectal neoplasia and also that of proximal neoplasia. The underlying framework assumes that FS is a suitable screening option when the screening participants do not have proximal lesions.

2. Materials and methods

The details of the study setting have been described elsewhere [12–17]. In short, a bowel cancer screening centre has been established in Hong Kong in 2008, and invited eligible Hong Kong residents aged 50–70 years who were asymptomatic of CRC to participate in a free CRC screening programme via media announcement. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong (protocol CRE-2008.404). All participants provided informed consent for the study.

2.1. Study design

Self-referred screening participants for CRC screening were recruited. The eligibility criteria for this study were (i) age 50–70 years; (ii) absence of existing or previous symptoms suggestive of CRC such as haematochezia, tarry stool, anorexia or change in bowel habit in the past 4 weeks, or weight loss of greater than 5 kg in the past 6 months; and (iii) not having received any CRC screening tests in the past 5 years. Exclusion criteria included personal history of CRC, colonic adenoma, diverticular disease, inflammatory bowel disease, prosthetic heart valve or vascular graft surgery. Participants with medical conditions which were contraindications for colonoscopy, like cardiopulmonary insufficiency and the use of double antiplatelet therapies were also excluded.

2.2. Study logistics

Eligible participants were invited to complete a self-administered questionnaire, including information on their socio-demographic details, past medical history and use of medications for chronic diseases. The completeness of questionnaires was checked by our centre's staff, and trained volunteers supported survey completion for illiterate subjects by reading the questions as exactly printed in the questionnaire. The body weight

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