Colon cancer screening

Local Perspective

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Incidence of colorectal cancer in Asia

Sung et al. (2005)
Increasing mortality from colorectal cancer in Asia

- Decreasing mortality in western world
- Increasing mortality in Asia

Sung et al. (2005)
Increasing incidence of colorectal cancer with age  The age-specific incidence of colorectal cancer in the general population was measured between 1988 and 1992 in men and women of all races. (Data from Surveillance, Epidemiology, and End Results (SEER) Program, 1973-1992.)
Factors Associated with Annual New Cases of Colorectal Cancer

- Sporadic: average risk - 75%
- Hereditary nonpolyposis colorectal cancer (HNPCC) - 5%
- Familial adenomatous polyposis (FAP) - 1%
- Inflammatory bowel disease (IBD) - 1%
- Family history (FH) - 15%-20%

Sporadic = men and women age 50 and older with no special risk factors; IBD = inflammatory bowel disease; FAP = familial adenomatous polyposis; HNPCC = hereditary nonpolyposis colorectal cancer; FH = positive family history.

Colonic polyps  Over 95 percent of colonic polyps are hyperplastic or adenomatous. Although these two types have some distinctive features on gross appearance, they cannot be reliably distinguished endoscopically. Panel A: typical small sessile hyperplastic polyp that is less than 5 mm in size. Panel B: typical pedunculated adenomatous polyp. Courtesy of James B McGee, MD.
Adenocarcinoma of the colon  Adenocarcinoma of the colon may have a variety of appearances on endoscopy. Panel A: a typical exophytic mass; Panel B: a friable polypoid mass; Panel C: circumferential adenocarcinoma. Courtesy of James B McGee, MD.
Pathogenesis of Colorectal Cancer – Adenoma-Carcinoma Sequence†

- Normal colon
  - Small adenoma
    - Large adenoma with villous component
      - Large adenoma with high-grade dysplasia
        - Large adenoma with invasive carcinoma

Adenoma to Carcinoma Pathway

- Normal Epithelium
- Hyper-proliferation
- Early Adenoma
- Intermediate Adenoma
- Late Adenoma
- Cancer

- APC loss
- K-ras mutation
- Chrom 18 loss
- p53 loss
According to the 3rd report of the National Cancer Registry, the most frequent cancer was:

- Breast cancer: 18.0%
- Large bowel cancer: 11.9%
- Lung cancer: 7.4%
NCR report: Variation by gender

**MALES**
- Large bowel cancer: 14.5%
- Cancers of the lung: 12.2%
- Nasopharynx: 7.8%

**FEMALES**
- Breast cancer: 31.3%
- Cancers of cervix uteri: 10.6%
- Large bowel cancer: 9.9%
NCR report: Large Bowel Cancer

Figure 5.7.2: Large Bowel International comparisons – Age-standardized Incidence per 100,000 population by sex, Peninsular Malaysia 2003-2006

<table>
<thead>
<tr>
<th>Country</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia, South</td>
<td>48.4</td>
<td>34.7</td>
</tr>
<tr>
<td>China, Hong Kong</td>
<td>38.6</td>
<td>28.3</td>
</tr>
<tr>
<td>China, Shanghai</td>
<td>26.5</td>
<td>19.5</td>
</tr>
<tr>
<td>China, Taiwan</td>
<td>28.8</td>
<td>23.5</td>
</tr>
<tr>
<td>India, Chennai (Madras)</td>
<td>6.7</td>
<td>4.1</td>
</tr>
<tr>
<td>India, Delhi</td>
<td>6.7</td>
<td>4.0</td>
</tr>
<tr>
<td>India, Mumbai</td>
<td>6.7</td>
<td>5.5</td>
</tr>
<tr>
<td>Malaysia, Chinese</td>
<td>31.5</td>
<td>26.2</td>
</tr>
<tr>
<td>Malaysia, Indian</td>
<td>15.7</td>
<td>12.9</td>
</tr>
<tr>
<td>Malaysia, Malay</td>
<td>12.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Singapore: Chinese</td>
<td>43.7</td>
<td>31.3</td>
</tr>
<tr>
<td>Singapore: Indian</td>
<td>12.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Singapore: Malay</td>
<td>20.0</td>
<td>15.9</td>
</tr>
<tr>
<td>Sweden</td>
<td>30.3</td>
<td>23.2</td>
</tr>
<tr>
<td>UK, England</td>
<td>35.4</td>
<td>22.8</td>
</tr>
<tr>
<td>USA, California, Los Angeles: Chinese</td>
<td>31.1</td>
<td>22.6</td>
</tr>
</tbody>
</table>

Lim et al. (2008)
NCPR-Colorectal Cancer
RATIONALE

The first colorectal cancer registry in Malaysia to systematically collect data on aspects of colorectal cancer relevant to its prevention, management and treatment evaluation in Malaysia.

To aid in improving colorectal cancer prevention, management and outcome

Sponsor
MOH and Clinical Research Centre (CRC)

Principal Investigators
Dr Muhammad Radzi
Hospital Sultanah Bahiyah

Registry coordinating centre/office
Clinical Research Centre, Hospital Sultanah Bahiyah, Alor Star, Kedah
Preliminary report 2008

- Clinico-Demographics
- Surgery Section
- Pathology Section
- Chemotherapy & Radiology Section
- Follow up Section/survival
A total of 622 patients with colorectal cancer were registered in the registry; 131 in 2007 and 491 in 2008. Males accounted for 60% and females, 40%. Age distribution showed that 18.3% were less than 50 years old and 80.7% were 50 years and above.
Age Distribution - Patient Population (2008-2012) (n=631)
## Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>% cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea, constipation, or other change in bowel habit</td>
<td>58 %</td>
</tr>
<tr>
<td>Weight loss</td>
<td>48 %</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>42 %</td>
</tr>
<tr>
<td>Blood in stool</td>
<td>32 %</td>
</tr>
<tr>
<td>Anemia</td>
<td>13 %</td>
</tr>
<tr>
<td>Intestinal Obstruction</td>
<td>11 %</td>
</tr>
</tbody>
</table>
Colorectal cancer is often found after symptoms appear, most people with early colon or rectal cancer have no symptoms of the disease. Symptoms usually appear only with more advanced disease. This is why getting the recommended *(Colorectal Cancer) screening tests* before any symptoms develop is so important.
In 2008, a total of 470 patients with confirmed histopathological diagnosis of colorectal cancer were registered. The majority (75.7%) had left sided tumours.
Stage at presentation & family history

- Majority in stage 3 and 4, advanced stage
- Less than 10% associated with family history
Conclusion

- It is hoped that this registry will be a valuable source of data for the assessment of colorectal cancer management and outcomes in Malaysia.
Screening is appropriate for colorectal cancer

- Natural history
- Early detection
- Treatment available and acceptable
- Change in outcome

Rerknimitr et al. (2006)
Simple Life Saving Steps

New Study: Boosting Five Preventive Services Would Save 100,000 Lives Annually
Colorectal Cancer Screening Guidelines
U.S. Preventive Services Task Force (USPTSF)*

“The USPSTF strongly recommends that clinicians screen men and women 50 years of age or older for colorectal cancer. Grade A Recommendation.”

*USPSTF. Ann Int. Med. 2002
Development of Colorectal Neoplasia

Genetically predisposed individual

Chromosomal changes

Colonic cell proliferation

Adenoma

Dysplasia

Carcinoma

Environmental Factors (Diet, smoking, inactivity)

Screening Strategies

Two-Stage Screening

FOBT (fecal occult blood test)

Colonoscopy
Fecal occult blood test (FOBT)

- Checks for hidden (occult) blood in the stool. Newer tests look for globin, DNA, or other blood factors including transferrin, while conventional stool guaiac tests look for heme.

- **PROS**
  - No direct risk to the colon
  - No bowel preparation
  - Sampling done at home
  - Inexpensive

- **CONS**
  - May produce false-positive test results
  - Colonoscopy will be needed if abnormal

[American Cancer Society® Colorectal Cancer Early Detection]
Objectives of Colorectal Cancer Screening

- **Prevent** cancers by detection and resection of adenomatous polyps
- **Detection** of surgically curable colorectal cancers (Stages 1, 2)
BLOOD PRODUCTS IN FECES

Hemoglobin

Heme

Globin

Guaiac; peroxidase.

Interference by
Meat, vegies, vitamin C, NSAIDs.

Detects bleeding from
Stomach, small & large intestine.

gFOBT

Immunochemical.

NO Interference.

Detects bleeding from
large intestine.

FIT

From: G. Young (2005)
iFOBT

- Adopted increasingly worldwide
- Specific for human haemoglobin
- Colon specific
- Sensitivity doubled cf gFOB
- Quantitative: threshold is adjustable
A rapid, one step test for the qualitative detection of Human Occult Blood in faeces
FIT rapid test

- Immunochromatographic assay for qualitative detection of Human Occult Blood in faeces
- No dietary restrictions
- Specific to human hemoglobin
- Sensitivity: detect levels of FOB as low as 50 ng/mL or 6 ug/g feces
- Test result in 5~10 minutes

Kit content:

> 25 test devices
> 25 collection tubes with extraction buffer

Storage: 2 - 30°C
Test Procedure

- Stab the collection stick into fecal at 3 different sites.
- Specimen prepared in collection tube may be stored for 3 days at room temperature (15-30°C)

POSTITIVE: two distinct colored lines appear
NEGATIVE: one colored line appears in control line region
INVALID: control line fails to appear
Flexible Sigmoidoscopy (Flex Sig)

RCT’s in progress
In US and UK
Sigmoidoscopy

- Disadvantages
  - Misses 40% - 50% of CRC and polyps
  - Risk of colon perforation is 1 to 2 per 10,000 exams

- Evidence for most effective screening interval is inconclusive
Colonoscopy

- 95% of CRC in reach of colonoscope
- Diagnostic use after positive results on FOBT or FS
- Recommended as initial screening test for high risk individuals
Colonoscopy

- The National Polyp Study observed a 76-90% reduction in CRC incidence after polypectomy
- RCT’s in progress

Winawer et al, NEJM 1993
Effect of Colonoscopic Polypectomy on Incidence of Colorectal Cancer

↓ Incidence

* U.S. National Polyp Study 76–90%
  + Italian Multicenter Study Group 66%

*Winawer, Zauber et al NEJM 1993
+Citarda et al GUT 2001
## Colorectal cancer screening tests

<table>
<thead>
<tr>
<th>Flexible sigmoidoscopy</th>
<th>Colonscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flexible sigmoidoscopy</strong></td>
<td><strong>Colonscopy</strong></td>
</tr>
<tr>
<td>the minimally invasive medical examination of the large intestine from the rectum through the last part of the colon</td>
<td>The endoscopic examination of the large bowel and the distal part of the small bowel with a CCD camera or a fiber optic camera on a flexible tube passed through</td>
</tr>
<tr>
<td><strong>PROS</strong></td>
<td><strong>PROS</strong></td>
</tr>
<tr>
<td>- Fairly quick and safe</td>
<td>- Can usually view entire colon</td>
</tr>
<tr>
<td>- Usually doesn’t require full bowel preparation</td>
<td>- Can diagnose other diseases</td>
</tr>
<tr>
<td><strong>CONS</strong></td>
<td><strong>CONS</strong></td>
</tr>
<tr>
<td>- Colonscopy will be needed if abnormal</td>
<td>- Full bowel preparation needed</td>
</tr>
<tr>
<td>- May some discomfort</td>
<td>- More expensive on a one-time basis than other forms of testing</td>
</tr>
</tbody>
</table>
CT Colonography

Rationale

• High level of sensitivity for cancer and large polyps

• Minimally invasive (rectal tube for air insufflation)

• No sedation required
CT Colonography

2-D view

3-D view

Courtesy of Beth McFarland, MD
CT Colonography: Issues

- Management of findings
- Inter-observer variability
- Bowel Prep
- Radiation
- Extracolonic findings
Blood or Stool..or Imaging?

Cancer Control Opportunity

The American Cancer Society estimates that 90% of colorectal cancer cases & deaths in the U.S. could be prevented.

ACS: Colorectal cancer facts and figures sp ed 2005
Colorectal Screening Rates Low:
Reasons (according to Patients)

- Low awareness of CRC as a personal health threat
- Lack of knowledge of screening benefits
- Fear, embarrassment, discomfort
- Time
- Cost
- Access
- “My doctor never talked to me about it!”
Participation

- The best test is useless if nobody does it
- Better is the enemy of good
- “Just do it!”
Physician’s CRC Recommendation

A recommendation from the doctor is the most powerful single factor in a patient’s decision about whether or not to obtain cancer screening.

How to Increase Colorectal Cancer Screening Rates in Practice: A Primary Care Clinician’s Evidence-Based Toolbox and Guide. Mona Sarfaty, MD, American Cancer Society & CDC, 2006.
"I'm inclined to agree with you."
CRC Screening in Malaysia: how to proceed?

- Second commonest cancer, commonest among elderly
- Aging of population and rising incidence of CRC
- Little health authority support for population-based screening programs
- National screening guidelines ?????
- Family doctors are under-utilized resource
- Low public awareness
- Team work and champions

*Identify high risk individuals for targeted screening*
2. OBJEKTIF
Untuk mengesan lesi pra-kanser dan kanser kolorektal seawal mungkin di kalangan populasi yang berumur antara 50-70 tahun.

3. KUMPULAN SASAR
Individu berumur antara 50 – 70 tahun, warganegara Malaysia.

4. KAWASAN PERLAKSANAAN PROGRAM SARINGAN
Semua Klinik Kesihatan dalam daerah Kota Setar dan Kuala Muda

Projek rintis saringan kolon kanser Kedah
5. **KAEDAH SARINGAN**

Kaedah yang digunakan untuk tujuan saringan kanser kolorektal adalah seperti berikut:

Individu berumur antara 50-70 tahun.

Menjalankan ujian kualitatif menggunakan *Immunological Faecal Occult Blood Test* (iFOBT), maksima sebanyak 2 kali bagi setiap individu.

Kes-kes positif iFOBT akan dirujuk ke Hospital Sultanah Bahiyah, Alor Setar atau Hospital Sultan Abdul Halim, Sungai Petani untuk ujian kolonoskopi.

Bagi kes-kes negatif iFOBT, jangkamasa ulangan saringan (screening interval) adalah setiap 2 tahun.

6. **SEBARAN MAKLUMAT TENTANG PROGRAM SARINGAN**

Radio Malaysia Kedah (RMK).

Poster dan *banner* di kawasan-kawasan umum.

Surat jemputan/tawaran untuk saringan kepada institusi-institusi kerajaan dan badan-badan berkanun di daerah Kota Setar dan Kuala Muda.
Issues

- Screening Guidelines
- Lifestyle Guidelines
- Provider Education
- Public Education
- Reimbursement
- Capacity and Access
- Barriers
- Evaluation
‘The barrier to reducing the number of death from colon cancer is not lack of scientific data but a lack of organisational, financial and societal commitment’

Daniel K Podoslsky MD
NEJM 7/02/00
Thank you for your kind attention

HAPPY CONFERENCING