UPDATE ON COLORECTAL CARCINOMA

JCB DAKUBO
Department of Surgery
U. G. M. S
INCIDENCE

• Colorectal cancers are common malignancies with annual incidence of about 1,000,000 new cases worldwide and mortality of 500,000 each year.

• It is the fourth most common cancer diagnosed and the second most common cause of cancer death in the U.S. accounting for an estimated 145,290 new cancer cases and 56,290 deaths in a year
<table>
<thead>
<tr>
<th>Age adjusted incidence rate per 100,000 population</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>43.0</td>
<td>N. America, UK, Europe, Scandinavia, Russia, Australia</td>
</tr>
<tr>
<td>21.0</td>
<td>Turkey, Italy, Greece, Brazil, Argentina, Chile</td>
</tr>
<tr>
<td>12.0</td>
<td>China, South Africa, Mexico</td>
</tr>
<tr>
<td>3.7</td>
<td>India, North Africa, Ethiopia, Kenya, Uganda, Middle East</td>
</tr>
<tr>
<td>&lt;2.0</td>
<td>Sub-Saharan African Countries</td>
</tr>
</tbody>
</table>
CRC statistics in Accra

• In Accra, Ghana
• Colorectal Cancer – 3th Commonest Cancer Diagnosed
• 10th cause of cancer deaths
• 8th cause of cancer deaths in males
• 9th cause of cancer deaths in females

(RB Biritwum 1996, E Wiridu 2005)
Published studies on colorectal cancer in Accra since 1956 to date and the population of Accra during the study periods.

<table>
<thead>
<tr>
<th></th>
<th>Badoe$^{12}$</th>
<th>Badoe$^{14}$</th>
<th>Naaeder et al$^{10}$</th>
<th>Dakubo et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>1956-1965</td>
<td>23</td>
<td>35</td>
<td>66</td>
<td>197</td>
</tr>
<tr>
<td>1970-1975</td>
<td>18</td>
<td>25</td>
<td>68</td>
<td>167</td>
</tr>
<tr>
<td>1987-1991</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997-2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>41</td>
<td>60</td>
<td>137</td>
<td>359</td>
</tr>
<tr>
<td>F</td>
<td>10</td>
<td>26.8</td>
<td>32.6</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>1/100,000/yr</td>
<td>1.3/100,000/yr</td>
<td>1.8/100,000/yr</td>
<td>1.2/100,000/yr</td>
</tr>
<tr>
<td>Population of Accra during study period</td>
<td>388,396$^{12}$</td>
<td>715,177$^{15}$</td>
<td>1,431,099 $^{16,17}$</td>
<td>2,905,726$^{18}$</td>
</tr>
</tbody>
</table>
Classification

Colorectal Cancers are classified as

1. Sporadic cancers. (Non-hereditary and hereditary)

2. Colitis associated cancers.
   These are cancers developing in the large bowels of patients with ulcerative colitis, Crohn’s disease and the Irritable Bowel Disease
COLITIS ASSOCIATED CRC

• In colitis associated CRC there is a generalised field change, genetically, and so multiple tumours can develop at the same time or soon after each other

• CRC account for about a third of deaths related to Ulcerative colitis and the risk depends on disease duration

  a. 2% of affected people by 10 yrs
  b. 8% of affected people by 20 yrs
  c. 18% of affected people by 30 yrs
Sporadic Colorectal Cancers are further divided into;
1. Hereditary cancers
2. Non-Hereditary cancers

Hereditary cancers are those associated with;
1. FAP *(there is truncation of the APC gene product)*
2. HNPCC
3. MAP *(Mut y associated polyposis)*

In Sporadic cancers the field change is usually focal and typically single but can be multiple
HISTOLOGICAL TYPES

I. Adenocarcinoma
II. Anaplastic
III. Colloid
IV. Mucin
V. Signet ring
VI. Neuroendocrine tumours
VII. Squamous cell carcinoma
VIII. Lymphoma
IX. Gastrointestinal stromal tumours (GIST)
X. Etc
MODES OF SPREAD

I. WITHIN BOWEL WALL
   a. Radial through the bowel wall
   b. Circumferential encircling the bowel wall
   c. Longitudinal, upwards and downwards

II. IN THE MESENTERY/ MESORECTUM
   Along lymphatics to pericolic or perirectal lymph nodes
   To intermediate lymph nodes to pre-aortic or para-aortic lymph nodes
III. OTHERS MODES OF SPREAD

a. Haematogenous to liver  *(considered the ‘sentinel node’ in haematogenous spread)*, lungs, bone, etc

b. Trans-ceilomic/trans-peritoneal
PATHOGENESIS
Carcinomas of the large bowel are tumours whose development are driven by 
*environmental, bowel luminal, genetic and epigenetic alterations.*

They develop through a prototypic stepwise accumulation of gene mutations that are handed down from one generation of cells to the other through cell division.
The initial morphological change noticeable is the adenoma which after 10-15 years develops into a carcinoma

1. Advanced age as a risk factor

*Peak incidence is in the 7th decade of life*
Figure 1, Sex and Age Specific incidence rate
2. Environmental factors

a. Imbalance in the energy equation; high energy intake against low energy expenditure
b. High intake of refined diets, rich in red meat, fat.
c. Alcohol abuse
d. Smoking
e. Low intake of vegetables, fruits, folate, fish etc
3. Luminal RISK FACTORS

- Long transit time of large bowel content
- Low amounts of short chain fatty acids (butyrate derived from bacterial fermentation of soluble non-starch polysaccharides is an obligate colonocyte fuel). High concentrations of it slows the progression of adenomas into large ones and also transition to malignancy.
- High colonic Ph
- High concentration of secondary bile salts
Bile Salts and field cancerization in colorectal cancer.

Bile salts induce

a. Oxidative/nitrosative stress to the mucosal cells
b. DNA damage and
c. Apoptosis

The epithelial cells of non-neoplastic colonic mucosa of individuals with CRC have reduced capacity to undergo induction of apoptosis by bile salts compared to epithelial cells of individuals without neoplasm.
4. Gene mutations

Colorectal cancers that develop through a prototypic stepwise accumulation of gene mutations that are handed down from one generation of cells to the other through cell division.
# Genes involved in colorectal cancer genesis

<table>
<thead>
<tr>
<th>Gene Category</th>
<th>Gene name</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proto-oncogenes</td>
<td>K-ras</td>
<td>Sporadic adenomas (large &amp; villous), cancer, ulcerative colitis</td>
</tr>
<tr>
<td></td>
<td>src, C-myc</td>
<td></td>
</tr>
<tr>
<td>Tumour Suppressor</td>
<td>APC, DCC, P53, P53, DPC4</td>
<td>FAP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Advanced adenomas &amp; cancers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor prognostic indicator</td>
</tr>
<tr>
<td>DNA mismatch repair</td>
<td>MSH2, MLH1, PMS1, PMS2, GTBP</td>
<td>HNPCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HNPCC</td>
</tr>
<tr>
<td>Risk modifiers</td>
<td>Phospholipase A 2, COX2, CD44v</td>
<td>Metastatic disease</td>
</tr>
</tbody>
</table>

8/9/2012
A typical series of gene mutations that precede a CRC development.

*Fearon and Vogelstein model (1990)*
Progression of morphological changes in colorectal cell towards carcinoma

Chromosome Unstable pathway (CIN) (Gatekeeper Pathway)

Microsatellite Unstable pathway (MSI) (Caretaker pathway)

Normal Epithelium

Early adenoma

Intermediate adenoma

Carcinoma

Dysplastic cells

Late adenoma
5. Epigenetic alterations

There are many mechanisms to this:

1. DNA Hypermethylation

This is hypermethylation of promoter CpG islands of tumour suppressor genes resulting in silencing of those genes.

This usually affects repair genes the silencing of which results in un-corrected errors in transcription and hence microsatellite instability.
2. Loss of imprinting
3. Histone acylation, methylation and phosphorylation
4. Modifier gene activity, eg. COX 2 gene activity
Genetics and Epigenetics of colorectal carcinogenesis

1. Genetic Abrasion; a) CIN pathway (85%)
   b) MSI Pathway (15%)

2. Epigenetic Change. This is hypermethylation of promoter CpG islands of tumour suppressor genes resulting in silencing of those genes

Tumours in Accra

*K-ras/B-raf mutations* > 90% and there is absence of *b-raf amplification typically associated with K-ras mutation*

MSI (41%), CIN (59%)
### Table 1: Frequency of microsatellite instable (MSI-High) tumors in African Americans and Native Africans from different studies.

<table>
<thead>
<tr>
<th></th>
<th>Ghana*</th>
<th>African Americans</th>
<th>African Americans</th>
<th>African Americans</th>
<th>Whites (MECC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSS</td>
<td>27 (39%)</td>
<td>11 (50%)</td>
<td>27 (53%)</td>
<td>222 (81.2%)</td>
<td>1221 (74%)</td>
</tr>
<tr>
<td>MSI-Low</td>
<td>14 (20%)</td>
<td>1 (5%)</td>
<td>2 (4%)</td>
<td>241 (15%)</td>
<td></td>
</tr>
<tr>
<td>MSI-High</td>
<td>29 (41%)</td>
<td>10 (45%)</td>
<td>22 (43%)</td>
<td>44 (19.8%)</td>
<td>191 (12%)</td>
</tr>
</tbody>
</table>

* Results of the present preliminary data
Figure 1: Representative images of MSI analysis in Ghana samples. Differences in fragment size and pattern between normal sample (upper part) and tumor (lower part) in BAT25 mononucleotide marker (A) and BAT26 mononucleotide marker (B).
Figure 2: Representative images of IHC staining of four MMR proteins in one of the tumors from Ghana. There is positive staining against MSH2 (A) and MSH6 (C), but there is no staining of the tumor cells against MLH1 (B) and PMS2 (D) in the same tumor.
DIAGNOSIS
## Statistics of stages at presentation with colorectal cancers

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5.1 %</td>
<td>13.7 %</td>
</tr>
<tr>
<td>II</td>
<td>27.1 %</td>
<td>27.9 %</td>
</tr>
<tr>
<td>III</td>
<td>58.8 %</td>
<td>37.7 %</td>
</tr>
<tr>
<td>IV</td>
<td>7.4 %</td>
<td>21.1 %</td>
</tr>
</tbody>
</table>

8/9/2012
Clinical Presentation

1. Rectal bleeding
2. **Change in bowel habits**
3. Constipation
4. Diarrhoea
5. Passing mucus PR
6. Unexplained Wt loss
7. Feeling of incomplete emptying of the bowel
8. Pain, Abdominal or rectal
9. Iron deficiency anaemia
10. Borbogrygmi
11. Tenesmus
12. Feeling of masses; abdominal and rectal
13. Emergency; intestinal obstruction or perforation
14. Fistulae, internal or external
<table>
<thead>
<tr>
<th>Index presenting symptom/condition</th>
<th>Number of patients (%)</th>
<th>Average duration of symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding PR</strong></td>
<td>185 (51.1)</td>
<td><strong>17.5 months</strong></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>76 (21.2)</td>
<td>5.4 months</td>
</tr>
<tr>
<td>Intestinal Obstruction</td>
<td>62 (17.3)</td>
<td>-</td>
</tr>
<tr>
<td>Intestinal Perforation</td>
<td>9 (2.5)</td>
<td>-</td>
</tr>
<tr>
<td>Anaemia</td>
<td>9 (2.5)</td>
<td>-</td>
</tr>
<tr>
<td>Change in bowel Habits</td>
<td>6 (1.7)</td>
<td>6.4 months</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>5 (1.4)</td>
<td>6.8 months</td>
</tr>
<tr>
<td>Internal faecal fistula</td>
<td>2 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>Fistula in Ano</td>
<td>2 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>Intussuception</td>
<td>1 (0.3)</td>
<td>-</td>
</tr>
<tr>
<td>Mucus discharge PR</td>
<td>1 (0.3)</td>
<td>12 months</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1 (0.3)</td>
<td>8.0 months</td>
</tr>
</tbody>
</table>
Clinical/Pathological Diagnosis of Lynch syndrome, Cont

Amsterdam Criteria II (1999)
- There should be at least three relatives with HNPCC-associated cancer (CRC, Endometrium, gastric, biliary, Small bowel, proximal Ureteric), of which one should be a first degree relative of the other two
- At least two successive generations should be affected
- At least one colorectal cancer should be diagnosed before the age of 50 years
- FAP should be excluded
- Tumours should be verified by a pathologist
- (Has a pooled sensitivity of 78% and a specificity ranging between 46%-68%)
Revised Bethesda Guidelines for testing for MSI: - Individuals meeting any one of the ff:

1. CRC diagnosed in individual under age 50yrs
2. Presence of synchronous, metachronous CRC, or other HNPCC-associated tumours regardless of age
3. CRC with the MSI-H histology (presence of tumour-infiltrating lymphocyte, crohn’s-like lymphocytic reaction, mucinous/signet-ring differentiation, or medullary growth pattern), in patient < 60yrs of age
4. CRC in 1 or more first degree relatives with an HNPCC-related tumour, with 1 of the cancers being diagnosed under 50yrs

5. CRC diagnosed in 2 or more first- or second-degree relatives with HNPCC-related tumour, regardless of age
INVESTIGATION
1. **LOCAL TUMOUR**

- DRE
- Endoscopy; proctoscopy, sigmoidoscopy, colonoscopy.
- Tumour biopsy
- Barium enema
- Endoluminal Ultrasound
2. **METASTATIC TUMOUR**

- Abdominal Ultrasound
- Abdominal & Pelvic CT scan
- Chest X-Ray
- IVU
- Bone Scintigraphy
- MRI

- “Serum CEA”
3. **Genetic testing**

- MSI (Immunohistochemistry)
- MSH 2, MSH 1, MLH 1, MLH 2, PMS 1, PMS 2
- K-ras
- B-raf
- Etc
TREATMENT
TREATMENT MODALITIES

1. SURGICAL RESECTION

2. IRRADIATION

3. ADJUVANT CHEMOTHERAPY (Folfox, Folfori, Xelox).  *Pre-operative or post-operative*

4. TARGET THERAPY (BIVACIZUMAB, CITUZUMAB, PANITUMUMAB)
Surgery

Accra, Ghana

- Rt Colon 97.2% (104/107)
- Left colon 84.5% (71/84)

USA

- Colon resections 91.6%
- Rectum 29.8% (50/168)

- Colon resections 90–92%
- Rectum 84%
Outcomes for colorectal cancer treatment are better in centres with higher caseload and specialisation.
Principles of standard surgery of the colon and rectum in cancer

Abdominal Exploration

We currently rely greatly on pre-operative staging techniques in cancers of the large bowel, employing ultrasonography, CT Scan, MRI etc.

But the standard still remains a thorough intra-operative exploration for metastatic and locally advanced primary and LN disease
A thorough examination includes inspection and palpation of the liver, peritoneal surface, omentum, retroperitoneum, and ovaries, if present.

Primary tumour is assessed for local adherence.

Palpation of periaortic, celiac, and portohepatic LN, when possible, is important for documentation.

The details of the exploration should be part of the surgical nodes.
• Resections should be categorised as follows
  a. R0 – all gross disease resected *en bloc* with margins histologically free of disease
  b. R1 – all gross disease resected by en bloc resection with margins positive for disease
  c. R2 – residual gross disease remains unresected

Patients who do not have histological assessment of radial tumour margins or who had R1 or R2 resection are considered to have incomplete resection for cure, ie, **Palliative**
Colon resections

Standard resections of the colon have been described as:

- Rt Hemicolecetomy (based on the rt colic Artery)
- Lt Hemicolecetomy (based on the Lt colic Artery)
- Transverse colectomy (based on the middle colic Artery)
- Sigmoid (pelvic) colectomy (based on the Artery to the sigmoid)
Ideal Bowel Resection and Margins

a. The ideal extent of a bowel resection is defined by removing the lymphovascular pedicle at the level of the origin of the primary feeding vessel.

b. When the primary tumour is equidistant from two feeding vessels, both vessels should be excised at their origin.

c. Ideally, the IMA should be excised at its origin, but this is currently not mandated by available supportive evidence.
Lymphadenectomy – this has both prognostic and therapeutic implications

1. This should extend to the origin of the primary feeding vessel.

2. In all cases for cure, the lymph node resection should be radical and should be removed *en-bloc*

3. Apical lymph node (at the origin of the primary feeding vessel) should be removed and tagged for pathological evaluation

4. Lymph nodes suspected of tumour but lie outside the field of resection should be sampled or biopsied
Lymphadenectomy results:

1. At least 15 lymph notes should be examined.
2. If biopsy results of suspicious lymph nodes are positive for disease and the LN are resected with the apical LN – resection is R0.
3. If biopsy results of suspicious LN are negative for disease and the positive apical LN is resected – resection is R0.
4. If biopsy results of suspicious LN are positive for disease or are clinically involved and the LN are not resected with the apical node – resection is incomplete = R2.
Surgical resection of the Rectum

Standard resections are:

a. ARR
b. Low ARR
c. Ultra low ARR
d. APRR
e. Local excision
Hemicorporectomy or translumbar amputation has been described as the most revolutionary of all operative procedures. Frederick E. Kredel, who first voiced the concept of the operation in 1950, referred to it as halfectomy.

Kredel envisioned hemicorporectomy as a curative operation for locally advanced cancer, limited to the pelvis, not encompassable by standard operative intervention. Additional indications are intractable decubitus ulcers with malignant change, particularly in paraplegics; pelvic organs, and bone infection with nonhealing fistulae; and crushing trauma to the pelvis.

The first hemicorporectomy operation was reported in 1960. Thirty-four operations have been recorded in the world literature. Two heretofore unreported cases are added, raising the total to 36. Review of these 36 cases confirms the conviction that hemicorporectomy is a humane and ethical alternative to the suffering encumbered by advancing, painful, malodorous malignant disease not treatable by conventional means.
Rectal resection as was described originally by Ernest Miles in 1907 was a mutilating procedure that entailed resection of a cylinder of central pelvic structures together with the anus.

Joseph Goliger affirmed this by commenting “that if the patient was not rendered impotent by the surgery then probably he is not cured of his rectal cancer”.

Today rectal surgery for cancer is not so. Sphincter saving procedures are frequently possible and erectile function can usually be maintained.
Fig. 3. Our concept of the field of spread.

Fig. 4. The fascial layers of the pelvis (after Stelzner).
In each case of rectal resection we are to balance the benefit of an extra chance of cure against the functional and anatomic price to be paid by the patient.

This implies that pre-operative assessment should supplement full clinical and endoscopic appraisal with a CT scan of the whole body for metastasis and a specialised MRI scan for appraisal of primary tumour within the pelvis.
Principles

1. **Length of rectum to resect** – There is currently no data to indicate that the length of bowel resected has an effect on local control and 5-year survival. **Resections here are influenced by available blood supply after appropriate vascular ligation and mesorectal excision**

After obtaining a 5cm proximal and 2cm distal margin there is no advantage in resecting additional rectum. **Emphasis here is to achieve an R0 resection**
2. **Distal and Proximal Bowel Margins** – The minimum distal edge is 2cm.

This length is measured in the fresh, anatomically restored ex vivo condition or in a formalinized, fixed specimen with the use of a correction factor of 12%.

**Distal intramural spread of tumour is rare and is found beyond 1 cm in 4% – 10% of rectal cancers. If it is found beyond 1.5 cm the tumour is usually poorly differentiated.**

Survival and local recurrence have been shown to be acceptable with at least 2 cm distal bowel margin.
It is currently accepted that:

1. Distal intramural spread beyond 1 cm occurs rarely

2. Distal spread beyond 1 cm is associated with tumours of advanced stage or histologically aggressive disease

3. The associated poor prognosis is not improved by a longer distal margin
3. Level of Proximal Lymphovascular Ligation for rectal Cancer

The appropriate proximal lymphatic resection for rectal cancer is provided by the removal of blood supply and lymphatics up to the level of origin of the primary feeding vessel i.e. the origin of superior rectal artery. There is a lack of evidence about the benefit of ligating the IMA at its origin. A more accurate staging may be obtained from high ligation of the IMA, but overall survival is not affected.
4. Mesorectal Excision

The mesorectum is defined as the lymphovascular, fatty and neural tissue that is circumferentially adherent to the rectum, starting at the level of the sacral promontory. It tapers and then diminishes just below Waldeyer’s fascia (the investing fascia of the levators) around the levator ani muscles at the level of the distal third of the rectum.

Its embryonic origins are the posterior mesentery (posteriorly all through) and anterior (anterior distal third of rectum) mesentery of the primitive distal hind gut.
Mesorectal spread can occur by direct tumour extension, as lymph node, perineural, or isolated mesenteric deposits.

Heald RJ 1998, demonstrated that mesorectal spread of cancer can go as far as 3 cm distal to the inferior border of the tumour. Therefore mesorectal excision should be at least 4cm from the inferior border of the tumour.

Mesorectal spread is an important indicator of disease severity, and surgical clearance of the mesorectum is an important technical variable.

There is greater local failure rates associated with lateral resection margins that are positive for disease.
5. **Extended Lateral Pelvic Lymph Node Dissection**

a. Evidence is insufficient to recommend an extended lateral lymphatic dissection for rectal cancer in a patient without lymph nodes that are clinically suspicious of disease.

b. If there are suspicious nodes, the dissection should attempt to remove these nodes.

c. A biopsy of suspicious LN that are beyond the surgical field of resection needs to be done for staging purposes.
**En Bloc Resection of Adherent Tumour**

CRC that are adherent to local structures are encountered in about 15% of these cancers. Structures that are frequently involved include uterus, adnexae, posterior vaginal wall, and urinary bladder.

En bloc resection is the ideal surgical method to manage these local extensions of rectal cancer.
Chemotherapy

This is given as adjuvant (when R0 resection has been done) or else palliative (when R1 or R2 resection has been done)

Combination chemotherapy regimens currently in use include:

a. 5-Florouracil and Leucovorin
b. 5-Florouracil/ Leucovorin and Oxaloplatin (FOLFOX)
c. 5-Florouracil/ leucovorin and Irinotican (FOLFIRI)
d. Capecitabine and Oxaloplatin (XELOX)

When Bevacizumab is added to these regimens progression Free survival is significantly improved in advanced CRC
Radiotherapy in rectal cancer.
Local recurrence is 15-45% without radiotherapy.
The purpose is to improve local control of the tumour.
It does not, in itself, impact on overall survival.
It does not downstage the tumour, it downsizes it.
Usually the long course chemotherapy is employed.
That is 50 Gy is delivered in about 180 cGy in 5 daily doses per week for 5 weeks.
There are two published data on short course radiotherapy by the Swedish group and the UK group, in which 25 Gy was given in a week. The outcomes were good.
Molecular (Target) therapy

Advances in molecular and cancer biology have led to the identification of a number of abnormal pathways in cancer cells that represent potential targets for anticancer drug development.

Two of these strategies include inhibitors of the epidermal growth factor receptor (EGFR) and angiogenesis inhibitors.

Before Cituzimab or Panutumumab can be used, K-ras mutation must be excluded.
Hepatic Resection

The liver is often the first site of metastatic disease and may be the only site of spread in as many as 30–40% of patients with advanced disease.

It has been postulated that because haematogenous spread usually occurs in a stepwise fashion, initially to the liver, with subsequent intrahepatic spread via the portal vein and further spread to the systemic circulation, surgical resection of isolated hepatic metastases from colorectal cancer may be curative.
Chemotherapy and hepatic resection

A small proportion of patients with completely resectable hepatic as well as extrahepatic metastatic disease may become long-term survivors.

Chemotherapy in combination with hepatic resection may prolong the time to recurrence after resection of hepatic metastasis.

Chemotherapy, the irinotican-based one may downsize to resectability previously judged inoperable hepatic metastasis.
Five year survival rates after hepatic resection

R0 resection has about 32%
R1 resection has about 7.2%
No resection has 0%
FOLLOW UP

• Three monthly in first year
• Six monthly for a year or two
• Bi-annually there after

For each visit at least CEA and abdominal ultrasound is done

Annual colonoscopy

If at any visit the CEA rises a complete diagnostic work-up must be done
Chemoprevention

• It is the attempt to use natural and synthetic compounds to intervene in the process of oncogenesis and early stages of cancer development.

• They prevent or block genetic mutations leading to cancer, or prevent or stop biological process leading to extensive cell division
• Dietary factor can prevent 75% of Colorectal cancer

• Selective inhibitors of prostaglandin synthesis and apoptosis inducers, eg., NSAIDS, Isothiocyanates (Sulforaphane), Selective COX 2 inhibitor, calcium etc are candidates for chemoprevention
• Dietary factor can prevent 75% of Colorectal cancer
• Selective inhibitors of prostaglandin synthesis and apoptosis inducers, eg., NSAIDS, Isothiocyanates (Sulforaphane), Selective COX 2 inhibitor, calcium etc are candidates for chemoprevention
Thank You