Colorectal Cancer

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Introduction

• Rooms at HSS and Westmead Private
• Outpatients at Westmead
• Multidisciplinary clinic Westmead

• Surgery and scopes
  – HSS
  – Westmead Public, Private and Children’s
  – Mt Druitt
Plan

• General overview

• Case presentations
  – New techniques
  – Non operative management
Incidence of Colorectal Cancer

- 2nd most common cause of cancer in both men and women
- 14860 new cases in 2010 in Australia
- 19960 predicted in 2020
- 3999 patients died from CRC in 2011
- 9.3% of all cancer deaths
- Highest rates in Australia and New Zealand
- By age 85, 1:10 men and 1:15 women
Survival rates for Colorectal Cancer

- Overall 5 yr survival 66%
- Stage I 93%
- Stage II 82%
- Stage III 59%
- Stage IV 8%
Improved cancer survival
Why?

- Screening
- Chemotherapy
- Radiotherapy
- Treatment of metastases

- MDT

- Surgery
Screening tools

- Faecal Occult Blood test (FOBT)
- Colonoscopy

- Flexible sigmoidoscopy

- CT colonography (expensive, non-therapeutic, poor pick up for small lesions, useful if colonoscopy is incomplete)

- *Not CEA*
Current status for screening

• FOBT is the standard tool for screening for colorectal cancer
• Shown to reduce the mortality from CRC 23%
• Recommended for over 50 years
• Cancer Council guidelines recommend performing FOBT every 2 years
• National bowel screening program every 5 years
• From 2017-2020, screening will be extended every 2 years from 50 to 75 years

Why start screening at 50?

Table 3.1 Absolute risk of Colorectal Cancer

<table>
<thead>
<tr>
<th>If a person is aged</th>
<th>Risk over the next 5 years</th>
<th>10 years</th>
<th>15 years</th>
<th>20 years</th>
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<tbody>
<tr>
<td>30</td>
<td>1 in 7000</td>
<td>1 in 2000</td>
<td>1 in 700</td>
<td>1 in 350</td>
</tr>
<tr>
<td>40</td>
<td>1 in 1200</td>
<td>1 in 400</td>
<td>1 in 200</td>
<td>1 in 90</td>
</tr>
<tr>
<td>50</td>
<td>1 in 300</td>
<td>1 in 100</td>
<td>1 in 50</td>
<td>1 in 30</td>
</tr>
<tr>
<td>60</td>
<td>1 in 100</td>
<td>1 in 50</td>
<td>1 in 30</td>
<td>1 in 20</td>
</tr>
<tr>
<td>70</td>
<td>1 in 65</td>
<td>1 in 30</td>
<td>1 in 20</td>
<td>1 in 15</td>
</tr>
<tr>
<td>80</td>
<td>1 in 50</td>
<td>1 in 25</td>
<td></td>
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</tr>
</tbody>
</table>

Note: Absolute risk is the observed or calculated likelihood of the occurrence of an event in a population under study (cf. relative risk, which is the ratio of the risk in a particular exposed group to the average risk in the population; see Table 6.1).

Source: AIHW 1996.
Practical points

• What does a positive FOBT mean?
  – \( \frac{1}{3} \) picking up a adenoma
  – \( \frac{1}{10} \) picking up an advanced adenoma (Tubulovillous polyps or tubular polyp>10mm or dysplasia)
  – \( 1 \) -\( 3 \) in 100 of picking up a cancer
  – \( \frac{1}{2} \) normal colonoscopy

<table>
<thead>
<tr>
<th>Normal</th>
<th>Small polyp</th>
<th>Advanced polyp</th>
<th>Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>33%</td>
<td>10%</td>
<td>1-3%</td>
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</table>
Management of Colorectal cancer

• Surgery is the best option for cure
• Aim of surgery is to perform a complete clearance of the tumour and draining lymph nodes (R zero)

• Rectal cancers are different
• Rectal cancers have higher tendency for local invasion
  – Tumour is found within a contained limited pelvic space
  – Closely associated with other pelvic organs such as vagina, prostate, sacrum iliac vessels and bladder
  – Different lymphatic drainage (non portal)
Treatment

Colon Cancer
• Surgery
  – Laparoscopic
  – Open
• Chemotherapy
  – Some T3
  – N+

Rectal Cancer
• Preop ChemoRTx
  – T3
  – N+
• Surgery
  – Laparoscopic
  – Open
  – Transanal
• Chemotherapy
  – Some T3
  – N+
  – Post Radiotherapy
Neoadjuvant Treatment

- Radiotherapy and chemotherapy
- Now standard for T3/T4 and N+ve disease
- RCTs showing both survival and LR benefit

• Swedish Rectal Cancer Trial
  NEJM 1997;336:980-987

<table>
<thead>
<tr>
<th></th>
<th>RT+</th>
<th>RT-</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>11%</td>
<td>27%</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>5 year survival</td>
<td>58%</td>
<td>48%</td>
<td>P=0.004</td>
</tr>
</tbody>
</table>
Radiotherapy

• Improves survival and local recurrence in T3+ rectal cancers
• Short (1 week) vs Long course (6 weeks)
• Sensitizing dose of chemo

• Improving
  – New techniques

• Side effects
Chemotherapy

- Usually 5-FU and oxaliplatin based
- Newer drugs are added if there is progression of disease
- Newer drugs = more side effects
- Gene targeted chemotherapy
- Immunotherapy

Common
- Cepcitabine (Xeloda) (oral)
- 5FU and Oxaliplatin (Folfox)
- Bevacizumab (Avastin)
Rectal cancer

• Different treatment options (RTx)
• More complicated surgery
• More recurrence (locally)

• How low is too low?

• ANTERIOR RESECTION
Rectal resection

- anterior resection
- ultra-low anterior resection
- abdominoperineal (AP) resection
OPERATIVE OPTIONS

- Open surgery
- Laparoscopic surgery
  - Multi vs single port vs hand assisted
- Robotic surgery
- NOSE
- NOTES
- Local resection
  - EMR ESD
  - Transanal excision
  - TEMS
- Dissection technique
- Anastomosis
- Stoma
- Intersphincteric resection
Total Mesorectal excision

• Reduced local recurrence rates from up to 30% to as low as 3%
• Norwegian Rectal Cancer Group
  – LR 28 to 8% with TME
  – 5YSR 55 to 71%  Wibe et al Colorectal Disease 2003;5:471-7

• Surgical technique
• Specialists vs Generalists (RR 0.3-0.8)

• Most early trials of RTx did not use TME and so had high LR rates
Staplers

• Allow faster operations
• As good as sutures
• Allows low rectal anastomosis

• Improvements in technology
• Still get leaks!
Open Vs Laparoscopic

• No oncologic difference
• No survival difference
• No local recurrence difference

• Laparoscopic has shorter time in hospital and quicker return to activities
• Laparoscopic equipment more expensive
Robotic Surgery

• Da Vinci robot
• Remote controlled with scrub nurse and surgical assistant with patient
• 3D view
• Improved view of pelvic structures
• 360 degree ROM
• Ergonomic improvement for surgeon
• BUT no haptic feedback
• ?improvement for patient
• Expensive
How low can we go?
How to get to lower third?

- Open surgery: St Mark’s retractor
- Laparoscopic surgery
- Robotic surgery
- New techniques?

- How to staple below cancer?
- Handsewn vs stapled anastomosis
Anastomosis

• Low anastomosis associated with poorer function (anterior resection syndrome)
• Anal instrumentation can damage sphincters
• Double stapled gives “best” results
• Not always able to easily staple below tumour

• MARGIN
APR vs Ultralow anterior resection

• Tumour Factors
  – Level
    • Need at least 2cm fresh
    • 1cm fixed
  – Sphincter involvement
  – Size
  – Response to radiotherapy

• Patient factors
  – Male vs Female
  – BMI
  – Buttock size
  – Preop continence
  – Patient wishes
Intersphincteric Resection

- Transanal dissection and removal of part or all of the INTERNAL sphincter
- External sphincter preserved
- Handsewn coloanal anastomosis
- Risk of incontinence and poor bowel function
- Higher risk of local recurrence due to closer margins
- Preop staging important
Transanal TME

- Direct view of cancer
- Pursestring suture below cancer guarantees margin
- Same TME plane
- Rectum more accessible than via pelvis
- Avoids robot
- Hand sewn or stapled anastomosis
GelPOINT Path Transanal Access Platform
Downsides of TAMIS

- Sphincter dilatation and possible damage
- Technically difficult
  - Different plane of dissection
  - Instrumentation
- Only for very low cancers
- Difficult if very large tumour
Case 1

- 49yo male
- Rectal bleeding and altered bowel habit
- At colonoscopy mobile cancer at 2cm above dentate line
- MRI and US stage T2N0
- No sphincter involvement
Discussion

- Abdominoperineal vs.
- Best chance of distal clearance
- Permanent stoma
- Laparoscopic vs. open
- Perineal wound
- Anterior resection
- Temporary ileostomy
- Risk of distal involvement requiring APR
- Lap vs. open
- Ileostomy closure
- BOWEL FUNCTION
- CONTINENCE
Operation

• Laparoscopic assisted ultralow anterior resection with loop ileostomy
• Completed with Pfannensteil incision
• Intersphincteric dissection at level of dentate line ie 2cm clearance
• Handsewn coloanal anastomosis

• Good recovery
Pathology

• pT1N0 cancer
• Mod diff, no venous or lymphatic invasion
• R0
• Margin 0.5cm

• Patient happy!
• No adjuvant therapy
Follow up

• Loop ileostomy closed at 8 weeks

• Initial frequency and urgency settled
• Now BM 2x a day. Up to 1x at night
• No flatus or faecal incontinence

• Yearly colonoscopy and CT to 5 years
• Patient very very happy!
Case Study 2

• 77 Female
• No co-morbidities
• Previous cholecystectomy and hysterectomy
• T3N0 locally invasive cancer at 3cm

• Preoperative chemoradiotherapy
• Good downstaging
Surgery

- Laparoscopic mobilisation of left colon and rectum to lower 1/3 level.
- IMA ligated
- Pursestring suture 2cm below cancer
- Full thickness incision in rectum to enter presacral space using Gelport device
Surgery

- Dissection planes from below joined with laparoscopic dissection
- Specimen extracted per anus
- Resection and anvil placed in colon
- Pursestring over drain at anorectal junction
Surgery

- Ischaemic colon noted on relaparoscopy requiring further resection (removed via ileostomy site)
- Single stapled anastomosis completed laparoscopically
- Loop ileostomy
- Good recovery
- Discharge day 7
Follow up

• Path: T3N0R0

• Ileostomy and chemo complications

• Ileostomy closed 3 months

• 2 years post ileostomy closure doing well with good bowel function
Not operating at all!

• Up to 15-30% of patients with rectal cancer will have a COMPLETE clinical and pathological response with chemoradiotherapy

• Some groups are now adopting a wait and see approach to these and operating if there is recurrence


• 5YSR 96% 5yDFS 72% (Habr-Gama Sao Paulo)
Complete Response CR

• After chemoradiation and time
• 15-20%
• Increasing with better and more treatment
• Best survival group post surgery

• No ulcer/mass/stenosis
• Normal biopsy
• Normal MRI
Watch and Wait

- Similar to Nigro Rx for anal SCC
- Stoma avoidance
- “Anterior resection syndrome”
- Local recurrence
- Systemic recurrence
- Quality vs quantity of life
- Colostomy free survival
Anterior Resection Syndrome

• Low capacity of neorectum and low anastomosis
• Complications of anastomosis

• Frequency
• Urgency
• Continence
• Tenesmus
• QoL
Issues with CR

• Clinical vs radiological vs pathological CR
• How to assess?
• How often?
• Is a recurrence after watch and wait worse?
• Lower stage (<T3) tumours?
• Does it change the operation?
• No RCT (ethically unable to randomise)
• Stoma free survival vs disease free survival
So what if it recurs after CR?

- Renehan et al Lancet Oncology May 2016
  - 129 watch and wait
  - 44/129 local regrowths (34%)
  - 36/41 “salvaged” (88%)
    - 31/41 surgery (30/31 R0 resection)
    - 5/41 local radiotherapy
  - Compared to resectional surgery at 3y
    - Disease free survival 88 vs 78% NS
    - Overall survival 96 vs 85% NS
    - Colostomy free survival 74 vs 47% p<0.0001
Benefit of watch and wait after CR

- Preserve rectum
- Avoid stoma
- About 1/3 will recur at 24 months
- Can reoperate if recur without necessarily affecting survival
<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of centers</th>
<th>No. of patients</th>
<th>Radiologic staging tools</th>
<th>T2</th>
<th>N+, %</th>
<th>Chemotherapy</th>
<th>Radiation dose, Gy</th>
<th>Adjuvant chemotherapy</th>
<th>cCR</th>
<th>Methods of defining cCR</th>
<th>Restaging time, wk</th>
<th>Follow-up, mo</th>
<th>Recurrence</th>
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<tbody>
<tr>
<td>Habr-Gama et al7</td>
<td>2</td>
<td>118</td>
<td>CT + EUS (when available)</td>
<td>T2N0, 19.5%</td>
<td>45</td>
<td>5-FU + LV</td>
<td>50.4</td>
<td>No</td>
<td>30.5%</td>
<td>DRE + proctoscopy + biopsy</td>
<td>6–8</td>
<td>36</td>
<td>27.0%</td>
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<tr>
<td>Rossi et al13</td>
<td>1</td>
<td>16</td>
<td>CT</td>
<td>NS NS</td>
<td>2 cycles 5-FU + LV</td>
<td>50.4 + 30.0 (brachytherapy)</td>
<td>No</td>
<td>6/16, 38%</td>
<td>DRE + proctoscopy + biopsy</td>
<td>10</td>
<td>238</td>
<td>5/6 (83.0%)</td>
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<tr>
<td>Nakagawa et al19</td>
<td>1</td>
<td>52</td>
<td>CT</td>
<td>No NS</td>
<td>2 cycles 5-FU + LV</td>
<td>45.0–50.4</td>
<td>No</td>
<td>19%</td>
<td>Proctoscopy + biopsy</td>
<td>3–4</td>
<td>321</td>
<td>NS fully</td>
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<tr>
<td>Habr-Gama et al8</td>
<td>2</td>
<td>265</td>
<td>CT + EUS</td>
<td>19.7%</td>
<td>22.5</td>
<td>5-FU + LV</td>
<td>50.4</td>
<td>No</td>
<td>26.8%</td>
<td>DRE + proctoscopy + biopsy + EUS (when available)</td>
<td>8</td>
<td>573</td>
<td>5/71 (7.0%)</td>
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<tr>
<td>Habr-Gama et al9</td>
<td>2</td>
<td>361</td>
<td>CT + EUS (when available)</td>
<td>14%</td>
<td>27.8</td>
<td>5-FU + LV</td>
<td>50.4</td>
<td>No</td>
<td>27.4%</td>
<td>CT + EUS (when available) + proctoscopy + excisional biopsy (some cases)</td>
<td>8</td>
<td>60</td>
<td>5/99 (5.0%)</td>
</tr>
<tr>
<td>Lim et al13</td>
<td>6</td>
<td>48</td>
<td>EUS (36%) or CT (60%) or MRI (4%)</td>
<td>T1(6%) and T2 (27%)</td>
<td>NS</td>
<td>2 cycles 5-FU (75%)</td>
<td>25–61 (median, 50)</td>
<td>No</td>
<td>56%</td>
<td>Proctoscopy</td>
<td>4–6</td>
<td>49</td>
<td>18/48 (37.5%)</td>
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<td>Hughes et al15</td>
<td>1</td>
<td>58</td>
<td>CT and EUS or MRI (5.5%)</td>
<td>No NS</td>
<td>Variable 5-FU (82%)</td>
<td>Capcitabine (8%)</td>
<td>Irinotecan/oxaliplatin (9%)</td>
<td>No</td>
<td>17%</td>
<td>Proctoscopy + CT or EUS or MRI (55%)</td>
<td>6–8</td>
<td>Not clear</td>
<td>60.0% local</td>
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<tr>
<td>Yu et al18</td>
<td>Multi-center</td>
<td>22</td>
<td>CT and MRI</td>
<td>NA NA</td>
<td>NA</td>
<td>Capcitabine</td>
<td>50.4–54.0</td>
<td>Adjuvant in some</td>
<td>Did not all achieve cCR</td>
<td>CT + MRI + proctoscopy</td>
<td>4</td>
<td>NA</td>
<td>41.0%</td>
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<tr>
<td>Meas et al11</td>
<td>1</td>
<td>21</td>
<td>MRI</td>
<td>24% T2N0 (1)</td>
<td>71.4</td>
<td>Capcitabine</td>
<td>Minimum 50.4</td>
<td>Adjuvant in some XELOX routinely</td>
<td>No</td>
<td>CT + MRI + proctoscopy</td>
<td>6–8</td>
<td>25</td>
<td>1/21 local (5.0%)</td>
</tr>
<tr>
<td>Dalton et al17</td>
<td>1</td>
<td>49</td>
<td>MRI</td>
<td>8.1%</td>
<td>75.5</td>
<td>Capcitabine</td>
<td>45</td>
<td>53% adjuvant chemotherapy</td>
<td>No</td>
<td>MRI + proctoscopy</td>
<td>6–8</td>
<td>26</td>
<td>6/12 (50.0%)</td>
</tr>
<tr>
<td>Smith et al18</td>
<td>1</td>
<td>32</td>
<td>EUS + CT</td>
<td>NS NS</td>
<td>5-FU or capcitabine</td>
<td>45–56</td>
<td>53% adjuvant chemotherapy</td>
<td>No</td>
<td>Variable DRE + proctoscopy</td>
<td>4–10'</td>
<td>17</td>
<td>3/32 local</td>
<td></td>
</tr>
</tbody>
</table>
Case 3 (August 2015)

- 62 yo male
- 1 year history of bleeding, urgency, tenesmus, frequency
- No urinary symptoms
- No weight loss

- PR obvious cancer at anal canal
- Palpable inguinal lymphadenopathy
Colonoscopy

• Semi circumferential cancer just at dentate line
• Otherwise normal

• Biopsy = adenocarcinoma

• CEA 120

• FNA Inguinal LN positive
Imaging

**CT**
- Locally invasive cancer
- Mesorectal, paraaortic, pelvic and inguinal lymphadenopathy
- No metastases in lungs or liver

**MRI**
- T4bN2
- Tumour extending into anal canal
- Beyond m.propria
- Involving mesorectal fascia
- Likely prostate involvement
- Mesorectal LN, lumbosacral LN, External iliac LN, Inguinal LN
Multidisciplinary meeting and clinic

- Likely incurable
- Long course chemoradiation started September 2015
- Only surgical option = abdominoperineal resection, cystoprostatectomy, bilateral inguinal, iliac and aortic lymphadenectomy
Restage December 2015

- Tolerated treatment well
- Symptoms improving
- Inguinal nodes no longer palpable
- Rectal tumour still present but much smaller

- 6 weeks of treatment then restaged after further 10 weeks
Re Staging

**PET**
- Primary tumour only seen
- Moderately hypermetabolic (SUV 6.7)
- No uptake in LN at all
- Tiny lung nodule? Significance

**MRI**
- Good tumour response with >75% fibrosis
- No LN enlargement
- Separate from prostate
- No longer involving levator and anal canal
- Restage T3aN0
MDT

- Patient very concerned
- Wanting operation (my bias)

Options:
- Radical surgery based on original findings
- APR based on post therapy findings
- Continued chemotherapy only
- Simple observation
Progress

• Full dose chemotherapy
• Cepcitabine, Oxaliplatin and Bevacizumab (Xelox and Avastin)

• Restage after 3 months
  – CT: no mets
  – PET: small focus uptake in rectum, no LN
  – MRI: “100% or near 100% fibrosis in rectum”
Progress

• No signs of cancer at colonoscopy April 2016
• Multiple biopsies all negative

• Symptom free
• Continuing with reduced dose Xelox and Avastin
• Plan to continue with maintenance dose indefinitely (palliative protocol)
• CEA 2.0

• Patient working still but planning retirement and holiday
Summary

• Surgical principles constant
• Surgical technology improving
• Adjuvant treatment improving
• Perioperative management improving

• Patients surviving longer
Future

• Improved adjuvant therapy
  – Newer chemo agents
  – Better radiotherapy
  – Immunotherapy

• Improved imaging (follow up)
• Use of biomarkers/genetics

• More minor salvage surgery
• Use chemoRTx in earlier stage cancers

• May eventually make surgery the rarer option
Multidisciplinary Team

• Weekly meeting
  – Fridays 8am
  – ICPMR meeting room

• Fortnightly clinic
  – Wednesdays 9-12am
  – Cancer centre

• Colorectal Surgeon
• Liver Surgeon
• Gynae Oncologist
• Medical Oncologist
• Radiation Oncologist
• Palliative Physician
• Geneticist
• Pathologist
• Stoma Nurse
• Oncology Nurse
Questions?

Thank you for your attention