Obesity in Gynaecology

The new Tsunami

Lewis Perrin
Obesity

• BMI increasing
• Associated malignancy rates
• Difficulty with treatment
• Approaches & opportunities to minimize risk
Obesity & Complications

- 68% of Australian women over 50 are overweight or obese
- 15-30% of cancer deaths in the US are attributed to obesity
- A major predictor of peri-operative morbidity
- A major predictor of reduced cancer specific survival across many tumour types
- Identified as a carcinogen
- Weight loss and lifestyle intervention studies will be extremely important over the next 10 years
BMI increasing

Persons aged 18 years & over - Proportion who were obese(a), 1995 to 2011-12

Source(s): Australian Health Survey: Updated Results, 2011-12
Global burden of cancer attributable to high body-mass index in 2012: a population-based study

Arnold et al. Lancet Oncol. 2015

• 3.6% of all new cancers attributed to obesity world wide
• 5.3% in high human index countries
• 64% of cancers were endometrial, post-menopausal breast & colon
**5kg/m² rise of BMI & Cancer Risk**

Renehan et al Nat.Rev Cancer 15 2015

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Summary risk estimate (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Endometrial</td>
<td>1.59 (1.50-1.68)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1.09 (1.00-1.12)</td>
</tr>
<tr>
<td>Postmenopausal Breast</td>
<td>1.12 (1.08-1.16)</td>
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Sex Hormone Hypothesis

• Conversion of androgenic precursors to oestradiol through increased aromatase activity peripheral adipose tissue

• Oestradiol increases endometrial cell proliferation and decreases apoptosis

• Oestradiol also increases IGF and IGFR

• Obesity associated with ovarian hyperandrogenism & reduced progesterone
Insulin Resistance & IGFs

- Insulin increases with BMI
- growth promoting signalling of hyperinsulinaemia
- associated reduced production of IGFBP with increased levels of free IGF
- leads to intracellular cascade of mitogenesis, anti-apoptosis and angiogenesis
Adipokines

• Leptin - mitogenic, anti-apoptotic and mediates immune suppression but epidemiological studies have been inconclusive

• Adiponectin - negative correlation with BMI, inverse correlation with levels and risk of obesity associated cancers

• Adiposity associated with chronic (subclinical) inflammation - CRP, TNF, IL
Weight loss & Biomarkers

- 10% weight loss associated with:
  - 1/3 reduction in free estradiol (E2 down & SHBG up)
  - 1/3 reduction CRP
  - Decreased TNF & IL-6 but not as marked
Impact of Obesity on Medical Treatment

- risk of underdosing chemotherapy as many as 40% of obese patients receive suboptimal dosage
- aromatase inhibitors less effective due to high circulating oestrogen
- Metformin effect on progesterone receptors inhibiting endometrial cell proliferation and aromatase expression
Impact of Obesity on Radiotherapy Treatment

- More difficult radiation dosimetry
- Increased setup errors
- Difficulty of high energy to central pelvis without overdosing peripheral tissues
Impact of Obesity on Surgical Treatment

- high risk of preoperative complications
- outcomes similar with increased weight but significant differences demonstrated when BMI approaching 40
- improved outcomes achievable with laparoscopic surgery
Surgical Considerations

- consider indication for surgery
- inform patient of risks
- Which surgical approach optimal
- Which modality of treatment optimal
Endometrial Cancer

Incidence (AUS): 2000+ new cases per annum
At QCGC: 400 patients
Stage 1A: 240 patients (60%)
  Of those with grade 1 tumours: 150 patients, 60%
These patients expect a very good prognosis
Still subjected to
  Hospital stay
  The risk of surgical adverse events
  Recovery
  Loss of fertility
Need smarter treatments

Until 2005
Serious Adverse events 15%

From 2005 to 2015
Serious Adverse events 8%

From 2015 (?) – personalize treatment
Indications

- Endometrial hyperplasia with atypia
- Stage 1A grade 1 endometrial cancer

- Young women who wish to retain fertility
- Women with co-morbidities making surgery unsafe
• Phase II Randomised 3 arm clinical trial
  • Mirena
  • Mirena + Metformin
  • Mirena + Weight loss programme
feMMe Trial

• Primary outcome measure
  • Pathological complete response
• Secondary outcome measure
  • Predict the outcome of treatment through blood & tissue molecular biomarkers
Exercise during Chemotherapy for Ovarian Cancer (ECHO) Trial

- Randomized controlled trial
- Assess exercise intervention during first line adjuvant chemotherapy for ovarian cancer
- primary objectives - physical wellbeing, function, QoL,
Exercise during Chemotherapy for Ovarian Cancer (ECHO) Trial

- chemotherapy-adverse events and adherence and progression-free survival
- Cost-effectiveness
- potential mechanistic pathways of exercise during chemotherapy
• Obesity prevention/treatment should be encouraged as part of cancer prevention
• Obese women should be regular cancer screening
• Metformin in women with NIDDM should considered for the prevention of both breast and endometrial cancers
• Surgery should be performed as in non-obese
• Chemotherapy doses calculated on actual body weight
• Aromatase inhibitors and bevacizamab may not be as effective
Lifestyle Risk Factors

- Weight
  - Aim to be a healthy weight throughout life
  - Be physically active every day

- Cancer Prevention
  - Limit red and processed meat
  - Limit foods high in calories and fat
  - Choose mostly plant foods

- Diet
- Physical Activity

Mater Education