Surgical Advances in Ovarian Cancer

MH MCCOMISKEY

BELFAST JUNE 2019

My background

- Consultant gynaecological cancer surgeon
- Team of 5 provide surgical care for all NI women

My background

- Consultant gynaecological cancer surgeon
- Team of 5 surgeons provide surgical care for all NI women
- Trained at Christie Hospital, Manchester

evolution of surgery for recurrent ovarian cancer……

Where Do We Come From?

What Are We?

Where Are We Going?

Setting the scene

- Ovarian cancer accounts for 5% of all cancer deaths in females in UK
- Approx 200 new cases of ovarian cancer in Northern Ireland every year
- Surgery can be primary (including delayed) or secondary
- Close relationship with chemotherapy

Primary cytoreduction principles

- General acceptance:
  - R0 associated with improved outcome
  - 6 cycles of platinum-based chemotherapy is optimum
- Unit to unit variation
  - Appetite for upfront surgery vs delayed primary surgery
  - Radical excisions

Where do we come from?

- 1970's - granulosa cell tumours became the most studied recurrence
- Radiotherapy common adjuvant treatment
- Varying chemo regimens and timings

- 1980's – relook laparotomy popular
- CT / USS being used to assess ovarian cysts

1990's

- Secondary debulking and its influence on survival – controversial
- Second-look surgery falling out of favour

- Cytoreduction of relapsing tumour masses seems to prolong survival
- Patients with a relapse free interval of more than 12 months

- Expectation of more selective operation strategies - new biologic indicators
- New developments in minimally invasive surgery

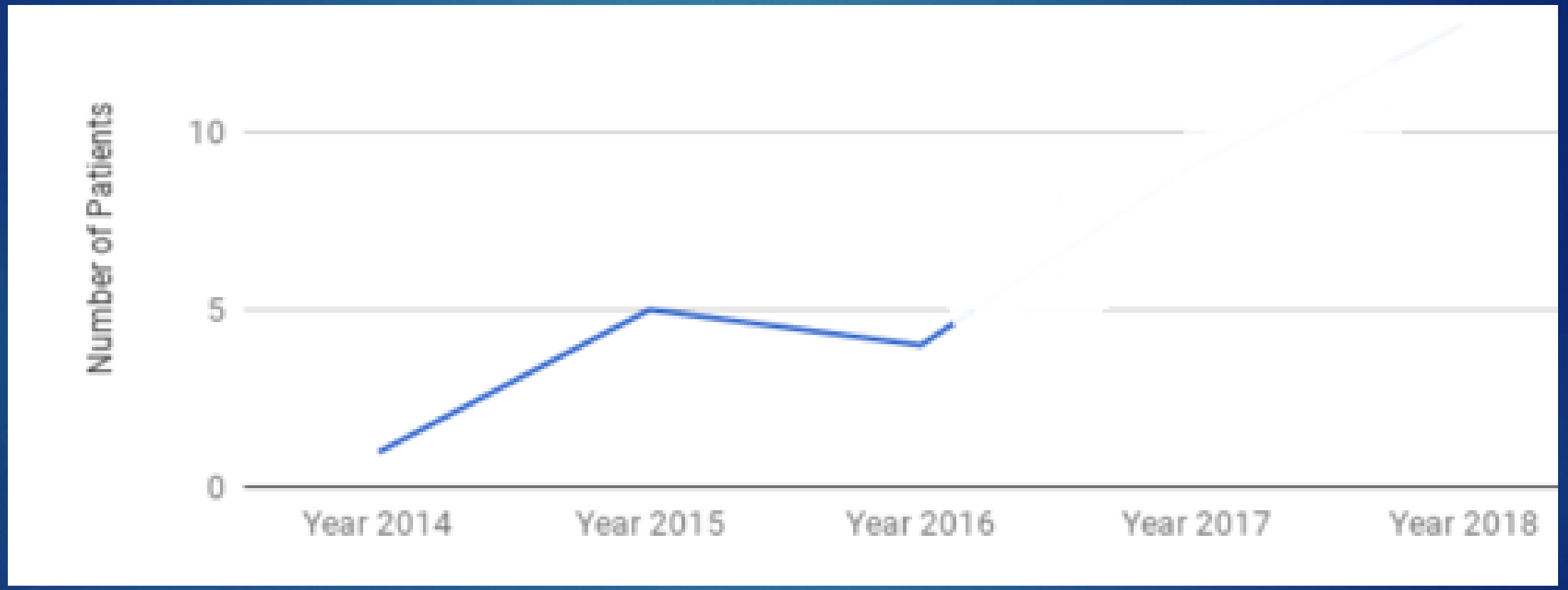
DESKTOP trials 1+2

- (Harter et al 2009, 2011)

- Helped create and validate a score to predict complete resection in recurrent ovarian cancer:

- Complete resection at first surgery
- Good performance status
- Absence of ascites

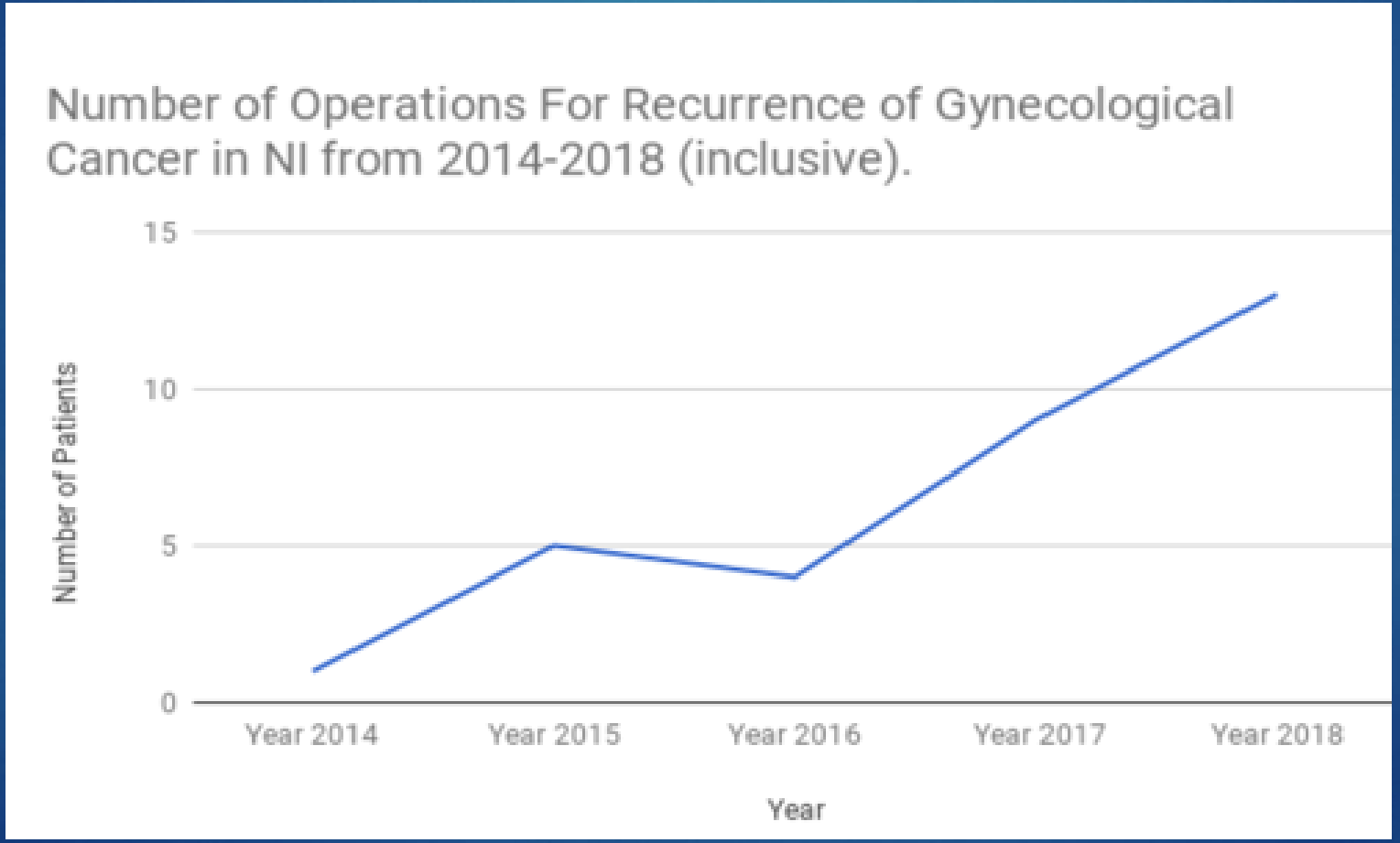
Belfast 2014 - 2016



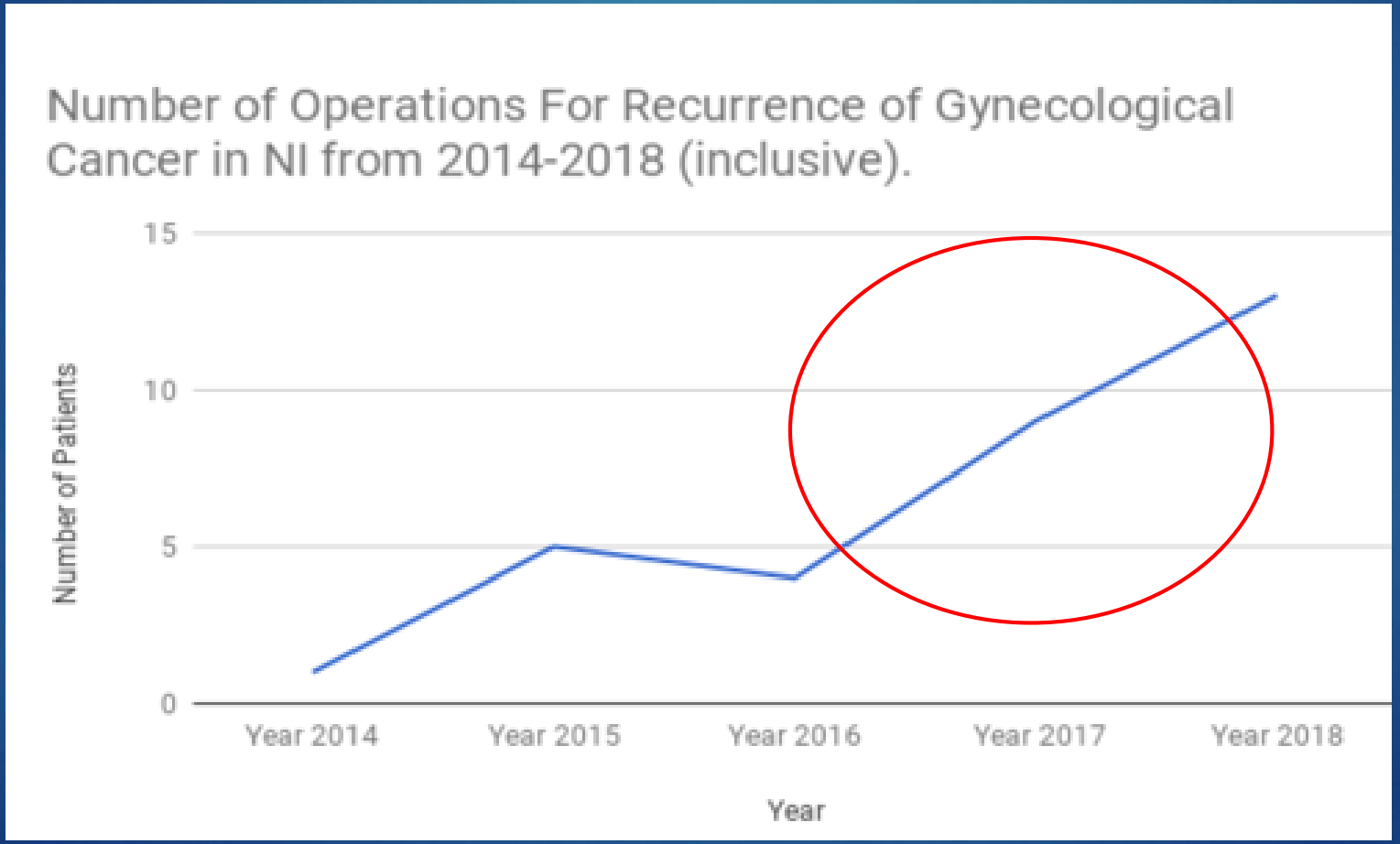
What are we?

- Growing body of evidence to support the theory that R0 resection is associated with improved disease-free survival and overall survival (Felsinger et al 2018)
- Some data suggest no improvement in overall survival (but improved progression free survival)(Coleman et al 2017)
- Evaluation carried out at regional cancer centre

Belfast past 5yrs



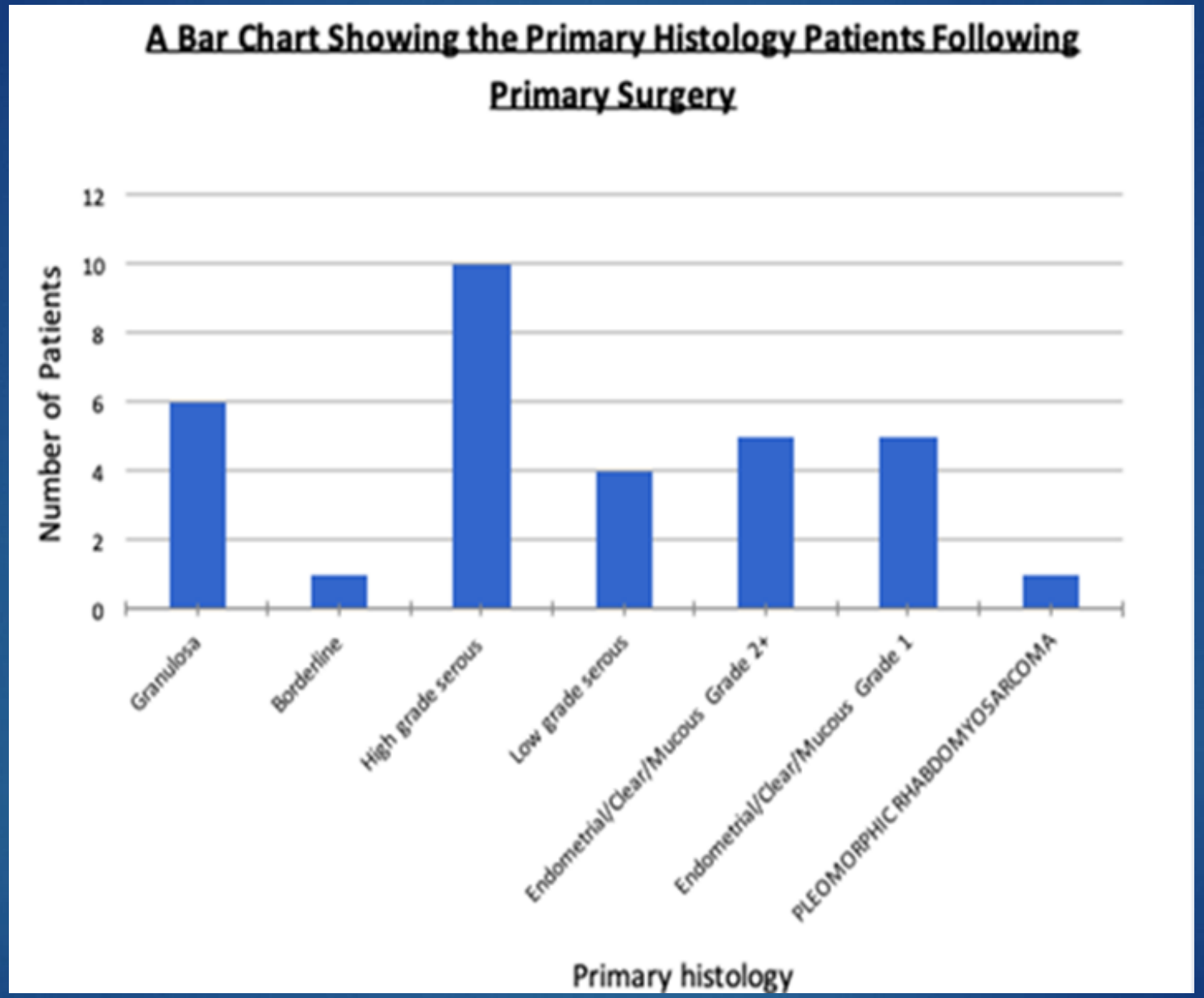
Belfast past 5yrs



Number of patients included: **32**

Mean age: **61**
Mean BMI: **30.6**

Comorbidities: **18** had one or more recorded
7 had none
7 had no information recorded
Comorbidities included; **Diabetes (2), Chronic lung diseases (7), Hypertension (2), Hyperlipidaemia (2)**


A Bar Chart Showing the Primary Histology Patients Following Primary Surgery
Number of Patients
12
10
8
6
4
2
0
Granulosa
Borderline
High grade serous
Low grade serous
Endometrial/Clear/Mucous Grade 2+
Endometrial/Clear/Mucous Grade 1
PLEOMORPHIC RHABDOMYOSARCOMA
Primary histology

Mean time from initial operation to recurrence: **51.6** months

Operation type: **30 laparotomy, 2 laparoscopic;**
(including 5 bowel resections, 2 ureteric stenting)

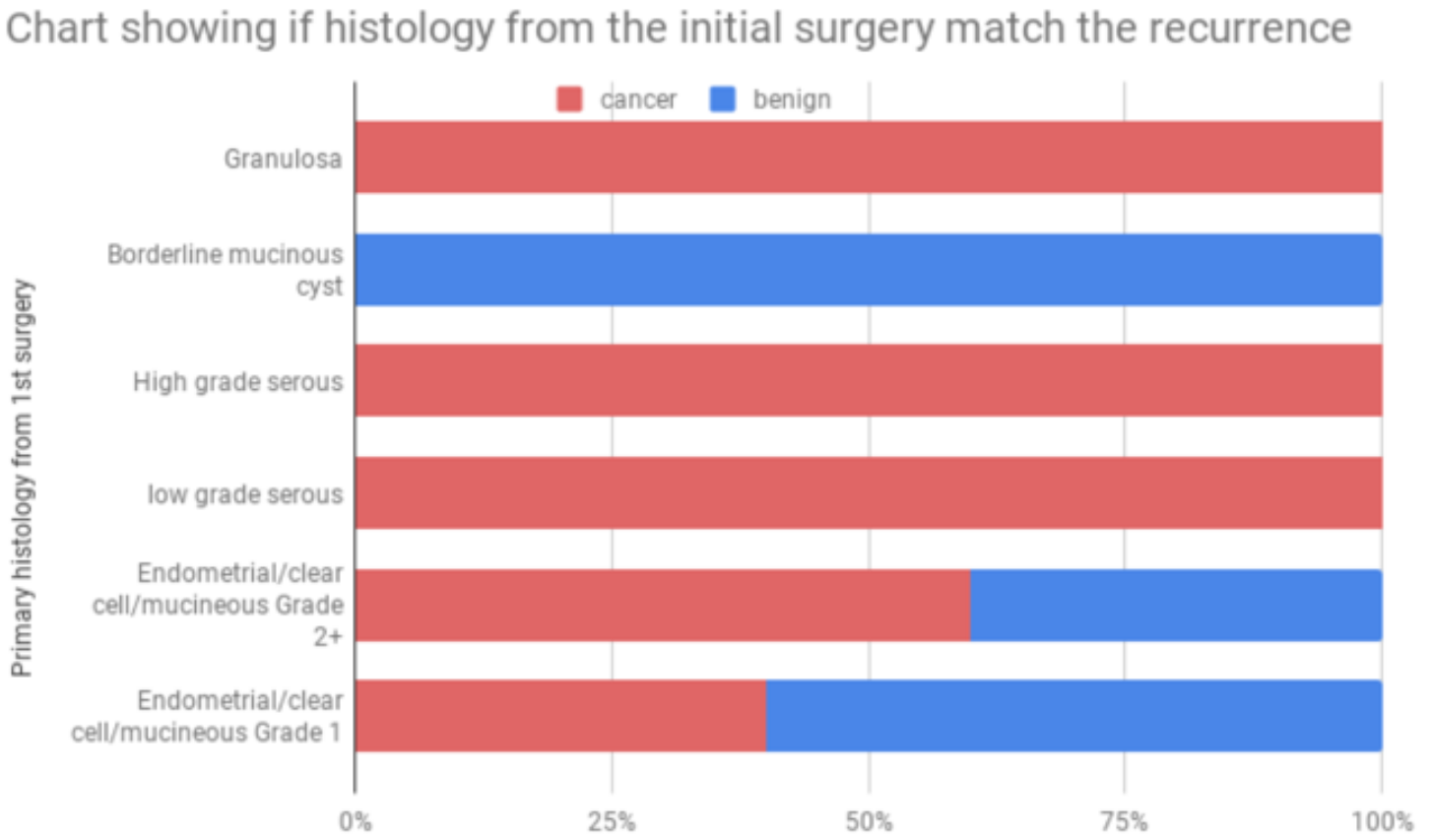
Buddy operations: **18 cases**

Complete cytoreduction: **29 patients**
Optimal debulking: **1 patient**

Histology of the recurrence matched initial surgery in **26 cases** and was benign in **6 cases**

Within this cohort there has been 1 death

→ **31 of the 32** patients are living



How to utilise these data?

- Small sample
- High complete cytoreduction rate to R0
- High survival rate

- Mucinous / endometrioid / clear cell “recurrences” should be carefully considered

- Secondary cytoreduction programme is safe and effective

Where are we going?

- Expectation of more secondary / tertiary cytoreduction as evidence builds – DESKTOP 3 (Du Bois et al 2017)

- Individualised treatment plans:
  - BRCA status (germline vs wildtype)(Marchetti et al 2018)
  - Artificial intelligence – disease free interval most important prognostic feature (Bogani et al 2018)
  - Biomarkers (Lheureux et al 2019)

HIPEC

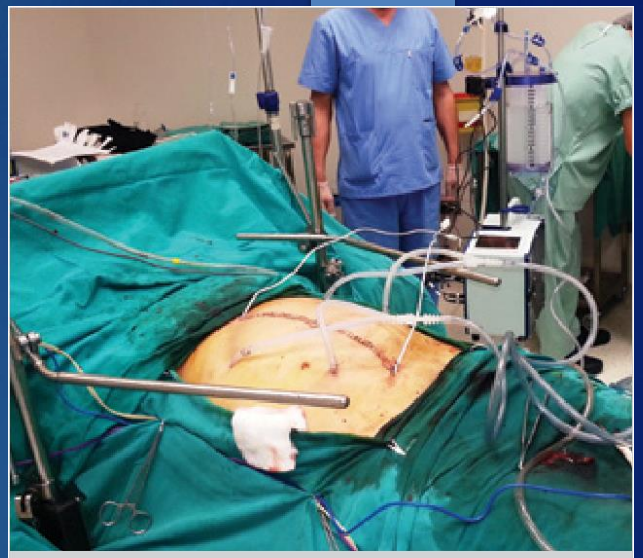


Figure 7. HIPEC application with closed abdominal technique

- Hyperthermic intra-peritoneal chemotherapy
- Used "routinely" in pseudomyxoma management
- Increasing use in ovarian cancer (Cianci et al 2018)
- Appears to improve survival in primary and recurrent ovarian disease - R0-cytoreduction was 95%
- Severe morbidity and mortality were observed in 15 % and 2%, respectively
- The 3 y OS was 77% in primary and 79% in recurrent ovarian cancer
- R1 cytoreduction and positive lymph nodes were risk factors in multivariate analysis(Arjona-Sanchez & Rufián-Peña 2018)

Take home messages

- Evolution of surgery for recurrence has come a long way in a few decades
- Local study of outcomes was reassuring and supportive of expanding the programme
- More evolutionary steps to be taken in new few decades

Thank you

References

- Arjona-Sanchez A1,2, Rufián-Peña S1,2. Int J Hyperthermia. 2017 Aug;33(5):554-561. doi: 10.1080/02656736.2017.1278631.Progress in the management of primary and recurrent ovarian carcinomatosis with peritonectomy procedure and HIPEC in a high volume centre.
- Andreas Du Bois, Ignace Vergote, Gwenael Ferron, Alexander Reuss, Werner Meier, Stefano Greggi. Randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer: AGO DESKTOP III/ENGOT ov20.
- Cianci S1, Ronsini C2, Vizzielli G3, Tropea A4, Biondi A5, Scambia G6, Fagotti A6. Updates Surg. 2018 Nov 8. doi: 10.1007/s13304-018-0600-y. [Epub ahead of print]Cytoreductive surgery followed by HIPEC repetition for secondary ovarian cancer recurrence.
- Bogani G1, Rossetti D2, Ditto A2, Martinelli F2, Chiappa V2, Mosca L2, Leone Roberti Maggiore U2, Ferla S2, Lorusso D2, Raspagliesi F2. J Gynecol Oncol. 2018 Sep;29(5):e66. doi: 10.3802/jgo.2018.29.e66. Epub 2018 Apr 23.Artificial intelligence weights the importance of factors predicting complete cytoreduction at secondary cytoreductive surgery for recurrent ovarian cancer.
- Marchetti C1, De Leo R2, Musella A1, D'Indinosante M2, Capoluongo E3, Minucci A3, Benedetti Panici P1, Scambia G2, Fagotti A4. Ann Surg Oncol. 2018 Nov;25(12):3701-3708. doi: 10.1245/s10434-018-6700-6. Epub 2018 Aug 20.BRCA Mutation Status to Personalize Management of Recurrent Ovarian Cancer: A Multicenter Study.
- Lheureux S1,2, Braunstein M3, Oza AM4,5.CA Cancer J Clin. 2019 May 17. doi: 10.3322/caac.21559. [Epub ahead of print]Epithelial ovarian cancer: Evolution of management in the era of precision medicine.
- Robert L. Coleman Danielle Enserro Nick Spirtos Thomas J. Herzog Paul Sabbatini Deborah Kay ArmstrongA phase III randomized controlled trial of secondary surgical cytoreduction (SSC) followed by platinum-based combination chemotherapy (PBC), with or without bevacizumab (B) in platinum-sensitive, recurrent ovarian cancer (PSOC): A NRG Oncology/Gynecologic Oncology Group (GOG) study.
- Felsinger M1, Minar L2, Weinberger V1, Rovny I3, Zlamal F4, Bienertova-Vasku J5. Eur J Obstet Gynecol Reprod Biol. 2018 Sep;228:154-160. doi: 10.1016/j.ejogrb.2018.06.036. Epub 2018 Jun 20.Secondary cytoreductive surgery - viable treatment option in the management of platinum-sensitive recurrent ovarian cancer.
- Harter P1, Sehouli J, Reuss A, Hasenburg A, Scambia G, Cibula D, Mahner S, Vergote I, Reinthaller A, Burges A, Hanker L, Pölcher M, Kurzeder C, Canzler U, Petry KU, Obermair A, Petru E, Schmalfeldt B, Lorusso D, du Bois A. Int J Gynecol Cancer. 2011 Feb;21(2):289-95. doi: 10.1097/IGC.0b013e31820aaafd.Prospective validation study of a predictive score for operability of recurrent ovarian cancer: the Multicenter Intergroup Study DESKTOP II. A project of the AGO Kommission OVAR, AGO Study Group, NOGGO, AGO-Austria, and MITO.
- Harter P1, du Bois A, Hahmann M, Hasenburg A, Burges A, Loibl S, Gropp M, Huober J, Fink D, Schröder W, Muenstedt K, Schmalfeldt B, Emons G, Pfisterer J, Wollschlaeger K, Meerpohl HG, Breitbach GP, Tanner B, Sehouli J; Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Committee; AGO Ovarian Cancer Study Group. Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial.