SURGICAL AND ADJUVANT TREATMENT OF MUCINOUS OVARIAN CARCINOMA: CURRENT APPROACH
MUZAFFER SANCı MD.
A dualistic approach to the classification of ovarian carcinoma

Type I
- Endometrioid
  - PTEN
  - PIK3CA
  - CTNNB
- Clear Cell
  - PIK3CA
  - ARID1A
- Mucinous
  - KRAS

Type II
- LGSOC
  - KRAS
  - BRAF
- HGSOC
  - TP53 / RB pathway
  - BRCA1/2
  - Chromosomal instability

DISTINCT DISEASES WITH DIFFERENT DRIVER ALTERATIONS
Falling incidence of primary mucinous ovarian carcinoma diagnosis

• Better recognition of the clinical importance of making the distinction
• Better histological distinction between metastases to the ovary and primary mucinous ovarian carcinoma
• Better preoperative work-up with imaging, and tumour markers
MUCINOUS OVARIAN TUMOURS

1.5% of all ovarian neoplasms

Continuum from benign → borderline → malignant

Benign mucinous cystadenoma ≈ 10-15%
Mucinous tumours of low malignant potential (mucinous borderline tumours) ≈ 67%

Invasive mucinous adenocarcinoma ≈ 4%

Tumours metastatic to the ovary ≈ 10-15%
PRIMAR Y OVARIAN MUCINOUS CARCINOMA
Types of Stromal Invasion

The diagnosis of invasive mucinous carcinoma requires stromal invasion measuring more than 5 mm or more than 10 mm² is detected.

1. Expansile: survival 100%

2. Infiltrative ("destructive"): poor prognosis
• The clinical features of mucinous ovarian neoplasms are distinct from their other epithelial counterparts.
• These tumors occur most commonly in women in their twenties to forties.
• Primary tumors tend to be larger and unilateral, compared with metastatic lesions.
• The mean size of primary mOCs has been documented as 16–20 cm, compared with 11–12 cm for metastatic cancers.
• Mucinous tumors can become extremely large and fill the entire abdominopelvic cavity.
PREOPERATIVE EVALUATION

- ULTRASOUND
- CT
- MRI
- PET-CT?

Imaging in gynecological disease: clinical and ultrasound features of mucinous ovarian tumors.
Moro F, Zannoni GF, Arciuolo D, Pasciuto T, Amoroso S, Mascilini F, Mainenti S, Scambia G, Testa AC.

A multilocular cyst with 2-10 locules is representative of a benign cystadenoma, whereas a multilocular cyst with > 10 locules is indicative of a GI-type borderline tumor. Most invasive tumors of mucinous GI-type contain solid components, the most typical ultrasound appearance being that of a multilocular-solid tumor. Papillary projections are typical features of endocervical-type borderline tumors.
Preoperative Evaluation

Clinical and ultrasound features of benign, borderline, and malignant invasive mucinous ovarian tumors.


The authors observed significant overlapping in ultrasound features among benign, borderline, and invasive ovarian mucinous tumors that renders a difficult accurate preoperative discrimination among these lesions.

Ultrasonography was helpful to evaluate the preoperative diagnosis and determining the surgical approach.
TUMOR MARKERS

• Carcinoembryonic antigen (CEA) is the most useful serum tumor marker to identify mOC preoperatively and to follow the progress. It is elevated in mOCs more than in nonmucinous ovarian carcinomas (88 % vs. 19 %).

• Serous tumors had elevated CA125, follicle-stimulating hormone, luteinizing hormone, and SMRP levels.

• Mucinous tumors had higher levels of CA72-4, matrix metalloproteinase-9, CD40L, insulin-like growth factor-binding protein-1, myeloperoxidase, and tissue plasminogen activator-1.
TUMOR MARKERS

Serum AGR2 can be a biomarker for diagnosis and prediction of mucinous ovarian cancers.
(Park.K., 2011)

*Obstet Gynecol Sci.* 2018 May;61(3):344-351
Preoperative serum levels of cancer antigen 125 and carcinoembryonic antigen ratio can improve differentiation between mucinous ovarian carcinoma and other epithelial ovarian carcinomas.
Choi JH, Sohn GS, Chay DB, Cho HB, Kim JH.

Pretreatment CCR might provide higher specificity and clinically relevant information as a criterion for the differentiation between ovarian mucinous carcinoma and other types of EOC.
Before establishing the diagnosis of primary mucinous ovarian tumor, always exclude the possibility of metastases.
PRIMARY vs METASTATIC MUCINOUS CARCINOMAS OF THE OVARY

Favor ovarian primary:
• Expansile pattern of invasion
• Complex papillary pattern
• Size >10 cm
• Smooth external surface
• Benign or borderline appearing areas

Favor metastases:
• Bilaterality
• Ovarian surface involvement
• Infiltrative pattern
• Nodular architecture
• Ovarian hilar involvement
• Single cell invasion and signet ring cells
• Vascular invasion
• Microscopic surface mucin

## Molecular alterations in ovarian and colorectal mucinous carcinomas

<table>
<thead>
<tr>
<th></th>
<th>Ovarian mucinous carcinomas</th>
<th>Colorectal mucinous carcinomas</th>
<th>Colorectal non-mucinous carcinomas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MSI-H</strong></td>
<td>22% &lt;sup&gt;36*&lt;/sup&gt;</td>
<td>31% (26–36) &lt;sup&gt;34–33&lt;/sup&gt;</td>
<td>4% (3–6) &lt;sup&gt;31,33†&lt;/sup&gt;</td>
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<tr>
<td><strong>KRAS mutations</strong></td>
<td>43% (32–56) &lt;sup&gt;34–37&lt;/sup&gt;</td>
<td>30% (23–38) &lt;sup&gt;39–40‡&lt;/sup&gt;</td>
<td>28% (24–33) &lt;sup&gt;40,41&lt;/sup&gt;</td>
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<tr>
<td><strong>BRAF mutations</strong></td>
<td>0% &lt;sup&gt;37&lt;/sup&gt;</td>
<td>20% (14–28) &lt;sup&gt;39,40,41&lt;/sup&gt;</td>
<td>8% (6–12) &lt;sup&gt;40,42&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>HER2 amplification</strong></td>
<td>18% &lt;sup&gt;43&lt;/sup&gt;</td>
<td>&lt;1% &lt;sup&gt;44&lt;/sup&gt;</td>
<td>2% (2–3) &lt;sup&gt;44,45&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>APC or CTNNB1 mutations</strong></td>
<td>9% &lt;sup&gt;46§&lt;/sup&gt;</td>
<td>24% &lt;sup&gt;42&lt;/sup&gt;</td>
<td>88% &lt;sup&gt;42&lt;/sup&gt;</td>
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<tr>
<td><strong>TP53 mutations</strong></td>
<td>26% &lt;sup&gt;34&lt;/sup&gt;</td>
<td>33% (20–48) &lt;sup&gt;42,47&lt;/sup&gt;</td>
<td>41% &lt;sup&gt;48&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

PROGNOSTIC FACTORS

• Stage
• Grade
• Expansile or infiltrative type
SURGICAL STAGING

✓ Exploration of the abdominal cavity,
✓ Peritoneal washing
✓ Total hysterectomy with BSO,
✓ Omentectomy,
✓ Resection of macroscopically suspicious lesions,
✓ Multiple peritoneal biopsies
✓ Pelvic and paraaortic lymphadenectomy
✓ Appendectomy
LAPARATOMY-LAPAROSCOPY

As the use of minimally invasive surgery has increased and the scope of indications has broadened, minimally invasive surgery has been increasingly used for the management of patients with mucinous ovarian tumors, even when they are quite large.

Multiple reports exist of the safe and feasible removal of mucinous tumors laparoscopically, with several techniques reported to effect removal without spillage of the cyst contents.

Morcellation in the peritoneal cavity or contamination of the peritoneal cavity and/or trocar sites should be absolutely avoided.

MAS for SSCR is feasible in properly selected cases. MAS is associated with favorable perioperative outcomes and similar oncologic outcomes, compared to LAP.
FROZEN SECTION (intraoperative consultation)

Approximately 25% of women had their diagnosis changed in the final diagnosis, this occurring more frequently in mucinous tumors.

Overall frozen section is only moderately accurate in distinguishing primary versus metastatic malignancies.

In any cystic tumor, as a general rule, all the locules should be opened and examined macroscopically.

Tissue for frozen section should be taken from solid areas. Because solid nodule may harbor a high-grade malignancy.
An Evaluation of Frozen Section and Lymph Node Dissection Results for Mucinous Ovarian Tumors.

Moroney MR, Post MD, Berning AA, Sheeder J, Corr BR.

Intraoperative identification of mucinous histology by frozen section is reliable with a concordance rate to final pathology of 97.2%. No lymph node metastases were present in any malignant or borderline primary ovarian cases.
LYMPHADENECTOMY

• Gynecol Oncol Rep. 2017 Sep 1;22:21-25. Morice P.
• Gynecol Oncol. 2017 Feb;144(2):414-419. Nasioudis D.
• BJOG. 2017 Feb;124(3):486-494. van Baal J.
• Int J Surg. 2017 May;41:1-5. Salgado-Ceballos I.
• Eur J Cancer. 2013 May;49(7):1600-8. Vergote I.
LYMPHADENECTOMY

• LNM are rare in early-stage G1 and G2 MOC without clinical suspicion of LNM.
• Lymphadenectomy could be omitted in patients with mucinous stage I grade 1 tumor and expansile type, but required in infiltrative type.
• Patients with clinical early-stage MOC had no DFS benefit from lymph node sampling.
• Complete surgical staging with lymph node dissection has no effect on recurrence, disease-free period, and overall survival of patients with early stage MOC.
• Reoperation for lymph node staging only should be discussed individually with caution.
• The therapeutic effect of the lymph node resection itself in apparent stage I Ovarian Cancer remains currently an unsolved debate with endless discussions.
LYMPHADENECTOMY

According to our study, lymph node metastasis in pT1 mucinous carcinoma has a rate of 22.2%. Therefore, we need to be careful about the omission of systematic lymphadenectomy in mucinous carcinoma.
Univariate analysis suggests that metastatic disease to the appendix and failure to perform complete staging including appendectomy are related to a worsened prognosis. A normal-looking appendix does not exclude metastatic disease, and because appendectomy is easily performed and does not increase morbidity, it should be performed during surgery for suspected mucinous ovarian cancer.
There is not sufficient evidence to support a routine appendectomy for patients with a grossly normal appendix in mBOT and MOC. A careful intra-operative exploration of the appendix is crucial, but appendectomy is only warranted when the appendix is abnormal.
FERTILITY SPARING SURGERY

Results of Fertility-Sparing Surgery for Expansile and Infiltrative Mucinous Ovarian Cancers.

21 patients: 12 with expansile and 9 with infiltrative cancer.
Ten had nodal staging surgery. Two patients recurred (one expansile and one infiltrative type). 6 patients became pregnant; four with expansile tumors and two with infiltrative tumors.

The type of mucinous cancer has no impact on the oncologic outcome; thus, FSS may be considered in both subtypes.
ADJUVANT THERAPY

use of
"ovarian" versus
"gastrointestinal" style chemotherapy
Potential treatment algorithm for primary mucinous ovarian carcinoma

Surgical Staging Identifies a Mucinous (Primary) Ovarian Tumour

- Advanced or recurrent MC
- MBOT or early stage MC

HER2 Testing

- Positive (+)
- Negative (-)

HER2 targeted therapy

- Respond to treatment

Fail treatment

KRAS Testing

- Positive (+)
- Negative (-)

Fail

Conventional chemotherapy?
- GI based
- Ovarian based
- Novel therapies/trials?

Cetuximab

- Respond to treatment
Mucinous epithelial ovarian cancer: a separate entity requiring specific treatment.


Patients with advanced mEOC have a poorer response to platinum-based first-line chemotherapy, and their survival is worse. Specific alternative therapeutic approaches should be sought for this group of patients, perhaps involving fluorouracil-based chemotherapy.
Mucinous ovarian carcinoma responds poorly to platinum based chemotherapy

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>RR (%)</th>
<th>PFS (mos)</th>
<th>OS (mos)</th>
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<tr>
<td>Hess et al., 2004²⁹</td>
<td>27</td>
<td>26.3</td>
<td>5.7</td>
<td>12.0</td>
</tr>
<tr>
<td>Pectasides et al., 2005³⁰</td>
<td>47</td>
<td>38.5</td>
<td>11.8</td>
<td>33.2</td>
</tr>
<tr>
<td>Pisano et al., 2005³²</td>
<td>19</td>
<td>42</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

RR, response rate; mos, months; NR, not reported.

Harrison et al; Int J Gynecol Cancer 2008: 209-214

Mucinous ovarian carcinoma may respond preferentially to oxaliplatin & 5FU

Sato et al; Cancer Science 2009 March, 100 (3) 546-551
Potential new approaches for mucinous ovarian carcinoma

- **Anti HER2 therapy:**
  - Trastuzumab, MGAH22, lapatinib, TDM-1,

- **Anti EGFR therapy for KRAS wt**
  - cetuximab, panitumumab

- **KRAS mut**
  - Phase 1 selumetanib + MK-2206: Durable response in 1 of 2 low grade ovarian with RAS mutation. Tolcher 2014

- **Chemotherapy**
  - phase II Japanese study of women with advanced or recurrent are undergoing treatment with oxaliplatin and S1, an orally active drug combining tegafur, gimeracil, oteracil


This population-based retrospective study is the first to demonstrate that the use of adjuvant abdominopelvic XRT after chemotherapy can improve survival in patients diagnosed as having stage I/II MC.
PROGNOSIS

Relatively Poor Survival of Mucinous Ovarian Carcinoma in Advanced Stage: A Systematic Review and Meta-analysis.

Patients with advanced-stage MOC have a significantly worse prognosis compared with patients with SOC, whereas in early stage, the prognosis of patients with MOC is better.
METASTATIC CARCINOMAS TO THE OVARY

- Stomach 76%
- Colorectum 11%
- Appendix 6%
- Breast 4%
- Pancreas/biliary tract 3%

Secondary tumors of the ovary account for 10-25% of all ovarian malignancies.

It requires different treatment.

Immunohistochemistry plays an important role in distinguishing primary ovarian tumors from extra-ovarian metastases.

The pathogenesis, diagnosis, and management of metastatic tumors to the ovary: a comprehensive review.
IMMUNOHISTOCHEMICAL PROFILE OF CK 7 AND CK20 IN OVARIAN AND COLONIC MUCINOUS TUMORS

• Ovarian mucinous carcinoma:
  CK7 + / CK20 +  ................... (93%)
  CK7 + / CK20 -  ................... (7%)

• Colonic mucinous carcinoma:
  CK7 + / CK20 +  ................... (9%)
  CK7 - / CK20 +  ................... (91%)

The role of secondary cytoreductive surgery for recurrent mucinous epithelial ovarian cancer (mEOC).


Optimal primary cytoreductive surgery for advanced mEOC was very important. Once it recurs, the prognosis is very poor. Patients with recurrent mEOC should be carefully assessed before performing secondary cytoreductive surgery, as this may have limited impact on the overall survival rates.
ADVANCED STAGE MEOC


A multicenter, retrospective department database review was performed to identify patients with stage III nonserous EOC who had undergone maximal or optimal primary CRS followed by six cycles of carboplatin/paclitaxel chemotherapy at seven gynecological oncology centers in Turkey.

218 women. Of these, 64 (29.4%) patients had endometrioid, 61 (28%) had mucinous, 54 (24.8%) had clear-cell and 39 (17.9%) had mixed epithelial tumors.

The extent of CRS seems to be the only modifiable prognostic factor associated with stage III nonserous EOC. Complete cytoreduction to no gross residual disease should be the main goal of management in these women.
ADVANCED STAGE MEOC

• Gynecol Oncol. 2005 May;97(2):436-41. the Hellenic Cooperative Oncology Group experience. Pectasides D.
• Cancer. 2010 Mar 15;116(6):1462-8 Bamias A.
• Ann Oncol. 2010 Dec;21(12):2377-81. the GINECO experience. Alexandre J, GINECO.
• J Gynecol Oncol. 2013 Apr;24(2):160-6. Ortaç UF.
• PLoS One. 2016 Jan 28;11(1) Morice P.
• Int J Gynecol Cancer. 2017 May;27(4):651-658. Simons M.
ADVANCED STAGE MEOC

• Residual disease after debulking surgery in MEOC negatively impacts prognosis.
• Patients with advanced stage mEOC have significantly lower response to first-line platinum-based chemotherapy.
• Advanced stage mEOC patients have a significantly worse prognosis and more poorer survival outcome when compared to advanced stage sEOC.
• Lethal recurrences were observed mainly in infiltrative type.
• New and different therapeutic strategies are needed.
Primary mucinous ovarian carcinoma (PMOC) across 3 tertiary medical centers

1976-2014

222 patients with PMOC were identified; all had undergone primary surgery.

Disease stage distribution was as follows: stage I, 163 patients (74%);
stage II, 8 (4%);
stage III, 40 (18%);
stage IV, 10 (5%).

99 (45%) of 219 patients underwent lymphadenectomy;
41 (19%) of 215 underwent fertility-preserving surgery.
68 (47%) had received chemotherapy-55 (81%) a gynecologic regimen and
13 (19%) a gastrointestinal regimen.

The 5-year progression-free survival (PFS) rates were 80% for patients with stage I to II disease and
17% with stage III to IV disease.

The 5-year PFS rate was 73% for patients who underwent fertility-preserving surgery.
The PFS outcomes were favorable for those with early-stage disease and lower but acceptable for those who underwent fertility preservation.
CONCLUSION

• Peritoneal staging surgery should be conducted, regardless of the type of mOC.
• Lymphadenectomy in expansile mOC cases might be omitted but required for infiltrative mOC cases, during either the initial or the restaging surgery.
• Appendectomy is only warranted when the appendix is abnormal?
• FSS may be considered in MOC. But should not be performed in patients with disease staged higher than FIGO Stage IA.
• Minimally invasive surgery is feasible in properly selected cases.
• A new strategy for chemotherapy in mEOC should be adopted.
THANK YOU

İzmir Tepecik Education and Research Hospital, Gynecologic Oncology Department
<table>
<thead>
<tr>
<th>Histopathologic Type</th>
<th>Number of patients (n:73)</th>
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<tbody>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>59</td>
</tr>
<tr>
<td>Mixt (clear cell + mucinous)</td>
<td>2</td>
</tr>
<tr>
<td>Mixt (serous+mucinous)</td>
<td>5</td>
</tr>
<tr>
<td>Mixt (endometroid + mucinous)</td>
<td>3</td>
</tr>
<tr>
<td>Primary appendiceal tumor</td>
<td>2</td>
</tr>
<tr>
<td>Colon Ca's metastasis to ovary</td>
<td>1</td>
</tr>
<tr>
<td>Mucinous ovarian ca + endometroid type endometrium ca</td>
<td>1</td>
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<td>GIS Endoscopic Analysis</td>
<td>Number of patients</td>
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<td>-------------------------------------------------------------</td>
<td>--------------------</td>
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<tr>
<td>No endoscopy</td>
<td>34</td>
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<tr>
<td>Endoscopic antral gastritis detected</td>
<td>35</td>
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<tr>
<td>Endoscopy completely normal</td>
<td>2</td>
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<tr>
<td>GIST detected</td>
<td>1</td>
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<tr>
<td>No colonoscopy</td>
<td>2</td>
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<tr>
<td>Colonoscopy is completely normal</td>
<td>31</td>
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<td>Patients who could not progress after 15-20 cm in colonoscopy</td>
<td>24</td>
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<tr>
<td>Benign polyps</td>
<td>10</td>
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<tr>
<td>Metastasis detected</td>
<td>6</td>
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<tr>
<td>Description</td>
<td>Count (Percentage)</td>
</tr>
<tr>
<td>--------------------------------------------------------------</td>
<td>--------------------</td>
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<tr>
<td>Tumor diameter (n:73)</td>
<td>18.8±5.22 cm</td>
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<tr>
<td>Patients with ascites</td>
<td>16 (21.9%)</td>
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<tr>
<td>Psodomixoma peritonei detected</td>
<td>4 (5.5%)</td>
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<td>Patients with peritonitis carcinomatosis</td>
<td>19 (26%)</td>
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<tr>
<td>Tumor detected in the appendix</td>
<td>15 (20.5%)</td>
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<tr>
<td>Appendectomy</td>
<td>54 (74%)</td>
</tr>
<tr>
<td>Right hemicolectomy + end-to-end anastomosis</td>
<td>3 (4.1%)</td>
</tr>
<tr>
<td>Optimal cytoreduction (TAH+BSO+PPLND+OMM+APP)</td>
<td>43 (79.5%)</td>
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<tr>
<td>Suboptimal cytoreduction</td>
<td>15 (20.5%)</td>
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<td>Unresectable tumor</td>
<td>15 (20.5%)</td>
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<td>Duration of surgery (n: 73)</td>
<td>152.0±52.0 min.</td>
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<td>Number of pelvic LNs (n: 42)</td>
<td>18.1±9.0</td>
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<tr>
<td>Number of paraaortic LNs (n: 34)</td>
<td>8.7±6.6</td>
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<td>GROUPS</td>
<td>AGE</td>
</tr>
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<td>--------------</td>
<td>------------</td>
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<tr>
<td>Stage 1a (n:36) 49,4%</td>
<td>53,2±16,0</td>
</tr>
<tr>
<td>Stage 1b (n:2) 2,7%</td>
<td>72,5±13,4</td>
</tr>
<tr>
<td>Stage 1c (n:9) 12,3%</td>
<td>46,7±11,4</td>
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<td>Stage 2b (n:1) 1,4%</td>
<td>46</td>
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<tr>
<td>Stage 3a (n:3) 4,1%</td>
<td>45,0±5,2</td>
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<tr>
<td>Stage 3c (n:20) 27,4%</td>
<td>55,4±10,6</td>
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<tr>
<td>Stage 4 (n:2) 2,7%</td>
<td>53,0±14,2</td>
</tr>
<tr>
<td>TOTAL (n:73) 100%</td>
<td>53,1±14,2</td>
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MUCINOUS OVARIAN TUMORS

BEFORE WHO 2014

• PRIMARY MUCINOUS OVARIAN TUMOR
• SEROMUCINOUS OVARIAN TUMOR
• METASTATIC MUSINOUS OVARIAL TUMOR
• PSODOMIXOMA PERİTONİİ
Comparison of advanced stage mucinous epithelial ovarian cancer and serous epithelial ovarian cancer

<table>
<thead>
<tr>
<th>Study (author, year)</th>
<th>Type</th>
<th>Patient population</th>
<th>No. of patients included in the study</th>
<th>No. of patients with mEOC</th>
<th>Stage</th>
<th>Summary</th>
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<tr>
<td>Omura et al. 1991 [5]</td>
<td>Retrospective</td>
<td>All EOC types</td>
<td>726</td>
<td>33</td>
<td>III/IV</td>
<td>mEOC is a poor prognostic factor.</td>
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<td>Pectasides et al. 2005 [16]</td>
<td>Retrospective</td>
<td>mEOC, sEOC</td>
<td>141</td>
<td>47</td>
<td>III/IV</td>
<td>mEOC has low response to platinum-based chemotherapy.</td>
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<tr>
<td>Pignata et al. 2008 [17]</td>
<td>Retrospective</td>
<td>All EOC types</td>
<td>408</td>
<td>20</td>
<td>I–IV</td>
<td>mEOC has low response rate to chemotherapy.</td>
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<tr>
<td>Shimada et al. 2009 [11]</td>
<td>Retrospective</td>
<td>mEOC, sEOC</td>
<td>719</td>
<td>64</td>
<td>I–IV</td>
<td>mEOC has low response rate to chemotherapy.</td>
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<tr>
<td>Alexandre et al. 2010 [9]</td>
<td>Retrospective</td>
<td>All EOC types</td>
<td>840</td>
<td>54</td>
<td>IIIB/IV</td>
<td>mEOC has low response rate to chemotherapy and has poor prognosis.</td>
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<tr>
<td>Bamias et al. 2010 [14]</td>
<td>Retrospective</td>
<td>mEOC, sEOC, clear cell</td>
<td>420</td>
<td>24</td>
<td>III/IV</td>
<td>mEOC but not clear cell histology is associated with poor prognosis.</td>
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<td>Mackay et al. 2010 [15]</td>
<td>Retrospective</td>
<td>All EOC types</td>
<td>8,704</td>
<td>264</td>
<td>III/IV</td>
<td>mEOC and clear cell carcinomas are independent predictors of poor prognosis in advanced stage EOC.</td>
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<td>Schiavone et al. 2011 [8]</td>
<td>Retrospective</td>
<td>All EOC types</td>
<td>40,571</td>
<td>4,811</td>
<td>I–IV</td>
<td>Advanced stage mEOC is associated with poor survival.</td>
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<td>Zaino et al. 2011 [7]</td>
<td>Prospective</td>
<td>All EOC types</td>
<td>3,435</td>
<td>44</td>
<td>III/IV</td>
<td>Advanced stage mEOC is associated with poor survival.</td>
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<tr>
<td>Present study</td>
<td>Retrospective</td>
<td>mEOC, sEOC</td>
<td>138</td>
<td>50</td>
<td>III/IV</td>
<td>mEOC has low response rate to chemotherapy and has poor prognosis.</td>
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Decision tree for differential diagnosis of primary ovarian versus metastatic carcinoma