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Characteristics and treatment outcomes of patients with expansile and infiltrative primary mucinous ovarian carcinoma – A 5-year retrospective study at a tertiary government hospital

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Abstract:

BACKGROUND: Primary invasive mucinous epithelial ovarian carcinoma (MOC) is a rare subtype of epithelial ovarian carcinoma (EOC). According to the 2020 World Health Organization (WHO) classification, the invasive patterns of MOC are classified into two categories: Infiltrative and expansile invasion. Studies examining the relationship between expansile and infiltrative primary MOCs are limited. In our local setting, there are no published studies to determine the impact of classifying primary MOCs between the two subtypes to treatment outcomes. This study, therefore, aims to determine the prevalence of primary MOC subtypes, their clinical and demographic characteristics, and clinical outcomes.

MATERIALS AND METHODS: This is a retrospective study of patients diagnosed with MOCs for a 5-year period from January 2013 to December 2017 in a public end-referral tertiary hospital. A pathological review was conducted using the 2020 WHO classification to determine the pattern of invasion. Demographic data were obtained and the treatment outcome of infiltrative invasion and expansile invasion of ovarian mucinous carcinoma were compared. Log–rank test was used to determine the overall survival (OS) with the specific type of MOCs.

RESULTS: A total of 29 cases were included in this study wherein 79.3% were expansile MOC type and 20.7% were infiltrative. Most of the patients had International Federation of Gynecology and Obstetrics Stage IA (27.6%). All patients had laparotomy and half of the patients received adjuvant therapy, 47.8% and 50% in expansile and infiltrative type, respectively. The factors associated with overall mortality were MOC type: expansile, hazard ratio (HR) = 0.3, 95% confidence interval (CI) = 0.07–0.91, $P = 0.047$, and infiltrative, HR = 3.3, 95% CI = 1.1–13.5, $P = 0.047$. Median OS was significantly higher in patients with expansile compared to infiltrative type (42 vs. 25 months, $P = 0.039$).

CONCLUSION: Infiltrative invasion was observed to be a prognostic factor showing worse outcomes for ovarian mucinous carcinoma compared to expansile invasion.

Keywords:

Expansile invasion, infiltrative invasion, mucinous ovarian carcinoma, prognosis

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Introduction and Significance of the Study

Ovarian cancer is the second most common gynecological malignancy and is the most lethal carcinoma of the female reproductive tract.[1] Epithelial ovarian carcinoma (EOC) is the most common histological type of ovarian carcinoma and classified based on molecular and clinicopathological differences into Type I and Type II tumors.[1] Type I tumors include low-grade serous carcinoma, endometrioid carcinoma, clear cell carcinoma, and mucinous epithelial ovarian carcinoma (MOC). They are often discovered at an early stage and have an indolent clinical course. In comparison, the Type II tumors, which include high-grade serous carcinoma are detected at an advanced stage and exhibit highly aggressive behavior.[2,3]

MOC is a rare histological Type I EOC, comprising 3%–5% of EOC cases.[3,4] The estimates of the frequency of primary MOC range from 6% to 25%, but a systematic review to exclude the tumors of low malignant potential and metastatic lesions from gastrointestinal, pancreatic, or other gynecologic primary tumors suggests that the true percentage of ovarian carcinomas represented by primary mucinous tumors is substantially less at 2.4%.[1] One local study showed that Filipinos have a different distribution of EOCs as compared to the international literature. Endometrioid type of EOCs comprised 22%, followed by mucinous types (24%), and serous type with the smallest proportion comprising 20%.[4]

In recent years, MOCs began to emerge as a separate entity, with a specific clinical presentation and biological behavioral pattern. Compared with all other types of EOCs, MOCs appeared to have worse outcomes leading to further research that has shown MOCs to be distinct from other forms of epithelial ovarian neoplasms.[4]

There are different classifications of MOCs that have been described. In 1973, Hart and Norris reported a category of "noninvasive mucinous carcinoma" based on more than three cell layers and severe nuclear atypia.[5] In 2000, the expansile and infiltrative types of MOC were described by Lee and Scully.[5,6] According to Lee and Scully, the expansile type is characterized by the absence of destructive stromal invasion, but exhibiting confluent or complex malignant glands, with or without minimal intervening stroma and exceeding 10 mm^2 in area (>3 mm in each of two linear dimensions). In contrast, the infiltrative type is characterized by obvious stromal invasion in the form of glands, cell clusters or individual cells, disorderly infiltrating the stroma and frequently associated with a desmoplastic stromal reaction. In 2014, to standardize the pathological report for MOC and borderline disease, the World Health Organization (WHO) classification proposed classifying primary mucinous cancers within these two groups defined by their growth patterns: Expansile and infiltrative. In 2020, the WHO adopted the definition of Lee and Scully in the classification of this type of tumor.[2,5]

In the Philippine General Hospital (PGH) unpublished census, the incidence of new patients seen with primary MOC for the past 2 years was 32 out of 186 ovarian carcinomas and 26 out of 132 ovarian carcinomas for 2019 and 2020, respectively. However, it is important to note that 25 out of 32 cases of MOCs for the year 2019 and 22 out the 26 cases of MOCs for the year 2020 have unknown pattern of invasion since pathologists have not routinely reported this finding.

Due to its rarity, the specific subtypes of MOCs are not routinely reported in pathologic reports and most clinical studies have grouped all EOCs together, leading to a common therapeutic approach. Studies examining the relationship between expansile and infiltrative primary MOCs are limited. In our local setting, there are no published studies to determine the impact of classifying primary MOCs between the two subtypes to treatment outcomes. This study, therefore, aims to determine the prevalence of primary MOC subtypes, its clinical and demographic characteristics, and their clinical outcomes.

Objectives of the study

This study aims to determine the treatment outcomes of patients with infiltrative and expansile primary mucinous ovarian carcinoma referred to or treated in a tertiary hospital. Specifically, it seeks:

1. To determine the overall prevalence of patients diagnosed with mucinous ovarian carcinoma at a tertiary hospital in a 5-year period
2. To determine the overall prevalence of patients in terms of the specific type of mucinous ovarian carcinoma (infiltrative or expansile) at a tertiary hospital in a 5-year period by conducting a pathologic review using the 2020 WHO criteria
3. To determine the clinicodemographic profile of patients according to the type of mucinous ovarian tumor in terms of:
   a. Age
   b. Symptom at presentation
   c. Tumor size
   d. Baseline CA-125
   e. Baseline CA 19-9
   f. Laterality
   g. International Federation of Gynecology and Obstetrics (FIGO) stage at diagnosis
   h. Form of treatment given: surgical procedure and adjuvant therapy received.
4. To determine the progression-free survival (PFS) and overall survival (OS) of patients with different type of MOCs

5. To determine the treatment outcomes of the different MOC types based on the particular type of treatment given, as follows:
   a. Surgery alone
   b. Surgery and systemic chemotherapy.

Materials and Methods

Study design, population, and sample size

This is a retrospective study. All patients diagnosed with MOCs from January 2013 to December 2017 referred to or treated in a tertiary hospital and gynecologic oncology referral center who will satisfy the inclusion (any stage of primary mucinous ovarian carcinoma, with available surgical, histological, and oncological data), and exclusion criteria (patients seen but not treated in the said institution, with missing medical records or incomplete records which could not be verified from any reliable external sources, and patients whose operations were performed in other institutions and/or the slides are no longer available for pathologic review) were included in the study. Total enumeration sampling was employed wherein all patient records eligible for the study were included.

Operational definition of terms

The major variables of the study are defined as follows:

1. Expansile mucinous ovarian carcinoma. The expansile subtype has no destructive stromal invasion but exhibits confluent or complex malignant glands (back to back glands) with or without minimal intervening stroma exceeding a 10 mm^2 area or >3 mm each of two linear dimensions based on the WHO 2020 criteria classification of MOC
2. Infiltrative mucinous ovarian carcinoma. The infiltrative type has stromal invasion in the form of glands, cell clusters, or individual cells, unsystematically infiltrating the stroma and often associated with a desmoplastic stromal reaction based on the WHO 2020 criteria classification of MOC
3. OS: Defined as the period from the day of primary debulking surgery to the day of death or the last confirmation of survival
4. PFS: Defined as the period from the day of primary debulking surgery to the day of death or recurrence/progression of the disease
5. Age: This refers to age of the patient at diagnosis
6. Symptom at presentation: This refers to the symptom that the patient experienced leading to consult. This will be recorded based on the "chief complaint" in the patient's chart during her first visit
7. Tumor size: This refers to the tumor size in centimeter. This variable will be obtained from the histopathologic report or operative technique in the patient's chart
8. Baseline CA-125: This refers to the baseline cancer antigen 125 level prior to operation as recorded in the chart. This tumor marker is measured in units per milliliter
9. Baseline CA 19-9: This refers to the baseline cancer antigen 19-9 level prior to operation as recorded in the chart. This tumor marker is measured in units per milliliter
10. Laterality: This refers to whether the ovarian mass is unilateral (pathology is confined to one ovary) or bilateral (when there is involvement of the contralateral ovary)
11. FIGO stage at diagnosis: This refers to the FIGO 2014 stage of the ovarian cancer after the primary debulking surgery as recorded in the chart
12. Form of treatment given. This refers to the form of treatment received by the patient whether surgical procedure only (laparotomy or laparoscopy) or with adjuvant therapy (including the specific chemotherapy given to the patient).

Description of study procedures, data collection tools, and analysis

The research hypothesis of this study is that the specific subtype of primary MOC of patients treated in a tertiary hospital has different treatments. The type of MOC, whether expansile or infiltrative, is the independent variable, and treatment outcome is the dependent variable.

The study group consists of all patients with mucinous ovarian carcinoma referred to or treated at the PGH Cancer Institute by the Division of Gynecologic Oncology in a 5-year period from January 1, 2013 to December 31, 2017, retroactively identified from the outpatient clinic census and conference files of the said institution. The outpatient clinic census includes all new and old patients seen by the center every year and is collated and stored in the office of the center. The medical charts, outpatient department records, and conference files from the said period were retrieved and compiled. An inclusion and exclusion criteria were used for the selection of patients.

Using the medical charts of the identified cases, data on patient demographics, tumor histology, intraoperative findings, extent of surgical procedure, adjuvant chemotherapy and/or radiation therapy, recurrence/progression, and survival were collected using a case registry form to meet the objectives of the study. All the patient records and files who had complete data, or missing data but verified from reliable sources were included.

The following data were collected and recorded using the case registry form to meet the objectives of the study:

- Date of diagnosis
- Age at diagnosis
- Symptoms

- Tumor size
- Laterality of the ovarian mass
- FIGO stage at diagnosis
- Histology (expansile vs. infiltrative type and degree of differentiation)
- Baseline CA-125
- Baseline CA 19-9
- Form of treatment given: surgical procedure and adjuvant therapy received
- Lymphadenectomy
- Amount of residual disease after primary surgery
- Date of last follow-up or death and cause of death to determine the treatment outcome.

Data on the intraoperative findings regarding tumor size and data on the surgical procedures performed were obtained and subdivided into either complete surgical staging with bilateral pelvic lymph node dissection, paraaortic lymph node sampling, incomplete surgical staging, or a fertility sparing surgery. Finally, information on the administration of adjuvant chemotherapy was also obtained.

The prevalence rates of MOCs by histologic subtypes were computed. Descriptive statistical measures were used for the clinicodemographic variables of the study participants. Records of all eligible patients from the initial diagnosis were reviewed to determine the OS and PFS. The primary outcome measures were the differences in the OS across patients according to different histologic subtypes, demographic factors, and treatment.

Pathology review

For the pathological review, available histopathological slides were retrieved from the section of surgical pathology and reviewed in the Department of Laboratories of the said institution. Histopathological slides were retrieved from the Department of Laboratories and all cases were reviewed by one pathologist. Primary MOCs were categorized as expansile or infiltrative according to the 2020 WHO classification of female genital tumors. Tumors with both expansile and infiltrative invasion patterns were classified under the group of invasive tumors. Only primary carcinomas were included and borderline mucinous tumors with microinvasive patterns as well as metastatic mucinous carcinomas were excluded. If the initial slide was not available or could no longer be retrieved for pathological review, the patient was excluded in the final analysis. If the slide was destroyed or there was difficulty classifying due to decay of the slide and the paraffin blocks were still available, reprocessing of the blocks were done for review.

Description of outcome measures

Data checking, compiling, and editing were performed manually by the researcher. Collected data were coded, entered into Microsoft Excel, and reviewed. STATA 14 (StataCorp LLC, Texas, USA) was used for the data analysis. Descriptive statistical measures, such as mean and standard deviation, were used to summarize the continuous quantitative variables, while frequency and proportion were used for the categorical variables.

Kaplan–Meier survival curves were used to describe OS. Log–rank test was used to compare OS across histology type and between surgery alone versus surgery with chemotherapy. The Chi-square test was used to determine which clinico-demographic variables were associated with OS. $P < 0.05$ was considered statistically significant.

Results

Patient and tumor characteristics

Seventy-four patients were identified who fulfilled the inclusion and exclusion criteria from the census and with available charts for review. Out of the 74 patients, only 34 patients had available slides for the pathologic review. Five patients were seen only once postoperatively; hence, their OS could not be included in the analysis.

A total of 29 cases were included in this study wherein the 5-year prevalence was 79.3% for expansile MOC type and 20.7% for the infiltrative type. The result of 29 patients was analyzed and the characteristics of MOC according to the invasive patterns are listed in Table 1.

The median age was 43 years for those with expansile type MOC and 53 years for those with infiltrative. The most common symptoms among those with expansile type MOC were increased abdominal girth (82.6%) and abdominal pain (30.4%). The most common symptom among those with infiltrative type MOC was increased abdominal girth (100.0%). One patient with infiltrative type MOC (16.7%) had bilateral disease compared to none in the expansile type (0.0%) ($P = 0.046$). A portion of the patients had FIGO Stage 1A (27.6%).

Upon the data collection, many of the patients lacked certain information in their charts including the tumor size, degree of differentiation, baseline tumor markers such as CA 125 and CA 19-9, and information on residual disease, hence these were not reported.

Surgical management

All patients had open surgery (exploratory laparotomy). Complete surgical staging was done in 95.6% of patients with expansile type MOC and 83.3% of those with infiltrative type. Appendectomy was done in 73.9% of patients with expansile type MOC and 66.7% of those with infiltrative type. Bilateral pelvic lymph node dissection was done in 91.3% of patients with expansile type MOC and 50.0% of those with infiltrative type.

Table 1: Characteristics of patients with expansile and infiltrative MOC (*n*=29)

	Expansile (*n*=23; 79.3%)	Infiltrative (*n*=6; 20.7%)	*P*
Age, median (IQR)	43 (12)	52 (9)	0.154
Gravidity, median (IQR)	3 (2)	4 (2)	0.623
Parity, median (IQR)	4 (2)	4 (2)	0.812
Symptoms			
Abdominal pain	7 (30.4)	1 (16.7)	0.502
Increased abdominal volume	19 (82.6)	6 (100.0)	0.271
Bleeding	3 (13.0)	1 (16.7)	0.819
Others	2 (8.7)	1 (16.7)	0.351
Tumor size diameter (cm), median (IQR)	15,740 (2954)	5260 (3295)	0.399
Bilateral	0	1 (16.7)	0.046
FIGO stage			
IA	7 (30.4)	1 (16.7)	0.492
IC1	3 (13.0)	0	
IC2	5 (21.7)	1 (16.7)	
IC3	2 (8.7)	0	
IIA	2 (8.7)	1 (16.7)	
IIB	2 (8.7)	1 (16.7)	
IIIB	1 (4.3)	0	
IIIC	1 (4.3)	1 (16.7)	
IVB	0	1 (16.7)	
Treatment			
Surgery			
Laparoscopy	0	0	N/A
Laparotomy	23 (100.0)	6 (100.0)	
Adjuvant chemotherapy	11 (47.8)	3 (50.0)	0.964
Complete surgical staging	22 (95.6)	5 (83.3)	0.289
Appendectomy	17 (73.9)	4 (66.7)	0.724
Bilateral pelvic lymph node dissection	21 (91.3)	3 (50.0)	0.017
Paraaortic lymph node dissection	16 (69.6)	3 (50.0)	0.369
Fertility sparing staging	6 (26.1)	2 (33.3)	0.724
Mortality	8 (34.8)	4 (66.7)	0.158

MOC: Mucinous epithelial ovarian carcinoma, IQR: Interquartile range, FIGO: International Federation of Gynecology and Obstetrics, N/A: Not available

Paraaortic lymph node dissection was done in 69.6% of patients with expansile type MOC and 50.0% of those with infiltrative type. Fertility sparing staging was done in 26.1% of patients with expansile type MOC and 33.3% of those with infiltrative type.

Chemotherapy

It was observed that 47.8% of those with mucinous ovarian carcinoma with expansile type had adjuvant systemic chemotherapy while 50.0% of those with infiltrative type MOC had adjuvant systemic chemotherapy.

Mortality

Mortality was higher in those with infiltrative type MOC (66.7%) compared to those with expansile type (34.8%), but the difference was not significant (P = 0.158). All patients who survived have no evidence of disease during the last follow-up time.

Response and survival

The factors associated with overall mortality were MOC type (expansile, hazard ratio [HR] = 0.3, 95% confidence interval [CI] = 0.07–0.91, P = 0.047 vs. infiltrative, HR = 3.3, 95% CI = 1.1–13.5, P = 0.047). This means that those with infiltrative type MOC were 3.3 times more likely to die. Bilateral disease was also associated with 14 times higher risk for mortality (HR = 14.0, 95% CI = 1.3–154.4, P = 0.031). Complete surgical staging was associated with 0.04 times decrease in risk for mortality (HR = 0.04, 95% CI = 0.003–0.4, P = 0.0007). The other variables tested did not show significant association with mortality [Table 2].

Median OS was significantly higher in patients with expansile type MOC (42 months) compared to infiltrative (25 months) (P = 0.039) [Figure 1].

Median OS was comparable between patients who had adjuvant therapy (46 months) and those who did not (38 months) (P = 0.562) [Figure 2].

Discussion

In this study, 23 (79.3%) cases with expansile and 6 (20.7%) with infiltrative invasion were included. This

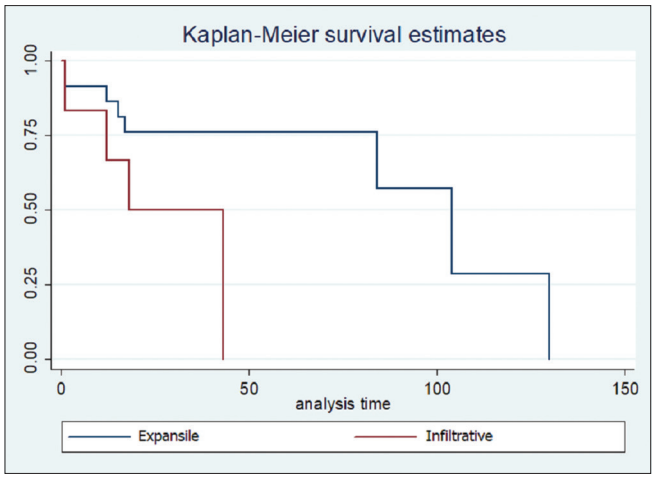

Figure 1: Kaplan–Meier survival for overall survival by MOC type

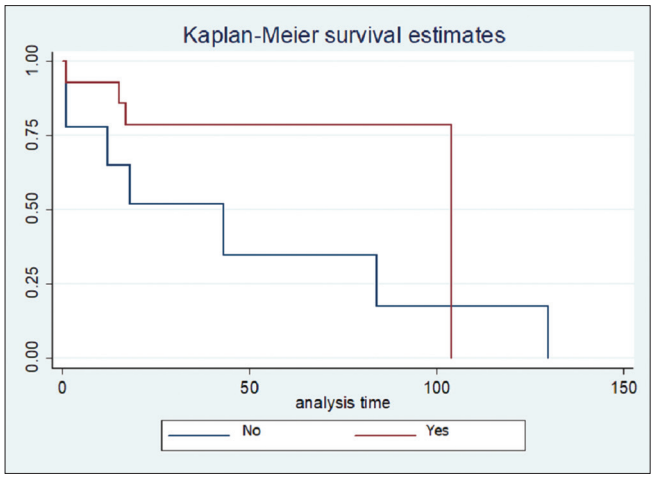

Figure 2: Kaplan–Meier survival for overall survival by adjuvant therapy

Table 2: Risk for mortality associated with each variable

	Hazard's ratio	*P*
MOC type		
Expansile	0.3 (0.07–0.91)	0.047
Infiltrative	3.3 (1.1–13.5)	0.047
Increasing age	1.0 (1.0–1.1)	0.561
Symptoms		
Abdominal pain	0.6 (0.1–2.8)	0.516
Increased abdominal volume	0.2 (0.04–1.3)	0.094
Bleeding	0.9 (0.1–7.4)	0.938
Urinary symptoms	1.0 (0.9–1.0)	1.000
Others	0.9 (0.1–6.3)	0.976
Increasing tumor size	1.0 (0.9–1.0)	0.230
Preoperative baseline Ca125	1.0 (0.9–1.0)	0.827
Bilateral	14.0 (1.3–154.4)	0.031
Increasing FIGO stage	1.0 (0.9–1.0)	0.331
Adjuvant chemotherapy	0.4 (0.1–1.4)	0.142
Complete surgical staging	0.04 (0.003–0.4)	0.007
Appendectomy	0.7 (0.2–2.4)	0.573
Bilateral pelvic lymph node dissection	0.5 (0.1–1.8)	0.273
Paraaortic lymph node dissection	0.5 (0.2–1.8)	0.305
Fertility sparing staging	0.8 (0.2–4.0)	0.797

MOC: Mucinous epithelial ovarian carcinoma, FIGO: International Federation of Gynecology and Obstetrics

overall prevalence of the specific type of MOC is different from other studies wherein, infiltrative invasion was relatively more frequently diagnosed (135 of 250 cases, 54%).[7]

In this study, the median age was 43 years for those with expansile type MOC and 53 years for those with infiltrative. Mucinous carcinoma usually occur as a large, multiloculated cystic mass with mucus-containing fluid and the mean size at presentation is 18 cm. Mucinous tumors can become extremely large and fill the entire abdominopelvic cavity.[1] In this study, the most common symptoms among those with expansile type MOC were increased abdominal girth (82.6%) and abdominal pain (30.4%). The most common symptom among those with infiltrative type MOC was increased abdominal girth (100.0%).

Most primary MOCs are unilateral. In one database, 79% of mucinous tumors were unilateral. Furthermore, in the said database analysis, 21.3% of women with primary MOCs had bilateral involvement significantly less than in serous ovarian cancers, in which 57.5% of women had bilateral involvement.[6] In our study, only one patient with infiltrative type MOC (16.7%) had bilateral disease and none in expansile type (0.0%) ($P = 0.046$).

Most of the patients had FIGO Stage IA (27.6%) disease. This is contrary to other studies wherein majority (83%) of patients with MOCs after surgery were diagnosed as Stage I and only 17% of patients with MOCs were Stage II or higher.[1,6]

This study also highlighted that the median OS was significantly higher in patients with expansile type (42 months) compared to infiltrative (25 months) ($P = 0.039$). Multivariate analysis also showed that overall mortality was associated with the MOC type (expansile, HR = 0.3, 95% CI = 0.07–0.91, $P = 0.047$ vs. infiltrative, HR = 3.3, 95% CI = 1.1–13.5, $P = 0.047$). This means that those with infiltrative type MOC are 3.3 times more likely to experience mortality. This finding was similar to Hada *et al*. wherein cases with an infiltrative invasion pattern were discovered at a more advanced stage, had a higher recurrence rate, and higher mortality rate (33% vs. 9%, $P < 0.01$) and showed worse prognosis than cases with expansile invasion.[8] Although previous reports identified MOC as a nonaggressive tumor,[9] MOC with infiltrative invasion was considered to be an aggressive subtype. The MOC type was associated with overall mortality as shown in this study (expansile, HR = 0.3, 95% CI = 0.07–0.91, $P = 0.047$ vs. infiltrative, HR = 3.3, 95% CI = 1.1–13.5, $P = 0.047$).

Studies reported recurrences in Stage II or III disease, but not in early Stage I.[9] In this study, the recurrence rate and PFS could not be accurately identified since imaging studies could no longer be located in the records and some patients were lost to follow-up. Only the OS can be accurately determined which is the period from the day of surgery to the day of death or the last confirmation of survival.

The favorable prognosis of MOC of the expansile type was demonstrated by Lee and Scully in 2000 who classified these tumors as noninvasive "intra-glandular carcinomas."[5,10] In this study of 29 patients with primary invasive mucinous carcinoma, for Stage I (n = 19), the invasion type was expansile in 17 patients and infiltrative in two patients. Six patients with expansile showed advance STAGE (II–IV) and four patients with infiltrative pattern.

Despite the low percentage of patients with epithelial ovarian cancer who have a primary MOC, the conclusions drawn from these randomized studies have been applied to MOCs until recently. This phenomenon is problematic for all rare tumors, as rare tumors are grouped together with more common tumors regardless of real differences. Multiple authors have shown MOCs to be platinum resistant. Published response rates among 24 women with MOC were 12.5%, compared to 67.7% among 189 women with serous ovarian carcinoma.[9]

Following the 2015 local guidelines of the Society of the Gynecologic Oncologist of the Philippines, the primary treatment for all primary MOCs is surgery. Those with Stage IC and higher requires adjuvant systemic chemotherapy. To date, there is still no widely accepted consensus whether to give adjuvant systemic chemotherapy but some clinicians may give systemic chemotherapy for infiltrative type of MOC.[11] It has been postulated that therapeutic strategy for MOC should be redefined, since these tumors behave more aggressively in the advanced stage and have different responsiveness to conventional cytotoxic therapy for epithelial ovarian cancers.[10] Mucinous ovarian carcinomas are not chemosensitive.[9] In one retrospective study in Japan, cases with infiltrative invasion were more frequently treated with adjuvant chemotherapy and more often showed recurrence.[8] Our study, however, showed different results in that almost same percentage of those with expansile type MOC (47.8%) and infiltrative type MOC (50%) received adjuvant chemotherapy, even though the aggressiveness of the latter is higher. In previous years, chemotherapy is considered in FIGO Stage IC ovarian epithelial cancers and above. In our study, the median OS was comparable between patients who had adjuvant therapy (46 months) and those who did not (38 months) (P = 0.562). Recently, adjuvant chemotherapy for Stage IA MOC infiltrative type is already being done. For the mucinous subgroup, the expansile or grade I type is associated with better prognosis and should not receive adjuvant chemotherapy, while the infiltrative form is associated with a high risk of relapse.[12]

The gold standard for the treatment of any suspected ovarian mass includes intact removal of the involved adnexa with intraoperative pathology evaluation. This has historically been laparotomy, total hysterectomy, bilateral salpingo-oophorectomy, and staging procedure including lymphadenectomy. Since most mucinous tumors of the ovary are large, most surgeons will perform an exploratory laparotomy with removal of the involved adnexa. If the patient is postmenopausal, a total hysterectomy and bilateral salpingo-oophorectomy may be considered regardless of the histology. However, many patients are premenopausal, and the unilateral nature of most mucinous tumors, whether benign, borderline, or invasive primary ovarian cancers, allow fertility preservation with conservation of the normal appearing uterus and contralateral ovary in apparent early stage disease.[9]

The benefit of complete surgical staging should also be emphasized. Mucinous carcinomas exhibiting expansile invasion have been reported to have a lower risk of metastasis than those exhibiting infiltrative invasion. The incidence of lymph node metastases in Stage I–II MOC is about 2.6% (versus 23.3% in Stage I–II serous ovarian cancers) in a review of eight studies with 155 patients.[8] Expansile MOC is mainly diagnosed in Stage I and is not associated with lymph node metastases, whereas in the same study, infiltrative MOC has a worse prognosis and is associated with lymph node metastases.[10] In this study, complete surgical staging was done in 95.6% of patients with expansile type MOC and 83.3% of those with infiltrative type.

Conclusion

The most common MOCs in this institution for 5 years were expansile type contrary to the literature abroad. The invasive patterns were associated with prognoses similar to previous reports. Particularly, infiltrative invasion was observed to be a prognostic factor showing worse outcomes for ovarian mucinous carcinoma compared to expansile infiltration.

The factors associated with overall mortality were: (1) MOC type wherein infiltrative type MOC are 3.3 times more likely to experience mortality; (2) Bilateral disease was also associated with higher risk for mortality, and (3) complete surgical staging was associated with decrease in risk for mortality.

Limitations and recommendations

This study had some limitations, including the small sample size from a single institution and retrospective

analysis. The next studies related to this topic should be prospective and higher number of cases is needed to confirm the clinical significance of the specific types of MOC. Future studies should also evaluate the clinicopathological factors and prognosis of MOC with infiltrative invasion, MOC with expansile invasion and other epithelial ovarian cancers such as serous carcinoma. A more comprehensive database should also be established with this specific type of ovarian cancer which includes demographics and other clinical and histopathological findings for easier retrieval of information in future.

Implication on clinical practice

Routine reporting of the specific subtypes of MOCs should already be included in histopathological reports since clinical outcomes between the different subtypes are different as shown in this study. In terms of clinical practice, a more aggressive administration of adjuvant treatment should be employed for infiltrative type of MOC. Treatment options tailored to the mucinous carcinoma should be considered in future studies since it has worse chemosensitivity compared to other epithelial ovarian cancers.

Authorship contributions

Jay Ian R. Argel - Involved in the conceptualization, methodology, validation, formal analysis, data curation, visualization, Writing- Original Draft, Writing- Review and Editing, supervision.

Renee Vina G. Sicam - Involved in the conceptualization, methodology, formal analysis, data curation, visualization, Writing- Review and Editing , supervision.

Jonathan P. Rivera - Involved in the conceptualization, methodology, validation, formal analysis, resources, Writing- Original Draft.

Joeanne Marie M. Salise - Involved in the conceptualization, methodology, validation, formal analysis, Writing- Original Draft, resources.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, J.I..R.A.

References

1. Brown J, Frumovitz M. Mucinous tumors of the ovary: Current thoughts on diagnosis and management. Curr Oncol Rep 2014;16:389.
2. WHO Classification of Tumors Editorial Board. Female Genital Organs. 5th ed. Lyon: International Agency for Research on Cancer; 2020.
3. Babaier A, Ghatage P. Mucinous cancer of the ovary: Overview and current status. Diagnostics (Basel) 2020;10:52.
4. Redaniel MT, Laudico A, Mirasol-Lumague MR, Gondos A, Uy GL, Toral JA, *et al.* Ovarian cancer survival population differences: A "high resolution study" comparing Philippine residents, and Filipino-Americans and Caucasians living in the US. BMC Cancer 2009;9:340.
5. Lee KR, Scully RE. Mucinous tumors of the ovary: A clinicopathologic study of 196 borderline tumors (of intestinal type) and carcinomas, including an evaluation of 11 cases with 'pseudomyxoma peritonei'. Am J Surg Pathol 2000;24:1447-64.
6. Boger-Megiddo I, Weiss NS. Histologic subtypes and laterality of primary epithelial ovarian tumors. Gynecol Oncol 2005;97:80-3.
7. Hess V, A'Hern R, Nasiri N, King DM, Blake PR, Barton DP, *et al*. Mucinous epithelial ovarian cancer: A separate entity requiring specific treatment. J Clin Oncol 2004;22:1040-4.
8. Hada T, Miyamoto M, Ishibashi H, Matsuura H, Sakamoto T, Kakimoto S, *et al.* Survival and biomarker analysis for ovarian mucinous carcinoma according to invasive patterns: Retrospective analysis and review literature. J Ovarian Res 2021;14:33.
9. Gouy S, Saidani M, Maulard A, Bach-Hamba S, Bentivegna E, Leary A, *et al*. Characteristics and prognosis of stage I ovarian mucinous tumors according to expansile or infiltrative type. Int J Gynecol Cancer 2018;28:493-9.
10. Muyldermans K, Moerman P, Amant F, Leunen K, Neven P, Vergote I. Primary invasive mucinous ovarian carcinoma of the intestinal type: Importance of the expansile versus infiltrative type in predicting recurrence and lymph node metastases. Eur J Cancer 2013;49:1600-8.
11. Society of Gynecologic Oncologists of the Philippines (Foundation), Inc. Clinical Practice Guidelines. 8th edition. Manila: OVT-Graphic Line Inc; 2019. p. 65-87.
12. Colombo N, Sessa C, Bois AD, Ledermann J, McCluggage WG, McNeish I, *et al*. ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. Int J Gynecol Cancer 2019;29:728-60.