Survival Outcomes by Histologic Subtype in Invasive Epithelial Ovarian Cancer: A Population-Based Study

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Background

- Epithelial ovarian cancer (EOC) comprises a diverse group of malignancies with distinct histologic subtypes—such as high- and low-grade serous, endometrioid, clear cell, and mucinous carcinomas—each exhibiting unique molecular profiles, clinical behavior, and survival outcomes. While high-grade serous carcinoma is the most common and initially responsive to chemotherapy, it often relapses and leads to poor long-term survival. In contrast, subtypes like clear cell and mucinous are more chemo-resistant, and low-grade serous and endometrioid carcinomas tend to have more favorable prognoses when detected early.
- Although recent population-based studies, including those using SEER data, have highlighted survival differences among these subtypes, gaps remain in understanding how these patterns vary across broader populations and healthcare settings. Further research using state-level cancer registry data is needed to refine prognostic tools, guide treatment decisions, and identify high-risk groups. This study aims to address these gaps by analyzing survival outcomes by histologic subtype using comprehensive data from the Louisiana Tumor Registry.

Objectives

Primary objective:
- To assess overall survival differences among ovarian cancer patients by histological subtype.

Secondary objective:
- To describe the distribution of histologic subtypes by demographic characteristics (e.g., age, race/ethnicity).

Kaplan Meier Curves

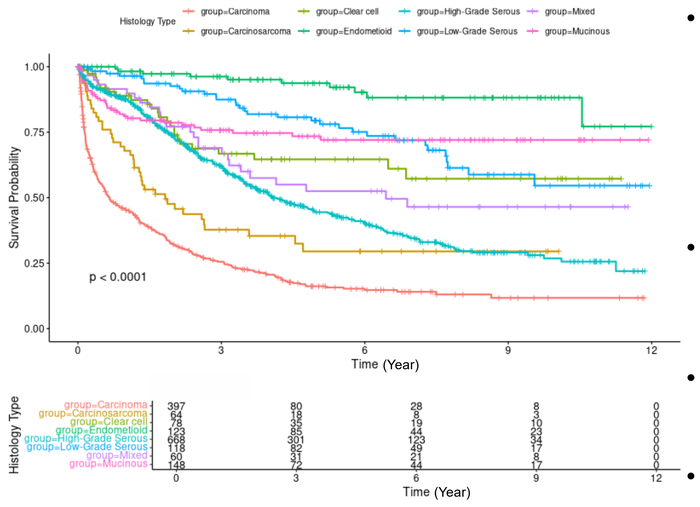

Figure 1: Kaplan-Meier survival curves of invasive epithelial ovarian cancer survival by histology type with log-rank test p-value < 0.0001.

- Log-rank test p-value is provided, indicating a significant difference in survival time among the histologic subtypes. Cox model yield similar results when the predictor is categorical and the proportional hazards assumption is satisfied.
- Carcinoma type has the lowest survival among all the histology types, while endometrioid type has the highest survival.
- Early divergence in the curves suggesting subtype-specific differences in early mortality.
- The numbers at risk for each histology type are listed in the lower panel.

Methods

- **Type of Study**: Retrospective cohort study
- **Eligibility Criteria**:
  1. Inclusion: First primary epithelial ovarian cancer diagnosed between 2010 and 2021; microscopically confirmed cases.
  2. Exclusion: Non-epithelial tumors (e.g., germ cell tumors, sex cord-stromal tumors); cases missing histology or vital status information.
- **Data Source**: Louisiana Tumor Registry
- **Variables**:
  1. *Continuous Variables*: Age at diagnosis, year of diagnosis
  2. *Sociodemographic Variables*: Race/ethnicity, marital status, insurance type, census-tract level poverty, urban/rural status
  3. *Clinical Variables*: Comorbidity, body mass index (BMI), stage at diagnosis, tumor grade.
- **Statistical Analysis**:
  1. Descriptive statistics for frequencies and proportions of histologic subtypes and demographic characteristics.
  2. Kaplan–Meier survival curves and log-rank tests to compare survival across histologic groups.
  3. Cox proportional hazards regression to estimate adjusted hazard ratios for death by histologic subtype, controlling for relevant covariates.
- **Software**: All analyses were conducted in R using the *survival*, *survminer*, and *ggplot2* packages.

Survival Rates by Histology Type

Category	1-Year Survival	2-Year Survival	5-Year Survival
Carcinoma	45.3% (40.5%–50.6%)	31.9% (27.5%–37.1%)	16.2% (12.6%–20.8%)
Carcinosarcoma	67.9% (57.2%–80.5%)	47.6% (36.5%–62.1%)	29.5% (19.0%–45.7%)
Clear cell	88.9% (81.9%–96.5%)	77.4% (67.8%–88.2%)	64.6% (53.6%–78.0%)
Endometioid	98.2% (95.8%–100.0%)	97.3% (94.3%–100.0%)	93.7% (88.9%–98.8%)
High-Grade Serous	87.6% (85.1%–90.2%)	73.4% (70.0%–77.1%)	44.5% (40.2%–49.2%)
Low-Grade Serous	96.5% (93.1%–99.9%)	92.6% (87.8%–97.7%)	79.4% (71.7%–88.0%)
Mixed	91.5% (84.6%–98.9%)	77.1% (66.9%–88.9%)	52.5% (40.0%–68.9%)
Mucinous	81.1% (74.8%–87.9%)	78.6% (72.0%–85.9%)	73.4% (66.0%–81.7%)

Table 1: (Survival Estimates by Histology (Cancer-Specific Death) 1, 2, and 5-Year Survival Rates with (95% Confidence Intervals)

Category	1-Year Survival	2-Year Survival	5-Year Survival
Carcinoma	42.5% (37.9%–47.7%)	29.4% (25.2%–34.3%)	14.5% (11.2%–18.7%)
Carcinosarcoma	67.9% (57.2%–80.5%)	45.8% (34.8%–60.4%)	27.2% (17.3%–42.8%)
Clear cell	83.6% (75.5%–92.5%)	70.2% (60.2%–81.8%)	58.7% (47.9%–71.9%)
Endometioid	94.9% (91.0%–99.0%)	92.2% (87.4%–97.2%)	84.5% (77.7%–91.9%)
High-Grade Serous	86.0% (83.3%–88.7%)	71.1% (67.5%–74.8%)	40.8% (36.7%–45.4%)
Low-Grade Serous	94.8% (90.9%–98.9%)	89.3% (83.7%–95.2%)	71.3% (62.9%–80.9%)
Mixed	91.5% (84.6%–98.9%)	74.0% (63.4%–86.2%)	47.5% (35.6%–63.5%)
Mucinous	78.6% (72.1%–85.7%)	73.1% (66.1%–81.0%)	67.5% (59.9%–76.2%)

Table 2: (Survival Estimates by Histology (All-Cause Death) 1, 2, and 5-Year Survival Rates with (95% Confidence Intervals)

From Table 1 & 2, we see the survival rates for carcinoma subtype are significantly lower than the rest of the histological subtypes in 1-, 2- and 5-years for both models, followed by the carcinosarcoma subtype. However, the differences are more obvious in the early time (i.e. 1-year survival).

Predictor	Hazard Ratio	95% CI Lower	95% CI Upper
Age at Diagnosis	1.01	1.01	1.02
Summary Stage: localized vs. distant	0.13	0.08	0.20
Regional vs. distant	0.38	0.29	0.48
Insurance: Medicare/Other public vs. Medicaid	1.00	0.74	1.36
Private vs. Medicaid	0.71	0.53	0.94
Uninsured/unknown vs. Medicaid	1.17	0.71	1.93
Grade: 2 vs. 1	1.85	1.04	3.31
3 vs. 1	1.87	0.92	3.81
4 vs. 1	2.16	1.03	4.50
BMI: Obese vs. Normal	0.82	0.65	1.04
Overweight vs. Normal	0.81	0.64	1.03
Under Weight vs. Normal	1.01	0.63	1.63
Unknown vs. Normal	0.67	0.46	0.98
Histology Type: Carcinosarcoma vs. Carcinoma	0.57	0.31	1.04
Clear cell vs. Carcinoma	0.62	0.35	1.12
Endometioid vs. Carcinoma	0.22	0.10	0.50
High-Grade Serous vs. Carcinoma	0.54	0.40	0.73
Low-Grade Serous vs. Carcinoma	0.32	0.16	0.61
Mixed vs. Carcinoma	0.72	0.43	1.22
Mucinous vs. Carcinoma	0.54	0.28	1.06
CCI: No vs. more	0.81	0.57	1.15
One vs. more	0.82	0.55	1.20
Marital Status: Not Married vs. Married	1.04	0.85	1.26
Race: NH-White vs. NH-Black	0.91	0.73	1.14
Poverty: 0%-<20% vs. >20%	1.00	0.82	1.21

Table 3: Cox Proportional Hazards Model Summary (cancer specific death)

Predictor	Hazard Ratio	95% CI Lower	95% CI Upper
Age at Diagnosis	1.02	1.01	1.03
Summary Stage: localized vs. distant	0.21	0.15	0.30
Regional vs. distant	0.41	0.33	0.51
Insurance: Medicare/Other public vs. Medicaid	0.87	0.66	1.15
Private vs. Medicaid	0.69	0.53	0.90
Uninsured/unknown vs. Medicaid	1.12	0.71	1.77
Grade: 2 vs. 1	1.77	1.11	2.82
3 vs. 1	1.94	1.06	3.53
4 vs. 1	2.13	1.14	4.00
BMI: Obese vs. Normal	0.84	0.67	1.05
Overweight vs. Normal	0.83	0.66	1.03
Under Weight vs. Normal	1.09	0.70	1.71
Unknown vs. Normal	0.77	0.55	1.09
Histology Type: Carcinosarcoma vs. Carcinoma	0.58	0.32	1.03
Clear cell vs. Carcinoma	0.59	0.34	1.03
Endometioid vs. Carcinoma	0.45	0.24	0.85
High-Grade Serous vs. Carcinoma	0.56	0.42	0.75
Low-Grade Serous vs. Carcinoma	0.42	0.23	0.76
Mixed vs. Carcinoma	0.71	0.43	1.18
Mucinous vs. Carcinoma	0.66	0.37	1.17
CCI: No vs. more	0.64	0.48	0.87
One vs. more	0.67	0.48	0.94
Marital Status: Not Married vs. Married	1.03	0.86	1.24
Race: NH-White vs. NH-Black	0.91	0.74	1.13
Poverty: 0%-<20% vs. >20%	1.03	0.86	1.24

Table 4: Cox Proportional Hazards Model Summary (all-cause death)

From Table 3 & 4, we found age, early-stage classification (summary_stage1localized/regional) and grade levels (grade_combined2-4), insurance, and histology subtype indicator for endometioid, high and low grade serous are all significant in both models. Note that the carcinoma histology subtype is used as the baseline group. Since all histology subtype indicators are negative, it indicates the carcinoma subtype has the lowest survival compared with other types. The Charlson comorbidity index (CCI) are significant in all-cause death model. This is because that CCI was originally developed to predict the 1-year mortality from a range of non-cancer comorbid conditions (e.g. heart disease, diabetes, COPD). Therefore, CCI is better at predicting non-cancer deaths than cancer-specific deaths.

Histology vs. Predictors

Predictor	P-Value	Carcinoma	Carcino-sarcoma	Clear cell	Endom-etioid	High-Grade Serous	Low-Grade Serous	Mixed	Mucinous
Age at Diag.	0.00	69.29	66.48	57.83	54.97	62.92	56.53	59.57	55.59
Stage: distant	0.00	304	42	22	17	456	59	26	33
localized		15	3	35	69	59	26	16	82
regional		57	16	20	36	147	33	18	30
Medicaid	0.00	65	9	11	22	98	19	6	41
Medicare/Other		184	26	14	25	229	34	14	29
Private		125	23	50	72	317	55	38	67
Uninsured		23	6	3	4	24	10	2	11
Grade: 1	0.00	9	1	0	48	0	52	5	41
2		10	1	5	75	0	66	9	57
3		70	22	34	0	520	0	27	16
4		5	6	7	0	148	0	9	2
BMI: Normal	0.01	96	25	22	27	167	29	16	43
Obese		127	21	33	54	222	45	24	54
Overweight		101	15	18	27	208	33	16	39
Under Weight		10	0	2	3	22	1	1	3
Unknown		63	3	3	12	49	10	3	9
CCI: more	0.00	68	3	5	9	56	4	5	14
No		257	57	65	93	485	102	48	118
one		72	4	8	21	127	12	7	16
Married or partner	0.00	138	31	45	61	354	51	37	63
Not Married		248	33	32	59	297	61	23	83
Race: NH-Black	0.04	120	19	15	24	165	30	8	41
NH-White		277	45	63	99	503	88	52	107

Conclusion

- **Histology type is a strong predictor of ovarian cancer survival:** Patients with carcinoma and carcinosarcoma exhibit significantly worse survival outcomes, while those with endometrioid histology show better survival rates.
- **Histology types correlate with key patient and tumor characteristics:** Significant associations were observed between histology and variables such as age at diagnosis, year of diagnosis, cancer stage, insurance type, cancer grade, BMI category, Charlson Comorbidity Index, and marital status.
- **Carcinoma and carcinosarcoma** are associated with older age at diagnosis, more advanced cancer stages, higher tumor grades, and a higher proportion of Non-Hispanic Black patients.

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