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Clinical Characteristics and Survival of Patients with Malignant Ovarian Tumors in Addis Ababa, Ethiopia

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Ovarian neoplasms • Ovarian cancer • Survival • Africa • Ethiopia

Abstract

Background. Ovarian cancer is the third leading cause of cancer death among women in Ethiopia, with about 2,550 diagnosed cases and 2,000 deaths each year. The incidence and mortality rates of this disease have been increasing in Ethiopia and other parts of sub-Saharan Africa over the past decades because of changing lifestyle and reproductive factors. In this study, we describe the clinical characteristics, treatment patterns, and survival of patients with ovarian cancer in Ethiopia.

Materials and Methods. This retrospective cohort study included 485 patients diagnosed between January 2009 and October 2015 at Addis Ababa University Hospital, Zewditu Memorial Hospital, or registered in the Addis Ababa population-based cancer registry. Follow-up data were obtained via telephone. Primary endpoint was all-cause mortality.

Results. The median age was 46 years (range, 11–95). The estimated 1- and 2-year overall survival rates were 78% (95% confidence interval [CI] 0.741–0.82.5) and 59% (95% CI, 0.538–0.646), respectively. Of those patients with result available (n = 423), 73.0% had epithelial cancers. Almost half were classified as Federation of Gynecology and Oncology stage III or IV (48.2%; stage available n = 201) resulting in worse outcomes (hazard ratio [HR], 2.91 [CI 0.67–12.64] and 3.03 [0.69–15.79], respectively). Four out of five patients received some form of surgery (82%), three out of five received platinum-containing chemotherapy. Patients with residual tumor after surgery (n = 83) showed worse survival outcome (HR, 2.23; 95% CI 1.08–4.49).

Conclusion. Our study revealed substantial treatment gaps with respect to surgery and adequate chemotherapy. Higher stage, residual tumor and lack of chemotherapy impaired the outcome. Access to higher standards of ovarian cancer treatment is urgently needed in Ethiopia. ***The Oncologist*** 2019;24:e303–e311

Implications for Practice: Ovarian cancer is often a fatal disease in high resource settings; now it is also becoming important in Ethiopia. This study included 485 women with malignant ovarian tumors treated in Addis Ababa who had a mean age of only 46 years because of the young population structure. Three quarters had the typical epithelial cancer, with half presenting with advanced stage III and IV. Improved oncologic surgery and sufficient chemotherapy could possibly improve their outcome. The relatively high proportion of women with nonepithelial cancer need adequate treatment options to have good prognosis.

Introduction

Ovarian cancer (OC) is the seventh most common cancer diagnosis and the eighth leading cause of cancer death in women worldwide, with 238,719 cases and 151,917 cancer deaths in 2012. Incidence rates vary geographically, with the highest rates reported from Northern America and Europe and the lowest from Africa and South America. Over the past decade incidence rates have increased in low- and middle-income countries. In sub-Saharan Africa and Ethiopia, OC is the third most common diagnosed cancer among women, with an estimated number of 12,705 and 2,550 cases in 2012, respectively [1–5].

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Studies suggest that there are high incidence rates of OC in countries with high development index (HDI); similarly HDI countries demonstrate higher prevalence of known OC risk factors including nulliparity/low parity, advanced age, hormone replacement therapy and family predisposition [6]. Increasing life expectancy and a more westernized lifestyle has led to rising numbers in countries with a low development index (LDI) [7, 8]. The above-mentioned risk factors are associated with epithelial tumors, which account for 90% of all ovarian cancers [9]. The remaining nonepithelial tumors include germ cell and sex cord-stromal tumors [10]. Risk factors, treatment, and prognosis vary greatly depending on the histologic subtype [11]. Borderline ovarian tumors behave like malignant tumors but in in less aggressive fashion with significantly better outcome over malignant ovarian tumors [12, 13]

Even in high-income countries, OC has poor prognosis [5]. The 5-year survival rate for OC is between 30%–41% [2, 11]. The absence of effective screening methods complicates early detection [14]. Survival is mainly effected by the extent of disease spread at diagnosis, reflected in the Federation of Gynecology and Oncology (FIGO) stage; access to adequate oncologic surgery, because optimal surgery with tumor free postoperative status is an important prognostic factor [15]; and the delivery of adequate platinum-taxane-based combination chemotherapy. Because of the poor prognosis of OC, palliative care and pain management are important aspects of OC therapy [16].

Ethiopia is the second most populous country in sub-Saharan Africa, with an estimated 102 million population in 2016 and more than 51 million women [17]. With approximately 80% of the population living in rural areas, Ethiopia is one of the least urbanized countries in the world [17, 18]. Generally, delay in diagnosis contributes to large proportion of OC in sub-Saharan African presenting in advanced stages of cancer, thus impairing outcome [8]. Low access to adequate medical care specialized for cancer treatment additionally negatively affects the outcome of patients with OC [19]. In 2013, only four gynecologic oncologists were performing surgeries on OC in Ethiopia [20]. Access to chemotherapy and palliative care is a challenge to oncology care in Ethiopia and other parts of Africa, compounded by the rising cancer burden [21]. In Ethiopia, 90% of all patients with cancer report problems accessing palliative care services [22].

The rising burden of ovarian tumors in Ethiopia is prospectively captured in a population-based cancer registry of Addis Ababa, Ethiopia [23]. The Addis Ababa City Cancer Registry (AACCR) registered patients reported from Addis Ababa health facilities with histological verification or strong clinical evidence from 19 centers in town, including pathology centers, oncology clinics, the main referral hospitals, and diagnostic facilities. The objective of our study was to evaluate clinical and pathological characteristics, along with therapy provided including pain and palliative care management, and overall survival of patients with ovarian malignancies (OM) of all histologic types. This analysis included patients treated at two major referral hospitals and the population-based cancer registry of Addis Ababa, Ethiopia. Because palliative care was not well developed in Ethiopia, special focus was given to ascertain information about symptoms and therapy received. This is the first study to report on the current pattern of ovarian malignancies and treatment outcome in referral hospitals in Ethiopia.

Materials and Methods

Patient Selection

We used data from consecutive patients treated from 2009–2015 in hospitals and a population-based cohort from 2011–2015 with malignant ovarian tumors to construct a retrospective cohort. We included women who were treated at the Department of Gynecology and the Oncology Center at Black Lion Hospital (BLH) Addis Ababa University and the Department of Gynecology at Zewditu Memorial Hospital (ZMH; referred to as "clinical patients"). The population-based cohort included patients registered in the AACCR (referred to as "registry patients") (Fig. 1). The AAACR cohort includes Addis Ababa residents from 19 centers in Addis Ababa city including BLH and ZMH hospital registry. In total, 263 registry patients were captured through the registry but additional clinical information was not traced. A total of 86 clinical patients were captured in both, 100 clinical patients were captured with diagnosis before start of the registry, and 36 clinical patients with files retrieved but missed by population-based registration. Patients are included into AAACR registry with histologic verification. We found no difference between the characteristics of the two groups and decided to analyze them together resulting in a cohort of 485 patients (total cohort) with OM in Addis Ababa region.

In BLH and ZMH, 683 patients received therapy for an ovarian abnormality; 222 of these patients with files available were diagnosed with malignant ovarian tumors between January 2009 and October 2015. Central review of histopathology was not possible; cases were processed according to standards of the ten local laboratories. For these clinical patients, patient characteristics, clinical information such as therapy, and outcome information were abstracted from patient files. Additionally, 349 patients with malignant ovarian tumors were registered in the AACCR between September 2011, when the cancer registry started, and October 2015. About half of the cases (n = 189, 54%) originated from BLH; the other participating hospitals registered 1–37 cases in this period. Of those 349 patients, 86 patients were duplicates in clinical cases from either BLH or ZMH registry, and those were merged. Finally, 263 cases were included in the study. For these registry patients, only data on the date of diagnosis, topology, and histology such as date of last contact was collected; no detailed information on clinical aspects or therapy was available.

Histologically verified diagnosis of an OM (International Classification of Disease for Oncology-O-3 codes C56.9) was available for 423 patients, and 5 patients had a positive cytology only. Tumor histology was grouped into epithelial tumor (n = 355), germ cell tumor (n = 40), sex cord-stromal tumor (n = 15), and borderline tumor (n = 13) using the World Health Organization classification of tumors of the ovary (updated version from 2013) [24]. Additionally, 57 patients were diagnosed based on strong clinical evidence without histological verification.

Follow-up information on survival status and date of last contact was collected via telephone contact with patients or

their relatives by trained staff of the AACCR. If a person could not be reached by telephone or the telephone number was missing, the last date recorded in the file was used as date of last contact (n = 126).

In 13 cases, the date of death given by the relatives was in contradiction to a later date of last contact in the file. Assuming the date in the file was reliable, date of death was assumed to be 3 months after the date of last contact in the file, because this was the time between regular follow-up visits.

Staging

Tumors were classified according to the International FIGO staging system [25]. Information on stage was extracted from surgical operative and pathology report. Patients without surgery were classified according to clinical findings and additional imaging such as chest x-ray, abdominal ultrasound, or computed tomography (CT) scan and, if performed, cytology of pleural effusion or ascites. In cases of distant metastases mentioned in chest x-ray, abdominal ultrasound, or CT scan, the stage was classified as IVB.

Treatment modalities

Characteristics of treatment were described for patients with information available. For clinical patients, information was taken from the patient clinical files. For registry patients, information from AACCR was supplemented by basic questions from the telephone interview about surgery and/or chemotherapy. For evaluation of survival, we included clinical patients with histologically verified epithelial tumors and who received an oncologic surgery (n = 125).

Surgeries reported included bilateral or unilateral salpingo-oophorectomy, abdominal hysterectomy, and omentectomy. Adjuvant chemotherapy was classified as cisplatinum/cyclophosphamide (6 cycles with 60–75 mg per m^2/650–900 mg per m^2), cisplatinum/paclitaxel (6 cycles with 60–75 mg per m^2/175 mg per m^2), carboplatin/paclitaxel (AUC-5 per $m^{2/}$175 mg per m^2), or cisplatinum only (doses unknown), according to international standard protocols. Information on the type of chemotherapy was missing in three cases. If the patient did not receive all six cycles of chemotherapy, therapy was considered as incomplete.

Statistical Analysis

The primary endpoint of the study analysis was overall survival. Person time was the time from the date of pathologic diagnosis or, if not available, from the date of first presentation to the hospital for this complaint (n = 51) to the date of last contact. The median follow-up time for the surviving patients was 21 months (range, 0.1–78.8). To estimate the adjusted and unadjusted hazard ratios and the corresponding 95% confidence intervals for prognostic factors, we used a multivariate cox proportional hazard regression model. We conducted analyses using statistical software SPSS (IBM, Armonk, NY).

Ethical approval was obtained from the Institutional Review Board of the College of Health Science Addis Ababa University and by the Ethiopian Public Health Research Institute.

Results

Patient Characteristics

The majority of patients originated from Addis Ababa (n = 375, 77%). The median age was 47 (range, 11–95), and mean number of pregnancies was three (range, 0–10). Data on contraceptive use and HIV status were rarely available; only 18 women indicated ever having used contraceptives (4%), and 10 women were known to be HIV positive (2.1%; Table 1). Epithelial tumor was the most common histology in the cohort (total n = 355, 73.0%; adenocarcinoma not otherwise specified [NOS] n = 184, serous n = 121, mucinous n = 41, endometroid n = 4, clear cell n = 2, transitional n = 2, carcinosarcoma n = 1). Second most common histology was germ cell tumor (total n = 40, 8.2%; immature teratomas, n = 24, dysgerminoma n = 5, choriocarcinoma n = 3, sarcoma n = 3, yolk sac tumor n = 2, germinoma n = 1, embryonal carcinoma n = 1, mixed germ cell tumor n = 1). Third most common type was sex cord-stromal tumor (total n = 15, 3.0%; of those granulosa cell tumor n = 11, signet ring stroma tumor n = 4). Borderline tumors were the least common (total n = 13, 2.7%; borderline serous n = 12, borderline mucinous n = 1). Information on histology was missing for 62 cases (13.0%).

Of the clinical patients with detailed information from patient files available (n = 222), the majority presented with late symptoms, and very few were detected incidentally. We found abdominal swelling and abdominal pain as the most common symptoms. Further symptoms and signs included weight loss, palpable abdominal mass, and preoperative ascites. An elevated tumor marker cancer antigen (CA) 125 was found in about half the cases. Almost two thirds of the patients were classified as FIGO stage II or III, only 33 cases as FIGO stage I, and 40 cases as FIGO stage IV (Table 2).

Treatment Modalities

The majority of the patients received surgery (n = 400, 82%). Out of the clinical patients (all histologic types) with detailed surgical information (n = 222), bilateral salpingo-oophorectomy was frequently performed (n = 146, 55.3%), 28 patients received unilateral salpingo-oophorectomy (10.6%), hysterectomy was performed in 154 cases (58.3%), and omentectomy was performed in 106 cases (40.2%). A total of 283 patients received chemotherapy (59%). Most of the clinical patients were treated with cisplatinum and cyclophosphamide (n = 54, 19.0%), 38 were treated with cisplatinum and paclitaxel (13.4%), 16 received carboplatin and paclitaxel (5.6%), and 16 other patients varied chemotherapeutics agents (5.6%). The type of chemotherapy was unknown in 160 cases (56.3%). Pain medication was given to 64 patients (29%) only (Table 3).

Survival

During follow-up of the total cohort (n = 485), 190 patients died (39.3%). The overall 1-year survival rate was 78.3% (95% CI, 0.741–0.82.5), and the 2-year survival rate 59.2% (95% CI, 0.538–0.646; Fig. 2). The median survival time was 32.5 (estimate + uncertainty) months. The clinical patients showed a higher overall 1-year survival rate of 82.7% (95% CI, 0.773–0.881) compared with the population-based registry patients (73.9%; 95% CI, 0.677–0.801); the 2-year survival

Table 1. Socio-demographic and reproductive patient characteristics of the total cohort (n = 485)

Patient characteristics	Total, count (%)	Histologic subtype of tumor, count (%)				
		Epithelial, 84.0%[a]	Germ cell, 9.4%[a]	Sex cord-stromal, 3.5%[a]	Borderline, 3.1%[a]	Cyto only/ no patho
Total	485	355	40	15	13	62
Origin						
Addis Ababa	375 (77)	294 (83)	33 (83)	10 (67)	7 (54)	31 (50)
Not Addis Ababa	100 (21)	56 (16)	5 (13)	5 (33)	5 (38)	29 (47)
Unknown	10 (2)	5 (1)	2 (5)		1 (8)	2 (3)
Age						
<30	60 (12)	41 (12)	8 (20)	3 (20)	1 (8)	7 (11)
30–39	106 (22)	83 (23)	7 (18)	4 (27)	4 (31)	8 (13)
40–49	109 (23)	78 (22)	5 (13)	3 (20)	4 (31)	19 (31)
50–59	102 (21)	73 (21)	8 (20)	4 (27)	1 (8)	16 (26)
60–69	60 (12)	47 (13)	5 (13)		2 (15)	6 (10)
>70	42 (9)	28 (8)	6 (15)	1 (7)	1 (8)	6 (10)
Unknown	6 (1)	5 (1)	1 (3)			
Age, median (range)		47 (11–95)	47 (12–77)	42 (16–82)	48 (25–76)	48 (14–72)
Parity						
0–1	73 (15)	37 (10)	7 (18)	4 (27)	8 (62)	17 (27)
2–3	49 (10)	29 (8)	2 (5)	1 (7)	3 (23)	14 (23)
>4	70 (14)	36 (10)	4 (10)	1 (7)	2 (15)	27 (44)
Unknown	293 (61)	253 (71)	27 (68)	9 (60)		4 (6)
Usage of contraceptives						
Yes	18 (4)	10 (3)			1 (8)	7 (11)
No	85 (17)	41 (12)	5 (13)	5 (33)	6 (46)	27 (44)
Unknown	382 (79)	304 (86)	35 (88)	10 (67)	6 (46)	28 (45)
HIV status						
Positive	10 (2)	3 (1)	3 (8)	1 (7)	1 (8)	2 (3)
Negative	7 (1)	5 (1)				2 (3)
Unknown	468 (97)	347 (98)	37 (93)	14 (93)	12 (92)	58 (94)

[a]Cases with known histologies.
Abbreviations: Cyto, cytology; patho, pathology.

rate was 66.3% (95% CI, 0.591–0.735) in clinical patients and 51.8% (95% CI, 0.438–0598) in registry patients (Fig. 3).

We tested whether assumed prognostic factors were associated with survival in patients with operated epithelial tumors: age, FIGO stage, addition of chemotherapy to surgery, and presence of residual disease. The outcome of patients receiving surgery without chemotherapy was similar compared with patients receiving combined surgery and chemotherapy (HR, 1.07; 95% CI, 0.54–2.11). The presence of a residual tumor after surgery was associated with a worse survival (HR, 2.23; 95% CI, 1.08–4.49, Table 4). Interestingly, age and stage were not significantly associated with the outcome considering the limited power of the assembled cohort.

Discussion

Our study is the first to present clinical characteristics and survival of patients with malignant ovarian tumors in Ethiopia. The overall 1-year and 2-year survival rates in this selected cohort from hospital and population-based cases were 78% and 59%, respectively. Most patients were diagnosed with epithelial type of ovarian cancer and presented with stage 3 disease. A majority of the patients received some form of surgery, but only two thirds received adjuvant chemotherapy. For patients with epithelial tumors, residual tumor after surgery was the most important prognostic factor for adverse outcome. A trend of worse outcome for higher stage was seen.

Patient Characteristics: Age Distribution

The median age in this study was 47 years (in all patients and in patients with epithelial tumors only). In high-income countries the average age at diagnosis is comparatively higher, (e.g., in the U.S., 63 years; in Germany, 69 years) [2, 26]. Reports from other sub-Saharan countries also show lower median ages, such as 45 years in Ghana, 52 years in Nigeria, and 49 years in Senegal [27–29]. The low median age in our patient cohort is attributable to the population structure in Ethiopia, where more than half of the population is younger than 20 years. It also reflects the higher proportion of germ cell and sex cord-stromal tumors in this cohort population,

Table 2. Clinical and pathological characteristics of the clinical patients (*n* = 222)

Clinical information	Total, count (%)	Histologic subtype of tumor, count (%)				
		Epithelial	Germ cell	Sex cord-stromal	Borderline	Cyto only/no patho
Total	222	127	13	7	13	62
Abdominal swelling						
Yes	160 (72)	81 (64)	11 (85)	5 (72)	12 (92)	51 (82)
No	24 (11)	14 (11)	2 (15)	1 (14)		7 (11)
Unknown	38 (17)	32 (25)		1 (14)	1 (8)	4 (6)
Abdominal distension/pain						
Yes	181 (82)	96 (75)	12 (92)	5 (72)	11 (85)	57 (92)
No	9 (4)	6 (5)	1 (8)	1 (14)		1 (2)
Unknown	32 (14)	25 (20)		1 (14)	2 (15)	4 (6)
Vaginal bleeding						
Yes	32 (14)	19 (15)		3 (43)		10 (16)
No	143 (64)	71 (56)	12 (92)	4 (57)	11 (85)	45 (73)
Unknown	47 (22)	37 (29)	1 (8)		2 (15)	7 (11)
Weight loss						
Yes	108 (49)	59 (46)	7 (54)	2 (29)	6 (46)	34 (54)
No	39 (17)	15 (12)	3 (23)	3 (42)	4 (31)	14 (23)
Unknown	75 (34)	53 (42)	3 (23)	2 (29)	3 (23)	14 (23)
Mass palpable						
Yes	126 (57)	61 (48)	9 (70)	3 (43)	10 (77)	43 (69)
Distended abdomen	36 (16)	19 (15)	2 (15)	2 (29)	2 (15)	11 (18)
No	54 (24)	42 (33)	2 (15)	1 (14)	1 (8)	8 (13)
Unknown	6 (3)	5 (4)		1 (14)		
Preoperative ascites						
Yes	79 (36)	40 (31)	3 (23)	3 (43)	4 (31)	29 (47)
No	65 (29)	26 (20)	6 (46)	3 (43)	4 (31)	26 (42)
Unknown	78 (35)	61 (48)	4 (31)	1 (14)	5 (38)	7 (11)
CA125 elevated						
Yes	120 (54)	77 (61)	4 (31)	3 (43)	11 (84)	25 (40)
No	51 (23)	17 (13)	4 (31)	3 (43)	1 (8)	26 (42)
Unknown	51 (23)	33 (26)	5 (38)	1 (14)	1 (8)	11 (18)
FIGO stage						
I	33 (15)	11 (9)	3 (23)	1 (14)	2 (15)	16 (26)
II	61 (27)	31 (25)	3 (23)	3 (43)	5 (38)	19 (31)
III	67 (30)	46 (36)	4 (31)	2 (29)	3 (23)	12 (19)
IV	40 (18)	22 (17)	3 (23)	1 (14)	2 (15)	12 (19)
Unknown	21 (10)	17 (13)			1 (8)	3 (5)

Clinical patients from two main referral hospitals in Addis Ababa.
Abbreviations: CA125, cancer antigen 125; cyto, cytology; FIGO, International Federation of Gynecology and Obstetrics; patho; pathology.

typically diagnosed in younger women. Data from Germany showed 27% of patients with OC with a mutation in at least one risk gene; 21% were BRCA 1–2 positive [30]. The low median age in our cohort may also suggest a high rate of genetic mutations; genetic testing or family history was not available. Long-term effects of cytoreductive surgeries as well as short and long-term toxicities from chemotherapy need to be considered in these young patients, highlighting the importance of cancer survivorship. An increase of ovarian cancer cases can also be expected because life expectancy is rising in Ethiopia (50 to 67 years between 1995–2015) [17].

Treatment modalities

In our cohort, 82% of all patients received surgery. Generally, the prognosis of ovarian malignancies and especially epithelial ovarian cancer is poor, especially in countries with low access to optimal treatment [31]. Surgery is a critical component of malignant ovarian tumor management, and all patients need access to surgical therapy [15]. We were unable to describe surgical procedures in detail in this retrospective study, but from 166 conclusive surgical notes we found 50% reporting residual disease. This shows the limited availability of optimal surgery. This is most likely due to

Table 3. Characteristics of first medical care, treatment and surgery results

	Histologic subtype of tumor, count (%)					
Therapy information	**Total**	**Epithelial**	**Germ cell**	**Sex cord-stromal**	**Borderline**	**Cyto only/ no patho**
First health facility (*n* = 222 clinical patients)						
Health center	44 (20)	19 (15)	1 (8)	1 (14)	5 (38)	18 (29)
Hospital	153 (69)	89 (70)	8 (61)	6 (86)	7 (54)	43 (69)
Referral hospital	16 (7)	13 (10)	3 (23)			
Unknown	9 (4)	6 (5)	1 (8)		1 (8)	1 (2)
Surgery received (*n* = 485 total cohort)						
Yes	400 (82)	283 (79)	35 (88)	12 (80)	13 (100)	57 (92)
No	85 (18)	72 (20)	5 (13)	3 (20)		5 (8)
Residual tumor (*n* = 215 operated patients among clinical patients)						
Yes	83 (39)	51 (41)	4 (31)	1 (14)	5 (38)	22 (39)
No	83 (39)	32 (26)	7 (54)	4 (57)	8 (62)	32 (56)
Unknown	49 (22)	42 (33)	2 (15)	2 (29)		3 (5)
Chemotherapy received (*n* = 485 total cohort)						
Yes	283 (59)	238 (67)	21 (53)	8 (53)	5 (38)	11 (18)
No	176 (36)	101 (28)	17 (43)	6 (40)	7 (54)	45 (72)
Unknown	26 (5)	16 (5)	2 (5)	1 (7)	1 (8)	6 (10)
Chemotherapy completed (*n* = 222 clinical patients)						
Yes	173 (78)	90 (71)	10 (77)	6 (86)	10 (77)	57 (92)
No	49 (22)	37 (29)	3 (23)	1 (14)	3 (23)	5 (8)
Pain medication received (*n* = 222 clinical patients)						
Yes	64 (29)	42 (33)	5 (38)	1 (14)	1 (8)	15 (24)
No	158 (71)	85 (67)	8 (62)	6 (86)	12 (92)	47 (76)

Clinical patients from two main referral hospitals in Addis Ababa.
Abbreviations: cyto, cytology; patho, pathology

Table 4. Unadjusted and adjusted hazard ratios for adverse outcome (death) of operated patients with epithelial ovarian cancers (*n* = 125)

Characteristic	**Unadjusted HR (95% CI)**	***p* value**	**Adjusted HR (95% CI)**	***p* value**
Age <40[a]				
40–59	1.02 (0.58–1.80)	.948	1.14 (0.64–2.04)	.657
≥60	1.48 (0.66–3.33)	.346	1.25 (0.52–3.00)	.612
FIGO stage 1[a]				
Stage 2	1.80 (0.41–7.92)	.439	1.89 (0.43–8.35)	.400
Stage 3	3.37 (0.79–14.34)	.101	2.91 (0.67–12.64)	.154
Stage 4	3.81 (0.83–17.42)	.085	3.03 (0.69–15.79)	.134
Unknown	2.00 (0.41–9.74)	.388	2.16 (0.44–10.65)	.344
Surgery + CT[a]				
Surgery	1.05 (0.55–1.97)	.887	1.07 (0.54–2.11)	.849
No residual tumor[a]				
Residual tumor	2.45 (1.25–4.83)	.009	2.23 (1.08–4.49)	.025
Unknown	1.09 (0.51–2.33)	.825	1.16 (0.52–2.56)	.714

Adjusted for treatment, age, FIGO stage, residual tumor.
[a]Reference category.
Abbreviations: CI, confidence interval; CT, chemotherapy; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio.

the very small number of well-trained oncologic surgeons and thus ovarian surgery is being performed by non-specialized surgeons, which has been shown to result in reduced optimal surgical outcomes [32]. In 2013, only four gynecologic oncologists trained to perform surgeries on malignant ovarian tumors practiced in Ethiopia, a small

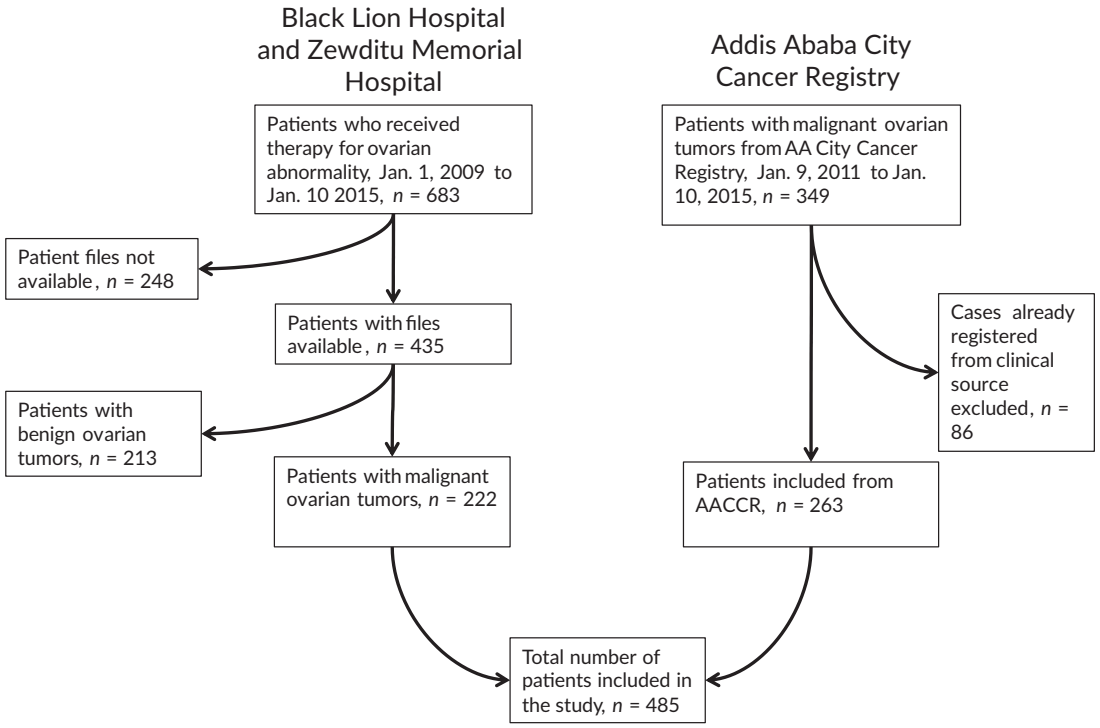

Figure 1. STROBE diagram. Patients included in the study were either diagnosed in Black Lion Hospital or Zewditu Memorial Hospital or registered in the AACCR.
Abbreviation: AACCR, Addis Ababa City Cancer Registry.

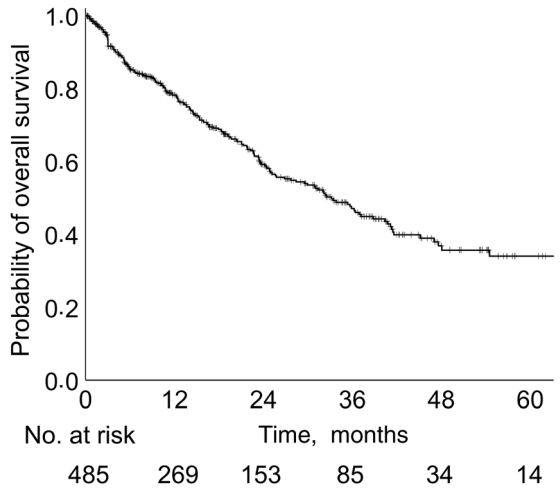

Figure 2. Estimated cumulative overall survival of the total cohort (*n* = 485; Kaplan-Meier method), hospital-based, and population-based data combined, all histologic subtypes included.

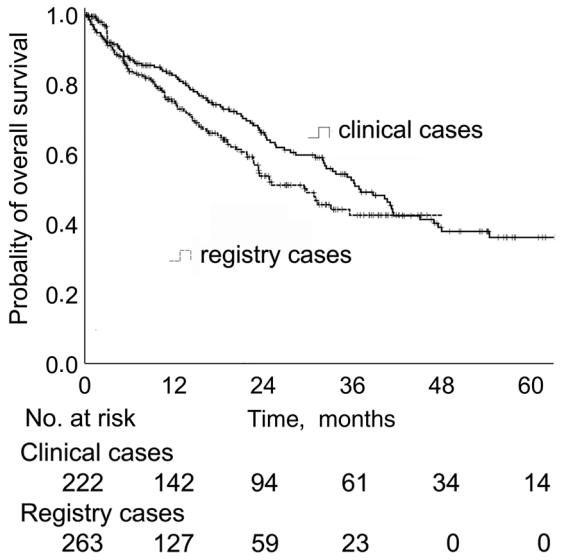

Figure 3. Estimated cumulative overall survival for clinical patients (*n* = 222) and registry patients (*n* = 263), mutually exclusive, all histologic subtypes included (Kaplan-Meier method).

number in relation to the 2,550 estimated yearly cancer cases in the whole country [20]. Furthermore, only three hospitals were equipped to perform complex oncologic surgeries and anesthetic as well as intensive care was limited. This clearly calls for action to improve quality and quantity of surgical oncologic services in Ethiopia. Patients with epithelial ovarian cancer stages higher than FIGO stage IA should receive a platinum-based adjuvant chemotherapy [15]. Chemotherapy was provided to 59% of patients in this cohort (all patients greater than stage IA); possible challenges to chemotherapy delivery include limited access to chemotherapy centers and shortage of chemotherapy drugs. Of patients with information on chemotherapy cycles, only 78% completed their total dose. Information on type of chemotherapy was incomplete but from the data available only a few patients (19%) received a taxane. Lack of financial resources and chemotherapy availability have been documented as barriers to chemotherapy delivery in sub-Saharan Africa [20]. Only 29% of clinical patients

received pain medication, a much lower than anticipated need considering the high proportion of advanced-stage diseases diagnosed in Ethiopia. Increasing access to palliative care is a global oncology priority.

Survival

The cumulative estimated crude overall 1-year and 2-year survival rate of our clinical patients (all histologic types) was 82.7% and 66.3%, respectively. The estimated 5-year survival rate was 33.9% (95% CI, 30.2%–37.6%), which is comparable to published data from Sudan (38%) but higher compared with data from Senegal (13%) [29, 33]. Compared with population-based data from the U.S. with a 1-year and 2-year survival rate of 78.3% and 66.8%, respectively, in 2012, our population-based registry patients had worse outcome (of 73.9% and 51.8%) but not as huge of a difference as possibly expected given the limited therapy available [26]. This could be partly explained by the fact that our patient cohort included a larger proportion of good-prognosis patients improving the outcome, such as germ cell tumors, sex cord-stromal tumors, and a sample of borderline epithelial tumors. However, at the same time, the relatively poor survival despite those good-prognosis patients may reflect patients with aggressive cancer and suboptimal therapy including suboptimal surgery, complete lack of surgery, or lack of standardized adjuvant chemotherapy. In addition, delay in diagnosis and long waiting times for surgery and chemotherapy contributes to disease progression and poor prognosis. Similar to other studies in epithelial cancer, overall survival was better in patients without residual tumor [34]. We assume that in Ethiopia, survival of all OMs is likely lower than reported in this study, accounting for the limited access to ovarian cancer diagnostic and treatment center across Ethiopia; a great number of patients are underdiagnosed in the rural settings. Patients without surgery are less likely to be registered in either clinical or population-based database and thus are not captured in this cohort.

Limitations

There are several limitations in this retrospective study. Firstly, the cohort is a mixture of population-based registered patients and patients with clinical records available. This does not allow comparison to studies reporting population-based data. All proportions described should be interpreted more behind the background of a selected hospital cohort. Second, the data quality was limited by the fact that patient files were handwritten and stored manually, and documentation was partly incomplete. Particularly, the operation notes were incomplete,and detailed information on size and position of residual tumors could not be gathered. Therefore, we only included $n = 125$ well-documented surgical cases in the assessment of prognostic factors on survival. Third, our cohort included 375 patients (77%) originating from Addis Ababa. As 80% of Ethiopia's population lives in rural areas, our cohort represented mainly a selected group of urban patients with good health care access. Fourth, the patient cohort was mostly generated from clinical operation registration books (clinical patients) and histologically verified and strong clinical evidence for OM (registry patients). Patients who were not operated on and without strong clinical evidence would likely not be referred to any facility with oncologic service. Because oncologic diagnostic service is still very limited in Ethiopia, there are no options to retrieve those underdiagnosed patients; thus, our total cohort and proportions described have a selection bias toward those patients with typical symptoms and access to good diagnostic facilities.

Conclusion

In this study, we presented for the first time a large cohort of Ethiopian patients diagnosed with malignant ovarian tumors. Knowing that these patients all over the world share a fatal outcome, we see room for improvement in Ethiopia. These considerably young patients (median, 46 years) had nonepithelial tumors in nearly one third of cases; in this respect they were markedly different from European or U.S. settings and thus call for local guideline development. The 62 patients without histologic confirmation (34 below the age of 50) definitely need better health service given the relatively high possibility of having a treatable nonepithelial tumor. The common presentation at high tumor stage shows the lack of screening strategies similar to other countries. Of this cohort, only four out of five women received surgery and only two out of three received chemotherapy, clearly indicating a need for access to therapy. Higher stage, residual tumor and lack of chemotherapy impaired the outcome of epithelial ovarian cancer cases. This shows the need for gynecologic oncology surgeons training in Ethiopia to provide access to adequate surgery and chemotherapy. Although almost half of the patients presented with FIGO stage III or IV tumors, only 29% received pain medication underlining the need to expand access to pain management and palliative care.

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Disclosures

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