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"The impact of debulking surgery in patients with node-positive epithelial ovarian cancer: Analysis of prognostic factors related to overall survival and progression-free survival after an extended long-term follow-up period"

Augusto Pereira [a, *], Tirso Pérez-Medina [b], Javier F. Magrina [c], Paul M. Magtibay [c], Ana Rodríguez-Tapia [d], Tatiana Cuesta-Guardiola [a], Irene Peregrin [e], Elsa Mendizabal [a], Santiago Lizarraga [a], Luís Ortiz-Quintana [a]

[a] Division of Gynecologic Oncology, Gregorio Marañón University General Hospital, C/Maiquez, 7, 28009 Madrid, Spain
[b] Department of Gynecologic Surgery, Puerta de Hierro University Hospital, C/Joaquin Rodrigo, 2, 28222 Madrid, Spain
[c] Division of Gynecologic Surgery, Mayo Clinic, 13400 East Shea Boulevard, Scottsdale, 85259 AZ, USA
[d] Department of Gynecology and Obstetrics, College of Medicine, Autonomous University, C/Arzobispo Morcillo, 4, 28029 Madrid, Spain
[e] Department of Obstetrics and Gynecology, Bronx-Lebanon Hospital Center, 1650 Grand Concourse, Bronx, 10457 NY, USA

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ABSTRACT

Objective: to estimate the prognostic factors associated with survival and progression free survival (PFS) in patients with node-positive epithelial ovarian cancer (EOC) after an extended long-term follow-up period.

Methods: Data was provided by the Tumor Registry of the Mayo Clinic, Scottsdale, Arizona on 116 node-positive EOC patients who underwent primary cytoreductive surgery observed over the period 1996–2014.

Results: At censoring date, 21 patients were alive (18%), 95 dead (82%), 18 without evidence of disease (NED) (15 alive, 3 dead) and 76 with evidence of disease (ED) (2 alive, 74 dead). Twenty-nine ED patients (38.2%) experienced a recurrence within 2 years, 53 patients (69.7%) before 5 years. No recurrences were recorded after 10 years. The median follow-up in alive patients was 169.8 months (1.20–207.9 months), 34.9 months (0.30–196.2 months) in dead patients, 128.4 months for NED patients (72.8–202.5 months) and 34.6 months (0.1–106.9 months) in ED patients. Multivariate analysis showed an increased risk of dead in patients with age ≥60 years (HR: 3.20; $p < 0.002$), stage IVA/B (compared with stage IIIA1/2, HR: 4.31; $p < 0.001$ and stage IIIB/C, HR: 5.31; $p < 0.010$) and incomplete surgery (compared with complete surgery, HR: 3.10; 95% CI, 1.41–6.77; $p < 0.003$) and a decreased PFS in stage IVA/B (compared with stages IIIB/C; $p = 0.003$ and stage IIIA; $p = 0.000$) and residual volume after surgery >0.6 cm (compared with residual disease <0.5 cm; $p < 0.023$).

Conclusions: prognostic factors for an extended long-term PFS are similar as those for survival, because after 17-year follow-up period, the majority of alive patients are NED patients.

1. Introduction

Epithelial ovarian cancer (EOC) is the second gynecological cancer in frequency and the first in mortality in developed countries [1]. In the USA, the estimated number of deaths from EOC was 7.7 per 100,000 women per year, that is, 2.4% of all cancer deaths in 2015 [2]. Survival of patients with ovarian cancer has improved by as much as 50% during recent years compared with previous decades [3] owing to a more specialized primary surgical approach and the use of standard chemotherapy.

Sixty percent of patients with epithelial ovarian cancer (EOC) are diagnosed in advanced stages [4]. Between 70% and 80% of patients achieve complete and partial response after primary debulking surgery and first-line chemotherapy [5–7], more than

* Corresponding author.
E-mail address: apereiras@sego.es (A. Pereira).

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Table 1
Clinical, tumor, and post-surgical characteristics.

Age (years)	N	Alive	Death	No evidence	Evidence	Unknown
<39	4	2	2	1	2	1
40–49	14	5	9	5	6	3
50–59	27	6	21	5	18	4
60–69	34	3	31	3	27	4
70–79	34	5	29	4	20	10
≥80	3	0	3	0	3	0
Histological type						
Serous type	76	13	63	12	47	17
Mucinous	2	1	1	0	2	0
Endometrioid	13	3	10	3	8	2
Mixed type	12	2	10	2	10	0
Clear cell	1	0	1	0	1	0
Brenner	2	0	2	0	1	1
Unclassified	3	1	2	0	3	0
Undifferentiated	7	1	6	1	4	2
Tumor grade						
II	3	1	2	2	1	0
III	50	10	40	8	34	8
IV	63	10	53	8	41	14
1988 FIGO stage						
IIIC	81	17	64	14	50	17
IV	35	4	31	4	26	5
2014 FIGO stage						
IIIA1i	9	2	7	2	5	2
IIIA1ii	14	6	8	6	5	3
IIIA2	3	2	1	2	1	0
IIIB	4	2	2	2	2	0
IIIC	67	7	60	5	49	13
IVA	4	0	4	0	4	0
IVB	15	2	13	1	10	4
Residual tumor after surgery						
0 cm	57	15	42	12	35	10
0.1–0.5 cm	20	4	16	4	13	3
0.6–1 cm	21	0	21	0	15	6
1.1–2 cm	10	1	9	1	7	2
>2 cm.	7	1	6	1	5	1
Unknown	1	0	1	–	1	-
Overall number of nodes removed						
>40	42	11	31	9	23	10
1–40	74	10	64	9	53	12
Number of positive nodes removed						
>10	30	6	24	3	19	8
1–10	86	15	71	15	57	14
Distant lymph nodes						
Negative	105	20	85	14	69	19
Positive	11	1	10	1	7	3
Inguinal	4	0	4	0	3	1
Suprarenal/celiac	5	1	4	1	2	2
Inguinal and suprarenal/celiac	1	0	1	0	1	0
Supraclavicular	1	0	1	0	1	0
Retroperitoneal invasion						
No	94	17	77	15	58	21
Yes	22	4	18	3	18	1
Ureteral obstruction/hydronephrosis	10	2	8	2	7	1
Proximal parametrial	5	2	3	1	4	0
Parametrial with ureteral obstruction/pelvic wall/recto-vaginal space	6	0	6	0	6	0
Pararectal space	1	0	1	0	1	0

N: number of patients. RV, residual volume.

50% achieve complete clinical response [8], and 25% achieve pathological complete remission [5,6]. Fifty percent of responders are positive for disease on second-look laparotomy within 3 years [8,9], and 10–15% of patients achieve long-term remission [10].

Once a diagnosis has been made, it is important to determine potential outcomes based on prognostic factors that will enable us to estimate the probability of recovery. In EOC, favorable independent predictors for 5-year overall survival (OS) include younger age, good performance status, histological type other than mucinous or clear cell, well-differentiated tumor grade, early stage, smaller tumor volume before surgical debulking, no residual tumor after debulking, and absence of ascites [11–16].

Close monitoring ensures that recurrence is readily identified and chemotherapy can be restarted in an attempt to turn the disease into a chronic process. Multiple studies have estimated progression-free survival (PFS) in EOC patients. The prognostic factors associated with PFS are maximal debulking surgery to minimize residual disease, adjuvant treatment, and systematic lymphadenectomy to guarantee the optimal accuracy of staging and debulking surgery [17–19].

Because EOC is the leading cause of death in patients with gynecological cancer, the number of survivors is low, thus implying that the studies were not long-term. Most prognostic factors of OS and PFS are associated with short-term survival, and predictors