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EARLY OVARIAN cancer (stage I and IIa according to the FIGO classification) is not rare amounting to approximately 30% of all ovarian cancers at initial diagnosis [1]. In the U.S., 5000–7000 new cases of early ovarian cancer are diagnosed per year [2] and in Europe, the figure is 7000–8000 cases [3]. The estimated numbers of deaths due to early ovarian cancer are, respectively, approximately 1500–2000 in the U.S. and 2000–2500 in Europe [2, 3]. Thus, the identification of effective treatments for this condition may have an impact at the public health level.

After completely resecting surgery, three kinds of therapy (chemotherapy, intraperitoneal or external radiotherapy) have been suggested as adjuvant treatment in early ovarian cancer. To define their role, and particularly for the scope of this debate, to define the utility of radiotherapy, we have to answer two questions:

- Has postoperative therapy shown any improvement in survival?
- Which therapy (chemotherapy or intraperitoneal or external radiotherapy) is the most efficacious as adjuvant treatment of ovarian cancer?

There is general agreement that sound scientific evidence comes from randomised controlled clinical trials. Thus, to

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Table 1. Results from selected studies comparing chemotherapy or radiotherapy versus no treatment in early ovarian cancer

	No. of patients		Recurrence (*n* (%))		Per cent 5-year survival	
	No treatment	Adjuvant treatment	No treatment	Adjuvant treatment	No treatment	Adjuvant treatment
No treatment versus chemotherapy						
Melphalan						
Hreshchyshyn and associates [6]	29	34	5 (17)	2 (6)	—	—
Young and associates [7]	38	43	4 (11)	1 (2)	94	98
Cisplatin						
Bolis and associates [8]	42	41	14 (33)	7 (17)	82	88
No treatment versus external radiotherapy						
Hreshchyshyn and associates [6]	29	23	5 (17)	7 (30)	—	—
Dembo and associates [4]	27	27	4 (15)	5 (19)	—	—

answer these questions we need to look at the results of randomised trials.

Before discussing the data on the role of adjuvant treatment in early ovarian cancer cases, it should be noted that survival after surgery in early ovarian cancer is around 60–70% [4], so the routine use of toxic treatment as adjuvant therapy is debatable. However, some subsets of patients, including women with low differentiated tumour or positive peritoneal cytology, are at a higher risk of relapse [5], and so most trials on adjuvant treatment of ovarian cancer include these patients.

To date, only a few randomised trials have compared external (chiefly abdominal) radiotherapy or chemotherapy with no treatment in early ovarian cancer cases [6–9], and indeed, no study has compared intraperitoneal radioactive chronic phosphate (^{32}P) with no treatment. Similarly, no randomised study has compared a combination of external radiotherapy plus intraperitoneal radioactive ^{32}P with no treatment or chemotherapy. However, this combination has been shown to be highly toxic [10].

Results of published studies are conflicting (Table 1). The three studies which compared chemotherapy with no treatment found a lower rate of recurrence in treated than untreated women, but the differences were not statistically significant [6–8]. In the studies comparing external radiotherapy with no treatment, the frequency of recurrences was higher in women who received abdominal radiotherapy [6, 9]. The studies on chemotherapy, showing favourable effect of adjuvant treatments in prevention of relapse, failed to show any difference in survival, probably due to the small sample size. Thus, we have no conclusive evidence for a role of any adjuvant treatment in improving survival of early ovarian cancer patients.

The data on the relative efficacy of intraperitoneal and external radiotherapy versus chemotherapy are also scanty. Table 2 shows a summary of the randomised studies comparing chemotherapy with radiotherapy as adjuvant treatment of early ovarian cancer [8, 11–14]. None of the studies showed any difference in overall survival among the treatments. A recent trial comparing cisplatin versus ^{32}P in 161 stage Ic patients showed a lower relapse rate in the cisplatin group, but no difference emerged in survival [8]. One study which included 190 ovarian cancer cases stage IB–III (non-residual) suggested that chemotherapy combined with pelvic irradiation prolonged disease-free survival, but did not reduce the number of recurrences [15].

In the absence of clear findings from randomised studies on the role of adjuvant treatment in early ovarian cancer and of any real benefit of intraperitoneal or external radiotherapy in comparison with chemotherapy, clinical considerations should also be taken into account in the decision to use radiotherapy in the postoperative treatment of this disease.

Following the suggestions of the Consensus statement [5], "high-risk patients (stage I grade 3 and stage Ic and stage II) with one chance in four of being alive at 5 years are presumably worth treating" with postsurgical treatment. For these patients, with a "disease prognosis similar to that of advanced-stage patients" the most rational treatment

Table 2. Results from selected studies comparing chemotherapy versus intraperitoneal or external radiotherapy in early ovarian cancer

	No. of patients			Recurrence (*n* (%))		Per cent 5-year survival	
	Chemotherapy	Radiotherapy	Stage	Chemotherapy	Radiotherapy	Chemotherapy	Radiotherapy
Cisplatin versus ^{32}P							
Vergote and associates [11]	127	138	I	—	—	81†	83†
Bolis and associates [8]	82	79	Iaii–Ibii–Ic	12 (15)	26 (33)	81†	79†
Melphalan versus ^{32}P							
Klaassen and associates [12]	106‡	44§	I–III	—	—	61†	66†
Young and associates [7]	68	73	I–II	13 (19)	14 (19)	81†	78†
Cisplatin versus abdominal RT							
Chiara and associates [13]	44	25	Ia–IIc	12 (27)	10 (40)	—	—
Melphalan versus abdominal RT							
Smith and associates [14]	28	19	I	—	—	90*	85*
	29	37	II	—	—	58*	55*
Klaassen and associates [12]	106‡	107‖	I–III	—	—	61†	62†

* 2-year survival; † 5-year survival; ‡ including 42 cases stage IIB–III; § including 22 cases stage IIB–III; ‖ including 41 cases stage IIB–III. RT, radiotherapy

Table 3. Frequency of major complications after chemotherapy or radiotherapy in early ovarian cancer cases (selected studies)

	No. of patients		Treatment-related deaths		Severe enteritis/ bowel complications		Nausea and/or vomiting		Myelosuppression	
	CT *n* (%)	RT *n* (%)	CT *n* (%)	RT *n* (%)	CT *n* (%)	RT *n* (%)	CT *n* (%)	RT *n* (%)	CT *n* (%)	RT *n* (%)
Cisplatin versus ^{32}P										
Vergote and associates [11]	171†	169†	—	—	4 (2)	18 (11)	n.r.	n.r.	n.r.	n.r.
Bolis and associates [8]	82	79	—	—	—	1 (1)	—	—	6 (8)	—
Melphalan versus ^{32}P										
Young and associates [7]	68	73	1 (2)	—	11 (16)	24 (33)	—	—	50 (74)	—
Cisplatin versus abdominal RT										
Chiara and associates [13]	44	25	—	1 (4)	—	7 (28)	44 (100)*	20 (80)*	16 (37)	11 (43)
Melphalan versus abdominal RT										
Smith and associates [14]	79	70	—	—	—	11 (16)	n.r.	n.r.	47 (59)	3 (4)

CT, chemotherapy; RT, radiotherapy; n.r., not reported.
* Estimated from published percentages; † including patients stage I–IV.

seems the one which is the most effective in stage III–IV: platinum-based chemotherapy [16].

Further, external and intra-abdominal radiotherapy is more toxic than the toxicity of chemotherapy. Table 3 shows the frequency of adverse effects after radiotherapy and chemotherapy in selected studies. Bowel complications are common after radiotherapy. Pooling the data from the studies considered, the frequency of severe enteritis and/or bowel complications was approximately 15% after treatment with ^{32}P and 20% after abdominal radiotherapy.

Besides the lack of evidence of the efficacy of radiotherapy and the high rate of complications after radiotherapy, theoretical considerations do not support its use after surgery for high risk early ovarian cancer cases. Extraperitoneal lymph nodal diffusion, that is probably not affected by treatment with ^{32}P, has been reported in approximately 10% of stage I ovarian cancers [17]. Most recurrences of early ovarian cancers are in the abdomen [8]. Thus, pelvic irradiation alone might lower the risk of pelvic recurrence, but not the overall risk of relapse. As such, most studies have used abdominal irradiation, a treatment with a higher rate of severe bowel complications than pelvic radiotherapy [9]. Finally, the rate of extra-abdominal relapse is approximately 5% [7]. Although this percentage is low, radiotherapy probably cannot affect these recurrences.

In conclusion, as scientific evidence is lacking, clinical and speculative considerations suggest that high risk early ovarian cases do not benefit from radiotherapy.

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