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Role of radiation therapy

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Because most patients with epithelial ovarian cancer have advanced disease at the time of initial diagnosis, radiation therapy usually does not play a major role in their treatment. Although ovarian carcinomas appear to be no less sensitive to radiation therapy than Müllerian carcinomas arising in other sites, the dose of radiation required to control gross disease, typically at least 60 Gy, cannot be safely delivered to the entire abdomen or even to large partial volumes of the pelvis and abdomen. Moreover, in most cases, localized radiation is ineffective because of the high risk of disseminated recurrence in peritoneal and extraperitoneal sites.

There is strong evidence that radiation therapy can be used to achieve prolonged disease-free intervals and even cure selected patients with epithelial ovarian cancer. The challenge is to determine the select few who stand to benefit from radiation therapy. In all cases, the potential benefits of treatment must be carefully weighed against the risks, particularly for patients who are referred after multiple operations and courses of chemotherapy. For patients with incurable ovarian cancer, radiation therapy can also be very effective as a tool for improving symptoms and quality of life.

Studies of adjuvant radiation therapy for ovarian cancer

During the third quarter of the 20th century, there was considerable interest in the use of radiation therapy (RT) to treat ovarian cancer. Early retrospective studies of pelvic treatment for patients with stage II disease demonstrated higher than expected survival rates for patients who had pelvic RT [1].

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However, most patients failed outside the RT fields, usually with intra-abdominal carcinomatosis. It was generally agreed that for RT alone to make a major impact on the disease, methods must be developed to address the characteristic pattern of transcoelomic metastasis from ovarian cancers. In the 1970s and 1980s, two approaches were explored: intraperitoneal installation of radioactive isotopes and whole abdominal external beam RT or whole abdominal RT (WART).

Intraperitoneal radioactive chromic phosphate

Radioactive chromic phosphate (^{32}P) can be instilled into the peritoneal cavity to deliver superficial RT to peritoneal surfaces. Retrospective studies have suggested that this treatment may benefit some patients with early-stage ovarian cancer. However, trials that compared intraperitoneal ^{32}P treatment with platinum-containing chemotherapy demonstrated lower relapse rates in patients treated with chemotherapy; the overall survival rates of patients who received these two treatments were not significantly different [2,3]. ^{32}P is difficult to administer and has been associated with significant bowel complications, particularly if the radiocolloid is unevenly distributed or combined with pelvic external beam irradiation. For these reasons, it is now rarely, if ever, used in the treatment of gynecologic cancers.

Early studies of adjuvant whole abdominal radiation therapy

In the beginning of the 1970s, a series of trials evaluated the benefit of WART for ovarian cancer. The two earliest randomized trials compared WART with the best chemotherapy of the time (a single alkylating agent) combined with pelvic RT. Because the maximum field size of contemporary treatment machines could not encompass the entire abdominopelvic cavity, WART was delivered using a "moving-strip" technique that sequentially treated overlapping strips of tissue over several weeks [4]. Although this technique appeared to be effective, the use of relatively low-energy cobalt-60 radiation beams and relatively high fractional radiation doses may have contributed to late complications in patients treated with WART in these trials.

In one randomized trial conducted at MD Anderson Cancer Center [5], 149 patients with stage I or II ovarian cancer received either WART or pelvic RT plus melphalan chemotherapy. Although no significant difference was reported in the overall survival of patients in the two arms, patients who received WART had a higher rate of major complications than those treated with chemotherapy. The treatment technique used in this early trial was subsequently criticized for not having fully covered the abdominal cavity; however, the discouraging results and the subsequent development of more effective chemotherapy agents led most US oncologists to abandon the use of RT for the initial management of ovarian cancer.

In a second trial conducted at Princess Margaret Hospital, 190 patients with stage IB, II, or III disease were randomized to receive either WART or a combination of pelvic RT and chlorambucil [6,7]. Patients who had incomplete pelvic surgical resections had a poor outcome with either treatment. However, patients who had more complete surgical procedures and those who had WART had a significantly higher relapse-free survival rate than those treated with pelvic RT and chemotherapy. In a subsequent trial, which was conducted after the development of modern linear accelerators, similar outcomes were reported for patients treated with the moving-strip technique or with a single-field "belly bath" technique; because of its relative ease of administration, the single-field technique became the standard WART technique in subsequent trials. The encouraging results of the Princess Margaret Hospital trials contributed to the more frequent use of adjuvant WART in Canada and some other countries. However, a multi-institutional Canadian trial [8] failed to confirm the superiority of WART over alkylating chemotherapy or ^{32}P; for patients who received WART in that trial, the authors noted an increased failure rate in patients for whom treatment fields failed to completely cover the abdominal cavity, emphasizing the importance of adequate radiation technique.

WART does appear to have the capacity to cure some patients with early-stage ovarian cancer or minimal residual disease after surgery. In a summary analysis of Princess Margaret Hospital trials, Carey et al. [9] found that the best outcomes were achieved in patients who had either stage I or II cancers with no gross residual disease or grade 1 or 2 cancers with minimal residual disease. In general,

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