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RADIATION THERAPY OF PARA-AORTIC LYMPH NODES IN CANCER OF THE UTERINE CERVIX

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From 1965 to 1986, 173 patients with gynaecological cancer received para-aortic radiation treatment using a biaxial-four-segmental-rotating field technique. Seventy-five patients with cervical cancer and proven lymph node involvement were eligible for analysis. Crude survival and disease-free survival in 37 patients with FIGO III and 15 patients with FIGO IVA, receiving initial para-aortic treatment were compared with the corresponding data from patients in whom para-aortic treatment was secondary applied when para-aortic metastases became clinically symptomatic. Five-year survival rates of 37.5% (FIGO III) and 27.3% (FIGO IVA) were encouraging as none of the patients in the secondary group survived for more than 16 months. The number of complications induced by the described method of para-aortic irradiation appears to be substantially lower than with other methods using equal doses. Five cases of severe but not life-threatening side-effects were observed among 173 treated patients.

Para-aortic lymph nodes contain metastases in a remarkable percentage of cervical cancer (1–3). In patients who have been treated successfully in the pelvis and who not have distant metastases, involvement of para-aortic nodes governs the prognosis (4). It has been demonstrated by Buchsbaum (5) and Nori et al. (6) that 'non-treatment' of inflicted para-aortal lymph nodes reduces the survival rate. Nevertheless, radiotherapy of para-aortic nodes is rarely applied. The main reason is the high percentage of side-effects, such as small bowel injury, ureter stenosis with hydronephrosis, and injuries of the spinal cord (7–12). Awareness of side-effects has led to a reduction of the dose resulting in the statement 'radiotherapy cannot sterilize positive nodes' (13). Therapy of the primary site might have to be interrupted because of severe acute side-effects due to simultaneously extended field irradiation. Furthermore, it is argued that patients with para-aortic nodes are very likely to have distant metastases (10) and therefore cannot be cured anyway. So the radiotherapist is faced with the question whether there is any benefit at all of extended field irradiation.

The presented data are concerned with patients with cervical cancer, treated from 1965 to 1986 in the University Hospital, Hamburg, Department of Gynaecological Radiology. The patients underwent either radiotherapy of the primary site as well as a consecutive irradiation of the para-aortic lymph nodes or received secondary radiation treatment of the para-aortic lymph nodes some time after the primary pelvic radiation treatment when para-aortic lymph nodes became symptomatic.

In order to reduce side-effects whilst applying a sufficiently high dose the biaxial-four-segmental-rotating field method was developed (14). Although the method was first described in 1970 there are, to our knowledge, no data available concerning the side-effects. Therefore, all patients (n = 173) who had received para-aortic treatment were analyzed in this respect.

Material and Methods

Patients. From 1965 to 1986, 173 patients with gynaecological cancer underwent extended field irradiation using a biaxial-four-segmental-rotating field technique. Patients'

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Table

Distribution of FIGO stages in patients with cervical cancer, receiving primary or secondary para-aortic irradiation

FIGO stage	Total primary	LN-pos* primary	Total secondary
I	2	2	5
IB			2
II			1
IIB	2	1	2
III	3	2	5
IIIA	4	3	
IIIB	37	32	4
IVA	18	15	1
Total	66	55	20

* LN-pos = proven para-aortic lymph node involvement

ages ranged from 18 to 82 years with a median age of 56 years. Of these patients, 141 underwent therapy of the primary site as well as a consecutive 'primary' irradiation of the para-aortic lymph nodes. Sixty-six patients presented with cervical cancers (Table). Para-aortic lymph node involvement was proven in 55 cases either by use of lymphangiography (n = 53) or CT-scanning (n = 2).

Another 32 patients received 'secondary' para-aortic irradiation when metastatic disease in the para-aortic lymph nodes became symptomatic some time after the primary local treatment. Twenty of these patients (Table) had cervical cancer. In all of them para-aortic involvement was proven by lymphangiography.

Irradiation technique. The para-aortic lymph node irradiation is performed using a biaxial-four-segmental-rotating field technique (14) on a ^{60}Co unit. The target volume is defined by the anatomic location of the para-aortic lymph nodes. Normally the lymph nodes are located close to the abdominal aorta but they can also be located as far dorsal as one-half of the vertebral body, lying lateral of the latter and ventral of the psoas muscle (15). Cranially, the fields do not have to reach beyond cisterna chyli (typically L1). Caudally, the fields are linked up with the portals for the primary site. Both gaps and overlappings have to be avoided. During the radiation treatment the patient lies in prone position and the lumbar spine is straightened horizontally. Dependant on the (bi-)lateral extension of the lymphatic chains – as verified by lymphangiography – the distance between the two rotation axes is either 4 or 6 cm. The axes are positioned 1.5 cm or 2 cm dorsal of the ventral spine margin respectively. Rotating angles are 0°–90° and 180°–270° for the right axis, 90°–180° and 270°–360° for the left axis (Fig. 1). Irradiation is applied to daily alternating axes consisting of one dorsal and one oblique ventral rotating field. The daily maximum dose (100% isodose) is 2 Gy, and the total maximum dose thus 50 Gy. The heart-shaped 80%-isodose covers the whole para-aortal and para-caval room. It also encloses the lateral vicinity of the vertebral body, but spares the spinal cord, which lies clearly outside the 60% isodose. The ureters receive less than 40% of the maximum dose. The actual total dose in the kidneys is approx. 20 Gy. Due to the rotating and alternating method (2 Gy/day in the maximum) the dose in the kidneys does not exceed 1.2 Gy/day and 0.4 Gy/day on the remote side respectively (14).

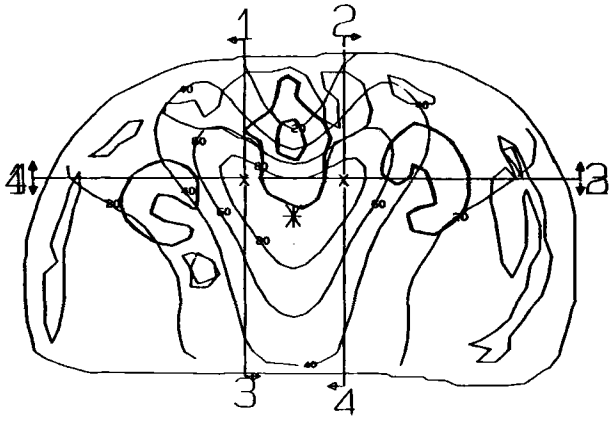

Fig. 1. Dose distribution obtained with the biaxial-four-segmental-rotating field technique (14).

Statistical evaluations. Evaluation of data was focused upon crude survival and disease-free survival for three groups of patients: FIGO stage III (n = 37) and IVA (n = 15) cervical cancer that received primary para-aortic irradiation and a third group (n = 20) which received secondary para-aortic irradiation. Patients were only included in this retrospective analysis when involvement of the para-aortic lymph nodes was proven by lymphangiography (n = 73) or CT-scans (n = 2).

Crude and disease-free survival curves were calculated by the Kaplan-Meier method (16). General mortality curves were also computed according to the figures of the Hamburg statistical year-book of 1978 matched for age with the patients.

Results

In patients with positive lymph nodes due to cervical cancer 5-year disease-free survival rates of 37.5% and 27.3% were achieved for FIGO stages III (Fig. 2) and IVA (Fig. 3) when para-aortic irradiation was part of the primary treatment.

Fig. 4 compares the crude survival of patients with lymphographically proven para-aortic lymph node involvement belonging to the primary treatment groups (FIGO stage III, n = 37; FIGO stage IVA, n = 15) and the secondary treatment group (n = 20). The survival rates after secondary treatment were rather discouraging.

In order to assess the rate of side-effects of the described method the whole collective of patients with gynaecological

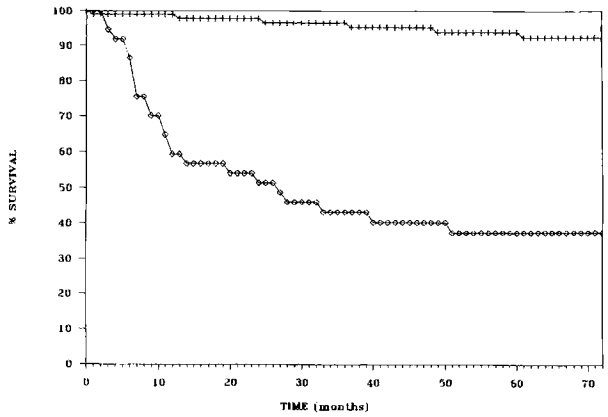

Fig. 2. Disease-free survival after primary para-aortic irradiation in patients with cervical cancer (FIGO III) and proven involvement of the lymph nodes (n = 37, ◇). In addition the general survival was computed according to life table analysis for age-matched females (+).

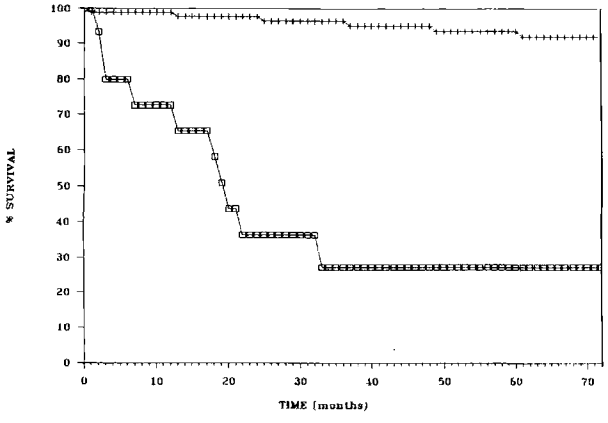

Fig. 3. Disease-free survival after primary para-aortic irradiation in patients with cervical cancer (FIGO IVA) and proven involvement of the lymph nodes (n = 15, □). In addition the general survival was computed according to life table analysis for age-matched females (+).

cancers was taken into consideration. Among the 173 patients who received para-aortic irradiation, the number of complications was very small. Three cases of ureter stenosis (14, 23 and 36 months after start of treatment) and two cases of bowel-related complications (9 and 12 months after start of treatment) were reported. All patients with therapy-related side-effects belonged to the primary group but in none of these patients had an operative staging of the lymph nodes been performed.

Discussion

Even in cervical cancers which, according to clinical staging are classified as early, there is a rather high rate of involved para-aortic lymph nodes (1–3). In such cases treatment of the pelvis alone must fail, if the inflicted

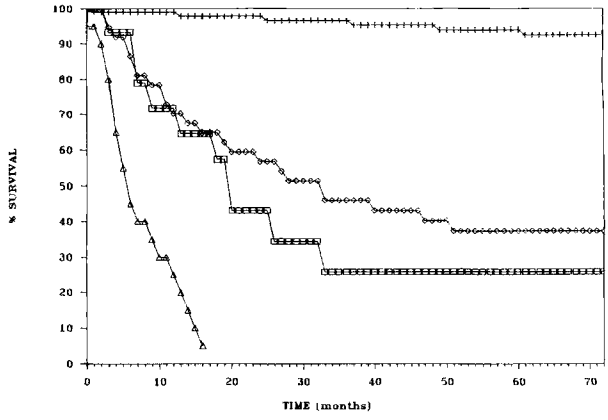

Fig. 4. Crude survival in patients who received primary para-aortic irradiation and had proven lymph node involvement (FIGO stage III; n = 37 ◇. FIGO stage IV A; n = 15, □) and in patients who received secondary para-aortic irradiation when the metastases became symptomatic (n = 20, △). The survival in an age-matched female population is also shown (+).

para-aortic lymph nodes remain untreated. Therefore, the American College of Radiology (4) recommends extended field irradiation in such cases. Many authors have analyzed the rational of para-aortic irradiation, with the background of the high rate of complications, which has been reported when irradiation and surgery are combined (1, 17–23). However, lymphangiography can detect even small metastatically involved lymph nodes without increasing the rate of complications and has, if adequately performed, high specificity and sensitivity (24–26). Heller et al. (25) found that wrong negative findings were reported only in 8% of the cases. Such results require an experienced radiologist. Therefore our department has put great emphasis on continuity concerning the technique of lymphangiography, especially as it is important for treatment planning when using para-aortic irradiation. Lymph-angiography and CT-scanning seem to have about the same value for staging as both have the same certainty factor (C2) (27).

Due to the reported high rate of complications most radiotherapists hesitate to treat para-aortic lymph nodes, especially on a 'prophylactic' basis. The high rate of side-effects (cf. 9, 11, 12) has led to new ways of treatment strategies. However, neither a split-course technique (28) applying 60 Gy, nor the reduction of the total dose (9, 21, 29, 30) has had the expected success.

In all our reported patients, para-aortic radiation treatment was regarded as necessary due to the fact that nodal involvement was proven (134 cases) or suspected (39 cases). In contrast to other authors (9, 11, 12), but in accordance to Podczaski et al. (3) and Rotman et al. (30), the incidence of side-effects was reasonably low. In only 5 out of the 173 patients severe, but not life-threatening, complications were observed. Podczaski et al. (30) found a para-aortic dose of 40–45 Gy sufficient to prolong survival considerably. Also in the study by

Rotman et al. (30) 44–45 Gy were applied. Very likely the low rate of side-effects in our patients was basically due to the biaxial-four-segmental-rotating field technique (14) which spares critical organs. Radiation doses exceeding 40 Gy are strongly restricted to the defined target volume.

In patients with FIGO stage III cervical carcinomas and proven para-aortic involvement (n = 37, Fig. 2) the five-year disease-free survival (37.5%) was remarkably high which suggests that patients in this stage may profit from para-aortic irradiation. The presented data are in good agreement with the conclusions of Podczaski et al. (3).

Also our patients with FIGO stage IVA had an encouraging high 5-year disease-free survival, suggesting a benefit from the para-aortic irradiation.

The situation was disastrous for the patients who received secondary para-aortic irradiation only (Fig. 4). These patients had not initially been treated with extended field irradiation, since lymphatic spread was neither suspected nor found (false negative lymphangiograms?) (Table). In contrast, the patients presenting initially with positive lymphangiograms and who received primary para-aortic irradiation had a considerably higher chance to survive for five years or more. Obviously doses exceeding 40 Gy can sterilize small lymph node metastases. The low rate of side-effects using the described method (14) appears to justify primary routine para-aortic irradiation in some groups of patients. However, in patients with clinically symptomatic para-aortic metastases one may assume that dissemination to an incurable extent has already taken place. Also accordingly to Piver et al. (31) para-aortic metastases which cause clinical symptoms are beyond treatability. As a consequence two randomized studies of para-aortic irradiation (9, 12) excluded patients with clinical evidence of para-aortic involvement.

However, in FIGO-stages Ib–IIb cervical cancer the RTOG 7920 trial showed a significantly better survival after extended field irradiation than after pelvic treatment alone (30).

In summary we are of the opinion, similar to Podczaski et al. (3) and Rotman et al. (30), that patients can profit from primary para-aortic irradiation. Especially the low rate of side-effects when using the biaxial-four-segmental-rotating field technique justifies routine application of primary para-aortic irradiation treatment in some defined groups of patients with cervical cancer.

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