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Original article

Non-closure of peritoneum after abdominal hysterectomy for uterine carcinoma does not increase late intestinal radiation morbidity

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ABSTRACT

Background/Aim: To evaluate whether non-closure of the visceral peritoneum after total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) in patients with uterine corpus carcinoma influences the volume of the small intestine within the irradiated volume during adjuvant radiotherapy or late radiation intestinal toxicity.

Materials and methods: A total of 152 patients after TAH + BSO with adjuvant pelvic radiotherapy were studied. The state of peritonealization was retrospectively evaluated based on surgical protocols. The volume of irradiated bowels was calculated by CT-based delineation in a radiotherapy planning system. The influence of visceral peritonealization upon the volume of the small intestine within the irradiated volume and consequent late morbidity was analyzed.

Results: Visceral peritonealization was not performed in 70 (46%) of 152 studied patients. The state of peritonealization did not affect the volume of the irradiated small intestine ($p = 0.14$). Mean volume of bowels irradiated in patients with peritonealization was 488 cm^3 (range 200–840 cm^3, median 469 cm^3); mean volume of bowels irradiated in patients without peritonealization was 456 cm^3 (range 254–869 cm^3, median 428 cm^3). We did not prove any significant difference between both arms. Nor did we observe any influence of non-peritonealization upon late intestinal morbidity ($p = 0.34$).

Conclusion: Non-closure of the visceral peritoneum after hysterectomy for uterine corpus carcinoma does not increase the volume of the small intestine within the irradiated volume, with no consequent intestinal morbidity enhancement.

1. Background

Until the last decade of the twentieth century, visceral peritonealization after hysterectomy was a standard of care all over the world. A closure of the visceral peritoneum has always been thought to be necessary to avoid postoperative ascending infections or adhesion formation with the risk of a consequent ileus. Several studies argued against this procedure at the turn of the millennium.[1–5,7]

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Prospective randomized trials of hundreds of patients revealed that peritoneal closure at abdominal hysterectomy provides no immediate postoperative benefits while unnecessarily lengthening surgical time and anesthesia exposure and increasing blood loss.[1,2] Omission of peritoneal closure seems to be safe, as fever, infection, hemorrhage or revision are similar to peritonealization.[3,4,5] On the contrary, a significantly lower number of postoperative irregular pyelograms was reported in cases without peritoneal closure after radical hysterectomy.[6] Moreover, resumption of bowel function may take place significantly earlier in patients with open peritoneum,[3] without a superior risk of subsequent ileus.[4,5] Study of pelvic and periaortic peritonealization in radical ovarian cancer surgery has showed that leaving the pelvic and periaortic peritoneum open significantly decreases the adhesion formation.[7] As s long-term sequelae, peritoneal non-closure after hysterectomy can cause an increase in peritoneal pelvic fluid, however, its clinical impact is supposedly insignificant.[8]

Referenced studies have suggested that the traditional practice of visceral peritoneal closure should be abolished at abdominal hysterectomy. Therefore, at present, a majority of gynecologists omit peritonealization in all patients undergoing hysterectomy for any reason. Unfortunately, some patients after total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) for uterine carcinoma require adjuvant pelvic radiotherapy. With regard to anatomical alterations, bowels usually fill up the empty space in the pelvis after radical hysterectomy. If the non-closure of visceral peritoneum increased the volume of the small intestine within the pelvis in these patients, a larger volume of the irradiated small intestine would consecutively lead to increased intestinal toxicity. There has been no study evaluating the influence of peritoneal non-closure upon the volume of the small intestine in the pelvis up to the present day.

The purpose of this study is to evaluate the influence of non-closure of the visceral peritoneum after TAH and BSO in patients with uterine carcinoma receiving adjuvant radiotherapy upon the volume of the small intestine within the irradiated volume and upon the risk of late radiation intestinal morbidity enhancement.

2. Materials and methods

2.1. *Patients*

A total of 235 Caucasian patients with uterine carcinoma had adjuvant pelvic radiotherapy between the January 2004 and December 2009 at the Department of Oncology and Radiotherapy, University Hospital in Hradec Králové. All patients underwent TAH with BSO. In 82 patients closure of the peritoneum was performed after hysterectomy, while visceral peritonealization was omitted in 70 patients. The state of peritonealization in other 83 patients was not clearly provable from the documentation; these patients were excluded from the study, thus 152 patients were left for statistical evaluation.

In 66 of the studied patients (43%), systematic pelvic lymphadenectomy was performed; median number of lymph nodes resected in these patients was 10 (range 1–36; mean 11). Detailed patient and treatment characteristics are listed in Tables 1 and 2.

Table 1 – Patient and treatment characteristics.

Age	MEAN: 64 years (±8.3 years)
FIGO stage (FIGO 1988)	FIGO IB: 33 (22%) patients FIGO IC: 64 (42%) patients FIGO IIA: 12 (8%) patients FIGO IIB: 24 (16%) patients FIGO IIIA: 12 (8%) patients FIGO IIIC: 7 (4%) patients
Histology	ENDOMETRIOID: 133 (88%) patients ADENOAKANTOMA: 11 (7%) patients CARCINOSARCOMA: 5 (3%) patients PAPILLARY SEROUS: 2 (1%) patients CLEAR CELL: 1 (1%) patient
Tumor grade	GRADE 1: 26 (17%) patients GRADE 2: 101 (66%) patients GRADE 3: 25 (17%) patients
Site of surgery	GYNECOL. CENTRE: 80 (53) patients DISTRICT HOSPITAL: 72 (47%) patients
Radiotherapy dose	50 Gy/25 FRACTIONS: 115 (76%) patients 45 Gy/25 FRACTIONS: 37 (24%) patients
Radiotherapy technique	CONVENTIONAL: 117 (77%) patients 3D-CONFORMAL: 31 (20%) patients IMRT: 4 (3%) patients

Values are given as a number (%); or mean ± standard deviation. FIGO, International Federation of Gynecology and Obstetrics; IMRT, intensity modulated radiotherapy.

2.2. *Small intestine delineation*

Following TAH with BSO, adjuvant pelvic radiotherapy was performed in all studied patients. In all patients, the radiation therapy was performed by a linear accelerator with photons of 6–18 MV energy. Majority of patients were treated by a conventional 4-field "box" technique; the other patients were treated by a 3D-conformal radiotherapy (3D-CRT) using 4-field individually shaped with a multi-leaf collimator (since 2007) or 7-field intensity modulated radiotherapy (IMRT; since 2009). All patients were treated in a supine position with standard leg-immobilization. No protocol for bowel preparation was used before planning.

Radiotherapy treatment planning was based on transversal CT scans of the whole pelvis; thickness of CT slices was mostly 10 mm (in 141 patients) or 5 mm (in 11 patients). Planning treatment volume consisted of the proximal vaginal stump; parametria; presacral, internal, external, and common iliac lymph nodes with cranial border of radiotherapy fields at L4/L5 spondylous discus in all patients; with 10 mm safety margins in all directions.

The contours of the small intestine were delineated within the whole irradiated volume, as defined by the ICRU 50 (International Commission on Radiation Units) recommendation, by the contouring function of the Eclipse radiotherapy treatment planning system (Eclipse; Varian Medical Systems Inc., Palo Alto, USA). Precise contours of the small intestine were performed in all transversal CT slices; every bowel loop was delineated separately omitting visceral adipose tissue; the

Table 2 – Distribution of lymphadenectomy, radiotherapy, and intestinal morbidity in the two groups.

	Peritoneal closure ($N = 82$)	Peritoneal non-closure ($N = 70$)
Lymphadenectomy	30 patients (37%)	36 patients (51%)
Radiotherapy technique		
Conventional 4-field	68 patients (83%)	48 patients (69%)
3D-conformal 4-field	14 patients (17%)	17 patients (24%)
IMRT	0 patients	5 patients (7%)
Dose of radiotherapy		
45 Gy in 25 fractions	14 patients (17%)	22 patients (31%)
50 Gy in 25 fractions	68 patients (83%)	48 patients (69%)
Late intestinal morbidity		
None observed	60 patients (73%)	56 patients (80%)
Grade 1	21 patients (26%)	9 patients (13%)
Grade 2	1 patient (1%)	5 patients (7%)

large intestine and rectum were not included (Fig. 1). All cases were delineated by one physician to avoid interpersonal variances. The volume of the small intestine within the irradiated volume was calculated in every patient by the automatic function of the Eclipse contouring system. The influence of visceral peritoneal closure upon the volume of the small intestine within the irradiated volume and upon the risk of late intestinal morbidity was analyzed as a dichotomous variable.

2.3. *Statistical analysis*

The normality of data distribution in both arms was confirmed by D'Agostino analysis; Fishers *F*-Test (Two Samples of Variances) was used to exclude unequal variances in both arms. The influence of visceral peritonealization upon the volume of irradiated small intestine was calculated by the unpaired *t*-Test (Two Sample Assuming Equal Variances). The null hypothesis assumed no difference in irradiated bowel volumes in both arms. The predictive factors of peritonealization, lymphadenectomy, site of surgery, radiotherapy technique, dose, and age for the volume of irradiated bowels were evaluated using a multiple regression analysis. Late intestinal adverse effects were retrospectively evaluated and classified according to the RTOG/EORTC late radiation morbidity scoring scheme. The predictive value of peritonealization for late intestinal morbidity was evaluated by logistic regression analysis. We considered $p < 0.05$ to be statistically significant. All statistical analyses were performed using the NCSS 2004 statistical software (NCSS, Keysville, Utah, USA).

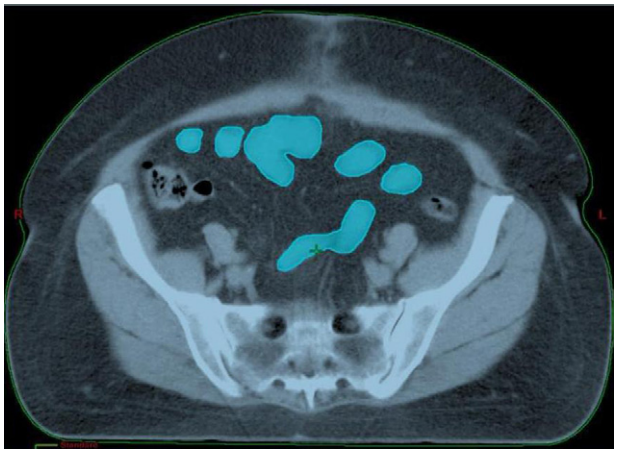

Fig. 1 – Small intestine delineation.

3. Results

The state of peritonealization was provable overall in 152 (65%) patients. Visceral peritonealization after hysterectomy was performed in 82 (54%) of these patients; while in the other 70 (46%) patients closure of the visceral peritoneum was omitted. Mean volume of bowels irradiated by adjuvant radiotherapy was 473 cm^3 (range 200–869 cm^3, median 450 cm^3). The state of peritonealization did not affect the volume of the irradiated small intestine ($p = 0.14$). Mean volume of bowels irradiated in patients with peritonealization was 488 cm^3 (range 200–840 cm^3, median 469 cm^3); mean volume of bowels irradiated in patients with peritoneal non-closure was 456 cm^3 (range 254–869 cm^3, median 428 cm^3). We did not prove any significant difference between both arms.

No statistically significant difference was found in the predictive value of peritonealization ($p = 0.42$), lymphadenectomy, site of surgery, radiotherapy technique, dose, or age for the volume of irradiated bowel in the multiple regression analysis.

The probability of peritonealization was significantly higher when the surgery was performed in smaller district departments rather than in our gynecological centre ($p = 0.003$; Chi-square test), as it was done in 67% (48/72) patients in district hospitals and in 43% (34/80) patients in our gynecological centre. Moreover, there was a significant decrease in the number of peritonealizations with accruing years ($p = 0.02$; Chi-square test).

Late intestinal morbidity was observed in 36 patients (24%): only of grade 1 in 30 patients or grade 2 in 6 patients (Table 2). Grade 1 toxicity consisted mostly of mild diarrhea or bowel cramping; grade 2 morbidity was predominantly moderate diarrhea or colics. The median follow-up for late morbidity evaluation was 40 months; eight patients were lost to follow-up. Logistic regression analysis showed significant predictive value of irradiated bowel volume upon the risk of late intestinal morbidity ($p = 0.013$; OR = 1.003, 95%CI 1.001–1.006); whereas there was no predictive value of the state of peritonealization ($p = 0.34$; OR = 1.467, 95%CI 0.684–3.144).

4. Discussion

In the present study, we did not prove any influence of non-closure of the visceral peritoneum after hysterectomy upon the volume of the small intestine irradiated by adjuvant radiotherapy. This finding supports the common practice whereby omission of peritonealization after hysterectomy for malignant disease is considered to be safe even in the case of adjuvant radiotherapy. On the contrary, closure of the visceral peritoneum can increase the risk of bowel adhesion formation, as reported by Kadanali et al.[7] Bowel loop adhesion in the small pelvis is a major problem in adjuvant pelvic radiotherapy, since it causes the application of great doses to the fixated loop with consequent morbidity. Again, this idea supports the practice of non-closure of the peritoneum after hysterectomy.

Unfortunately, we were not able to study all 235 patients treated at our department in this period. This deficiency was caused by retrospective evaluation, as only accessible data from surgical protocols could answer the question whether the peritonealization was performed or omitted. In 83 patients the surgical protocols could not answer this question. That is quite a big loss, and a theme for retrospect.

Acute gastrointestinal toxicity, especially acute diarrhea, is the most common adverse event of adjuvant pelvic radiotherapy in gynecological malignancies. Acute diarrhea is rarely the reason for treatment interruption or termination. Intestinal adverse events are directly proportional to the volume of bowels irradiated,[9] hence we can deduce that surgical techniques which may enlarge the volume of the small intestine within radiation fields may cause greater post radiation morbidity.

It seems that non-closure of the pelvic peritoneum is not that case; however, the clinical impact of our observation is not clear, as we have no reliable data about patients' acute gastrointestinal toxicity (retrospective evaluation; not-standardized acute toxicity questionnaire).

In our study, we found no influence of the state of visceral peritonealization upon the risk of late intestinal toxicity after pelvic radiotherapy. Nonetheless, grade 2 intestinal morbidity was slightly more frequent in patients without peritonealization. On the other hand, we found a significant predictive value of irradiated bowel volume upon late morbidity, as we had expected from the Quantec data.[9] Once again, there seems to be no hazard related to peritoneal non-closure in patients with tumors of the uterus who may require postoperative whole pelvic radiotherapy.

Finally, we discovered that the probability of peritonealization was significantly lower for surgeries performed in our gynecological centre rather than district hospitals. Moreover, there was a significant decrease in the number of peritonealizations with accruing years as well, with no peritonealizations performed in the year 2009 (12 patients studied that year). These data show the convincing tendency in modern surgical techniques to leave the peritoneum open.

In the last few years, several randomized trials in early endometrial carcinoma raised some doubt about the value of external beam radiotherapy in this setting.[10–15] The experience from our study may therefore seem less important in the current era. Nevertheless, we hope our findings can provide a sufficient evidence and consequently moderate potential uncertainty for surgeons or radiation oncologists.

5. Conclusion

Non-closure of the visceral peritoneum after abdominal hysterectomy and BSO in patients with uterine corpus carcinoma receiving adjuvant radiotherapy does not increase the volume of the small intestine within the irradiated volume. Likewise, there is no consequent intestinal morbidity enhancement in these patients.

Conflict of interest

There are no conflicts of interest.

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