Laparoscopic debulking of bulky lymph nodes in women with cervical cancer: indication and surgical outcomes

R Tozzi,a F Lavra,a T Cassese,a R Garruto Campanile,a V Pedicini,b M Bignardi,b M Scorsetti,b A Bertuzzi

a Department of Gynaecologic Oncology, Radiology b Department of Radiotherapy and c Department of Medical Oncology, IRCCS Humanitas Clinical Institute, Rozzano, Milan, Italy

Correspondence: Dr R Tozzi, Department of Gynecologic Oncology and Mini-invasive Surgery, IRCSS Humanitas Clinical Institute, Via Manzoni 56, 20089 Rozzano, Milan, Italy. Email roberto.tozzi@humanitas.it

Objective To describe the technique and the surgical outcome of laparoscopic resection of bulky lymph nodes before adjuvant treatment.

Design Prospective pilot study.

Setting Gynaecological oncology cancer centre.

Population From January 2006 to February 2008, 22 consecutive women presented with cervical cancer and bulky metastatic lymph nodes (>2 cm).

Methods All women underwent resection of bulky lymph nodes by laparoscopy. A prospective record of the main surgical outcomes was performed.

Main outcome measures Safety and efficacy of laparoscopic resection of bulky lymph nodes, conversion to laparotomy, intra- and perioperative morbidity.

Results All the operations were completed by laparoscopy. Median operative time was 197 minutes (range 180–320). Median blood loss was 60 cc (range 10–100), two women experienced complications: one thermal injury of the sciatic root provoking postoperative leg palsy and one chylous ascites. The woman with the thermal injury has recovered most leg function with physiotherapy and the woman with chylous ascites recovered within 2 weeks, slightly delaying the adjuvant treatment. All women were discharged within 4 days from the operation (range 2–4). Pathology reports confirmed the presence of tumour metastases and the lymph nodes size. The adjuvant treatment started at a median time of 12 days (range 3–22).

Conclusion Debubling of large pelvic and para-aortic lymph nodes was effectively accomplished by laparoscopy in all 22 women with 9% complication rate. The surgical outcome is similar to historical series on women operated on by laparotomy, with the advantage of a faster recovery and an early start of adjuvant treatment.

Keywords Cervical cancer, bulky, laparoscopy, lymph nodes, surgery.


Introduction

The lymph nodal status is the most important prognostic factor for survival in women with cervical cancer. Lymph node metastases, both pelvic and para-aortic, are clearly worsening the prognosis. Despite several studies confirming the prognostic value of tumour metastasis to the lymph nodes, the official International Federation of Obstetrics and Gynecology (FIGO) staging system for women with cervical cancer is based on clinical findings and does not take the lymph nodal status into account. However, in the current practice, the presence of lymph node metastasis demands the use of radiotherapy. If the lymph node involvement is recognised before surgery, radiotherapy substitutes surgery. In fact, the cure rate of radical radiotherapy is similar to radical surgery, while the combination of the two treatment modalities adds to the overall morbidity with no demonstrated benefit on survival. Usually the area of the lymph nodes is treated with 50–60 Gy given with an external beam using a linear accelerator. Such dose should not be exceeded to avoid severe or fatal toxicity to adjacent organs, chiefly the small bowel. According to classic studies of radiotherapy, 60 Gy are required to sterilise 90% of a 2-cm lesion.

The primary central pelvic tumour can be treated with the combination of external beam and brachytherapy (BT) with
an overall dose of 70–90 Gy. An equivalent dose is intolerable if
given to the pelvic sidewall or to the para-aortic area. Therefore,
women with cervical cancer and bulky pelvic and/or para-
aortic lymph nodes larger than 2 cm still represent a challenge
for radiotherapy and/or chemotherapy. In the past, few studies
proposed the removal of such bulky lymph nodes before the
radiotherapy.6–9 The surgery was always performed by la-par-
rotomy. This is a pilot study on the laparoscopic technique of
‘lymph node debulking’, reporting on the feasibility and on
the surgical outcomes.

Methods
Between January 2006 and February 2008, 22 consecutive
women referred to the Department of Gynaecologic Oncology
of the Humanitas Clinical Institute, Milan, Italy, were diag-
nosed with cervical cancer and the presence of at least one
bulky, pelvic and/or para-aortic lymph node. A lymph node
was defined bulky if the size was >2 cm. Twelve women were
affected by a primary tumour and 10 women by a recurrent
tumour. In 8 of 10 women, previous surgery included pelvic
lymphadenectomy. Ten of 22 (45%) women had bulky para-
aortic and 12 of 22 (55%) women beard bulky pelvic lymph
nodes. Previous treatments, patients and tumour character-
istics are described in Tables 1 and 2. The decision for the
women to undergo surgery, together with the entire manage-
ment, was undertaken at a multidisciplinary level well in
advance to the operation. The indication for surgery was
the position and the size of the lymph node, affecting the
ability of radio and/or chemotherapy to effectively treat the
woman. All 22 women underwent positron emission tomo-
graphy (PET) scan to rule out widespread disease. The last 10
women underwent an angio-computed tomography (CT)
with three-dimensional reconstruction to display the an-
tomic relation of the bulky lymph node to the vessels.

All women were admitted to the hospital the day before the
surgery to receive bowel preparation (X-prep; ASTA, Milan,
Italy) to confirm the consent and to test the compatibility of
blood units. At least 4 blood units were made available and
kept as a standby. All women were placed supine in a litho-
tomy position with closed legs. The technique of pelvic and
para-aortic transperitoneal lymphadenectomy has been fully
described by Prof. Schneider and his team in Jena,
Germany.10–13 The operation started with the debulking
phase. According to the information gained with the angio-
CT, abnormal vessels were coagulated and the cleavage plane
with the vessel was sought in the most favourable area. In the
pelvis, the ureter was isolated at the cross with the iliac vessels.
The pelvic sidewall was dissected from lateral to medial, with
access to obturator fossa leaving the external iliac vessels
medially. The obturator nerve and the lumbo-sacral trunk
were visualised and isolated to avoid injuries. The lymph node
was carefully mobilised from the pelvic sidewall with preven-
tive bipolar coagulation before any tissue was cut. The aim
was to avoid the rupture of the lymph node capsule. Once the
bulky lymph node was mobilised from the pelvic sidewall, it
was dissected medially along the internal iliac vessels. Finally,
with enough space on both sides, the lymph node was freed
from its dorsal connections by careful traction. To delineate
the field of radiotherapy, the para-aortic lymphadenectomy
was performed to the level of the inferior mesenteric artery on
the left side and to the inset of the ovarian vessels in the cava
on the right side. If these lymph nodes were found positive at
frozen section, the lymphadenectomy was continued to the
level of the left renal vein. In women with bulky para-aortic
lymph nodes, the attention was immediately focused on the
bulky lymph node. If the debulking was successfully com-
pleted, it was regularly followed by an infrarenal lymphade-
nectomy to the level of the left renal vein. The technique
was to isolate and mobilise the ureter and then to approach the
lymph node. The dissection was started from the aorta and
then continued to the cava. In two women, the bulky lymph
node was on the right side, lateral to the aorta and intimately
adherent to the cava. In these women, the conventional place-
ment of the optic in the umbilical trocar provided only a lim-
ited exposition of the cava. Therefore, an additional 10-mm
trocar was inserted in the right side, thus placing the cava in
the foreground. At the end of the surgery, some endoclips
were placed to mark the area where the bulky lymph node
was removed. All specimens were extracted via an endobag
and, depending on the extension of the surgery, one or two
drains were positioned (one in the pelvis and the other in the
para-aortic area) to avoid lymph accumulation. Analgesia
was provided with nonopioid drugs and the urinary catheter
was removed 24 hours after the surgery. Oral assumption started
day after the surgery. The drains were removed once the
daily discharge was <50 cc.

Adjuvant treatment was provided by external beam radio-
therapy (EBR). A total dose of 45–59.4 Gy was prescribed in
daily fractions of 1.8 Gy, five fractions per week, to a total of 25–
33 fractions. Both pelvic and para-aortic targets were treated
with an 18 MV X-ray beam by multiple field conformal tech-
niques (either a classical four fields box technique or a 3–4 fields
nonorthogonal beam arrangement). The upper limit of the

Table 1. Characteristics of 22 women with cervical cancer and
bulky lymph node

<table>
<thead>
<tr>
<th>Age, median (range)</th>
<th>56 (39–72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous abdominal operations, mean (range)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>Previous treatment, type (no. of women)</td>
<td>Surgery + chemoradiation (n = 5)</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy + surgery + radio (n = 3)</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy + surgery (n = 2)</td>
</tr>
</tbody>
</table>
para-aortic field was fixed to L1. In case of infrarenal-positive lymph nodes, the field was extended to the level of T10. All women treated with radical intention were undergoing BT and were referred to a local institution. They were treated with either high dose rate (HDR) or pulsed dose rate (PDR) after-loading mode, using an intracavitary Iridium-192 source. The aim was to give an estimated overall dose of 80–85 Gy to point A and 50–60 Gy to point B. If BT was undeliverable or in women with residual disease after debulking, an additional external beam boost was administrated. Chemotherapy was based on cisplatin given during the EBR at the dose of 40 mg/m²/week. The end-points of the study were to investigate the morbidity and the success rate of the procedure. Therefore, we prospectively recorded the rate of conversion to laparotomy, the complications and the number of women in whom the bulky lymph node could be completely resected.

**Results**

In all women, the PET scan was positive for the bulky lymph node and negative for widespread disease. All the operations were concluded by laparoscopy with no conversion to laparotomy. In 21 of 22 women, the lymph node was removed intact. In one woman, affected by recurrent disease and still radiotherapy naive, the bulky lymph node was 3.1 cm, with the more distal and also smaller part surrounding the lumbar-sacral trunk. Despite several attempts to mobilise the lymph node, it was not safely separable from the nerve. In view of the possibility to offer radiotherapy, it was decided to leave some tissue behind, trying to avoid capsule rupture and potential tumour spread. The pathology report described a 1.8-cm structure completely replaced by tumour. The simulation CT showed a 1-cm residual structure. In addition to the debulking of the lymph node, 12 women had, during the same operation, inframesenteric para-aortic lymphadenectomy and 10 women had infrarenal lymphadenectomy to define the radiotherapy field. Median operative time for the entire operation was 197 minutes (range 180–320) and median blood loss was 60 cc (range 10–100). In addition to the bulky lymph node, a mean of eight (range 1–18) para-aortic lymph nodes were removed. Pathology reports confirmed tumour metastases in the bulky lymph node of all women. The median size of the lymph nodes, as from the pathology report, was 3.8 cm (range 1.8–6.9 cm). Two of 10 (20%) women with primary disease and pelvic bulky lymph node, underwent para-aortic lymphadenectomy and were found with histologically positive para-aortic lymph nodes missed at the PET scan. One woman with a positive PET scan in the para-aortic area was found to have 12 negative para-aortic lymph nodes. Two women experienced complications: one thermal injury of the sciatic root provoking postoperative leg palsy and one chylous ascites. The woman with the thermal injury has slowly recovered most of the leg function and the woman with chylous ascites was settled within 2 weeks, slightly delaying the adjuvant treatment. All women were discharged within 2 days from the operation, except for the two women with complications who remained until day 4. The adjuvant treatment was started at a median time of 12 days (range 3–42). Excluding the two women with complications, all women underwent adjuvant treatment within 7 days. All women received chemoradiation, 10 to an extended field including the para-aortic area, 4 to the para-aortic area alone and 8 to the standard pelvic field.

**Discussion**

The most significant prognostic factor for survival in women with cervical cancer is the status of the lymph nodes, independently of the FIGO stage or histological grade of disease.1–3 On the basis of five major trials published in 1999–2000,10,11,14–16 significant changes have been made in the treatment of women with cervical cancer. Although none of the trials has compared surgery versus chemoradiation and only one16 of the five trials included women undergone surgery, chemoradiation has become the standard of treatment for all women with FIGO stage >IB2, completely replacing surgery. In the last few years, for these women not candidate to surgery, a surgical staging by laparoscopy has been proposed to identify microscopic involvement of the lymph nodes, particularly the para-aortic.17 In fact, the presence of tumour involved lymph nodes beyond the pelvis remains valuable information, mandating extension of the radiotherapy field to the para-aortic area.

For all these women, however, the finding of bulky lymph nodes poses a serious challenge. As from classic studies,5,18 the probability of tumour control by radiotherapy depends on the capacity to eliminate up to the last clonogenic cells. The rate

---

**Table 2. Tumour characteristics of 22 women with cervical cancer and bulky lymph node**

<table>
<thead>
<tr>
<th>Original tumour</th>
<th>Pelvic/para-aortic bulky lymph node</th>
<th>FIGO stage women p</th>
<th>Size of the bulky lymph node, median (range), cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix (n = 22)</td>
<td>12 pelvic</td>
<td>IIIB (n = 4); IIIB (n = 3)</td>
<td>Pelvic 4.8 (3.1–7.2)</td>
</tr>
<tr>
<td></td>
<td>10 para-aortic</td>
<td>IIIA (n = 2); IB2 (n = 2)</td>
<td>Para-aortic 3.7 (2.8–4.8)</td>
</tr>
</tbody>
</table>

p, primary; r, recurrent
of success is proportional to the dose, but, since cell killing is a random process, the relation is not linear. Several factors are influencing the rate of success, related to the tumour (volume, oxygenation, regeneration and repair of damages) and the treatment modality. With the limits of tumour heterogeneity, tumour control probability curves have been designed. Readjusting for tumour volume, higher dose is required for larger tumours. According to these curves, a dose of about 75 Gy is required to achieve 100% control of a 2-cm tumour. In designing dose–response curves,\textsuperscript{5,18} the effect of the dose on the normal tissues must be taken into account. The dose–response curves for adverse effects are steeper than for tumour because normal tissues are more homogenous, but also adverse effects are directly related to the dose. Usually the dose is prescribed according to the tumour volume and the presence in the field of treatment of dose-limiting tissue. The pelvic sidewall is treated with a maximum of 60 Gy and the para-aortic area with a dose of 45–50 Gy. The dose is limited because the intestine, mainly the small bowel, is inevitably reached by the radiotherapy and has a minimal tolerance dose of 50 Gy and a maximal tolerance dose of 60 Gy.\textsuperscript{3} In case of women with bulky pelvic or para-aortic lymph nodes (>2 cm), such dose is insufficient to achieve tumour control. However, dose escalation to 75 Gy, required to sterilise such tumour volume, is intolerable for the surrounding organs, mainly small bowel. Therefore, the only option is to reduce the tumour burden. This can be achieved either by chemotherapy or by surgery. There are enough data, mainly on women with cervical cancer, on the efficacy of the chemotherapy and/or surgery on large lymph nodes. The option of surgical resection of bulky lymph nodes has already been proposed in previous reports.\textsuperscript{1,3,6–9,19} The outcomes of interest were feasibility, morbidity and survival. The surgery was performed by laparotomy, with an extra- or transperitoneal technique. The feasibility can be assessed by the rate of women in which the procedure was abandoned and by the complication rate. In two studies,\textsuperscript{1,6} the operation was successfully performed on all women with a feasibility of 100%. In other two reports,\textsuperscript{7,8} one being the update of a previously published paper, there is a group of women in which the bulky lymph node was unrectable. The rate of women with such finding was 21.1% (20 of 94 women with bulky lymph node). In another study\textsuperscript{19} focused on women with positive para-aortic lymph nodes, little details are provided on the size of the bulky lymph node and on the number of women harbouring such lymph nodes. There is a group of women with gross residual disease (17 of 43 women with six of them having undergone fine needle aspiration). Unfortunately, the group of women with no residual disease (26 of 43 women) includes women with initial microscopic disease. Therefore, the rate of women actually having their surgery abandoned cannot be drawn. In the report from Goff et al.,\textsuperscript{3} 9 of 33 (27%) women with bulky lymph nodes (defined as size >1.5 cm) were unresectable. No details are provided on the site of the unresectable lymph nodes. It is difficult to isolate from all these studies the rate of surgical complications solely related to the resection of bulky lymph nodes. In fact, the complication rate refers to the whole study group, also including women with microscopic positive lymph nodes but no bulky lymph nodes or women undergone radical hysterectomy at the same time. Additionally, because one of the greatest concerns against pre-treatment surgery has been the increase of radiotherapy complications, most studies report on overall treatment morbidity (surgery and adjuvant treatment). Thus, the complications rate for the resection of bulky lymph nodes is broadly stretched between 10.6 and 23.4% as in most studies the women have undergone additional procedures. However, these studies report major vascular accidents occurring in three women\textsuperscript{3} and in one woman.\textsuperscript{6} With respect to the survival rate, two studies\textsuperscript{7,8} had a control group, that is, women with positive but unresectable bulky lymph nodes. The most impressive information is the dismal prognosis of women whose lymph node could not be resected (0–5%, 3 years over-all survival [OS]). In both studies, the complete resection of enlarged, bulky positive lymph nodes was providing a survival benefit over women with unresectable bulky lymph nodes. This finding was also confirmed in studies focused on women with bulky para-aortic lymph nodes.\textsuperscript{19} Moreover, the 5-year OS rate of women with macroscopic/palpable but resected lymph nodes (43%, 5-year OS) was found to be similar to the survival of women with microscopic positive lymph nodes (50%, 5-year OS).\textsuperscript{7,8} In 2002, a paper by Kupets et al.,\textsuperscript{20} reviewing the literature on pelvic lymph node debulking and readjusting after the standard survival rate, concluded that very few women with cervical cancer would profit from such procedure. This paper was strongly contested in a letter to the editor from Tammela et al.\textsuperscript{21} The letter was extremely precise and we do fully agree with their data estimation and conclusions. In addition, it must be emphasised that so far no alternative has been proposed for these women with large lymph nodes, whose prognosis is very poor if the lymph nodes are not resected. Therefore, the aim should be to resect the lymph node and reduce the surgical morbidity to accelerate the start of the adjuvant treatment.

**Conclusion**

To our knowledge, there are no previous studies on the use of laparoscopy in removing bulky lymph nodes. The results of the current study show that the procedure of debulking was effective in all women, with 21 of 22 (95%) women having the bulky lymph node completely removed and none requiring conversion to laparotomy. The morbidity rate (9%) is similar to the rate reported in the literature on women undergone the
same surgery by laparotomy, with no vascular injury occurring and a minimal blood loss. Also, a major potential advantage of the laparoscopy compared with the laparotomy may be the reduction of the overall complications rate (surgery + radiotherapy). This issue, yet to be confirmed, should be related to a lower rate of adhesions formation following laparoscopy, with less restriction of small bowel mobility and, consequently, limiting the enteric morbidity. While the research in radiotherapy is attempting to increase the dose to the target organ sparing the adjacent organs with stereotaxis and intensity modulated radiotherapy, surgery remains the only resource for women with bulky lymph nodes. With respect to survival outcomes, our follow up is far too short to draw conclusions. However, this study was merely looking at the surgical outcomes, showing that the procedure was feasible by laparoscopy in all women with an acceptable morbidity. The major benefit of the laparoscopy was the early recovery of the women and the opportunity to accelerate the start of the adjuvant treatment. The reduction of overall treatment-related morbidity because of less adhesions formation is possible but remains unproven. Studies including more women and longer follow-up periods are required to validate the results provided in this pilot study.

Disclosure of interest
No relevant financial, personal, political, intellectual or religious interest needs to be disclosed.

Contribution to authorship
All authors contributed in the clinical part of the study. R.T. has contributed in the conception of the protocol, performance of the surgeries and writing the manuscript.

Details of ethics approval
No ethical approval was requested as this type of procedure is well recognised in clinical practice.

Funding
No funding was requested for this publication.

Acknowledgements
The authors thank Lavinia Segurini and Jon Shore for editorial assistance.

References
17 Hertel H, Kohler C, Elhawawy T, Michels W, Possover M, Schneider A. Laparoscopic staging compared with imaging techniques in the staging of advanced cervical cancer. Gynecol Oncol 2002;87:46–51.