



# Comparison of surgical and pathological parameters after laparoscopic transperitoneal pelvic/para-aortic lymphadenectomies

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## HIGHLIGHTS

- Safety and feasibility of laparoscopic and para-aortic lymphadenectomy is not impaired by body mass index
- High volume training may lead to reduced intra-operative complications
- As new members join a team of gynecologic oncology surgeons, the results may be maintained without a new increase in intra-operative complications.

## ABSTRACT

**Objective** Lymphadenectomy is an integral part of surgical staging and treatment for patients with gynecologic malignancies. Since its introduction, laparoscopic lymphadenectomy has proved feasible, safe, and oncologically adequate compared with open surgery while morbidity is lower and hospital stay considerably shorter. The aim of this study was to examine if surgical outcomes may be improved after the initial learning curve is complete.

**Methods** An analysis of 2535 laparoscopic pelvic and/or para-aortic lymphadenectomies was performed between July 1994 and March 2018 by one team of gynecologic oncology surgeons but with the consistent supervision of a consultant surgeon. Data were collected prospectively evaluating operative time, intra-operative and post-operative complications, number of lymph nodes, and body mass index (BMI). Previously published data of 650 patients treated after introduction of the method (period 1, 1994–2003) were compared with the latter 524 patients (period 2, 2014–2018).

**Results** The median age of the 2535 patients was 43 years (IQR 34–57). The most common indication for pelvic and/or para-aortic lymphadenectomy was cervical cancer (n=1893). Operative time for para-aortic lymph node dissection was shorter in period 2 (68 vs 100 min,  $p<0.001$ ). The number of harvested lymph nodes was increased for pelvic (19.2 (range 2–52) vs 21.9 (range 4–87)) and para-aortic lymphadenectomy (10.8 (range 1–52) vs 14.4 (range 4–64)),  $p<0.001$ . BMI did not have a significant influence on node count or operative time, with BMI ranging from 14.6 to 54.1 kg/m<sup>2</sup>. In contrast to period 1 (n=18, 2.9%), there were no intra-operative complications in period 2 (n=0, 0.0%,  $p<0.001$ ) whereas post-operative complications were similar (n=35 (5.8%) in period 1; n=38 (7.6%) in period 2;  $p=0.32$ ).

**Conclusion** In this large cohort of patients who underwent laparoscopic transperitoneal lymphadenectomy, lymph node count and peri-operative complications improved after the initial learning curve.

## INTRODUCTION

According to national and/or international guidelines, laparoscopic pelvic and/or para-aortic lymphadenectomy is an integral part of surgical staging and treatment of patients with gynecologic malignancies. In many gynecologic oncology centers worldwide, it is performed as a staging procedure in locally advanced cervical cancer,<sup>1,2</sup> radical trachelectomy,<sup>3,4</sup> laparoscopic and vaginal-assisted laparoscopic radical hysterectomy,<sup>5–7</sup> early ovarian cancer,<sup>8,9</sup> groin-node positive vulvar cancer,<sup>10</sup> endometrial cancer,<sup>11,12</sup> and other rare entities.

After their introduction in the 1990s,<sup>13,14</sup> large single-center and multi-center studies demonstrated feasibility, low morbidity, and oncologic adequacy but also showed longer operation times for the laparoscopic approach.<sup>15–17</sup> Comprehensive laparoscopic and robotic staging allows for individual treatment according to intra-operative findings and histologic results of frozen and permanent section, even in obese patients.<sup>11,18,19</sup> There is disagreement regarding the number of procedures needed to gain proficiency in these meticulous operations.<sup>20</sup> To date, the extent to which further experience after the initial learning curve can improve surgical/oncological results has not yet been investigated. Therefore, the aim of this study is to compare surgical and pathological parameters between the first 650 patients and the latter 524 patients of a large cohort of laparoscopic lymphadenectomies performed by one team of gynecologic oncologists.

## METHODS

A total of 2535 laparoscopic pelvic and/or para-aortic lymphadenectomies were performed by one team of gynecologic oncologists between July 1994 and



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**Table 1** Indications for pelvic and/or para-aortic lymphadenectomy

Indication for pelvic/para-aortic lymphadenectomy	1994–2018	1994–2003 (eligible for analysis)	2014–2018 (eligible for analysis)
Cervical cancer	1893	407	394
Endometrial cancer	361	112	72
Early ovarian cancer	99	44	16
Vulvar cancer – inguinal lymph node positive	62	9	20
Others	120	34	22
Total	<b>2535</b>	<b>606</b>	<b>524</b>

March 2018. Data of 1130 patients were included in this analysis. The team members changed over the years but the procedures were always performed under the supervision of a consultant gynecologic oncologist. The standardized technique of transperitoneal lymphadenectomy using five trocars has been described elsewhere and was not modified substantially over time.<sup>16</sup> There was no restriction regarding age or body mass index (BMI). Each patient undergoing any type of lymph node dissection (complete pelvic and/or para-aortic lymphadenectomy, sentinel node biopsy, pelvic  $\pm$  para-aortic lymph node sampling, removal of bulky lymph nodes) was registered in the database. From 2001, the data were maintained prospectively. Indications for the 2535 lymphadenectomies are summarized in Table 1.

The results of the first 650 procedures between 1994 and 2003 have been previously published.<sup>16</sup> Due to incomplete data with respect to lymph node number and separate operation time for different parts of lymphadenectomy, lymphadenectomies between October 2003 and December 2013 are not included in this study. Hence, this is a comparison between lymphadenectomies performed in period 1 (1994–2003) and period 2 (2014–2018). The following parameters were monitored: operation time, intra-operative and post-operative complications (grade I–V Clavien–Dindo classification), number of lymph nodes, and BMI. The time for each step of lymphadenectomy (pelvic right/left side, right para-aortic, left inframesenteric, infrarenal) as well as intra-operative complications related to lymphadenectomy were registered. Registration of post-operative complications had the limitation that not all patients were followed in our institution. Lymph node number and BMI were extracted from pathology reports and patients' charts.

Parameters were collected in an Excel database. Statistical analysis was performed using t-test, Levene test, and Mann–Whitney

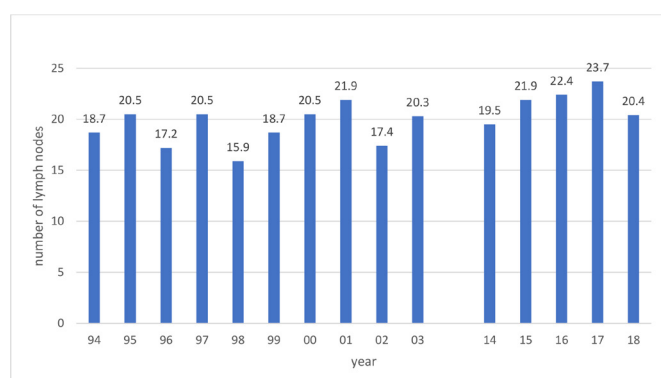
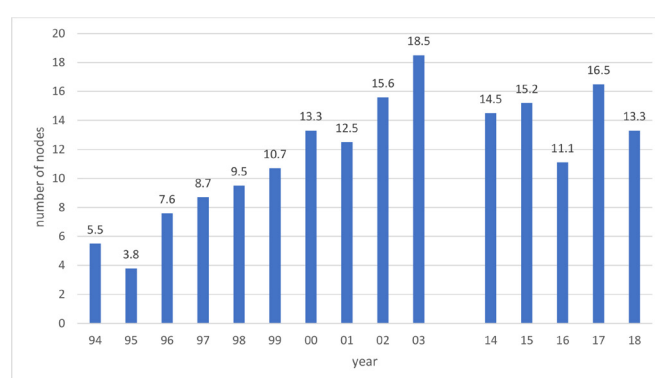
U tests. The institutional review board agreed with the purposes of this retrospective study and approved it.

## RESULTS

A total of 1130 patients were included in the analysis. This included 606 patients in period 1 and 524 patients in period 2. The majority of laparoscopic pelvic  $\pm$  para-aortic lymphadenectomies in both periods was performed for cervical cancer (75.2% and 66.0%, respectively). Further indications are listed in Table 1. In period 1, 466 (77%) of 606 eligible patients underwent pelvic lymphadenectomy, 433 complete and 33 lymph node sampling. Para-aortic lymphadenectomy was performed in 468 women, 445 complete and 23 sampling procedures. In 362 patients, a complete pelvic and para-aortic lymphadenectomy was performed. Mean patient age in period 1 was 49 years (range 14–85) and mean BMI was 25.9 kg/m<sup>2</sup> (range 14.6–49.7).

Of the 524 patients treated during period 2, 358 patients underwent complete pelvic lymphadenectomy and 128 patients underwent sentinel node biopsy exclusively. Para-aortic lymphadenectomy was performed in 210 patients, 170 complete and 40 sampling procedures. Complete pelvic and para-aortic lymphadenectomy was performed in 177 patients. Mean patient age was 45 years (range 20–84) and mean BMI was 26.1 kg/m<sup>2</sup> (range 15.6–54.1). There was no significant difference with respect to age and BMI between the two periods ( $p=0.5$ ). For the comparison between periods 1 and 2, only complete lymphadenectomies were included.

In patients who underwent complete pelvic lymphadenectomy, a mean of 19.2 lymph nodes (range 2–52) were removed in period 1 and 21.9 nodes (range 4–87) in period 2 ( $p<0.001$ ) (Figure 1).

**Figure 1** Number of harvested pelvic lymph nodes.**Figure 2** Number of harvested para-aortic lymph nodes.

**Table 2** Pelvic lymphadenectomy: correlation of lymph node number and operative time with body mass index (BMI)

BMI (kg/m <sup>2</sup> )	No of patients		No of lymph nodes		Operative time (min)			
					Right side		Left side	
	1994–2003	2014–2018	1994–2003	2014–2018	1994–2003	2014–2018	1994–2003	2014–2018
<20	40	15	19	22	28	22	27	23
20–24.9	192	134	20	21	28	23	28	24
25–29.9	149	118	18	23	27	26	27	26
>30	85	91	18	22	27	27	29	27

During complete para-aortic lymphadenectomy, a mean of 10.8 lymph nodes (range 1–52) was harvested in period 1 compared with 14.4 (range 4–64) in period 2 ( $p < 0.001$ ) (Figure 2). BMI had no significant impact on the number of harvested pelvic lymph nodes. Mean lymph node numbers per sub-group are shown in Table 2. The correlation between operative time and BMI for pelvic and para-aortic lymphadenectomy is shown in Tables 2 and 3. There was no significant reduction in operative time for pelvic lymphadenectomies between the two periods (56 vs 51 min;  $p = 0.078$ , t-test). In contrast, the mean operative time for complete para-aortic lymphadenectomy was 100 min in period 1 and 68 min in period 2 ( $p < 0.001$ ).

Between 1994 and 2003, 18 (2.9%) intra-operative and 35 (5.8%) post-operative complications occurred. Between 2014 and 2018 there were no intra-operative complications: no conversion to laparotomy or transfusion was necessary ( $p < 0.001$ ). The post-operative complication rate was 7.6%. Most post-operative complications were temporary paresthesia ( $n = 22$ ), followed by lymphoceles ( $n = 11$ ), fever of unknown origin ( $n = 2$ ), temporary shoulder weakness due to shoulder blockers, paralytic ileus, and fulminant pulmonary embolism (one each).

## DISCUSSION

Laparoscopic lymphadenectomy was added to the armamentarium of gynecologic surgery at the end of the last century,<sup>13 14</sup> robotic lymphadenectomy following the approval by FDA in 2005.<sup>21 22</sup> Techniques for laparoscopic/robotic transperitoneal or retroperitoneal lymphadenectomy may be considered routine procedures. Shortly after their introduction, minimally invasive lymphadenectomy demonstrated oncological adequacy compared with open surgery with respect to radicality and number of lymph nodes,<sup>23 24</sup> with the latter very much depending on examining pathologists.<sup>25</sup> In our center we adhere to a standardized transperitoneal laparoscopic approach, which allows for inspection of the abdominal cavity, washings, and biopsies. The decision for either transperitoneal or retroperitoneal lymphadenectomy and straight-stick laparoscopy versus robotic lymphadenectomy is mostly related to surgeon preference and availability rather than based on scientific data.<sup>26 27</sup>

Most studies on laparoscopic/robotic lymphadenectomy demonstrate lower blood loss, shorter hospital stay, equal or higher number of lymph nodes, and a lower complication rate, especially in obese patients, but a significantly longer operative time compared with open surgery.<sup>15–17</sup> In our study there was no significant reduction in operative time for pelvic lymphadenectomies between the two

periods (56 vs 51 min;  $p = 0.078$ ). Operative time for pelvic lymphadenectomy alone is rarely provided in studies as it is often part of larger procedures. The few studies available demonstrate a time range of 31–156 min, removing 10.7–41.6 lymph nodes.<sup>28</sup> Our operative time falls into the lower end of this range without compromising the number of harvested nodes (19 and 21, respectively). Para-aortic lymphadenectomy up to the renal vessels is the most challenging procedure. The published operative time ranges from 96 to 340 min for the removal of 5.7–21 nodes.<sup>22 29</sup> We significantly reduced the time for complete para-aortic lymphadenectomy from 100 to 68 min between periods 1 and 2. At the same time we increased the number of nodes from 10.8 in period 1 to 14.4 in period 2. In contrast to the findings in previously published data, higher BMI did not significantly impair the number of para-aortic lymph nodes during period 2.<sup>16</sup>

As the operation technique and instruments used have changed very little over the years, the most obvious causes for improved surgical and pathological results are greater proficiency, high volume training, and newer imaging equipment. Teaching laparoscopic lymphadenectomy is an important aspect in any fellowship program.<sup>23 24</sup> However, only a few studies have focused on the learning curve of laparoscopic lymphadenectomy. Togami et al reported significantly reduced blood loss and surgical time after 20 patients<sup>30</sup> and Chong et al reported fewer complications after 50 procedures.<sup>20</sup> Quality improved after 23 patients in the series by Reade et al<sup>31</sup> and after 125 patients in the series by Melendez et al.<sup>32</sup> Reaching consistent outcomes seems more feasible when using robotic surgery. Seamon et al achieved proficiency after only 20 patients with robotic surgery for endometrial cancer.<sup>33</sup> Lim et al had lower intra-operative complication rates in their first 122 robotic cases (0.8%) than their first 122 laparoscopic cases (5.7%).<sup>29</sup> In our analysis of the first 606 patients who underwent pelvic ± para-aortic lymphadenectomy, a consistent performance was achieved after 20 pelvic and 100 para-aortic procedures.<sup>16</sup> After having performed over 2000 laparoscopic lymphadenectomies, we reduced the intra-operative complication rate from 2.9% to 0.0% whereas the post-operative complication rate was similar between both periods. This low overall rate of complications is in accordance with the literature.<sup>15 17</sup>

Our study has strengths and weaknesses. It is a single-center retrospective study of a prospectively maintained database and the results of the first period have already been published. Moreover, due to missing data, not all 2535 lymphadenectomies were analyzed. However, to the best of our knowledge, this is the largest series of transperitoneal laparoscopic lymphadenectomies performed using

**Table 3** Para-aortic lymphadenectomy: correlation of lymph node number and operative time with body mass index (BMI)

BMI kg/m <sup>2</sup>	Para-aortic lymphadenectomy							
	No of patients		No of lymph nodes		Operative time (min)			
	1994–2003	2014–2018	1994–2003	2014–2018	Right paraaortic	Left inframesenteric		
<20	49	8	13	15	36	28	36	15
20–24.9	191	71	11	14				18
25–29.9	156	67	11	14				19
>30	79	53	10	14				21

a standardized technique. Our results suggest that, even after the initial learning curve, the operative time for specific parts of lymphadenectomy and the intra-operative complication rate can still be reduced even in the setting of higher BMI. This continued learning effect has not previously been addressed in the literature.

## CONCLUSION

This study has shown that standardized laparoscopic transperitoneal pelvic ± para-aortic lymphadenectomy is safe and oncologically adequate with minimal morbidity. As long as the procedures are performed under the supervision of a consultant gynecologic oncologist, the operative duration and lymph node count may be improved over time.

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