

Intra-operative and postoperative complications depend on operating approach and body mass index in patients with malignant uterus body neoplasm

A. Mladěnka¹, P. Mladěnka², O. Simetka¹, J. Klát¹

¹Oncogynaecologic center, Department of Gynecology and Obstetrics, University Hospital, Ostrava; ²Department of Pharmacology and Toxicology, Charles University in Prague, Faculty of Pharmacy in Hradec Králové, Prague (Czech Republic)

Summary

Purpose: Cancer of the uterus body is the fourth most frequent tumor in females. The standard approach is a hysterectomy. Although laparoscopy (LPS) is advantageous, to date, no complex, conclusive data have compared the complication rates between LPS and laparotomy (LT) in real clinical settings, with a long-term follow up. This study aimed to compare these two approaches in terms of peri-operative, and early postoperative, and late postoperative complications, and to analyze associations between complications and patient characteristics (e.g., body mass index). **Materials and Methods:** The outcomes of hysterectomy were retrospectively analyzed in 812 consecutive patients with uterus body tumors. **Results:** The frequency of peri-operative complications was similar between LPS (3.4%) and LT (2.9%). However, in the early postoperative period, complication rates were 26.6% for LT and only 3.4% for LPS ($p < 0.001$). A similar trend was found in the late complication rates (51.3 vs. 24.4%, respectively; $p < 0.001$). Higher degrees of obesity were associated with increased complication frequencies after LT in the early postoperative period ($p = 0.03$). Increases in BMI were linearly related to the risk of postoperative complications ($p = 0.002$). This relationship was not observed after LPS for any type of complication. Interestingly, the frequencies of incisional hernia and dehiscence were highly dependent on which surgeon performed the LT ($p = 0.002$). **Conclusions:** In extremely obese patients, the first method of choice should be LPS.

Key words: Surgery complications; Uterus body; Neoplasm; Body mass index; Incisional hernia.

Introduction

Cancer of the uterus body is the fourth most frequent tumor among females [1]. The incidence of malignant tumors of the uterus body is 34.3 cases per 100,000 inhabitants in the Czech Republic [2], which is higher than the incidence of cervical cancer [3]. The standard treatment for endometrial carcinoma is hysterectomy with bilateral salpingo-oophorectomy, and eventually, pelvic, and para-aortal lymphadenectomy [4, 5]. Women with endometrial cancer frequently have co-existing morbidities, including severe obesity, diabetes mellitus (DM), and cardiovascular diseases. These conditions increase the risk of postoperative complications and mortality, which can often complicate an adequate treatment. A few lines of evidence have supported laparoscopy (LPS) as the treatment of choice: 1) LPS was associated with similar overall- and disease-free survival rates, reduced operative morbidity, and reduced hospital stays in patients with early-stage tumors [6, 7]. 2) LPS showed distinct advantages for obese patients; in these patients, LPS was associated with shorter postoperative hospital stays and a lower wound infection incidence than laparotomy (LT) [8]. To date, the available data have been

insufficient to support a relationship between late postoperative complications and body mass index (BMI). The aim of the present study was to compare LPS and LT according to the rates of peri-operative, early postoperative, and late postoperative complications in consecutively operated patients. Moreover, the authors analyzed the possible influence of different patient characteristics, particularly BMI, the presence of DM, and cardiovascular disease, on the complication rates.

Materials and Methods

Eight-hundred thirty-one patients with malignant neoplasm of the uterus body were treated operatively in the Oncogynaecologic Department of the University Hospital of Ostrava from June 2002 to December 2013. Because the number of patients with vaginal hysterectomy was very small ($n=19$), only cases of hysterectomy performed with LPS or LT were included in this study. The final number of patients was 812 (Table 1).

All operations were performed under the supervision of an experienced oncogynaecologist. Four experienced oncogynaecologic surgeons performed 81.6% of the operations in patients that were followed regularly. These four surgeons performed operations consistently throughout the study period. All data were collected

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Table 1. — Basic patient characteristics.

Characteristics	LT, n (%)	LPS, n (%)	Total, n (%)	Comparison
Patients	665 (81.9)	147 (18.1) ¹	812 (100)	-
BMI, kg/m ² ; mean (range)	32 (16-62)	31 (19-53)	32 (16-62)	n.s.
Age, years; mean (range)	65 (26-91)	58 (30-81)	64 (26-91)	<i>p</i> < 0.001
Blood loss, ml; mean (range)	411 (50-2000)	215 (20-900)	376 (20-2000)	<i>p</i> < 0.001
Transfusions, volume per patient; mean (range)	0.32 (0-33)	0.07 (0-9)	0.28 (0-33)	<i>p</i> = 0.05
Length of hospitalization, days; mean (range)	14 (4-68)	7 (4-17)	13 (4-68)	<i>p</i> < 0.001
Disease characteristics				
FIGO I	453 (76.8)	137 (23.2)	590 (72.7)	<i>p</i> < 0.001
FIGO II	82 (92.1)	7 (7.9)	89 (11.0)	
FIGO III	118 (97.5)	3 (2.5)	121 (14.9)	
FIGO IV	12 (100.0)	0 (0)	12 (1.4)	
Endometrial	471 (78.9)	126 (21.1)	597 (73.5)	<i>p</i> = 0.001
Adenosquamous	70 (81.4)	16 (18.6)	86 (10.6)	
Serous	41 (93.2)	3 (6.8)	44 (5.4)	
Sarcoma	41 (95.4)	2 (4.6)	43 (5.3)	
Undifferentiated	22 (100.0)	0 (0)	22 (2.7)	
Clear cell	13 (100.0)	0 (0)	13 (1.6)	
Mucinous	7 (100.0)	0 (0)	7 (0.9)	

Values represent the number of patients (%), unless otherwise indicated. ¹Conversion from LPS to LT was necessary in 9.3% of patients that received LPS.

from a secure hospital database. Perioperative complications were defined as all documented complications that occurred during the operation. Early postoperative complications were defined as all complications that influenced the hospital stay and were documented in a discharge report. Late postoperative complications were defined as all subjective or objective data that might be associated with the surgery and were recorded in visits during the three- to sixth-month follow ups; the follow up period was assigned according to the stage of disease. The authors used the FIGO 2009 classification to determine the disease stage; all cases recorded before 2009 were reclassified according to this norm.

For analyses, patients were divided into groups according to BMI as follows: normal weight (BMI under 25), overweight (25-30), first degree obesity (30-35), second degree (35-40), third degree obesity (40 and above). Comparisons between LPS and LT were performed with the *t*-test (quantifiable values) and the chi-square test (numbers of cases). The latter was also used to assess the influence of different variables. All statistics were performed with the Excel Real Statistics module. Correlations between BMI and complications were evaluated with the Pearson and Spearman correlation tests, followed by analyses of linear or non-linear regression. For this purpose, the authors used GraphPad Prism, version 6.00.

Results

This retrospective analysis of cases of uterine carcinoma treated in the present hospital from 2002 to 2013 showed that in real clinical settings, the LT approach was the preferred operation for these patients. The percentage of patients that underwent the LPS approach increased from 0% in 2002 to 58% in the last few years of the study period. Compared to patients that received LPS, patients that received LT were older and were more likely to have a more advanced stage or more a severe histological type of disease (Table 1), but they had similar BMIs. As expected, compared to LT, LPS was associated with less blood loss, less

need for transfusion, and shorter hospital stays (Table 1).

Perioperative complications occurred at a similar frequency for both treatments (3.4% for LPS and 2.9% for LT, n.s.). These complications mainly included severe bleeding, injury to the urinary bladder or ureter, and injury to the bowel. For both types of operations, the complication rate did not depend on either the BMI or the operating approach.

In the early postoperative period, complications occurred significantly more often in patients treated with LT (26.6%) compared to those treated with LPS (3.4%, *p* < 0.001). The most common early complications were wound dehiscence and a need for reoperation. The chi-square test showed significant differences in complication rates among different BMI groups for patients treated with LT (*p* = 0.03). In contrast, the complication rates were not dependent on BMI among patients treated with LPS (Figure 1). A correlation analysis did not show any direct relationship between BMI and the percentage of complications; this was probably because only patients with high degrees of obesity (second and third degrees) experienced a high percent of complications after LT. Further analysis of patients treated with LT revealed that the frequency of wound dehiscence was dependent on both BMI (*p* < 0.001) and the presence of DM; dehiscence occurred in 10.7% and 16.1% of patients without and with DM, respectively (*p* = 0.05). Interestingly, the frequency of dehiscence in patients treated with LT also depended on the surgeon (*p* = 0.008, Figure 2). The risk of complications was not significantly influenced by the type of treatment for DM, including diet (13.6%), oral anti-diabetics (15.7%), or insulin (23.7%). The complication rate was not significantly related to the presence of hypertension or coronary heart disease.

Regular follow-ups were performed for 76.4% of patients

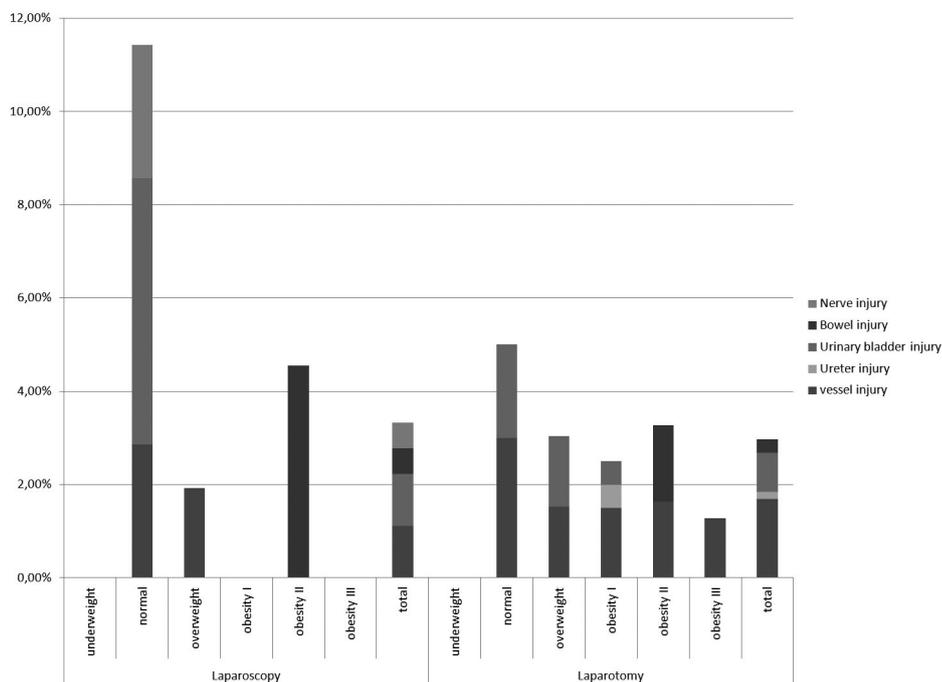


Figure 1. — Dependence of early postoperative complications on BMI. This graph shows the percentage of early postoperative complications for both LPS and LT in relation to different BMI groups. The chi-square test did not find any significant differences among BMI groups in patients treated with LPS, but a significant effect was found in those treated with LT ($p = 0.03$)

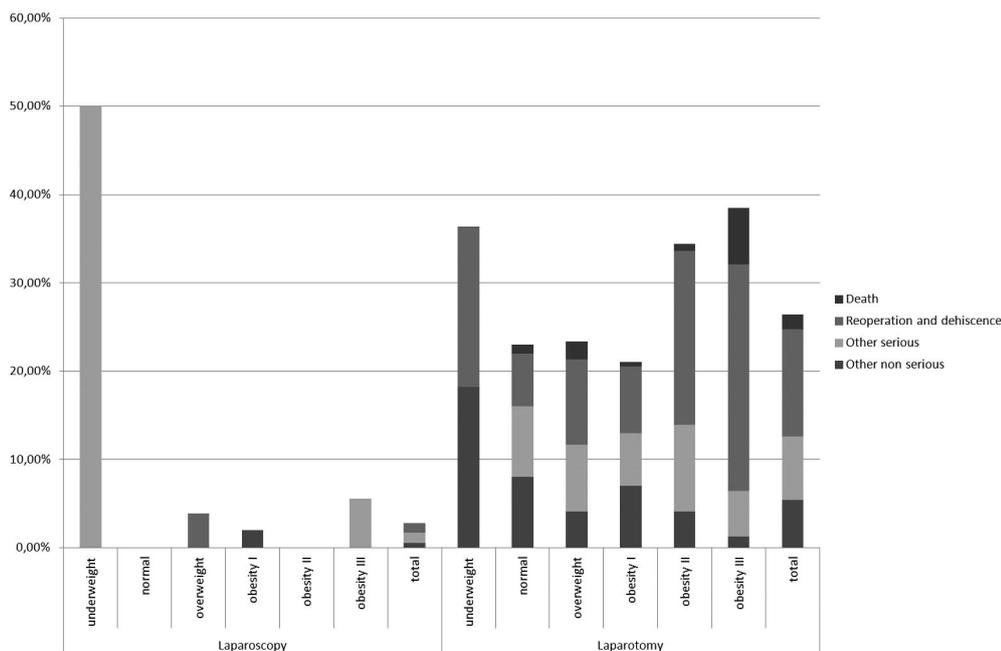


Figure 2. — Influence of different surgeons on the rate of dehiscence. This graph shows the percentage incidence of dehiscence that occurred with different surgeons. Four of the most experienced surgeons (A-D) performed the majority of operations. The chi-square test found a significant relationship between the surgeon and the incidence of dehiscence ($p = 0.008$)

($n=620$), and 3.9% of patients ($n=32$) received only one follow-up. The dropout rate of 19.7% ($n=160$) was due to death or failure to return for follow-up visits. Late complications were found in 24.4% of patients that underwent LPS and in 51.3% of patients that underwent LT ($p < 0.001$). The most common complication was incisional hernia (24.4%), which represented the main difference between operational approaches. Among patients that

underwent LPS, no clinically important incisional hernias were recorded. Among patients that underwent LT, a high BMI appeared to be linked to a high risk of incisional hernia. Although the chi-square test did not show significant differences among the BMI groups, a correlation analysis revealed a high correlation between BMI and the risk of late complications (Pearson correlation coefficient - $r_S=0.9857$, $p = 0.002$). This relationship was highly linear

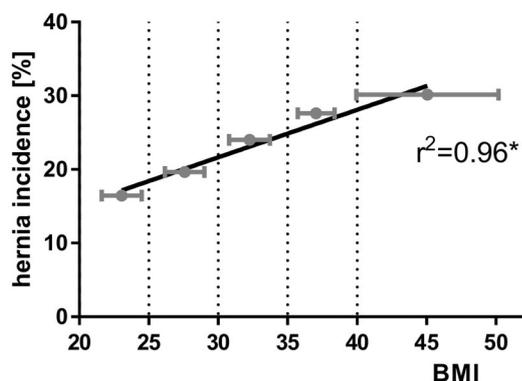


Figure 3. — The incidences of incisional hernias that occurred in laparotomy among groups of patients with different BMIs. The relationship between the hernia incidence and BMI was linear; based on this relationship, the expected incidence of incisional hernias could be predicted based on BMI, as follows: hernia (%) = $0.72 \times \text{BMI} + 1.28$

($r^2 = 0.97$, $p = 0.002$, Figure 3). The frequency of hernias did not depend on the type of DM treatment, the presence of hypertension, or the presence of coronary heart disease. Moreover, the frequency of hernias did not correspond to wound dehiscence or the reoperation frequency, the operation time, or the need for adjuvant therapy. The frequency of hernias among patient without adjuvant therapy was 26.9%. Interestingly, the frequency of this complication clearly depended on the performing surgeon ($p = 0.002$, Figure 4).

Discussion

From a historical point of view, LT is an older, more established operation than LPS. This point was particularly true for the present hospital; from 2002 to 2013 the majority of operations were LTs. The importance of this study lies in the fact that the authors analyzed all consecutive cases of uterine body tumors that were treated in this hospital; in other words, no exclusion criteria were applied. Only hysterectomies performed with a vaginal approach were excluded from this analysis, because the very small number of cases would have hindered a reasonable statistical analysis. This broad inclusion of participants rendered this study more relevant to clinical praxis than the most common clinical studies. For this reason, there were differences in the ages of patients. Patients in the LT group were older than those in the LPS group, probably mainly due to the fact that capnoperitoneum was contraindicated in very old women. However, accidentally, there was not a significant difference in BMIs between the LPS and LT groups, and this fact strengthened the results of this study.

The risk of uterus body neoplasm generally increases with age, and the frequency of high BMIs also increases with age. Therefore, the effect of BMI on complications is relevant in this patient group. The fact that there was no significant difference in BMIs between groups may lay in the fact that BMI was not a selection factor for assigning patients to the LT or LPS approach.

It is well known that, compared to a LT, the LPS is associated with less blood loss and less subsequent need of blood transfusion. This association was confirmed in this study. Consistent with previous findings, we confirmed that LPS provided a reduction in postoperative complications and shorter hospital stays compared to LT [9]. Bijen *et al.* inferred that LPS in obese patients with BMIs $>35 \text{ kg/m}^2$ was cost-ineffective [10], but they did not follow late postoperative complications, such as hernias, which would certainly increase the total cost of patient treatment. Other studies found that, compared to LT, LPS was also beneficial for obese patients, due to the reduced postoperative complications and shorter hospital stays, but they found insignificant effects on peri-operative complications and disease free survival [9, 11].

The results of this study concerning severe post-operative morbidity were not in accordance with previous studies. The review from Galaal *et al.* [6] reported no significant differences between LPS and LT. In contrast, Zullo *et al.* found advantages in early postoperative complications for LPS over LT, but no difference in the peri-operative complication rate [12]. Incisional hernias comprise the most frequent, long-term, general complication in abdominal surgery. They cause morbidity, and sometimes, patient death [13-16]. Despite studies that have indicated the optimal closing technique for LTs, the risk of incisional hernias after midline incision remains about 11-20% [17, 18]. Moreover, this rate may rise to 26-39% in higher-risk groups, such as highly obese patients, or those treated surgically for abdominal aortic aneurysms [19]. In our study, the total frequency of incisional hernia was 24.4%, and the incidence in obesity group III was 32.7%; however, this difference was not statistically significant. In the future, the incidence can likely be reduced by using a prophylactic mesh on the abdominal wall closure. A recent study has shown that this method can reduce the occurrence of incisional hernias, regardless of the risk factors [20]. Currently, we await long-term results from the prospective trial, which aimed to compare the primary suture closure with a mesh-augmented closure in patients with BMIs over 27 [21]. On the basis of short-term results, primary mesh augmentation can be considered as a safe procedure with only an increase in seroma formation, but without an increased risk of surgical site infection [22].

The most important finding in this study was that a higher BMI corresponded to a higher complication risk in patients treated with LT, but not those treated with LPS. Previous studies showed that the BMI was independent of peri-op-

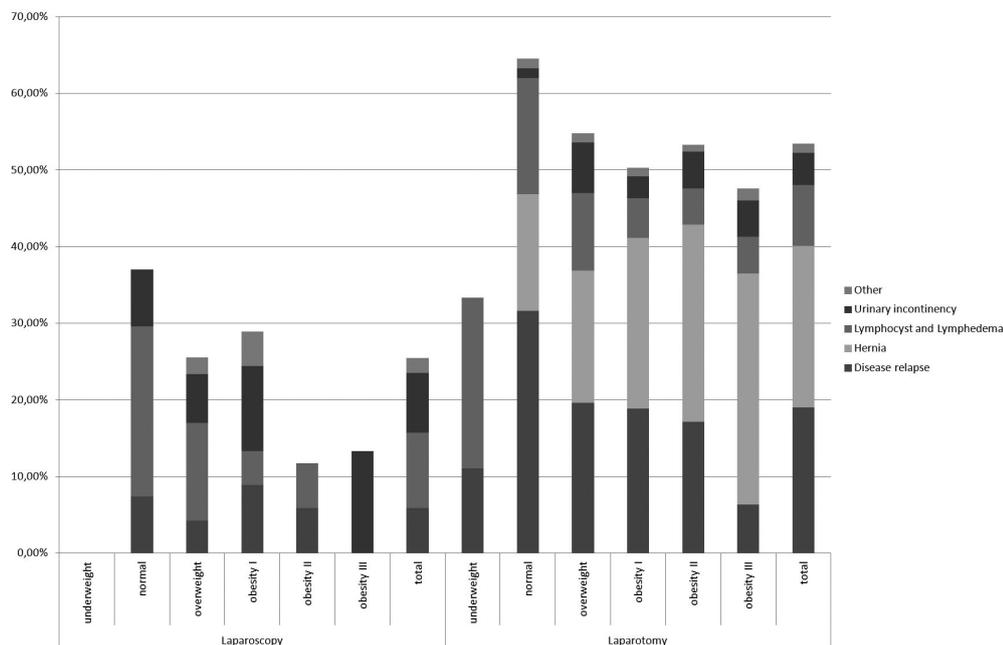


Figure 4. — Dependence of incisional hernia incidence on the performing surgeon. The graph shows the percent incidence of incisional hernias that occurred after LT for each operating surgeon. Four of the most experienced surgeons (A-D) performed most operations in patients that underwent regular follow ups. The chi-square test showed a significant relationship between the surgeon and the rate of incisional hernias ($p = 0.002$).

erative and early complications associated with LPS treatments [23-26]. However, to the present authors' knowledge, no data on the incidence of hernias or late complications, in general, have been published to date. Previous studies on both the early and late postoperative periods have suggested that higher BMIs were associated with higher risk of complications. The present study clearly documented this relationship, particularly during the early postoperative period, where BMI was significantly associated with the risk of complications. In the late postoperative period, the percentage of complications increased linearly with increases in BMI, but the differences between BMI groups were not significant. Most likely, a larger cohort of patients will be needed to demonstrate significant differences between the groups. In light of the highly linear relationship observed, the differences between BMI groups are probably significant, but to achieve sufficient statistical power, a multicenter study will be required.

The most unexpected finding was the impact of the operating doctor on the frequencies of incisional hernias and dehiscences. All four of the experienced surgeons worked under the same conditions; i.e., the same type of suture material, the same operation tools, and the same postoperative care. Moreover, many times, the operations were performed by two of these experienced surgeons together in one operation team. Therefore, the present authors would have expected that all experienced doctors practicing in this hospital would have a similar operation technique for the abdominal wall closure. In contrast to these assumptions, the authors found that the most experienced oncogynecologic surgeon had the highest incidence of incisional hernias, despite very few peri-operative and early postoperative complications in LT (e.g., reoperations and wound dehiscence), a very short operation time, and the least need for blood transfusion, compared to the other surgeons. In the literature, the authors found studies that showed a clear role for the surgeon in incisional hernia repairs [27], but to the present authors' knowledge, no studies have described a clear role for the surgeon or a role for BMI in the incidence of incisional hernias after LT surgery for a uterus body malignancy.

Incisional hernias incur additional financial expenses [28]. There is a need to update our view on closure techniques and to consider using prophylactic mesh in patients with risk factors; these changes could reduce the total treatment costs.

Conclusion

The present results showed that perioperative complications were independent of BMI or the operating approach. In contrast, with LT, early postoperative complications were dependent on both BMI and the operating approach, and late complications were dependent on the operational approach; moreover, the frequency tended to increase with increasing BMIs. The present authors also found that with LPS, no peri- or postoperative complications were dependent on BMI. Therefore, in extremely obese patients, the method of choice should be LPS, when possible.

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