

Evaluation of perioperative stress after laparoscopic and abdominal hysterectomy in premalignant and malignant disease of the uterine cervix and corpus

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Summary

Objective: To compare the differences in laparoscopic and abdominal hysterectomy in surgery of premalignant and malignant uterine disease.

Design: Prospective study.

Setting: Baby Friendly Hospital, Kladno, Czech Republic.

Subject: A total 32 patients underwent hysterectomies for premalignant and malignant uterine conditions.

Interventions: Patients were assigned to either laparoscopic-assisted vaginal hysterectomy or total abdominal hysterectomy (LAVH), with bilateral salpingo-oophorectomy and lymph node dissection.

Measures: Clinical data and value of total creatine kinase and C-reactive protein were measured.

Results: All 32 procedures were successfully completed. There were no major complications. Mean order of CRP concentrations was significantly lower ($p=0.001$) in patients with LAVH. Mean order of total CK activities was also significantly lower in these patients ($p=0.003$) and the median hospital stay was 4.1 days ($p=0.05$).

Conclusions: Laparoscopic procedures were followed by shorter hospital stays and the proposed evaluation of tissue damage using serum enzymes and proteins demonstrates that the laparoscopic approach to hysterectomy and accessory procedures has considerable importance in decreasing perioperative patient stress. The presented results are supported by clinical experience and should have a decisive impact on the chosen approach to the course and duration of convalescence in patients undergoing a hysterectomy in premalignant and malignant disease of the uterine cervix and corpus.

Key words: Perioperative stress; Hysterectomy; Serum enzyme; C-reactive peptide.

Introduction

Laparoscopic hysterectomy was introduced to clinical practice by Reich ten years ago [1]. Hysterectomy is currently the most frequent type of gynecological surgery. There has been a significant move away from an abdominal approach to hysterectomy to less invasive procedures such as laparoscopic hysterectomy. In this context, a number of studies were conducted with the aim of comparing the objective acquisition and results of the operation with abdominal hysterectomy [2-5]. Laparoscopic hysterectomy and lymph node dissection have lately been reported as an alternative to an open procedure for the treatment of malignant gynecological conditions. Reich performed the first transperitoneal laparoscopic pelvic lymphadenectomy in November 1988 to stage ovarian cancer and the same time performed a laparoscopic hysterectomy. Querleu [6] in France performed the same procedure one week later to stage cervical cancer. Childrens and Survit [7] described laparoscopic assisted staging of endometrial cancer, combining laparoscopic lymph node dissection with laparoscopic assisted vaginal hysterectomy (LAVH). The laparoscopic operative technique has been evaluated and compared in terms of

safety, feasibility and effectiveness. Standard methods evaluating the duration of surgery, blood loss, perioperative morbidity, damage of tissue, subsequent pain, duration of hospital stay and hospitalization costs were used as comparative criteria [8, 9, 10]. Some authors, however, do not consider the assessment of the surgical method using the above-mentioned criteria to be sufficiently objective [11]. Other authors evaluated metabolic changes, blood enzymes, cytokines, cortisol and serum proteins to try to explain differences in preoperative morbidity between open and endoscopic surgery [12, 13, 14].

For these reasons we decided to verify the possibility of using creatine kinase (CK) and C-reactive peptide (CRP) as further objective criterion of perioperative stress after laparoscopic hysterectomy in comparison to abdominal hysterectomy in premalignant and malignant disease. The trial is a part of a long-term study conducted within our department [15].

Materials and Methods

The preoperative comparative study was performed at Baby Friendly Hospital, Kladno. Hysterectomies were performed on 32 women during the period from 1/1/1998 to 31/5/1998. Removal of the uterus by one of two alternative procedures was performed on the consecutively selected women for premalignant and malignant uterine disease. Group I included 17 women

Received October 22, 1998
revised manuscript accepted for publication November 27, 1998

on whom laparoscopic-assisted vaginal hysterectomies (LAVH) were performed. Classical or extended abdominal hysterectomies were performed on 15 women in group 2. The type of surgery and characteristics of patients are shown in Table 1.

Biochemical procedures

Two blood samples were collected from the brachial vein at 6 a.m. on the day of surgery and 24 hours later, respectively.

Only patients who had undergone surgery during the morning were included in the study. The interval between the end of surgery and post-surgery sample collections varied between 16-20 hours. The overall activity of creatine kinase (CK, EC 2.7.3.2) was assessed using the kinetic method under ultraviolet (UV), isoenzyme CK MB was assessed by immuno-inhibition of the M-subunit. Total CK activity was measured with the standardized IFCC method in 37 °C (Dade, U.S.A.) with calibrator traceable to enzyme-reference materials ERM 1 and ERM 2. The limit for females was 2.4 µkat/l. Physiological range values are shown in Table 2. CRP was measured by turbidimetric immunoassay at 37 °C (Merck, Germany) with calibrator traceable to CRM 470. The upper limit of reference values was 10 mg/l.

Operative techniques

Laparoscopic procedure

Laparoscopy was performed in the lithotomy position using videomonitoring equipment. The telescope was inserted in the subumbilical position and one 5 mm or 10 mm port of entry was made suprapubically and medially. Finally two or three 5 mm ports were placed in each lower quadrant at the lateral border of the straight abdominal muscle. Transperitoneal pelvic lymph node dissection was started by opening the broad ligamentum and lateral pelvic peritoneum between the round ligament and the infundibulopelvic ligament. We dissected the lymph node up to the level of bifurcation of common iliac artery and along the aorta up to the level of the mesenteric inferior artery. We performed systematic pelvic lymphadenectomy and only lymph node sampling from the para-aortal bilateral areas. The nodal package was removed from the operative field through the upper 10 mm trocar. During laparoscopic-assisted vaginal hysterectomy the bladder was dissected from the lower uterine segments; inspection was carried out to visualize the ureter and uterine artery. In most cases we performed only desiccation of the uterine artery. Clips or needles were used occasionally, whereas electrocautery was effective in most cases. The uterine vessels and ligaments were performed the same way as in a conventional vaginal hysterectomy. The procedures were carried out without morcelation of the uterus. A final check was made by laparoscopy to control hemostasis.

Open procedure

Standard abdominal hysterectomies were performed on 6 women through the suprapubic access and in 9 women the incision of the abdominal wall was directed from the navel in a medial line and with enlargement above the navel in patients with lymphadenectomy. Adnexal removal was advanced in all women according to histological and clinical findings. These criteria were also followed in the endoscopic group of patients. A summary of accessory operations in assessed alternative hysterectomies is listed in Table 2.

We used the technique of radical abdominal hysterectomy and lymphadenectomy described by Burghardt and Winter [16], corresponding approximately to a combination of the class II and III extended hysterectomies described by Piver *et al.* [17].

Table 1. — Type of surgery and characteristics of women

Type of hysterectomy	Number	Age (years)	Average weight (kg)
LAVH	1	43.0	67.0
LAVH, PLN	1	41.0	71.0
LAVH, BSO	10	64.7	78.1
LAVH, BSO, PLN	4	59.1	76.5
LAVH, BSO, PLN, PALN	1	58.0	82.0
Total (or average)	17	60.6	76.9
		range (41-71)	
TAH, BSO	6	61.8	83.5
TAH, BSO, PLN	5	59.7	78.3
TAH, BSO, PLN (Wertheim)	4	51.6	77.2
Total (or average)	15	57.6	79.7
		range (27-76)	

Abbreviations: LAVH = Laparoscopic-assisted vaginal hysterectomy
 BSO = Bilateral salpingo-oophorectomy
 PLN = Pelvic lymph node dissection
 PALN = Para-aortic lymph node dissection
 TAH = Total abdominal hysterectomy

Table 2. — Physiological ranges of values CK and CRP

(serum levels in females at 37 °C)	
Substance	Range
CK	0.40 - 2.83 µkat/l
CK MB	< 0.40 µkat/l
CRP	< 10 mg/l

Table 3. — Outcomes of surgery and histopathological findings

Clinical data	Laparoscopic group	Open group
Duration of procedure (min)	111	117
Hospital stay (days)	4.1 (p=0.05)	5.9
Blood loss: estimated (ml)	130	150
Post-operative complications:		
Fever	1	2
Secondary wound healing	0	1
Vaginal discharge	1	0
Pelvic haematoma	1	0
Urinary tract infection	2	1
Histopathological findings		
CIN III (CIS)	3	1
Invasive cervical carcinoma	1 (Ia2)	4 (Ib)
Atypical hyperplasia	3	2
Endometrial cancer	10 (stage Ib, c 5x)	8 (stage Ib, c 6x)

Table 4. — Criteria for grading of expected tissue damage during hysterectomy

Grade of damage Criteria	Severe	Moderate	Mild
Duration of procedure	> 2 hours	≅ hours	≅ 90 min
Extension of tissue dissection	large	small	small
Obese patients, dense adhesions and abnormal anatomy	yes	yes	no

Characteristics of the group were complemented with data such as duration of surgical procedure, duration of hospital stay, histopathological findings, staging and complications (Table 3). All procedures were performed under general anesthesia using the same type of muscle relaxant.

Statistical analysis

For evaluation of the differences in perioperative stress between particular types of hysterectomy, the patients were divided into two basic groups. We used the non-parametric Wilcoxon-White test for two independent groups. The test is based on the comparison of mean order with theoretical order in case of no difference between groups. We calculated the probability of differences between the respective two groups. Clinical data were compared by the Chi-square test.

For analysis of the main clinical criteria, which allowed us to assess the grade of post-operative trauma during hysterectomy, the following method was used. As criteria of presumed tissue trauma these parameters were chosen:

Table 5. — Absolute frequency of CRP concentrations in three different ranges

Value (mg/l)	number of LAVH	number of TAH
< 50	11	1
51-70	4	4
> 70	2	10

Table 6. — Absolute frequency of CK total activity in three different ranges

Value (μ kat/l)	number of LAVH	number of TAH
< 3.0	9	2
3.01-10.0	5	5
> 10.0	3	8

Table 7. — CK values in relation to presumed grade of tissue damage based on known clinical criteria in LAVH and TAH

LAVH	Group 6 (severe)	Group 5 (moderate)	Group 4 (mild)
Value range	1.36-15.5	1.18-6.89	0.76-4.16
Mean value	6.66	3.64	2.01
TAH	Group 3 (severe)	Group 2 (moderate)	Group 1 (mild)
Value range	2.39-28.82	4.72-10.86	4.16-15.15
Mean value	14.85	8.63	9.85

Table 8. — CRP values in relation to presumed grade of tissue damage based on known clinical criteria in LAVH and TAH

LAVH	Group 6 (severe)	Group 5 (moderate)	Group 4 (mild)
Value range	23.6-77.9	16.3-80.9	10.0-69.5
Mean value	49.2	34.7	44.6
TAH	Group 3 (severe)	Group 2 (moderate)	Group 1 (mild)
Value range	56.8-98.4	45.5-97.5	60.9-62.7
Mean value	76.6	74.5	61.8

1) Duration of procedure.

2) Extent of tissue dissection, particularly the length of abdominal wall incision.

3) Obese patient, abnormal anatomy and dense adhesions.

Considering the difficulties in making an objective differentiation, the second criterion referring to the extent of tissue dissection, was divided into two groups only. The large tissue dissection group included: wide incision of abdominal wall, extensive adhesiolysis and parametrial and peritoneal resection. Other criteria are listed in Table 4.

Based on these criteria, three subgroups of presumed severe, moderate and mild tissue damage were composed. The presence of at least two basic criteria led to inclusion in one of these subgroups. Other methods of classification would create more subgroups, each with only a small number of patients, and would not allow a valid statistical analysis.

Results

All values of CK and CRP collected before surgery were within the physiological range (for CK 0.4-2.4 μ kat/l, for CRP less than 10.00). All recorded CK MB values were in the physiological range. Statistical evaluation was made by the Wilcoxon-White test. The increase in CRP values was statistically significant in both groups. Mean order of CRP concentrations was significantly lower ($p=0.001$) in patients with LAVH. Mean order of total CK activities was also significantly lower in these patients ($p=0.003$). Absolute frequencies of CK and CRP are shown in Tables 5, 6. CK and CRP values in six subgroups of clinical evaluation of presumed tissue trauma are listed in Tables 7, 8. The high average CK value of 14.85 (and CRP value of 76.6) in group 3 (open) is further evidence of the critical contribution of the endoscopic approach to perioperative stress in connection with hysterectomies. Subgroup 3 includes patients with radical hysterectomy and extended abdominal wall incision due to lymphadenectomy. The patients with laparoscopic lymphadenectomy procedure are included in subgroup 6 (mean value of CK = 6.66 and CRP = 49.2). Nearly identical low average CK and CRP values were observed in patients with LAVH from groups 4, 5, 6. Clinical data and histopathological findings are shown in Table 3.

Discussion

The traditional approach to surgery of premalignant and malignant disease of the uterine cervix and body is almost always conventional or radical hysterectomy. The primary disadvantage of laparotomy is a prolonged recovery period – mainly due to a longer period of tiredness.

This may be because of a longer abdominal incision and the laparotomic procedure itself. Blass *et al.* [18] suggest that patients with early stage endometrial cancer have cure rates with vaginal surgery comparable to abdominally-staged patients, while morbidity and mortality are higher. Most frequent reasons for laparoscopic hysterectomy were complaints due to uterine myomas, endometriosis and ovarian benign pathology. The door to laparoscopic surgery for pelvic malignancies was opened when laparoscopic hysterectomy and lymphadenectomy procedures became possible [6, 7].

Traumatic tissue damage after surgery results in a series of local and general metabolic changes and response to stressful situations [19]. Moore (1952) speaks even about postoperative disease characterized by catabolic and anabolic phases [20]. In a recent study done by Volz *et al.* [13] the course of metabolic changes in patients after laparoscopic surgery and after laparotomy demonstrated statistically significant differences. Severe intraperitoneal postoperative metabolic acidosis was found in patients after laparoscopic surgery, which afterwards continued for a short time. Prolonged metabolic intraabdominal acidosis may lead to damage of the organism. Other authors evaluated CK levels to try to explain differences in perioperative stress and morbidity between open and endoscopic surgery of benign pelvic conditions [14, 21]. A great amount of literary information exists about the activity of serum creatine kinase and its isoenzyme CK MB in connection with cardio-surgical operations. Serum CK and CK MB values are used to estimate the extent of necrotic focus in patients with myocardial infarction [22]. Analysis of the CK MB portion of overall CK activity allows us to differentiate the origin of isoenzyme from skeletal or uterine muscle origin. As indirectly demonstrated, the proportion of CK BB and CK MB activity of the overall CK activity was insignificant in the last study [14]. The above presented results show high average CK values in patients with an open procedure and bring further evidence of the critical contribution of the laparoscopic approach to perioperative stress in connection with hysterectomies.

On the other hand, Ellstrom *et al.* [12] found the extent of surgical trauma did not differ between the two operative methods. They compared laparoscopic and abdominal hysterectomy with regard to the aim of the study to determine whether or not hysterectomy leads to cytokine, cortisol and C-reactive protein release, activation of neutrophils, and activation of the complement cascade. Their results indicate serious tissue trauma during both laparoscopic and conventional abdominal hysterectomy. We found that CRP was significantly increased 24 hours after surgery and the mean order of this one concentration was significantly lower ($p=0.0001$) in patients with laparoscopic hysterectomy. CRP peaks the third day after surgery and returns to preoperative levels within one week [22]. Monitoring of CRP concentrations is a suitable tool for postoperative stress detection and early detection of complications, especially infections.

Clinical experience demonstrates that perioperative stress is lower during laparoscopic surgery than during laparotomy [9, 10]. The presented results from our first study supported this clinical experience [15]. Based on this premise, we believe that examining CK and CRP may be used as one of the objective quantifications of operative stress after hysterectomy for benign and malignant disorders of the female pelvis.

Acknowledgements

The authors would like to acknowledge the help of P. Kasal ing. (Olympus) and Mrs M. Rohlova (Dept. Obst. Gynec., Hospital Kladno) for their assistance and support of the study.

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