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ORIGINAL ARTICLE

Influence of the operative treatment of leiomyomas on lipid profile

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Abstract

OBJECTIVE: The aim of this study was to asses the influence of operative treatment of leiomyomas on lipid profile. The study was conducted from April 1, 2000, through April 30, 2002 in The Department of Septic Gynecology and Obstetrics at Collegium Medicum of the Jagiellonian University.

METHODOLOGY*:* Most hysterectomies are performed because of leiomyomas, which are the most common benign tumors of the female reproductive organ. Pathogenesis and evolution of uterine leiomyomas are not well understood. Treatment of leiomyomas is divided into operative and inoperative. Operative methods include generally laparoscopic myomectomy, conservative myomectomy and hysterectomy. 130 women with diagnosed leiomyomas were analyzed in four groups.

CONCLUSION*:* Regardless of the type of performed surgery, decrease in cholesterol, HDL and LDL are observed 10 days after operation, with return to preoperative values at 6 months after surgical procedure. The highest level of cholesterol and LDL (6 moths from surgery) is observed in patients who underwent hysterectomy with bilateral oophorectomy.

Introduction

Most hysterectomies are performed because of leiomyomas, which are the most common benign tumors of the female reproductive organ [2]. The prevalence ranges from 25% to 30% after the age of 30 [2, 13, 14]. Pathogenesis and evolution of uterine leiomyomas are not well understood. Some investigators have suggested that residual undifferentiated cells in the myometrium are the progenitor cells of leiomyomas [2, 19]. Other authors assume that acquired chromosomal aberrations play a pathogenetic role in uterine leiomyomas [12, 13, 14, 18]. Uterine fibroids appear and enlarge during the reproductive years. This observation suggests that steroid hormones secreted by the ovaries are necessary for the continued growth of these tumors [2]. They may cause abnormal uterine bleeding, they are often associated with reproductive failure and are the most frequent indication for hysterectomy [2,14]. Approximately one third of women with uterine fibroids have symptoms that may eventually require medical or surgical intervention. Treatment of leiomyomas is divided into operative and inoperative. Operative methods include generally laparoscopic myomectomy, conservative myomec-

tomy and hysterectomy. Hysterectomy with uni- or bilateral oophorectomy can provoke premature menopause. The classic symptom of menopause, the hot flash, is related to declining estrogen levels, and is reported by 85% of menopausal American women [5, 9]. Other problems observed in this population include: irritability, fatigue, nervousness, insomnia, sweating, depression, and vaginal dryness [9]. There is also increased risk of cardiovascular disease and stroke, related to lipids disturbances. According to S. Jedrzejczyk et al., increased levels of triglycerides and low-density lipoprotein (LDL) and decreased levels of high-density lipoproteins (HDL) are also recorded [8]. Only proper hormonal replacement therapy can protect against menopausal symptoms and complications. Results of several studies indicate that patients generally believe in effectiveness of hysterectomy, 91% – 100% of women reported being glad that they had undergone the surgery [2, 5, 17].

Subject: The aim of this study was to asses the influence of the operative treatment of leiomyomas on lipid profile.

Material and Methods

The study was conducted from April 1, 2000, through April 30, 2002 in The Department of Septic Gynecology and Obstetrics at Collegium Medicum of the Jagiellonian University. 130 women with diagnosed leiomyomas were studied in four groups. Patients were divided into four groups based on:

- age,
- parity,
- number and size of leiomyoma,
- macroscopic examination of ovaries during operation,
- contraindications for laparoscopic myomectomy.

The first group consisted of patients who underwent hysterectomy with bilateral oophorectomy, the second one included those after hysterectomy with unilateral oophorectomy, the third one – those after hysterectomy without bilateral oophorectomy. The fourth group involved patients in whom the conservative variant of myomectomy was performed.

Exclusion criteria comprised all general dysfunctions that can affect clinical and psychological tests:

- *diabetes mellitus*,
- thyroid and parathyroid dysfunction,
- psychiatric disorders,
- circulatory and heart disorders,
- liver and kidney disorders.

Demographic data collected included patient age, weight, parity, education and employment status.

Before surgery, gynecological bimanual examination, exfoliative cytology, transvaginal ultrasonography and assessment of the Ca-125 antigen were performed. Other factors examined included general symptoms before and blood loss during the operation.

All patients after hysterectomy with bilateral oophorectomy received 10mg intra-muscle injection of *oestradiolum valerianicum* and underwent subsequent hormonal replacement therapy.

Data from the post-surgical period included: body temperature, antibiotics, complications within healing of the vagina (inflammation or abscess) and result of pathological examination of removed uterus and ovaries.

Total cholesterol, low-density lipoprotein (LDL), high-density lipoproteins (HDL) and triglycerides (TG) were measure before surgery and at 10 days, and 6 months after operation.

Differences in demographic and biochemical data between the four groups were evaluated with χ^2 test.

Results

One hundred and thirty patients were enrolled in the trial. Patients were distributed into four groups based on the type of surgery (Table 1).

The four groups were similar with respect to demographic variables, including weight, parity, education and employment status. The only difference referred to age: patients in Group I were older than the others ($p<0.05$).

As it appeared in patients' medical history, the most common symptoms on admission were:

- 61 (46.9%) menometrorrhagia,
- 34 (26.2%) pain in the lower part of the abdomen,
- 18 (13.8%) bleeding not related to menstruation,
- 9 (7%) difficulties with urination,
- 5 (4%) sacral pain,
- 3 (2.3%) pressure effect, vesical tenesmus.

According to gynecological examination of the vagina, in 42 patients (32.3%) descends of the anterior and posterior wall of the vagina were recorded, and 32 patients (24.6%) had *vaginitis*. No pathological lesions on the cervix were diagnosed in 80 cases (61.5%). Laceration of the cervix was found in 21 patients (16.1%). As revealed in clinical evaluation of the uterus, 80 patients (61.5%) had regular enlargement of the uterus, while 34 subjects (26.1%) had irregular one.

Location of the leiomyomas were as follows:

- in 52 patients (40%) – on the anterior wall,
- in 36 patients (27.7%) – on the posterior wall,
- in 23 patients (17.7%) – both on the anterior and posterior wall,
- in 12 patients (9.2%) – inside the cornu of the uterus,
- in 7 patients (5.4%) – isthmo-cervical site.

Mean size of the leiomyomatic uterus in terms of pregnant uterus was the highest in Group I – 14.2 gestational weeks.

Table 1: Four groups of participants.

Participants	General population N=130	Group I hysterectomy with bilateral oophorectomy N=80	Group II hysterectomy with unilateral oophorectomy N=20	Group III hysterectomy without bilateral oophorectomy N=15	Group IV conservative myomectomy N=15
age	45.1+/–5.2	49.2+/–3.85	42.34+/–2.23	39.8+/–3.9	38.4+/–4.87
range	26–58	34–58	35–47	29–43	26–45

Table 2: Lipids serum concentration during the trial.

Examination	Before surgery	10 days from surgery	6 months from surgery	Statistical significance
		GROUP I		
Cholesterol (mM)	5.68	5.31	6.18	P<0.001
TG (mM)	1.46	1.92	1.56	P<0.001
HDL (mM)	1.51	1.19	1.69	P<0.001
LDL (mM)	3.58	3.19	3.88	P<0.001
		GROUP II		
Cholesterol (mM)	5.87	5.28	5.74	P<0.001
TG (mM)	1.51	1.86	1.56	P<0.05
HDL (mM)	1.63	1.14	1.65	P<0.001
LDL (mM)	3.59	3.27	3.32	P>0.05
		GROUP III		
Cholesterol (mM)	5.10	4.66	5.48	P<0.01
TG (mM)	1.29	1.56	1.01	P<0.001
HDL (mM)	1.37	1.20	1.75	P<0.001
LDL (mM)	3.05	2.84	3.29	P>0.05
		GROUP IV		
Cholesterol (mM)	5.52	4.90	5.13	P<0.01
TG (mM)	1.32	1.43	1.16	P>0.05
HDL (mM)	1.71	1.23	1.52	P<0.001
LDL (mM)	3.24	3.07	3.07	P>0.05

Blood loss during surgery in 96 patients (73.8%) remained below 300ml; in 18 cases (13.8%) ranged from 300ml to 400ml; in 8 subjects (6.1%) it ranged from 400 to 500ml, and in 8 other cases (6.1%) reached 500ml and more. In Group I, 67 patients (83.7%) were administered antibiotic treatment, versus 17 subjects (85%) in Group II, 7 subjects (46.6%) in Group III, and 11 patients (73.3%) in Group IV.

No severe complications after operations were recorded, such as bleeding or infections.

According to pathological examinations, the majority of patients – 90 subjects (69.2%) featured *leiomyoma*, 26 (20%) *leiomyoma partim hyalinisans, and* 14 (10.7%) developed *leiomyoma cellulare*.

Gynecological follow-up visit 6 months from surgery revealed

- 82 patients (63%) experiencing no pathological changes,
- 30 patients (23%) with moderate vaginitis,
- 14 patients (10.7%) with severe *vaginitis*,
- 2 patients (1.5%) complaining about pain in the lower part of the abdomen,
- 2 patients (1.5%) after conservative myomectomy still having menometrorrhagia.

Total cholesterol, TG, HDL and LDL were assessed from patient's blood sample before surgery and at 10 days, and 6 months after operation. On the basis of mean results of serum lipids (general population), decrease in total cholesterol, LDL and HDL was observed at 10 days from surgery, with return to preoperative value at 6 months from surgery (Fig. 1). These differences were statistically significant ($p<0.001$). Different behaviour was recorded in the case of triglycerides: higher level at 10 days from surgery with return to preoperative value after 6 months.

Within the groups analyzed, the same tendency was observed in serum lipids concentration (Table 2). Regardless of the type of surgery performed, decrease in cholesterol, HDL and LDL was observed at 10 days after operation, with return to preoperative values at 6 months after surgical procedure (Fig. 2, Fig. 4, Fig. 5). Different situation was observed in the case of TG (Fig. 3).

The highest level of total cholesterol and LDL (6 moths after operation) was reported in patients who

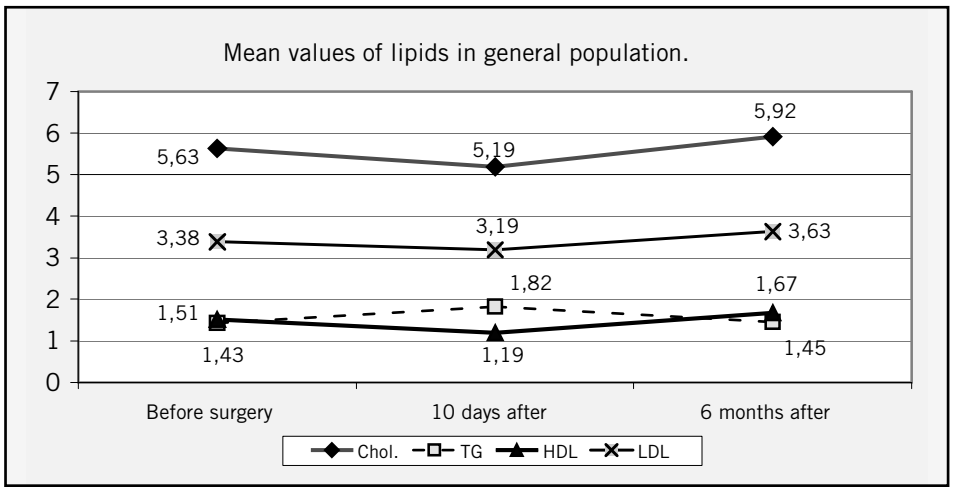

Figure 1. Mean values of lipids in general population.

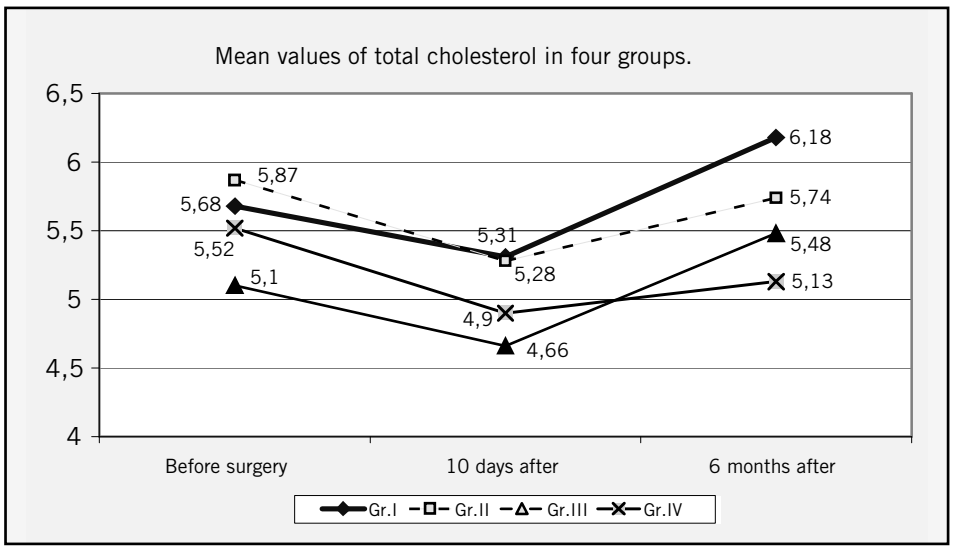

Figure 2. Mean values of total cholesterol in four groups.

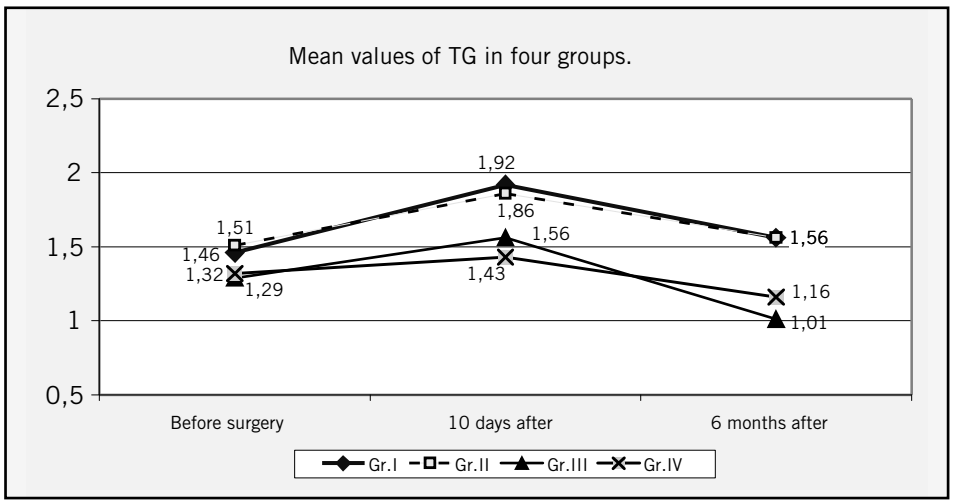

Figure 3. Mean values of TG in four groups.

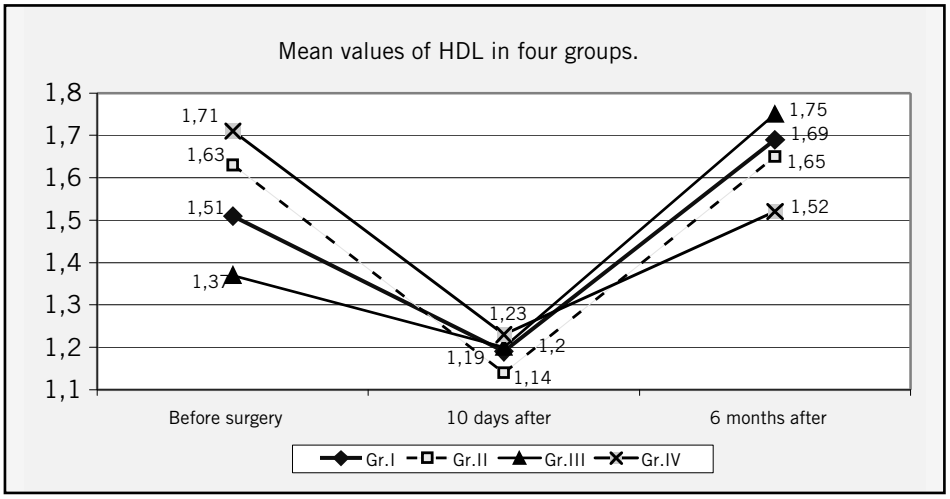

Figure 4. Mean values of HDL in four groups.

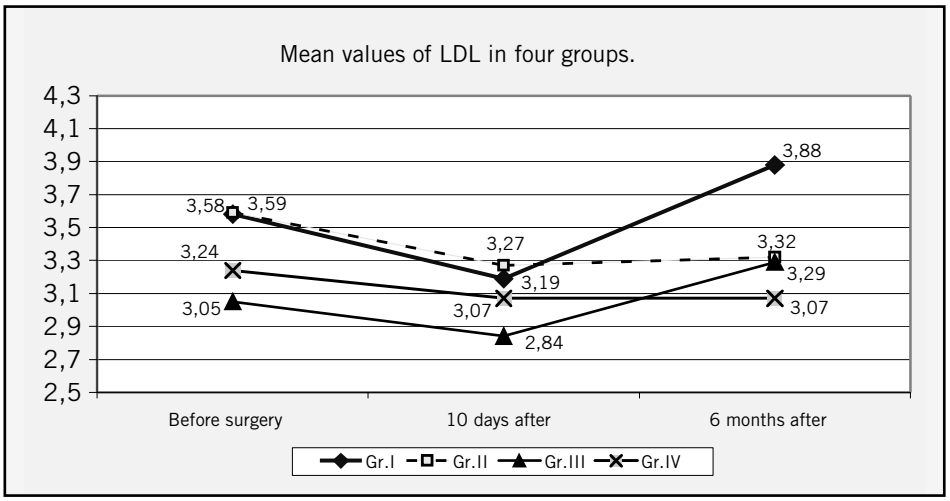

Figure 5. Mean values of LDL in four groups.

underwent hysterectomy with bilateral oophorectomy (Fig. 2, Fig. 5). Women in Groups I and II had the highest level of TG at 6 months after gynecological procedure (Fig. 3). Patients who underwent hysterectomy without bilateral oophorectomy were reported the highest rate of HDL (Fig. 4).

Discussion

According to Farish E. et al. and Notelovitz M. et al., who investigated effects of bilateral oophorectomy on lipoprotein metabolism, decrease in total cholesterol, LDL and HDL was reported at early stage after surgical procedure and returned to preoperative value at 6 months later – which was similar to our results [4]. Women's lipids metabolism six years after surgery on account of uterine leiomyomas was assessed by Kaminski B. et al. They concluded that in younger women with partial oophorectomy no changes of lipid metabolism were found. In older women after hysterectomy with bilateral oophorectomy, a marked increase in LDL and decrease in HDL were observed, which promote development of atherosclerosis [11]. Changes of the lipid profile in the blood serum may be connected with hormonal homeostatic disturbances, decreased level of estrogens and rising level of gonadotropins – the early period after surgical ovariectomy is characterized by decrease in concentration of 17β-estradiol and increase of atherogenic lipid parameters [7].

Goldman G. et al. tried to explain the effect of endogenous estrogen on lipid and lipoprotein metabolism in premenopausal and postmenopausal women. They claimed that no significant differences were found in the serum lipid and lipoprotein profile, before castration and 6 months later [6]. We cannot agree with their conclusion that the effect of endogenous estrogen on lipid metabolism is doubtful and should be further investigated. We also cannot accept the results of the trial carried out by Carranza-Lira S. et al., in which they observed that hysterectomy does not have a deleterious effect on hormone or lipid levels, nor on bone density [3].

Patients with estrogen deficiency – after hysterectomy with bilateral or unilateral oophorectomy – had the highest level of total cholesterol and LDL 6 months from surgery. This supports the theory that estrogens

have significant influence on lipid metabolism [10, 15]. All women after such surgery should undergo subsequent hormonal replacement therapy. In the study by Paganini-Hill A. et al., the aim was to assess the relationships of lipid and lipoprotein levels with hormone replacement therapy. They studied 292 patients and discovered that estrogens users (with and without progestin) had lower total cholesterol and LDL and higher HDL – which protects against coronary heart disease and stroke [16]. The effect of surgical menopause and subsequent estrogen replacement therapy was also investigated by Bruschi F. et al. Their findings suggest that surgical menopause induces improper changes in the lipid profile three months from surgery, and that estrogen replacement therapy soon reverses them [1].

Peters H. et al. claimed that total cholesterol, LDL and apolipoprotein B form primary cardiovascular risk factors affected by menopause [17]. According to the study by Sultan N. et al., decrease in estradiol level and the associated decrease in HDL-C, observed in postmenopausal women, may be responsible for the increased risk of coronary heart disease after menopause [20]. Several short-term randomized or crossover studies have shown that adding a progesterone-derived progestin to estrogen replacement therapy decreased the benefit of estrogen replacement therapy on the HDL level [5,9].

Conclusions: Regardless of the type of surgery performed, decrease in cholesterol, HDL and LDL are recorded at 10 days after operation, with return to preoperative values at 6 months after surgical procedure.

The highest level of cholesterol and LDL (6 moths from surgery) is observed in patients who underwent hysterectomy with bilateral oophorectomy.

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