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ORIGINAL ARTICLE

Analysis of the metabolic profile and comorbidities in women with endometriosis before and after surgical treatment

Análise do perfil metabólico e comorbidades em mulheres com endometriose antes e depois do tratamento cirúrgico

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Abstract

Aim: this study aimed to evaluate the effects of surgical treatment for endometriosis on the metabolic profile of women diagnosed with deep endometriosis. **Methods**: we conducted a prospective observational study with a sample of 30 women in the menacme diagnosed with deep endometriosis who underwent videolaparoscopic surgery in a reference center in Brazil between October 2020 and December 2021. A total of 30 women performed clinical and laboratory tests regarding their metabolic profile on two occasions, during preoperative tests and six months after video-laparoscopy. **Results**: patients had lower average levels of Total Cholesterol (TC), Low-Density Cholesterol (LDL-c), Triglycerides (TGC), and Fasting Glycemia (FG) after the surgical procedure. The average TC level was 8.2% lower after surgery, LDL-c was 12.8% lower, TGC was 10.9% lower, and FG was 7.3% lower. The results showed a statistically significant difference for all these parameters ($p < 0.001$). **Conclusions**: video-laparoscopy was associated with a favorable lipid profile compared to the preoperative lipid profile, with a significant improvement in the average levels of LDL-c, HDL-c, TC, TGC, and FG. Long-term follow-up studies are needed to determine whether surgical treatment for endometriosis can improve the metabolic parameters of women with endometriosis and favor a lower predisposition to atherogenesis.

Keywords: endometriosis; videolaparoscopy; dyslipidemia; inflammatory response; pelvic pain.

Resumo

Objetivo: Aeste estudo teve como objetivo avaliar os efeitos do tratamento cirúrgico da endometriose no perfil metabólico de mulheres com diagnóstico de endometriose profunda. **Métodos:** foi realizado um estudo observacional prospectivo com uma amostra de 30 mulheres na menacme, com diagnóstico de endometriose profunda, que foram submetidas à videolaparoscopia em um centro de referência no Brasil, entre outubro de 2020 e dezembro de 2021. As mulheres realizaram exames clínicos e laboratoriais quanto ao seu perfil metabólico em duas ocasiões, durante exames pré-operatórios e seis meses após a videolaparoscopia. **Resultados**: as pacientes apresentaram níveis médios mais baixos de Colesterol Total (CT), Colesterol de Baixa Densidade (LDL-c), Triglicerídeos (TGC) e Glicemia de Jejum (GJ) após o procedimento cirúrgico. O nível médio de CT foi 8,2% menor após a cirurgia, o LDL-c foi 12,8% menor, o TGC foi 10,9% menor e a GJ foi 7,3% menor. Os resultados mostraram diferença estatisticamente significativa para todos esses parâmetros ($p < 0,001$). **Conclusões**: a videolaparoscopia foi associada a um perfil lipídico favorável em comparação ao perfil lipídico pré-operatório, com melhora significativa nos níveis médios de LDL-c, HDL-c, CT, TGC e GJ. Estudos de acompanhamento a longo prazo são necessários para determinar se o tratamento cirúrgico da endometriose pode melhorar os parâmetros metabólicos de mulheres com endometriose e favorecer uma menor predisposição à aterogênese.

Palavras-Chave: endometriose; videolaparoscopia; dislipidemia; resposta inflamatória; dor pélvica.

INTRODUCTION

Endometriosis is a chronic gynecological and neuroinflammatory disorder affecting about 10% of reproductive-aged women[1,2]. Characterized by the presence of endometrium tissue outside the uterine cavity, studies have shown its association with chronic systemic inflammation, increased oxidative stress, and atherogenic lipid profile[3-6]. Systemic inflammation associated with endometriosis may predispose to increased levels of circulating inflammatory markers in the peritoneal fluid, facilitating implantation, proliferation, and infiltration of endometrial cells in the pelvis[7].

Given this scenario, one can mention the relationship between two important conditions, atherosclerosis, and endometriosis, apparently unconnected but which put inflammatory markers and lipoproteins together in the peritoneal fluid, with the consequent oxidation of Low Density Cholesterol (LDL-cholesterol)[8-11]. That is supported by the hypothesis that women with endometriosis have an increased frequency of dyslipidemia, and the products of lipid peroxidation have profound effects on the growth and aggregation of endometrial cells in the pelvic cavity[12].

Given the negative impact and association between systemic inflammation and endometriosis, with emerging evidence that endometriosis may predispose patients to a spectrum of comorbidities, including high blood pressure,

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hypercholesterolemia, dysglycemia, and cardiovascular disease, this study aimed to evaluate the effects of surgical treatment for endometriosis on the metabolic profile of women diagnosed with the disease[13-15].

METHODS

It is a prospective observational study carried out at the Endometriosis outpatient clinic of the Assis Chateaubriand Maternity Hospital, a reference center for endometriosis treatment in Fortaleza – Brazil, from October/2020 to October/2021. The Research Ethics Committee of the Assis Chateaubriand Maternity Hospital (MEAC, acronym in Portuguese) of the Federal University of Ceará (UFC, acronym in Portuguese) approved the project under No. 4312679, following Resolution of the National Health Council of the Ministry of Health (CNS/MS) No. 466/12, which deals with research involving human beings.

After applying the inclusion and exclusion criteria, from a total of 72 women interviewed, 30 met the criteria. All patients were tested for their metabolic profile on two occasions, during preoperative tests and six months after the surgical treatment. They were evaluated through physical examination and laboratory tests.

The surgeries were scheduled and took place according to the clinical service routine, regardless of this study. Menacme patients diagnosed with deep endometriosis by ultrasound with mapping and confirmed by laparoscopy were eligible to participate in the study.

The investigation to diagnose endometriosis was carried out through anamnesis, physical examination, and ultrasound mapping for endometriosis. Participants were tested for symptoms of endometriosis, including chronic pelvic pain, dyspareunia, and progressive dysmenorrhea. Surgery indications were for symptomatology of pelvic pain unresponsive to medical treatment (pill or levonorgestrel intrauterine device - IUD); ultrasound diagnosis of deep endometriosis, with intestinal or ureteral compromise; and image of ovarian endometrioma > 4 cm.

Exclusion criteria were: women with obesity grade 2 or 3 (Body Mass Index - BMI ≥ 35 kg/m²); women with a family history of dyslipidemia, diabetes mellitus, or systemic arterial hypertension; women who did not have a surgically confirmed diagnosis of deep endometriosis; women who did not sign the consent form or who did not perform all stages of the evaluation.

After the clinical diagnosis of endometriosis, the women were tested for their metabolic profile through laboratory tests before surgical treatment. The same tests were repeated six months after surgery for those women who had surgical confirmation of endometriosis. The metabolic profile was evaluated through a physical examination, with the collection of anthropometric data (weight in kg, height in meters, waist circumference in cm), calculation of BMI (kg/m²), measurement of systolic (SBP) and diastolic (DBP) blood pressure, and laboratory tests for dyslipidemia (TC–Total Cholesterol; HDL – High-Density Cholesterol; LDL – Low-Density Cholesterol; TGC–Triglycerides) and dysglycemia (Fasting Glycemia). The diagnoses were reached according to the following parameters:

- Arterial hypertension: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg (ESH/ESC guidelines)[16].
- Obesity: overweight (BMI 25 – 29,9 kg/m²); class 1 obesity (BMI 30 - 34,9 kg/m²) (WHO criteria)[16].
- Dyslipidemia: Total cholesterol > 200mg/dL, and/or LDL-cholesterol > 130 mg/dL, and/or HDL-cholesterol < 40 mg/dL and/or triglycerides > 150mg/dL (ESH/ESC guidelines)[16].
- Dysglycemia: Fasting glycemia ≥ 100mg/dL (ADA criteria)[17].
- Diabetes mellitus: two fasting glycemia measurements ≥ 126 mg/dL or any glycemia ≥ 200 mg/dL (ADA criteria)[17].

Baseline data included information on BMI, use of hormonal medications, habits, and comorbidities such as arterial hypertension and diabetes mellitus. All patients were using combined contraceptives or oral progestin for clinical treatment of endometriosis prior to surgery. After the surgical treatment, the patients kept habits regarding environmental, dietary, lifestyle, and reproductive factors, except for hormonal medication, which 100% of the patients had discontinued after the surgery.

Statistical analysis: on two occasions, the Wilcoxon signed-rank test was used to compare the quantitative variables for paired samples. Descriptive statistics of mean and standard deviation expressed the results obtained regarding quantitative variables. The results obtained regarding qualitative variables were expressed through frequencies and percentages, and a P-value less than 0.05 was statistically significant. Data were entered into the RedCap Platform, and a diagnostic agreement analysis was performed. Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 22.0 (USA), and software R 3.3.1.

RESULTS

The sample consisted of women aged between 23 and 46 years, with an average of 38.5 (± 7.1) years and nine years of schooling. The weighting profile and average blood pressure levels showed no statistical difference between preoperative tests and after surgery: average BMI of 31.23 (± 1.91) kg/m² and 30.47 (± 1.50) kg/m², respectively; average SBP of 119 (± 7.8) mmHg and 120 (± 7.1) mmHg, respectively, and average DBP of 76 (± 5.4) mmHg and 78 (± 5.2) mmHg, respectively. No patient had arterial hypertension or changes in lifestyle habits, such as diet or physical activity. Of the patients studied, 60% were overweight, and 40% had class 1 obesity, not including class 2 or 3 obesity patients.

Before laparoscopy, the patients were observed to have higher

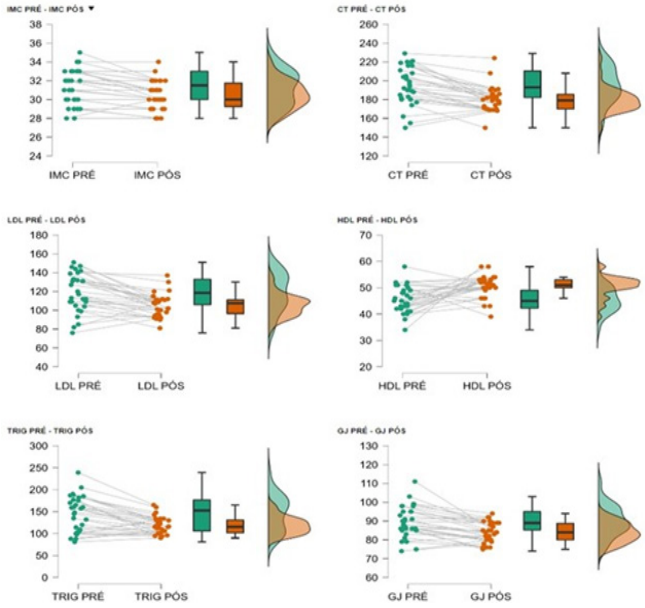
levels of total cholesterol, LDL-cholesterol, triglycerides, and fasting glycemia compared to six months after surgery. As described in Table 1 and illustrated in Figure 1, the average total cholesterol level was 8.2% lower after the surgical procedure (194.57 ± 20.08 mg/dL vs 179.77 ± 13.53 mg/dL, p < 0.001), the LDL cholesterol was 12.8% lower (119.07 ± 20.56 mg/dL vs 105.6 ± 12.18 mg/dL, p < 0.001), triglycerides 10.9% lower (145.47 ± 40.79 mg/dL vs 132.77 ± 19.68 mg/dL, p < 0.001), and fasting glycemia 7.3% lower (89.8 ± 8.37 mg/dL vs 83.67 ± 5, 3 mg/dL, p < 0.001. A difference was also observed in the analysis of HDL-cholesterol level, which was 9.9% higher after surgery (45.53 ± 5.04 mg/dL vs 50.53 ± 4 .15 mg/dL, p < 0.001).

Table 1. Clinical and laboratory variables before and six months after videolaparoscopy.

Variables	Preoperative tests Mean/SD	Postoperative tests Mean/SD	P*
TC (mg/dL)	194.5 / 20.08	179.7 / 13.5	< 0.001
LDL (mg/dL)	119 / 20.56	105.6 / 12.18	< 0.001
HDL (mg/dL)	45,5 / 5.04	50.53 / 4.15	< 0.001
TGC (mg/dL)	145.4 / 40.79	118.7/19.6	< 0.001
FBG (mg/dL	89.8 / 8.3	83.87 / 5.30	< 0.001

Note: Teste de Wilcoxon*
Legenda: VLP (Videolaparoscopy); TC (Total Cholesterol); LDL (Low Density Cholesterol); HDL (High Density Cholesterol), TGC (Triglycerides); FBG (Fasting Blood Glucose)

Figure 1. Graphical relationship between the parameters studied preoperatively and 6 months after the surgical treatment of endometriosis.



DISCUSSION

The present data show that patients with endometriosis have an unfavorable lipid profile. Although there was a statistical difference between the average levels of all lipoproteins before and after surgical treatment, the difference was more substantial for LDL and triglyceride levels, 12.8% and 10.9% lower, respectively, after surgery. Likewise, total cholesterol, triglycerides, and glycemic levels were lower in women with endometriosis after surgery, showing some improvement after surgical treatment.

Endometriotic lesions occur in a highly complex and dynamic environment through a combination of hormonal dysregulation and activation of inflammatory processes, with elevated levels of inflammatory markers in the peritoneal fluid and the serum of women with endometriosis18. A higher prevalence of systemic diseases, such as cardiovascular and metabolic diseases, has been documented and corroborated in women with endometriosis[15].

The inflammatory response associated with endometriosis may also predispose these women to an increased risk of arterial hypertension and hypercholesterolemia. Hypertension is a determinant of vascular remodeling, with an inflammatory response in the arterial wall and increased circulating inflammatory markers and peritoneal fluid levels, facilitating adhesion, implantation, proliferation, and infiltration of endometrial cells in the pelvis[8,10,15].

The clinical importance of LDL elevation derives from the involvement of this lipid in atherogenesis. Oxidized LDL can cause endothelial damage, with platelet aggregation and cytokines and chemotactic substances released by the endothelium. That favors the internalization of oxidized LDL particles and the migration of myocytes from the middle layer to the intima of the artery, forming atheromatous plaques[10,11]. Before laparoscopic surgery, the present study showed higher LDL levels in women with endometriosis.

Verit et al. (2008) detected an atherogenic lipid profile in women with endometriosis, with higher TC, LDL, and TGC levels and lower HDL levels among patients with endometriosis, which was also confirmed in the present study. However, those investigators included women with minimal endometriosis in their study, while this study involved patients with moderate or severe endometriosis and who also did not discontinue hormone medications prior to lipid profile determination, which may represent a bias[19].

In a prospective cohort study carried out by Mu et al. (2016), women with a laparoscopically confirmed diagnosis of endometriosis had a higher risk of hypercholesterolemia and arterial hypertension, regardless of family history, anthropometric characteristics, and lifestyle. The authors also observed that women with hypercholesterolemia were at greater risk of confirming a subsequent diagnosis of endometriosis on video laparoscopy, showing an association in both directions. The outcome was worse for women ≤ 40 years old and associated with a higher frequency of hysterectomy/ oophorectomy at an earlier age[9].

Donnez et al. (2016) also showed that endometriosis is associated with changes in the lipid profile and the development of atherosclerotic disease by the implication of oxidative stress and chronic inflammation20. That was confirmed by a large study carried out by Tan et al. (2019). Women with endometriosis were at greater risk of association with dyslipidemia, arterial hypertension, and atherosclerosis, which was related to many circulating inflammatory mediators[13].

An inverse causality was shown by Byun et al. (2020). Endometriosis was responsible for changes in hepatic metabolism and consequent induction of other metabolic changes, which may even explain the fact that women with endometriosis present weight loss and lower BMI values[21]. A study carried out by Carsons et al. (2020), in turn, highlighted that obese women with endometriosis tend to develop more severe forms of the disease[22].

Unlike the present study, Pretta et al. (2007) and Santoro et al. (2015) did not detect differences in the lipid profile of women with endometriosis. However, their study included patients who were not using hormonal medication (oral hormonal contraceptive, GnRH analog) to treat endometriosis, which may be an additional confounding factor to consider when analyzing the data[23,24]. This study may have a limitation in analyzing the lipid profile since it analyzed women with endometriosis in hormone treatment before surgery and without hormone treatment after surgery.

Finally, this study represents an analysis of representative metabolic domains for the female population, observing the relationship between endometriosis and dyslipidemia and suggesting early identification of young women at risk for vascular disease and prone to atherogenesis.

CONCLUSIONS

The lipid profile of patients diagnosed with endometriosis in the present study after laparoscopic surgical treatment was favorable compared to their preoperative lipid profile. There was an improvement in the average levels of LDL-cholesterol, HDL-cholesterol, total cholesterol, and triglycerides and an improvement in glycemic levels. Long-term follow-up studies are needed to determine whether surgical treatment for endometriosis can improve the metabolic parameters of women with endometriosis and favor a lower predisposition to atherogenesis.

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