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Carotid intima-media thickness: a new marker of patients with uterine leiomyoma

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ABSTRACT

Objective: To determine whether or not there are any significant differences in carotid intima-media thickness between patients with uterine leiomyoma and controls.
Study Design: Patients whose ages were between 40 and 50 years, with body mass index <30 kg/m^2, and with a pathological diagnosis of uterine leiomyoma constituted the study group. Control subjects had no uterine leiomyoma proven by sonography. Demographic, clinical, and drug history data were collected. Right, left and mean carotid intima-media thickness measurements were obtained by ultrasonography.
Results: Carotid intima-media thickness and serum high-density lipoprotein (HDL) levels were significantly different between the groups ($p = 0.0001$ and $p = 0.001$ respectively), being respectively higher and lower in the leiomyoma group than in controls. Stepwise binary logistic regression analysis revealed that uterine leiomyoma development ratio was 159.32 times higher when carotid intima-media thickness was over 0.61 mm ($p = 0.0001$). In patients with uterine leiomyoma, carotid intima-media thickness was significantly less in patients taking statins compared to those not on these drugs ($p = 0.0001$).
Conclusion: The present study demonstrated a positive association between carotid intima-media thickness and the presence of uterine leiomyoma. Conversely, an inverse association was suggested between HDL and uterine leiomyoma. These findings suggest that women with uterine leiomyoma might have an increased risk of subclinical atherosclerosis.

1. Introduction

Cardiovascular diseases are among the most prevalent causes of morbidity and mortality in developed communities. Classical cardiovascular risks have not been observed in nearly one-half of these diseases. Therefore their association with new risk factors, and other factors (if any) are still being investigated. Uterine leiomyomas (ULs) are the most frequently encountered benign uterine tumors both in the world and in our community [1,2]. Although ULs are rarely associated with mortality, they usually cause significantly increased health care costs and negative health experiences. In several countries, UL is the leading cause of hysterectomy, accounting for one-third to one-half of these surgeries [3–5]. We intended to investigate the following question: can such a widely seen tumor be a risk factor for the development of atherosclerosis during the child-bearing age and postmenopausal period?

Recent studies have shown a positive association between UL and cardiovascular risk factors such as hypertension, diabetes mellitus, obesity, and smoking [6–11]. These factors are also related to atherosclerosis. Similarly, previous results from our clinic have shown that hypertension, diabetes mellitus and smoking are associated with UL risk [6].

The shared patterns support the hypothesis that the development of UL and the development of atherosclerosis may share a common biological mechanism. In the present study, we aimed to determine whether there were any significant differences between patients with UL and controls in carotid intima-media thickness (IMT), which is good marker of atherosclerosis.

2. Materials and methods

2.1. Study design

Before beginning the research, human subject approval was obtained from the Ethical Committee of Trakya University: informed consent was obtained from all participants. The investigation conforms to the principles outlined in the Declaration of

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Helsinki. The current study was conducted at the cardiology and gynecology & obstetrics clinics in Trakya University between July 2011 and May 2012.

Two hundred and ninety-two patients diagnosed with UL and thus scheduled for surgery were included in the study (Fig. 1). Preoperatively, detailed physical and cardiac examinations were performed, biochemical parameters were analyzed in blood samples obtained after a 10-hour fasting period, and finally carotid IMT measurements were conducted. Patients aged between 40 and 50 years with a body mass index (BMI) <30 kg/m^2 and a diagnosis of UL based on clinical, laboratory and radiological test results constituted the study group.

The study population was composed of 292 UL patients and 185 control subjects without UL. Controls were patients with intact uteri who had visited the same department for a routine check-up or complaints of pelvic pain, dysuria, poly- or dysmenorrhea, anemia and infertility that included a pelvic examination and uterine sonogram. Control subjects had no UL proven by uterine sonography. Patients with hepatic, renal or coronary failure, coronary or pulmonary artery disease, history of heart attack, history of peripheral artery disease, cerebrovascular diseases, malignancies, infection, pelvic inflammatory disease, and chronic pelvic pain were not included in the study. Patients with a BMI >30 kg/m^2, low-density lipoprotein (LDL) >160 mg/dl, high-density lipoprotein (HDL) <30 mg/dl, triglyceride (TG) >200 mg/dl and creatinine >1.5 mg/dl were excluded from the study. Of 292 patients with a pathological diagnosis of UL, 88 patients were excluded because they were not eligible for our study. Patients in whom diagnostic interventions were performed for diseases other than UL were also excluded.

2.2. Outcome parameters

The following clinical and demographic parameters were recorded: age, sex, weight, height, serum creatinine level, triglyceride, LDL and HDL. History of cardiovascular risk factors such as smoking habit, hypertension, hyperlipidemia and diabetes mellitus; use of angiotensin-converting enzyme (ACE) inhibitor, calcium channel blocker, antidiabetic drugs and use of statin and fibrat were recorded.

For the measurement of the carotid IMT, the patients were laid supine with their heads inclined backwards and turned slightly away from the examined side. Carotid IMT of the patients was evaluated by high-resolution ultrasound using the Logiq 7 (GE Medical Systems, Milwaukee, Wisc., USA) system and a 12-MHz linear array transducer. Ultrasonographic evaluation was performed by the same radiologist, who was blinded to the patients and the rest of the team. The common carotid artery has been used in most of the IMT measurements. Because of its tortuosity and hardly visible nature, internal carotid artery has not been preferred. The measurements were performed on longitudinal images and on a nearly 1-cm-segment starting from the bulbus determined on a 2-cm distal segment of common carotid artery taking care to obtain the most precise images. Concordance between IMT estimates of the posterior wall based on ultrasonographic and histological parameters was found to be relatively better. Therefore, only a 1 cm^2 area of the posterior (remote) wall was selected for IMT measurements. The average of measurements obtained from three different angles (anterior oblique, lateral and posterior oblique) was calculated. For ultrasonographic analyses, IMT was measured based on the characteristic echogenicities of the lumen-intima and media-adventia interfaces. Calculations were performed manually by a single operator. Right, left and mean carotid IMT measurements were used for the study.

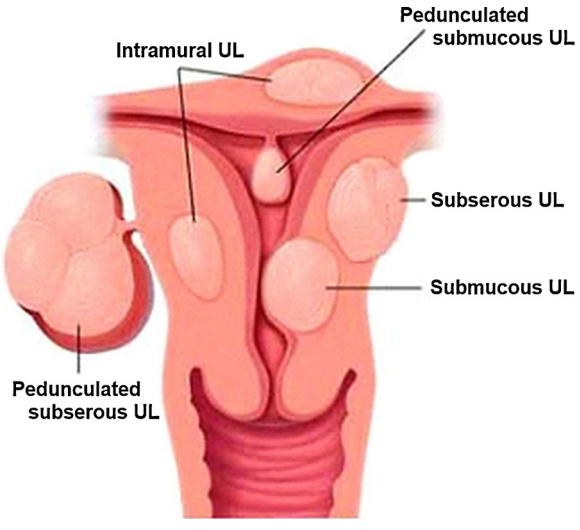

Fig. 1. Illustration showing the types of uterine leiomyoma (UL: Uterine leiomyoma).

2.3. Statistical analyses

Data were analyzed using the Statistical Package for Social Sciences 19.0 for Windows (SPSS Inc., Chicago, IL). A normal distribution of the quantitative data was checked using the Kolmogorov–Smirnov test. Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. The independent-samples *t*-test was used to compare independent groups. To calculate correlation coefficients Pearson's *r* was used. The distribution of categorical variables in both groups was compared using Pearson's chi-square test. A univariate analysis of potential risk factors was performed with the log-rank test for categorical factors and with the univariate Cox analysis for continuous variables. The cut-off points were calculated by the MedCalc software as the points with the best sensitivity-specificity balance. The results for all items were expressed as mean ± SD, presented as 95% confidence internal (95% CI). A value of $p < 0.05$ was considered statistically significant.

3. Results

Two hundred and four patients with UL and 185 controls met the eligibility criteria for the study and agreed to participate. Of the patients with UL, the mean age was 44.57 ± 2.43 (range 40–49) years; while it was 45.22 ± 2.56 (range 40–50) years in the control group.

The comparison of demographic and clinical variables of women with UL and controls is shown in Table 1. When compared with the control group, a marked increase in carotid IMT was detected in the myoma group (0.66 ± 0.04 vs 0.57 ± 0.02 $p = 0.0001$). Besides, significantly lower serum HDL levels were

Table 1
Comparison of demographic and clinical variables.

	Case ($n = 204$) *mean ± SD*	Control (n = 185) *mean ± SD*	*p* value
Age (years)	44.57 ± 2.43	45.22 ± 2.56	0.012
BMI (kg/m^2)	26.47 ± 2.37	26.60 ± 2.23	0.555
Carotid IMT (mm)	0.66 ± 0.04	0.57 ± 0.02	0.0001
Serum creatinine (mg/dL)	0.90 ± 0.20	0.89 ± 0.19	0.453
HDL (mg/dL)	39.82 ± 8.02	43.65 ± 12.97	0.001
LDL (mg/dL)	123.68 ± 23.20	121.03 ± 27.67	0.309
Triglyceride	112.96 ± 26.08	112.56 ± 24.74	0.876

SD: standard deviation; BMI: body mass index; IMT: intima-media thickness; HDL: high-density lipoprotein; LDL: low-density lipoprotein.