Histologic changes caused by nonabsorbable sutures after ovarian suspension

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Summary

Purpose: To evaluate intraovarian histologic changes caused by polypropylene and silk sutures that commonly are used in ovarian suspension. *Materials and Methods:* Twenty-four female rats were randomly allocated to three study groups: a sham group receiving no ovarian suspension; the other two groups that had right ovarian suspension with polypropylene and silk sutures. At 90 days after surgery, the histologic changes and ovarian weight reduction in the suspended ovaries and severity of pelvic adhesions were evaluated. *Results:* There were no differences between study groups in focal inflammation, cystic structures, or vascularity. Adhesion severity and ovarian weight reduction in suspended ovaries and cysts around the suspended ovary were significantly greater in the silk than sham group. The frequency of hematoma within the suspended ovary was significantly greater in the polypropylene than sham group. *Conclusions:* Polypropylene suture caused less adhesion severity or ovarian weight reduction than silk suture. This suggests that polypropylene suture may be the better suture for ovarian suspension procedures.

Key words: Inflammation; Adhesions; Cysts; Ovary; Polypropylene; Silk.

Introduction

During the reproductive years, the ovaries are very sensitive to the harmful effects of pelvic irradiation. The frequency of ovarian failure after radiation therapy is from 12% to 66% [1, 2]. Therefore the ovaries should be protected from the harmful effects of pelvic radiation therapy.

Ovarian suspension is a surgical procedure in which the ovary is transposed to a different location and fixed using transparenchymal sutures. The procedure is done to protect the ovaries from the harmful effects of radiation during pelvic radiation therapy or to prevent recurrent ovarian torsion. Nonabsorbable suture materials such as polypropylene or silk may be used in ovarian suspension procedures [3-7]. The ovaries may be detached from the uterus and suspended with their blood supply at a region outside the pelvis, usually the lateral paracolic gutter above the pelvis. Ovarian suspension performed before radiation therapy may preserve ovarian function in 16% to 90% patients [8, 9]. Failure of ovarian suspension to preserve ovarian function may be associated with age of the patient, not shielding the ovaries during radiation therapy, scattered radiation, adjuvant chemotherapy, and decreased blood supply to the suspended ovary. In addition, foreign bodies such as sutures placed in ovarian tissue during suspension may impair ovarian function.

Oophoropexy, also known as ovariopexy, is performed to prevent recurrent ovarian torsion. This procedure is similar to ovarian suspension. The surgical technique includes suturing the ovary with a transparenchymal suture to the pelvic side wall or the round ligament and plicating the utero-ovarian ligament [7, 10].

Previous studies have evaluated histologic changes or paraovarian adhesion formation during ovarian reconstruction using various suture materials [11-13]. However, there is limited information available about the effects of nonabsorbable suture materials on the ovary, such as inflammatory changes in the ovary or pelvic adhesions that occur after ovarian suspension. This information may be important because ovarian parenchymal changes may have detrimental effects on ovarian function and fertility.

The purpose of this experimental study was to evaluate intraovarian histologic changes caused by polypropylene and silk sutures that commonly are used in ovarian fixation procedures.

Materials and Methods

Animals

This experimental study was performed with 24 female Sprague Dawley rats that were randomly allocated into three study groups (eight rats per group): a sham group receiving no ovarian suspension, a group that had right ovarian suspension with polypropylene sutures, and a group that had right ovarian suspension with silk sutures. The study was approved by the animal experimentation local ethics board of Hacettepe University.

Procedure

Intraperitoneal anesthesia was induced with ketamine hydrochloride (50 mg/kg) and xylazine hydrochloride (10 mg/kg). In

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all rats, a two-cm abdominal incision was made, both ovaries were identified, and left ovariectomy was performed. In the rats in the polypropylene and silk groups, right ovarian suspension was performed; the connection between the right ovary and the uterine horn was cut, and the ovary was fixed with the vascular pedicle to the peritoneum in the right paracolic region superiorly using transparenchymal sutures (polypropylene 5-0 or silk 5-0). The excised left ovaries were weighed and the abdomen was closed with silk 3-0 suture in two layers.

After surgery, the animals were housed in a temperature- and humidity-controlled environment at 22°C on an alternating cycle of light (12 hours) and darkness (12 hours). The rats were fed typical laboratory food and tap water ad libitum. At 90 days after the initial surgery, the same type of anesthesia was induced, and similar laparotomy was performed. The severity of pelvic adhesions was graded in each animal with a standardized scale and a corresponding score was obtained for each rat in a blinded manner; adhesion severity was described and scored as absent adhesions (0 points); thin, filmy adhesions (1 point); definite localized adhesions (2 points); dense multiple visceral adhesions (3 points); or dense adhesions extending from the abdominal wall to visceral organs (4 points) [14]. Hematoma within the suspended ovaries and cysts around the suspended ovaries were recorded. The suspended ovaries were removed and weighed. The weight difference of ovaries after 90 days was calculated between control (left) and suspended (right) ovaries in each rat.

Histology

The histologic changes in the suspended or sham ovaries were investigated. Fresh tissue samples were rapidly fixed in 10% phosphate buffered formalin, dehydrated through graded alcohol solutions, and processed for routine light microscopy. All specimens were embedded in paraffin blocks, and five-µm sections were cut and stained with hematoxylin-eosin. Sections were examined using a microscope and photographed. A single histologist evaluated the histologic changes in a blinded manner. The histologic examination evaluated superficial inflammatory changes, cystic structures, vascularity, and follicular maturation.

Superficial inflammatory changes adjacent to the suture were graded as none, mild, moderate, and severe and were assigned numerical values of 0 to 3 as previously described [15]. Mild inflammatory changes were defined as a focal inflammatory infiltrate involving < 25% ovary with adjacent normal ovarian structure. Moderate inflammatory changes were defined as 25% to 75% involvement of the ovary. Severe inflammatory changes were defined as > 75% involvement of the ovary.

Cystic structures (dilation of lymphatic vessels containing exudate without red blood cells) were graded based on the number of cystic structures in an area with ten-fold magnification (grade 1 had one to ten cystic structures; grade 2 had 11 to 20 cystic structures; and grade 3 had > 20 cystic structures). Vascularity was scored similar to cystic structures. The grading systems were assigned numerical values for statistical analysis. In addition, primordial and maturing follicles (primary, secondary, and antral follicles) were evaluated for each rat.

Statistical analysis

Data analysis was performed with statistical software (SPSS version 20). The scores of focal inflammation, cystic structures, vascularity, and adhesion severity were not normally distributed; the non-parametric Kruskal-Wallis test was used to compare these variables between the groups. Pairwise differences were evaluated with Mann-Whitney test with Bonferroni adjustment for multiple comparisons. Weight differences between the ovaries were normally distributed and were compared with one-way analysis of variance. Pairwise post hoc analysis was performed with Tukey test. The χ^2 test (chi-square test) or Fisher exact test was used to compare proportions of hematoma within, and cysts around, suspended ovaries in different groups. Bonferroni adjustment was applied for multiple comparisons. Statistical significance was defined by $p \leq 0.05$.

Table 1. — *Histologic changes associated with ovarian suspension in rats*[*]

Variable	Sham	Polypropylene	Silk	$p \leq$ [†]
Number	8	8	8	
Focal inflammation	1.4 ± 0.5	1.5 ± 0.5	1.6 ± 0.5	NS
Cystic structures	1.3 ± 0.5	1.6 ± 0.5	1.4 ± 0.7	NS
Vascularity	1.5 ± 0.5	1.4 ± 0.5	1.5 ± 0.8	NS
Adhesion severity	0.4 ± 0.5	0.5 ± 0.9	2 ± 1	0.01[a]
Weight difference (mg)[d]	2 ± 5	-5 ± 8	-9 ± 5	0.005[e]
Hematoma within suspended ovary	0 (0)	6 (75)	2 (25)	0.002[b]
Cyst around suspended ovary	0 (0)	1 (13)	4 (50)	0.03[c]

[*]N = 24 rats. Results at 90 days after sham surgery or ovarian suspension with polypropylene or silk transparenchymal sutures. Data reported as mean ± SD or number (%).

[†]NS, not significant ($p > 0.05$).

[a,b,c] With multiple comparisons and Bonferroni adjustment, differences were significant between sham *vs* silk groups for adhesion severity, sham *vs* polypropylene groups for hematoma within suspended ovary and sham *vs* silk groups for cyst around suspended ovary.

[d] Weight difference between control (left) and suspended (right) ovaries.

[e] With post hoc test, difference between sham and silk groups was significant.

Results

At 90 days after ovarian suspension, there were no differences between study groups in focal inflammation, cystic structures, or vascularity (Table 1). Inflammation, cystic structures, and vascularity in the suspended ovary typically were grade 1 or 2 in all rats (Table 1, Figure 1). In the silk group, only one rat presented with grade 3 cystic structures and vascularity in the suspended ovary (Figures 2, 3).

Adhesion severity was significantly greater in the silk than sham group (Table 1). Ovarian weight reduction in suspended ovaries was significantly greater in the silk than sham group, and there was no difference in weight reduction between the polypropylene and sham group (Table 1).

The frequency of hematoma within the suspended ovary was significantly greater in the polypropylene than sham group, and cysts around the suspended ovary were significantly greater in the silk than sham group (Table 1). There was one abscess (2 × 2 cm) noted around the suspended ovary in the polypropylene group.

In all study groups, each animal had normal primordial and maturing follicles (primary, secondary, and antral follicles) in the suspended or sham ovary (Figures 4, 5).

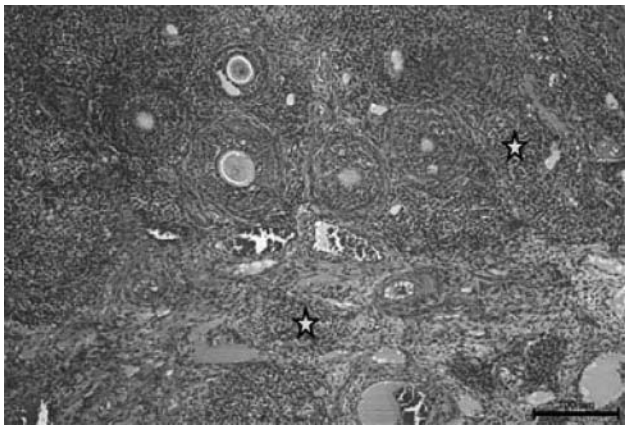

Figure 1. — Inflammation (grade 1) (stars) in ovarian stroma in a rat from the sham group that received no ovarian suspension (hematoxylin-eosin, original magnification ×10).

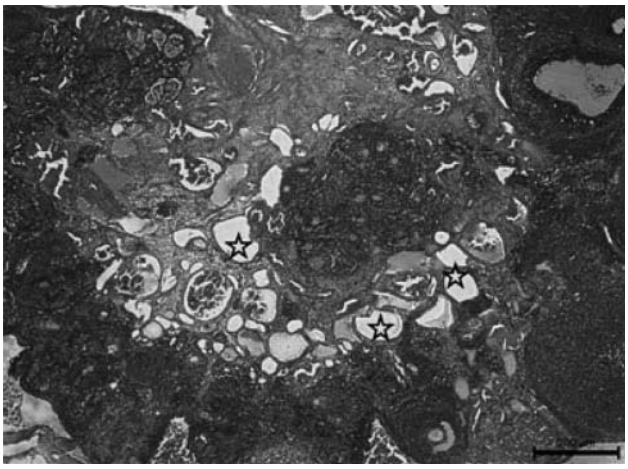

Figure 2. — Cystic structures (grade 3) (stars) noted in one rat that had ovarian suspension with silk suture (hematoxylin-eosin, original magnification ×5).

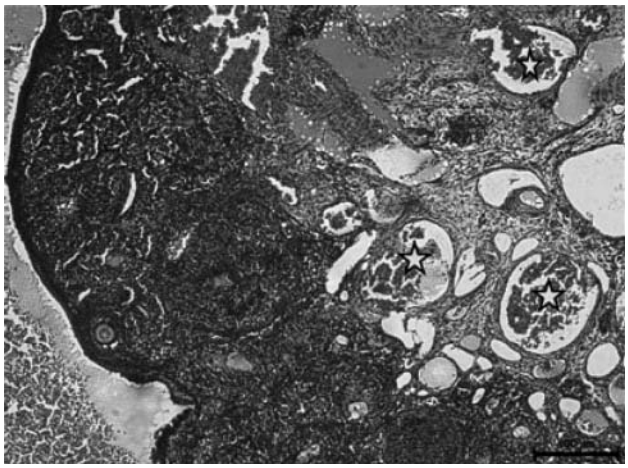

Figure 3. — Vascularity (grade 3) (stars) noted in one rat that had ovarian suspension with silk suture (hematoxylin-eosin, original magnification ×10).

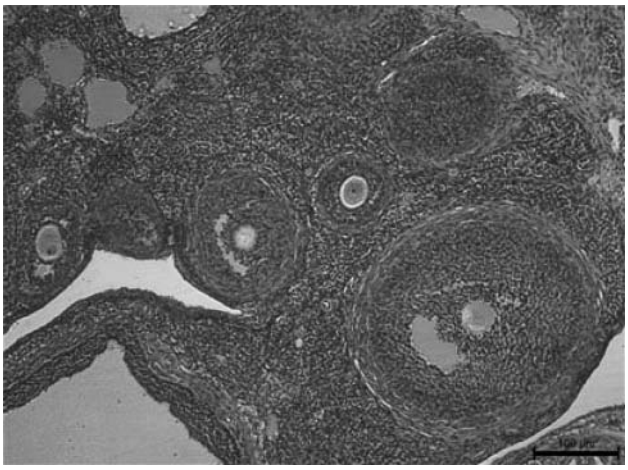

Figure 4. — Normal primordial and maturing follicles in a rat that had ovarian suspension with polypropylene suture (hematoxylin-eosin, original magnification ×10).

Discussion

This experimental study showed that suspension of the ovary with transparenchymal polypropylene or silk sutures was associated with no significant histologic changes in focal inflammation, cystic structures, or vascularity within the suspended ovaries compared with sham ovaries (Table 1). Severity of adhesions in the pelvis, weight reduction in the suspended ovary, and frequency of cysts around the suspended ovary were significantly greater in the silk than sham group (Table 1). Both polypropylene and silk sutures had no effect on primordial and maturing follicles (Figure 4).

Surgical procedures on ovary such as ovarian suspension, ovarian reconstruction, or cystectomy are performed with various types of sutures that are placed inside the ovary. However, very limited data are available about the effects of suture materials within ovarian tissue. Therefore, comparison between the present and previous studies is limited.

Figure 5. — Nonaffected antral follicle in a rat from the sham group that received no ovarian suspension (hematoxylin-eosin, original magnification ×10).

In a previous experimental study that compared ovarian reconstruction using rapid acting human fibrin glue, polyglactin absorbable suture, and no suture, results with the different materials were similar in adhesions, ovarian size, presence of cysts, and histologic scores [13]. In contrast, the present study showed that nonabsorbable suture material caused changes in adhesions, ovarian weight, hematoma, and cysts (Table 1).

Atrophy or weight reduction in the suspended ovary, greater in the silk than sham group, may have been caused by vascular compromise in the suspended ovary caused by the suture. Edema may develop in response to suture materials and may potentially mask the actual weight reduction in the suspended ovary, and this may explain why no significant weight reduction was demonstrated with polypropylene suture (Table 1).

Previous studies showed that ovarian suspension may cause the development of cystic structures in 23% to 24% ovaries [8, 16]. Although the authors observed no intraovarian cysts in suspended ovaries, cystic structures around the suspended ovary with clear serous fluid were detected with propylene and silk sutures but not in the sham group (Table 1). These cystic structures around the suspended ovaries had the appearance of peritoneal inclusion cysts, which may be caused by peritoneal adhesions after ovarian suspension [17]. Therefore, the differential diagnosis of postoperative ovarian cysts in suspended ovaries may include peritoneal inclusion cysts.

Although good functional outcomes have been reported in ovaries after suspension [18], the effects of suture materials on developing or mature follicles within the suspended ovary have not been evaluated in detail. In five young girls with radiosensitive brain tumors who had laparoscopic ovarian suspension with polypropylene suture before radiation therapy, ovarian biopsy after radiation therapy showed > ten germinal follicles per high power field [19]. Therefore, ovarian suspension may enable preservation of ovarian germinal follicles [19]. In the present study, primordial and maturing follicles also were not affected by suture material. The absence of harmful effects of suture materials on ovarian follicles may explain, in part, the frequent preservation of ovarian function after suspension.

Ovarian suspension may cause postoperative adhesions and interfere with the anatomic relation between pelvic organs. In two previously reported patients who had laparoscopic ovarian suspension with polypropylene suture before radiotherapy, no adhesions were noted on laparoscopy at three months after radiation therapy [20]. This is consistent with the present results that showed similar adhesion severity in the pelvis between polypropylene and sham groups (Table 1). However, the silk group had significantly greater adhesion severity than the sham group (Table 1). Therefore, polypropylene may be better than silk suture in minimizing the development of pelvic adhesions after ovarian suspension.

Limitations of the present study included the possibility that the animal model may not necessarily mimic typical ovarian suspension in human clinical practice. In addition, the short study duration (90 days) precluded the determination of long-term histologic and functional outcomes. Nevertheless, the study improves the available information about the effects of transparenchymal suture materials within ovaries after suspension and may serve as a model for the evaluation of ovarian suspension in humans.

Conclusions

This study focused on ovarian tissue reactions to two different types of suture materials in an animal model and provided information about tissue reactions at 90 days after suture placement. Transparenchymal polypropylene and silk sutures caused no significant histologic changes in focal inflammation, cystic structures, or vascularity between the suspended and sham ovaries. Polypropylene suture caused less adhesion severity or ovarian weight reduction than silk suture. This suggests that polypropylene suture may be the better suture for ovarian suspension procedures. However, further study is necessary to determine the long-term histopathologic and functional changes associated with these suture materials in the ovary.

Competing interests: the authors declare that they have no competing interests.

Authors' contributions: SH participated in the design of the study and in drafting the manuscript and carried out experiments. LKS carried out histologic assessments and helped to draft the manuscript. FFK carried out histologic assessments and helped to draft the manuscript DH participated in the study design and coordination and helped to draft the manuscript. HT participated in the study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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