A conservative approach to unilateral ovarian torsion in a rat model

Ebru Dikensoy, MD, Ahmet Gocmen, MD, Ibrahim Sari, MD.

ABSTRACT

Objective: To determine whether surgical detorsion is effective in preventing surgical resection in a rat model of ovarian torsion.

Methods: This study was performed between July 2002 and May 2003 in the Department of Obstetrics and Gynecology of Gaziantep University Hospital, Gaziantep, Turkey. Fifty adult female rats were randomized into 10 groups. The right ovaries in the study groups were manually twisted under general anesthesia. The duration of ovarian torsion was 24, 48, 72, or 96 hours. Each group was also divided into 2 subgroups according to the time lapse following detorsion (24 or 72 hours). During autopsy, both ovaries from each animal were removed for histopathological examination. Tissue injury was graded from 0 (no injury) to 3 (necrosis).

Results: Follicle development was observed in all specimens. After 24 hours following detorsion, the histopathology scores of the twisted right ovaries were significantly higher compared to the untwisted left ovaries in groups with torsion periods of 48 (p=0.04), 72 (p=0.03), and 96 hours (p=0.04). The histopathology scores of the twisted right ovaries at 24 hours following detorsion were significantly higher than those at 72 hours following detorsion in all groups (p<0.05).

Conclusions: The results show that conservative management by surgical detorsion in rats, even in those with a torsion period of 96 hours, can restore ovarian tissue viability. Furthermore, recovery observed in the twisted ovaries was better at 72 hours compared to that at 24 hours following detorsion

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From the Departments of Obstetrics and Gynecology (Dikensoy, Gocmen), and Pathology (Sari), Gaziantep University, Gaziantep, Turkey.

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Address correspondence and reprint request to: Dr. Ebru Dikensoy, Department of Obstetrics and Gynecology, Gaziantep University School of Medicine, Gaziantep, Turkey. Tel. +90 (342) 3606060 Ext.76352. Fax. +90 (342) 3606306. E-mail: dikensoy@yahoo.com

varian torsion is a serious gynecological problem and the 5th most common gynecologic emergency, with a reported incidence of 3% in one series of acute gynecologic complaints.^{1,2} It is more prevalent among women of reproductive age, and ovulation induction, pelvic infections, ovarian tumors, and pregnancy are the most common indices of ovarian torsion. Early diagnosis and treatment are crucial for the preservation of fertility and prevention of pelvic infections, which can even cause mortality.¹⁻³ However, delay in diagnosis may occur because of non-specific clinical presentation such as acute unilateral cramping pain located in the lower abdominal quadrant, attributable to a wide range of acute abdominal emergencies.^{2,3} Although ultrasonography can visualize the twisted adnexa,⁴ direct visualization with laparoscopy is frequently required for definitive diagnosis as well as for treatment in most cases.⁵ Historically, ovarian torsion has been treated with salpingo-oophorectomy to avoid the potential complication of thrombotic emboli from the ovarian vein.⁶⁻¹³ In 1946, Way¹⁴ initially advocated conservative management of ovarian torsion by untwisting of the ovary followed by ovarian cystectomy. Although this conservative approach has been accepted worldwide, there is no consensus on issues such as selection of the appropriate case and the method. The aim of this study is to investigate whether surgical detorsion in a rat model of ovarian torsion is an effective method of avoiding salpingo-oophorectomy in rats with torsion periods of 24, 48, 72, and 96 hours.

Methods. This prospective controlled study, approved by our institutional review board, was performed on 50 female Wistar rats between July 2002 and May 2003 in the Department of Obstetrics and Gynecology of Gaziantep University Hospital, Gaziantep, Turkey. The surgical procedures were performed according to the National Institutes of Health Guide for the care and use of laboratory animals. Animals were randomly divided into

10 groups for histopathological examinations for the selected ischemia and detorsion periods (Figure 1). Female Wistar rats at 70 days of age and weighing 120 ± 13.2 grams, were housed and fed in a standardized environment and conditions. On the day of the surgical procedures, each rat was weighed and anesthetized with a single intramuscular injection of 50 mg/kg ketamine hydrochloride. Animals were placed in the prone position, and their abdominal region was shaved and cleaned with 10% povidone before surgery. A small (-2 cm) incision was made at the midline abdomen to visualize the uterine horns and ovaries. Ovarian torsion was created by twisting the ovary at right side 720° clockwise and fixing it to the abdominal wall with a 5/0 vicryl suture. Sham operations were performed in control groups by putting a 5/0 vicryl suture between the ovary and tube and the abdominal wall without twisting the ovary. Animals in sham groups were reopened to remove the suture. The abdominal wall was sutured with 3/0 silk after torsion was performed. Detorsion was performed following ischemia periods under general anesthesia, as described above, and by opening the same surgical line and removing the sutures to release the ovaries to their natural position. Prophylaxis with 100 mg/kg intraperitoneal ampicillin was performed following each laparotomy. At the end of each detorsion periods, animals were sacrificed by cervical dislocation, and both ovaries were surgically removed for histopathological examination. All ovarian tissues were fixed in 10% buffered formalin, embedded in paraffin, cut into 5-µm sections, and stained with hematoxylin-eosin. Histopathological examinations were performed separately by 2 different pathologists, who were blinded to the groups. Tissue injury was graded from 0 to 3: 0=Normal interstitium; 1=Interstitial hemorrhage; 2=Focal necrosis; 3= Diffuse necrosis (foci for necrosis >1). Left ovaries were used as the second control for each animal.

Statistical analysis. The statistical analyses were performed using ANOVA, the Mann Whitney-U test, and Wilcoxon's signed-rank test where appropriate, using SPSS 9.0 software. The p<0.05 was accepted as statistically significant. Values were given as mean \pm standard deviation (SD).

Results. There were no significant differences in demographics among animals (p>0.05). The mean operation time was approximately 4 ± 1 minutes and was similar between the groups. The twisted ovaries in all groups were macroscopically observed to be dark purple during the second laparotomy performed for detorsion. During the autopsies performed to remove ovaries following the detorsion periods, all of the ovaries appeared to have returned to their original healthy-pink color. Histopathological examinations of these torsioned-detorsioned ovaries identified follicle development in all specimens. The histopathological examinations of the never-twisted left ovaries were normal in all animals in the study, including the sham groups. The histopathological injury scores of twisted ovaries at 24 hours following detorsion were significantly higher than those of the never-twisted left ovaries in groups with torsion periods of 48 (1.8 \pm 0.8 versus 0, p=0.04), 72 (1.8 ± 0.8 versus 0, p=0.03), and 96 hours $(2.2 \pm 0.4 \text{ versus } 0, p=0.04)$. However, there was no statistically significant difference at 24 hours following detorsion in the comparison of histopathological injury scores of the twisted right and never-twisted left ovaries in the group with a 24-hour torsion period (1.8 ± 1.6) versus 0.4 ± 0.5 , p > 0.05).

In all study groups, the twisted right ovaries exhibited significantly higher histopathological injury scores compared to those in the sham groups at 24 hours following detorsion. There was no such difference at 72 hours following detorsion except for the group with a torsion period of 48 hours, which had significantly higher histopathological injury scores compared to the

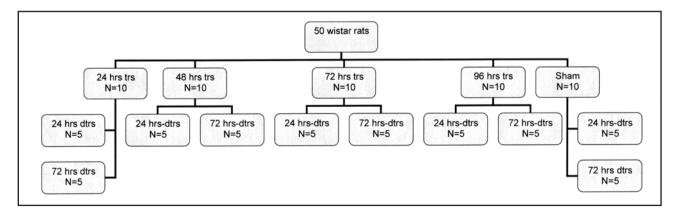


Figure 1 - Flow diagram showing the groups that underwent torsion (trs) and detorsion (dtrs) for certain time periods.

sham group at 72 hours following detorsion $(0.8 \pm 0.4 \text{ versus } 0, p > 0.05)$. Histopathological injury scores of the twisted right ovaries at 24 hours following detorsion were significantly higher than those at 72 hours following detorsion, regardless of the torsion period (24 hours torsion: 1.8 ± 1.6 versus 0, p=0.04; 48 hours torsion: 1.8 ± 0.8 versus 0.8 ± 0.4 , p=0.04; 72 hours torsion: 1.8 ± 0.8 versus 0.6 ± 0.5 , p=0.04; 96 hours torsion: 2.2 ± 0.4 versus 0, p=0.03).

Discussion. Management of ovarian torsion is a controversial topic. Concern that untwisting the ovary will precipitate thrombotic events such as pulmonary embolus has frequently led physicians to manage ovarian torsion with salpingo-oophorectomy.⁹ The overall incidence of fatal pulmonary emboli in women <40 years old undergoing all types of pelvic surgery is reported to be between 0.1-0.5%.¹⁵ Four series from outside the United States report 97 cases of ovarian torsion treated by surgical detorsion followed by salpingo-oophorectomy, cystectomy, or cyst aspiration.¹⁶⁻¹⁹ Eighty-two patients in these series underwent surgical ovarian detorsion, and 61 of these ovaries were saved. No thrombotic complications were seen. Although the numbers of the case series, which advocate ovarian detorsion in such cases, have increased recently, there is no consensus on patient selection. Management issues addressing patient selection and procedural timing and approach remain to be clarified. $\overline{4}, 5, 7, 10, 12$

In theory, occurrence of necrosis in the twisted ovary is less likely because of the very good blood supply from both ovarian and uterine arteries. Some previous studies reported that the macroscopic dark purple appearance in the twisted ovary occurs secondary to venous stasis and is not always associated with tissue necrosis, as was also indicated in the present study.^{5,16} We macroscopically observed during the second laparotomy performed for detorsion that the twisted right ovaries were dark purple in all study groups; however, all twisted right ovaries had returned to the original healthy-pink color at autopsy following a detorsion period. Follicle development was observed in the histopathological examinations of all specimens at either 24 or 72 hours following detorsion. These findings support those of previous studies suggesting that the dark purple color observed in twisted ovaries does not indicate necrosis. The histopathology scores of the twisted right ovaries in all groups were significantly higher compared to those of right ovaries in the sham group at 24 hours following detorsion. However, the same comparison did not identify any significant difference at 72 hours following detorsion, with one exception: the group with 48 hours of torsion had significantly higher histopathology scores compared to the sham group. These data from an experimental animal model suggest that ischemia resulting from ovarian torsion lasting up to 96 hours causes some degree of reversible histopathological changes in the ovaries. Further, untwisting these ovaries allows reperfusion, producing better recovery when the detorsion is prolonged from 24-72 hours. The group that underwent a 48-hour torsion period received higher histopathology scores for the twisted right ovaries compared to the sham group at 72 hours following detorsion; however, the histopathology scores of the twisted ovaries were significantly lower compared to those from the 48hour torsion group that underwent only 24 hours of detorsion. The same comparison showed no significant difference between the 96-hour torsion group and the sham group at 72 hours following detorsion; thus, we believe that the higher histopathology scores in the 48-hour torsion group were not related to the ischemia period. The small number of animals included in each group might explain this bias. Regardless of torsion time, histopathology scores were significantly higher at 24 versus 72 hours post-detorsion. These data support our previous suggestion that longer reperfusion allows better recovery of ovarian tissue. Histopathological examination of the untwisted ovaries in each group showed no sign of tissue injury, and neither was there any identified in the control groups. This finding was contrary to that of a previous report by Cakmak et al,¹⁹ who suggested that unilateral ovarian torsion in a rabbit model caused decreasing ultrastructural damage in the untwisted ovaries at 8 and 24 hours of torsion. It should be kept in mind that this is an animal study and one should be cautious to extrapolate the results of this study to human populations.

In conclusion, our results show that the dark purple color following torsion does not indicate necrosis, and conservative management by surgical detorsion in rats, even in those with a torsion period of 96 hours, can restore ovarian tissue viability. Furthermore, recovery observed in the twisted ovaries was better at 72 hours compared to that at 24 hours following detorsion.

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Related topics

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