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# Oophorectomy versus salpingo-oophorectomy in Turner syndrome patients with Y-chromosome material: clinical experience and current practice patterns assessment

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ABSTRACT

*Background/purpose:* Gonadectomy is recommended in Turner syndrome (TS) patients with Y-chromosome material due to high risk of tumor in the dysgenetic gonads. No recommendations exist on whether concurrent salpingectomy should be performed.
*Methods:* A retrospective chart review of surgical procedure and histopathology in TS patients with Y-chromosome enrolled in a TS database was undertaken at Cincinnati Children's Hospital Medical Center. An electronic survey was sent to members of the International Pediatric Endosurgery Group to assess prevalent practice patterns and attitudes on gonadectomy and concurrent salpingectomy in this population.
*Results:* In March 2011, 12/158 (8%) TS girls (mean age 6.6 years) enrolled in the database had TS with Y-chromosome. Gonadoblastoma was identified in 4/12 (33%) patients and 2/4 had malignant transformation to dysgerminoma and teratoma. Approach to gonadectomy was varied and 3/12 had concurrent salpingectomy. Fifty-four laparoscopic surgeons responded to the survey with no clear consensus on whether salpingectomy should be concurrently performed.
*Conclusions:* TS patients with Y-chromosome have an increased risk of gonadal tumor development and gonadectomy is recommended. While there is no consensus among pediatric laparoscopic surgeons on concurrent salpingectomy, it is reasonable to consider this combination procedure.


Turner syndrome (TS) is a common chromosomal abnormality with prevalence of approximately 1 in 2,000 live female births [1]. Girls with TS have a variable phenotype and age at diagnosis [2]. Fifty percent of patients with TS have a 45,X karyotype, and the remaining patients have either mosaicism with a 45,X cell line or a structural X anomaly [2]. About 5% of patients with TS have Y-chromosome material in the peripheral blood karyotype and another 3% have a marker chromosome (a chromosome fragment of the X or Y chromosome) [3,4]. The patients with Y-chromosome material have a high risk for development of germ cell tumors in their dysgenetic gonads. This was previously reported with a prevalence of 15–30%, with some reports of risk as high as 40% [3,5]. Recent studies point to a lower prevalence (7–25%) [6,7]. Gonadoblastoma is the most commonly found tumor and considered an in-situ neoplastic lesion with further risk for malignant transformation to a dysgerminoma or another invasive germ cell tumor (such as yolk sac tumor, embryonal cell carcinoma and malignant teratoma) [6]. Prophylactic gonadectomy is currently recommended in all TS patients with Y-chromosome material [5]. While laparoscopic gonadectomy has been the preferred approach, there are no specific recommendations that address whether concurrent salpingectomy should be performed. With the consideration of pregnancy through assisted reproductive techniques (ART) in this population, the status of the tubes may be an important consideration.

We conducted a retrospective review of medical records to identify patients with TS with Y-chromosome derived material, and we describe the gonadectomy approach and histopathological findings in these patients. We also surveyed prevalent techniques and practice patterns of pediatric surgeons regarding performance of salpingectomy at the time of gonadectomy in these patients.

## 1. Materials and methods

Patients at Cincinnati Children's Hospital Medical Center (CCHMC) with a karyotype-confirmed diagnosis of TS were enrolled. These TS patients had been followed in the CCHMC Turner Syndrome Center clinic and had been prospectively enrolled in an Institutional Review Board (IRB) approved clinical database. Informed consent for data entry and review was obtained from subjects if ≥18 years of age or from parents/guardians for subjects <18 years, with assent obtained

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from the child. The TS database was queried in March 2011 to identify subjects with Y-chromosome material in their karyotype. Characteristics of the peripheral blood mononuclear cell karyotype, operative procedure summary, and histopathology reports for all subjects were abstracted retrospectively using additional hospital information systems and medical records. Turner syndrome mosaicism with Y-chromosome derived material was diagnosed based on a peripheral blood karyotype at the time of initial evaluation. Some of the patients had previously been evaluated at outside centers prior to a referral to CCHMC. The retrospective portion of the study was approved by the IRB and was compliant with the Health Insurance Portability and Accountability Act (HIPAA).

To assess prevalent surgical practice patterns, a link to an electronic Survey Monkey™ questionnaire was sent to all members of the International Pediatric Endosurgery Group (IPEG) in June of 2011. Survey questions assessed the surgeon's experience, preferred technique for gonadectomy, whether salpingectomy was concurrently done, and reasons for a specific procedure. The survey also asked surgeons' opinions on salpingectomy and on benefits and risks of the procedure in TS. (A copy of the survey is included in the supplemental material). Response to the survey indicated implied consent of the surgeons to participate in this survey data collection.

## 2. Results

### 2.1. Retrospective review of the TS database

Out of 158 subjects with TS in the database at the time of the query, 12 (8%) were identified as having Y-chromosome material in the peripheral blood karyotype. Mean age at diagnosis of TS in these 12 subjects was 6.6 years (y) (range: prenatal to 15). Mean age at gonadectomy was 7.3 y (range: 1.5–15). The details of the individual cases are noted in Table 1. The 45,X/46,XY karyotype was seen in 8/12 subjects, 3/12 had 45,X/46,X,isodicentric Y and one subject had 45,X/47,XYY. Two subjects (numbers 1 and 11 in Table 1) had a TS phenotype with ambiguous genitalia and had been classified as mixed gonadal dysgenesis. These two patients were included in this report because they still presented with characteristics that fit the clinical phenotype of TS and we chose to include all patients with a clinical presentation of TS in this report. Both underwent feminizing genitoplasty (at 16 and 18 months of age) and gonadectomy (at ages 1.5 y and 2.5 y). Neither of them had evidence of a tumor in the resected gonads. Four of the remaining 10 subjects had a gonadoblastoma on histopathology of the resected gonad (33%). A dysgerminoma and a teratoma were also identified in 2/4 of these subjects. All resected Fallopian tubes were examined carefully for tumors and none were found in our series. Three of 10 subjects had laparoscopic bilateral salpingo-oophorectomy, 2/10 had laparoscopic oophorectomy with Fallopian tube preservation, 2/10 subjects had oophorectomy by inguinal approach with Fallopian tube preservation and herniorrhaphy, and 2/10 had gonadectomy at an outside hospital with unknown Fallopian tube status. The remaining subject (operated at 15 y) had undergone two abdominal surgeries for a pelvic mass.

### 2.2. International pediatric endosurgery group survey

Fifty-four surgeons from 14 countries responded to the survey (10% response rate) with 96% preferring the laparoscopic approach. By self-report, 6/54 surgeons (11%) had operated on 5–10 cases of TS, 13/54 (24%) had operated on 3–5 cases, 18/54 (33%) had operated on 1–2 cases, 16 (29%) had not operated on a TS patient and were answering a hypothetical question and one surgeon did not respond to this question. There was no clear consensus among surgeons on whether salpingectomy should be done concurrent with gonadectomy. The majority of the respondents felt there was no indication for salpingectomy (33/54; 61%). When done, the reasons for performing a concurrent salpingectomy included: technical ease ($n = 6$), risk of devascularization of the fallopian tubes ($n = 4$), potential risk of malignancy in the fallopian tubes ($n = 7$) and risk of future ectopic pregnancy after ART ($n = 4$). Among the six more experienced surgeons (who had operated on 5–10 cases), three (50%) preferred salpingo-oophorectomy, while two (33%) favored leaving the Fallopian tubes behind, and one was undecided.

## 3. Discussion

The proportion of TS girls with Y-chromosome material in our series was 8%. This is consistent with the 5-12% previously reported [3,7,8]. A higher incidence of Y-chromosome material has been reported when polymerase chain reaction (PCR) and fluorescent in situ hybridization (FISH) techniques were used in addition to peripheral blood karyotyping [7,9]. Some have argued that false positives may be problematic with the use of oversensitive methods [10]. Others have suggested that the finding of gonadoblastoma in TS

**Table 1**
Description of individual TS girls with Y-chromosome material: genotype, surgical procedure and histopathology.

| N | Genotype | Age at surgery (years) | Histopathological findings (and phenotype) | Surgery |
|---|---|---|---|---|
| 1 | 45,X/46,XY | 1.5 | Ambiguous genitalia Dysgenetic gonads | Bilateral gonadectomy, inguinal hernia repair, and feminizing genitoplasty |
| 2 | 45,X/46,XY | 3.4 | Streak ovaries | Bilateral salpingo-oophorectomy |
| 3 | 45,X/46,XY | 11.25 | Bilateral gonadoblastoma with dysgerminoma on the left | Bilateral salpingo-oophorectomy |
| 4 | 45,X/46,XY | 1.5 | Dysgenetic ovaries with gonadoblastoma on the left | Inguinal approach gonadectomy and herniorrhaphy |
| 5 | 45,X/46,XY | 11.7 | Microscopic gonadoblastoma | Laparoscopic oophorectomy |
| 6 | 45,X/46,XY | 15 | Left ovary: grade 1 teratoma Right streak gonad: gonadoblastoma | Resection of pelvic mass followed by second surgery for bowel obstruction and right sided mass removal (outside hospital) |
| 7 | 45,X/46,XY | 1.25 | Not available | Gonadectomy (outside hospital) |
| 8 | 45,X/46,XY | 11.8 | Not available | Laparoscopy and oophorectomy (outside hospital) |
| 9 | 45,X/47,XYY | 2.9 | Bilateral streak ovaries in hernial sac | Inguinal approach gonadectomy and herniorrhaphy |
| 10 | 45,X/46,X,idicY* | 11.3 | Left ovo-testis, right ovary: both with cysts and with normal fallopian tubes | Bilateral salpingo-oophorectomy |
| 11 | 45,X/46,X,idicY* | 2.5 | Ambiguous genitalia Right dysplastic gonad, left streak gonad adherent to fallopian tube | Laparoscopic gonadectomy with dissection of gonad from tube, genital reconstruction |
| 12 | 45,X/46,X,idicY* | 13.5 | Bilateral streak ovaries with cysts | Laparoscopic oophorectomy and right inguinal herniorrhaphy |

* idicY: isodicentric Y.