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# Infertility | Treatment | Update™

## Prevalence of Occult Uterine Sarcomas After Laparoscopic Morcellation of Leiomyomas

power morcellators used to remove the fibroids in small fragments through the laparoscopy incision have raised concern about the potential risk for intraperitoneal dissemination of unsuspected uterine sarcoma (leiomyosarcoma). Thus, the U.S. Food and Drug Administration has issued a warning against using power morcellators to remove uterine fibroids.

Unexpected uterine sarcoma is rare, but the risk rises with age, from <1:500 for those aged <30 years to 1:100 for patients aged 75 to 79 years. Unfortunately, evidence in the literature about occult uterine sarcoma after laparoscopic morcellation of presumed benign fibromas in reproductive age is lacking. Pados et al from Aristotle University of Thessaloniki, Greece, reviewed records of 1216 women (mean age, 36.4 ± 5.21 years; 2582 apparently benign leiomyomas) who had undergone laparoscopic myomectomy performed by 1 gynecologist at 1 hospital from June 2003 through December 2015. Preoperatively, the women were free of any preinvasive or invasive cervical or uterine cancer.

**L**aparoscopic myomectomy is the gold standard surgical method to remove benign uterine fibroids, or leiomyomas, in symptomatic women who wish to preserve their fertility. However,

Specimen slides examined by a single experienced pathologist revealed the following:

- 0 leiomyosarcoma
- 6 atypical-bizarre leiomyomas
- 1 mitotically active leiomyoma
- 34 adenomyomas
- 45 leiomyomas with infarcts
- 81 cellular myomas
- 133 degenerated leiomyomas

No patient experienced complications associated with the morcellation procedure, and in no case was conversion to laparotomy required.

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Based on this retrospective study, laparoscopic power morcellation of apparently benign leiomyomas performed after a careful preoperative workup appears to be safe for women of reproductive age. With less pain and postoperative morbidity, along with a shorter hospital stay, the procedure has clear advantages over open myomectomy.

*Pados G, Tsolakidis D, Theodoulidis V, et al. Prevalence of occult leiomyosarcomas and atypical leiomyomas after laparoscopic morcellation of leiomyomas in reproductive-age women. Hum Reprod 2017;32:2036-2041.*

## Predictors of High Pregnancy Rates with Single-embryo Transfer

**B**ecause single-embryo transfer (SET) has reduced the multiple-birth rate (MBR) associated with transfer of multiple embryos, the American Society for

Reproductive Medicine and the Society for Assisted Reproductive Technology (SART) have recommended its use after in vitro fertilization (IVF). This advice has been inconsistently followed in the United States, perhaps because there have been no means to successfully estimate the likelihood of pregnancy and the concurrent risk of multiple gestation.

Using data compiled by the national SART Clinic Outcome Reporting System, Mersereau et al from the University of North Carolina analyzed factors associated with high live-birth rate (LBR) and low MBR after SET and after double-embryo transfer (DET). They defined a live birth as gestational duration of  $\geq 22$  weeks and a birth weight of  $\geq 300$  g, and a multiple birth as  $\geq 2$  live births from the same pregnancy.

The study population comprised 181,523 women (mean age,  $33.5 \pm 4.2$  years) undergoing a first cycle of IVF with autologous oocytes and fresh embryo transfer, and 27,033 women (mean age,  $41.4 \pm 5.3$  years) undergoing a first cycle of IVF with donor oocytes and fresh embryos. In the case of an unsuccessful first cycle, a second cycle using autologous fresh embryo transfer (37,658 women)

or autologous frozen–thawed cycle (35,446 women) was attempted.

For both autologous and donor fresh first cycles, the following LBR patterns emerged:

- LBRs were lower in cycles when no embryos were cryopreserved.
- Blastocyst embryo transfer resulted in higher LBRs than did transfer at the cleavage stage.
- While older maternal age was a factor in lowering the LBR for the autologous cycles, it was not a factor in the donor cycles.
- When SET was used, the chance of multiple birth was generally  $< 2\%$ , but if  $\geq 2$  embryos were transferred, the chance of multiple birth increased to  $> 49\%$ .

For the second fresh cycle, the same LBR patterns emerged, decreasing with maternal age.

- When  $\geq 1$  embryos were frozen, the LBR was 35% to 57% for blastocysts and was considered “quite high.”
- Transfer of 3 embryos did not increase the LBR significantly, and the MBR was similar to that seen with the transfer of 2 embryos.

## Conclusions and Clinical Implications

These data from a large national cohort of women undergoing IVF showed that younger maternal age, transfer of a blastocyst and having additional embryos cryopreserved were favorable prognostic factors for SET. Although the LBR was 10% to 15% lower than with DET, the MBR decreased from 49% with DET to 2% with SET when favorable prognostic factors were present. The authors viewed these findings as “an opportunity to increase the rate of SET across the United States and thereby reduce the MBR and its associated poor perinatal outcomes with [assisted reproductive technology] pregnancies.”

*Mersereau J, Stanhiser J, Coddington C, et al. Patient and cycle characteristics predicting high pregnancy rates with single-embryo transfer: an analysis of the Society for Assisted Reproductive Technology outcomes between 2004 and 2013. Fertil Steril 2017;108:750-756.*

**Table 1.** Conventional sperm quality parameters (mean  $\pm$  SEM) for fresh, slow frozen–thawed and vitrified–warmed groups

Parameter	Fresh	Slow frozen–thawed	Vitrified–warmed
Progressive motility (%)	47.67 $\pm$ 4.08	11.33 $\pm$ 2.70 <sup>a,b</sup>	18.17 $\pm$ 2.70 <sup>a,b</sup>
Immotility (%)	34.39 $\pm$ 4.06	72.89 $\pm$ 4.59 <sup>a,b</sup>	65.28 $\pm$ 4.53 <sup>a,b</sup>
Normal morphology (%)	28.10 $\pm$ 1.48	16.35 $\pm$ 1.77 <sup>a,b</sup>	22.24 $\pm$ 1.14 <sup>a,b</sup>
Head damage (%)	44.83 $\pm$ 3.05	53.03 $\pm$ 3.77	47.88 $\pm$ 2.87
Mid-piece damage (%)	15.82 $\pm$ 1.28	16.02 $\pm$ 2.00	17.92 $\pm$ 4.13
Cytoplasmic droplet (%)	3.12 $\pm$ 0.44	1.76 $\pm$ 0.38	3.49 $\pm$ 1.71
Tail damage (%)	25.98 $\pm$ 2.94	51.62 $\pm$ 3.38 <sup>a,b</sup>	36.88 $\pm$ 3.11 <sup>a,b</sup>
Vitality (%)	87.75 $\pm$ 1.66	55.13 $\pm$ 4.79 <sup>a,b</sup>	76.38 $\pm$ 1.53 <sup>a,b</sup>
TZI	1.24 $\pm$ 0.04	1.46 $\pm$ 0.05 <sup>a,b</sup>	1.33 $\pm$ 0.05 <sup>b</sup>

<sup>a</sup>Groups are significantly different from control ( $p < .05$ ). <sup>b</sup>Study groups are significantly different from each other ( $p < .05$ ). SEM, standard error of the mean; TZI, Teratozoospermia index, i.e., the number of abnormalities present per abnormal spermatozoon.

## Evaluating a New Method to Freeze Sperm

**S**low freezing, in which sperm are cooled progressively, is the most common technique currently

used for cryopreservation of sperm. Labor- and time-consuming, the procedure causes dramatic changes in sperm structure and function related to the addition and removal of cryoprotectants and the formation of ice crystals. One newly developed method to improve sperm cryopreservation is vitrification, which increases and decreases the temperature ultra-rapidly with or without nonpermeable cryoprotectants. Aizpurua et al from the University of Alicante, Spain, compared the effects of slow freezing with those of vitrification on sperm structure and function.

Normozoospermic samples obtained from 18 healthy men (age range, 31–40 years) seeking treatment at a fertility clinic revealed an average sperm count of  $83.44 \pm 13.73 \times 10^6 \text{ mL}^{-1}$  and an average volume of  $3.79 \pm 2.41 \text{ mL}$ . The sperm samples were divided into 3 groups of 200 spermatozoa per sample each: fresh (F), slow freezing–thawing (S) and vitrification–warming (V). Sperm count, motility, morphology and vitality were assessed immediately after liquefaction for the F samples and after thawing and warming for the S and V samples. The number and type of abnormalities were calculated and compared, along with

spontaneous acrosome reaction and DNA fragmentation; sperm cytoskeleton was evaluated by detecting patterns of the protein  $\alpha$ -tubulin.

Compared with F samples, both S and V sperm samples showed a significant decline in all conventional quality parameters. After vitrification, however, motility and vitality were reduced significantly less, with better preservation of morphology than after slow freezing. The number of abnormalities did not differ significantly between the F and V samples but was significantly higher in the S samples (Table 1). Compared with slow freezing, vitrification also preserved acrosomes better and had lower levels of DNA fragmentation, while showing a distribution pattern of  $\alpha$ -tubulin similar to that of the F sperm samples. Sperm samples showed a significantly different frequency of  $\alpha$ -tubulin patterns.

## Conclusions and Clinical Implications

In all parameters, this study found vitrification to be superior to slow freezing of sperm. The authors concluded that vitrification is “an efficient and reliable alternative to conventional freezing methods.” However, because the study involved only normozoospermic samples, studies using pathological samples are needed to evaluate the application of this method to clinical outcomes.

Aizpurua J, Medrano L, Enciso M, et al. New permeable cryoprotectant-free vitrification method for native human sperm. *Hum Reprod* 2017; 32:2007–2015.

## Pain Cognition And Quality Of Life with Endometriosis

**C**hronic endometriosis pain can substantially affect a woman's life. Because psychological factors have been shown to

play an important role in the experience of pain, van Aken et al from Radboud University Medical Centre, the Netherlands, explored the influence of pain cognition on the health-related quality of life (HRQoL) in women with chronic endometriosis. This includes pain catastrophizing and anxiety, constant vigilance for pain sensations, and exaggerated feelings of helplessness and pessimism, all of which can negatively affect therapy.

All of the 92 participants (50 women with confirmed endometriosis, 42 controls; age range, 18–49 years) used hormone treatment or hormone contraception, ruling out the influence of hormone cycles. The women completed 5 questionnaires: the standardized Short Form Health Survey (SF-36), version 2.0, to measure general HRQoL; the Endometriosis Health Profile 30 (EHP-30) to measure disease-specific quality of life; the Pain Catastrophizing Scale (PCS); the Pain Vigilance and Awareness Questionnaire (PVAQ); and the Pain Anxiety Symptoms Scale (PASS). The endometriosis group was also asked to indicate the severity of pain during the past month, ranging from 0 (no pain) to 10 (unbearable pain), using the verbal Numerical Rating Scale, the most commonly used subjective measure to score pain intensity.

Forty-eight endometriosis patients and 35 controls returned the questionnaires. Responses on the SF-36 showed a statistically significant reduction in HRQoL for the endometriosis group compared with the control group in 8 of 9 domains, as well as in the total score. Only the "health change" domain was not significantly different between the 2 groups. On the disease-specific EHP-30 questionnaire, the endometriosis group had higher scores than did the control group, corresponding to a lower quality of life.

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All 3 pain cognition questionnaires showed a statistically significant difference between the 2 groups, corresponding with a more negative pain cognition in women with endometriosis (Table 2). Despite the fact that 74% of the patients were classified as having moderate-to-severe endometriosis according to the American Society for Reproductive Medicine's revised classification, fewer than half reported a pain intensity score of  $\geq 4$ .

### Conclusions and Clinical Implications

Pain cognition was independently associated with the HRQoL of women with endometriosis. The authors urged clinicians to consider these psychological aspects and treat pain symptoms in a multidimensional, individualized way.

van Aken MAW, Oosterman JM, van Rijn CM, et al. Pain cognition versus pain intensity in patients with endometriosis: toward personalized treatment. *Fertil Steril* 2017;108:679-686.

**Table 2.** Results of questionnaires

Questionnaire	Patients (n = 48)	Controls (n = 35)	p value
<b>Quality of life</b>			
SF-36	521.31 ± 174.85	743.11 ± 103.50	<.001 <sup>a</sup>
EHP-30	189.41 ± 102.52	57.85 ± 65.55	<.001 <sup>a</sup>
<b>Pain cognition</b>			
PCS	16.88 ± 10.40	7.26 ± 6.32	<.001 <sup>a</sup>
PVAQ	35.73 ± 14.32	24.94 ± 12.21	.001 <sup>a</sup>
PASS	31.00 ± 17.98	14.74 ± 11.15	<.001 <sup>b</sup>

Data presented as mean ± standard deviation. SF-36 and EHP-30 represent total score.

<sup>a</sup>Independent samples t-test. <sup>b</sup>Mann-Whitney U test.