

# Autotransplantation of fragmented ovarian cortical tissue: a laparoscopic demonstration

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**Objective:** To describe and demonstrate a simple and secure procedure for laparoscopic autotransplantation of fragmented ovarian cortical tissue in women with diminished ovarian reserve as part of in vitro activation (IVA) of ovarian follicles.

**Design:** Step-by-step video explanation of the surgical procedure with still pictures and surgical video clips to demonstrate the detailed technique.

**Setting:** Fertility clinic and obstetrics and gynecology department at a university hospital.

**Patient(s):** Women with idiopathic diminished ovarian reserve and indication for in vitro fertilization (IVF), aged 25 to 39 years with an antral follicle count bilaterally of  $\leq 5$ , antimüllerian hormone level of  $\leq 5$  pmol/L, and two ovaries.

**Intervention(s):** The laparoscopic autotransplantation consists of six steps: [1] obtaining ovarian cortical biopsy samples, [2] preparing the peritoneal pocket, [3] fragmenting the ovarian cortical tissue into pieces of approximately 1 mm<sup>3</sup>, [4] installing the tissue fragments into a catheter, [5] transplanting the tissue fragments into the peritoneal pocket, and [6] closing the peritoneal pocket with a surgical clip. After the procedure, the patients are evaluated with blood samples and ultrasound scans followed by controlled ovarian stimulation. Ethics committee approval was obtained.

**Main Outcome Measure(s):** Feasibility of a six-step laparoscopic autotransplantation procedure using fragmented ovarian cortical tissue.

**Result(s):** A simple, fast laparoscopic procedure for taking biopsy samples and autotransplanting cortical tissue fragments in an all-in-one procedure ensures the rapid handling and correct placement of the small tissue fragments. The procedure is performed in an outpatient setting with an operation time of 1 hour. We have performed this procedure on 20 patients with no complications.

**Conclusion(s):** In vitro activation is a new, developing option for women in fertility treatment who have diminished ovarian reserve. Fragmentation of murine ovarian tissue has shown to suppress the Hippo pathway, thereby initiating proliferation and growth. This surgical procedure resembles that used when transplanting pieces of frozen-thawed ovarian tissue for fertility restoration, but the fragmented ovarian tissue is only 1 mm<sup>3</sup>, which makes it difficult to transplant. Until now no surgical procedures for transplanting small IVA fragments of cortical tissue has been published. With this video we report in detail a simple way of autotransplanting small fragments of IVA cortical tissue using what is already accessible in the operating theater. Among the many advantages of this procedure are its short duration (1 hour) and outpatient setting, which enable fast recovery and minimal postoperative pain. The procedure also allows fast handling and minimal manipulation of the tissue (limited to the fragmentation). The effect of autotransplantation of fragmented tissue in women with diminished ovarian reserve is currently being studied in ongoing trials. If the technique is combined with chemical IVA, a better outcome may be seen. (Fertil Steril® 2018;110:1181–3. ©2018 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

**Key Words:** Autotransplantation, diminished ovarian reserve, in vitro activation, laparoscopy, premature ovarian failure

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## **Autotrasplante de tejido cortical ovárico fragmentado: una demostración laparoscópica**

**Objetivo:** Describir y demostrar un procedimiento sencillo y seguro para el autotrasplante de tejido cortical ovárico fragmentado en mujeres con reserva ovárica disminuida como parte de una activación in vitro (IVA) de folículos ováricos.

**Diseño:** Explicación paso a paso del procedimiento quirúrgico por medio de video, con imágenes fijas y fragmentos de videos para demostrar la técnica detalladamente.

**Escenario:** Clínica de fertilidad y el departamento de obstetricia y ginecología de un hospital universitario.

**Pacientes:** Mujeres con reserva ovárica disminuida e indicación de fertilización in vitro (IVF), dentro de un rango de edad de 25 – 39 años con un conteo bilateral de folículos antrales  $\leq 5$ , nivel de hormona antimülleriana  $\leq 5$  pmol/L y dos ovarios.

**Intervenciones:** El autotrasplante laparoscópico consiste de seis pasos: [1] obtener muestras de biopsia cortical ovárica, [2] preparar la bolsa peritoneal, [3] fragmentar el tejido ovárico cortical en pedazos de aproximadamente  $1\text{mm}^3$ , [4] instalar los fragmentos de tejido dentro de un catéter, [5] trasplantar los fragmentos de tejido dentro de la bolsa peritoneal, y [6] cerrar la bolsa peritoneal con una grapa quirúrgica. Después del procedimiento, las pacientes son evaluadas con la toma de muestras de sangre y ultrasonido seguido por una estimulación ovárica controlada. Se obtuvo la aprobación del comité de ética.

**Medida de resultados principales:** La factibilidad de un procedimiento laparoscópico de seis pasos utilizando fragmentos de tejido cortical ovárico.

**Resultados:** Un procedimiento laparoscópico simple y rápido para la toma de muestras de biopsia y autotrasplante de fragmentos de tejido cortical todo en uno asegura el rápido manejo y la correcta colocación de los pequeños fragmentos de tejido. El procedimiento se realiza de manera ambulatoria con un tiempo de operación de 1 hora. Hemos realizado este procedimiento en 20 pacientes sin complicaciones.

**Conclusiones:** La activación in vitro es una nueva opción de desarrollo para mujeres sometidas a tratamientos de fertilidad con reserva ovárica disminuida. La fragmentación de tejido ovárico de ratones ha demostrado poder suprimir el camino del hipopótamo, de este modo iniciando la proliferación y el crecimiento. Este procedimiento quirúrgico se parece al utilizado cuando se trasplantan pedazos de tejido ovárico congelado-descongelado para la restauración de la fertilidad, pero el tejido ovárico fragmentado es de solo  $1\text{ mm}^3$ , lo cual lo hace difícil al momento de trasplantar. Hasta ahora ningún procedimiento no quirúrgico para el trasplante de pequeños fragmentos de tejido cortical IVA ha sido publicado. Con este video reportamos en detalle una forma sencilla de autotrasplantar pequeños fragmentos de tejido cortical IVA utilizando lo que ya se encuentra accesible en el quirófano. Entre las muchas ventajas de este procedimiento están, su corta duración (1 hora) y el modo ambulatorio, lo cual permite una rápida recuperación y dolores post-operatorios mínimos. El procedimiento también permite un rápido manejo y mínima manipulación del tejido (limitado a la fragmentación). El efecto del autotrasplante de tejido fragmentado en mujeres con reserva ovárica disminuida se está estudiando en investigaciones en curso. Si la técnica se combina con IVA químico, se podría obtener un mejor resultado.