The effect of laparoscopic ovarian cystectomy of endometrioma versus cyst deroofing on ovarian reserve as determined by Anti-mullerian hormone and antral follicle count: a prospective randomized study

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Contents

List of figures

List of tables

List of Abbreviations

AFC: Antral follicle count

AFCs: Antral follicle counts

ALK2, 3, 6: Activin receptor-like kinase (2, 3, 6)

AMH: Antimüllerian hormone

AMHKO: Antimüllerian knockout

ART: Assisted reproductive technique

BMP: Bone morphogenetic proteins

TMB: Tetramethylbenzidine

CA-125: Carcino emberyonic antigen 125

CCCT: Clomiphene citrate challange test

CV: Coefficients of variation

DF: Degrees of freedom

E2: Estradiol

EFFORT: Exogenous FSH Ovarian Reserve Test

ELISA: Enzyme Linked Immunosorbent Assay

FHA: Functional hypothalamic amenorrhea

FOR: Functional ovarian reserve

FSH: Follicle stimulating hormone

GAS: Gonadotrophins agonist stimulation test

GC: Granulosa cells

GFs: Growing follicles

GnRH : Gonadotropin releasing hormone

Het: Heterozygous

Hom: Homozygous

HRP: Horseradish peroxidase

INH (A): Inhibin (A)

INH (B): Inhibin (B)

IVF: In vitro fertilization

kDa: Kilodalton

LH: Luteinizing hormone

MIF: Mullerian inhibitory factor

MIS: Mullerian inhibitory substance

MRI: Magnetic resonance imaging

NGF: Non-growing follicle

NGFs: Non-growing follicles

Norm: Normal

OD: Optical Density

OHSS: Ovarian hyperstimulation syndrome

OR: Ovarian reserve

PCOS: Polycystic ovary syndrome

POF: Premature ovarian failure

R^2: Correlation coefficient

rFSH: Recombinant FSH

rp: Round per minute

rAFS: Revised American Fertility Society

SSE: Sums or Squares Error

TAFC: Total antral follicle count

TGF-ß: Transforming Growth Factor beta

TOR: Total ovarian reserve

TVS: Transvaginal ultrasound

Introduction

Endometriosis is defined as the presence of endometrial glands and stroma at extra-uterine sites. These ectopic endometrial implants are usually located in the pelvis, but can occur nearly anywhere in the body. Endometriosis is a common, benign, chronic, estrogen-dependent disorder. It can be associated with many distressing and debilitating symptoms, such as pelvic pain, severe dysmenorrhea, dyspareunia and infertility, or it may be asymptomatic, and incidentally discovered at laparoscopy or exploratory surgery ***(Schenken RS et al., 2010).***

Endometriosis is found to be 7%–10%, but among infertile women it increases up to 50% ***(Streuli et al., 2012).***

Endometrioma is found to be in 17%–44% of patients with endometriosis ***(Celik et al., 2012).*** Represents 35% of benign ovarian cysts requiring surgery ***(Busacca et al., 2009).***

One of the major concerns about excision of endometriomas is their negative effect on ovarian reserve because of follicle loss, removal of endometriomas has been associated with poorer performance in IVF procedures, and decreased ovarian volumes have also been reported after surgery ***(Celik et al., 2012).***

The term "ovarian reserve" is used to define the quality and quantity of primordial ovarian follicles inside a woman at a given chronological age, which is an indirect measure of her reproductive age ***(Gupta et al., 2009).***

Total ovarian reserve mostly consists of NGFs (largely primordial follicles) and to a lesser degree of maturing growing follicles (GFs) after recruitment. But only the latter reflect the so-called functional OR (FOR) ***(Gleicher et al., 2011).***

AMH belongs to the transforming growth factor- β family, and is produced by the granulosa cells of primary to small antral follicles cells to

prevent depletion of the primordial follicle pool; recently it has been shown that the serum AMH levels may be a valuable marker of the ovarian reserve. AMH is the only marker of ovarian reserve, which is menstrual cycle-independent and is unaffected by the use of oral contraceptive pills or gonadotrophin-releasing hormone agonist. Therefore, the serum AMH levels currently represent the most reliable and easily measurable maker of ovarian reserve ***(Kwee et al., 2008).***

Not surprisingly, several independent researchers have used serum AMH concentration also to investigate the effects of surgical excision of ovarian endometriomas, in recent years, the detrimental impact of the removal of these pseudo cysts has stimulated the interest of the scientific community, in women who had ovarian endometriomas excised, responsiveness to hyper stimulation is reduced ***(Somigliana et al., 2011)*** and menopausal transition occurs earlier ***(Coccia et al., 2011),*** some cases of post-surgical ovarian failure have been documented in women operated on for

bilateral endometriomas ***(Somigliana et al., 2012).***

The total AFC (defined as the total number of antral follicles, sized 2-5 or 2-10mm, present in both ovaries) more than half of the antral follicles detected by TVS in young women could be in early or late stages of atresia. Unfortunately, the quality status (growing or atretic) of follicles cannot be assessed using its ultrasound appearance. With female aging, the decline in primordial follicle numbers parallels the decrease in size of the FSH-sensitive antral follicle cohort ***(Broekmans et al., 2009)***. There is no significant differences between right sided and left sided AFC within the same individual ***(Hendriks et al., 2005).***

It was found a good prediction tool for IVF response (poor and hyper) and even superior or at least equivalent to ovarian volume measurements and endocrine challenge tests ***(Kwee et al., 2007).***

Traditionally, endometrioma was removed by the laparotomy approach, with advances in

laparoscopic technique; most endometrioma can be treated by laparoscopy. In recent years, laparoscopy has become the gold standard for the treatment of ovarian endometriotic cysts. When compared to laparotomy, operative laparoscopy is associated with shorter hospital stay, faster patient recovery, decreased costs and lower incidence of de novo adhesion formation ***(Al-Shahrani et al., 2006).***

Aim of the work

Is to evaluate the impact of laparoscopic ovarian cystectomy versus laparoscopic cyst deroofing on ovarian reserve measured by serum levels of anti mullerian hormone and antral follicle count in patients with endometriomas.