

LAPAROSCOPIC OOPHOROPEXY FOR OVARIAN FUNCTION RESERVATION IN CANCER PATIENT

Dr. Ragaa Mohomed Hussien

Consultant OB/GY,MSD JUBAIL KANB ,KSA

ABGO ,DGO ,DMAS

Member of Saudi OB/GYN Association

Member of Sudan OB/GYN Association

Member of WALS

Project submitted towards completion of Diploma in Minimal Access surgery at Laparoscopy Hospital New Delhi , India , July 2008

ABSTRACT

Minimally invasive technique for ovarian transposition (oophoropexy) can offered to any age premenopausal women with Hodgkins disease ,brain tumors ,cervical ,vaginal ,and others whose under going total Lymph Node Irradiation (TNI) deliver as a dose of 200-400 Centigray (CGY) It is safe and effective procedure for ovarian function preservation with pregnancy rate of nearly 90% .If minimal or no Chemotharpy used .

KEYWORD

Minimally Invasive Surgery (MIS). Laparoscopy Oophoropexy .Hodkins Disease Total Lymph Node Irraditation (TNI) .Premature Ovarian Failure (POF). Fertility Preservation

AIMS

The aims of this review is to evaluate is effectiveness and safety of Laparoscopy Oophoropexy in Fertility preservation. The following parameters where evaluated .ovarian function .pregnancy rate .Premature Ovarian Failure (POF) and discuss limitations of others fertility preservation methods .

MATERIAL AND METHODS

A literature search was performed ,using midline and search engine Google ,the following search terms where used "Laparoscopic Oophoropexy In cancer" .Fertility preservation in cancer, 300 citation, found in total. Selected papers were screened for further references . Criteria for selection of literature were number of cases (excluded if less than 15),methods of analysis (statistical or nonstatistical) operative procedure (only accepted procedure were selected and institution where the study was done (specialized institution for good Laparoscopy Surgery).

Introduction

The female reproductive axis inherently different than males in ways that women is born with all the oocytes she will ever have and fertilization and subsequent development of the fetus occur within the female reproductive tract.

Minimal access surgery has been proved to be a useful surgical technique .New standards have been established for various indications, patients comforts is a greater consideration in 21 st century .The acquisition of recent technology and skill now a allords a better choice of mode of surgery .this documents reviews the recent advances in technique applicable to Laparoscopy Oophoropexy, examines a literatures, and suggest guidelines for Oophoropexy in patients with cancer.

Contents

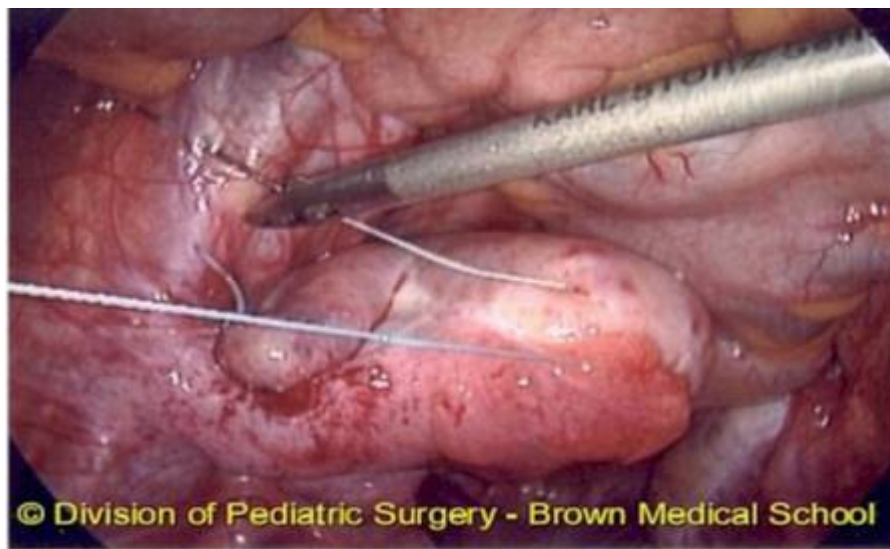
Evaluation of Laparoscopic Oophoropexy

Laparoscopic Oophoropexy is being done at the time when; Laparoscopy surgery has shown definite benefit over open technique which is done only when open surgery is indicated for staging of the cancer or when chemotherapy is used .

Laparoscopy Oophoropexy is now a gold stander for younger girl and premenopausal women who is going for total Lymphnode Irradiation (TNI) and has virtually nearly replace open Oophoropexy .still numerous factors need to be in the deciding the ideal and most appropriate surgical technique .

It is important the patients care physician should understand the available methods to preserve fertility in cancer patients and communicate this information to the patients.

In paediatric Minimal Access Surgery (MAS) has lagged behind because fertility may be the last thing on most physician mind when they are facing a younger girl who has just been diagnosed with cancer but now is rapidly expanding since a grater number of young patient who survive and living healthy wants to conceive later and this become an important issue .



Effect of a irradiation on ovarian follicle

The ovarian follicle are remarkably vulnerable to damage form ionizing radiation which results in ovarian atrophy and reduced follicle stores . on cellular level oocytes show rapid onset of pyknosis ,chromosomal condensation ,disruption of nuclear envelope and cytoplasmic vaculation .

Serum FSH and LH rise within 4-8 weeks after exposer .

Degree of damage and suppression of ovarian function is related to the patient age and the dose of irradiation delivered to the ovaries .

Schiman et al found that a younger age at transplantation predicted return to ovarian function and this is confirmed in number of studies.

Irradiation has invariably results in premature ovarian failure (POF) unless the ovaries transplanted out of the field.

Many studies indicated that the cut off for radiation- induced ovarian failure is around 300 cetergray (CGY) 11%-13% of patients have ovarian failure if exposed to radiation below 300 CGY versus 60%-63% if above that value .

The table below show effect of radiation dose and age on ovarian function

Ovarian dose in CGY	result
60	No deleterious effect
150	No deleterious in young women. some risk for sterilization in women older than 40
250-500	In women 15-40 60%perminently sterilized .reminder may suffer amenorrhea ,in women older than 40 permanently sterilized
500-800	In women age 15-40 ,60%-70% permanently sterilized .reminder may experience temporary amenorrhea. No data available for women over 40.
>800	100% permanently sterilized

Laparoscopic oophoropexy and chemotherapy

Prepubertal girls seems less susceptible than young women to cytotoxic drugs .depending on the type of chemotherapy used some alkylating agent such as cyclophosphmide is permanently damage the gonad and others like 5-flurouracil -etopside-doxorubician do not induce permanent ovarian failure and if this later agent used with irradiation to cancer patient Oophoropexy can be done with it .

Consideration in operative technique

The procedure should be simple -safe -minimal invasive

- can be offered to any age premenopausal women .
- ample blood supply to the recipient site
- feasible access for follicle aspiration
- performed in patient just prior to undergoing radiation therapy

when the ovaries are transpositioned out of the field of irradiation the ovarian dose is reduced to approximately 5%-10% of that in untransposed ovaries which receive 100 % radiation dose .

to improve the quality of life and preserve fertility in these young women ovarian function has been maintain for over three decades by transposing the ovaries out of the field of irradiation

Site of Oophoropexy -Pregnancy Rate -Fetal Outcome

In lateral ovarian transposition .the ovary is mobilized with its blood vessels to the paracolic gutters.

Bidzinski{ 13} confirmed that ovarian function was preserved if the ovaries were transposed at least 3cm from upper border of the field or above the iliac crest with care to ovarian vessels from injury .when vaginal and cervical cancer are treated with brachytherapy laparoscopic Oophoropexy can be performed under the same anesthesia .interestingly in his study 89% of pregnancy spontaneous 75% occurring without ovarian repositioning (repositioning only in case of infertility)11% of those patient conceived with IVF(22)

Tulandi [32] reported cases of laparoscopic lateral ovarian transposition in patient with rectal Adeno-carcinomas he divide the utero -ovarian ligament but the ovaries remained attached to the distal fallopian tube to improve the chance for ovarian pickup and the patients achieved spontaneous pregnancies (24)

Covens [13] and **Swerd** [23] confirmed that there were no excess cases of still birth ,low birth ,congenital malformation ,abnormal karyotype or cancer in offspring of women Treated with laparoscopic Oophoropexy .

Some consideration during the procedure

- Ovarian failure may result after Laparoscopic Oophoropexy
- If the ovaries are not moved far enough out of irradiation field
- Compromise ovarian vessels from surgical technique or radiation injury to the vascular pedicle.
- Development of symptomatic ovarian Cyst

It is more common with open Oophoropexy than Laparoscopic (4.9%-7.6%) versus (1%-5.2%) and to avoid its occurrence Laparoscopic Oophoropexy should be done just before the start of irradiation

- If conception occur less than a year after radiation exposure patient has an increase in low birth weight and spontaneous abortion and advice is to delay pregnancy a year after radiation exposure.

Other ovarian preserving function

These include cryopreservation of oocytes, embryo and ovarian tissue

Some of these techniques like cryopreservation of oocytes have significant increase in ovarian preserving function and success report with recent introduction of technical modification but still many cryo damage occur.

In the other like cryopreservation of pre implantation of human Embryo and ovarian tissue cryopreservation and transplantation are still experimental procedure and study effect of cryopreservation insult on ovarian tissue have been limited .

Newton et al demonstrated that human ovarian tissue loose 90% of primordial follicle when using glycerol as cryo protectants(CPA) compare with 25%-15% and 55% using DMSO, Ethanol Glycol(EG) and Propylene Glycol(PG) respectively.

Conclusion

Laparoscopic Oophoropexy that is done immediately before pelvic irradiation is safe and very effective in preserving ovarian function in nearly all patients with Hodkins disease some gynecological cancer and others who are to under go total lymphatic irradiation and receive minimal or no chemotherapy compared with high risk of ovarian dysfunction seen in girl who did not under go Oophoropexy.

References

1. Blumenfeld Z., Avivi I., Linn S., et al. Prevention of irreversible chemotherapy-induced ovarian damage in young women with lymphoma by a gonadotrophin-releasing hormone agonist in parallel to chemotherapy. *Hum. Reprod.* 1996; 11:1620-6.
2. Blumenfeld Z., Haim N. Prevention of gonadal damage during cytotoxic therapy. *Ann. Mod.* 1997; 29:199-206.
3. Blumenfeld Z., Dann L., Avivi I., et al. Fertility after treatment for Hodgkin's disease. *Ann. Oncol.* 2002; 13:138-47.
4. Familiari G., Caggiati A., Nottola S., et al. Ultrastructure of human ovarian primordial follicles after combination chemo-therapy for Hodgkin's disease. *Hum. Reprod.* 1993; 8: 2080-7.
5. Meirow D., Schenker J., Rosier A. Ovarian hyperstimulation syndrome with low oestradiol in nonclassical 17 alpha-hydroxylase. 17,20-lvase deficiency: what is the role of oestrogens? *Hum. Reprod.* 1996; 11: 2119-21.
6. Damewood MD and Grochow LB Prospects for fertility after chemotherapy or radiation for neoplastic disease. *Fertil. Steril.* 1986; 45:443-59.
7. Meirow D., Nugent D. The effects of radiotherapy and chemotehrpay on female reproduction. *Hum. Reprod. Update.* 2001; 7: 533-43.
8. Clough K., Goffinet F., Labib A., et al. Laparoscopic unilateral ovarian transposition prior to irradiation: prospective study of 20 cases. *Cancer.* 1996; 77: 2638-45.

9. Gaetini A., De Simone M., Urgesi A., et al. Lateral high abdominal ovariopexy: an original surgical technique for protection of the ovaries during curative radiotherapy for Hodgkin's disease. *J. Surg. Oncol.* 1988; 39:22-8.
10. Williams R., Littell R., Mendenhall N. Laparoscopic oophoropexy and ovarian function in the treatment of Hodgkin's disease. *Cancer.* 1999; 86:2138-42.
11. Howell S., Shalet S. Fertility preservation and management of gonadal failure associated with lymphoma therapy. *Curr. Oncol. Rep.* 2002; 4:443- 52.
12. Howell S., Shalet S. Gonadal damage from chemotherapy and radiotherapy. *Endocrinol. Metab. Clin. N. Am.* 1998; 27:927-3.
13. Covens A., Van der Putten H., Fyles A., et al. Laparoscopic ovarian transposition. *Eur. J. Gynaecol. Oncol.* 1996; 17:177-82.
14. Belinson J., Doherty M., McDay J. A new Fenig E., MIshaeli M., Kalish Y., et al. Pregnancy and radiation. *Cancer. Treat. Rev.* 2001; 1:27-7.
15. Fujiwara K., Mohri H., Yoshida T., et al. Subcutaneous transposition of the ovary following hysterectomy. *Int J. Gynaecol. Obstet.* 1997; 58:223-8.
16. Todorow S., Siebzehnruhl E., Spitzer M., et al. Comparative results on survival of human and animal eggs using different cryoprotectants and freeze-thawing regimens. II. Human. *Hum. Reprod.* 1989; 4:812-6.
17. Porcu E. Freezing of oocytes. *Curr. Opin. Obstet. Gynecol.* 1999; 11:297-300.
18. Oktay K., Nugent D., Newton H., et al. Isolation and characterization of primordial follicles from fresh and cryopreserved human ovarian tissue. *Fertil. Steril.* 1997; 67:4816.
19. Oktay K., Karlikaya G., Aydin B. Ovarian cryopreservation and transplantation: basic aspects. *Mol. Cell. Endocrinol.* 2000; 169:105-8.
20. Assisted reproductive technology in the United States 1998 results generated from the American Society for Reproductive Medicine/Society for Assisted Reproductive Technology Registry. *Fertil. Steril.* 2002; 77:18-31.
21. Oktay K., Buyuk E., Davis O., et al. Fertility preservation in breast cancer patients: IVF and embryo cryopreservation after ovarian stimulation with tamoxifen. *Hum. Reprod.* 2003;18: 90-5.
22. Paynter S., Cooper A., Fuller B., et al. Cryopreservation of bovine ovarian tissue: structural normality of follicles after thawing and culture in vitro. *Cryobiology.* 1999; 38:301-9.
23. technique for ovarian transposition. *Surg. Gynecol. Obstet.* 1984; 159:157-60.

24. Bidzinski M., Lemieszczuk B., Zielinski J. Evaluation of the hormonal function and features of the ultrasound picture of transposed ovary-in cervical cancer patients after surgery and pelvic irradiation. *Eur. J. Gynaecol. Oncol.* 1993; 14:77- 80.
25. Feeney D., Moore D., Look K., et al. The fate of the ovaries after radical hysterectomy and ovarian transposition. *Gynecol. Oncol.* 1995; 56:3-7.
26. Chambers S., Chambers J., Holm C., et al. Sequelae of lateral ovarian transposition in unirradiated cervical cancer patients. *Gynecol. Oncol.* 1990; 39:155-9.
27. Bashist B., Friedman W., Killackey M. Surgical transposition of the ovary: radiologic appearance. *Radiology.* 1989; 173:857-60.
28. Kier R., Chambers S. Surgical transposition of (he ovaries: imaging findings in 14 patients. *AJR Am J Roentgenol.* 1989; 153:1003-6.
29. Treissman M., Miller D., McComb P. Laparoscopic lateral ovarian transposition. *Fertil. Steril.* 1996; 65:1229-31.
30. Yarali H., Demiroglu A., Bukulmez O., et al. Laparoscopic high lateral transposition of both ovaries before pelvic irradiation. *J. Am. Assoc. Gynecol. Laparosc.* 2000; 7:237-9.
31. Morice P., Thiam-Ba R., Castaigne D., et al. Fertility results after ovarian transposition for pelvic malignancies treated by external irradiation or brachytherapy. *Hum. Reprod.* 1998; 13:660-3.
32. Tulandi T., Al-Touk S. Laparoscopic ovarian suspension before irradiation. *Fertil. Steril.* 1998; 70:381-3.
33. Bisharah M., Tulandi T. Laparoscopic preservation of ovarian function: an underused procedure. *Am. J. Obstet. Gynecol.* 2003; 188:367-70.
34. Swerdlow A., Jacobs P., Marks A., et al. Fertility, reproductive outcomes, and health of offspring, of patients treated for Hodgkin's disease: an investigation including chromo-some examinations. *Br. J. Cancer.* 1996; 74:291-6.

For more information please log on to <http://www.laparoscopyhospital.com>