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# Laparoscopic Approach to Ovarian Cysts in Women over 40 Years of Age

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For many years, the traditional treatment of ovarian cysts has been laparotomy. This approach is characterized, however, by elevated morbidity given that the majority of these cysts are very often benign. The main problem regarding the laparoscopic approach to the ovarian cyst is the risk of treating an ovarian cancer. As a consequence, there can be a worsening of prognosis, due to spillage at the time of laparoscopic surgery.

According to the literature, the incidence of ovarian carcinoma among patients who have undergone operative laparoscopy for adnexal masses varies from 0.1% to 4.2%.<sup>1-8</sup> Canis *et al.*<sup>6</sup> reported 19 cases of ovarian tumors out of 819 adnexal masses in 757 patients. The 19 ovarian tumors (2.32%) were classified as ( $n = 7$ ) ovarian carcinomas and low malignant potential tumors ( $n = 12$ ). If we consider the incidence of these tumors in relation to age, 1.8% were found in women under 50 and 7.6% were found in women over 50 years of age.

In a retrospective study, Maiman *et al.*<sup>2</sup> reported a total of 42 cases of malignancy after laparoscopic treatment of ovarian masses. However, only 12% of the physicians interviewed had used tumor markers, and only 40% had requested an intraoperative frozen section. Moreover, four of the most accepted benign characteristics of cysts, that is, diameter less than 8 cm, cystic neoplasm, unilaterality, and unilocularity, were present in 31% of the cases.

Some retrospective studies<sup>9-13</sup> on the problem of spillage have reported that surgical rupture of the capsule in stage I epithelial ovarian cancer has an adverse influence on survival prognosis. However, other retrospective studies have reported that surgical rupture of a malignant cyst is not a negative prognostic factor, at multivariate analysis. In fact, some authors affirm that prognosis is not influenced at all if the patient is immediately treated.<sup>14-16</sup>

We would like to stress that the majority of ovarian cysts (87%) are benign<sup>17</sup> and are therefore eligible for endoscopic treatment. Following strict guidelines (echographic criteria of benignity: unilaterality, unilocularity, absence of septa > 3 mm and intracystic vegetation, and pure borders; CA 125 levels < 35 IU/ml; benign laparoscopic appearance of cyst and the peritoneal cavity) and using cautious management, laparoscopic treatment of ovarian cysts can be reliable and safe.

On the other hand, Canis *et al.*<sup>6</sup> reported on two malignant tumors that had been macroscopically suspicious and were treated as benign masses. The false negative diagnoses (1.5%) were due to inadequate sampling. Thus, Canis suggested that the

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complete cyst, and not only a fragment or small bioptic sample, be submitted for intraoperative histologic examination. Chapron *et al.*<sup>18</sup> treated 26 patients with suspected signs of ovarian malignancy using laparoscopic adnexectomy with an endoscopic bag. The results of the intraoperative histological examination for all these patients were benign. The definitive histological results confirmed the frozen section findings. Using the same strategy, we have been able to avoid laparotomy, especially in postmenopausal patients, who, at ultrasound, present with complex adnexal masses. Laparotomy should not be considered a complication when managing suspicious adnexal masses. Immediate vertical laparotomy remains the gold standard for macroscopically suspicious masses. Although this approach is acceptable in postmenopausal patients,<sup>6</sup> laparoscopic adnexectomy of suspicious masses at ultrasound is not acceptable in young patients. The false positive rate of diagnosis of malignancy at ultrasound is still very high.

One pressing question must be asked: Can we distinguish a benign tumor from a malignant one? Appropriate patient selection for laparoscopic ovarian surgery requires information on the characteristics of the cyst. This can be obtained by ultrasound examination. One of the most important advances in gynecological ultrasound diagnosis has been the introduction of transvaginal sonography, which gives a good image of the pelvic organs given the closeness of the ultrasound transducer to the genital organs.

The protocol at our department for the diagnosis and management of ovarian persistent cysts is based on a multimodal approach using clinical examination, case history, transabdominal and transvaginal ultrasonography, transvaginal color Doppler, and serum values of CA125 and other markers (CA19.9, CA15.3, CA72.4, CEA,  $\alpha$ FP,  $\beta$ hCG).

The echographic criteria for distinguishing benign cysts are the following: unilateral mass, unilocular cyst, absence of both septa  $> 3$  mm and intracystic vegetations, and pure borders.<sup>19,20</sup> However, using Sassone's score, which considers 9 as the cut-off point used to distinguish malignant from nonmalignant cysts,<sup>21</sup> several complex benign cysts, such as dermoid cysts, could be considered malignant.

If the above-mentioned criteria are respected, such as those evaluated by a transvaginal probe, and the dosage of CA125 employed is  $< 35$  IU/ml,<sup>8</sup> the probability of finding a benign formation is very high. Some authors have noted that by using these specific ultrasonographic criteria, the negative predictive value has been 96%<sup>19</sup>; in post-menopausal women, the same values range from 95% to 100%.<sup>22,23</sup> When an ovarian mass is sonographically defined as a unilocular and nonechogenic cyst, the negative predictive value reported has been between 90% and 95%.<sup>19,24</sup> Other authors have reported 100% specificity by using a combination of the clinical examination, CA125 dosage  $< 35$  IU/ml, and transvaginal ultrasound.<sup>25,26</sup>

In a prospective study that included 1769 asymptomatic postmenopausal patients, Conway<sup>27</sup> found ovarian cysts in 116 patients at ultrasound. The prevalence was 6.6%. Out of the 116 patients, 27 (23.28%) had simple cysts that disappeared spontaneously, 60 (50.48%) had persistent cysts, and 20 (17.24%) were lost to follow-up study. Eighteen out of the 60 women (26.09%) with persistent simple ovarian cysts underwent surgery. No malignant ovarian aspects were identified. Simple ovarian cysts are more common in postmenopausal women than had been previously believed. However, given that such cysts are unlikely to be or become malignant, con-

servative treatment can be followed. In fact, Kroon *et al.*<sup>28</sup> reported that 12 out of 32 (37.5%) cysts had spontaneously disappeared in a group of postmenopausal women with small, simple anechoic ovarian cysts.

Recently, the use of transvaginal color Doppler (TV-CDS) has allowed us to increase our knowledge on the state of neovascularization of the ovarian cyst wall.<sup>29,30</sup> It has become clear that this technique is a valuable tool for differentiating benign from malignant ovarian tumors.<sup>30-33</sup>

A low pulsatility index (PI) or resistance index (RI) indicates a low impedance to blood flow in the distal vasculature, as seen in neoplasias; a high PI or RI (associated with absent intratumoral neovascularization with color Doppler) is said to exclude ovarian cancer. According to the literature, the percentage of true positives varies from 80% to 100%, with a false positivity of 0%–20%. Fleischer<sup>33</sup> compared transvaginal color-Doppler ultrasonography with histologic findings in 126 ovarian masses. He reported a sensitivity level of 92%, a specificity level of 86%, a PPV of 86%, and a NPV of 98%. Furthermore, in 3 out of the 126 cases, the CD was highly suggestive of ovarian cancer, although the morphologic findings had not been suspicious. The mean and SD of the PI values in the benign group ( $1.4 \pm 0.6$ ) showed a statistically significant difference when compared to the malignant groups ( $0.6 \pm 0.4$ ) ( $p = 0.04$ ). However, there was overlap in the range of PI values of the benign (0.8 to 2.0) and malignant groups (0.3 to 1.2).

According to Zanetta,<sup>34</sup> color Doppler is more accurate than conventional ultrasound and CA125 in discriminating malignancies from benign tumors. The best uses of this technique seem to be the gathering of ulterior preoperative information concerning masses with uncertain sonographic characteristics, and that of allowing better timing and tailoring of surgery.

CA125 is an antigen, identified by OC125 monoclonal antibody, found in cells cultured from patients with serous papillary ovarian carcinoma. Eighty percent of patients with known epithelial ovarian cancer respond positively to CA125 assay. It is correlated with tumor volume, but the percentage can be high in benign epithelial cysts such as endometrioma, adenomyosis, myoma, and PID. In the presence of certain factors such as a pelvic mass, however, a serum level of CA125 > 50 IU/ml and postmenopausal age, the probability of a malignant neoplasia is from 80 to 90%.

Furthermore, during laparoscopy we can obtain information by observing both the cyst and the peritoneal cavity. An aspiration of the peritoneal fluid sample, a careful examination of the cystic ovary, and a complete inspection of the pelvic peritoneum, the contralateral ovary, and the omentum can be performed using laparoscopy. Endoscopic bags can be used to remove the cyst or the whole ovary without spillage. Thus, intraoperative histological examination can be performed. In this way, it is possible to reduce the risk of treating an ovarian cancer during laparoscopy.<sup>1,3,35</sup>

Canis *et al.*<sup>6</sup> compared the accuracy of laparoscopic diagnosis with that of histodiagnosis in 819 adnexal masses. They found that all the malignant tumors that had been considered cancerous or suspicious at laparoscopy were confirmed histologically (sensitivity 100%). The positive predictive value was 41.3%, and the negative predictive value was 100%.

During laparoscopy, we can also study the ovarian cyst by laparoscopic ultrasound imaging (LUI). LUI is performed by using a high-frequency, multiple focus

transducer (7.5 MHz): sector, convex, or linear. The possibility of having real-time multiplane imaging of the organs increases the accuracy of diagnosis.

The transducer (UST-5521, Aloka, Japan) is a 7.5-MHz linear array designed for easy insertion through a 10-mm trocar; it is applicable to SSD 620 (Aloka, Japan) ultrasound equipment and can be used to perform intraoperative ultrasound examinations.

The closeness of the LUI probe to the ovary, the use of a high-frequency transducer with high resolution, and the possibility of using color Doppler are among the advantages of this technique. It is even possible to identify very small papillary formations on the internal wall of the cysts. Identification of these formations is not possible when using conventional abdominal ultrasonography: it is difficult even when using transvaginal ultrasonography.

After using this imaging approach, our preliminary evaluation of LUI is that this type of ultrasonography can be a reliable diagnostic tool during gynecological operative endoscopy. It can also be helpful in intraoperative decision-making.<sup>36</sup>

An ovarian cyst may be sometimes histopathologically diagnosed as being a carcinoma of low malignant potential or a borderline ovarian tumor. Unilateral salpingo-oophorectomy, or, in some cases, cystectomy, is a valid alternative treatment in young women with localized (stage IA) disease.<sup>37</sup> These borderline tumors present a high survival rate (93%) at five years. A study of 254 cases was carried out by Mangioni *et al.*,<sup>38</sup> and they reported that not one of these patients had died because of the malignancy. Conservative surgery is a valid alternative in those patients still at reproductive age. Pelvic and para-aortic lymphadenectomy are indicated in stage III subjects with peritoneal spread: laparoscopic follow-up is suggested. However, even if no specific sonographic aspect exists for the identification of borderline tumors, ultrasonography is the best way to detect their recurrence. Conservative treatment of borderline ovarian tumors includes a laparoscopic procedure. Even if there appears to be a high risk of intraoperative rupture, the rate of recurrence is similar to that of laparotomic treatment.<sup>39</sup> Available data indicate that fertility, pregnancy outcome, and survival in such patients remain excellent.<sup>40</sup>

In 1993, the Italian Society of Endoscopy and Laser Therapy in Gynecology (S.I.E.L.G.) decided to perform a multicenter prospective study. The aim of the study was to verify whether laparoscopic treatment of ovarian cysts could be reliable and safe even in women over 40, when cautious management and strict guidelines were used. Forty-seven Italian Centers of Gynecological Endoscopy participated (from June 1994 until December 1995). The safety of laparoscopic treatment in women over 40 with ovarian persistent cysts was evaluated. Four hundred and six patients over 40 years of age (37.2% in postmenopause) took part in the study. All patients were divided into two groups according to the ultrasonographic characteristics of the cysts (benign or suspect). A comparison was made between 289 patients with benign ultrasonographic findings (group A) and 117 patients of the same age with ultrasonographic criteria that included septa, vegetation, solid components, or complex masses (group B).

The average age of group A subjects was  $51.4 \pm 8$ . Age ranged from 40 to 78 years. Histological diagnosis of the 289 ultrasonically identified benign cysts confirmed that they were all nonmalignant. In the 117 patients with suspicious ultrasonographic criteria (group B), four cases of malignancy were found: two were cases

of serous cystoadenocarcinoma, one was a moderately differentiated Leydig cell tumor, and one was a low-malignant-potential tumor.

Statistical elaboration was carried out using the  $\chi^2$  method. Considering the prevalence of carcinoma in relation to the ultrasonographic findings, there was a significant statistical difference between the two groups ( $p = 0.009$ ). Moreover, in the patients with no benign ultrasonographic criteria, there were no significant statistical differences between those in premenopause and those in postmenopause ( $p = 0.612$ ).

At our department we treated a series of 276 ovarian cysts using laparoscopy. Sixty-eight patients were over 40 years of age. In 15 of the 68 cases (22%), the serum levels of the tumoral ovarian markers were abnormal. The ovarian markers were abnormal in endometriotic cysts and in dermoid cysts, as well as in paraovarian and in simple serous cysts. The diameters of all the cysts were  $43 \pm 13$  mm (range 5–80). The duration of surgery was  $59 \pm 26$  min (range: 15–120 min.). In two cases where severe adhesion was present, two laparoscopic (0.7%) procedures were converted into laparotomies. The duration of hospital stay was  $2.6 \pm 1.3$  days. No relapses were noted at follow-up in the ultrasonographic controls. In this series we performed excision of the cyst in 45% of the cases and an adnexectomy in 55% of the cases. We did not find any case of malignancy.

In conclusion, operative laparoscopy represents a valid alternative for the treatment of benign adnexal masses, even in women over 40. The majority of cysts in this age group of women are benign. Patient selection for laparoscopic surgery is very important. Patient selection should be based on transvaginal ultrasound, color Doppler, dosage of CA125, clinical examination, and case history. This multimodal approach is fundamental for avoiding treatment of malignant masses. If the benign ultrasonographic criteria, (unilateral mass, unilocular cysts, absence of septa  $>3$  mm and intracystic vegetations, defined borders) are respected and the serum level of CA125 is  $<35$  IU/ml, the probability of the presence of a benign cyst is very high. Furthermore, during laparoscopy, we can obtain information from the cyst itself and from the peritoneal cavity. Endoscopic bags can be used to remove the cyst or the whole ovary without any spillage. Thus, intraoperative histological examination can be carried out. In this way, it is possible to reduce the risk of treating an ovarian cancer at laparoscopy.

Laparoscopic treatment of ovarian masses can be considered useful and safe, even in post-menopausal patients. However, the following criteria must be met: benign sonographic aspects, CA125  $<35$  IU/ml, and benign laparoscopic features. On the other hand, if vegetation, septa, and/or solid or complex cysts are present, there is no diagnostic possibility of eliminating the risk of finding and treating ovarian malignant masses. Ultrasonography is perhaps the most important tool available for distinguishing benign from malignant adnexal masses.

#### REFERENCES

1. PARKER, W. & J. BEREK. 1990. Management of selected cystic adnexal masses in postmenopausal women by operative laparoscopy: a pilot study. *Am. J. Obstet. Gynecol.* **163**: 1574–1579.
2. MAIMAN, M., V. SELTZER & J. BOYCE. 1991. Laparoscopic excision of ovarian neoplasms subsequently found to be malignant. *Obstet. Gynecol.* **77**: 563–565.

3. MANN, W.J. & H. REICH. 1992. Laparoscopic adnexectomy in postmenopausal women. *J. Repr. Med.* **37**: 254–256.
4. NEZHAT, F., C. NEZHAT, C.E. WELANDER, *et al.* 1992. Four ovarian cancers diagnosed during laparoscopic management of 1011 women with adnexal mass. *Am. J. Obstet. Gynecol.* **167**: 790–796.
5. METTLER, R., G. CAESAR, S. NEUNZLING & K. SEMM. 1993. Value of endoscopic ovarian surgery: critical analysis of 626 pelviscopically operated ovarian cysts at the Kiel University Gynecologic Clinic 1990–1991. *Geburtshilfe Frauenheilk.* **53**: 253–257.
6. CANIS, M., G. MAGE, J.L. POULY, *et al.* 1994. Laparoscopic diagnosis of adnexal masses: a 12-year experience with long term follow-up. *Obstet. Gynecol.* **83**: 702–712.
7. SHALEV, E., S. ELIYAHU, D. PELEG, *et al.* 1994. Laparoscopic management of adnexal cystic masses in postmenopausal women. *Obstet. Gynecol.* **83**: 594–596.
8. GUGLIELMINA, J.N., G. PENNEHOAT, B. DEVAL, *et al.* 1997. Treatment of ovarian cysts by laparoscopy. *Contracept. Fertil. Sex.* **25**: 218–229.
9. PUROLA, E. & U. NIEMINEN. 1968. Does rupture of cystic carcinoma during operation influence the prognosis? *Ann. Chir. Gynaecol. Fenn.* **57**: 615–617.
10. WEBB, M.J., D.G. DECKER, E. MUSSEY & T.J. WILLIAMS. 1973. Factors influencing survival in Stage I ovarian cancer. *Am. J. Obstet. Gynecol.* **116**: 222–228.
11. EINHORN, N., B. NILSSON & S. KERSTIN. 1985. Factors influencing survival in carcinoma of the ovary. *Cancer* **55**: 2019–2025.
12. FINN, C.B., B.M. LUESLEY, E.J. BUXTON, *et al.* 1992. Is Stage I epithelial ovarian cancer overtreated both surgically and systemically? Results of a five-year cancer registry review. *Br. J. Obstet. Gynecol.* **99**: 54–58.
13. SAINZ DE LA CUESTA, R., B.A. GOFF, A.F. FULLER, *et al.* 1994. Prognostic significance of intraoperative rupture of malignant ovarian neoplasm. *Gynecol. Oncol.* **52**: 111.
14. DEMBO, A.J., M. DAVY, A.E. STENWIG, *et al.* 1990. Prognostic factors in patients with stage I epithelial ovarian cancer. *Obstet. Gynecol.* **75**: 263–272.
15. SIGURDSSON, K., P. ALM & B. GULLBERG. 1983. Prognostic factor in malignant epithelial ovarian tumours. *Gynecol. Oncol.* **15**: 370–380.
16. SEVELDA, P., N. VAVRA, M. SCHEMPER & H. SALZER. 1990. Prognostic factors for survival in Stage I epithelial ovarian carcinoma. *Cancer* **65**: 2349–2352.
17. CREASMAN, W.T. & J.T. SOPER. 1986. The undiagnosed adnexal mass after the menopause. *Clin. Obstet. Gynecol.* **29**: 446–450.
18. CHAPRON, C., J.B. DUBUISSON, O. KADOCH, *et al.* 1998. Laparoscopic management of organic cysts: is there a place for frozen section diagnosis? *Hum. Reprod.* **13**: 324–329.
19. HERRMANN, U.J., G.W. LOCHER & A. GOLDBIRSCH. 1987. Sonographic patterns of malignancy: prediction of malignancy. *Obstet. Gynecol.* **69**: 777–781.
20. GRANDBERG, S., A. NOSTROM & A. WIKLAND. 1990. Tumors in the pelvis as imaged by vaginal sonography. *Gynecol. Oncol.* **37**: 224–229.
21. SASSONE, A.M., I.E. TIMOR-TRITSCH, A. ARTNER, *et al.* 1991. Transvaginal sonographic characterization of ovarian disease: evaluation of a new scoring system to predict ovarian malignancy. *Obstet. Gynecol.* **78**: 70–76.
22. RULIN, M.C. & A.L. PRESTON. 1987. Adnexal masses in postmenopausal women. *Obstet. Gynecol.* **70**: 578–583.
23. GOLDSTEIN, S.R., B. SUBRAMANYAM, J.R. SNYDER, *et al.* 1989. The postmenopausal cystic adnexal mass: the potential role of ultrasound in conservative management. *Obstet. Gynecol.* **73**: 8–10.
24. MEIRE, H.B., P. FARRANT & T. GUTHA. 1978. Distinction of benign from malignant ovarian cysts by ultrasound. *Br. J. Obstet. Gynecol.* **85**: 893–897.
25. FINKLER, N.J., B. BENACERERRAF, P.T. LAVIN, *et al.* 1988. Comparison of serum CA 125, clinical impression and ultrasound in the preoperation evaluation of ovarian masses. *Obstet. Gynecol.* **72**: 659–664.
26. JACOBS, I., I. STABILE, J. BRIDGES, *et al.* 1988. Multimodal approach to screening for ovarian cancer. *Lancet* **1**: 268–273.
27. CONWAY, C., I. ZALUD, M. DILENA, *et al.* 1998. Simple cyst in the postmenopausal patient: detection and management. *J. Ultrasound Med.* **17**: 369–372.
28. KROON, E. & E. ANDOLF. 1995. Diagnosis and follow-up of simple ovarian cysts detected by ultrasound in postmenopausal women. *Obstet. Gynecol.* **85**: 211–214.

29. LEIBMAN, A.J., B. KRUSE & M.B. MCSWEENEY. 1988. Transvaginal sonography: comparison with transabdominal sonography in the diagnosis of pelvic masses. *Am. J. Roentgenol.* **151**: 89–92.
30. BOURNE, T., S. CAMPBELL, C. STEER, *et al.* 1989. Transvaginal colour flow imaging: a possible new screening technique for ovarian cancer. *Br. Med. J.* **299**: 1367–1370.
31. KURJAK, A., I. ZALUD & Z. ALFIREVIC. 1991. Evaluation of adnexal masses with transvaginal color ultrasound. *J. Ultrasound Med.* **10**: 295–297.
32. FLEISCHER, A.C., W.H. RODGERS & B.K. RAO, *et al.* 1991. Assessment of ovarian tumor vascularity with transvaginal color Doppler sonography. *J. Ultrasound Med.* **10**: 563–568.
33. FLEISCHER, A.C., J.A. CULLINAN, C.V. PEERY, *et al.* 1996. Early detection of ovarian carcinoma with transvaginal color Doppler ultrasonography. *Am. J. Obstet. Gynecol.* **174**: 101–106.
34. ZANETTA, G., P. VERGANI & A. LISSONI. 1994. Color Doppler ultrasound in the preoperative assessment of adnexal masses. *Acta Obstet. Gynecol. Scand.* **73**: 637–641.
35. LEVINE, R.L. 1990. Pelviscopic surgery in women over forty. *J. Reprod. Med.* **35**: 597–600.
36. COCCIA, M.E., G.L. BRACCO & G. SCARSELLI. 1994. Laparoscopic sonography and multimodal diagnostic approach in case of endoscopic treatment of ovarian cyst. *In* Growth and Differentiation in Reproductive Organs. A.R. Genazzani, F. Petraglia, A.D. Genazzani & G. D'Ambrogio, Eds.: 173–175. CIC Edizioni Internazionali. Roma.
37. LIM TAN, S.K., H.E. CIGAS & R.E. SCULLY. 1988. Ovarian cystectomy for serous borderline tumors: a follow-up study of 35 cases. *Obstet. Gynecol.* **72**: 755–778.
38. MANGIONI, C. & U.A. BIANCHI. 1996. Tumori maligni dell'ovaio. *In* La Clinica Ostetrica e Ginecologica. II Edizione. G.B. Candiani, V. Danesino & A. Gastaldi, Eds.: 1723–1725. Masson. Milano, Italy.
39. DARAI, E., J. TEBOUL, F. WALKER, *et al.* 1996. Epithelial ovarian carcinoma of low malignant potential. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **66**: 141–145.
40. GOTLIEB, W.H., S. FLIKKER, B. DAVIDSON, *et al.* 1998. Borderline tumors of the ovary: fertility treatment, conservative management, and pregnancy outcome. *Cancer* **82**: 141–146.