Transvaginal ultrasound assessment of the premenopausal ovarian mass

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Abstract The evaluation of the premenopausal ovarian mass with transvaginal ultrasound and color Doppler is reviewed.

Keywords Ovarian mass · Color Doppler · Ovarian cancer screening

It is clear to anyone who practices infertility that the transvaginal probe has revolutionized our ability to examine the adnexa. The study by Padilla et al. clearly demonstrates the lack of sensitivity of bimanual examination in identifying both uterine as well as ovarian tumors [1]. In fact this sensitivity did not improve when medical students were compared to experienced attending gynecologists. As a consequence of screening asymptomatic premenopausal women, we have learned that cystic masses are not uncommon. Shulman et al. identified cystic masses greater than 2.5 cm in 13% of premenopausal women [2]. From the series of Osmer et al., at a large centralized European site, it can be estimated that at least 50–60% of these will be functional. Among 1,072 premenopausal ovarian masses, 570 were functional cysts and corpus lutea, 264 were endometriotic cysts, 192 were benign neoplasms, and 46 malignancies [3].

Incorrect interpretation of transvaginal ultrasound findings can clearly lead to unindicated surgeries. The corpus

luteum and particularly the resorbing hemorrhagic corpus luteum can be extremely complex in appearance and can be easily mistaken as a neoplasm (Fig. 1a and b). Women with prior pelvic surgery or inflammatory processes can have remarkable fluid filled adhesions and loculations which should not be mistaken for neoplasm (Fig. 2). Color Doppler as an adjunct to transvaginal gray scale-imaging can be a useful tool in improving diagnostic accuracy but misuse of arbitrary velocimetry cut-offs can also lead to unnecessary surgeries [4]. Similarly, false positive elevations of CA-125, which are particularly common in the premenopause, may lead us to suspect ovarian carcinoma.

Three diagnostic goals have been previously described for evaluation of the ovary (1) Identify hemorrhagic corpus luteum, functional cysts, hydrosalpinges, and peritoneal adhesive disease, and avoid operative interventions for them if possible. (2) Differentiate benign from malignant disease of the ovary and Fallopian tube. (3) Discriminate gastrointestinal and uterine pathology from ovarian or Fallopian tube processes. Our lab has long relied on a multi-parameter approach of the evaluation of the suspect adnexal mass. This includes age, history, reported findings of bimanual examination, transvaginal ultrasound, trans-abdominal ultrasound if indicated, and various tumor markers as clinically indicated. As will be outlined CT scans and MRI may be required.

To achieve the goals noted above, the clinician must have a clear understanding of the epidemiology of ovarian neoplasm both benign and malignant as the premenopausal women ages. Using the data of Koonings et al.: At age 20–29, cystic teratomas, serous cystadenomas, and mucinous cystadenomas are responsible for 72, 15, and 11% of benign ovarian neoplasms, respectively. At age 40–49, the same three tumor types make up 43, 46, and 8%, of benign neoplasms. The risk of a neoplasm being borderline is 2.4%

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Fig. 1 **a** A hemorrhagic corpus luteum is noted. Retracting clot is noted on the inner cyst wall. Circumferential blood flow is noted on color Doppler. Spontaneous resolution was noted at subsequent scan. **b** Another hemorrhagic cyst is noted. A much larger retracting clot is seen. The absence of color Doppler flow within the echogenic material is reassuring that this is not a solid neoplasm. Spontaneous resolution was noted

at 20–29 and 6.3% at 40–49. The risk for frank malignancy is 4% at 20–29 and 35% at 40–49 [5]. This last percentile may be seen inflated, but it must be remembered that the denominator does not include women with endometriomas, adhesive disease and functional cysts.

Several assumptions can be made that most practitioners will be comfortable with. In women aged 20–29, a cystic mass, either simple or complex is most likely a functional cyst, a hemorrhagic corpus luteum, a pelvic inflammatory process (population-dependent), an endometrioma, a cystic teratoma, or a cyst-adenoma. A small percentage of these patients will have borderline or frank malignancy. If a frankly malignant tumor is present it is more likely to be a malignant germ cell tumor or granulosa cell rather than epithelial. By age 40–49 the differential is similar except

Fig. 2 This patient was experiencing pelvic pain 3 months status post myomectomy. An echogenic Fallopian tube is noted surrounded by a loculated fluid filled adhesion

the cyst-adenomas start occurring more frequently. More importantly, the percentage of these neoplasms which are malignant neoplasms increases. If a frank ovarian malignancy is present after age 40 it is epithelial 90% of the time.

After 15 years of exhaustive study it is clear that color Doppler velocimetry as an isolated test, reveals diagnostic overlap between benign and malignant masses. Neither a $PI \leq 1.0$ or an $RI \leq 0.4$ are specific enough to differentiate a benign from malignant mass. Using a pulsatility index of ≤ 1.0 , Fleischer et al. in 1993, clearly demonstrated that although there was a clear tendency for malignant ovarian neoplasms to have low resistance vessels, there was diagnostic overlap [6]. This author in fact was an early advocate of the multi-parameter approach to the suspect adnexal mass. Tekay and Jouipilla in 1994 were able to

Fig. 3 A complex mass cystic and solid is noted in this perimenopausal patient. Power Doppler revealed low-resistance vessels within this mass. A Stage III-C ovarian carcinoma was identified at exploratory laparotomy

demonstrate an $RI \leq 0.4$ in 30% of benign premenopausal ovarian masses [7]. Other authors have advocated using a time averaged maximum velocity of 12.5 cm/s or greater for identifying ovarian malignancy [8]. Initial enthusiasm for color Doppler energy or power Doppler has been tempered by issues with motion artifact. Several recent logistic regression analyses have found that 95% of ovarian malignancies display two common regression analyses two common features. These two features are solid elements and central vasculature flow within these elements [9, 10] (Figs. 3 and 4a and b). Typically these vessels display very unusual architecture.

Caution must be used in using color Doppler for routine screening. Although color Doppler typically will show a ring of flow around a corpus luteum, if taken at a more oblique angle these vessels can be seen to be quite complex and branching in appearance (Fig. 5a and b). Retracting clot within a corpus luteum can also be mistaken for a papillary

Fig. 4 **a** A solid excrescence is noted on the inner cyst wall of this complex ovarian cyst. **b** Power Doppler examination of the mass shown in Fig. 4a revealed multiple intermediate resistance vessels. A Stage I–C epithelial ovarian cancer was found at laparotomy

Fig. 5 **a** A hemorrhagic corpus luteum is noted with circumferential flow. A few vessels appear to perforate and branch more centrally in the mass. **b** By angulation of the transducer multiple perforating vessels are demonstrated centrally. This hemorrhagic corpus luteum regressed spontaneously. To those unfamiliar with the vessel pattern of the corpus luteum this physiologic structure can be misinterpreted as a malignant neoplasm

excrescence. Partial or complete resolution with the next menses is reassuring.

The combination of color Doppler and pattern recognition is the foundation on which are lab and particularly our ovarian cancer screening program stand. In our experience endometriomas and cystic teratomas can be specifically identified with 90% accuracy [11]. Endometriomas typically are filled with uniform low level echoes on transvaginal imaging (Fig. 6). Some areas of echogenic speckling can be noted. These masses may be unilocular or multilocular. Doppler flow is confined to the cysts walls or septa between the locules. If central branching vascular flow is noted, a granulosa cell tumor must be considered (Fig. 7). An acute hemorrhagic corpus luteum may look very similar to an endometrioma [12]. Usually we will rescan in 6–8 weeks at the start of the cycle to check for resolution.

Fig. 6 A typical endometrioma filled with low-level echoes is noted. Color flow reveals no flow centrally. Flow can be seen in the septa between loculations (not demonstrated on this image). More normal ovarian tissue is noted at the upper right

Hemorrhagic corpus lutea will either be resolved or retracting clot noted. Cystic teratomas can be highly complex and are variable in appearance. They usually contain sebaceous material, hair, and cartilage [13] (Fig. 8). Posterior shadowing is frequently noted and color Doppler is usually seen only at the periphery of the mass. Central flow may be seen if there are immature neural elements or struma-ovarri. Cystadenomas may be unilocular or multilocular. They typically have smooth walls (Fig. 9).

A variant of the cystadenoma, the cyst-adenofibroma is a great masquerader for malignancy. The solid elements may be highly bizarre in appearance. Color Doppler will usually reveals no central vascularity with the solid elements (Fig. 10). If multiple excrescences are noted, a borderline

Fig. 7 This mass was initially interpreted to be either a granulosa cell tumor or a corpus luteum. The mass did not resolve in 6 weeks time at the beginning of the cycle. A Stage IA granulosa cell tumor was found at surgical staging. The key was reimaging the patient

Fig. 8 A fairly typical cystic teratoma. This complex cystic mass contained hair, cartilage, and sebaceous material. These masses can be quite complex in appearance. Shadowing posterior to echogenic regions is demonstrated about 90% of the time. (Not demonstrated this image) Color Doppler investigation was unremarkable. Color Doppler of cystic teratomas rarely reveals flow except at the junction between the mass wall and normal ovary. The echogenic material within the masses doesn't display flow. An exception is if struma-ovarri, carcinoid tumor, or malignant elements are noted. Moving material within these masses can cause false positive vascular flow on power Doppler. If there is a concern for malignant teratoma, AFP and HCG levels should be obtained

tumor becomes more likely. Color Doppler will not show flow into these excrescences about 30% of the time.

CA-125 should only be used in the pre-menopause as an adjunct test in a women with a suspect adnexal mass. The work of Jacob et al. suggest that CA-125 is approximately 30% sensitive with a 1% false positive rate for Stage I

Fig. 9 A multiloculated cystadenoma is noted. No solid elements are noted. Flow may be seen in the cyst walls particularly with the mucinous varieties. If there is back to back crowding of the cysts or if the cysts are greater than 10 cm. borderline tumor or frank malignancy should be included in the differential even if no solid elements are identified

Fig. 10 This complex cyst with two areas of excrescence was found to be a adeno-fibroma at laparoscopy. Color Doppler doesn't display flow within the excrescences. The differential diagnosis includes borderline malignancy. In our unpublished experience about 70% of cystic teratomas will reveal flow in the excrescences or solid elements of the tumor

disease in menopausal women. A large clinical trial of 200,000 postmenopausal women is now underway in England [14]. The 10–15% false positive rate in premenopausal women makes the test inappropriate for screening in the premenopause. In a premenopausal women with a known adnexal mass many authorities recommend CA-125 testing. Elevations can be seen with endometriosis, pelvic inflammatory disease, leiomyomas, cystic teratomas, pleural infections, and the menstrual cycle. It is an extremely nonspecific marker. If a mucinous tumor is suspect a CA 19-9 marker is commercially available. In young women with a suspect germ cell tumor HCG and AFP levels are appropriate. Many other markers are available which are beyond the scope of this review. The role of laser enhanced mass spectroscopy, proteomics testing, is controversial [15].

MRI with gadolinium contrast should be considered to confirm pedunculated and interligamentous leiomyomas [16]. MRI is also useful in identifying fat within cystic teratomas and blood or endometriotic fluid within ovarian masses. Computerized tomographic imaging with contrast is extremely useful for the evaluation of suspect gastrointestinal pathology, abscesses, lymph node status, and locating the ureters as well as ureteral pathology.

The role of ultrasound in screening for ovarian cancer remains controversial. Studies with primarily low-risk women have found that women will be detected at Stage I more frequently if they undergo surveillance with ultrasound [17, 18]. Excluding borderline tumors the sensitivity of annual ultrasound in low-risk women may approximate 40–50%. In expert hands approximately 10–25 surgeries will be performed for each malignancy identified. This number may be even higher if simple cystic masses are not

followed expectantly [19]. For high-risk women ultrasound and in particular women with BRCA mutations, ultrasound is poorly sensitive in identifying early stage ovarian cancer [20, 21]. There is no evidence that the addition of 3D Doppler investigation of normal size ovaries improves sensitivity. There are preliminary papers that have evaluated the role of 3D Doppler examination of suspect masses [22–24].

In summary it is critical for the clinician to recognize that in the reproductive age group many masses are physiologic or residuals of adhesive disease. History is critical in avoiding operating on women for residuas of pelvic inflammatory disease or post-operative adhesions. (Myomectomies and transplants are two prime examples) Patience will frequently prevent unnecessary surgery. Most adnexal pathology in the reproductive age group can be identified with pattern recognition. If solid elements or ascites are noted think about the possibility of malignancy. Color Doppler may improve accuracy in predicting malignancy. Color Doppler velocimetry measurements may be taken, but it is the pattern of central flow within solid elements which is most predictive. Serum markers should be chosen as clinically indicated. Routine screening with CA-125 in the premenopausal women is not indicated. CT scan and MRI are two powerful tools that should be used when the differential diagnosis is cloudy.

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