January 2013

Ovarian masses: is multi-detector computed tomography a reliable imaging modality?

Yasir Jamil
Agha Khan University, yasir.jamil@aku.edu

Saima Hafeez

Tariq Alam
Aga Khan University, tariq.alam@aku.edu

Madiha Beg

Mohammad Awais

See next page for additional authors

Authors
Yasir Jamil, Saima Hafeez, Tariq Alam, Madiha Beg, Mohammad Awais, and Imrana Masroor

RESEARCH ARTICLE

Ovarian Masses: Is Multi-detector Computed Tomography a Reliable Imaging Modality?

Yasir Jamil Khattak, Saima Hafeez, Tariq Alam, Madiha Beg*, Mohammad Awais, Imrana Masroor

Abstract

Background: Ovarian cancer continues to pose a major challenge to physicians and radiologists. It is the third most common gynecologic malignancy and estimated to be fifth leading cancer cause of death in women, constituting 23% of all gynecological malignancies. Multi-detector computed tomography (MDCT) appears to offer an excellent modality in diagnosing ovarian cancer based on combination of its availability, meticulous technique, efficacy and familiarity of radiologists and physicians. The aim of this study was to compute sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of 64- slice MDCT in classifying ovarian masses; 95% confidence intervals were reported. Materials and Methods: We prospectively designed a cross-sectional analytical study to collect data from July 2010 to August 2011 from a tertiary care hospital in Karachi, Pakistan. A sample of 105 women aged between 15-80 years referred for 64-MDCT of abdomen and pelvis with clinical suspicion of malignant ovarian cancer, irrespective of stage of disease, were enrolled by non-probability purposive sampling. All patients who were already known cases of histologically proven ovarian carcinoma and having some contraindication to radiation or iodinated contrast media were excluded. Results: Our prospective study reports sensitivity, specificity; positive and negative predictive values with 95%CI and accuracy were computed. Kappa was calculated to report agreement among the two radiologists. For reader A, MDCT was found to have 92% (0.83, 0.97) sensitivity and 86.7% (0.68, 0.96) specificity, while PPV and NPV were 94.5% (0.86, 0.98) and 86.7% (0.63, 0.92), respectively. Accuracy reported by reader A was 90.5%. For reader B, sensitivity, specificity, PPV and NPV were 94.6% (0.86, 0.98) 90% (0.72, 0.97) 96% (0.88, 0.99) and 87.1% (0.69, 0.95) respectively. Accuracy computed by reader B was 93.3%. Excellent agreement was found between the two radiologists with a significant kappa value of 0.887. Conclusion: Based on our study results, we conclude MDCT is a reliable imaging modality in diagnosis of ovarian masses accurately with insignificant interobserver variability.

Keywords: Malignant - sensitivity and specificity - computed tomography - ultrasound - confidence intervals - Pakistan

Asian Pacific J Cancer Prev, **14 (4)**, 2627-2630

Introduction

Ovarian cancer continues to pose a major challenge to physicians and radiologists. It is third most common gynecologic malignancy (Silverberg et al., 1990; Tawani et al., 2005) and estimated to be the fifth leading cancer cause of death in women (Landis et al., 1998) after lung, breast, colon, and pancreatic cancer and constitutes 23% of all gynecological malignancies (Woodward et al., 2004). Nearly two thirds of all ovarian carcinomas have progressed to disease stage III or IV at time of first diagnosis because they may remain clinically asymptomatic for extended periods (Nagell et al., 1990; Kombacher et al., 1992). The "silent" nature of disease and lack of established population-based screening programmes are the major factors why the majority of women present with advanced disease and consequently have a poor prognosis. Seventy-six percent of patients with ovarian cancer survive only 1 year after diagnosis (Timpani et al., 2000).The incidence and mortality rates of ovarian cancer increases with age and for all stages, the 5-year survival rate is 45% (American Cancer Society, 2007).

Ovarian tumors are classified as epithelial tumors, germ cell tumors, sex cord–stromal cell tumors, and metastatic tumors on the basis of tumor origin (Koonings et al., 1989).As most patients with ovarian carcinoma have distant or widespread disease at the time of diagnosis, this fact underscores the importance of early detection and improved characterization of ovarian masses and is of paramount and utmost importance in the preoperative evaluation, enabling the surgeon to anticipate carcinoma of the ovary before the operation, so that adequate procedures are planned (Hermann et al., 1987; Mugel

*The Aga Khan University Hospital, Karachi, Pakistan *For correspondence: madiha.beg@aku.edu, drmadiha@gmail.com*

et al., 1993; Osmers et al., 1996; Sengupta et al., 2000). Bimanual pelvic examination and serum CA-125 levels have failed to allow consistent detection of ovarian malignancy. Because the sensitivities of these techniques are often below 50%, imaging modalities have become indispensable (Jacobs et al., 1989; Taylor et al., 1994; Kurtz et al., 1999; Ferozabadi et al., 2011). Sonography has been shown to be a sensitive, but relatively nonspecific method, leading to unnecessary surgical resection of many benign lesions (Outwater et al., 1995). Besides clinical examination, CA 125 levels, and ultrasonography, CT scan is also used as a diagnostic technique for ovarian carcinoma and is superior to US in assessment of the nature of ovarian masses. It has proven as an excellent modality in the diagnosis of women believed to have ovarian cancer based on combination of its ready availability, meticulous technique, efficacy and familiarity of radiologists and physicians (Spencer et al., 2005). With the advent of 64-slice multidetector Computed Tomography (MDCT), it has become possible to acquire several thin slices and image reconstruction in axial, coronal and sagittal planes contributing valuable information towards preoperative surgical and management planning (Parish, 2007).

Materials and Methods

A cross sectional analytical study was designed to collect data from the Department of Radiology, Aga Khan University Hospital Karachi from July 2010 to August 2011. Female patients (age range 15-80 years) referred for 64-MDCT of Abdomen and pelvis with clinical suspicion of malignant ovarian cancer irrespective of stage of disease was included. Patients with signs and symptoms of weight loss, abdominal or pelvic mass detected on examination by physician deemed suspicious for ovarian cancer were included in the study. Patients who were already known case of histologically proven ovarian carcinoma and, having some contraindication to radiation or iodinated contrast media were excluded. MDCT scan of abdomen and pelvis performed from dome of the diaphragm to the pubic symphysis by 64 slice Aquilion, Toshiba Medical System at 120 kvp and 350 mAs by a trained technologist with 5 years' experience in MDCT scanning. All patients received intravenous non-ionic contrast medium omnipaque-300 (the dose of which was decided according to age and weight of the patient) and given by a computer-controlled injector at rate of 4 ml/second. First, volume data with 0.5 mm slice thickness were acquired in Porto-venous phase, followed by multiplanar reconstruction in axial, coronal and sagittal planes with a slice thickness of 5 mm each. MDCT reporting regarding presence of carcinoma ovary was done by consensus between two consultant radiologists with 5 and 8 years' clinical experience in women imaging. Histopathological findings regarding malignancy were obtained from medical/histopathology records of patients.

Data analysis procedure

Data were entered and analyzed by utilizing SPSS windows package 19.0 version. Descriptive analysis was conducted i.e. frequencies and percentages for categorical variables like malignant (positive for ovarian carcinoma) or benign (negative for ovarian carcinoma) and mean and standard deviation for the continuous variables like age.

Sensitivity and Specificity of 64-slice MDCT were calculated and 95% Confidence Intervals (CI) reported. Positive, negative predictive values and accuracy were computed. The agreement between MDCT and histopathological findings for ovarian carcinoma was computed using kappa statistic between both readers.

Sample size calculation

Reported sensitivity of MDCT for the detection of ovarian carcinoma is 90% (Jain, 1994; Jung et al., 2002) taking confidence interval of 95%, bound on error of 6%, the calculated sample size N=97. We enrolled 106 patients in the study.

$$n=Z^2_{1-\alpha/2}\text{-}P(1\text{-}P)/B^2$$

Results

During the study duration 105 women with a diagnosis of ovarian mass (mean age 53.13±SD 9.7 years) were enrolled in the study. Age range reported as 49 years, minimum and maximum 33, and 82 respectively. Out of 105 ovarian lesions, 73 cases (69.5%) were read by First radiologist as malignant and 32 (30.5%) as benign.

The second radiologist read 74 cases (70.5%) as malignant and 31 (29.5%) as benign. On later histopathological findings, 75 of 105 cases (71.4%) were proven to be malignant while 30 (28.6%) turned out to be benign.

Malignant lesions included Serous adenocarcinomas (n=32), mucinous adenocarcinomas (n=24), endometrioid carcinomas (n=12), malignant mullerian tumor (n=5) and Granulosa cell tumors (n=2). Benign lesions were endometriomas (n=15), benign cyst adenomas (n=5), teratomas (n=5), dermoid (n=3), corpus luteal cysts (n=2), simple ovarian cyst (n=1).

In case of the first radiologist, there were four false positive cases: The first case on MDCT appeared as a predominantly solid lesion with patchy areas of necrosis. The interface with the adjacent fallopian tube was not clear and appeared adherent to it. On histology this mass proved to be degenerated subserosal fibroid. Since there was minimal amount of ascites associated with it as well, it was implicated as suspicious considering the post menopausal status of the patient. Amongst the other three patients two had multiple enhancing nodular peritoneal deposits with pelvic adhesions secondary to previous tuberculosis giving a bizarre appearance. One of the patients had endometrioma deposit near the broad ligament which was read as malignant. Three of these cases were also read as malignant by the second reader as well. All the four cases had associated mild to moderate ascites as additional finding which further raised suspicion for malignancy.

There were six false negatives in case of first radiologist: Three of these cases were considered benign on account of their small size, all less than 4 cm. Two amongst these proved to be endometroid carcinoma. Amongst these three cases, one was falsely negative by

Table 1. Radiologist A and B

64-MDCT		Gold-standard (Histopathology)	
		Present (+ve)	Absent (-ve)
Radiologist A:			
Present (+ve)	True positive (a)	69	
	False Positive (b)		4
Absent (-ve)	False Negative (c)	6	
	True Negative (d)		26
Radiologist B:			
Present (+ve)	True positive (a)	71	
	False Positive (b)		3
Absent (-ve)	False Negative (c)	4	
	True Negative (d)		27

the second radiologist. The remaining three false negative cases were apparently simple cysts with internal septations which all proved to be mucinous adenocarcinomas. Two of these cases were read as negative for malignancy by the second reader as well. Thus, for the first reader there were 69 true positives, 4 false positives, 26 true negative, and 6 false negative results. For the second reader there were 71 true positives, 3 false positives, 27 true negative, and 4 false negative results on MDCT based assessment. Overall in case of first reader, MDCT was found to have 92%, 95%CI (0.83,0.97) sensitivity, 86.7%, 95%CI (0.68,0.96) specificity, while PPV and NPV were 94.5%, 95%CI (0.86,0.98) and 86.7%, 95%CI (0.63,0.92), respectively. (Table 1; Radiologist B).

The sensitivity, specificity, PPV and NPV were 94.6%, 95%CI (0.86,0.98) 90%, 95%CI (0.72,0.97) 96%, 95%CI (0.88,0.99) and 87.1%, 95%CI (0.69,0.95) respectively for the second reader (Table 1; Radiologist B).

Kappa statistics for measure of agreement was calculated between both readers for MDCT findings. Excellent agreement was established between the two radiologists with a significant kappa value of 0.887. Very Good (k=0.771) and excellent (k=0.838) agreement was also found between the MDCT and histopathological findings for both readers with significant kappa values.

Discussion

Ovarian malignancy usually has a delayed presentation due its non-specific symptoms. Most adnexal masses are suspected when patients presents with complaint of abdominal mass , or pain which later on is further evaluated by ultrasonography. Once we come across a neoplastic ovarian mass, it is imperative to decide whether the mass is benign or malignant to determine further treatment plan, and this is based largely on imaging appearances in addition to laboratory findings (Buy et al., 1991; Parkin et al., 2005)

The most commonly employed imaging modality for pelvic pathologies and adnexal masses is ultrasonography. Although it is the standard method for the preliminary assessment, due to its low cost, easy availability and high sensitivity of approximately 85-100%, it is still lagging behind CT and MRI due to its variable specificity rate (50-100%). On the other hand, the recent advances in CT technology has allowed better detection and improved role, not only in differentiation of benign and malignant ovarian masses, but also evaluation of metastatic deposits and extent of disease. Adequate determination of nature of mass and disease extent proves useful in planning of treatment which saves the patient unnecessary surgery and expense (Tamai et al., 2006; Tsili et al., 2008).

The values of sensitivity and specificity of MDCT in differentiation of ovarian masses are comparable to those reported in literature (Kinkel et al., 2005; Tsili et al., 2008; Gatreh-Samani et al., 2011). A sensitivity and specificity of 81% and 87% has been reported by Kinkel et al. (2005) in their Meta-analysis. Similarly Tsili et al. have reported that MDCT can categorize adnexal masses into benign and malignant with a sensitivity and specificity of up to 90.5% and 93.7% respectively. In our study, two separate radiologists recorded the MDCT findings. Overall in case of first reader, MDCT was found to have 92% sensitivity and 86.68% specificity, while the second reader reported a sensitivity and specificity 94.6%, 90% respectively. The difference between the results of two radiologists was not statistically significant. The relatively better results for the second reader could be related to the difference of experience between the two readers. Excellent agreement was found between the findings reported by the two readers and the histopathological results. Also, in our study all patients underwent biopsy (Gold-standard), thus minimizing verification bias and reporting accurate sensitivity rate.

With the advancement in technology and availability of MDCT with multiplanar reformation has resulted in significantly improved characterization of adnexal masses.

One of the other advantages of MDCT is its fast acquisition in addition to providing a detailed evaluation of both adnexa and abdomen. The thin sections and high resolution provides good details of internal architecture of masses, leading to significantly improved characterization of adnexal masses and a reliable differentiation between benign and malignant ones. Moreover the near-isotropic imaging possible with a 64 slice MDCT enabled the acquisition of high resolution multiplanar and 3D-reconstructed images. These acquisitions added to the detection of additional findings like ascites, invasion of pelvic viscera and pathological lymph nodes which further substantiated the confidence of readers in the diagnosis of malignancy. The ability to perform these thin section scans and reformatted images in different planes with spatial resolution similar to the original scanning plane has provided MDCT a pivotal role in staging and planning of further surgical management.

There are myriad types of ovarian masses and CT appearances vary widely. Accurate histologic characterization is thus not always possible however some tumors have certain radiologic features which predominate and knowledge of these key findings may help in reaching a specific diagnosis.

We in our study reported a diagnostic accuracy of 90.5% and 96% respectively by reader A and B. These findings are comparable to those reported in literature (Kinkel et al., 2005; Gatreh et al., 2011).There were few false negative and false positive cases in this study. The presence of ascites in a post-menopausal patient with associated adnexal mass implicates possibility

of malignancy. The presence of these findings made it difficult to exclude malignancy leading to false positives. Cysts smaller than 4 cm containing smooth non enhancing internal septations is a characteristic of benign lesion, however few such cases turned out to be mucinous adenocarcinomas on histopathology in our study population. Previously studies (Tsili et al., 2008; Adel et al., 2011; Satoh et al., 2011) have been carried out on same topic; however no interobeserver agreement was calculated.

This study had a few limitations as well. First, all the patients sent for MDCT were included in the study which could result in selection bias. Patient population for ovarian lesions were relatively small.

In conclusion, based on our study we can conclude that MDCT is a reliable imaging modality in diagnosis of ovarian masses accurately and with insignificant interobserver variability.

References

Adel El-Badrawy, Eman O, Ashraf K, Mohamed A, Adel H (2011). 64 Multidetector CT with multiplanar reformation in evaluation of bilateral ovarian masses. *Egypt J Radiology and Nuclear Medicine*, **42**, 147-5

Buy JN, Ghossain MA, Sciot C, Bazot M, Guinet C (1991). Epithelial tumors of the ovary: CT findings and correlation with US. *Radiolog*, **178**, 811-8.

Droegumueller W (1994). Screening for ovarian carcinoma: hopeful and wishful thinking. *Am J Obstet Gynecol*, **170**, 1095-8.

Ferozabadi RD, Zarchi MK, Mansurian HR, Mogliadam BR, Teimoori S (2000). Evaluation of diagnostic value of CT scan, physical examination and ultrasound based on the pathological findings in patients with pelvic masses. *Asian Pac J Cancer Prev*, **12**, 1745-7.

Gatreh-Samani F, Tarzamni MK, Olad-Sahebmadarek E, Dastranj A, Afrough A (2011). Accuracy of 64-multidetector computed tomography in diagnosis of adnexal tumors. *J Ovarian Res*, **4**, 15

Herrmann UI Jr, Locher GW, Goldhirsh A (1987). Sonographic patterns of ovarian tumors: prediction of malignancy. *Obstet Gynecol*, **69**, 777-81.

Jacobs I, Bast RC Jr (1989). The CA 125 tumor-associated antigen: a review of the literature. *Hum Reprod*, **4**, 1-12.

Kinkel K, Lu Y, Mehdizade A, Pelte MF, Hricak H (2005). Indeterminate ovarian mass at ultrasound: incremental value of second imaging test for characterization-meta analysis and Bayesian analysis. *Radiology*. **236**, 85-94.

Kombächer P, Hamm B, Becker R, et al (1992). Tumors of the adnexa: a comparison of magnetic resonance tomography, endosonography and the histological findings [Original article in German, English version available]. *Rofo Fortschr Geb Röntgenstr Neuen Bildgeb Verfahr*, **156**, 303-8.

Koonings PP, Campbell K, Mishell DR Jr, Grimes DA (1989). Relative frequency of primary ovarian neoplasms: a 10- year review. *Obstet Gynecol*, **74**, 921-6.

Kurtz AB, Tsimikas JV, Tempany CM, Hamper UM, Arger PH et al (1999). Diagnosis and staging of ovarian cancer: comparative values of doppler and conventional US, CT, and MR imaging correlated with surgery and histopathologic analysis - report of the radiology diagnostic oncology group. *Radiology*, **212**, 19-27

Landis SH, Murray T, Bolden S, Wingo PA (1998). Cancer statistics. *Cancer*, **47**, 6-29.

Mugel T, Ghossain M, Buy JN, Malbec L, Vadrot D (1993). Value of CT scan and MRI in primary tumors of the ovary. *J Chir (Paris)*, **130**, 486-91.

Nagell JR, Higgins RV, Donaldson E (1990). Transvaginal sonography as a screening method for ovarian cancer: a report of the first 1000 cases screened. *Cancer*, **65**, 573-7.

Osmers R (1996). Sonographic evaluation of ovarian mass and its therapeutical implications. *Ultrasound Obstet Gynecol*, **175**, 428-34.

Outwater EK, Dunton C (1995). Imaging of the ovary and adnexa: clinical issues and applications of MR imaging. *Radiology*, **194**, 1-18.

Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108

Parrish FJ (2007). Volume CT: state-of-the-art-reporting. *Am J Roentgenol*, **189**, 528-34.

Sengupta PS, Shanks JH, Buckley CH (2000). Requirement for expert histopathological assessment of ovarian cancer and borderline tumors. *Br J Cancer*, **82**, 760-2.

Silverberg E, Boring CC, Squires TS (1990). Cancer statistics. *Cancer*, **40**, 9-26.

Spencer JA (2005). A multidisciplinary approach to ovarian cancer at diagnosis. *Br J Radiol*, **78**, 94-102.

Tanwani AK (2005). Prevalence and pattern of ovarian lesions. *Ann Pak Inst Med Sci*, **1**, 211-4.

Taylor K, Schwartz P (1994). Screening for ovarian cancer. *Radiology*, **192**, 1-10.

Tempany CM, Zou KH, Silverman SG, Brown DL, Kurtz AB (2000). Staging of advanced ovarian cancer: comparison of imaging modalities--report from the radiological diagnostic oncology group. *Radiology*, **215**, 761-7.

Teneriello MG, Park RC (1995). Early detection of ovarian cancer. *CA Cancer J Clin*, **45**, 71-87.

Tsili AC, Tsampoulas C, Argyropoulou M, et al (2008). Comparative evaluation of multidetector CT and MR imaging in the differentiation of adnexal masses. *Eur Radiol*, **18**, 1049-57.

Tsili AC, Tsampoulas C, Argyropoulou M, et al (2008). Comparative evaluation of multidetector CT and MR imaging in the differentiation of adnexal masses. *Eur Radiol*, **18**, 1049-57

Woodward PJ, Hosseinzadeh K, Saenger JS (2004). Radiologic staging of ovarian carcinoma with pathologic correlation. *Radiographics*, **24**, 225-46