doi: 10.13241/j.cnki.pmb.2017.02.018

计算机辅助超声诊断提高卵巢癌诊断的准确性 *

杨 娜[1] 韩燕燕[1△] 张梅娜[1] 张英涛[2] 宫丽华[1] 曲延峻[1]

(1 哈尔滨医科大学附属第一医院妇产超声科 黑龙江 哈尔滨 150001;2 哈尔滨工业大学计算机学院 黑龙江 哈尔滨 150001)

摘要 目的:评估应用计算机辅助阴式超声诊断卵巢癌是否优于单独阴式超声诊断。**方法:**收集 2013 年 9 月 -2015 年 3 月在我院进行手术切除的卵巢肿块患者的术前阴式超声(TVS)图像资料,共 124 例(病理诊断良性 80 例,恶性 44 例),平均年龄 54.2± 9.7 岁。建立的图像样本库,每名患者取 4 幅超声图像,共有 496 幅图像被分析。首先对图片库内的超声图像进行多模式序列超声识别系统的处理,应用灰度共生矩阵法,获得肿块的各种特征,将感兴趣区域分类为正常组织,良性肿块和恶性肿瘤。两名超声医生人工肉眼对卵巢肿块的原始阴式超声图片进行分析诊断,随后两名医师对计算机辅助诊断(CAD)处理后的图片再次分析诊断,以病理诊断为金标准,利用 ROC 曲线下肿块区域的面积参数评价单独 TVS 和 TVS 结合 CAD 诊断卵巢癌的准确度差异。比较应用 CAD 前后的特异性、敏感性、阳性预测值,阴性预测值等指标的差异。**结果:**TVS 结合 CAD 诊断准确度高于单独 TVS,单独 TVS 诊断 ROC 曲线下面积(Az)为 0.791,95%可信区间 [0.725-0.857], TVS 结合 CAD 诊断 Az 为 0.927,95%可信区间[0.883-0.970]; TVS 结合 CAD 组诊断卵巢癌的精确度(0.774 vs 0.919,P<0.05)、特异性(0.738 vs 0.933,P<0.05)及阳性预测值(0.650 vs 0.889,P<0.05)较单独 TVS 诊断明显提高。**结论:**计算机辅助诊断技术可以辅助超声医师提高卵巢癌诊断的准确度。

关键词:卵巢癌的诊断;阴式超声;计算机辅助诊断

中图分类号:R737.3;R445 **文献标识码:**A **文章编号:**1673-6273(2017)02-276-04

A Computer-Aided Diagnostic Algorithm can Improve Accuracy in Diagnosis of Ovarian Cancer*

YANG Na[1], HAN Yan-yan[1△], ZHANG Mei-na[1], ZHANG Ying-tao[2], GONG Li-hua[1], QU Yan-jun[1]

(1The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, 150001, China;

2 School of Computer Science and Technology, Harbin Institute of Technology, Harbin, Heilongjiang, 150001, China)

ABSTRACT Objective: We compared the efficacy of the transvaginal sonography (TVS) assisted with a computer-aided diagnostic (CAD) algorithm to it of TVS in discriminating the benign tumor from malignant adnexal masses. **Methods:** Women (n=124, with pathological diagnosis of benign 80 cases and malignant 44 cases) scheduled for surgical removal of at least one ovary and had TVS image data in First Affiliated Hospital of Harbin Medical University during from September, 2013 to March, 2015. The average ages of the patients are 54.2± 9.7 years. We established the image database. In total, 496 images were acquired, and 4 images of each case were chosen for image processing. We used the multi-mode ultrasound sequence recognition system to reanalyze the images, applicated gray co-occurrence matrix method to obtain tumor texture features of the region of interest (ROI) and to classify the ROI as normal tissue, benign tumors and malignant tumors, then we compared the accuracy of diagnosis of ovarian cancer TVS group and TVS+ CAD group which are executed by 2 ultrasound doctors. The mean area under the ROC curve (Az) was preformed to evaluate the diagnostic accuracy using pathological diagnosis as the gold standard. Furthermore, the comparing parameters we calculated are include the accuracy, the specificity, the sensitivity, the positive predictive value, and the negative predictive value within before and after application of CAD. **Results:** The diagnostic accuracy was improved after CAD application compared to TVS alone, ROC area under the curve (Az) was 0.791 [95% CI 0.725-0.857] in TVS alone, and 0.927 [95% CI 0.883-0.970] in TVS+ CAD; Comparing TVS and TVS+ CAD ,the accuracy (0.774 vs 0.919, P<0.05), the specificity (0.738 vs 0.933, P<0.05) and the positive predictive value (0.650 vs 0.889,P<0.05) were significantly improved. **Conclusions:** The CAD algorithm is significantly useful to improve the diagnostic accuracy in Ovarian cancer and decrease false negative rates.

Key words: Ovarian cancer diagnosis; Transvaginal sonography(TVS); Computer-aided diagnosis (CAD)

Chinese Library Classification(CLC): R737.3; R445 Document code: A

Article ID: 1673-6273(2017)02-276-04

* 基金项目:黑龙江省卫生厅科研课题(2013013)

作者简介:杨娜(1982-),硕士,主治医师,主要研究方向:妇科肿瘤的超声诊断,E-mail:984yangnasunny@163.com

△通讯作者:韩燕燕(1960-),学士,副主任医师,主要研究方向:妇科肿瘤的超声诊断,电话:13674618904,E-mail:circulation0311@163.com

(收稿日期:2016-08-09 接受日期:2016-09-02)

前言

在妇科肿瘤中，卵巢癌是首要的致死病因，容易转移，预后相对差，而且早期多无症状不易发现。近年来其发病呈上升趋势，高病死率已经在很大程度上被归结为一个事实，即确诊时多数卵巢癌已是晚期阶段（≥ III 期）。如何早期诊断并给与合理干预，取决于对附件肿块的精确鉴别诊断，恶性肿瘤建议肿瘤专科医院治疗，良性肿块则由普通妇产科医生处理[1,2]。近年超声影像技术飞速发展，超声对于诊断妇科肿瘤的价值已得到肯定，但仍然存在很多亟待解决的问题[3-5]。主要表现在：① 对仪器成像质量的依赖；② 超声医生的诊断还是依靠主观判断，做出的诊断结果势必因会受到医生经验以及专业知识水平影响；③ 当患者量较大时候，超声医生很容易因为劳累疲劳等原因遗漏掉某些细微的改变；④ 良恶性声像图特征存在交叉。故亟需探索准确、有效、快速的检查手段。医学图像的计算机辅助分析的方法应运而生，计算机辅助诊断（CAD）的主要优点是数据处理迅速，检查结果一致性好、可重复性高，能够给出比较客观、准确的辅助诊断意见，可以明显主观原因引起的漏误诊，如减少因年轻医生经验不足或者是视觉疲劳等，CAD 辅助超声诊断就更为准确更为科学。这与目前卵巢肿瘤阴式超声（TVS）诊断中亟待解决的问题不谋而合，本研究拟应用计算机辅助诊断技术辅助超声医师以提高卵巢癌诊断的准确性。

1 资料与方法

1.1 临床资料

收集 2013 年 9 月 -2015 年 3 月在我院进行手术治疗的卵巢肿瘤患者的术前超声检查图像资料，共 124 例，（其中病理诊断良性 80 例，恶性 44 例），平均年龄 54.2± 9.7 岁。观察并记录肿块的大小、形态，边界，肿块内部回声，是否有囊壁，囊壁的厚度，囊壁是否光滑等，所获得的满意图片建立图像样本库，每名患者取 4 幅超声图像，共有 496 幅图像被分析。

1.2 方法

所有超声图片由 GE Voluson E8 三维超声诊断仪（阴式探头，频率在 7.5-12 MHz）获取，按孙等[6]所用图像处理方法，对图片库内的超声图像进行多模式序列超声识别系统的处理，采用人工手动勾勒感兴趣区大致位置，结合基于主动轮廓技术的图像分割的方法来获取图像中的肿块位置，应用灰度共生矩阵法，采用 5 种统计分量（能量、对比度、相关、熵和同一性）获得肿块的各种纹理特征，将感兴趣区域分类为正常组织，良性肿块和恶性肿瘤。两名超声医生人工肉眼对卵巢的原始超声图片进行分析，并不告知患者的临床资料及病理结果，按照卵巢肿瘤的诊断标准进行诊断，随后两名超声医师对计算机处理后的图片再次分析得出诊断，以病理诊断为金标准，比较两名超声医生应用计算机辅助诊断技术前后准确度差异，比较应用计算机辅助阴式超声和单独阴式超声在诊断卵巢癌的特异性、敏感性、阳性预测值和阴性预测值等指标的差异。

1.3 统计学分析

统计学方法计量资料以均数± 标准差表示，计数资料以百分率表示。ROC 曲线用来判断超声医师诊断的准确度。单独 TVS 诊断与 TVS 结合 CAD 诊断的精确度、敏感性、特异性、阳性预测值及阴性预测值差异采用卡方检验。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 患者特征

纳入本研究的患者特点见表 1 总结。研究的 124 例附件肿块切除患者中，以中年绝经期妇女为多（71%），且多数因发现症状性包块而就医，近半数就医患者肿瘤标志物 CA125 阳性，本组患者最终病理证实恶性 44 例，良性 80 例。

表 1 患者特征

Table 1 Patient characteristics

Variable	n=124
Age (year)	54.2± 9.7
Menopausal (yes/no)	88/36
CA125（≥ 35/＜35）	57/67
Reason for surgery	
Symptomatic adnexal mass	77(62%)
Asymptomatic discovered at gynaecological examination/TVS	47(38%)
Adnexal mass pathology (benign / Malignant)	80/44

2.2 应用 CAD 前后 ROC 曲线比较

我们比较了应用 CAD 前后 ROC 曲线，分别为 TVS 单独诊断（TVS），TVS 结合 CAD 诊断（TVS+CAD），见图 1、表 2。从图中可以看出，TVS+CAD 的诊断准确度要高于单独 TVS。我们又计算了应用 CAD 前后的 ROC 曲线下面积（Az），其中 TVS：A1=0.791，95%可信区间[0.725-0.857]；TVS+CAD：A2=0.927，95%可信区间[0.883-0.970]。

2.3 敏感性特异性等分析

我们比较单独 TVS，TVS 结合 CAD 的精确度、敏感性、特异性、阳性预测值和阴性预测值，见表 3。当应用 CAD 技术后，大多数诊断指标都有显著提升。五个指标的平均值分别如下，TVS：① 精确度 0.774；敏感性：0.887；特异性：0.738；阳性预测值：0.650；阴性预测值：0.922。② TVS+CAD：精确度 0.919；敏感性：0.909；特异性：0.936；阳性预测值：0.889；阴性预测值：0.949。在这五个指标中，应用 CAD 后，精确度、特异性和阳性预测值明显提升（TVS+CAD vs TVS，均 $P<0.05$），而敏感性、阴性预测价值提升不明显（TVS+CAD vs TVS，均 $P>0.05$）。

3 讨论

卵巢癌可见于所有年龄的妇女。为了优化卵巢癌的管理，避免不必要的诊断程序，术前超声鉴别非常重要，近年阴式超声广泛用于卵巢肿瘤的检查。但阴式超声的局限是其高的假阳性检测率，多个中心荟萃分析显示假阳性率高达 17%（95%可信区间：12-24%）。许多方法尝试提高阴式超声的敏感性和特异性，包括使用形态评分系统[7,8]或通过形态学与超声定量分析[9,10]组合，但这些方法作用有限。在本研究中，我们参考孙等[6]，应用形态重组和动态分析序列图像等计算机算法，评估计算机

表 2 应用 CAD 前后 ROC 曲线分析

Table 2 Az of radiologists' diagnosis before and after CAD

	Az	P value	SE	95%CI
TVS	0.79	<0.001	0.034	0.725-0.857
TVS+CAD	0.927	<0.001	0.022	0.883-0.970

注:TVS:TVS 单独诊断;TVS+CAD:TVS 结合 CAD 诊断。

Note: TVS: Diagnosis with TVS alone,TVS+CAD : Diagnosis with TVS assisted with CAD. SE: Standard Error, CI: Confidence Interval.

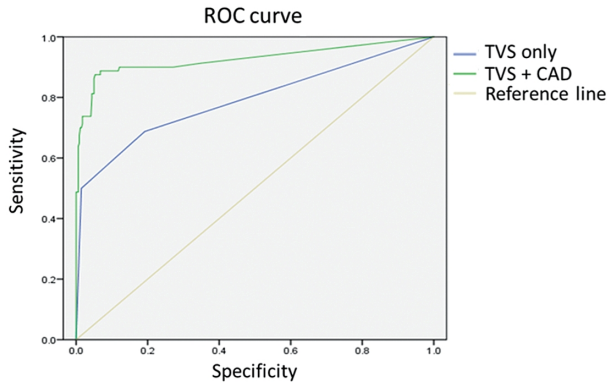

图 1 TVS, TVS+CAD 的 ROC 曲线分析

Fig. 1 Receiver operating characteristic curves for radiologists using TVS alone, and TVS assisted with CAD

重大临床研究价值。现阶段 CAD 研究比较成熟的主要是是在肺部疾病[11,12]和乳腺疾病[13,14]两个方面,国内外医学家专家在该领域业已并取得可喜的成果;而 CAD 在虚拟腔镜[15-17]、肝脏疾病[18,19]、脑部肿瘤[20]等很多方面的研究还在起步阶段,距离开发新技术应用于临床患者,可能还有很长路要走。

总之,计算机辅助阴式超声诊断卵巢癌的诊断高度敏感,同时保持良好的特异性,是盆腔肿块的非侵入性检查的一个行之有效的手段。计算机辅助诊断可以充分利用所获取的临床影像资料将数据量化,可以去除人为的主观因素,能够最大限度的避免因为个人专业知识和经验的差异所导致的临床偏倚;因此它的结果更为准确、更为科学,具有广阔的临床应用前景。

表 3 应用 CAD 前后的精确度、敏感性、特异性、阳性预测值和阴性预测值

Table 3 Accuracy, sensitivity, specificity, PPV and NPV before and after CAD

	Accuracy	Sensitivity	Specificity	PPV	NPV
TVS	0.774(96/124)	0.887(39/44)	0.738(59/80)	0.650(39/60)	0.922(59/64)
TVS+CAD	0.919(114/124)*	0.909(40/44)	0.936(75/80)*	0.889(40/45)*	0.949(75/79)

注:精确度 = (TP+TN)/(TP+TN+FP+FN);敏感性 =TP/(TP+FN);特异性 =TN/(TN+FP);阳性预测值(PPV)=TP/(TP+FP);阴性预测值(NPV)=TN/(TN+FN)。FN,假阴性病例数;FP,假阳性病例数; TN,真阴性病例数;TP,真阳性病例数。* 与 TVS 比较,P<0.05。

Note: Accuracy = (TP + TN)/(TP + TN + FP + FN); sensitivity = TP/(TP + FN); specificity= TN/(TN + FP); positive predictive value (PPV) = TP/(TP + FP); negative predictive value (NPV) = TN/(TN + FN). FN, false negatives; FP, false positives; TN, true negatives; and TP, true positives. *compared to TVS, P<0.05.

辅助阴式超声诊断的的精确度、敏感性、特异性、阳性预测值和阴性预测值,发现 CAD 结合阴式超声诊断卵巢癌的精确度、特异性、阳性预测值均优于单独阴式超声诊断,说明计算机辅助诊断技术可以辅助超声医师提高卵巢癌诊断的准确度,减少假阳性率。

超声诊断的准确性不仅依赖超声仪器的先进,更依赖于超声医师的临床经验。在操作相同超声仪器的前提下,高年资的超声医生的临床诊断的误诊率往往低于低年资医生。对于低年资医生来说,这种差异是不可避免的。但即使是具有丰富经验的超声医生,由于繁重的临床工作,过度疲劳,注意力下降等因素仍然使误诊、漏诊事件时有发生。计算机辅助诊断技术对于低年资和高年资超声医生都有应用意义,对于低年资医师尤为重要。

CAD 技术与医学交叉研究自上个世纪 90 年代就已开始,近年随着计算机技术和人工神经元网络的飞速发展,这种边缘交叉学科已经成为当今医学影像领域研究的热点,具有

参 考 文 献(References)

[1] Vaes E, Manchanda R, Autier P, et al. Differential diagnosis of adnexal masses: sequential use of the risk of malignancy index and HistoScanning, a novel computer-aided diagnostic tool [J]. Ultrasound Obstet Gynecol, 2012, 39(1): 91-98

[2] Kaijser J, Sayasneh A, Van Hoorde K, et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis[J]. Hum Reprod Update, 2014, 20(3): 449-462

[3] Diane M. Twickler, ElysiaMoschos. Ultrasound and Assessmentof Ovarian Cancer Risk[J]. AJR, 2010, 194: 322-329

[4] Campbell S. Ovarian cancer: role of ultrasound in preoperative diagnosis and population screening [J]. Ultrasound Obstet Gynecol, 2012, 40(3): 245-254

[5] Testa AC, Ludovisi M, Mascilini F, et al. Ultrasound evaluation of intra-abdominal sites of disease to predict likelihood of suboptimal cytoreduction in advanced ovarian cancer: a prospective study [J].

UltrasoundObstet Gynecol, 2012, 39(1): 99-105

[6] Sun L, Li Y, Zhang YT, et al. A computer-aided diagnostic algorithm improves the accuracy of transesophageal echocardiography for left atrial thrombi: a single-center prospective study[J]. J Ultrasound Med, 2014, 33(1): 83-91

[7] Kaijser J, Sayasneh A, Van Hoorde K, et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis [J]. Hum Reprod Update, 2014, 20(3): 449-462

[8] Ferrazzi E, Zanetta G, Dordoni D, et al. Lissoni AA Transvaginal ultrasonographic characterization of ovarian masses: comparison of five scoring systems in a multicenter study [J]. Ultrasound ObstetGynecol, 1997, 10: 192-197

[9] Alcazar JL, Ruiz-Perez ML, Errasti T. Transvaginal color Doppler sonography in adnexal masses: which parameter performs best? [J]. Ultrasound ObstetGynecol, 1996: 114-119

[10] Valentin L. Prospective crossvalidation of Doppler ultrasound examination and gray-scale ultrasound imaging for discrimination of benign and malignant pelvic masses [J]. Ultrasound ObstetGynecol, 1999, 14: 273-283

[11] Kligerman S, CaiL, WCS. The effect of computer-aided detection on radiologist performance in the detection of lung cancers previously missed on a chest radiograph [J]. J Thorac Imaging, 2013, 28(4): 244-252

[12] Magalhães Barros Netto S, Corrêa Silva A, Acatauassú Nunes R, et al. Automatic segmentation of lung nodules with growing neural gas and support vector machine [J]. Comput Biol Med, 2012, 42(11): 1110-1121

[13] Moon WK, Lo CM, Chang JM, et al. Computer-aided classification of breast masses using speckle features of automated breast ultrasound images[J]. Med Phys, 2012, 39(10): 6465-6473

[14] Dromain C, Boyer B, Ferré R, et al. Computed-aided diagnosis (CAD) in the detection of breast cancer[J]. Eur J Radiol, 2013, 82(3): 417-423

[15] Mang T, Hermosillo G, Wolf M, et al. Time-efficient CT colonography interpretation using an advanced image-gallery-based, computer-aided "first-reader" workflow for the detection of colorectal adenomas[J]. Eur Radiol, 2012, 22(12): 2768-2779

[16] Cheng JZ, Ni D, Chou YH, et al. Computer-Aided Diagnosis with Deep Learning Architecture: Applications to Breast Lesions in US Images and Pulmonary Nodules in CT Scans[J]. Sci Rep, 2016, 15(6): 244-254

[17] Suzuki K. A review of computer-aided diagnosis in thoracic and colonic imaging[J]. Quant Imaging Med Surg, 2012, 2(3): 163-176

[18] S S Kumara, R S Monib, J Rajeesh. An automatic computer-aided diagnosis system for liver tumours on computed tomography images [J]. Computers & Electrical Engineering, 2013, 39(5): 1516-1526

[19] Gaurav Sethi, Barjinder S Saini. Computer aided diagnosis system for abdomen diseases in computed tomography images[J]. Biocybernetics and Biomedical Engineering, 2016, 36(1): 42-55

[20] Andrés Ortiza, Juan M Górrizb, Javier Ramírez. LVQ-SVM based CAD tool applied to structural MRI for the diagnosis of the Alzheimer's disease Pattern Recognition Letters[J]. Pattern Recognition Letters, 2013, 34(14): 1725-1733

（上接第 271 页）

[8] Heng EL , Gatzoulis MA, Babu-Narayan SV. Tailoring counselling after pulmonary valve surgery in repaired tetralogy of Fallot[J]. Heart, 2015, 101(21): 1695-1696

[9] Zhang Hui-feng, Jia Bing, Ye Ming, et al. Real-time three-dimensional echocardiographic assessment of tetralogy of fallot the value of right heart function after surgery [J]. Chinese practical pediatric clinical journal, 2014, 29(11): 825-827

[10] Downing TE, Kim YY. Tetralogy of Fallot: General Principles of Management[J]. Cardiol Clin, 2015, 33(4): 531-541

[11] Talwar S, Kumar R, Bhoje A, et al. Anatomical Repair of an Unusual Combination of Tetralogy of Fallot and Atrio ventricular Septal Defect With Unroofed Coronary Sinus[J]. J Card Surg, 2015, 30(11): 849-852

[12] Bokma JP, Winter MM, Oosterhof T, et al. Individualised prediction of pulmonary homograft durability in tetralogy of Fallot [J]. Heart, 2015, 101(21): 1717-1723

[13] Wadhawa V, Mishra A, Kothari J. Anomalous right coronary from aortopulmonary window in tetralogy of Fallot [J]. Asian Cardiovasc Thorac Ann, 2015, 23(9): 1140

[14] McCartney SL, Machovec K, Jooste EH. Uncorrected Tetralogy of Fallot, Biventricular Dysfunction, and a Large Pericardial Effusion[J]. J Cardiothorac Vasc Anesth, 2015, 29(5): 1391-1395

[15] Müller J, Hager A, Diller GP, et al. Peak oxygen uptake, ventilatory efficiency and QRS-duration predict event free survival in patients late after surgical repair of tetralogy of Fallot [J]. Int J Cardiol, 2015, 196: 158-164

[16] Boutsikou M, Uebing A Kilner P, et al. Brock procedure: 52 years of effective palliation for Tetralogy of Fallot [J]. Int J Cardiol, 2015, 19 (9): 195-196

[17] Zile MR, Gregg D. Is Biventricular Fibrosis the Mediator of Late Complications in Tetralogy of Fallot?[J]. JACC Cardiovasc Imaging, 2015, 9(1): 11-13

[18] Yao Q, Hu XH, Shen QL, et al. Differential Effect of the Ratio of Right Ventricular Volume to Left Ventricular Volume in Children with Repaired Tetralogy of Fallot[J]. Cardiology, 2016, 133 (3): 135-140

[19] Vida VL, Zucchetta F, Stellin G. Pulmonary valve-sparing techniques during repair of tetralogy of Fallot: The delamination plasty [J]. J Thorac Cardiovasc Surg, 2016. DOI: 10.1016/j.jtcvs.2016.02.015