

## Diagnostic performance of different imaging tests for ovarian tumors: Meta-analysis

WU Ying<sup>1\*</sup>, PENG Hongling<sup>2</sup>, ZHAO Xia<sup>2</sup>

(1. Department of Ultrasound, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu 610072, China; 2. Department of Gynecology and Obstetrics, West China Second Hospital, Sichuan University, Chengdu 610041, China)

**[Abstract]** **Objective** To evaluate the overall diagnostic performance of CEUS, contrast-enhanced MRI (CE-MRI), functional MRI and CT for ovarian masses. **Methods** Embase and Medline databases were systematically searched for relevant articles on the diagnosis of ovarian masses using CEUS, CE-MRI, functional MRI or CT. Data were pooled to yield summary sensitivity, specificity and the area under the SROC curve (AUC). Z-value test was performed to determine whether the diagnostic value of two independent diagnostic tests had significant difference. **Results** The pooled sensitivity of CEUS, CE-MRI, functional MRI and CT was 0.89, 0.93, 0.83 and 0.88, and the pooled specificity was 0.91, 0.90, 0.79 and 0.91, as well as the AUC was 0.9619, 0.9710, 0.9090 and 0.9444, respectively. The results of Z-test revealed there were no significant differences in diagnostic performance between CEUS, CE-MRI and CT, and the diagnostic performance of functional MRI were significant inferior to that of CEUS or CE-MRI. **Conclusion** CEUS, CE-MRI, functional MRI and CT all have high diagnostic performance in diagnosis of malignant ovarian tumors, with their advantages and limitations.

**[Key words]** Contrast-enhanced ultrasound; Magnetic resonance imaging; Tomography, X-ray computed; Ovarian neoplasms; Meta-analysis

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## 不同影像学检查诊断卵巢肿瘤:Meta分析

吴 莹<sup>1\*</sup>,彭鸿灵<sup>2</sup>,赵 霞<sup>2</sup>

(1. 四川省医学科学院 四川省人民医院超声科,四川 成都 610072;  
2. 四川大学华西第二医院妇产科,四川 成都 610041)

**[摘要]** **目的** 评价CEUS、增强MRI、功能性MRI和CT对卵巢肿瘤的诊断价值。**方法** 检索Embase、Medline数据库,收集关于CEUS、增强MRI、功能性MRI及CT诊断卵巢肿瘤的文献资料。进行统计分析得到各组诊断性试验的合并敏感度、特异度及SROC曲线下面积(AUC)。采用Z检验比较组间独立诊断试验的诊断效能。**结果** CEUS、增强MRI、功能性MRI和CT诊断卵巢恶性肿瘤的合并敏感度分别为0.89、0.93、0.83和0.88;合并特异度分别为0.91、0.90、0.79和0.91。四组影像学方法的AUC值分别为0.9619、0.9710、0.9090和0.9444。Z检验结果显示:CEUS、增强MRI、CT三者的诊断效能差异无统计学意义( $P>0.05$ );功能性MRI的诊断效能低于CEUS和增强MRI( $P$ 均 $<0.05$ )。**结论** CEUS、增强MRI、功能性MRI和CT四种影像学方法对卵巢恶性肿瘤均具较高的诊断效能,对卵巢肿瘤的诊断各有优势和不足。

**[关键词]** 超声造影;磁共振成像;体层摄影术,X线计算机;卵巢肿瘤;Meta分析

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**[第一作者]** 吴莹(1977—),女,四川成都人,博士,副主任医师。研究方向:妇产科超声。

**[通信作者]** 吴莹,四川省医学科学院 四川省人民医院超声科,610072。E-mail: wuyingxiongxiong@163.com

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卵巢癌是致死率最高的妇科恶性肿瘤,因缺乏有效的早期诊断方法,约70%的患者发现时已属晚期<sup>[1]</sup>。应用影像学方法更早更准确地评估卵巢肿瘤的良恶性,有助于患者治疗方案的选择及预后改善。尤其是针对初次影像学检查或临床检查疑似恶性的卵巢包块,如何通过更精确地影像学检查方法帮助妇科医生对这部分患者作出更全面综合的临床决策一直是影像学研究的重点。本研究通过Meta分析,比较CEUS、传统增强MRI、功能性MRI[包括动态对比增强磁共振成像(dynamic contrast-enhanced MRI, DCE-MRI)、DWI及MRS]、CT对初期检查疑似恶性的卵巢肿瘤的诊断价值,旨在为临床医生应用这些技术得到更多地诊断信息、做出效益最大化的选择,提供有力的信息。

## 1 资料与方法

1.1 文献检索 检索 Embase、Medline数据库,辅以文献追溯、手工检索等方法,收集公开发表的关于CEUS、增强MRI、功能性MRI及CT诊断卵巢肿瘤的文献资料。检索年限截止至2014年12月31日,以人类为研究对象,语言限制为英文。检索词为:“ovarian/adnexal”,“neoplasm/carcinoma/tumor/cancer/mass/lesion”,“contrast enhanced/contrast media/contrast agent”,“ultrasound/ultrasonography/sonography”,“magnetic resonance”,“computed tomography”,“sensitivity/specificity/accuracy/diagnostic value”。

1.2 文献选择 纳入标准:①文献是关于采用CEUS、增强MRI、功能性MRI、CT鉴别诊断卵巢良性肿瘤,卵巢肿瘤为初次影像学检查或临床检查疑似恶性的卵巢包块;②诊断“金标准”为组织病理学结果或临床综合诊断;③可提取诊断试验四格表数据;④病例数≥20;⑤QUADAS评分≥11分;⑥数据无重复发表。排除标准:①综述、病例报道、信件及述评类文献;②对同一医学中心或同一作者发表的有重复数据的文献,只纳入样本量最大者。

1.3 文献质量评价 采用诊断性试验准确性质量评价(the Quality Assessment of Diagnostic Accuracy Studies, QUADAS)工具<sup>[2]</sup>评价文献质量及发生偏移的可能性,评分≥11分,则认为研究具有较高的方法学质量,存在偏倚的可能性较低。

1.4 资料提取 提取每篇纳入文献的第一作者、发表时间、国籍、患者的平均年龄、设计类型、影像学诊断方法、QUADAS评分、病灶数、诊断试验四格表数据等。

1.5 统计学分析 文献选择、质量评价、资料提取均由2位研究者独立进行,有分歧时由第3位研究者通过讨论协助解决。对所有数据采用Meta-Disc 1.4和STATA 12.0软件进行分析。 $P<0.05$ 为差异有统计学意义。

1.5.1 异质性检验 采用Q检验和 $I^2$ 统计量进行异质性检验( $P<0.1$ 为有统计学意义)。对诊断阈值效应的检验,采用ROC平面散点图和Spearman相关系数。

1.5.2 合并效应量并绘制SROC曲线 采用随机效应模型或固定效应模型,得到合并的敏感度、特异度及相应95%可信区间;拟合汇总受试者工作特征曲线(SROC曲线),获得SROC曲线下面积(area under curve, AUC)。通过AUC值评价、比较诊断试验的诊断效能, $AUC>0.9$ ,表示诊断价值较高。采用Z检验比较组间独立诊断试验的准确性。

1.5.3 Meta回归分析 将CEUS组造影剂种类(第一代vs第二代)和声学诊断标准(TIC曲线定量分析vs血管形态学定性分析)作为自变量,将增强MRI组文献发表年限(2000年前vs2000年及2000年后)作为自变量,进行Meta回归分析。

1.5.4 发表偏倚分析 使用Deeks漏斗图评估发表偏倚。

## 2 结果

2.1 纳入文献基本特征 共纳入合格文献45篇。CEUS组纳入文献10篇<sup>[3-12]</sup>,579个病灶,9篇前瞻性研究<sup>[3-6,8-12]</sup>,1篇回顾性研究<sup>[7]</sup>,发表年限2000—2013年。主要有2种声学诊断标准,即TIC曲线定量分析<sup>[5-7,9,11]</sup>和血管形态学定性分析<sup>[3-4,8,10,12]</sup>。使用2代造影剂,即第一代造影剂Leovis<sup>[4,9-12]</sup>和第二代造影剂(SonoVue和Definity)<sup>[3,5-8]</sup>。增强MRI组纳入文献17篇<sup>[13-29]</sup>,1473个病灶,12篇前瞻性研究<sup>[14-20,23,24,26,28-29]</sup>,4篇回顾性研究<sup>[13,21,25,27]</sup>,1篇文献设计类型不详<sup>[22]</sup>,发表年限1991—2014年,其中2000年前发表文献6篇<sup>[17,21-22,24-25,28]</sup>,2000年及2000年后发表文献11篇<sup>[13-16,18-20,23,26-27,29]</sup>。功能性MRI组纳入文献11篇<sup>[30-40]</sup>(DCE-MRI3篇<sup>[30,37,39]</sup>、DWI7篇<sup>[31,33-36,38,40]</sup>和MRS1篇<sup>[32]</sup>),912个病灶,4篇前瞻性研究<sup>[32-33,35,38]</sup>,6篇回顾性研究<sup>[30-31,34,36-37,40]</sup>,1篇文献设计类型不详<sup>[39]</sup>,发表年限2008—2014年。CT组纳入文献7篇<sup>[26,35,41-45]</sup>,947个病灶,5篇前瞻性研究<sup>[26,35,41-42,44]</sup>,2篇回顾性研究<sup>[43,45]</sup>,发表年限1991—2014年。所有纳入文献的QUADAS评分均≥11分。

**2.2 统计学分析结果** 异质性检验:CEUS组各研究间敏感度( $I^2 = 50.8\%$ ,  $P = 0.03$ )和特异度( $I^2 = 82.1\%$ ,  $P < 0.01$ )均存在明显异质性;增强MRI组各研究间特异度( $I^2 = 74.0\%$ ,  $P < 0.01$ )存在明显异质性,敏感度( $I^2 = 46.2\%$ ,  $P = 0.02$ )不存在明显异质性;功能性MRI组各研究间敏感度( $I^2 = 87.0\%$ ,  $P < 0.01$ )和特异度( $I^2 = 75.2\%$ ,  $P < 0.01$ )均存在明显异质性;CT组各研究间特异度( $I^2 = 91.0\%$ ,  $P < 0.01$ )存在明显异质性,敏感度( $I^2 = 39.4\%$ ,  $P = 0.13$ )不存在明显异质性。四组影像学方法ROC平面散点图均呈非典型的“肩袖型”,不存在阈值效应( $P > 0.05$ )。

四组影像学方法诊断指标汇总结果见表1、图1~4。Z检验结果显示:CEUS、增强MRI、CT三者的诊断效能差

异无统计学意义( $P > 0.05$ );功能性MRI的诊断效能低于CEUS和增强MRI( $P$ 均 $< 0.05$ )。

Meta回归分析结果显示,CEUS组造影剂种类( $P = 0.49$ )和声学诊断标准( $P = 0.76$ ),增强MRI组文献发表年限( $P = 0.82$ ),不存在研究间异质性。

Deeks'漏斗图结果显示,CEUS组( $P = 0.33$ )、功能性MRI组( $P = 0.95$ )、CT组( $P = 0.47$ )纳入的研究发表偏倚不明显;增强MRI组纳入的研究存在发表偏倚( $P = 0.02$ )。

### 3 讨论

CEUS是在常规超声检查的基础上,应用声学造影剂在微血管床灌注的基础上使组织和器官显影增强的影像学检查技术,其显著提高了超声对卵巢肿瘤微血管及微循环的探测能力,能够更准确地评估卵巢肿瘤血管形态分布及循环灌注特点,为卵巢肿瘤的诊断提供了新的机会,具有经济、无创伤、无放射辐射损害、操作简便、实时动态、不良反应少等特点。传统MRI具有良好的软组织分辨率及空间分辨率,具有

多序列、多平面和多方位成像特点,能够清晰地显示卵巢肿块的来源、部位、形态、内部成分以及是否侵犯周围脏器等,对卵巢肿瘤良恶性鉴别诊断、分期诊断及制定手术方案具有重要意义。近年来,随着MRI技术的发展,功能性MRI,如DCE-MRI、DWI及MRS等,得到越来越广泛地应用,为卵巢肿瘤的诊断提供了新的思路和方法。DCE-MRI可从血流动力学角度反映卵巢肿瘤的微循环<sup>[37]</sup>。DWI可反映卵巢肿瘤内水分子的扩散运动及变化情况,MRS可无创分析卵巢肿瘤代谢物浓度的变化,使MRI对人体的研究深入至细胞分子水平<sup>[32,34]</sup>。传统增强MRI可对卵巢肿瘤进行较为客观、准确地评估,而DCE-MRI、DWI和MRS等功能

表1 四组影像学方法诊断指标汇总结果

影像学方法	敏感度	特异度	AUC
CEUS( $n=10$ )	0.89(0.83~0.94)	0.91(0.88~0.93)	0.9619
增强MRI( $n=17$ )	0.93(0.90~0.95)	0.90(0.88~0.92)	0.9710
功能性MRI( $n=11$ )	0.83(0.79~0.86)	0.79(0.75~0.83)	0.9090
CT( $n=7$ )	0.88(0.83~0.91)	0.91(0.88~0.93)	0.9444

注:括号内数据为95%可信区间

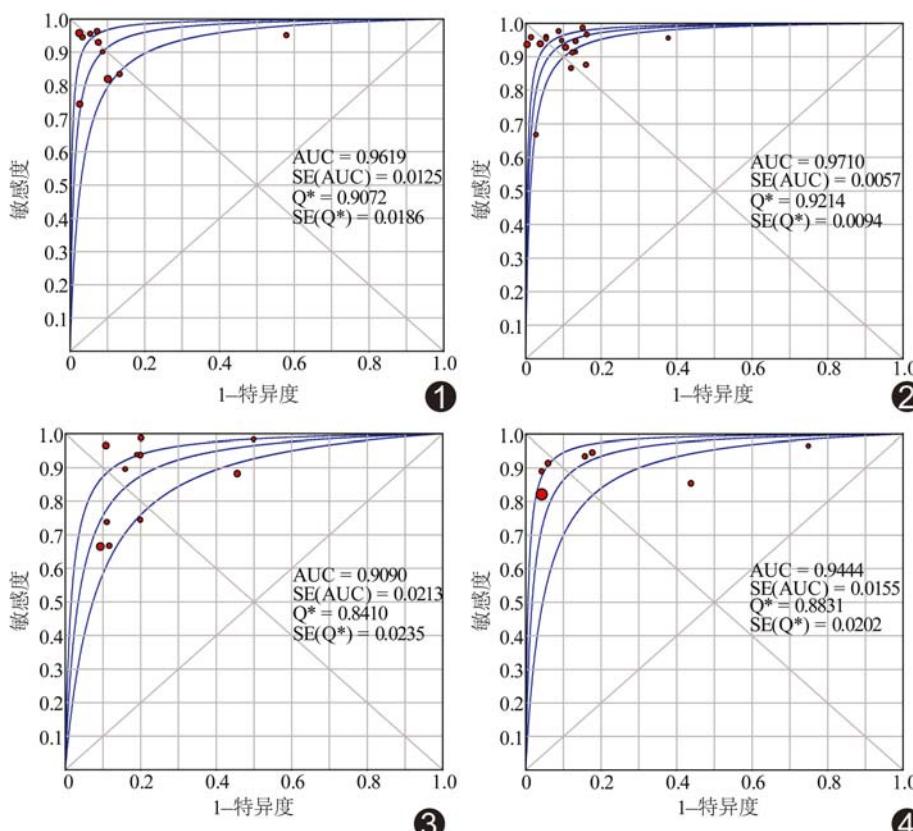


图1 CEUS组SROC曲线  
图2 增强MRI组SROC曲线  
图3 功能性MRI组SROC  
图4 CT组SROC曲线

成像技术能提供形态学以外的生物学信息及功能参数,为卵巢肿瘤良恶性鉴别诊断及病理类型分析提供了新的可能。CT具有较好的断层解剖功能和组织对比,能够较清楚地显示卵巢肿瘤位置、大小、形态、内部结构及与周围邻近组织器官的关系。

综合分析本研究结果,四组影像学方法对卵巢恶性肿瘤的诊断效能及各自的优势和不足如下:①CEUS、增强MRI、功能性MRI和CT对卵巢恶性肿瘤均具较高的诊断效能。②CEUS作为卵巢肿瘤诊断的一项新技术,是实时显示组织微循环灌注的最佳影像学技术,有利于早期发现卵巢恶性肿瘤,具有经济、操作简便和不良反应少的特点,可以作为可疑卵巢肿瘤影像学检查的优选方法;不足主要体现在对肿瘤周边组织有无侵犯及有无远处转移判断较差。③功能性MRI能够提供形态学以外的生物学信息及功能参数,使MRI对人体的研究深入至细胞分子水平,是诊断卵巢肿瘤最有应用潜力的影像学方法,可以做为常规MRI的有益补充,为从形态学上难以鉴别的卵巢肿瘤提供有价值的信息。但是目前研究资料有限,有待增大样本量进一步探讨其在卵巢肿瘤诊断方面的应用。④传统增强MRI,技术较成熟,具有良好的软组织分辨力及空间分辨力,在卵巢肿瘤鉴别诊断、分期及手术方案制定方面具有重要作用;不足主要体现在检查费用高、操作困难和对比剂不良反应。⑤CT作为一项传统技术,对卵巢恶性肿瘤亦具有较高的诊断效能,但由于其操作不如CEUS简便且能实时观察肿瘤微循环,空间分辨力及软组织分辨力不及MRI,且具有辐射,因此不作为卵巢肿瘤良恶性鉴别诊断的首选方法。

本研究文献检索、资料提取以及文献质量评价均由2名研究者独立进行,进行了全面地文献检索和详细的资料提取,所有纳入文献的QUADAS评分均≥11,表明纳入研究均具有较高的方法学质量,存在偏倚的可能性较低。

本研究存在的不足:①各组纳入的研究间存在异质性,虽进行了Meta回归分析,但仍不能完全解释和处理研究间的异质性。②一些影像学领域的新技术,如CEUS、DCE-MRI、DWI、MRS等,存在研究样本量不足、缺乏统一的检测方法和诊断标准等问题,需要更多高质量大样本量的试验进一步深入研究。③仅检索了公开发表的文献,阳性结果文献更易于发表,有可能有一些阴性结果的文章未被刊出,导致文章发表偏倚,在一定程度上可能高估了诊断试验的诊断效能。

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## Extraskeletal myxoid chondrosarcoma in right lower extremity: Case report 右下肢骨外黏液样软骨肉瘤1例

李方燕,王波,王红

(贵州医科大学附属医院影像科,贵州 贵阳 550004)

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[关键词] 骨外黏液样软骨肉瘤;下肢

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图1 右下肢骨外黏液样软骨肉瘤 A. CT平扫示右侧大腿根部肌间隙内见浅分叶状稍低密度团块影,内见斑片状稍高密度影(箭);B. CT增强扫描示肿块强化不均匀,内见条片状强化影(箭);C. 病理检查(HE,×100)示肿瘤细胞呈圆形或短梭形(黑箭),呈网格状、带状或假滤泡状排列,稀疏分布于黏液样基质中(星号),部分区域见出血(白箭)

患者男,41岁,主因“发现右大腿根部包块6个月”入院。查体:右大腿上段内侧包块,约10 cm×7 cm,形态欠规则,质软,无明显压痛。CT检查:平扫示右侧大腿根部肌间隙内见浅分叶状稍低密度团块影,边界较清,内部可见斑片状稍高密度影(图1A);增强扫描肿块呈不均匀强化,内见条片状强化影(图1B)。CT诊断:神经鞘瘤。遂行肿瘤切除术,术中见右侧大腿上段肌间隙内鱼肉状椭圆形实质性包块,边界清楚。病理检查:肿块大体呈灰褐色,约10 cm×6 cm×9 cm,切面呈胶冻状;光镜下可见肿瘤细胞被纤维分隔成小叶或结节状,圆形或短梭形的肿瘤细胞呈网格状、带状或假滤泡状排列,稀疏分布于黏液样基质中,肿瘤部分区域可见出血、囊变(图1C)。免疫组化:Vimentin(+),S-100(+),Syn(+),EMA(+),

SMA(-),Ki67(阳性细胞约2%)。病理诊断:骨外黏液样软骨肉瘤(extraskeletal myxoid chondrosarcoma, EMC)。

**讨论** EMC是一种较罕见的软组织低度恶性肿瘤,约占软组织肿瘤中的3%,主要见于35岁以上成年人,男性患者多于女性。约80%的EMC发生于四肢近端深部软组织,皮肤及骨组织极少受累。EMC生长缓慢,多表现为逐渐增大的软组织肿物,可伴疼痛或触痛。病理学检查可见EMC肿瘤细胞呈卵圆形或短梭形,网格状、带状或假滤泡状排列,且被纤维分隔成小叶或结节状,肿瘤细胞之间为黏液样基质。免疫组化中Vimentin是EMC唯一相对恒定的阳性指标,多数S-100为阳性,个别EMA可为阳性。EMC的CT主要表现为分叶状低或稍低密度肿块,常伴出血或坏死,较少出现钙化及骨组织侵犯,增强后肿瘤强化不均匀。EMC需与神经鞘瘤、黏液样脂肪瘤、滑膜肉瘤等相鉴别。EMC发病率低,临床表现及影像学表现缺乏特异性,最终确诊需依赖病理学检查。

[第一作者] 李方燕(1989—),女,贵州独山人,在读硕士。

E-mail: 1272181625@qq.com

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