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弹性成像技术在子宫肌瘤射频治疗中的应用价值*

段景域 董晓秋[△] 张立维 孔德娇 邵小慧

(哈尔滨医科大学附属第四医院超声科 黑龙江 哈尔滨 150001)

摘要 目的:探讨实时超声弹性成像(Real-time ultrasound elastography, RTE)在子宫肌瘤射频消融治疗(radiofrequency ablation, RFA)中的应用价值。**方法:**对34例行RFA治疗的子宫肌瘤患者(共38个病灶)于术前、术后1小时、术后3个月进行阴式超声、RTE及超声造影(contrast-enhanced ultrasonography, CEUS)检查。在2D、RTE、CEUS三种条件下分别测量病灶的直径。分析术前弹性图特征并分组,测量病灶弹性应变比率(E/E_0),对比分析组间、组内的 E/E_0 。比较2D、RTE、CEUS条件下病灶直径之间的差异。术后以弹性图像上病灶显示蓝绿相间为判定消融不全的标准,与CEUS对比,分析RTE与CEUS对消融程度评估的一致性。**结果:**根据术前肌瘤弹性图像将病灶分为蓝色组8个(21.1%),蓝色为主组20个(52.6%),绿色为主组10个(26.3%),术前3个月病灶之间 E/E_0 差异明显,术后1小时、术后3个月 E/E_0 差异无统计学意义($P>0.05$),组内RFA术后1小时、3个月病灶 E/E_0 较术前明显增大,术后3个月 E/E_0 大于术后1小时($P<0.05$);术前RTE检测病灶直径大于2D及CEUS($P<0.05$),术后1小时2D测量直径大于RTE及CEUS($P<0.05$),三种成像技术在术后3个月测量病灶直径差异无统计学意义($P>0.05$);RFA术后1小时及术后3个月RTE对病灶消融程度评估结果与CEUS基本一致,Kappa值分别为0.46、0.54。**结论:**RFA术后肌瘤逐步变硬,RTE检查能够反映这种硬度变化,并且能够评估消融病灶的范围并预估消融程度,因此RTE在子宫肌瘤RFA治疗中有一定的应用价值。

关键词:子宫肌瘤;射频治疗;弹性成像

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Application Value of Ultrasound Elastography Techniques in the Treatment of Uterine Fibroids Radiofrequency Ablation*

DUAN Jing-yu, DONG Xiao-qiu[△], ZHANG Li-wei, KONG De-jiao, SHAO Xiao-hui

(Department of Ultrasonography, the fourth Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, 150001, China)

ABSTRACT Objective: To investigate the application value of real-time ultrasound elastography in the treatment of fibroids radiofrequency ablation (RFA). **Methods:** Transvaginal ultrasonography, Real-time ultrasound elastography (RTE) and contrast-enhanced ultrasonography (CEUS) were performed on 34 patients with a total of 38 uterine fibroids who had the treatment of RFA before, 1 hour and 3 months after the treatment of RFA. Detected the diameters of the lesions with the three methods of CEUS, RTE and 2D. Analysed the elastic image features and divided into groups, Measured the elastic strain ratio and compared the E/E_0 in and between the group. The difference of lesion diameter between 2D, RTE and CEUS was compared. When the image of lesions showed blue and green was taken as the criterion of incomplete ablation after RFA, compared with CEUS, analysed the consistency of RTE and CEUS in evaluating the degree of ablation. **Results:** The lesions were divided into 3 groups according to the preoperative elastic image, with 8 (21.1%) in the blue group, 20 (52.6%) in blue-based and 10 (26.3%) in green-based group. The difference was obvious in E/E_0 between the 3 groups before RFA. There was no significant difference in E/E_0 between 1 hour and 3 months after RFA ($P>0.05$). In each group the E/E_0 of lesions were significantly increased at 1 hour and 3 months after the treatment of RFA, and the hardness of 3 months after RFA was harder than that of 1 hour after RFA ($P<0.05$). The diameter measured by RTE was larger than that by 2D and CEUS before RFA ($P>0.05$). The diameter measured by 2D was larger than that by RTE and CEUS at 1 hour after RFA ($P<0.05$). No statistically significant difference was found in the lesion diameters among the three methods of 2D, RTE and CEUS at 3 months after the treatment of RFA ($P>0.05$). CEUS and RTE had the basic consistent in the evaluation of lesions ablation degree at 1 hour (kappa=0.46) and 3 months (kappa=0.54) after the treatment of RFA. **Conclusions:** After RFA, the myoma gradually hardens, and RTE can reflect the change of the hardness, RTE can clearly show the boundary of uterine fibroids especially after the treatment of RFA, can be used in the prediction of lesions ablation degree, so there was a certain application value of RTE used in RFA.

Key words: Uterine fibroids; Radiofrequency ablation; Real-time ultrasound elastography

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作者简介:段景域(1990-),硕士研究生,电话:13845166343, E-mail: 1135762679@qq.com

[△] 通讯作者:董晓秋,博士,硕士生导师,主任医师,主要研究方向:腹部、妇产科及小器官的超声诊断与介入治疗,

电话:(0451)82576705, E-mail: dongxq0451@163.com

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前言

子宫肌瘤是女性生殖系统最常见的良性肿瘤,30-50 岁的女性发病率约为 20 %^[1]。RFA 是在超声的引导及监视下将自凝刀置于病灶内部,致病灶局部产生生物高热效应,使病灶发生凝固性坏死,以改善患者临床症状,提高患者生活质量的微创治疗方法。该方法用于子宫肌瘤的治疗较传统外科手术而言具有创伤小,安全性高,治疗费用低,临床效果确切等优点^[2]。目前临床上对于热消融病灶的评估常以增强 CT、MRI 作为影像学评估的金标准,而近年来 CEUS 用于消融病灶评估方面的价值也得到了广大学者的认可并在临床广泛应用^[3-5]。但以上方法存在价格昂贵、有创、操作复杂等不足。本研究旨在探讨 RTE 在子宫肌瘤 RFA 中的应用价值。

1 资料与方法

1.1 临床资料

收集 2014 年 9 月至 2016 年 4 月在我院自愿接受 RFA 治疗的肌壁间肌瘤患者 34 例,共 38 个病灶,年龄 31-52 岁,平均(4 2.2± 4.7)岁,肌瘤直径≤ 5 cm,平均(3.4± 0.9)cm,且肌瘤中心点距阴式探头距离≤ 3 cm。所有患者均已婚且无再生育要求,无其他妇科疾病,无凝血功能障碍和心脏病等手术禁忌症。术前向患者及家属详细交待手术过程及术中可能出现的风险、术后并发症等,签署知情同意书。

1.2 仪器与方法

1.2.1 仪器与药品 应用配备有 RTE 软件的 Logiq E9 彩色多普勒超声诊断仪,具有低机械指数实时谐波超声造影功能。腹部探头频率 1.0-5.0 MHz,阴式探头频率 5.0-9.0 MHz。RFA 治疗采用 BBT-RF-E 妇科多功能射频治疗仪,工作频率(550± 40) kHz,最大输出功率为 50 W。造影剂为声诺维(SonoVue),使用时加入 5 mL 注射用生理盐水,用力振摇混匀后,抽取 2.4 mL 微泡混悬液以团注方式经肘前静脉快速注入,随后推注 5 mL 生理盐水冲注。

1.2.2 方法 全部病例在 RFA 治疗前、术后 1 小时及术后 3

个月行阴道二维超声检查。观察肌瘤位置、数量、回声水平、血流情况并测量其最大直径。在阴式超声检查基础上加用 RTE 技术。取样框范围尽可能包括全部病灶及部分周边正常组织。手持探头在病灶部位做微小振动,位置高的肌瘤配合腹部加压,待压力质量指示标尺变为绿色,压力曲线频率及幅度均匀,弹性图像稳定时冻结图像,弹性图像上由红到蓝代表组织由软到硬,观察病灶弹性图特征并分组,利用机身自带的弹性测量方法选取病灶区域(E)和相邻正常肌组织区域(E₀),感兴趣区要尽量等大且保持在同一深度,计算 E/E₀,并且测量弹性图上肌瘤最大直径。RFA 治疗前、术后 1 小时及术后 3 个月行 CEUS。观察病灶造影剂灌注情况,于平衡期时测量病灶最大直径。消融程度判定标准是肌瘤内部无造影剂灌注为完全消融,反之,为消融不全^[6],对于术后 1 小时消融不全者,再次补针消融。术后 1 小时 E/E₀ 结果以补充消融后为准。所有测值均测量三次取平均值。

1.2.3 RFA 治疗 患者取截石位,将电极板置于腰骶部,射频治疗仪功率设置为 20-40 W,根据肌瘤大小、位置、肌瘤血供情况制定个性化消融方案,在经腹超声引导下经阴道进入自凝刀进行 RFA 治疗。

1.3 统计方法

用 SPSS 23.0 统计软件包对数据进行处理。计量资料以均数± 标准差($\bar{x} \pm s$)表示,以 P<0.05 为差异有统计学意义。多组间数据采用方差分析。以 Kappa 值评价 RTE 与 CEUS 评估病灶消融程度的一致性,Kappa>0.75 为高度一致,0.75≥ Kappa≥ 0.4 为基本一致,Kappa<0.4 为一致性差。

2 结果

2.1 肌瘤病灶 E/E₀ 的比较

根据术前弹性图特征将病灶分为 3 组,蓝色组 8 个(21.1 %),蓝色为主组 20 个(52.6 %),绿色为主组 10 个(26.3 %),术前组间 E/E₀ 差异明显,术后 1 小时及 3 个月差异无统计学意义(P>0.05),组内 RFA 术后 1 小时、3 个月病灶 E/E₀ 较术前明显增大,术后 3 个月 E/E₀ 大于术后 1 小时(P<0.05),见表 1。

表 1 不同弹性特征病灶的 E/E₀($\bar{x} \pm s$)

Table 1 E/E₀ of different elastic characteristics of lesions($\bar{x} \pm s$)

Groups	Number of lesions(%)	Before RFA	1 hour after RFA	3 months after RFA	P
Green-based	10(26.3)	1.5± 0.4	3.5± 0.4	3.9± 0.4	<0.05
Blue-based	20(52.6)	2.5± 0.3	3.4± 0.3	3.8± 0.4	<0.05
Blue	8(21.1)	3.1± 0.3	3.6± 0.3	4.1± 0.3	<0.05
P		<0.05	>0.05	>0.05	

2.2 2D、RTE、CEUS 三种方法测量病灶直径的比较

术前 RTE 测量病灶直径大于 2D 及 CEUS(P<0.05),术后 1 小时 2D 测量直径大于 RTE 及 CEUS(P<0.05),三种成像方法在术后 3 个月测量病灶直径差异无统计学意义(P>0.05),见表 2、图 1、图 2。

2.3 术后 1 小时及 3 个月 RTE 与 CEUS 对病灶消融情况评估结果(补充消融前)的比较

RFA 术后 1 小时及术后 3 个月 RTE 对病灶消融情况评估结果与 CEUS 基本一致(Kappa 值分别为 0.47、0.54),见表 3。

3 讨论

1991 年由 O'phir^[7]等提出了超声弹性成像概念,它是根据不同组织的弹性系数差异进行成像的一种技术。近年来发展的 RTE 成像原理是将组织内部的弹性模量等力学属性的差异示以不同颜色,以直观显示不同组织的相对硬度。目前,RTE 在鉴别乳腺、甲状腺等浅表器官肿瘤良、恶性中的价值已得到证实^[8-10]。子宫肌瘤是由增生的平滑肌细胞和数量不等的纤维结缔组织细胞构成,理论上其硬度较正常子宫肌层硬,国内外亦有

研究表明,典型的子宫肌瘤弹性图像表现为肌瘤内部以蓝色为主^[11,12]。RFA 治疗使肌瘤组织升温,使肌瘤细胞发生脱水、蛋白变性、凝固性坏死^[13],消融病灶硬度与周边正常组织差异增大。

理论上 RTE 能反映这种变化,并可以用来评价子宫肌瘤消融范围及消融程度。但是,RTE 用于子宫肌瘤热消融治疗前、后的研究目前尚处于离体及动物实验阶段^[14,15]。

表 2 2D、RTE、CEUS 技术显示病灶直径的比较 (cm, $\bar{x} \pm s$)
Table 2 Comparison of diameter by 2D, RTE and CEUS (cm, $\bar{x} \pm s$)

Methods	Before RFA	1 hour after RFA	3 months after RFA
2D	3.3 $\pm$ 0.9 ¹	3.7 $\pm$ 0.9 ^{*#}	2.0 $\pm$ 0.9
RTE	3.6 $\pm$ 0.8 ¹²	3.6 $\pm$ 0.9 [#]	1.9 $\pm$ 0.9
CEUS	3.4 $\pm$ 0.9 ²	3.5 $\pm$ 0.9 [*]	1.9 $\pm$ 0.9

Note: 1,2,*,*P<0.05.

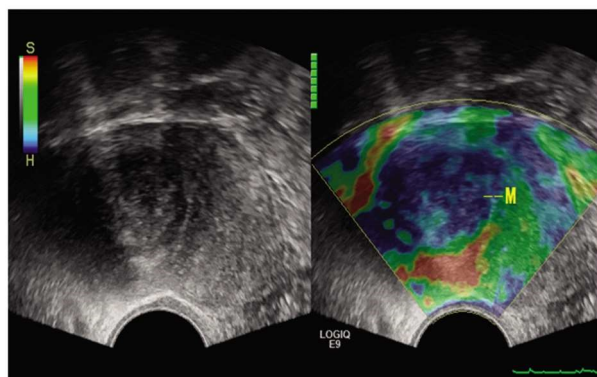


图 1 RFA 术后 1 小时 RTE

Fig.1 RTE at one hour after RFA

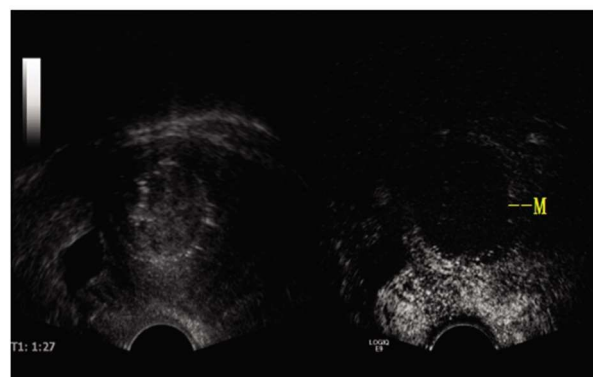


图 2 RFA 术后 1 小时 CEUS

Fig.2 CEUS at one hour after RFA

表 3 术后 1 小时及 3 个月 RTE 与 CEUS 比较 (n=38)

Table 3 Comparison of RTE and CEUS at 1 hour and 3 months after RFA

RTE	Number of lesions	CEUS of 1 hour after RFA		Number of lesions	CEUS of 3 months after RFA	
		No perfusion	Uneven hypoperfusion		No perfusion	Uneven hypoperfusion
Blue	32	29	3	33	31	2
Blue and green	6	2	4	5	2	3
Number of lesions	38	31	7	38	33	5

Note: 1 hour after RFA Kappa=0.46, 3 months after RFA Kappa=0.54.

本研究中根据术前肌瘤弹性图特征将其分为三组,蓝色组占 21.1%,蓝色为主占 52.6%,绿色为主者占 26.3%,组间术前 E/E_0 差异明显。既往研究表明^[16,17],子宫肌瘤的硬度与平滑肌细胞、结缔组织含量的多少及肌瘤细胞的排列方式关系密切。肌瘤细胞以束状排列为主,间质水肿,质地相对较软,病灶呈现以绿色为主, E/E_0 小;肌细胞呈编织状交替排列,含纤维支架成分较多,排列规则,则质地较硬,病灶呈现以蓝色为主, E/E_0 较大。但无论术前病灶软硬,术后 1 小时、术后 3 个月消融灶呈现完全被蓝色覆盖或以蓝色为主, E/E_0 较术前均明显升高,且术后 3 个月 E/E_0 较术后 1 小时升高更明显,分析原因与 RFA 治疗术后病灶的病理演变过程相关。RFA 术后,肌瘤细胞脱水、凝固性坏死,故硬度增加,随时间继续推移,坏死组织分解和液化,遗留下的组织缺损区由肉芽组织充填予以修复,最后演变为瘢痕组织。所以,术后 3 个月时除部分病灶因术后局部血管新生,出现硬度略变软之外,大部分病灶的 E/E_0 均较术后 1 小时升高。另外我们推测术后某一段时间由于坏死组织液化,会出现肌瘤变软,即 E/E_0 减小的过程,本研究未对此方向

进行研究。

本研究分别在 2D、RTE、CEUS 条件下对病灶直径进行测量,结果显示术前 RTE 检测病灶直径大于 2D 及 CEUS,术后 1 小时 2D 检测病灶直径大于 RTE 及 CEUS,术后 3 个月 3 种方法检测病灶直径差异无统计学意义。子宫肌瘤膨胀性生长压迫周围的子宫肌层形成假包膜,2D 超声通过肌瘤假包膜及肌瘤组织与周边正常肌组织的声阻抗差识别边界;RTE 检查是根据不同组织的弹性系数差异进行成像,通过图像上病灶与周围正常组织的颜色差异识别边界;CEUS 成像原理是滤除基波成分而有选择性地接受造影剂微泡产生的谐波信号而进行成像,临床通过病灶内部的血流灌注与正常肌组织的差异评估病灶直径,并已获得临床认可。经过分析,本研究中术前部分较软子宫肌瘤弹性成像显示蓝绿相间绿色为主,与周边黄绿色的正常肌组织分界不清晰,导致测量直径较 2D、CEUS 偏大。但是 RFA 治疗后 1 小时,肌瘤假包膜受到破坏,而且治疗所产生的气体尚未完全消散,二维图像受干扰严重,因此显示消融病灶边界常不清晰。国内外也有研究表明消融病灶强回声大小与实际消

融范围无良好的相关性,不能用强回声范围来预测消融范围^[18,19]。RTE 检查不受气体影响,而且由于消融后病灶硬度均较术前增加,所以与周围肌层分界明显,所测直径与 CEUS 下消融病灶无灌注区范围^[20]差异无统计学意义。术后 3 小时,二维图像不再受气体干扰,病灶较之前变硬,故无论在 2D、RTE、CEUS 哪种条件下消融病灶均能较好的显示边界,故三者对病灶直径的评估差异无统计学差异。因此,RTE 检查虽然在术前因受部分较软的肌瘤影响造成对肌瘤大小的评估出现一定偏差,但在用于 RFA 术后消融范围的评估时,可以弥补二维超声的不足,且无创、方便。

在 RFA 治疗中,正确判断消融病灶的消融程度,是保证消融质量及疗效的关键。采用 CEUS 提供的消融病灶的微循环情况评价其消融程度,已得到广大学者公认。本研究中将术后 1 小时及 3 个月时(均为补充消融前)RTE 与 CEUS 结果进行分析,发现以消融病灶蓝绿相间为评判病灶消融不全的标准时,与 CEUS 结果基本一致。但是,研究中发现 RFA 术后 1 小时 5 例病灶、术后 3 个月 4 例病灶两种方法评估结果不一致。弹性图像显示为蓝绿相间,而 CEUS 显示病灶全程无灌注,可能与肌瘤体积及术前硬度相关。肌瘤体积较大时,其受力不均匀,组织产生的形变大小不一,故弹性图像可以表现为蓝绿相间。另外研究表明^[16]质地较软的肌瘤内部细胞成分不均匀,热量容易分散,内部消融不均匀,故血管虽然已全部灭活,但短期内弹性图像仍可能表现为蓝绿相间。弹性图像显示病灶完全被蓝色覆盖,但是 CEUS 呈现不均匀低增强,这种偏差与 RTE 无法评价病灶的血流状态的成像原理有关。周洪雨等^[21]离体动物实验研究表明,弹性图的蓝色区域可代表热消融后组织细胞的凝固性坏死区,但本研究由于肌瘤特殊的组织结构,部分肌瘤术前弹性图像也表现为完全被蓝色覆盖。所以 RFA 治疗后病灶总体硬度较高,但当局部尚有一些微小血管存在活性时,由于 RTE 无法评价消融灶的血流状态,而 CEUS 能清晰的显示小血管内低速、细小血流,因此造成评估结果出现假阴性。本研究认为 RTE 虽尚不能完全取代 CEUS,但可以在 CEUS 之前初步预估病灶消融程度。由于本研究入组病例少,故尚需大量临床及基础研究为 RTE 用于消融病灶消融程度的评估提供定量的诊断指标及依据。

综上所述,RFA 术后肌瘤逐步变硬,RTE 检查能够反映这种硬度变化;RTE 能够评估子宫肌瘤尤其是 RFA 术后病灶的范围并预估消融程度,故 RTE 检查在子宫肌瘤 RFA 治疗中的应用前景可期。

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