

· 临床研究 ·

收缩达峰时间离散度评价食管癌患者放疗前后左心室收缩同步性的应用价值

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【摘要】目的 探讨收缩达峰时间离散度(PSD)评价食管癌患者放疗前后左心室收缩同步性的应用价值。**方法** 选取2017年10月至2018年7月在苏北人民医院首次接受胸部放射治疗的食管癌患者60例作为放疗组。同期选取年龄、性别相匹配的健康志愿者25例作为对照组。分别于放疗前、放疗中期(放疗14次后)、放疗结束及放疗结束后1个月采用超声心动图机检查相关参数指标并比较。采用SPSS 25.0软件进行统计分析。变量间相关性采用Spearman相关性分析。**结果** 与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后1个月的常规超声心动图参数差异无统计学意义($P>0.05$)。与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后1个月的基底段纵向峰值应变达峰时间(TTPLS)[(361.0±29.0)、(376.6±35.1)、(382.7±33.8)和(370.6±36.9)ms]、以及基底段[(92.86±7.39)、(105.67±25.18)、(124.57±31.61)和(110.98±29.93)ms]和中间段[(66.57±23.64)、(87.56±20.13)、(101.57±17.48)和(84.32±23.81)ms]的纵向应变达峰时间最大差值(Tls-dif)均显著延长($P<0.05$), 与放疗结束时相比, 放疗结束后1个月的上述参数有缩短趋势($P<0.05$)。与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后1个月的PSD均显著增加[(33.20±7.65)、(36.83±8.20)、(40.91±8.36)和(38.53±9.89)ms], 而整体纵向峰值应变(GLPS)均显著降低($P<0.05$)。与放疗结束时相比, 放疗结束后1个月的PSD与GLPS均有向放疗前恢复的趋势($P<0.05$)。Spearman相关性分析结果显示, GLPS绝对值与PSD呈显著负相关($r=-0.61, P<0.01$)。**结论** 应用PSD能够评价食管癌患者放疗前后左心室收缩同步性, 为临床监测放疗患者心功能, 及时调整放疗方案提供帮助。

【关键词】 超声心动图; 食管癌; 左心室功能; 应变; 达峰时间离散度

【中图分类号】 R445

【文献标志码】 A

【DOI】 10.11915/j.issn.1671-5403.2020.08.134

Value of peak strain dispersion for assessment of left ventricular contraction synchronization in patients with esophageal carcinoma before and after radiotherapy

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【Abstract】 Objective To explore the application value of peak strain dispersion (PSD) for assessment of left ventricular (LV) synchronization in patients with esophageal carcinoma before and after radiotherapy. **Methods** A total of 60 patients with esophageal carcinoma who received chest radiotherapy for the first time in the Northern Jiangsu People's Hospital from October 2017 to July 2018 were enrolled in this study. Another 25 age-and sex-matched health volunteers at the same period served as control. Routine echocardiography examinations were performed before, in the middle of (after 14 times of radiotherapy), after and in 1 month after radiotherapy, and the obtained parameters were compared between the two groups. SPSS statistics 25.0 was used to analyze the data. Spearman correlation analysis was employed for correlation analysis. **Results** There were no significant differences in the echocardiographic parameters before and in the middle, end and in 1 month after radiation ($P>0.05$). In the above time points, the time to peak longitudinal strain (TTPLS) in basal segment was (361.0±29.0), (376.6±35.1), (382.7±33.8) and (370.6±36.9) ms, respectively, maximum difference of TTPLS (Tls-dif) in basal segment was (92.86±7.39), (105.67±25.18), (124.57±31.61) and (110.98±29.93) ms, respectively, and it in middle segments was (66.57±23.64), (87.56±20.13), (101.57±17.48) and (84.32±23.81) ms. The differences were gradually extended from the middle to the 1 month after radiotherapy ($P<0.05$). Compared with the end of radiotherapy, the above parameters showed a shortening trend in 1 month after radiotherapy ($P<0.05$). Compared with the values before radiation,

收稿日期: 2019-09-11; 接受日期: 2019-11-05

基金项目: 扬州市重点研发计划(社会发展)项目(YZ2016075)

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PSD was increased gradually from the middle to the 1 month after radiotherapy [(33.20±7.65) vs (36.83±8.20) vs (40.91±8.36) vs (38.53±9.89) ms], while the absolute value of global longitudinal peak strain (GLPS) was decreased gradually ($P<0.05$). The PSD and GLPS values gradually recovered to the pre-radiotherapy levels in 1 months after radiation when compared with those at the end of radiotherapy ($P<0.05$). Spearman correlation analysis indicated that the absolute value of GLPS was negatively correlated with PSD ($r=-0.61$, $P<0.01$). **Conclusion** PSD can be used to evaluate the left ventricular contraction synchronization in esophageal carcinoma patients before and after radiotherapy, and is helpful for monitoring their cardiac function and timely adjusting radiotherapy regimen in clinical practice.

[Key words] echocardiography; esophageal carcinoma; left ventricular function; strain; peak strain dispersion

This work was supported by Yangzhou Key R & D (Social Development) Program(YZ2016075).

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食管癌是我国男性第五大高发肿瘤和第四大致死肿瘤^[1]。放射治疗是治疗食管癌的一种非常有效的方法,但经胸部放射治疗所产生的心脏毒性亦会损害癌症患者的健康,甚至会影响其生活质量^[2]。因此,对食管癌放疗患者进行定期心脏功能监测至关重要。常规超声心动图检测的敏感度较差,且精确度不高,难以发现心脏潜在的收缩功能损害。基于二维超声的斑点追踪成像(two-dimensional speckle tracking echocardiography, 2D-STE)技术被广泛用于冠心病、肥厚性心肌病、高血压、心肌淀粉样变等疾病的临床诊断,近年来,该项技术也逐渐被应用于肿瘤患者心脏病的动态监测。左室收缩达峰时间离散度(peak strain dispersion, PSD)是2D-STE的重要参数之一,笔者着重探讨PSD评价食管癌患者放疗前后左心室收缩同步性的应用价值。

1 对象与方法

1.1 研究对象

选取2017年10月至2018年7月在苏北人民医院首次接受胸部放射治疗的食管癌患者60例作为放疗组,年龄48~78(64.9±8.5)岁,其中男性41例,女性19例,鳞癌54例,腺癌6例。全部患者均经病理证实为食管癌,除外心脑血管疾病及心脏相关不适或记录,且入院时心电图和心肌酶谱检查均无异常,放疗前均未接受过化疗。

同期选取年龄、性别相匹配的健康志愿者25例作为对照组,年龄45~75(62.5±9.0)岁,男性17例,女性8例。

本研究经我院伦理委员会批准(2016KY-011),受试者均知情同意。

1.2 方法

对符合要求的食管癌患者及健康志愿者采集身高、体质量、血压等基本资料。放疗组采用调强放疗法投射,5次/周,1.80~2.14 Gy/次,连续5~6周。根据中国食管癌放疗的治疗指南^[3],放疗总量:大

体肿瘤靶区60 Gy/28次,临床靶区56 Gy/28次,计划靶区50.4 Gy/28次,采用同步推量技术,总量50.4~60.0 Gy。分别于放疗前、放疗中期(放疗14次后)、放疗结束及放疗结束后1个月采用超声心动图机(GE Vivid E9, M5S心脏探头,频率1.7~3.3 mHz,帧频40~80 Hz)检查相关参数指标^[4]。嘱受检者取左侧卧位,平静呼吸,同步记录胸导联心电图;所有测量值最少记录3个心动周期,取其平均值。

1.3 检测指标

1.3.1 常规参数 记录左室舒张末期内径(left ventricular dimension in diastole, LVEDD)、左室收缩末期内径(left ventricular dimension in systole, LVESD)、舒张末期室间隔厚度(interventricular septal thickness in diastole, IVST)、舒张末期左室后壁厚度(posterior wall thickness in diastole, PWT),另分别采集心尖两腔、三腔、四腔切面连续3个心动周期的二维动态图像,以DICOM格式储存于优盘。应用双平面simpson法测量左室舒张末期容积(left ventricular end-diastolic volumes, LVEDV)、收缩末期容积(left ventricular end-systolic volumes, LVESV)及左室射血分数(left ventricular ejection fraction, LVEF)。

1.3.2 2D-STE 应变参数 采用EchoPAC工作站、Q-analysis软件进行图像分析。分别手动描绘左室长轴3个切面动态图像的心内膜,系统自动将左室长轴每个切面分为6个节段,左心室短轴每个水平分为6个节段,共18节段(按美国超声心动图协会推荐的18节段划分法),软件自动显示相应的收缩期纵向峰值应变(global longitudinal peak strain, GLPS)及纵向峰值应变达峰时间(time to peak longitudinal strain, TTPLS)牛眼图,从牛眼图上可以得到左室每个节段与心动周期对应的LPS和TTPLS。在最终给出的TTPLS牛眼图的界面,系统会提供基于所有节段达峰时间的标准差,即PSD和整体纵向峰值应变(global longitudinal peak strain, GLPS)。计算左

室基底段、中间段、心尖段的 TTPLS 最大差值 (maximum differences of TTPLS, Tls-dif) 及左心室基底段、中间段、心尖段的收缩达峰时间。各值均测量 3 次, 取平均值。

1.4 统计学处理

采用 SPSS 25.0 软件进行统计分析。计量资料采用均数±标准差 ($\bar{x} \pm s$) 表示, 组间比较采用单因素方差分析。变量间相关性采用 Spearman 相关分析。 $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 2 组常规超声心动图参数比较

与对照组相比, 放疗组患者放疗前的常规超声心动图参数 LVEDD、LVESD、IVST、PWT、LVEF 差异均无统计学意义 ($P > 0.05$)。与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后 1 个月的常规超声心动图参数差异亦无统计学意义 ($P > 0.05$; 表 1)。

2.2 2 组基底段、中间段、心尖段的 TTPLS 和 TLS-dif 比较

与对照组比较, 放疗组患者放疗前基底段、中间段、心尖段的 TTPLS 和 TLS-dif 差异均无统计学意义 ($P > 0.05$)。与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后 1 个月的基底段 TTPLS、以及基底段和中间段的 Tls-dif 均显著延长 ($P <$

0.05), 与放疗结束时相比, 放疗结束后 1 个月的上述参数有缩短趋势, 差异有统计学意义 ($P < 0.05$; 表 2)。典型病例 2D-STE 牛眼图如图 1 所示。

2.3 2 组 PSD 和 GLPS 比较

与放疗前相比, 放疗组患者放疗中期、放疗结束及放疗结束后 1 个月的 PSD 均显著增加, 而 GLPS 均显著降低, 差异有统计学意义 ($P < 0.05$)。与放疗结束时相比, 放疗结束后 1 个月的 PSD 与 GLPS 均有向放疗前恢复的趋势, 两两比较差异均有统计学意义 ($P < 0.05$; 表 3)。Spearman 相关分析结果显示, GLPS 绝对值与 PSD 呈显著负相关 ($r = -0.61$, $P < 0.01$; 图 2)。

3 讨 论

研究表明^[5,6], 放疗诱发的心脏疾病反映了不同细胞种类和结构对射线的敏感性差异, 心肌细胞敏感性低, 但微循环对放疗较敏感。放疗产生的氧自由基可使 DNA 断裂, 首先损伤微循环系统, 导致血管内皮细胞受损、管腔闭塞、微循环障碍、心肌缺血, 进而影响心脏收缩功能。临幊上常用 LVEF 评价放疗导致的急性收缩功能损伤^[7], 但本研究结果表明, 食管癌患者放疗前后的常规超声心动图参数 (LVEDD、LVESD、IVST、PWT、LVEF) 的差异无统计学意义, 提示常规的超声心动图对食管癌放疗患者心功能监测并无显著意义。

表 1 2 组常规超声心动图参数比较

Table 1 Comparison of conventional echocardiographic parameters between two groups

($\bar{x} \pm s$)

Group	n	LVEDD(mm)	LVESD(mm)	IVST(mm)	PWT(mm)	LVEF(%)
Control	25	44.93±4.18	28.94±3.03	9.37±1.39	10.27±0.81	61.74±4.26
Radiotherapy	60					
Before therapy		44.72±3.98	29.13±3.15	9.50±0.99	9.70±0.94	62.00±3.83
During therapy		43.56±5.17	29.35±3.65	10.04±1.28	9.53±1.57	61.76±3.75
End of therapy		43.84±4.67	29.78±4.13	9.72±1.02	9.60±0.84	61.07±4.02
1 month after therapy		44.02±5.12	29.60±3.58	9.57±1.08	9.50±1.78	61.21±3.66

LVEDD: left ventricular dimension in diastole; LVESD: left ventricular dimension in systole; IVST: interventricular septal thickness in diastole; PWT: posterior wall thickness in diastole; LVEF: left ventricular ejection fraction.

表 2 2 组基底段、中间段、心尖段的 TTPLS 和 TLS-dif 比较

Table 2 Comparison of TTPLS and TLS-difference parameters of basal, middle and apical segments between two groups (ms, $\bar{x} \pm s$)

Group	n	TTPLS			TLS-difference		
		Basal	Middle	Apical	Basal	Middle	Apical
Control	25	358.0±28.5	355.1±24.4	336.7±30.0	89.70±6.90	69.37±14.47	36.74±14.89
Radiotherapy	60						
Before therapy		361.0±29.0	345.6±26.7	341.6±28.9	92.86±7.39	66.57±23.64	38.50±17.71
During therapy		376.6±35.1*	348.4±30.4	340.3±25.6	105.67±25.18*	87.56±20.13*	47.54±23.95
End of therapy		382.7±33.8*	354.0±38.5	343.6±39.6	124.57±31.61*	101.57±17.48*	51.75±31.09
1 month after therapy		370.6±36.9**	441.5±39.6	339.8±30.2	110.98±29.93**	84.32±23.81**	43.56±26.54

TTPLS: time to peak longitudinal strain; TLS-difference: the maximum differences of TTPLS. Compared with before therapy, * $P < 0.05$; compared with end of therapy, ** $P < 0.05$.

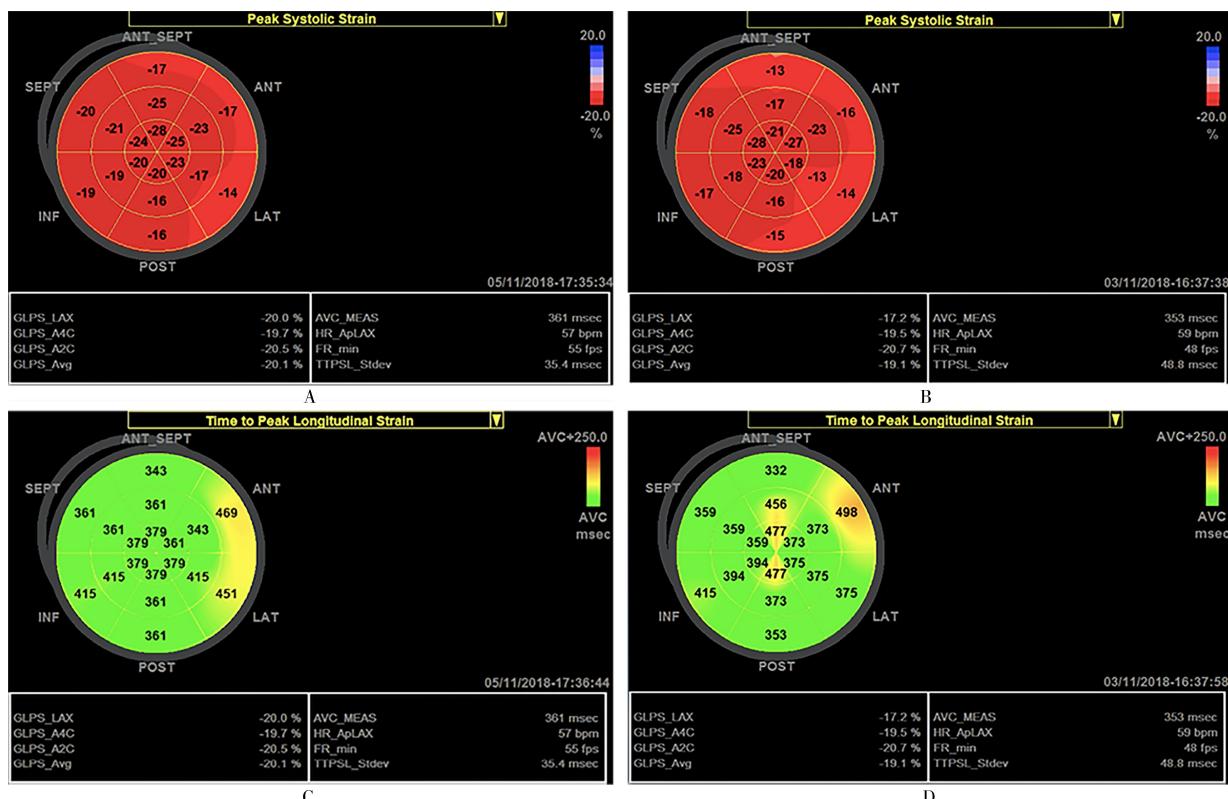


图1 典型病例2D-STE牛眼图

Figure 1 2D-STE bull eye chart for one typical patient

A: peak systolic strain before radiotherapy; B: peak systolic strain at the end of radiotherapy; C: time to peak longitudinal strain before radiotherapy; D: time to peak longitudinal strain at the end of radiotherapy. 2D-STE: two-dimensional speckle tracking echocardiography.

表3 2组 PSD 和 GLPS 比较

Table 3 Comparison of PSD and GLPS between two groups

Group	n	PSD (ms, $\bar{x} \pm s$)	GLPS (% , $\bar{x} \pm s$)
Control	25	32.38±5.89	21.25±3.05
Radiotherapy	60		
Before therapy		33.20±7.65	20.87±4.04
During therapy		36.83±8.20*	18.35±3.75*
End of therapy		40.91±8.36*	17.60±1.82*
1 month after therapy		38.53±9.89**#	18.67±5.57**#

PSD: peak strain dispersion; GLPS: global longitudinal peak strain.
Compared with before therapy, * $P<0.05$; compared with end of therapy, ** $P<0.05$.

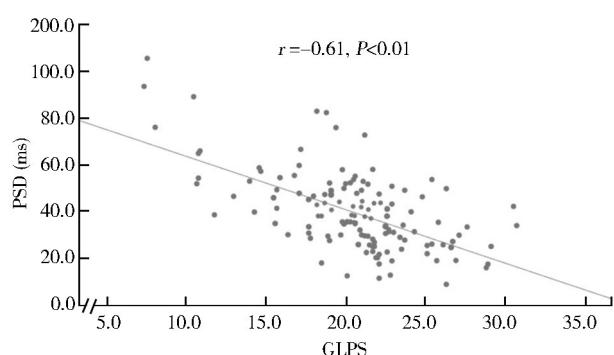


图2 GLPS 绝对值与 PSD 的相关性分析

Figure 2 Correlation analysis between absolute value of GLPS and PSD

PSD: peak strain dispersion; GLPS: global longitudinal peak strain

2D-STE 技术已被美国超声心动图学会提议作为一种无创检测放疗诱导的心肌毒性早期亚临床症状的手段^[8]。有研究表明,食管癌患者在放疗剂量累计达 40 Gy 时,左室 GLPS 降低^[9]。本研究亦发现,食管癌患者与放疗前相比,放疗中期、放疗结束及放疗结束后 1 个月的 GLPS 均显著降低。提示食管癌患者放疗后存在亚临床的心肌损伤。

既往研究表明, GLPS 和 TTPLS 具有良好的一致性,可以作为左心室功能指标的参考值^[10]。因此, TTPLS 在牛眼图上能够直接评价某一节段心肌的收缩功能:健康心肌表现为绿色;当心肌缺血等原因导致心肌收缩功能下降时,TTPLS 延长,表现为黄色或红色。PSD 是基于 2D-STE 技术衍生的用于表达左心室 TTPLS 离散程度的新参数,是左心室各节段心肌长轴应变达峰时间的标准差,能够直观表示左室心肌各节段之间的同步性^[11]。本研究采用 TTPLS 评价左室收缩功能,PSD 及 Tls-dif 作为评估左心室收缩同步性的指标,PSD 及 Tls-dif 越大,左室收缩不同步性越显著^[12]。

本研究通过 Pearson 相关分析发现, PSD 与 GLPS 绝对值呈负相关, GLPS 绝对值越低,代表整体收缩功能越差, PSD 越大,代表同步性越差,这与

文献结果相似^[11],这说明收缩功能和同步性一致。本研究还发现,放疗后左室基底段收缩功能减低,而中间段、心尖段收缩功能未见明显改变。左室整体收缩存在不同步性,其中又以左室基底段、中间段的不同步性更为显著,这说明收缩不同步可能比整体收缩功能下降更为敏感,这可能是因为大动脉不像小动脉那样容易受到影响,大动脉管腔直径大,血流速度快,不易形成斑块;且大动脉的管壁较厚,其内含有更多的抗辐射细胞^[13,14]。因此,放疗多导致某一节段的微血管损伤,使该节段心肌细胞不能正常供血,但未影响整体收缩功能^[2]。

本研究还发现,与放疗结束相比,放疗后1个月收缩功能较前有所恢复,其左室基底段、中间段不同步性也有所减弱,这说明放疗所造成的心肌损伤是可逆的,停止放疗后一段时间有望恢复至正常。但是不排除某些患者放疗后1个月收缩功能同步性继续下降的可能,我们将继续扩大样本量,密切随访,找到这些患者与其他患者的不同之处,从而有针对性的采取干预措施或者改变放疗方案,减少对放疗敏感人群的心肌毒性。还有研究表明^[15],放疗导致的心脏疾病临床症状通常出现在放疗很长时间之后,因此还要在放疗半年、1年后增加随访观察,有利于更好地评估放疗患者的慢性心脏损伤。

综上所述,食管癌放疗患者放疗后存在亚临床的心肌损伤,应用PSD能早期评估放疗导致的左心室收缩功能下降及同步性减低,为临床及时治疗及调整放疗方案提供帮助。该方法的缺陷在于对二维图像清晰度要求较高,一旦出现声窗条件差的病例将无法获取理想图像,致使误差增大。

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