doi: 10.13241/j.cnki.pmb.2020.19.028

图像引导下精确放疗治疗宫颈癌的价值分析 *

张荣繁[1] 于 芹[1] 庞 鑫[1] 周 源[1] 牛丽红[2△]

（内蒙古医科大学附属人民医院 1 肿瘤放射治疗科；2 妇瘤科 内蒙古 呼和浩特 010020）

摘要 目的：探讨与分析图像引导下精确放疗治疗宫颈癌的价值。**方法：**2016 年 1 月至 2017 年 12 月选择在本院进行诊治的宫颈癌患者 120 例，根据治疗方法的不同把患者分为观察组 80 例与对照组 40 例。对照组给予常规放疗方法，观察组给予图像引导下精确放疗，记录与随访两组的预后情况。**结果：**治疗后观察组的总有效率为 85.0 %，显著高于对照组的 60.0%(P<0.05)。观察组治疗期间的放射性直肠损伤、放射性膀胱损伤、消化道反应、血液系统反应等毒副反应发生率显著低于对照组(P<0.05)。观察组治疗后的 IgG 与 IgA 值都显著高于治疗前(P<0.05)，也高于对照组(P<0.05)，对照组治疗前后对比差异无统计学意义(P>0.05)。Kaplan-meier 法分析显示观察组的无疾病进展生存时间和总生存时间都显著长于对照组(P<0.05)。**结论：**图像引导下精确放疗治疗宫颈癌能促进患者免疫功能的恢复，提高治疗效果与减少毒副反应的发生，从而延长患者的生存时间。

关键词：图像引导；精确放疗；宫颈癌；免疫功能；毒副反应

中图分类号：R737.33 **文献标识码：**A **文章编号：**1673-6273(2020)19-3732-04

Value Analysis of Image-guided Precise Radiotherapy for Cervical Cancer*

ZHANG Rong-fan[1], YU Qin[1], PANG Xin[1], ZHOU Yuan[1], NIU Li-hong[2△]

(1 Department of Radiation Oncology; 2 Department of Gynecologic Oncology, People's Hospital Affiliated to Inner Mongolia Medical University, Hohhot, Inner Mongolia, 010020, China)

ABSTRACT Objective: To investigate and analyze the value of image-guided precise radiotherapy for cervical cancer. **Methods:** From January 2016 to December 2017, 120 patients with cervical cancer who were treated in our hospital were selected and were divided into the observation group (n=80) and control group (n=40) accorded to different treatment methods. The control group were given conventional radiotherapy, and the observation group were given image-guided precise radiotherapy. The prognosis of the two groups were recorded and followed up. **Results:** The total effective rates of the observation group after treatment were 85.0%, which were significantly higher than that of the control group (60.0%)(P<0.05). The incidence of toxic side effects such as radiation rectal injury, radiation bladder injury, digestive tract reaction and blood system reaction during the treatment in the observation group were significantly lower than that of the control group (P<0.05). The IgG and IgA values in the observation group after treatment were significantly higher than those before treatment(P<0.05), and were also higher than the control group(P<0.05), and there were no significant difference in the the control group compared before and after the treatment (P>0.05). Kapplan-meier analysis showed that the disease-free survival time and overall survival time of the observation group were significantly longer than the control group (P<0.05). **Conclusion:** Image-guided precise radiotherapy for cervical cancer can promote the recovery of immune function, improve the treatment effect and reduce the occurrence of toxic and side effects, thus prolonging the survival time of patients.

Key words: Image-guided; Precise radiotherapy; Cervical cancer; Immune function; Toxic side effects

Chinese Library Classification(CLC): R737.33 Document code: A

Article ID: 1673-6273(2020)19-3732-04

前言

当前宫颈癌在我国的发病率有所增加，是前三位妇科肿瘤之一[1,2]。宫颈癌的治疗手段包括手术、放疗、化疗等，其中手术治疗基本不适合中晚期[3]，而放疗为主要的治疗方式，传统放疗方法包括盆腔前后两野、箱式照射与四野对穿放射放疗，虽然能够达到更好的靶区剂量分布，但是容易引起放疗并发症[4,5]。特别是联合同期化疗可延长放疗时间，降低了治疗效果，并使患者经济负担加重[6,7]。随着医学技术的发展，三维适形放射治疗(Three-dimensional conformal radiation therapy，3D-CRT)调强放射治疗(Intensity-modulated radiation therapy，IMRT)得到了广泛应用，其能更好地保护正常组织，达到剂量分布与靶区一致，降低了毒副反应的发生[8,9]。而螺旋断层放射治疗 (Helical tomotherapy，HT)为一种融合 CT 的图像引导调强放射治疗技术，

* 基金项目：内蒙古自治区自然科学基金项目（YKD2017KJ ）

作者简介：张荣繁（1974-），女，硕士研究生，副主任医师，研究方向：妇科肿瘤的放射治疗，电话：15904717765，E-mail：ZRF7765@126.com

△ 通讯作者：牛丽红（1970-），女，本科，副主任医师，研究方向：妇科肿瘤的规范治疗，电话：15248015863，E-mail：honhliniu@qq.com

（收稿日期：2019-12-30 接受日期：2020-01-27）

最大程度上降低由于患者膀胱和肠道体积变化所导致的摆位误差,实现了剂量分布的适形性和均匀性,可达到精准治疗的目的[10,11]。本文具体探讨了图像引导下精确放疗治疗宫颈癌的价值,以明确图像在放疗中的应用价值与改善患者预后。

1 资料与方法

1.1 研究对象

选择 2016 年 1 月至 2017 年 12 月在本院诊治的宫颈癌 120 例,病理证实为宫颈鳞癌;具有同期放化疗的指征;年龄 18-80 岁;初次接受放疗;患者知情同意;获得医院伦理委员会批准。排除标准:临床资料不完整者;存在放疗禁忌症。

根据治疗方法的不同把患者分为观察组 80 例与对照组 40 例,两组一般资料有可比性。见表 1。

表 1 一般资料对比

Table 1 General information comparison

Groups	n	Age (years)	BMI (kg/m^2)	Mass diameter (cm)	Clinical stages (Ⅲ/ⅢIa/ⅢIb)	Lymph node metastasis (yes / no)	Differentiation type(high / medium / low)
Observation group	80	58.25± 4.10	23.19± 2.87	6.29± 1.05	44/20/16	30/50	28/30/22
Control group	40	59.56± 5.10	22.00± 0.95	6.48± 1.53	20/16/4	12/18	14/15/11

1.2 治疗方法

对照组:给予常规放疗方法,采用体外放疗加常规后装近距离放疗。

观察组:给予图像引导下精确放疗,采用图像引导下的调强放疗及三维腔内后装放疗。

定位:采用热塑体模进行固定,患者仰卧位时固定体位,保持膀胱充盈。采用 CT 进行扫描,扫描层厚 5 mm,扫描范围从坐骨结节下肾门平面至坐骨结节下 5 cm。靶区的设定:CTV 上界为髂血管分叉平面,下界为瘤体下 3 cm,GTVnd 为影像可见的阳性淋巴结,PTV 为 CTV 前后左右分别外放 0.7 cm,头脚方向外放 1.0 cm,PGTVnd 为 GTVnd 三维外放 0.5 cm。

总放疗时间为 8 周,同期给予顺铂进行单药周方案化疗,40 mg/m^2 体表面积,同期化疗 5 周期。

1.3 观察指标

(1)疗效标准:参照实体瘤疗效为标准,CR+PR 表示有效。完全缓解(Complete remission,CR):可以测量的肿瘤全部消失;部分缓解 (Partial remission,PR):肿块缩小≥ 50 %;病变稳定(Lesion stable,SD):肿块增大≤ 25 %或缩小≤ 50 %;病变进展(Pathological devolop,PD):新病变出现或单个或者多个病变增大≥ 25 %。(2)记录两组在治疗期间出现的放射性直肠损伤、放射性膀胱损伤、消化道反应、血液系统反应等毒副反应情况。(3)在治疗前后收集患者静脉血,检测免疫球蛋白 G(IgG)、免疫球蛋白 A(IgA)等免疫功能指标含量。(4)所有患者随访至今,笔记无疾病进展生存时间和总生存时间。

1.4 统计方法

选择 SPSS22.00,通过($\bar{x}\pm s$)来表示计量资料,行 t 检验,通过%表示计数数据,使用卡方分析对比计数数据,生存因素分析采用 Kapplan-meier 法分析,所有的检验为双侧检验,P<0.05 为差异显著。

2 结果

2.1 总有效率对比

治疗后观察组的总有效率为 85.0%,显著高于对照组的 60.0%(P<0.05)。见表 2。

表 2 总有效率对比(例,%)

Table 2 Comparison of total efficiency between the two groups (n, %)

Groups	n	CR	PR	SD	PD	Total effective rate
Observation group	80	36	32	10	2	68(85.0%)*
Control group	40	12	12	10	8	24(60.0%)

Note: Compared with the control group, *P<0.05.

2.2 毒副反应情况对比

观察组治疗期间的放射性直肠损伤、放射性膀胱损伤、消化道反应、血液系统反应等毒副反应发生率低于对照组(P<0.05)。见表 3。

表 3 毒副反应情况对比 (例,%)

Table 3 Comparison of toxic and side effects (n, %)

Groups	n	Radiation rectal injury	Radiation bladder injury	Radiation bladder injury	Blood system reaction
Observation group	80	2(2.5%)*	2(2.5%)*	5(6.3%)*	7(8.8%)*
Control group	40	7(17.5%)	6(15.0%)	11(27.5%)	12(30.0%)

Note: Compared with the control group, *P<0.05.

2.3 免疫功能变化对比

观察组治疗后的 IgG 与 IgA 值都显著高于治疗前(P<0.05)，也高于对照组(P<0.05)，见表 4。

表 4 两免疫功能变化对比 (g/L，$\bar{x}\pm s$)

Table 4 Comparison of immune function changes (g/L, $\bar{x}\pm s$)

Groups	n	IgG Pretherapy	Post-treatment	IgA Pretherapy	Post-treatment
Observation group	80	7.72± 0.31	19.87± 1.33*#	1.14± 0.10	4.56± 0.42*#
Control group	40	7.70± 0.24	7.56± 0.34	1.15± 0.12	1.19± 0.13

Note: Compared with the pretherapy, *P<0.05; compared with the control group of Post-treatment, #P<0.05.

2.4 生存情况对比

Kapplan-meier 法分析显示观察组的无疾病进展生存时间和总生存时间都显著长于对照组(P<0.05)。见表 5。

表 5 两组生存时间对比(月，$\bar{x}\pm s$)

Table 5 Comparison of survival time between the two groups (month, $\bar{x}\pm s$)

Groups	n	Disease-free progress survival time	Total survival time
Observation group	80	18.28± 1.24*	22.01± 2.15*
Control group	40	15.49± 1.42	17.66± 1.77

Note: Compared with the control group, *P<0.05.

3 讨论

宫颈癌很多患者在治疗后容易复发，导致治疗效果欠佳[12,13]。放疗可以显著提高晚期宫颈癌患者的局控率，但是放疗的毒副反应大[14,15]。精确放疗可以达到更好的靶区分布和显著降低危及器官的受照射体积，从而可以降低直肠、膀胱、处方剂量水平受照射体积[16]。特别是图像的应用可增加了摆位准确的精度，实现靶区更好剂量分布，通过调整照射野内剂量，同时降低周围正常组织受量[17]。本研究显示治疗后观察组的总有效率高于对照组；观察组治疗期间的放射性直肠损伤、放射性膀胱损伤、消化道反应、血液系统反应等毒副反应发生率显著低于对照组，表明图像引导下精确放疗能提高放疗效果，减少毒副反应的发生。

宫颈癌是一种临床常见的恶性肿瘤，具有疗难度大、死亡率高、发病率高、隐匿性强等特点[18]，很多患者常合并基础疾病且器官生理功能衰退，无法进行手术治疗[19]。宫颈癌的放疗括体外放疗和腔内放疗，也经历了普通放疗、调强放疗、三维适形放疗、螺旋断层放射等技术发展过程[20,21]。图像引导的应用可实时了解膀胱和直肠充盈程度，降低由于患者膀胱和肠道体积变化所导致的摆位误差，从而达到精确放疗的目的[22-24]。本研究显示观察组治疗后的 IgG 与 IgA 值都显著高于治疗前，也高于对照组，对照组治疗前后对比差异无统计学意义，表明图像引导下精确放疗能促进患者免疫功能的恢复。并且图像引导的应用有明显的剂量学优势，可使得周围危及器官的辐射剂量比较少，使病灶得到较高照射剂量的同时，有效的保护周围的正常组织[25-27]。

图像引导下精确放疗是一种 CT 图像引导调强放射治疗技术，可实现剂量分布的高度均匀性与适形性，能实现更好的危及器官保护[28-30]。本研究显示 Kapplan-meier 法分析显示观察组的无疾病进展生存时间和总生存时间都显著长于对照组，表明该方法的应用能延长患者的生存时间。不过本研究也存在一定的局限性，具体的作用机制还不明确，也没有进行剂量学分析，将在下一步研究中进行深入分析与探讨。

总之，图像引导下精确放疗治疗宫颈癌能促进患者免疫功能的恢复，提高治疗效果与减少毒副反应的发生，从而延长患者的生存时间。

参 考 文 献(References)

[1] Li X, Zhao J, Liu M, et al. Determination of radiotherapeutic target zones for thoracic esophageal squamous cell cancer with lower cervical lymph node metastasis according to CT-images [J]. Oncotarget, 2016, 7(24): 35865-35873

[2] Biete A, Oses G. Intraoperative radiation therapy in uterine cervical cancer: A review [J]. Rep Pract Oncol Radiother, 2018, 23 (6): 589-594

[3] Bowen S R, Yuh W T C, Hippe D S, et al. Tumor radiomic heterogeneity: Multiparametric functional imaging to characterize variability and predict response following cervical cancer radiation therapy [J]. J Magn Reson Imaging, 2018, 47(5): 1388-1396

[4] Chargari C, Deutsch E, Blanchard P, et al. Brachytherapy: An overview for clinicians[J]. CA Cancer J Clin, 2019, 69(5): 386-401

[7] Gebremariam A, Yalew A W, Hirpa S, et al. Application of the rapid ethical assessment approach to enhance the ethical conduct of longitudinal population based female cancer research in an urban setting in Ethiopia[J]. BMC Med Ethics, 2018, 19(1): 87

[8] Jan Y T, Chang C L, Tai H C, et al. The air matters - sleeve air cavity as a marker guiding image-guided helical tomotherapy to target cervical cancer[J]. J Contemp Brachytherapy, 2016, 8(1): 82-87

[9] Jurgenliemk-Schulz I M, Beriwal S, De Leeuw A a C, et al. Management of Nodal Disease in Advanced Cervical Cancer[J]. Semin Radiat Oncol, 2019, 29(2): 158-165

[10] Koper K, Dziobek K, Makarewicz R, et al. The analysis of the

long-term outcomes in elderly women treated for locally advanced cervical cancer[J]. J Contemp Brachytherapy, 2018, 10(5): 411-417

[11] Onodera K, Sato N, Kobayashi K, et al. A Pulmonary Mucoepidermoid Carcinoma with Anaplastic Lymphoma Kinase Fusion Responding to Alectinib Hydrochloride [J]. Kyobu Geka, 2019, 72(11): 889-892

[12] Palled S R, Tanvirpasha C a R, Naveen T, et al. Magnetic resonance image-based 3D volume interstitial brachytherapy using polyether ether ketone catheters in advanced cervical cancer - a feasibility study [J]. J Contemp Brachytherapy, 2019, 11(4): 307-311

[13] Mastmeyer A, Pernelle G, Ma R, et al. Accurate model-based segmentation of gynecologic brachytherapy catheter collections in MRI-images[J]. Med Image Anal, 2017, 42(2): 173-188

[14] Mezquita G, Muruzabal J C, Perez B, et al. Para-aortic plus pelvic lymphadenectomy in locally advanced cervical cancer: A single institutional experience[J]. Eur J Obstet Gynecol Reprod Biol, 2019, 236: 79-83

[15] Rodgers J R, Murry K, Leung E, et al. Toward a 3D transrectal ultrasound system for verification of needle placement during high-dose-rate interstitial gynecologic brachytherapy [J]. Med Phys, 2017, 44(5): 1899-1911

[16] Yu J, Ouyang W, Li C, et al. Mapping patterns of metastatic lymph nodes for postoperative radiotherapy in thoracic esophageal squamous cell carcinoma: a recommendation for clinical target volume definition[J]. BMC Cancer, 2019, 19(1): 927

[17] Song Y, Erickson B, Chen X, et al. Appropriate magnetic resonance imaging techniques for gross tumor volume delineation in external beam radiation therapy of locally advanced cervical cancer [J]. Oncotarget, 2018, 9(11): 10100-10109

[18] Verma V, Choi J I, Sawant A, et al. Use of PET and Other Functional Imaging to Guide Target Delineation in Radiation Oncology [J]. Semin Radiat Oncol, 2018, 28(3): 171-177

[19] Morsing A, Hildebrandt M G, Vilstrup M H, et al. Hybrid PET/MRI in major cancers: a scoping review [J]. Eur J Nucl Med Mol Imaging, 2019, 46(10): 2138-2151

[20] Zheng Q, Li X, Cheng X, et al. Granulocyte-macrophage colony-stimulating factor increases tumor growth and angiogenesis directly by promoting endothelial cell function and indirectly by enhancing the mobilization and recruitment of proangiogenic granulocytes[J]. Tumour Biol, 2017, 39(2): 1010428317692232

[21] Briens A, Castelli J, Barateau A, et al. [Adaptive radiotherapy: Strategies and benefits depending on tumor localization][J]. Cancer Radiother, 2019, 23(6-7): 592-608

[22] Cegla P, Burchardt E, Roszak A, et al. Influence of Biological Parameters Assessed in [18F]FDG PET/CT on Overall Survival in Cervical Cancer Patients[J]. Clin Nucl Med, 2019, 44(11): 860-863

[23] Fischerova D, Cibula D. The role of ultrasound in primary workup of cervical cancer staging (ESGO, ESTRO, ESP cervical cancer guidelines)[J]. Ceska Gynekol, 2019, 84(1): 40-48

[24] Gosset M, Chargari C, Bentivegna E, et al. Should We Cease to Perform Salvage Hysterectomy After Chemoradiation and Brachytherapy in Locally Advanced Cervical Cancer?[J]. Anticancer Res, 2019, 39 (6): 2919-2926

[25] Kahramanoglu I, Meydanli M M, Taranenka S, et al. SATEN II-I-Splitting Adjuvant Treatment of stage III ENdometrial cancers: an international, multicenter study[J]. Int J Gynecol Cancer, 2019, 29(8): 1271-1279

[26] Karaca S, Kirli M. Adaptive radiation therapy for cervical esophageal cancer: dosimetric and volumetric analysis [J]. J Gastrointest Oncol, 2019, 10(3): 506-512

[27] Kumar T, Achkar S, Haie-Meder C, et al. Multimodal imaging guided brachytherapy: the example of cervical cancer [J]. Cancer Radiother, 2019, 23(6-7): 765-772

[28] Li C, Zhang J, Wang H. Predictive value of LN metastasis detected by (18)F-FDG PET/CT in patients with papillary thyroid cancer receiving iodine-131 radiotherapy[J]. Oncol Lett, 2019, 18(2): 1641-1648

[29] Muresan B T, Sanchez Juan C, Artero A, et al. Diagnosis of pre-sarcopenia from a single selectional crosscut at C3 region, using CT scans before radiotherapy[J]. Nutr Hosp, 2019, 36(5): 1101-1108

[30] Schad M D, Moore J, Camacho F, et al. Predictors of quality of care and survival in a three-state cohort of locally advanced cervical cancer patients and development of a predictive model to identify women at risk of incomplete treatment[J]. Medicine (Baltimore), 2019, 98(33): e16874