

doi: 10.13241/j.cnki.pmb.2021.14.029

调强适形放疗联合替莫唑胺对脑胶质瘤患者生命质量及血清 VEGF、EGF 水平的影响 *

曹 杰¹ 张 杰¹ 李 民¹ 孟发财¹ 蔺鹏帧¹ 黄卫东¹ 于 娇²

(1 陕西省人民医院神经外科 陕西 西安 710068; 2 陕西省人民医院放疗科 陕西 西安 710068)

摘要 目的:探讨调强适形放疗联合替莫唑胺对脑胶质瘤患者生命质量及血清表皮生长因子(EGF)、血管内皮生长因子(VEGF)水平的影响。**方法:**选取我院于 2015 年 3 月到 2017 年 2 月期间收治的脑胶质瘤患者 86 例,分为对照组($n=43$,调强适形放疗治疗)和研究组($n=43$,对照组的基础上联合替莫唑胺治疗),比较两组患者疗效、生命质量、生存率血清 VEGF、EGF 水平以及不良反应。**结果:**治疗 6 个疗程后,研究组的总有效率为 69.77%(30/43),高于对照组的 48.84%(21/43)($P<0.05$)。治疗 6 个疗程后,两组血清 VEGF、EGF 水平均较治疗前降低,且研究组低于对照组($P<0.05$)。两组不良反应发生率对比无差异($P>0.05$)。治疗 6 个疗程后,两组生活质量量表(QOL)、卡劳夫斯基(KPS)评分升高,且研究组高于对照组($P<0.05$)。研究组治疗后 1 年、2 年、3 年生存率均高于对照组($P<0.05$)。**结论:**调强适形放疗联合替莫唑胺治疗胶质瘤患者疗效较好,可有效降低患者血清 VEGF、EGF 水平,且不增加不良反应发生率,同时还可有效改善患者生命质量。

关键词:调强适形放疗;替莫唑胺;脑胶质瘤;生命质量;血管内皮生长因子;表皮生长因子

中图分类号:R739.4;R730.55 **文献标识码:**A **文章编号:**1673-6273(2021)14-2735-04

Effects of Three Dimensional Conformal Radiotherapy Combined with Temozolomide on Quality of Life and the Levels of Serum VEGF, EGF in Patients with Glioma*

CAO Jie¹, ZHANG Jie¹, LI Min¹, MENG Fa-cai¹, LIN Peng-zhen¹, HUANG Wei-dong¹, Yu Jiao²

(1 Department of Neurosurgery, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, 710068, China;

2 Department of Radiotherapy, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, 710068, China)

ABSTRACT Objective: To investigate the effects of three dimensional conformal radiotherapy combined with temozolomide on quality of life and the levels of serum epidermal growth factor(EGF), vascular endothelial growth factor(VEGF) in patients with glioma. **Methods:** 86 patients with glioma who were admitted to our hospital from March 2016 to February 2017 were selected. They were divided into control group ($n=43$) and study group ($n=43$), the patients in the control group were treated with three dimensional conformal radiotherapy, the study group were treated combine with temozolomide on the basis of the control group, the curative effect, quality of life, survival rate, the levels of serum VEGF, EGF and adverse reactions in patients of the two groups were compared. **Results:** After 4 courses of treatment, the total efficiency rate of the study group was 69.77% (30/43), which was higher than 48.84% (21/43) of the control group ($P<0.05$). After 4 courses of treatment, the levels of VEGF, EGF in the two groups were lower than those of the before treatment, and the study group were lower than those of the control group ($P<0.05$). After 4 courses of treatment, the quality of life scale (QOL), Kalovsky (KPS) scores of the two groups were higher than those of the before treatment, and the study group were higher than those of the control group ($P<0.05$). The 1,2,3-year survival rate of the study group were higher than those of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Three dimensional conformal radiotherapy combined with temozolomide treat the patients with glioma has good curative effect, can effectively reduce the levels of serum VEGF, EGF of the patients, and does not increase the incidence of adverse reactions, which can effectively improve the quality of life of the patients at the same time.

Key words: Three dimensional conformal radiotherapy; Temozolomide; Glioma; Quality of life; Vascular endothelial growth factor; Epidermal growth factor

Chinese Library Classification(CLC): R739.4; R730.55 **Document code:** A

Article ID: 1673-6273(2021)14-2735-04

* 基金项目:陕西省自然科学基金基础研究计划项目(2016JM8073)

作者简介:曹杰(1975-),男,在职博士研究生,副主任医师,研究方向:脑血管病、脑肿瘤及脑积水,E-mail:cj18092895019@163.com

(收稿日期:2020-09-04 接受日期:2020-09-28)

前言

脑胶质瘤是临床常见的颅内神经上皮恶性肿瘤,具有高发率及高致死率的特点^[1]。该病可见于任何年龄段,以中老年群体为主,男性多见^[2]。临床主要表现为颅内压增高、认知功能障碍等症状,同时还可引起多种神经功能系统障碍,影响患者生活质量^[3]。调强适形放疗具有精确设计计划、精确定位、精确治疗等优点,通过三维软件进行治疗计划的设计,在杀伤癌细胞的同时可最大限度的减少对瘤周边正常组织的伤害的作用,有效控制肿瘤的增长、转移、扩散^[4-6]。然而也有部分患者经调强适形放疗治疗后效果欠佳,临床价值有限。替莫唑胺是临床常用于治疗复发或进展的多形性胶质母细胞瘤或间变性星形细胞瘤,是一种具有抗肿瘤活性的烷化剂^[7,8]。本研究通过将调强适形放疗联合替莫唑胺治疗应用于我院收治的部分脑胶质瘤患者,观察其治疗效果。

1 资料与方法

1.1 基线资料

选取我院于2015年3月到2017年2月期间收治的脑胶质瘤患者86例。纳入标准:(1)符合《WHO(2016)中枢神经系统肿瘤组织学分类》^[9]中脑胶质瘤相关标准;(2)患者及其家属知情本研究且签署了同意书;(3)病理检查确诊为脑胶质瘤,肿瘤单发且行手术切除治疗,病理分级为III~IV级;(4)血常规、肝肾功能、心电图、凝血功能正常;(5)生命体征平稳;(6)卡劳夫斯基(KPS)行为状况评分在60分以上。排除标准:(1)合并其他恶性肿瘤者;(2)有脑出血和脑梗死病史者;(3)接受过化疗或头颈部肿瘤增敏放疗者;(4)存在放疗禁忌证及对本研究药物过敏者;(5)伴精神疾病者;(6)未能完成随访研究者。根据随机数字表法分为两组对照组、研究组,其中对照组43例,女20例,男23例,病理类型:间变性少突胶质细胞瘤16例,III~IV级星形胶质细胞瘤17例,混合性胶质瘤10例;年龄38~60岁,平均(48.89±3.27)岁;病理分级:IV级19例,III级24例。研究组43例,女18例,男25例,病理类型:间变性少突胶质细胞瘤15例,III~IV级星形胶质细胞瘤16例,混合性胶质瘤12例;年龄36~63岁,平均(47.95±4.42)岁;病理分级:IV级17例,III级26例。两组一般资料比较无差异($P>0.05$),具有可比性。

1.2 方法

两组患者均于术后2~6周行调强适形放疗,具体如下:患者取仰卧位,头部采用热塑头颈肩膜面罩固定,于飞利浦大孔径CT行CT增强扫描,头顶至上颈部层距、层厚各3mm,将

CT定位扫描图像传输至Pinnacle治疗计划系统工作站,将术前、术后增强MRI及CT定位图像融合进行靶区勾画,肿瘤大体靶区(GTV)为MRI T1增强或T2/FLAR异常信号区,GTV外扩2-2.5cm并包括T2/FLAR显示的水肿区、术后瘤腔为一程临床靶体积(CTV-1),二程增量临床靶体积(CTV-2)为GTV或术后瘤腔外扩2cm,CTV-1、CTV-2分别外扩3mm为计划靶体积(PTV)-1和PTV-2,放疗计划:PTV-1 DT 46Gy/23f(2Gy/f, 5f/w),之后缩野至PTV-2推量DT 14Gy/7f(2Gy/f, 5f/w)。研究组在对照组的基础上联合替莫唑胺(Merck Sharp & Dohme Limited,规格:100mg)治疗,放疗过程中75mg/(m²·d),放疗结束14d后开始辅助化疗,100~200mg/(m²·d),服用5d后间隔23d。两组均以28d为一个疗程,治疗6个疗程。放化疗期间均予托烷司琼或格拉司琼止吐,粒细胞集落刺激因子升白细胞,甘露醇、糖皮质激素、维生素以防治脑水肿等对症处理。

1.3 观察指标

(1)疗效标准:目标性病灶进展或出现新病灶(病情进展)。基线病灶缩小<30%或增加<20%,出现1个及以上非目标病灶或肿瘤标志物异常(疾病稳定)。可测病灶及不可测病灶长径总值缩小≥30%(部分缓解)。目标及非目标病灶完全消失,肿瘤标志物正常(完全缓解);总有效率=完全缓解率+部分缓解率^[10]。(2)采集患者清晨空腹肘静脉血4mL,采血时间:治疗前、治疗6个疗程后。经离心半径14cm,4500r/min离心13min,分离上清液待测。参考试剂盒(美国sigma公司)说明书步骤,采用酶联免疫吸附法测定血管内皮生长因子(VEGF)、表皮生长因子(EGF)水平。(3)于治疗前、治疗6个疗程后采用KPS评分^[11]、生活质量量表(QOL)^[12]评价患者生存质量及生活质量,其中KPS评分为0~100分,得分越高表示生存质量越好。QOL包括12个维度,每个维度评分1~5分,得分越高表示生活质量越好。(4)两组均以门诊复查、电子通信的方式随访3年或死亡,比较两组治疗后1年、2年、3年生存率。

1.4 统计学方法

采用SPSS25.0进行数据分析,以率的形式表示计数资料,行卡方检验,以均值±标准差的形式表示计量资料,行t检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 疗效比较

研究组治疗6个疗程后的总有效率为69.77%(30/43),高于对照组的48.84%(21/43)($P<0.05$);详见表1。

表1 两组疗效比较[例(%)]

Table 1 Comparison of curative effect between the two groups[n(%)]

Groups	Complete remission	Partial remission	Disease stability	Disease progression	Total efficiency
Control group (n = 43)	6(13.95)	15(34.88)	14(32.56)	8(18.60)	21(48.84)
Study group (n = 43)	11(25.58)	19(44.19)	9(20.93)	4(9.30)	30(69.77)
χ^2					3.903
P					0.048

2.2 VEGF、EGF 水平比较

治疗前,两组血清VEGF、EGF水平比较($P>0.05$),治疗6

个疗程后,两组血清 VEGF、EGF 水平降低,且研究组较对照组 低($P<0.05$),详见表 2。

表 2 两组血清 VEGF、EGF 水平比较($\bar{x}\pm s$, ng/L)Table 2 Comparison of levels of serum VEGF, EGF between the two groups($\bar{x}\pm s$, ng/L)

Groups	VEGF		EGF	
	Before treatment	After 6 courses of treatment	Before treatment	After 6 courses of treatment
Control group (n = 43)	276.89±19.65	164.67±17.95*	121.23±17.25	78.39±12.87*
Study group (n = 43)	278.36±21.02	108.14±15.79*	120.81±20.36	44.97±8.95*
t	0.335	15.506	0.103	13.980
P	0.738	0.000	0.918	0.000

Notes: Compared with before treatment, * $P<0.05$.

2.3 生命质量比较

疗程后 QOL、KPS 评分升高,且研究组较对照组高($P<0.05$),详

治疗前,两组 KPS、QOL 评分比较($P>0.05$),两组治疗 6 个 见表 3。

表 3 两组生命质量比较($\bar{x}\pm s$, 分)Table 3 Comparison of quality of life between two groups($\bar{x}\pm s$, score)

Groups	VEGF		EGF	
	Before treatment	After 6 courses of treatment	Before treatment	After 6 courses of treatment
Control group (n = 43)	276.89±19.65	164.67±17.95*	121.23±17.25	78.39±12.87*
Study group (n = 43)	278.36±21.02	108.14±15.79*	120.81±20.36	44.97±8.95*
t	0.335	15.506	0.103	13.980
P	0.738	0.000	0.918	0.000

Notes: Compared with before treatment, * $P<0.05$.

2.4 两组生存率比较

(74.42%)生存率均高于对照组(69.77%)、(62.79%)、(53.49%)

研究组治疗后 1 年 (90.70%)、2 年 (83.72%)、3 年 ($P<0.05$);详见表 4。

表 4 两组生存率比较【例(%)】

Table 4 Comparison of survival rates between the two groups[n(%)]

Groups	1 year survival rate	2-year survival rate	3-year survival rate
Control group (n = 43)	30(69.77)	27(62.79)	23(53.49)
Study group (n = 43)	39(90.70)	36(83.72)	32(74.42)
χ^2	5.939	4.807	5.560
P	0.015	0.028	0.018

2.5 两组不良反应发生情况比较

两组不良反应发生率对比($P>0.05$),详见表 5。

表 5 两组不良反应发生情况比较【例(%)】

Table 5 Comparison of adverse reactions between the two groups[n(%)]

Groups	Nausea and vomiting	Leukopenia	Alopecia	Myelo suppression	Total incidence
Control group (n = 43)	4(9.30)	2(4.65)	5(11.63)	4(9.30)	15(34.88)
Study group (n = 43)	3(6.98)	2(4.65)	5(11.63)	3(6.98)	13(30.23)
χ^2					0.212
P					0.645

3 讨论

脑胶质瘤可引起空间 " 占位 " 效应,进而出现头痛、视物模糊等一系列临床症状,导致患者生活质量明显下降,其 5 年生存率不到 40%^[13-15]。目前临床有关脑胶质瘤的具体发病机制

尚未完全阐明,其发生发展可能与外环境因素、机体因素以及基因变异有关,而在这之中,肿瘤血管生成学说得到了较多学者的认可^[16-18]。脑胶质瘤的细胞增生导致细胞组织处于缺氧状态,从而刺激肿瘤细胞释放 VEGF、EGF 等血管活性因子,进而驱动癌细胞浸润性生长^[19,20]。因此,临床不仅可将 VEGF 和

EGF 作为脑胶质瘤的血清学标志物,同时还可将其用作判断患者预后的辅助指标。手术作为脑胶质瘤的主要治疗方案,可获得一定的治疗效果,但由于脑胶质瘤处于脑部的重要功能区,术中无法彻底清除病灶,导致术后复发率较高。故临床通常在术后给予放化疗治疗。

肿瘤放疗的理想目标是只针对病灶部位而不损伤周边正常组织。以往常用的放射治疗无法准确的调整靶区剂量使得治疗效果较差^[21]。调强适形放疗可在实体虚拟图像上对剂量分布实际情况进行计算,有效控制患者病灶周围正常组织的受量,并对照射效果进行评价,最大程度的减少对正常周围组织的损害,提高患者耐受性,化疗药物的应用使生存期限明显延长^[22,23]。以往有研究结果显示^[24],单纯术后放疗的长期生存率不尽人意。邹勤舟等人^[25]研究显示,脑胶质瘤患者在化疗期间联合替莫唑胺辅助治疗,可提高治疗效果,延长生存期限。替莫唑胺具有广谱抗肿瘤活性,对处于有丝分裂时期的癌细胞发挥抑制作用,阻止细胞增殖,发挥抗肿瘤效应^[26,27]。本研究组研究的总有效率高于对照组,主要是因为调强适形放疗联合替莫唑胺从不同的作用机制出发,发挥抗肿瘤效应,同时替莫唑胺还可有效增加放疗敏感性,共同促进疗效提升。进一步观察患者血清指标发现,两组血清 VEGF、EGF 水平均较治疗前降低,且研究组低于对照组。替莫唑胺在生理酸碱度下,可转换为活性产物 5-(3-甲基)-1-咪唑基-4-氨基甲酰,促使肿瘤 DNA 甲基化,破坏其 RNA 和蛋白质结构,阻止肿瘤细胞增殖,减少对肿瘤细胞的刺激,进而有效改善 VEGF、EGF 等血管活性因子^[28,29]。脑胶质瘤疾病本身可对患者身心均造成巨大损伤,进而导致其生命质量明显下降,本研究中相比于单纯的放疗患者,联合替莫唑胺治疗的生命质量改善更为显著,可能是因为联合治疗可更好的控制患者病情,减轻患者身体不适感,对患者日常生活、工作的影响相对较轻,故而该类患者生命治疗更高。此外,两种治疗方案不良反应发生率对比未见差异,主要是因为替莫唑胺在酸性环境下较为稳定,与其他药物联合使用时无叠加毒性,故不增加不良反应发生率,安全可靠^[30]。同时,通过随访研究发现,研究组治疗后 1 年、2 年、3 年生存率均高于对照组,可能是与联合治疗可更好的控制患者病情,减少复发发生风险有关。

综上所述,调强适形放疗联合替莫唑胺治疗胶质瘤患者疗效较好,可降低血清 VEGF、EGF 水平,有效改善患者生命质量,具有一定的临床应用价值。

参考文献(References)

- [1] Venkatesh HS, Morishita W, Geraghty AC, et al. Electrical and synaptic integration of glioma into neural circuits [J]. *Nature*, 2019, 573(7775): 539-545
- [2] Gutmann DH, Kettenmann H. Microglia/Brain Macrophages as Central Drivers of Brain Tumor Pathobiology [J]. *Neuron*, 2019, 104(3): 442-449
- [3] Lukas RV, Wainwright DA, Horbinski CM, et al. Immunotherapy Against Gliomas: is the Breakthrough Near?[J]. *Drugs*, 2019, 79(17): 1839-1848
- [4] Wei X, Jiang Y, Zhang X, et al. Neoadjuvant Three-Dimensional Conformal Radiotherapy for Resectable Hepatocellular Carcinoma With Portal Vein Tumor Thrombus: A Randomized, Open-Label, Multicenter Controlled Study[J]. *J Clin Oncol*, 2019, 37(24): 2141-2151
- [5] Kivanc H, Gultekin M, Gurkaynak M, et al. Dosimetric comparison of three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for left-sided chest wall and lymphatic irradiation [J]. *J Appl Clin Med Phys*, 2019, 20(12): 36-44
- [6] Jirkovska M, Novak T, Malinova B, et al. Three-dimensional conformal radiotherapy versus intensity modulated radiotherapy with simultaneous integrated boost in the treatment of locally advanced head and neck carcinoma[J]. *Neoplasma*, 2019, 66(5): 830-838
- [7] Strobel H, Baisch T, Fitzel R, et al. Temozolomide and Other Alkylating Agents in Glioblastoma Therapy[J]. *Biomedicines*, 2019, 7(3): 69
- [8] Yi GZ, Huang G, Guo M, et al. Acquired temozolomide resistance in MGMT-deficient glioblastoma cells is associated with regulation of DNA repair by DHC2[J]. *Brain*, 2019, 142(8): 2352-2366
- [9] Louis DN, Ohgaki H, Wiestler OD, et al. WHO(2016) 中枢神经系统肿瘤组织学分类[J]. *诊断病理学杂志*, 2016, 23(8): 638-640
- [10] 易立, 王旭亚, 初曙光, 等. 脑胶质瘤疗效评价进展[J]. *中国现代神经疾病杂志*, 2019, 19(11): 826-831
- [11] Halid MA, Achakzai IK, Ahmed Khan S, et al. The use of Karnofsky Performance Status (KPS) as a predictor of 3 month post discharge mortality in cirrhotic patients [J]. *Gastroenterol Hepatol Bed Bench*, 2018, 11(4): 301-305
- [12] Estoque RC, Togawa T, Ooba M, et al. A review of quality of life (QOL) assessments and indicators: Towards a "QOL-Climate" assessment framework[J]. *Ambio*, 2019, 48(6): 619-638
- [13] Lee J, Chaloner Winton Hall R. The Impact of Gliomas on Cognition and Capacity[J]. *J Am Acad Psychiatry Law*, 2019, 47(3): 350-359
- [14] Venkataramani V, Tanev DI, Strahle C, et al. Glutamatergic synaptic input to glioma cells drives brain tumour progression [J]. *Nature*, 2019, 573(7775): 532-538
- [15] Glombova M, Petrak B, Lisy J, et al. Brain gliomas, hydrocephalus and idiopathic aqueduct stenosis in children with neurofibromatosis type 1[J]. *Brain Dev*, 2019, 41(8): 678-690
- [16] Malouff TD, Peterson JL, Mahajan A, et al. Carbon ion radiotherapy in the treatment of gliomas: a review [J]. *J Neurooncol*, 2019, 145(2): 191-199
- [17] Conte GM, Altabella L, Castellano A, et al. Comparison of T1 mapping and fixed T1 method for dynamic contrast-enhanced MRI perfusion in brain gliomas[J]. *Eur Radiol*, 2019, 29(7): 3467-3479
- [18] Falchetti ML, D'Alessandris QG, Pacioni S, et al. Glioblastoma endothelium drives bevacizumab-induced infiltrative growth via modulation of PLXDC1[J]. *Int J Cancer*, 2019, 144(6): 1331-1344
- [19] Mair DB, Ames HM, Li R. Mechanisms of invasion and motility of high-grade gliomas in the brain[J]. *Mol Biol Cell*, 2018, 29(21): 2509-2515
- [20] Todorova PK, Fletcher-Sananikone E, Mukherjee B, et al. Radiation-Induced DNA Damage Cooperates with Heterozygosity of TP53 and PTEN to Generate High-Grade Gliomas[J]. *Cancer Res*, 2019, 79(14): 3749-3761

- 点的文献调查分析[J].江苏中医药, 2020, 52(4): 74-80
- [14] 苗青,丛晓东,王冰,等.新型冠状病毒肺炎的中医认识与思考[J].中医杂志, 2020, 61(4): 286-288
- [15] 范伏元,樊新荣,王莘智,等.从“湿毒夹燥”谈湖南新型冠状病毒肺炎的中医特点及防治[J].中医杂志, 2020, 61(7): 553-556
- [16] 李鑫,代甜,王虹,等.2019 冠状病毒病(COVID-19)疑似患者合并焦虑和抑郁的临床分析 [J]. 浙江大学学报 (医学版), 2020, 49(2): 203-208
- [17] 程丽,郑丽平,晏苏玉,等.新型冠状病毒肺炎患者焦虑现状及影响因素分析[J].浙江医学, 2020, 42(4): 315-317
- [18] Liu S, Yang L, Zhang C, et al. Online mental health services in China during the COVID-19 outbreak [J]. *Lancet Psychiatry*, 2020, 7 (4): e17-e18
- [19] Qiu J, Shen B, Zhao M, et al. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations[J]. *Gen Psychiatr*, 2020, 33 (2): e100213
- [20] 董人齐,周霞,焦小楠,等.新型冠状病毒肺炎疫情期间隔离人员心理状况调查研究[J].康复学报, 2020, 30(1): 7-10
- [21] 尚东梅,曹靖惠.康艾注射液联合音乐疗法对老年非小细胞肺癌胸腔镜术后化疗血清肿瘤标志物及心理健康的影响[J].中国老年学杂志, 2019, 39(20): 4958-4961
- [22] Dai WS, Huang ST, Xu N, et al. The effect of music therapy on pain, anxiety and depression in patients after coronary artery bypass grafting[J]. *J Cardiothorac Surg*, 2020, 15(1): 81-85
- [23] Lin CJ, Chang YC, Chang YH, et al. Music Interventions for Anxiety in Pregnant Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials[J]. *J Clin Med*, 2019, 8(11): 1884
- [24] Kukreja P, Talbott K, MacBeth L, et al. Effects of Music Therapy During Total Knee Arthroplasty Under Spinal Anesthesia: A Prospective Randomized Controlled Study [J]. *Cureus*, 2020, 12(3): e7396
- [25] Liu X, Niu X, Feng Q, et al. Effects of five-element music therapy on elderly people with seasonal affective disorder in a Chinese nursing home[J]. *J Tradit Chin Med*, 2014, 34(2): 159-161
- [26] Yang Y, Fang YY, Gao J, et al. Effects of Five-Element Music on Language Recovery in Patients with Poststroke Aphasia: A Systematic Review and Meta-Analysis[J]. *J Altern Complement Med*, 2019, 25(10): 993-1004
- [27] Lu Y, Qu HQ, Chen FY, et al. Effect of Baduanjin Qigong Exercise on Cancer-Related Fatigue in Patients with Colorectal Cancer Undergoing Chemotherapy: A Randomized Controlled Trial [J]. *Oncol Res Treat*, 2019, 42(9): 431-439
- [28] Zou L, Yeung A, Quan X, et al. Mindfulness-Based Baduanjin Exercise for Depression and Anxiety in People with Physical or Mental Illnesses: A Systematic Review and Meta-Analysis [J]. *Int J Environ Res Public Health*, 2018, 15(2): 321
- [29] Liu SJ, Ren Z, Wang L, et al. Mind-Body (Baduanjin) Exercise Prescription for Chronic Obstructive Pulmonary Disease: A Systematic Review with Meta-Analysis [J]. *Int J Environ Res Public Health*, 2018, 15(9): 1830
- [30] Zou L, Yeung A, Quan X, et al. A Systematic Review and Meta-Analysis of Mindfulness-Based (Baduanjin) Exercise for Alleviating Musculoskeletal Pain and Improving Sleep Quality in People with Chronic Diseases[J]. *Int J Environ Res Public Health*, 2018, 15(2): 206

(上接第 2738 页)

- [21] Marjanovic D, Plesinac Karapandzic V, Stojanovic Rundic S, et al. Implementation of intensity-modulated radiotherapy and comparison with three-dimensional conformal radiotherapy in the postoperative treatment of cervical cancer[J]. *J BUON*, 2019, 24(5): 2028-2034
- [22] Lin WC, Chang CL, Hsu HL, et al. Three-Dimensional Conformal Radiotherapy-Based or Intensity-Modulated Radiotherapy-Based Concurrent Chemoradiotherapy in Patients with Thoracic Esophageal Squamous Cell Carcinoma[J]. *Cancers (Basel)*, 2019, 11(10): 1529
- [23] Wang C, Lu M, Zhou T, et al. Intensity-modulated radiotherapy does not decrease the risk of malnutrition in esophageal cancer patients during radiotherapy compared to three-dimensional conformal radiation therapy[J]. *J Thorac Dis*, 2019, 11(9): 3721-3731
- [24] Taurone S, Spoleitini M, Chiappetta C, et al. Brain gliomas and growth factors: immunohistochemical, immunofluorescence, flow cytometry and RT-PCR profile in pediatric age [J]. *J Biol Regul Homeost Agents*, 2019, 33(5): 1451-1463
- [25] 邹勤舟,张晓军,张福正,等.高级别脑胶质瘤术后同期加量调强放疗联合替莫唑胺化疗的临床观察[J].临床肿瘤学杂志, 2018, 23 (11): 1032-1036
- [26] 董必锋,陈玲,李亮,等.贝伐单抗联合替莫唑胺对老年胶质母细胞瘤术后患者预后的影响 [J]. 现代生物医学进展, 2017, 17(21): 4079-4081, 4085
- [27] Whitelaw BC. How and when to use temozolomide to treat aggressive pituitary tumours [J]. *Endocr Relat Cancer*, 2019, 26(9): R545-R552
- [28] Le Rhun E, Devos P, Houillier C, et al. Romiplostim for temozolomide-induced thrombocytopenia in glioblastoma: The PLATUM trial[J]. *Neurology*, 2019, 93(19): e1799-e1806
- [29] Farago AF, Yeap BY, Stanzione M, et al. Combination Olaparib and Temozolomide in Relapsed Small-Cell Lung Cancer [J]. *Cancer Discov*, 2019, 9(10): 1372-1387
- [30] Karachi A, Yang C, Dastmalchi F, et al. Modulation of temozolomide dose differentially affects T-cell response to immune checkpoint inhibition[J]. *Neuro Oncol*, 2019, 21(6): 730-741