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乳腺癌患者焦虑抑郁水平现状及研究进展*

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[摘要]　随着心理社会肿瘤学的兴起与发展,国内外众多学者开始重视心理社会因素在乳腺癌发生、发展及诊疗过程中的重要作用。焦虑抑郁是乳腺癌患者诊疗过程中普遍出现的心理健康问题,早期进行焦虑抑郁筛查,并给予相应的社会心理干预可改善心理痛苦症状,提高治疗依从性和生存质量。但乳腺癌患者负面心理症状筛查和治疗仍有一定的局限性,且缺乏高质量证据。该文从乳腺癌患者焦虑抑郁的流行病学、病理生理学、症状筛查和治疗4个方面进行综述,旨在为肿瘤临床医生与护理人员针对乳腺癌患者焦虑抑郁症状的预防与管理提供参考。

[关键词]　乳腺癌;焦虑;抑郁;社会心理干预;综述
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Current situation and research progress of anxiety and depression in breast cancer*

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[**Abstract**]　With the rise and development of psychosocial oncology, many scholars at home and abroad have begun to pay attention to the important role of psychosocial factors in the occurrence, development and diagnosis and treatment of breast cancer. Anxiety and depression are common mental health problems in breast cancer diagnosis and treatment. Early screening for anxiety and depression and corresponding psychosocial interventions can improve psychological distress symptoms, treatment compliance and quality of life. However, the screening and treatment of negative psychological symptoms in breast cancer patients still have certain limitations, and there is a lack of high-quality evidence. This article searches the relevant literature on the level of anxiety and depression in breast cancer, and reviewed the epidemiology and pathophysiology of breast cancer anxiety and depression, symptom screening and treatment. The purpose of this study is to provide reference for the prevention and management of breast cancer anxiety and depression symptoms for oncology clinicians and nurses.

[**Key words**]　breast cancer; anxiety; depression; psychosocial intervention; review

乳腺癌是女性常见的癌症类型,其发病率(11.7%)逐年上升,已超过了肺癌(11.4%)和前列腺癌(11.0%),位居全世界女性恶性肿瘤首位[1],其中我国女性乳腺癌占新诊断癌症总人数的19.9%,发病年龄逐渐年轻化[2]。基于癌症筛查的普及及诊疗技术的快速进步,乳腺癌治疗后5年及10年生存率均可达到80%以上[3]。随着国内心理社会肿瘤学研究的兴起,肿瘤患者的心理和行为因素逐渐得到重视,众多学者开始关注心理因素在恶性肿瘤的发生、发展和预后中的作用[4]。由于术后形体的改变、放化疗副作用及工作压力、经济压力等,患者不仅面临着疾病本身及治疗带来的生理症状,而且需要承受复发的恐惧及医疗负担等心理社会挑战,在长期的不良刺激下患者可能会出现一系列心理问题[5-6]。焦虑和抑郁是乳腺癌患者诊疗过程中常见的情绪障碍,影响患者的治疗效果及生活质量、免疫系统功能(包括细胞免疫和体液免疫),增加乳腺癌复发和转移的风险,甚至缩短生存时间,增加癌症死亡率[7-8]。既往国内关于乳

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腺癌患者焦虑抑郁的综述较少，临床上对焦虑、抑郁症状往往忽视和管理不足。本文对近年来乳腺癌患者焦虑抑郁的相关研究进行了综述，以期为临床上改善患者焦虑抑郁水平，提高生存质量提供参考依据。

1 乳腺癌患者焦虑、抑郁现状

与健康人及其他妇科肿瘤患者相比，乳腺癌患者并发焦虑、抑郁的风险更高[9-11]。MAASS等[9]调查了乳腺癌患者和健康人焦虑抑郁的患病率，结果显示乳腺癌患者焦虑(18.6%)、抑郁(10.6%)的患病率高于健康人(16.3%、4.9%)，其中处于严重焦虑和严重抑郁程度的比例明显高于健康人。根据BURGESS等[12]的研究，在确诊乳腺癌时焦虑抑郁的患病率较高，达33%，确诊后1年升高至48%，但在之后的2～5年内逐渐下降，分别为25%、23%、22%和15%，提示随着治疗及生存期的延长，患者对不良刺激的自我调节能力逐渐恢复，进而达到一定的适应状态，其焦虑、抑郁的症状逐渐缓解。FAYE-SCHJØLL等[13]对293例乳腺癌患者进行长期随访发现，焦虑抑郁的患病率在确诊时最高，为29.4%，确诊1年(焦虑21.2%；抑郁7.9%)后有所下降，但在3年(焦虑23.1%；抑郁8.6%)和5年(焦虑26.3%；抑郁9.6%)后略有上升。由于化疗疗效的不确定性和毒副作用给患者造成了巨大的心理压力，焦虑和抑郁症状更为常见，HAJJ等[14]的研究发现乳腺癌化疗患者焦虑的患病率高达56.2%，抑郁的患病率为43.4%。随着乳腺癌年轻化趋势，年轻的患者伴发焦虑抑郁的可能性高于年长的患者。LAN等[15]前瞻性纳入114例年龄在35岁以下的中国乳腺癌术后患者，8.8%的患者出现中等程度以上焦虑，23.7%的患者出现中等程度以上抑郁。

2 乳腺癌患者焦虑、抑郁的影响因素

独居、文化程度、未婚、职业、手术及诊疗方案等各方面不良刺激都可能影响患者的心理应对能力。乳腺癌的确诊本身就是一种不良刺激，治疗疗效的不确定及治疗时间的长期性、术后性征的变化、社交及工作的限制、治疗副作用、疼痛及经济压力等因素均可能加重患者身体及心理上的负担，进而导致心理障碍的出现[16]。NAKAMURA等[7]和HAJJ等[14]的研究证实乳腺癌患者化疗期间抑郁和焦虑的发生率远远高于化疗前，其严重程度与未婚、社交活动减少及睡眠质量低下呈正相关。年轻的乳腺癌患者较为重视自身的形象，疾病或术后导致第二性征的改变、对婚姻及生育的担忧加重了患者的心理压力，BERHILI等[17]的研究证实接受保乳手术的患者发生焦虑抑郁的风险低于接受根治性乳房切除术的患者。此外，年龄、婚姻状况、疾病分期、家庭月收入及受教育程度也会影响焦虑、抑郁的发生[18]。有学者[19-20]研究提示丧偶、老年女性及受教育程度低的乳腺癌患者焦虑、抑郁的发生率较高，与生活质量呈负相关。

3 乳腺癌患者焦虑、抑郁的病理生理学研究

疾病本身及治疗带来的生理及心理各方面不良刺激均可对患者的免疫系统产生影响，在长期或严重的应激状态下可促进肿瘤的发生、血管生成和转移扩散，影响治疗效果及预后，导致身体自我调节功能及生存质量的降低，增加死亡风险[21]。机体炎症水平的变化与癌症相关痛苦存在明显的联系，有研究发现乳腺癌早期治疗(如手术、放疗和化疗)后炎症细胞因子[干扰素-γ(IFN-γ)、白细胞介素(IL)-1、IL-6、肿瘤坏死因子-α(TNF-α)]和C反应蛋白表达水平的改变与焦虑、抑郁症状的发生及严重程度存在纵向相关性，特别是在接受化疗的患者中其相关性表现明显[21]。此外，焦虑抑郁症状的出现可能激活儿茶酚胺和GCs产生的生理通路，抑制自然杀伤细胞活性，降低$CD3^+$、$CD4^+$表达水平，$CD4^+/CD8^+$比值下降，从而抑制细胞介导免疫[22]。此外，焦虑抑郁等心理痛苦的出现与癌症患者体内的行为、神经内分泌途径和交感神经系统相关[23]。具体表现为下丘脑-垂体-肾上腺(HPA)轴的激活，导致调节情绪和新陈代谢的基因表达发生变化，血浆皮质醇和去甲肾上腺素水平升高。随着疾病的进展及治疗不良反应的增加，皮质醇和去甲肾上腺素调节失衡，导致焦虑抑郁等负性情感的发生及加重[24]。另外，敏感性相关基因变异(FKBP5 rs9394309，NR3C2 rs5525和CRHR1 rs12944712)与乳腺癌患者疲劳、焦虑和抑郁心理症状的严重程度有关[25]，TNF-α中的2个单核苷酸多态性(SNP)位点(rs1799964和rs3093662)、儿茶酚-O-甲基转移酶中的rs4680及FK506结合蛋白5中的3个SNP位点(FKBP5-rs1360780；rs9296158；rs9470080)可能与焦虑水平存在相关性，IL-1β中的等位基因(rs1800795；rs2069840)、IFN-γ受体1中的rs9376268及脑源性神经营养因子的rs6265可能与较高的抑郁风险相关[26]。有研究推测多巴胺(DA)、去甲肾上腺素(NA)、血清素(5-HT)和犬尿氨酸(KYN)水平的改变可能使乳腺癌患者更易产生焦虑和抑郁[27]。虽然炎症和乳腺癌焦虑、抑郁可能是双向相关的[16]，但尚未得到充分研究，关于大脑对慢性应激(焦虑抑郁)作出的反应与肿瘤微环境之间的联系仍了解甚少。

4 乳腺癌患者焦虑、抑郁的筛查

一些指南和研究强调了焦虑、抑郁筛查及管理对乳腺癌预后的重要性，为患者提供高质量的综合性服务已成为肿瘤临床工作的最主要目标，建议对乳腺癌患者焦虑、抑郁症状进行合理的评估和常规筛查，并进行针对性干预[4,20]。根据ABU-ODAH等[28]的研究，96.8%的癌症患者存在中等程度以上的护理支持需求，包括日常生活、身体和心理等方面的需求，其中近90%的患者存在焦虑、抑郁症状[28]。目前常用于焦虑、抑郁筛查的是自我报告量表评估[29]，有效的评估工具包括：心理痛苦温度计(DT)、医院焦虑抑郁量

表(HADS)、焦虑自评量表(SAS)、广泛性焦虑障碍量表(GAD-7)、抑郁自评量表(SDS)、流行病学研究中心抑郁量表(CES-D)、贝克抑郁量表(BDI)和爱丁堡抑郁量表(EDS)等[9,12-15,30-31]。此外,国内ZHANG等[32]的研究发现存在焦虑、抑郁症状的女性在癌症(乳腺癌和宫颈癌)的筛查中容易漏诊。因此诊断焦虑、抑郁的人群可能是乳腺癌的高危人群,应提高焦虑和抑郁的筛查,以提高癌症筛查率。然而,在我国对乳腺癌高危人群或乳腺癌确诊患者进行焦虑、抑郁症状的早期筛查仍存在一定的限制,因为焦虑、抑郁的早期表现是情绪低落,在临床上易认为是患者正常的情绪反应而被忽视。

5 乳腺癌患者焦虑抑郁的治疗及预后

5.1 药物干预

使用药物治疗和非药物治疗的方式均可预防或减轻乳腺癌患者的焦虑、抑郁症状。一些药物治疗方案已在临床研究中被证实对乳腺癌患者焦虑抑郁症状有明显的改善作用。选择性5-羟色胺再摄取抑制剂、去甲肾上腺素再摄取抑制剂和依西酞普兰可有效缓解乳腺癌焦虑抑郁症状,明显改善患者的生活质量,且耐受性良好,可成为改善心理行为失调、提高生存质量的治疗选择[33-34]。特异性抗抑郁药细胞色素P4502D6(CYP2D6)抑制剂(如氟西汀、帕罗西汀)可对内分泌药物他莫昔芬的药物疗效产生很大的干扰,甚至可能增加乳腺癌复发转移和死亡的可能性,因此乳腺癌患者在选择该类药物时应考虑是否有联合他莫昔芬的使用[35]。与褪黑素能受体和5-羟色胺能受体亚型(5-HT2b、5-HT2C)结合的新型抗抑郁药物阿格美拉汀在临床上也开始得到广泛使用[36],但上述药物在乳腺癌焦虑抑郁的治疗疗效仍需要纳入更多的患者或进行多中心的临床试验来证实。

5.2 非药物干预

非药物干预治疗通常指运动治疗、音乐治疗和心理干预治疗等,与药物治疗相比,其干预手段易被临床医护人员掌握及患者接受,不会对乳腺癌的临床治疗产生干扰或出现额外的毒副作用[37-43]。虚拟现实(VR)技术应用于当前医疗中,能有效分散患者的注意力,从而改善治疗相关的痛苦及减少心理负担[37]。对于新确诊的乳腺癌患者,早期心理干预不仅可以有效预防疲乏、焦虑、抑郁及失眠等心理问题的发生,而且能提高患者的免疫功能。与未接受心理干预的患者相比,接受早期心理干预的患者促炎因子信号的表达明显降低,其特点是自然杀伤细胞活性恢复速率明显加快,TNF-α表达水平降低,IL-6和IFN-γ表达水平升高[38]。国内有研究表明为期12周的以认知行为治疗为基础的管理干预在治疗后、治疗后1个月及3个月均可提高乳腺癌患者的睡眠质量,减轻焦虑和抑郁症状[39]。八段锦及针灸是中医学的传统疗法,通过运动干预或针灸能明显改善乳腺癌患者的焦虑、抑郁及睡眠障碍,减少疲劳对认知功能的负面影响[41-42]。随着互联网的快速发展,通过电子邮件和电话等网络方式进行心理行为干预及症状管理受到广泛关注[40,43]。随着国内心理社会肿瘤学的兴起,临床上对乳腺癌患者心理问题开始得到重视,期待未来有更多关于非药物治疗的研究从明确乳腺癌患者发生焦虑、抑郁的具体危险因素出发,结合心理社会行为和精神药理学,制订适当的干预和预防方法,从而提供最佳的预防效果。

6 小 结

综上所述,乳腺癌患者普遍存在焦虑、抑郁症状,临床上对患者未被满足的支持护理开始得到重视,将心理社会领域的内容结合到乳腺癌的综合治疗及全程管理中是医学发展的必然[20]。早期实施焦虑抑郁筛查可以早期识别患者未被满足的支持性护理需求,通过有效的应对策略来预防和管理心理问题,药物治疗和心理干预均可用于焦虑、抑郁症状的改善[44]。在乳腺癌全程管理中应采用肿瘤、心理、药理等多学科协作治疗,基于支持患者表达、提高认知和正念的干预可能对心理和癌症预后有益。一项针对焦虑抑郁症状是否接受相应治疗的研究发现,60.4%的患者选择药物治疗,仅有26.3%的患者选择接受心理支持干预[45],且高中或以下文化程度的患者接受心理咨询(OR=0.43,95%CI:0.19~0.95)和中西医结合服务(OR=0.30,95%CI:0.12~0.72)的可能性低于受教育程度较高的患者[46]。目前我国对于乳腺癌患者焦虑抑郁的研究存在以下问题:(1)虽然多项研究强调了心理因素的重要性,但临床上对于乳腺癌患者焦虑、抑郁的识别率及重视仍然很低;(2)针对不同人群心理症状的评估工具众多,且信效度存在较大差异;(3)受国内传统文化的影响,患者对心理问题常处于逃避态度,因此对焦虑抑郁的早期筛查受到一定的限制;(4)焦虑抑郁的发生对乳腺癌的影响及相关分子机制仍需进一步的研究;(5)我国心理干预效果的临床资料相对匮乏,缺乏说服力,针对乳腺癌患者的标准化心理干预模式还未建立;(6)对于社会心理干预在调节乳腺癌患者心理适应方面的作用我国尚处于发展阶段,很少将社会心理干预作用与应激生理变化、免疫变化及对生活质量的长期影响进行研究等。

未来可以从以下几个方面展开深入研究:(1)对国外已开发的心理症状评估量表进行中文版翻译,在我国评估乳腺癌心理筛查研究中进行信效度验证;(2)着眼于心理干预治疗具体的作用机制,对心理干预治疗组采取更密集的干预措施,或者针对心理困扰程度高的患者进行大样本、多中心、随机临床试验,并对其模式进行指导调整,以便更好地指导肿瘤心理干预在临床实践中的应用;(3)基于我国的家庭模式结构,充分发挥家属优势,探索强化家属参与的心理疏导模式对乳腺癌患者的康复作用;(4)结合我国传统

的中医针灸技术，鼓励将中医穴位按摩或中频脉冲电刺激穴位融入乳腺癌常规护理当中，有望为改善乳腺癌患者心理状态，减轻痛苦提供新策略；(5)肿瘤临床医生及护理人员应对乳腺癌患者心理评估与筛查开展知识宣教与支持，提高患者个人、家庭及社会对心理症状评估和预防筛查的重视程度，有望为乳腺癌的整体诊疗和全程管理提供新的治疗理论。

参考文献

[1] SUNG H,FERLAY J,SIEGEL R L,et al. Global Cancer Statistics 2020:GLOBOCAN estimates of Incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin,2021,71(3):209-249.

[2] FENG R M,ZONG Y N,CAO S M,et al. Current cancer situation in China:good or bad news from the 2018 Global Cancer Statistics? [J]. Cancer Commun (Lond),2019,39(1):22.

[3] AL-RASHDAN A,XU Y,QUAN M L,et al. Higher-risk breast cancer in women aged 80 and older:exploring the effect of treatment on survival[J]. Breast,2021,59:203-210.

[4] 程绪平,陈萍,冯丹,等. NCCN 指南 2018 心理痛苦管理第二版对我国癌症患者心理痛苦管理实践的启示[J/CD]. 中华肺部疾病杂志(电子版),2019,12(4):536-538.

[5] MOKHTARI-HESSARI P,MONTAZERI A. Health-related quality of life in breast cancer patients:review of reviews from 2008 to 2018 [J]. Health Qual Life Outcomes,2020,18(1):338.

[6] DINAPOLI L,COLLOCA G,DI CAPUA B,et al. Psychological aspects to consider in breast cancer diagnosis and treatment[J]. Curr Oncol Rep,2021,23(3):38.

[7] NAKAMURA Z M,DEAL A M,NYROP K A,et al. Serial assessment of depression and anxiety by patients and providers in women receiving chemotherapy for early breast cancer[J]. Oncologist,2021,26(2):147-156.

[8] ANUK D,ÖZKAN M,KIZIR A,et al. The characteristics and risk factors for common psychiatric disorders in patients with cancer seeking help for mental health[J]. BMC Psychiatry,2019,19(1):269.

[9] MAASS S,BOERMAN L M,VERHAAK P F,et al. Long-term psychological distress in breast cancer survivors and their matched controls:a cross-sectional study[J]. Maturitas,2019,130:6-12.

[10] HO D,KIM S Y,KIM S I,et al. Insomnia,anxiety,and depression in patients first diagnosed with female cancer[J]. Psychiatry Investig,2021,18(8):755-762.

[11] CARREIRA H,WILLIAMS R,DEMPSEY H,et al. Quality of life and mental health in breast cancer survivors compared with non-cancer controls:a study of patient-reported outcomes in the United Kingdom[J]. J Cancer Surviv,2021,15(4):564-575.

[12] BURGESS C,CORNELIUS V,LOVE S,et al. Depression and anxiety in women with early breast cancer:five year observational cohort study[J]. BMJ,2005,330(7493):702.

[13] FAYE-SCHJØLL H H,SCHOU-BREDAL I. Pessimism predicts anxiety and depression in breast cancer survivors:a 5-year follow-up study[J]. Psychooncology,2019,28(6):1314-1320.

[14] HAJJ A,HACHEM R,KHOURY R,et al. Clinical and genetic factors associated with anxiety and depression in breast cancer patients:a cross-sectional study[J]. BMC Cancer,2021,21(1):872.

[15] LAN B,JIANG S,LI T,et al. Depression,anxiety,and their associated factors among Chinese early breast cancer in women under 35 years of age:a cross sectional study[J]. Curr Probl Cancer,2020,44(5):100558.

[16] THAKUR M,SHARMA R,MISHRA A K,et al. Prevalence and psychobiological correlates of depression among breast cancer patients[J]. Indian J Surg Oncol,2021,12(2):251-257.

[17] BERHILI S,OUABDELMOUMEN A,SBAI A,et al. Radical mastectomy increases psychological distress in young breast cancer patients:results of a cross-sectional study[J]. Clin Breast Cancer,2019,19(1):e160-165.

[18] 王静,李菲菲,李娅岐,等. 乳腺癌确诊患者心理痛苦轨迹变化的调查及影响因素分析[J]. 中华现代护理杂志,2021,27(27):3723-3728.

[19] OLIVEIRA F F B,DE BARROS SILVA P G,DE SANT'ANA R O,et al. How does genetic testing influence anxiety,depression,and quality of life? A hereditary breast and ovarian cancer syndrome suspects trial[J]. Support Care Cancer,2021,29(7):3521-3530.

[20] 唐丽丽,庞英,宋丽莉. 心理社会肿瘤学发展概

述及展望[J]. 中国肿瘤临床与康复,2021,28(11):1406-1408.
[21] RENNA M E,SHROUT M R,MADISON A A,et al. Within-person changes in cancer-related distress predict breast cancer survivors' inflammation across treatment[J]. Psychoneuroendocrinology,2020,121:104866.
[22] CASARIL A M,DOMINGUES M,BAMPI S R,et al. The antioxidant and immunomodulatory compound 3-[(4-chlorophenyl)selanyl]-1-methyl-1H-indole attenuates depression-like behavior and cognitive impairment developed in a mouse model of breast tumor[J]. Brain Behav Immun,2020,84:229-241.
[23] ANTONI M H,DHABHAR F S. The impact of psychosocial stress and stress management on immune responses in patients with cancer[J]. Cancer,2019,125(9):1417-1431.
[24] BERRY A,COLLACCHI B,CAPOCCIA S,et al. Chronic isolation stress affects central neuroendocrine signaling leading to a metabolically active microenvironment in a mouse model of breast cancer[J]. Front Behav Neurosci,2021,15:660738.
[25] LI H,MARSLAND A L,CONLEY Y P,et al. Genes involved in the hpa axis and the symptom cluster of fatigue,depressive symptoms,and anxiety in women with breast cancer during 18 months of adjuvant therapy[J]. Biol Res Nurs,2020,22(2):277-286.
[26] CHAIR S Y,LAW B M H,CHAN J Y W,et al. Association of genetic polymorphisms with psychological symptoms in cancer:a systematic review[J]. Asia Pac J Oncol Nurs,2022,9(1):12-20.
[27] PEREZ-TEJADA J,LABAKA A,VEGAS O,et al. Anxiety and depression after breast cancer:the predictive role of monoamine levels[J]. Eur J Oncol Nurs,2021,52:101953.
[28] ABU-ODAH H,MOLASSIOTIS A,YAT WA L J. Analysis of the unmet needs of Palestinian advanced cancer patients and their relationship to emotional distress:results from a cross-sectional study[J]. BMC Palliat Care,2022,21(1):72.
[29] KERRIGAN K,PATEL S B,HAALAND B,et al. Prognostic significance of patient-reported outcomes in cancer[J]. JCO Oncol Pract,2020,16(4):e313-323.
[30] SUN H,THAPA S,WANG B,et al. A Systematic review and meta-analysis of the distress thermometer for screening distress in asian patients with cancer[J]. J Clin Psychol Med Settings,2021,28(2):212-220.
[31] 徐莹,郭素萍. 心理痛苦管理筛查工具及个性化干预在肺癌住院患者中的应用[J]. 护理实践与研究,2019,16(7):42-43.
[32] ZHANG X,MKUU R,SAMMAN E,et al. Anxiety and depressive symptoms and missing breast cancer and cervical screening:results from Brazos valley community health survey[J]. Psychol Health Med,2020,25(4):402-409.
[33] BUSBY J,MILLS K,ZHANG S D,et al. Selective serotonin reuptake inhibitor use and breast cancer survival:a population-based cohort study[J]. Breast Cancer Res,2018,20(1):4.
[34] TOFTEGÅRD A L,VOIGT HANSEN M,ROSENBERG J,et al. Pharmacological treatment of depression in women with breast cancer:a systematic review[J]. Breast Cancer Res Treat,2013,141(3):325-330.
[35] HUSSAARTS K,BERGER F A,BINKHORST L,et al. The risk of QTc-interval prolongation in breast cancer patients treated with tamoxifen in combination with serotonin reuptake inhibitors[J]. Pharm Res,2019,37(1):7.
[36] ALSTON M,CAIN S W,RAJARATNAM S M W. Advances of melatonin-based therapies in the treatment of disturbed sleep and mood[J]. Handb Exp Pharmacol,2019,253:305-319.
[37] CHIRICO A,MAIORANO P,INDOVINA P,et al. Virtual reality and music therapy as distraction interventions to alleviate anxiety and improve mood states in breast cancer patients during chemotherapy[J]. J Cell Physiol,2020,235(6):5353-5362.
[38] WITEK J L,TELL D,MATHEWS H L. Mindfulness based stress reduction provides psychological benefit and restores immune function of women newly diagnosed with breast cancer:a randomized trial with active control[J]. Brain Behav Immun,2019,80:358-373.
[39] LAI H L,CHEN C I,LU C Y,et al. Cognitive behavioral therapy plus coping management for depression and anxiety on improving sleep quality and health for patients with breast cancer[J]. Brain Sci,2021,11(12):1614.

(下转第2868页)

tug1,and promotes the cortex cytoskeleton formation in vsmcs[J]. Gene,2017,616:52-57.
[27] XIE M Y,DENG Y T,HUANG Y J,et al. LncRNA tug1 regulates autophagy in atherosclerosis by sponging miR-145-5p[J]. Int J Cardiol,2022,369:47.
[28] ZHANG Y,ZHANG H,HU L,et al. LncRNA tug1 regulates hyperuricemia-induced renal fibrosis in a rat model[J/OL]. Acta Biochim Biophys Sin (Shanghai),2022,54(9):1365-1375.
[29] TAN W Q,YUAN L,CAO X,et al. Overexpression of LncRNA tug1 enhances the efficacy of dccik immunotherapy in neuroblastoma in vitro and in vivo[J]. Cancer Biomark,2023,36(1):53-61.
[30] FARZANEH M,GHASEMIAN M,GHAED RAHMATI F,et al. Functional roles of LncRNA-tug1 in hepatocellular carcinoma[J]. Life Sci,2022,308:120974.
[31] VERKHRATSKY A,NEDERGAARD M. Physiology of astroglia[J]. Physiological Rev,2018,98(1):239-389.
[32] HAJ-YASEIN N N,VINDEDAL G F,EILERT-OLSEN M,et al. Glial-conditional deletion of aquaporin-4 (aqp4) reduces blood-brain water uptake and confers barrier function on perivascular astrocyte endfeet[J]. Proc Natl Acad Sci U S A,2011,108(43):17815-17820.
[33] KITCHEN P,SALMAN M M,HALSEY A M,et al. Targeting aquaporin-4 subcellular localization to treat central nervous system edema[J]. Cell,2020,181(4):784-799.
[34] ZHANG G,LI T,CHANG X,et al. Long noncoding RNA snhg14 promotes ischemic brain injury via regulating miR-199b/aqp4 axis[J]. Neuro Chem Res,2021,46(5):1280-1290.
[35] WANG H,ZHENG X,JIN J,et al. LncRNA malat1 silencing protects against cerebral ischemia-reperfusion injury through mir-145 to regulate aqp4[J]. J Biomedl Sci,2020,27(1):40.
[36] GASTFRIEND B D,NISHIHARA H,CANFIELD S G,et al. Wnt signaling mediates acquisition of blood-brain barrier properties in naïve endothelium derived from human pluripotent stem cells[J]. Elife,2021,10:e70992.
[37] GUÉRIT S,FIDAN E,MACAS J,et al. Astrocyte-derived wnt growth factors are required for endothelial blood-brain barrier maintenance[J]. Prog Neurobiol,2021,199:101937.

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(上接第2863页)

[40] LALLY R M,KUPZYK K,GALLO S,et al. Use of an unguided,web-based distress self-management program after breast cancer diagnosis: sub-analysis of caringguidance pilot study[J]. J Med Int Res,2020,22(7):e19734.
[41] WEI X,YUAN R,YANG J,et al. Effects of Baduanjin exercise on cognitive function and cancer-related symptoms in women with breast cancer receiving chemotherapy: a randomized controlled trial[J]. Support Care Cancer,2022,30(7):6079-6091.
[42] ZHANG Y,SUN Y,LI D,et al. Acupuncture for breast cancer:a systematic review and meta-analysis of patient-reported outcomes[J]. Front Oncol,2021,11:646315.
[43] MCFARLAND D C,JOHNSON S M,HARRIS K,et al. ReCAP: would women with breast cancer prefer to receive an antidepressant for anxiety or depression from their oncologist?[J]. J Oncol Pract,2016,12(2):172-174.
[44] DOUBOVA S V,PÉREZ-CUEVAS R. Association of supportive care needs and quality of patient-centered cancer care with depression in women with breast and cervical cancer in Mexico[J]. Psychooncology,2021,30(4):591-601.
[45] NISSEN E R,ZACHARIAE R,O'CONNOR M,et al. Internet-delivered mindfulness-based cognitive therapy for anxiety and depression in cancer survivors: predictors of treatment response[J]. Internet Interv,2021,23:100365.
[46] TREVINO K M,IYENGAR N,LI Q,et al. Receipt of psychological counseling and integrative medicine services among breast cancer survivors with anxiety[J]. Breast Cancer Res Treat,2020,184(2):301-310.

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