

·论著·

超声评估远隔缺血适应对动脉瘤性蛛网膜下腔出血患者脑血流的影响

齐猛,王宁,程玮涛,蒋丽丹,陈文劲,曲鑫,徐跃峤

作者单位
首都医科大学宣武医院神经外科
北京 100053
基金项目
北京市科技计划首都临床特色应用研究与成果推广(No. Z151100004015095);
北京市215高层次卫生技术人才学术骨干项目(No. 2015-3-092);
首都医科大学宣武医院基础临床研究项目(No. XWYY201709)
收稿日期
2020-11-16
通讯作者
徐跃峤
xuyueqiao@sina.com

摘要 目的:探讨远隔缺血适应(RIC)对动脉瘤性蛛网膜下腔出血(aSAH)患者脑血流的影响。方法:选择2017年11月至2018年5月首都医科大学宣武医院神经外科重症监护病房连续收治的aSAH患者24例,所有患者在aSAH后72 h内接受动脉瘤夹闭和栓塞治疗,术后7 d内进行RIC干预5次。在RIC干预前、后采用经颅超声多普勒(TCD)评估脑血流,包括前循环:双侧大脑前动脉(ACA)、双侧大脑中动脉(MCA)、同侧MCA/颈内动脉(ICA)终末段血流速度比值(ratio);后循环:双侧大脑后动脉(PCA)、双侧椎动脉颅内段(VA)、基底动脉(BA)。RIC干预结束后复查头颅CT或MRI,判断有无新发脑梗死。结果:RIC干预后,患者前循环血流R-MCA、L-ACA及R-ratio较干预前升高(均 $P<0.05$),升高幅度均 $<20\%$,其余参数差异无统计学意义(均 $P>0.05$)。RIC干预后,患者后循环血流L-VA及BA较干预前升高(均 $P<0.05$),升高幅度均 $<20\%$,其余参数差异无统计学意义(均 $P>0.05$)。RIC干预结束后,CT或MRI均未发现新发脑梗死。结论:RIC干预在aSAH应用中对脑血流影响不明显,未导致新发脑梗死,其安全性得到初步证实。

关键词 颅内动脉瘤;蛛网膜下腔出血;远隔缺血适应;经颅超声多普勒;脑血流

中图分类号 R741;R741.04;R741.05;R743 **文献标识码** A **DOI** 10.16780/j.cnki.sjssgncj.20200830

本文引用格式:齐猛,王宁,程玮涛,蒋丽丹,陈文劲,曲鑫,徐跃峤. 超声评估远隔缺血适应对动脉瘤性蛛网膜下腔出血患者脑血流的影响[J]. 神经损伤与功能重建, 2021, 16(2): 76-78, 94.

Effect of Remote Ischemic Conditioning on Cerebral Blood Flow Evaluated by Transcranial Doppler in Patients with Aneurysmal Subarachnoid Hemorrhage QI Meng, WANG Ning, CHENG Wei-tao, JIANG Li-dan, CHEN Wen-jin, QU Xin, XU Yue-qiao. Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

Abstract **Objective:** To explore the effect of remote ischemic conditioning (RIC) on cerebral blood flow in patients with aneurysmal subarachnoid hemorrhage (aSAH). **Methods:** Included in this study were 24 aSAH patients consecutively admitted to the Intensive Care Unit of the Department of Neurosurgery at Xuanwu Hospital from November 2017 to May 2018. All patients underwent aneurysm clipping and embolization treatment within 72 hours of aSAH and received RIC 5 times within 7 days after treatment. Before and after RIC intervention, transcranial doppler (TCD) was used to evaluate cerebral blood flow in the anterior circulation, including that of the bilateral anterior cerebral arteries (ACA), bilateral middle cerebral arteries (MCA), and the ipsilateral MCA/internal carotid artery (ICA) terminal section flow velocity ratio (ratio). The posterior circulation blood flow was also evaluated, including that at the bilateral posterior cerebral arteries (PCA), bilateral vertebral arteries (VA), and basilar artery (BA). Head CT or MRI recheck was performed after RIC intervention to evaluate the fresh infarctions. **Results:** Compared to data before RIC intervention, cerebral blood flow after intervention at the R-MCA, L-ACA, and R-ratio of the anterior circulation were increased (all $P<0.05$), with this increase being less than 20%, and the remaining parameters showed no significant difference ($P>0.05$). After RIC intervention, blood flow at the L-VA and BA of the posterior circulation were increased compared to those before intervention (all $P<0.05$), with this increase being less than 20%, and the other parameters showed no significant difference ($P>0.05$). Neither CT nor MRI showed fresh cerebral infarction after RIC intervention. **Conclusion:** RIC had no obvious effect on cerebral blood flow in patients with aneurysmal subarachnoid hemorrhage and did not trigger fresh cerebral infarctions. This study confirms the preliminary safety of RIC.

Key words intracranial aneurysm; subarachnoid hemorrhage; remote ischemic conditioning; transcranial doppler; cerebral blood flow

缺血预适应(ischemic preconditioning, IPC)于1986年由Murry等^[1]率先提出,指预先给予一个器官非致死性的、短暂轻度缺血处理后,会对以后致死性的缺血产生耐受。Przyklenk等^[2]于1993年提出了远隔器官缺血预适应的概念,即一个器官的短暂缺血会诱导另一个器官的缺血适应。近年临床及基础研究发现,远隔缺血预适应(remote

ischemic preconditioning, RIPC)对包括脑和心脏在内的缺血性卒中具有保护作用,已成为当前卒中治疗中的研究热点之一^[3,4]。本研究拟探讨远隔缺血适应(remote ischemic conditioning, RIC)对动脉瘤性蛛网膜下腔出血(aneurysmal subarachnoid hemorrhage, aSAH)患者脑血流的影响。

1 资料与方法

1.1 一般资料

本研究通过首都医科大学宣武医院伦理委员会审核批准。前瞻性设计纳入2017年11月至2018年5月首都医科大学宣武医院神经外科重症监护病房连续收治入院的aSAH患者24例,其中男9例,女15例;年龄36~73岁,平均(55.5±9.0)岁。

纳入标准:①年龄18~75岁;②脑血管造影证实动脉瘤,Hess-Hunt分级≤IV级;③在发病48 h内入院,通过栓塞和(或)夹闭治疗了责任动脉瘤;④纳入时间在发病72 h内;⑤本人或法定代理人同意参加本研究。

排除标准:①发病48 h以后入院;②未针对破裂的动脉瘤进行治疗或无法治疗;③治疗动脉瘤需要放置支架;④伴有严重心血管疾病、肢体血管闭塞性疾病及其他无法耐受治疗的疾病或状况;⑤既往有脑梗死或术后24 h内CT显示脑梗死。

1.2 方法

所有RIC干预均在患者常规治疗的基础上进行。在aSAH后72 h内接受动脉瘤夹闭和栓塞治疗,术后7 d内进行RIC干预5次。具体方法:血压袖带加压,予以肢体180 mmHg压力(若患者收缩压>180 mmHg,则加压为患者收缩压以上20 mmHg);每周期包括加压充气(直至远端动脉搏动消失)5 min,放气再灌注5 min^[5];每次干预5个周期。干预期间常规监测患者血压、心率、呼吸变化。对于意识清楚患者进行疼痛视觉模拟评分,如患者不能耐受,则终止干预,患者退出本研究。

在RIC干预前、后采用经颅超声多普勒(transcranial doppler, TCD)评估脑血流,包括前循环:双侧大脑前动脉(anterior cerebral artery, ACA)、双侧大脑中动脉(middle cerebral artery, MCA)、同侧MCA/颈内动脉(internal carotid artery, ICA)终末段血流速度比值(ratio);后循环:双侧大脑后动脉(posterior cerebral artery, PCA)、双侧椎动脉颅内段(vertebral artery, VA)、基底动脉(basilar artery, BA)。RIC干预结束后复查头颅CT或MRI,判断有无新发梗死。

1.3 统计学处理

采用SPSS 17.0统计软件进行数据处理与分析,符合正态分布以及方差齐性的计量资料以($\bar{x}\pm s$)表示,组间比较采用独立样本均数 t 检验;计数资料以率表示,组间比较采用 χ^2 检验; $P<0.05$ 为差异有统计学意义。

2 结果

RIC干预后,患者前循环血流R-MCA、L-ACA及R-ratio较干预前升高(均 $P<0.05$),升高幅度均<20%,其余参数差异无统计学意义(均 $P>0.05$),见表1。RIC干预后,患者后循环血流L-VA及BA较干预前升高(均 $P<0.05$),升高幅度均<20%,其余参数差异无统计学意义(均 $P>0.05$),见表2。RIC干预结束后,CT或MRI均未发现新发脑梗死。

表1 RIC干预对aSAH患者前循环脑血流的影响(cm/s, $\bar{x}\pm s$)

部位	RIC干预前流速	RIC干预后流速	t 值	P 值
L-MCA	142±54	169±59	-1.832	0.080
R-MCA	138±51	159±61	-2.410	0.024
L-ACA	127±41	153±51	-2.923	0.008
R-ACA	117±42	128±39	-1.255	0.222
L-ratio	1.25±0.70	1.43±0.70	-1.519	0.142
R-ratio	1.25±0.73	1.55±1.07	-2.697	0.013

注:“L”:左;“R”:右

表2 RIC干预对aSAH患者后循环脑血流的影响(cm/s, $\bar{x}\pm s$)

部位	RIC干预前流速	RIC干预后流速	t 值	P 值
L-PCA	74±21	78±19	-0.768	0.450
R-PCA	69±21	79±28	-1.950	0.063
L-VA	64±20	74±20	-2.254	0.034
R-VA	63±15	66±17	-0.994	0.331
BA	66±14	78±19	-2.716	0.012

注:“L”:左;“R”:右

3 讨论

有研究提示,RIPC对远隔组织器官的保护作用可能涉及介质-受体-基因表达等多个环节及多种机制^[6]。近年研究证实,RIPC对多个靶器官包括心脏、肺、肾脏等具有保护作用^[7-11],而且其神经保护作用可见于缺血性脑损伤及缺血性脊髓损伤,为脑与脊髓的缺血性损伤提供了一种潜在的治疗方式^[12]。对重度颈动脉粥样硬化性狭窄患者在行颈动脉支架置入术前给予RIPC治疗^[13],可通过改善机体炎性反应降低术后相关栓塞发生率。对于颅内动脉粥样硬化患者,使用血压计加压行短暂重复双上肢缺血,可以改善脑灌注,减少卒中复发^[14]。

RIPC在出血性脑血管病中的研究尚不多,尤其针对SAH的研究,需要深入探索。aSAH在所有卒中类型中占比较低($<5\%$)^[15],但因40~60岁为发病高峰,发病年龄相对较轻,病情一般较其他类型卒中更严重,是神经外科临床和基础研究的热点之一。随着显微神经外科手术技术、介入治疗技术及材料和影像诊断技术的进步,aSAH的病死率在过去20年内显著下降并在近年仍呈下降趋势^[16,17],但约2/3的患者遗留神经功能缺损。早期脑损伤、SAH后继发的脑血管痉挛、脑血管自动调节功能损伤、微血栓等多种因素造成的迟发性脑缺血损伤都是影响预后的重要因素。约30%的aSAH患者出现缺血性卒中症状,15%~20%的患者发生致残性的脑梗死^[18,19]。aSAH后脑血管痉挛、早期脑损伤及迟发性脑缺血的作用越来越受到重视并开展了相关研究^[20,21]。而在SAH后缺血性脑损伤发生前RIPC有治疗的窗口期。有研究显示,既往存在缺血性脑血管病的“自然IPC”患者,脑血管痉挛发生率下降。IPC可以对急性缺血性脑损伤发挥保护作用^[22]。

RIC干预对患者的安全性,在不同疾病中需要进行全面评估。本研究对aSAH患者进行TCD评估脑血流,并以CT或MRI评估有无新发梗死,以评估该干预的安全性。在安全性得以保证的前提下,有利于进一步开展对该干预的有效性评估,以及该干预措施在临床中的推广应用。

Gonzalez等^[23]于2013年针对4例aSAH患者进行RIPC的干预研究发现,在aSAH后2~12 d内,非连续地进行3~4次RIPC干预,每次4个周期,每周周期包括5 min加压充气至收缩压之上30 mmHg,直至TCD确认远端足背动脉搏动消失,5 min放气再灌注,每次干预前后120 min进行ICP及TCD持续监测。结果显示患者颅内压在干预时可增高,与意识清楚患者疼痛和其他生命体征无关;RIPC干预后,早期MCA下降($P=0.039$),提示脑血管扩张,但持续时间不长,在干预后24~48 h无特异性的变化趋势。本研究结果虽然提示部分区域脑血流在干预后有变化,但变化幅度均 $<20\%$,且无明显特异性。aSAH患者在出血后5~7 d是脑血管痉挛的高峰期,本身脑血流速度即可能出现升高,因本研究缺乏对照组,因此部分血管脑血流的变化是否与RIC有关,仍有待商榷和进一步研究。此外,干预后头颅CT或MRI复查,均未见明确新发脑梗死,说明RIC的应用并未发现脑缺血的表现,但是否能预防aSAH相关脑梗死的发生,也需增加对照组进行下一步研究和探讨。

RIC在aSAH中的应用研究较缺血性脑血管病起步晚,研究仍然不够深入^[24,25]。我们在前期研究中,初步验证了RIC对aSAH患者凝血功能影响的安全性^[5],本研究则进一步验证了经TCD及CT或MRI评估的RIC干预对aSAH脑血流影响的安全性。但因较严格的纳入和排除标准,符合入组标准的病例数偏少,因此未设置对照组进行观察对比。后续需设立对照组进行进一步研究,并对该干预措施的有效性进行评估,以期有更多的证据来证明RIC干预在动脉瘤性SAH中的应用前景。

参考文献

- [1] Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium[J]. *Circulation*, 1986, 74: 1124-1236.
- [2] Przyklenk K, Bauer B, Ovize M, et al. Regional ischemic 'preconditioning' protects remote virgin myocardium from subsequent sustained coronary occlusion[J]. *Circulation*, 1993, 87: 893-899.
- [3] Schmidt MR, Rasmussen ME, Botker HE. Remote ischemic conditioning for patients with STEMI[J]. *J Cardiovasc Pharmacol Ther*, 2017, 22: 302-309.
- [4] Dezfulian C, Garrett M, Gonzalez NR. Clinical application of preconditioning and postconditioning to achieve neuroprotection[J]. *Transl Stroke Res*, 2013, 4: 19-24.
- [5] 齐猛, 徐跃桥, 王宁, 等. 远隔缺血适应干预对动脉瘤性蛛网膜下腔出血患者凝血功能的影响[J]. *中国卒中杂志*, 2018, 13: 1148-1152.
- [6] Lim SY, Yellon DM, Hausenlo DJ. The neural and humoral pathways in remote ischemic preconditioning[J]. *Basic Res Cardiol*, 2010, 105: 651-655.
- [7] Hausenlo DJ, Candilio L, Evans R, et al. Remote ischemic preconditioning and outcomes of cardiac surgery[J]. *N Engl J Med*, 2015, 373: 1408-1417.
- [8] Li C, Xu M, Wu Y, et al. Limb remote ischemic preconditioning attenuates lung injury after pulmonary resection under propofol-remifentanyl anesthesia: a randomized controlled study[J]. *Anesthesiology*, 2014, 121: 249-259.
- [9] Zarbock A, Kellum JA. Remote ischemic preconditioning and protection of the kidney—a novel therapeutic option[J]. *Crit Care Med*, 2016, 44: 607-616.
- [10] Leung CH, Caldarone CA, Wang F, et al. Remote ischemic conditioning prevents lung and liver injury after hemorrhagic shock/resuscitation: potential role of a humoral plasma factor[J]. *Ann Surg*, 2015, 261: 1215-1225.
- [11] Li C, Li YS, Xu M, et al. Limb remote ischemic preconditioning for intestinal and pulmonary protection during elective open infrarenal abdominal aortic aneurysm repair: a randomized controlled trial[J]. *Anesthesiology*, 2013, 118: 842-852.
- [12] Yunoki M, Kanda T, Suzuki K, et al. Ischemic tolerance of the brain and spinal cord: a review[J]. *Neurol Med Chir (Tokyo)*, 2017, 57: 590-600.
- [13] Zhao W, Meng R, Ma C, et al. Safety and efficacy of remote ischemic preconditioning in patients with severe carotid artery stenosis before carotid artery stenting[J]. *Circulation*, 2017, 135: 1325-1335.
- [14] Meng R, Asmaro K, Meng L, et al. Upper limb ischemic preconditioning prevents recurrent stroke in intracranial arterial stenosis[J]. *Neurology*, 2012, 79: 1853-1861.
- [15] van Gijn J, Kerr RS, Rinkel GJ. Subarachnoid haemorrhage[J]. *Lancet*, 2007, 369: 306-318.
- [16] Lovelock CE, Rinkel GJ, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: population-based study and systematic review[J]. *Neurology*, 2010, 74: 1494-1501.

- [10] Granella F, Sances G, Pucci E, et al. Migraine with aura and reproductive life events: a case control study[J]. *Cephalalgia*, 2000, 20: 701-707.
- [11] Hansen JM, Charles A. Differences in treatment response between migraine with aura and migraine without aura: lessons from clinical practice and RCTs[J]. *J Headache Pain*, 2019, 20: 96.
- [12] Negro A, Delaruelle Z, Ivanova TA, et al. Headache and pregnancy: a systematic review[J]. *J Headache Pain*, 2017, 18: 106.
- [13] Ertresvag JM, Zwart JA, Helde G, et al. Headache and transient focal neurological symptoms during pregnancy, a prospective cohort[J]. *Acta Neurol Scand*, 2005, 111: 233-237.
- [14] Serva WA, Serva VM, de Fátima Costa Caminha M, et al. Course of migraine during pregnancy among migraine sufferers before pregnancy[J]. *Arq Neuropsiquiatr*, 2011, 69: 613-619.
- [15] Petrovski BE, Vetvik KG, Lundqvist C, et al. Characteristics of menstrual versus non-menstrual migraine during pregnancy: a longitudinal population-based study[J]. *J Headache Pain*, 2018, 19: 27.
- [16] Delaruelle Z, Ivanova TA, Khan S, et al. Male and female sex hormones in primary headaches[J]. *J Headache Pain*, 2018, 19: 117.
- [17] Pakalnis A. Migraine and Hormones[J]. *Semin Pediatr Neurol*, 2016, 23: 92-94.
- [18] Gupta S, Mccarson KE, Welch KM, et al. Mechanisms of pain modulation by sex hormones in migraine[J]. *Headache*, 2011, 51: 905-922.
- [19] Bolay H, Berman NE, Akcali D. Sex-related differences in animal models of migraine headache[J]. *Headache*, 2011, 51: 891-904.
- [20] Lai J, Dilli E. Migraine Aura: Updates in Pathophysiology and Management[J]. *Curr Neurol Neurosci Rep*, 2020, 20: 17.
- [21] Chauvel V, Multon S, Schoenen J. Estrogen-dependent effects of 5-hydroxytryptophan on cortical spreading depression in rat: Modelling the serotonin-ovarian hormone interaction in migraine aura[J]. *Cephalalgia*, 2017, 38: 427-436.
- [22] Chauvel V, Schoenen J, Multon S. Influence of ovarian hormones on cortical spreading depression and its suppression by L-kynurenine in rat[J]. *PLoS One*, 2013, 8: e82279.
- [23] McEwen BS, Milner TA. Understanding the broad influence of sex hormones and sex differences in the brain[J]. *J Neurosci Res*, 2017, 95: 24-39.
- [24] Pavlovic JM, Akcali D, Bolay H, et al. Sex-related influences in migraine[J]. *J Neurosci Res*, 2017, 95: 587-593.
- [25] 赖小燕, 胡幼平, 艾虹静, 等. 雌激素对偏头痛的影响及机制[J]. *中国疼痛医学杂志*, 2016, 22: 851-853.
- [26] Puri V, Cui L, Liverman CS, et al. Ovarian steroids regulate neuropeptides in the trigeminal ganglion[J]. *Neuropeptides*, 2005, 39: 409-17.
- [27] Cetinkaya A, Kilinc E, Camsari C, et al. Effects of estrogen and progesterone on the neurogenic inflammatory neuropeptides: implications for gender differences in migraine[J]. *Exp Brain Res*, 2020, 238: 2625-2639.
- [28] Gintzler AR, Storman EM, Liu NJ. Estrogens as arbiters of sex-specific and reproductive cycle-dependent opioid analgesic mechanisms[J]. *Vitam Horm*, 2019, 111: 227-246.
- [29] Finocchi C, Ferrari M. Female reproductive steroids and neuronal excitability[J]. *Neurol Sci*, 2011, 32: S31-35.
- [30] Bushnell CD, Jamison M, James AH. Migraines during pregnancy linked to stroke and vascular diseases: US population based case-control study[J]. *BMJ*, 2009, 338: b664.
- [31] Wabnitz A, Bushnell C. Migraine, cardiovascular disease, and stroke during pregnancy: systematic review of the literature[J]. *Cephalalgia*, 2015, 35: 132-139.
- [32] Jarvis S, Dassan P, Piercy CN. Managing migraine in pregnancy[J]. *BMJ*, 2018, 360: k80.
- [33] Skajaa N, Szépligeti SK, Xue F, et al. Pregnancy, Birth, Neonatal, and Postnatal Neurological Outcomes After Pregnancy With Migraine[J]. *Headache*, 2019, 59: 869-879.
- [34] Grossman TB, Robbins MS, Govindappagari S, et al. Delivery Outcomes of Patients with Acute Migraine in Pregnancy: A Retrospective Study[J]. *Headache*, 2017, 57: 605-611.
- [35] Sanchez SE, Williams MA, Pacora PN, et al. Risk of placental abruption in relation to migraines and headaches[J]. *BMC Women Health*, 2010, 10: 30.
- [36] Aukes AM, Yurtsever FN, Boutin A, et al. Associations Between Migraine and Adverse Pregnancy Outcomes: Systematic Review and Meta-analysis[J]. *Obstet Gynecol Surv*, 2019, 74: 738-748.
- [37] Burch R. Epidemiology and Treatment of Menstrual Migraine and Migraine During Pregnancy and Lactation: A Narrative Review[J]. *Headache*, 2020, 60: 200-216.
- [38] Afridi SK. Current concepts in migraine and their relevance to pregnancy[J]. *Obstet Med*, 2018, 11: 154-159.
- [39] Amundsen S, Øvrebø TG, Amble NMS, et al. Risk perception, beliefs about medicines and medical adherence among pregnant and breastfeeding women with migraine: findings from a cross-sectional study in Norway[J]. *BMJ Open*, 2019, 9: e026690.
- [40] Sader E, Rayhill M. Headache in Pregnancy, the Puerperium, and menopause[J]. *Semin Neurol*, 2018, 38: 627-633.

(本文编辑:唐颖馨)

(上接第78页)

- [17] 何强, 许进. 动脉瘤性蛛网膜下腔出血患者行介入栓塞术与夹闭术的对照研究[J]. *神经损伤与功能重建*, 2019, 14: 578-580.
- [18] Connolly ES Jr, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association[J]. *Stroke*, 2012, 43: 1711-1737.
- [19] Diringer MN, Bleck TP, Claude Hemphill J 3rd, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference[J]. *Neurocrit Care*, 2011, 15: 211-240.
- [20] Rabinstein AA, Lanzino G, Wijdicks EF. Multidisciplinary management and emerging therapeutic strategies in aneurysmal subarachnoid haemorrhage[J]. *Lancet Neurol*, 2010, 9: 504-519.

- [21] 张彬, 马肃. 初始压力反应性指数对动脉瘤性蛛网膜下腔出血患者迟发性脑缺血的预测价值[J]. *神经损伤与功能重建*, 2019, 14: 571-573.
- [22] Kim YW, Zipfel GJ, Ogilvy CS, et al. Preconditioning effect on cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage[J]. *Neurosurgery*, 2014, 74: 351-358.
- [23] Gonzalez NR, Hamilton R, Bilgin-Freiert A, et al. Cerebral hemodynamic and metabolic effects of remote ischemic preconditioning in patients with subarachnoid hemorrhage[J]. *Acta Neurochir Suppl*, 2013, 115: 193-198.
- [24] Koch S, Gonzalez N. Preconditioning the human brain: proving the principle in subarachnoid hemorrhage[J]. *Stroke*, 2013, 44: 1748-1753.
- [25] 齐猛, 徐跃峤. 远隔缺血预适应在动脉瘤性蛛网膜下腔出血中的应用的研究进展[J]. *中国脑血管病杂志*, 2018, 15: 220-224.

(本文编辑:唐颖馨)