

《脊髓损伤神经修复治疗临床指南(中国版)2021》 解读

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【摘要】 中国神经修复学会根据近年发表的有关脊髓损伤临床治疗证据,对《脊髓损伤神经修复临床治疗指南(中国版)2016》进行修订和更新,并于2021年3月发布《脊髓损伤神经修复治疗临床指南(中国版)2021》[以下简称“中国指南(2021)”],其内容涵盖脊髓损伤伤情评估和诊断、院前急救、治疗原则、康复训练和并发症管理等。本文拟就“中国指南(2021)”中修订和更新的内容进行解读,以为临床医师和研究人员提供治疗标准或参考。

【关键词】 脊髓损伤; 康复; 指南; 中国

Interpretation of "Clinical guidelines for neurorestorative in spinal cord injury (2021 China version)"

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【Abstract】 According to the clinical treatment evidence of spinal cord injury (SCI) published in recent years, the Chinese Association of Neurorestoratology (Preparatory) had revised and updated the "Clinical therapeutic guideline for neurorestoration in spinal cord injury (Chinese version 2016)", and released the "Clinical guidelines for neurorestorative in spinal cord injury (2021 China version)" in March 2021. "2021 China version" provided comprehensive management strategies for SCI, which contains evaluation and diagnosis, pre-hospital first aid, treatment principle, rehabilitation training, and complication management. This paper intends to interpret the revisions and updates of the "2021 China version", and provide treatment standards or references for clinicians and researchers.

【Key words】 Spinal cord injuries; Rehabilitation; Guideline; China

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脊髓损伤(SCI)可造成损伤平面以下运动、感觉和自主神经功能障碍^[1],由于尚无有效治疗方法使其神经修复治疗至今仍面临诸多挑战。2016年,中国神经修复学会和国际神经修复学会中国委员会首次发布《脊髓损伤神经修复临床治疗指南(中国版)2016》[以下简称“中国指南(2016)”]^[2],不仅为

脊髓损伤患者伤情评估和诊断、院前急救、治疗原则、康复训练和并发症管理提供标准参照,而且有效地推动我国脊髓损伤临床研究的快速发展。为了适应临床诊断与治疗的需要,中国神经修复学会于2021年3月制定并发布《脊髓损伤神经修复治疗临床指南(中国版)2021》[以下简称“中国指南(2021)”]^[3],在保留“中国指南(2016)”主要内容的基础上,根据2020年12月31日之前公开发表的有关脊髓损伤的临床治疗证据分别对伤情评估、院前急救、治疗原则和并发症管理等内容进行更新;其中有别于“中国指南(2016)”的是,“中国指南(2021)”将原有脊髓损伤分期由3个疾病阶段(急性

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期、亚急性期和慢性期)改为4个阶段,即急性期(<48小时)、亚急性期(48小时至14天)、中期(14天至6个月)和慢性期(>6个月)^[4]。本文拟基于脊髓损伤分期对“中国指南(2021)”的修订及更新内容进行解读,以期更为深入地理解指南并指导临床。

一、急性期和亚急性期脊髓损伤

1. 诊断 (1)影像学检查:包括X线、CT及MRI检查,各有特点,互为补充。“中国指南(2021)”认为,X线对脊柱骨折存在一定的漏诊率,故不建议其作为颈髓损伤的首选影像学检查方法。CT是诊断脊柱骨折或椎体脱位最常用的成像方法,可以轴向和三维显示椎管和小关节,并可检出X线难以发现的较小病变或隐匿病变。MRI适用于评估椎间盘、韧带、脊髓、马尾和神经根完整性、损伤部位、严重程度和累及范围^[5],可准确评估脊髓损伤程度并指导分类和外科手术治疗^[5-7];而且手术前后均行MRI检查更助于判断预后^[8];除常规扫描序列外,“中国指南(2021)”还推荐应用扩散张量成像(DTI)等新的定量MRI检查技术以反映脊髓白质的微观病理变化。(2)脊髓损伤神经学分类:无论是“中国指南(2021)”还是“中国指南(2016)”均认为,在诊断过程中首先应明确损伤节段与严重程度、脊柱骨折和(或)椎体脱位类型,以及脊柱稳定性。为此“中国指南(2021)”详细阐述美国脊髓损伤协会(ASIA)《脊髓损伤神经学分类国际标准(ISNCSCI)2019》中对运动评分、感觉评分,以及部分保留带(ZPP)定义的重大修订^[9]。其中,ASIA A级(完全损伤)为S₄₋₅无感觉或运动功能保留;ASIA B级(不完全感觉损伤),神经平面以下包括S₄₋₅无运动但有感觉功能保留,且双侧运动平面以下均无3个节段以上的运动功能保留;ASIA C级(不完全运动损伤),单个损伤平面1/2以上的关键肌肌力<3级;ASIA D级(不完全运动损伤),单个损伤平面约1/2或以上的关键肌肌力≥3级;ASIA E级(正常),既往脊髓损伤后出现神经功能障碍,ISNCSCI检查提示感觉和运动功能均正常^[10]。其中,C级和D级患者保留肛门括约肌自主收缩功能,或S₄₋₅感觉功能且一侧运动平面以下3个节段以上运动功能^[10]。新修订的脊神经分级标准可充分反映脊髓损伤后的神经功能状态,且对伤情记录更详细、更全面,有助于明确诊断。

2. 治疗原则 对于急性期脊髓损伤患者,“中国指南(2021)”指出多学科诊疗模式(MDT)可降低死亡率并缩短住院时间;建议成立区域脊髓损伤治疗

中心,包括急诊科、神经外科、骨科、普通外科、重症监护医学、放射科、神经科和麻醉科等的多学科脊髓损伤救治团队;患者入院后,救治团队应迅速对伤情进行评估,确定损伤节段和严重程度,并立即开始治疗。(1)院前急救:相对于“中国指南(2016)”,“中国指南(2021)”对于患者搬运和转运方法则更强调转运途中应提供必要的生命支持,如保持呼吸道通畅,必要时给予呼吸、循环支持,并使用远程通信设备实现医疗指示实时转达,以确保救治中心在知晓患者整体情况的前提下快速接收患者,为后续治疗节省时间。(2)药物治疗:“中国指南(2021)”另一项值得关注的内容是,针对急性期脊髓损伤患者是否采取甲泼尼龙冲击治疗的临床推荐有所变化。既往认为,脊髓损伤8小时内大剂量甲泼尼龙冲击治疗有助于急性期的神经修复^[11],而美国急性脊髓损伤研究(NASCIS) I期和II期结果显示,甲泼尼龙冲击治疗效果低于预期且存在严重并发症;因此,自2013年以来,美国神经外科联盟(AANS)和神经外科医师大会(CNS)发布的脊髓损伤临床指南不再推荐甲泼尼龙冲击治疗作为急性期用药^[3],而2017年国际脊柱学会(AOSpine)临床指南推荐,脊髓损伤8小时内可选择甲泼尼龙冲击治疗^[12]。综合上述研究结果,目前的共识是,脊髓损伤后采取大剂量甲泼尼龙冲击治疗证据不足^[13],且存在呼吸系统感染、消化道出血、心律失常,甚至死亡等严重并发症,故不再作为急性期常规推荐用药。然而,对于不完全性颈髓病变等特殊损伤类型,特别是需要施行外科减压治疗的脊髓型颈椎病患者,甲泼尼龙可作为治疗选项^[13],但须注意发病时间窗、给药剂量,以及禁忌证。另外,尽管神经节苷脂(100 mg/d)联合甲泼尼龙可以改善急性脊髓损伤患者伤后早期的肢体感觉、肌力和肛门括约肌功能^[14],但鉴于外源性神经节苷脂抗体可以使继发吉兰-巴雷综合征(GBS)的风险显著增加^[15],故目前不推荐该药作为急性期脊髓损伤的常规用药,尚需大样本临床试验明确其疗效^[8]。其他急性期用药还包括促红细胞生成素、利鲁唑、米诺环素、性激素、神经营养因子、七叶皂苷钠、轴突生长促进剂、粒细胞集落刺激因子、镁剂和纤维母细胞生长因子^[1]等,但这些药物中部分正在临床试验阶段,有些虽然已在临床应用,但目前尚缺乏支持其常规应用的高水平证据^[4,16-18]。另外,静脉注射血管加压药如去甲肾上腺素虽具有改善脊髓损伤后局部脊髓灌注压和血

流动力学的作用^[19],但其对神经功能恢复的影响尚不确定,且可增加心脏不良事件如心律失常和心肌损伤的风险,故不作为推荐^[20]。(3)亚低温治疗:“中国指南(2016)和(2021)”关于亚低温治疗的宗旨略有不同,前者认为局部低温(6℃)和全身亚低温(34℃)均可降低损伤组织新陈代谢和耗氧量;而后者指出,亚低温治疗以全身低温诱导至32~34℃效果最佳,硬膜外或硬膜下局部低温(6℃)也有一定疗效^[21-25]。提示目前关于急性脊髓损伤亚低温治疗的适应证或禁忌证尚未取得共识,建议在医疗条件允许和患者生命体征平稳的情况下,可同时进行全身亚低温和局部低温治疗^[22-23]。(4)手术治疗:“中国指南(2021)”推荐,患者入院后应采用下颈椎损伤分类与损伤程度评分系统(SLICs)、胸腰椎损伤分类与损伤程度评分系统(TLICs)分别对脊柱脊髓损伤进行分类并评估损伤程度,≤3分者推荐保守治疗,4分者视伤情选择外科手术或保守治疗,≥5分则建议外科手术治疗;但无论是“中国指南(2016)”还是“中国指南(2021)”均强调应于损伤早期施行脊柱固定和脊髓减压^[26]。目前认为,于急性期进行脊柱复位、固定安全、有效,既可改善神经功能、缩短住院时间,亦有利于降低并发症发生率,尤其是急诊脊髓减压术不仅可以减少继发性损伤、保护存活轴突的神经功能,而且可以防止脊髓进一步损伤。以骨筋膜室综合征为例,重型急性脊髓损伤后继发的脊髓室综合征(SCCS)亦称为脊髓髓内高压,是脊髓继发性损伤的一种机制^[27-31];脊髓缺血、水肿、挫裂伤,以及椎管容积变小均可以导致髓内高压,从而进一步加重脊髓缺血、水肿和变性坏死损伤,如此恶性循环加重继发性损伤。此外,早期施行脊髓减压术有利于脊髓功能恢复,因此无论是完全性损伤(ASIA A级)还是不完全性损伤(ASIA B~D级)患者均应尽早(<24小时)施行减压术和内固定术^[27,32];对于转运困难或难以在伤后24小时内完成术前检查和术前准备的患者,亦应于伤后3天内进行外科手术治疗^[26]。“中国指南(2021)”强调,急性脊髓损伤后出现广泛性脊髓水肿的患者应及时行硬脊膜切开术和硬脊膜成形术,由于后者尚未达成共识,故“中国指南(2021)”仅列出硬脊膜切开术的适应证,包括ASIA A~C级且存在广泛性脊髓水肿(>2个节段),或合并MRI提示局部脑脊液循环中断,以及椎板切除术后无脑脊液搏动^[29,33]。值得注意的是,硬脊膜切开术存在增加脑脊液漏和脑膜

炎的风险,是否选择硬脊膜切开术以缓解脊髓水肿,应权衡潜在获益与较长手术时间和其他并发症的风险^[34]。此外,保留蛛网膜完整性的硬脊膜切开术可降低大部分脊髓内压力,而且不存在导致脑脊液漏以及炎性因子进入脑脊液和脊髓的风险^[33],适用于硬脊膜切开后脊髓水肿且无明显蛛网膜下腔出血的患者。(5)细胞治疗:急性脊髓损伤可以导致损伤区域发生水肿和炎症,而损伤早期于病灶区域予以细胞注射可加剧损伤,因此“中国指南(2016)和(2021)”均不建议在急性期进行损伤局部细胞注射治疗,“中国指南(2021)”指出,鞘内或静脉注射间充质基质细胞可以改善急性期全身或局部炎症反应^[35]。

3. 并发症管理 脊髓损伤后,损伤平面以下的交感神经受到抑制,导致心率减慢、外周血管扩张,易发生低血压和休克^[36]。而脊髓血供呈节段性分布的特点使其侧支血流少,缺血代偿能力差^[37],脊髓损伤后一旦发生低血压即可导致脊髓灌注不足。“中国指南(2021)”建议,脊髓损伤后平均动脉压(MAP)维持在85~90 mm Hg以上对患者有益^[38-39];而且适当补充体液扩容或应用去甲肾上腺素,对改善损伤后局部脊髓灌注压、缓解脊髓缺血有益^[40]。低钠血症是颈髓损伤的常见并发症,“中国指南(2021)”建议,轻度低钠血症患者可采取高盐饮食并限制液体摄入量,同时密切监测血清钠水平;中至重度稀释性低钠血症患者则需在高盐饮食的基础上输注氯化钠溶液;而低血容量性低钠血症既要扩容又要补充钠盐^[26,41-42]。对于深静脉血栓形成患者,“中国指南(2021)”建议物理疗法(下肢气压泵、弹力袜等)联合应用低分子量肝素以预防静脉血栓形成,不推荐常规应用下腔静脉滤器^[26]。

二、中期和慢性期脊髓损伤

“中国指南(2021)”首次引入“中期脊髓损伤”的概念,系指损伤后14天至6个月,6个月以后则为慢性期^[2,4,43]。在此阶段,应在评估患者神经功能状态、脊柱序列和稳定性、脊髓损伤程度,并综合患者全身情况的基础上,制定最佳治疗计划。(1)手术减压:“中国指南(2016)和(2021)”均认为,对于出现严重脊髓压迫症状的中期和慢性期脊髓损伤患者,手术减压可促进神经功能恢复。(2)神经桥接:神经桥接可恢复慢性期完全性脊髓损伤患者的某些神经功能^[44],主要有以下3种方法,其一,受伤平面以上的周围神经(如副神经或肋间神经)桥接至

受伤平面以下瘫痪肌肉的神经根或周围神经^[45];其二,受伤平面以上的L₅或S₁腹侧根桥接至受伤平面以下支配膀胱的S₂或S₃腹侧根^[46-47];其三,取外周神经插入胸髓腹侧束(皮质脊髓束)4~5 mm,神经远端连接下肢肌肉的神经-肌肉接头^[48]。晚近临床研究证实,上述神经桥接方法对脊髓损伤后的神经功能恢复有一定促进作用^[49-51]。(3)神经刺激/神经调控:硬膜外刺激训练可以激活神经回路,促进完全性脊髓损伤患者的神经重塑和功能恢复^[52]。例如,经颅电刺激对治疗慢性脊髓损伤后的神经性疼痛有效^[53],功能性电刺激可以挽救永久性失神经-肌肉的肌肉质量和功能^[54];此外,电刺激还可以减少全身并发症^[55]、缓解疼痛、改善躯干稳定性^[56-57]。(4)脑机接口和神经假肢:脑机接口和人工神经假肢可以帮助瘫痪患者进行日常生活活动并促进神经重塑^[58];通过外骨骼机器人进行康复治疗,有助于步态康复、使脊髓损伤平面下降并可改善肌肉痉挛^[59-60]。(5)细胞治疗:目前有多种类型细胞适用于中期和慢性期脊髓损伤患者的细胞移植治疗,已成为此阶段脊髓损伤患者的重要治疗方法,包括嗅鞘细胞、间充质基质细胞、外周血单核细胞、骨髓和脐带血单核细胞、骨髓造血干细胞、施万细胞以及胚胎干细胞等^[43,61-67]。细胞注射可通过血管内输注、鞘内或脊髓实质注射以及多种途径联合治疗以改善患者部分神经功能和生活质量^[61-66]。然而,该疗法对少数患者无效^[68-69]。(6)相关临床研究进展:新近临床研究显示,切除急性或慢性期完全性脊髓损伤患者的脊髓坏死组织和瘢痕组织,然后以神经再生支架和脐带间充质干细胞进行原位填充^[70-71]。但“中国指南(2021)”并不推荐开展此类手术,认为脊髓损伤急性期或亚急性期行此类手术可能会丧失神经功能自我恢复的机会,而慢性期完全性脊髓损伤患者可能会因此失去前述细胞治疗、神经调控、神经桥接等神经修复和康复的可能^[72]。

三、总结与展望

综上所述,采用单一神经修复的治疗方法患者获益有限,而多种方法相结合的综合治疗方是今后的发展方向。尽管“中国指南(2021)”根据现有临床证据对“中国指南(2016)”进行部分修订和更新,但仍存在许多问题尚未解答或不够详尽。随着大规模多中心随机对照临床试验的开展,相信未来将会获得更多和更充分的改变临床实践的证据以造福患者。

利益冲突 无

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· 小词典 ·

中英文对照名词词汇(二)

- 脊髓室综合征 spinal cord compartment syndrome(SCCS)
- 脊髓损伤 spinal cord injury(SCI)
- 脊髓损伤神经学分类国际标准
International Standards for Neurological Classification of Spinal Cord Injury(ISNCSCI)
- 脊髓小脑性共济失调6型
spinocerebellar ataxia 6(SCA6)
- 简易智能状态检查量表
Mini-Mental State Examination(MMSE)
- 交叉相关 cross-correlation(CC)
- 进行性核上性麻痹 progressive supranuclear palsy(PSP)
- 经后路腰椎间融合术
posterior lumbar interbody fusion(PLIF)
- 经椎间孔腰椎间融合术
transforaminal lumbar interbody fusion(TLIF)
- 颈动脉支架成形术 carotid artery stenting(CAS)
- 颈内动脉 internal carotid artery(ICA)
- 颈椎功能障碍指数 Neck Disability Index(NDI)
- 颈椎前路椎间盘切除椎间融合术
anterior cervical discectomy and fusion(ACDF)
- 聚合酶链反应 polymerase chain reaction(PCR)
- 均方根误差 root mean square error(RMSE)
- 抗核抗体 anti-nuclear antibody(ANA)
- 抗凝血酶 antithrombin(AT)
- 抗心磷脂抗体 anti-cardiolipin antibody(ACA)
- 抗中性粒细胞胞质抗体
antineutrophil cytoplasmic antibody(ANCA)
- 扩散张量成像 diffusion tensor imaging(DTI)
- 狼疮抗凝物 lupus anticoagulant(LA)
- 毛细管电泳 capillary electrophoresis(CE)
- 美国国立卫生研究院卒中量表
National Institutes of Health Stroke Scale(NIHSS)
- 美国急性脊髓损伤研究
National Acute Spinal Cord Injury Study(NASCIS)
- 美国脊髓损伤协会
American Spinal Injury Association(ASIA)
- 美国介入和治疗性神经放射学学会/美国介入放射学学会
侧支循环分级系统
American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology
Collateral Flow Grading System(ASITN/SIR ACG)
- 美国神经外科联盟
American Association of Neurological Surgeons(AANS)
- 美国医学遗传学和基因组学会
American College of Medical Genetics and Genomics
(ACMG)
- 蒙特利尔认知评价量表
Montreal Cognitive Assessment(MoCA)
- 脑白质高信号 white matter hyperintensity(WMH)
- 脑桥预警综合征 pontine warning syndrome(PWS)
- 脑实质血肿 parenchymal hematoma(PH)
- 脑血流量 cerebral blood flow(CBF)
- Alberta 脑卒中计划早期CT评分
Alberta Stroke Program Early CT Score(ASPECTS)
- 内囊预警综合征 capsular warning syndrome(CWS)
- 平均通过时间 mean transmit time(MTT)
- 奇异值分解 singular value decomposition(SVD)
- 全外显子组测序 whole exome sequencing(WES)
- 日本骨科协会评分
Japan Orthopedic Association Scores(JOA)