· 指南与共识 ·

脊髓损伤神经修复临床治疗指南（IANR/CANR 2019 年版）

国际神经修复学会暨中国神经修复学会

【摘要】 脊髓损伤(SCI)患者的功能恢复是神经修复领域最具挑战的任务之一。为探索 SCI 急性、亚急性和慢性期的有效神经修复方法，中国神经修复学会(CANR)于 2016 年首次发布了《脊髓损伤神经修复临床治疗指南(中国版 2016)》。鉴于近年该领域的快速发展，国际神经修复学会(IANR)和 CANR 共同修订发布了《脊髓损伤神经修复临床治疗指南(IANR/CANR 2019 年版)》，本刊在此全文首发《脊髓损伤神经修复临床治疗指南(IANR/CANR2019 年版》中文版。该指南为 SCI 患者提供了全面的管理策略，包括评估与诊断、院前急救、治疗策略、康复训练以及并发症管理。当前，诸多临床试验已经证明很多神经修复策略对于促进 SCI 患者功能恢复和改善生活质量是有益的。此外，临床前期研究成果为 SCI 治疗提供了许多有前景的神经修复策略。本指南可为临床医生和研究人员提供一种神经修复治疗标准和(或)参考，最大程度恢复 SCI 患者的神经功能，改善生活质量。

【关键词】 脊髓损伤；神经修复；临床治疗指南

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Interpretation of clinical neurorestorative therapeutic guidelines for spinal cord injury (IANR/CANR version 2019)

(International Association of Neurorestoratology and Chinese Association of Neurorestoratology)

【Abstract】 Functional restoration after spinal cord injury (SCI) is one of the most challenging tasks in neurological clinical practice. With a view to exploring effective neurorestorative methods in the acute, subacute, and chronic phases of SCI, "Clinical Therapeutic Guidelines of Neurorestoration for Spinal Cord Injury (China Version 2016)" was first proposed in 2016 by the Chinese Association of Neurorestoratology (CANR). Given the rapid advances in this field in recent years, the International Association of Neurorestoratology (IANR) and CANR formed and approved the "Clinical Neurorestorative Therapeutic Guidelines for Spinal Cord Injury (IANR/CANR version 2019)". This guideline provided comprehensive management strategies for SCI, which contains the evaluation and diagnosis, pre-hospital first aid, treatments, rehabilitation training, and complications management. Nowadays, amounts of neurorestorative strategies have been demonstrated to be benefit in promoting the functional recovery and improving the quality of life for SCI patients by clinical trials. Also, the positive results of preclinical research provided lots of new neurorestorative strategies for SCI treatment. These promising neurorestorative strategies are worthy of translation in the future and can promote the advancement of SCI treatments. These guidelines can provide a neurorestorative therapeutic standard or reference for clinicians and researchers in clinical practice to maximally restore functions of patients with SCI and improve their quality of life.

【Key words】 Spinal Cord Injury; Nerve rehabilitation; Clinical treatment guide

脊髓损伤(spinal cord injury，SCI)是指脊柱骨折或脱位引起的脊髓或马尾神经的损伤，伴或不伴开放性损伤。中国有超过 100 万的脊柱脊髓损伤患者，并且还在以每年 12 万的速度增长。SCI 的全球患病率情况不一，其中美国最高(每百万 906 人)，法国罗纳-阿尔卑斯(Rhone-Alpes)最低(每百万 250 人)[1-7]。脊柱骨折患者中约 14%患有 SCI，大多数损伤是单节段性的。SCI 常发生在 30～40 岁人群中。SCI 患者的死亡率高于年龄匹配的对照组[8]。近年来，由于急性期院前急救和治疗的进步以及护理技术的提高，脊柱

损伤和脊髓损伤的受害者死亡率已从 4.42%降至 0.44%。诸多干预方式的进步改善了 SCI 患者的生活质量,并延长了寿命。

如今,许多神经修复策略已被用于临床实践,并获得了疗效[9-21]。鉴于该领域的快速发展,国际神经修复学会(International Association of Neurorestoratology, IANR)和中国神经修复学会(Chinese Association of Neurorestoratology, CANR)基于已发布的指南,共同推荐《脊髓损伤的临床神经修复治疗指南(IANR / CANR 2019 年版)》[22]。该文件已由 IANR 理事会和 CANR 委员会批准。本指南是基于 2019 年 6 月 30 日之前针对急性、亚急性和慢性 SCI 的临床治疗证据。本文所描述和列出的针对急性、亚急性和慢性 SCI 恢复的干预措施,大部分都是在临床实践中已广泛应用或者正处于临床研究阶段。在非人模型上进行的神经修复实验研究和临床前研究的阳性结果应鼓励其早日转化为临床研究。建议将这些指南作为 SCI 临床神经修复治疗的全球医学界和科学界的参考标准。尽管指南中的方法可以在一定程度上恢复 SCI 患者的功能,但要使 SCI 患者完全恢复功能,我们还有很多工作要做。

1 SCI 急性期和亚急性期

1.1 评估、诊断与治疗

1.1.1 评估 体格检查:SCI 后 3d 内应进行全面的神经系统检查,以评估严重程度并估计治疗的可能结果。约 1/4 的颈椎损伤合并 SCI 的患者可合并颅脑损伤,而胸腰段 SCI 也可伴有胸、腹、骨盆及四肢损伤。因此,有必要进行全面的体格检查,以避免误诊[3,23-24]。神经功能评估最常用的定量诊断方法是美国脊髓损伤协会(American Spinal Cord Injury Association ,ASIA)神经功能评分[25](见图 1)。SCI 患者的日常生活或生存质量推荐采用国际神经修复协会脊髓损伤功能评定量表评估[26],见表 1。

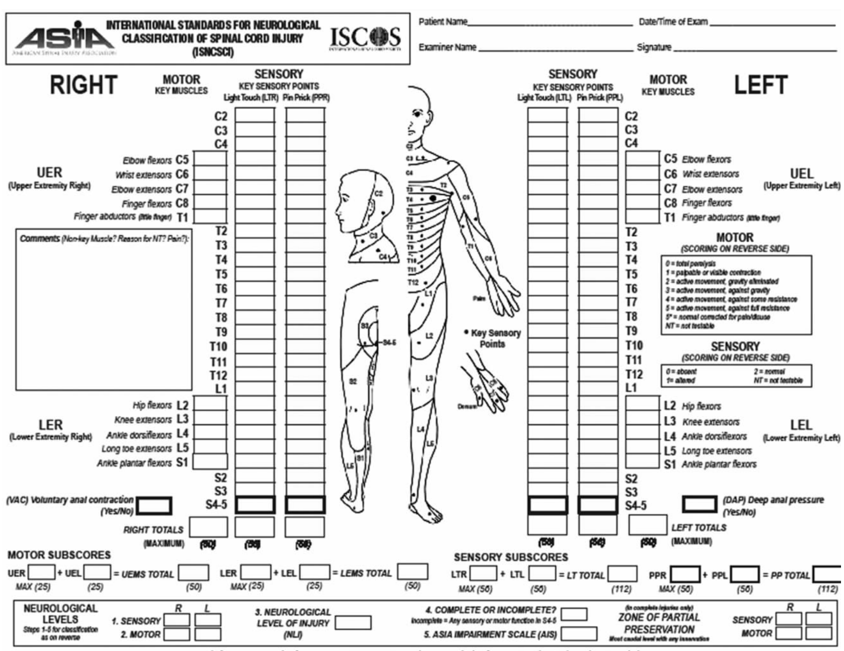

图 1 美国脊髓损伤协会(ASIA)的神经学评分

Figure 1 Neurological score of American Spinal Cord Injury Association

补充检查 X 线平片:拍片包括前后位及侧位片,但应首先检查侧位片来限制患者活动。某些情况下,应检查双斜位影像。主要观察椎体的对位、骨折或脱位的类型、附件骨折及椎间隙变窄或变宽等。电子计算机断层扫描(computer tomography, CT):CT 是诊断 SCI 患者脊柱骨折或脱位的常用技术[27-28]。CT 轴位和三维扫描可显示椎管和小关节的形态。对于有合并伤的病例,强烈建议对合并损伤的患者 CT 扫描。磁共振成像(magnetic resonance imaging, MRI):MRI 是评估 SCI 患者椎间盘、韧带、脊髓和神经根完整性、损伤部位、严重程度和累及范围的首选检查方法[29]。MRI 还可显示椎管内受损椎间盘和韧带的移位碎片以及水肿和(或)出血[30]。体感诱发电位(somatosensoyr evoked potential, SSEP):SSEP 是检查损伤脊髓感觉功能完整性的可靠方法[31-32]。在伤后 24 h 和几周的反复检查中未能检测到 SSEP,表明感觉功能完全丧失,反之判定为不完全损伤。

1.1.2 诊断 SCI的诊断应包括受伤节段与严重程

表 1　国际神经修复学会脊髓损伤功能评定量表(IANR-SCIFRS)

Table 1　Spinal cord injury rating scale of International Association of Neurorestoratology

1. 上肢运动	(10)穿衣
(1)进食和饮水	正常 3 分
正常 3 分	独立完成,有困难 2 分
独立完成有困难 2 分	部分辅助 1 分
部分帮助 1 分	完全依赖 0 分
完全依赖 0 分	5. 括约肌控制
(2)洗漱	(11)膀胱控制
正常 3 分	正常 3 分
独立完成有困难 2 分	有部分感觉的反射性排尿或控制 2 分
部分帮助 1 分	无感觉的反射性排尿或控制 1 分
完全依赖 0 分	完全尿失禁或导尿/膀胱造瘘 0 分
(3)书写	(12)排便控制
正常 3 分	正常 3 分
动作缓慢或粗糙;多数字迹清晰 2 分	有感觉的部分控制 2 分
多数字迹不清晰 1 分	无感觉的部分控制或无部分感觉的控制 1 分
无法握笔 0 分	完全性失禁 0 分
2.下肢运动	6.(13)肌张力(指肌肉对运动的张力或阻力的大小)
(4)不带支具站立	正常 3 分
正常 3 分	轻微亢进/减退或轻度痉挛 2 分
独立站立但不稳 2 分	大幅度亢进/减退或显著痉挛 1 分
需要辅助支具 1 分	极度僵硬或痉挛 0 分
无法站立 0 分	7.(14)出汗
(5)不带支具行走	正常 3 分
正常 3 分	轻微减少 2 分
独立行走但缓慢或不稳 2 分	显著减少 1 分
需要辅助支具 1 分	无汗 0 分
无法行走 0 分	8.(15)皮肤情况
3. 躯干运动	正常 3 分
(6)坐位	部分分解 2 分
正常 3 分	明显分解,常合并水肿 1 分
静止时稳定,但运动时不稳定 2 分	持久褥疮或皮肤破损;严重水肿 0 分
静止时不稳定 1 分	9.(16)疼痛
无法坐 0 分	无疼痛 3 分
(7)翻身	轻度疼痛,普通止痛药有效 2 分
正常 3 分	重度疼痛,需要吗啡类镇痛药 1 分
独立完成有困难 2 分	极度疼痛,未控制 0 分
部分辅助 1 分	10.(17)性功能(仅针对男性的比率;不包括在总评分中)
完全依赖 0 分	正常 3 分
4. 一般运动	可以实现勃起和性渗透,但感觉或射精的问题 2 分
(8)转移:卧床到椅子/轮椅	可以实现勃起,但没有性快感或射精 1 分
正常 3 分	无法实现勃起 0 分
独立完成,有困难 2 分	
部分辅助 1 分	
完全依赖 0 分	
(9)洗澡	
正常 3 分	
独立完成,有困难 2 分	
部分辅助 1 分	
完全依赖 0 分	

该量表包括 9 个类别,共 16 个项目(加上一个可选类别)。最高评分为 48;最低评分为 0. 功能评定量表评分的解释:48,所有类别的功能正常;35-47,轻度功能障碍(大部分独立);18-34,中度功能障碍(部分依赖);0-17,严重的功能障碍程度(显著影响日常生活)。

度、伤椎骨折与(或)脱位的节段和类型、脊柱的稳定性等。SCI 的严重程度根据 ASIA 损伤量表[25]进行分类。AISA A 级:肛周感觉和肛门括约肌随意收缩均缺失。ASIA B 级:在损伤节段水平以下保留了部分感觉,但运动评分为 0。ASIA C 级:在损伤节段以下存在部分运动功能,但运动评分累计达不到正常的 50%。ASIA D 级:在损伤节段以下运动评分累计为正常水平的 50% 或高于 50%。

1.1.3　脊髓损伤治疗方法　继发性损伤是 SCI 后微环境失衡的主要原因[26],治疗应着重减轻 SCI 急性期和(或)亚急性期的继发性损伤。急性脊髓损伤的处理原则包括限制主动和被动运动,早期固定,联合髓外和髓内减压,合理的细胞疗法,早期康复治疗以及预防并发症[3,23-24,33-34],见图 2。

1.1.3.1　院前急救　在外伤后,急救人员应迅速评估患者,并在将患者转运至医院途中进行复苏。必要时应随时提供生命支持(气道、呼吸和循环)。应限制搬运以避免头部和整个脊柱过度移动。处理 SCI 患者的最佳方法:在三个或更多人的帮助下将患者水平抬起,移动到平板或专用担架上,由救护车或直升机运送到专科医院[3]。

1.1.3.2　药物治疗　神经保护是 SCI 急性期和亚急性期最重要的神经修复方法之一,尽量减少和(或)防止继发性病变的扩展,从而减少细胞凋亡或坏死,促进神经元细胞和轴突存活。

皮质类固醇:早期大剂量甲基强的松龙(MP)治疗曾被认为对脊髓损伤急性期的神经修复有积极作用[35-38]。美国国家 SCI 研究(NASCIS I 和 II 期)进行的临床研究结果显示该法疗效中等,但可能存在严重的并发症。到目前为止,还没有明确的证据支持其常规应用。美国神经外科医师协会(American Association of Neurosurgeons, AANS)和神经外科医师代表大会(自 2013 年起)的指南中不推荐使用 MP。最近的研究表明,在神经系统恢复方面,尚无足够证据表明大剂量 MP 疗法可用于急性 SCI,且由于感染、呼吸系统损伤、胃肠道出血、甚至死亡等并发症,大剂量 MP 疗法已不再作为急性 SCI 的常规使用方法,但在某些情况下仍是一种可选的治疗方法[19,39-42]。MP 仍可用于不完全性颈髓病变,特别是在需要减压的脊髓型颈椎病患者中。如果要使用 MP,建议注意以下几点:(a)时间窗口(<8h):在大剂量 MP 的应用中,应严格控制正确的输注速度,并准确测量体重和剂量[42]。在 SCI 之后的前 3h,MP 应在 15min 内以 30 mg / kg 的推注剂量给予,然后以 5.6 mg / kg /h 的速度连续输注 23 h;对于 SCI 后 3 到 8h 的时间间隔,

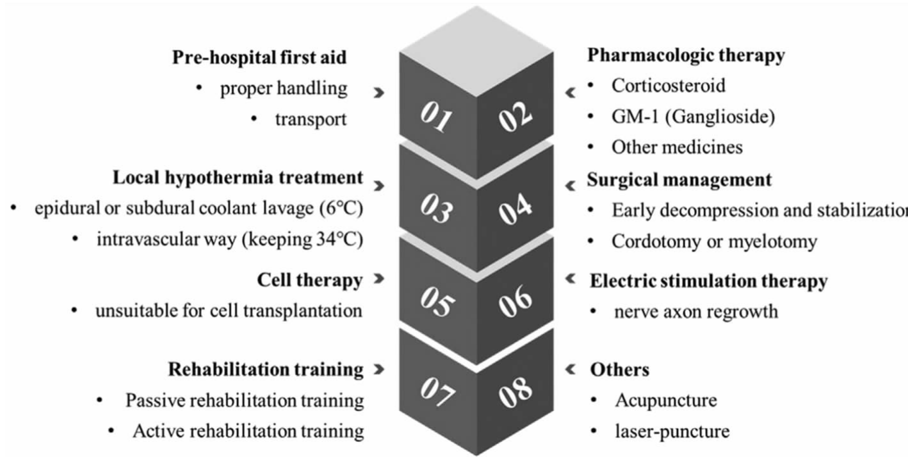

图 2 SCI 急性和亚急性期的神经修复治疗策略

Figure 2 Neural repair strategies in the acute and subacute phases of SCI

应在 15min 内以 30 mg / kg 的推注剂量给予 MP，然后连续 23 h 输注 5.4 mg / kg /h。(b)对于先前神经系统症状已缓解的患者，应尽早停止 MP 使用，以减少毒副作用风险。(c)大剂量 MP 治疗的禁忌症：无神经功能缺损的脊柱损伤；脊髓贯穿伤和枪击伤，以及伤后 8h 以上；胃肠道出血；糖尿病；有肺炎高危因素的老年患者。

神经节苷脂 GM1：一项随机对照研究表明，神经节苷脂 GM1 尽管对神经功能恢复有益，但并未显示出明显的促神经功能恢复作用[43]。一项最近的研究表明，将 GM1(100 mg/d)与 MP 联合用于早期急性 SCI 可促进神经功能的恢复，可改善预后[44]。另一项随机安慰剂对照的研究表明，每天 100 mg(静脉，30 d)服用 GM1 可以改善感觉功能，但不能改善运动功能。在通过大样本临床试验以确定 GM1 能否恢复神经功能并降低急性脊髓损伤患者的死亡率和发病率之前，不建议将 GM1 用于急性脊髓损伤患者的常规治疗[40,45-47]。

以上列出的干预措施在大多数急性 SCI 的临床实践中均被接受。

其他药物：促红细胞生成素具有神经胶质保护和神经保护特性，可减少髓质空洞化、细胞浸润和神经元凋亡。然而它不能改善创伤性完全或不完全的颈椎 SCI 患者的功能预后[48]。临床试验表明，米诺环素、纳洛酮和替拉扎德对 SCI 患者的治疗效果有限。甘露醇能减轻继发性脊髓水肿，在无禁忌症的情况下可早期应用[49]。

1.1.3.3 亚低温治疗 低温包括全身和局部低温的治疗方法，可减少受伤组织的新陈代谢并减少耗氧量。32～34℃似乎是全身治疗的最有效范围[50-54]。局部低温治疗也有效[55]，可通过开放式或封闭式技术进行硬膜外或硬膜下冷却液灌洗(6℃)[56]。亚低温疗法仍处于探索阶段。到目前为止，针对急性 SCI，尚无公认的适应证或禁忌症。治疗建议是，如医疗和患者条件允许，应同时进行局部低温治疗和全身低温治疗[57-59]。

1.1.3.4 手术管理 早期减压和稳定：椎板成形术或椎板切除术可通过椎体复位和固定脊柱恢复稳定性，并恢复椎管容积。急性 SCI 时进行脊柱对线复位和稳定(24 h 内)是安全的，可改善神经结局，缩短住院时间，减少并发症。急性 SCI 后脊髓减压可减轻继发性损伤，保留存活轴突的神经功能，并防止进一步破坏脊髓组织。

手术时间窗口：目前证据表明，对于存在明显神经功能缺损的患者，无论损伤是完全损伤(ASIA A 级)还是不完全损伤(ASIA B-D 级)，均应在没有危及生命的情况下尽早(< 24 h)进行减压和内固定[60-65]。但由于运输、术前检查和准备等问题，很多患者无法在 24 h 内接受手术。一项临床研究对脊髓损伤进行早期手术干预(< 3 d)显示，手术治疗越早，获益越大[3,66-67]。

脊髓切开术：硬膜外减压是治疗急性脊髓损伤患者的重点。目前脊髓坏死和出血引起继发性损伤尚未引起人们的重视。SCI 相关脊髓肿胀和任何持续的外部压力都可能会阻断正常脑脊液(cerebrospinal fluid, CSF)流动，并进一步增加脊髓水肿。脊髓切开术和坏死早期清创可阻止继发性损伤的进一步扩大，降低其余组织和 CSF 的压力，保留存活的轴突和备用脊髓组织，延缓白质中的胶质细胞死亡，从而有利于防止完全瘫痪和获得更多的神经功能恢复。

硬脊膜减压可降低人和动物 SCI 的继发性损伤水平。临床研究报道了脊髓切开术对急性 SCI 患者

的神经功能的改善作用[3,22,66-69]。但仍缺乏前瞻性随机对照临床试验。

损伤类型和减压手术由于脊髓完全横断在临床上相当少见，因此应在显微镜下结合 CT 和 MRI 信息进行髓内减压，以保留神经功能受损患者的存活轴突。以下是四种类型的脊髓损伤及其相应的手术干预和效果，见图 3。

第一类：蛛网膜粘连，脊髓搏动消失，脑脊液阻塞，脊髓苍白肿胀。干预措施是减轻蛛网膜的粘连，恢复脑脊液流动和脊髓搏动。

第二类：表现为髓内血肿，骨碎片或异物。干预是清除血肿、骨碎片或异物并探查脊髓。

第三类：脊髓部分受损。一旦打开硬脊膜，液化组织可能会涌出。干预措施包括探查损伤部位，清除坏死组织并用生理盐水轻轻冲洗该部位。

第四类：表现为髓内软化。干预措施是在软化区域进行 0.3～0.5 cm 的纵向切口，去除软化组织，并用生理盐水轻轻冲洗腔体。

由于挫伤脊髓与正常脊髓之间的边界在早期尚不清楚，因此应注意不要过度扩大髓内减压范围。

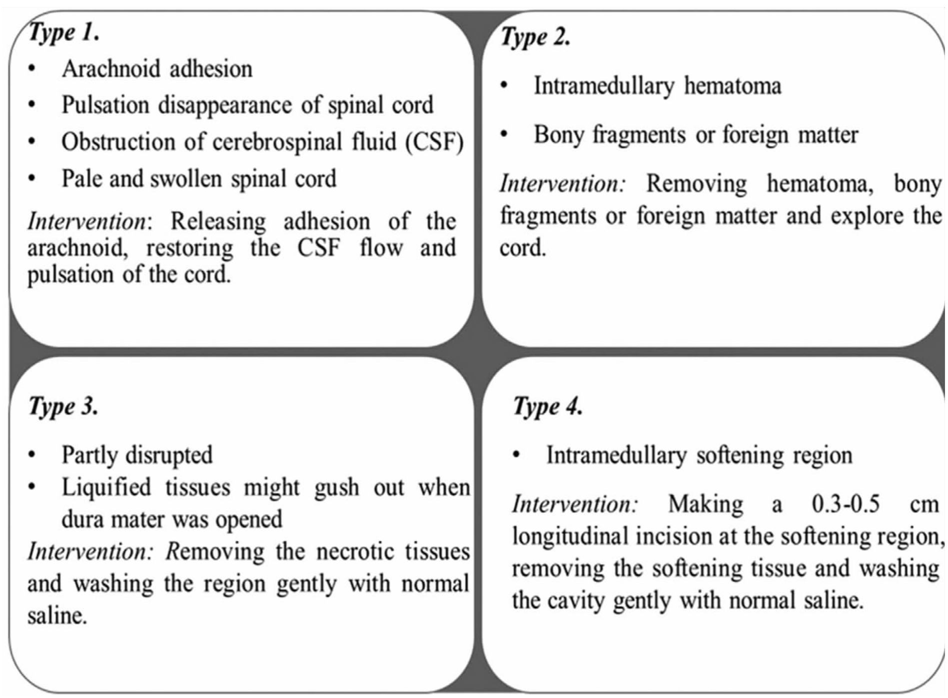

图 3　SCI 急性期和亚急性期的损伤类型和减压程序

Figure 3　Types of injury and decompression procedures in the acute and subacute phases of SCI

1.1.3.5　神经电生理评估　急性或亚急性 SCI 患者的术中神经电生理评估可提供其他方法无法获得的有关脊髓功能信息，这些信息可以正确预测神经系统预后。

在过去 100 年里，这些神经修复手术一直在发展进步中，而且这些手术或脊髓切开术还在进一步研究中，以制定急性和亚急性 SCI 的标准治疗方案。

1.1.3.6　细胞疗法　细胞治疗是 SCI 一种很有前景的治疗选择。用于 SCI 细胞疗法的机制包括轴突再生和髓鞘再生、神经重塑、神经保护、神经调节、神经结构修复、抗炎反应或免疫调节、神经组织再生、血管再生、减少瘢痕和空洞形成以及细胞替代[13,49,70-72]。迄今为止，一些细胞疗法治疗急性或亚急性 SCI 的临床试验已经进行[73-75]。在动物急性 SCI 研究中也获得令人振奋的结果[71-72]。在一项动物研究中，当延迟至横断性损伤后 2～4 周移植神经细胞和应用神经营养因子时，运动功能恢复显著[76]，这可能是得益于病变区域急性炎症和巨噬细胞浸润消退所致。因此，急性 SCI 可能不适合将细胞直接移植到受伤区域。目前，需要在急性和亚急性 SCI 中评估细胞疗法的疗效。细胞疗法可作为一种促进急性脊髓损伤修复的具有前景的方法。但还需要进一步评估感觉运动修复机制。

1.1.3.7　电刺激疗法　神经系统依靠电信号进行信息传递，局部电刺激可以改善并诱导轴突再生[77]。电刺激有几种类别。首先，最先采用的是神经肌肉电刺激，期望延缓在瘫痪期间肌肉失用性效应。第二类是瘫痪者电刺激调控[78-79]。第三类是从对周围神经结构的功能性电刺激发展到对脊髓的电刺激。这种方法很有前景，但仍在进一步探索提高治疗效果[80]。第

四类是通过物理、药物、神经电生理以及各种神经生物刺激的综合干预来促进 SCI 运动控制。以上方法可通过刺激和抑制,有效调整神经功能,并继续探索提高有效程度[81]。

1.4　康复训练

1.4.1　理疗　被动康复训练:术后被动康复训练(如按摩和压力治疗)不仅可以降低压疮和深静脉血栓的发生率而且可以恢复神经功能。自我激励疗法在康复中有重要作用[82]。此外,在康复期间和康复之后接受指导的患者,其自我效能感应得到更大的提高,并且也减少额外住院时间[83]。主动康复训练:一旦患者病情允许,就可开始在手术后借助头颈和腰背部支具进行积极主动的康复训练。这包括职业培训、运动培训和水疗等。积极训练原则是:主动运动-目标强化-神经康复,依据这一原则训练,有助于患者最大化神经功能恢复[27]。

机器人技术正在融合到物理治疗中,可以维持和延长 SCI 后恢复期的运动功能,并制定出促进运动功能恢复的控制程序。同时。运动功能神经可塑性研究,有助于与其他物理治疗方法共同促进功能恢复[84]。

1.4.2　职业治疗　职业疗法是解决患者职业(自理、工作和休闲问题)综合康复的一部分。该疗法目的包括帮助患者适应社交生活和其它环境[85]。在神经修复治疗后,早期职业和物理治疗非常重要。我们强烈建议早期进行康复运动或治疗,包括职业治疗、物理治疗、中频电刺激、低频电刺激和磁治疗,特别是神经修复治疗后的主动运动训练(如果条件允许)[86]。针灸[87]和激光治疗[88]可以促进急性或亚急性 SCI 患者的功能恢复且风险较小。对急性完全 SCI 患者鞘内使用人源抗 Nogo-A 抗体的治疗,患者耐受性良好,并显示出一定疗效[89]。

1.5　并发症和处理

1.5.1　循环系统并发症

低血压:颈部脊髓损伤后,交感神经(而非副交感神经)活动受到抑制,导致患者痰多、心率减慢、血压下降。山莨菪碱可静脉给药(20 mg 配 500 mL 生理盐水),速度为每 11～15 滴每分钟;儿童速度应根据体表面积进行调整。药物作用通常包括心率加快、平均动脉压升高和痰液减少。

低钠血症:各项临床试验证明,这是颈脊髓损伤常见而严重的并发症,发生率为 45%～100%。低钠血症常发生在伤后 6.4～8.9 d,伤后 8.7～17.3 d 检测到最低血钠浓度,在第(21.8±10.2)d 开始升高。一般低钠血症在 30.4～6.0 d 后消失。低钠血症的相关原因包括脊髓损伤节段、感染、使用呼吸机和药物(如脱水剂和利尿剂)。精制尿素可用于(口服给药,30 mg/d)抗利尿激素分泌不当综合征;氟氢可的松(口服给药,0.1～0.2 mg/d)可治疗脑性盐耗综合征。由于这两类综合征难以区分,氟氢可的松(加入生理盐水)对于特发性性低钠血症是安全有效的[90-91]。

深静脉血栓形成:SCI 后具有临床症状深静脉血栓形成(deep vein thrombosis, DVT)的发生率约为 16.3%,而其发生率通过超声或静脉造影成功检测率为 79%。DVT 预防措施包括四肢运动和穿弹性袜。一旦形成,应给予抗凝治疗。血栓形成有导致心脏、肺和脑栓塞的风险。

1.5.2　呼吸系统并发症　呼吸困难和肺部感染是脊柱脊髓损伤后主要呼吸系统并发症。包括反复肺炎、肺不张和胸腔积液;SCI 也可能导致睡眠呼吸暂停和呼吸衰竭[84]。呼吸系统并发症是慢性 SCI 患者死亡的主要原因[86]。颈椎 SCI 达 C4 水平以上的患者可出现膈肌麻痹,咳嗽反射减弱甚至消失,导致呼吸困难和肺部感染。此时,可能需要做气管切开,以便于吸痰和呼吸机支持。适当体位有助于预防或减少呼吸道感染的出现和恶化。此外,定时位置变化有助于预防并发症,尤其是压疮和循环问题。应鼓励患者尽早坐起,或在坐轮椅之前抬高床头进行训练,以防止发生多种与呼吸有关的并发症。当然,在体位变换过程中,应密切观察患者,防止体位性低血压发生[92-94]。

1.5.3　泌尿系并发症　尿路感染是脊柱脊髓损伤后主要的泌尿系统并发症。必须使用导尿管时,定期更换导尿管并定期清洗膀胱,以避免肾积水和肾功能衰竭。

2　慢性期

2.1　评价、诊断与治疗

2.1.1　体格检查　神经功能可采用 ASIA 评定标准[25]。日常生活功能可采用国际神经修复学会脊髓损伤功能评定量表[27]进行评估,见图 4。

磁共振成像:MRI 可清晰显示损伤脊髓的当前状况,如萎缩、脊髓软化、囊腔甚至脊髓空洞,以及形成的疤痕和脊髓压迫(如果存在)。

电生理检查:椎旁 SSEP 可以评估和判断脊髓损伤的感觉水平。肌电图用于评估受伤部位的运动水平。

2.1.2　诊断　慢性 SCI 的临床诊断包括确定损伤脊髓的水平和严重程度[25],日常生活质量[27],损伤脊髓是否仍有受压[30]。神经生理学检查和 MRI 可能有助于准确了解运动和感觉的结构[31]和功能状况[95-98]。

2.1.3　治疗方法　对于患有慢性 SCI 和严重脊髓受

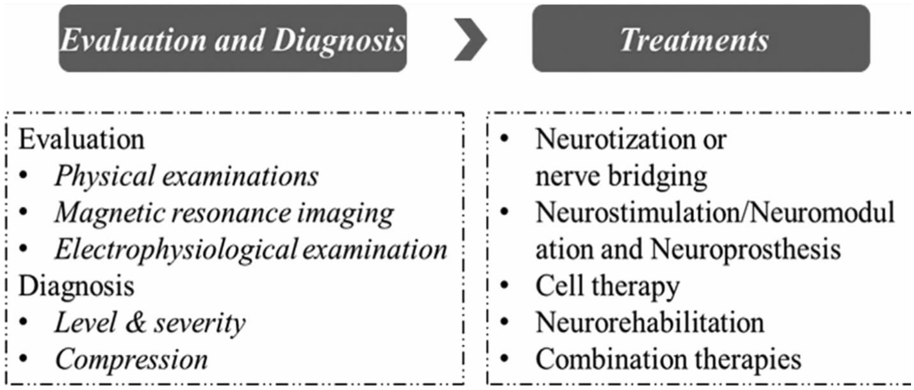

图 4 SCI 慢性期的临床神经修复治疗指南

Figure 4 Guidelines for the treatment of clinical nerve repair in the chronic phase of SCI

压的患者,减压治疗最有可能促进某些功能性神经系统恢复。

神经桥接:50 年前已有报道:将神经移植到失神经支配的部位进行神经桥接可以恢复完全性慢性 SCI 患者的某些功能[99-100],尤其是在做身体康复情况下。主要有以下三种方法。

1).切除受伤部位上方的周围神经(例如:副神经或肋间神经),桥接至受伤部位下方瘫痪的肌肉的神经根或周围神经[101-102]。2).从受伤部位上方的腰五或骶一节段切除腹侧根,与正常支配膀胱的骶 2 或 3 节段腹侧根相连[103-104]。3).切断周围神经,将神经插入胸椎脊髓(皮质脊髓束)腹侧束 4～5mm,神经远端连接下肢肌肉神经接点[105-106]。

最近几项临床报告描述了这些方法在 SCI 患者神经功能恢复中的作用[107-109]。

神经刺激/神经调节和神经假体:硬膜外刺激训练能激活以前沉默的备用神经回路并促进神经可塑性改变。这些干预措施是完全性慢性 SCI 患者功能恢复的可行临床方法[17,110-111]。经颅电刺激可有效治疗慢性 SCI 后的神经性疼痛[112-113]。在完全性慢性下运动神经元病变患者中,对永久失神经支配肌肉进行功能性电刺激,是一种有效治疗方法,可挽救肌肉质量及功能。同时也改善腿部外观和增强座椅舒适效果[114-115]。此外,电刺激可以改善慢性 SCI 患者的神经可塑性并减少全身并发症[116]。

脑机接口与人工神经假肢可以帮助长期瘫痪的患者进行一些必要的日常生活活动[117-119]。感觉传入、反馈输入和相关大脑随意运动命令(后者通过脑机接口)有助于为仿生站立和步态辅助的机器人引擎提供无线信息力。最近一项研究表明,可以通利用瘫痪患者脑中皮质内记录的信号来控制肌肉活动[120]。

细胞疗法:细胞疗法已成为慢性 SCI 患者重要治疗选择方法[70]。越来越多的临床证据表明,细胞疗法是一种安全可行疗法。已经发现几种适合移植的细胞类型,例如嗅鞘细胞、雪旺细胞[121-122]、间充质基质细胞、外周血单核细胞、骨髓造血干细胞[123]、脐带血单核细胞、骨髓单核细胞和胚胎干细胞[124]。细胞移植到脐带实质中、鞘内给予(病变区域或腰椎蛛网膜下腔)、血管内输注细胞或多途径给药后,患者部分功能和生活质量得到了改善[22,125-135]。

细胞移植手术技术:大多数脊髓损伤是将细胞移植在损伤部位或邻近损伤部位,用细针或玻璃毛细管注射少于 25μL 的细胞悬浮液[136]。也有尝试做鞘内注射将细胞移植至受伤脊髓。髓内移植是细胞移植最佳途径,它可以与宿主环境直接相互作用,以激活或触发功能异常的神经元或轴突,帮助轴突再生和萌芽,使轴突髓鞘再生,并替代已丧失细胞。但是不适当的细胞注射方法可能会损害脊髓,因技术不当致细胞移植无效,会导致出现错误结果和结论。脊髓实质内注射风险包括针头穿刺损伤、注射过程中脊髓移动损伤、实质内压力梯度增加和血液动力学改变致脊髓缺血等额外伤害。了解这些因素可最大程度提高注射移植安全性,避免损坏其它结构。临床操作要求:(a)通过减少注射次数来减少注射性创伤,尤其是对于颈椎和 T11-L1 段的 SCI 和不完全的 SCI。(b)缩短手术时间(理想情况下)。(c)实验室采集细胞、细胞转运至细胞移植应在 2h 内完成。(d)微创手术(减小切口大小)可缩短术后恢复时间。(e)用细针头,较高浓度细胞以减少总注射量[49,137]。

神经康复:高强度运动和生物反馈训练可以改善慢性不完全性脊髓损伤患者的运动功能[138-140]。强化训练是指每周进行 6～7d,每天 6h 的站立和行走运动。虽然单纯高强度运动对慢性 SCI 患者的益处有

限,但这对接受神经修复疗法患者的运动恢复是必不可少的[27],可帮助患者改善神经功能和生活质量。在中枢神经系统受伤后会发生一种称为“习得性废用”的现象,而高强度重复运动可以逆转肌肉和神经组织的萎缩。通过“基于活动的恢复,一例 C-2 ASIA A 级脊髓损伤患者实现实质性功能恢复(两个 ASIA 级)[141]。多模式强化运动可以显著改善慢性完全性脊髓损伤患者的运动功能,该方法可作为其他恢复性疗法的辅助手段。1 例慢性 SCI ASIA A 级的患者在强化物理治疗和机器人运动训练后,行走能力明显改善[142]。然而这些研究的样本量较小,故需要更多大样本研究。

药物神经修复疗法:酸性成纤维细胞生长因子和粒细胞集落刺激因子治疗可能对慢性 SCI 有益,但需要更高等级证据证实[143-145]。

组合疗法:目前单一神经修复策略的神经功能恢复程度仍然有限。针对完全性慢性 SCI 的组合疗法有望实现更大程度的功能恢复,包括通过两种或多种途径相同细胞移植、移植两种或三种具有协同作用的细胞、细胞治疗与神经康复联合、细胞疗法与激光针灸联合和神经康复联合[27,88,146-147]。此外,神经康复与功能性电刺激相结合[148]或基于脑机接口的步态训练方案可部分恢复行走能力[149]。植入电极可通过电刺激强化神经康复,部分恢复慢性完全性 SCI 患者的站立和行走能力[150-151],并改善日常生活质量[152-156]。

曾有报道在完全切除损伤脊髓后,应用神经再生支架和人脐带血间充质基质细胞修复慢性 SCI 患者[157]。但是,目前应禁止切除脊髓损伤区域脊髓组织的手术,因慢性完全性脊髓损伤患者通过上述细胞疗法、神经调控、神经桥接、神经康复等神经修复方法仍有机会恢复部分功能。然而更好组合疗法设计将面临更多的挑战。

3 小结

近年来,针对 SCI 患者的临床神经修复治疗取得了很大进步[20,2,158]。本指南将能为临床医师更好治疗 SCI 患者提供新的知识和信息。随着更大程度恢复神经功能、改善 SCI 患者生活质量的新治疗措施的积累,本指南将进一步修订和完善。

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