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Intracerebral Hemorrhage: Issues in Rehabilitation

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Abstract

While the advancements in the management of the spontaneous intracerebral hemorrhage (SICH) have resulted an increase in survival, this has also resulted in the number of survivors with significant functional morbidity that require long-term care and rehabilitation services. SICH can lead to various impairments, and the deficits related to SICH may include impairment in motor and sensory functions, emotional lability, language dysfunctions, perception deficits and cognitive dysfunctions. In the present chapter, we present an overview of the issues in rehabilitation which are faced by medical personnel's while managing the patients with SICH.

Keywords: intracerebral hemorrhage, physical impairment, disability, rehabilitation

1. Introduction

Spontaneous intracerebral hemorrhage (SICH) is characterized by nontraumatic bleeding into the brain parenchyma [1]. Further the term “primary spontaneous intracerebral hemorrhage” denotes a spontaneous hemorrhage into the brain parenchyma without any secondary cause (i.e., vascular abnormality, brain tumor, etc.) [2]. SICH accounts for approximately 10–20% of all stroke cases, carries a 30-day mortality of up to 50%, and causes significant and persistent disability in survivors [3–7]. Advances in the management of the SICH have resulted an increase in survival, particularly in cases of smaller lesions; however, larger SICH lesions remain a significant cause of morbidity and mortality globally [8, 9]. Literature suggests that in comparison with ischemic stroke, SICH causes more morbidity and mortality [10]. SICH can lead to various impairments including motor and cognitive deficits, sensorimotor impairment, impaired mobility, depression, swallowing dysfunctions, constipation and urinary incontinence [11]. The rehabilitation in SICH patients is targeted to facilitate the recovery process, avoid complications and optimize the functional outcomes acute as well as in post-acute recovery phase [11].

2. Overall management

The management of SICH can be divided into medical management, surgical management (when indicated) and rehabilitation both in acute as well as post-acute recovery phase [12]. The medical and surgical management intend to stabilize the general as well as the neurological condition of the patient and to prevent the secondary brain injury (either due to mass effect or presence of clotted blood in the brain parenchyma) [13–15]. In the acute phase, the major medical complications that can occur includes pneumonia (because of dysphagia and aspiration), aspiration, respiratory failure/distress, pulmonary embolism and sepsis [16, 17]. The most important step in the initial management, is the control of hypertension, which is the major risk factor that increases the risk of developing SICH by approximately four times [2].

3. Rehabilitation concepts

The deficits related to SICH are variable and may include impairment in motor and sensory functions, emotional lability, language dysfunctions, perception deficits, and cognitive dysfunctions [18]. A number of factors decide the functional outcome as well as the treatment protocol for a given patient. While assessing a patient with SICH for rehabilitation, we need to identify whether the stroke has affected the dominant or nondominant side, whether the patient is having monoplegia, hemiplegia, or any other paralytic syndromes, are there any cognitive or speech disturbances (i.e., aphasia, dysphasia, dysarthria or fluency disorder), whether there is impairment of swallowing or if the patient is on tracheostomy. Additionally, this detailed evaluation should detect the presence of any pressure ulcers, their numbers and sites. Neuroplasticity is often regarded as a physiological basis for recovery after brain insults [19]. There is a dearth of reliable efficient post-stroke rehabilitative therapy implying a significant clinical need [20–22], and there is a significant “therapeutic window” that exists for the SICH patients to recover functionally [23].

4. Rehabilitation and recovery

In the case of hemorrhagic stroke, it has been documented in the literature that gait, limb motor and sensory function generally continue to recover until 3 months after onset; however, gait could improve up to 6 months from onset and it has been shown that upper limb recovery could persist up to an year [24]. This prolonged recovery is a witness to the beneficial outcome of rehabilitation during the subacute phase of recovery in stroke patients [25]. Neuronal plasticity is a subject of dedicated study today and is defined as the ability of the brain to recover functionally due to neuronal reorganization after a cerebral insult. It can usually occur actively following any cerebral insult, albeit for a limited time. It has been postulated that in acute phase and early stages of recovery following SICH delayed metabolic changes, continued neuronal damage and apoptosis in perihematoma tissue can continue

to cause more active inflammatory damage, which is mediated by cellular and noncellular components, leading to more widespread consequences [26–30]. Thus, in comparison with an equivalent-sized ischemic infarct, in patients with SICH, an intraparenchymal blood leads to an increased inflammation and a greater cell death [26, 31]. There is growing evidence that recovery in functions is better in patients with SICH than in patients with ischemic strokes [6, 32–42]. The recovery process starts in the acute phase and can continue for months in the recovery phase [38, 43, 44].

5. Right versus left hemisphere stroke

There is a conflicting evidence whether which hemisphere stroke corroborates with a better outcome [45–47]. The controversy stems from various factors including the varied outcome scales used, measurement domain, presence of hemineglect and the timing of evaluation; for example, in considering vocational rehabilitation, patients with the right hemisphere stroke appear to have a better outcome [48]. The left hemisphere controls speech and language function along with the right half of the body. Strokes in this half of the brain demonstrate a right hemiplegia and aphasia [49]. Preservation of language function is considered one of the primary reasons for a higher percentage of right afflicted people returning to work; however, this cohort of patients are usually the one who most frequently develop social shortcomings in contrast to the left-sided stroke patients [50]. Further studies with exclusion of hemineglect patients may help to exemplify the difference in the disabilities between left and right hemisphere stroke patients [51].

6. Impaired motor function

Restoration of the motor function and mobility is one of the most important components of stroke rehabilitation [52]. Although most stroke patients regain walking independence, many have continuing problems with mobility due to impaired balance, motor weakness, and decreased walking velocity [18]. Impaired motor functions can be due to paralysis or paresis of the muscles (depending on the site of the lesion), which results from the damage to the brain parenchyma (motor cortex or descending/ascending pathways in the internal capsule and corona radiata), resulting in abnormal regulation of spinal motoneurons, alterations in postural and stretch reflexes and loss of voluntary movements [18, 53–56]. If the lesions involve the internal capsule, thalamus, periventricular white matter, and/or premotor cortex, the recovery of the upper limb motor functions is poorer [25, 57]. Regarding the functions in the lower limbs, in a study, it was shown that approximately 51% of subjects were without walking function at the time of admission to the rehabilitation unit and 12% of the subjects needed assistance during ambulation [58]. One of these patients was subjected to rehabilitation protocol, and the number of subjects with no walking function was reduced to 18% [58].

7. Sensory dysfunctions

Stroke survivors may have sensory impairment that may be either central or peripheral. The latter includes loss of primary sensory modalities such as hypoesthesia/paresthesia, proprioception and position sense loss or loss of pain and temperature sensations, or they may have more complex sensory impairments such as agraphesthesia and astereognosis, which are impairments of the central sensory mechanisms [49]. These contribute to requiring additional assistance for these patients to relearn cognitive and motor skills. The processing of sensory modalities begins with reception which is the registration of the pure sensations and stimuli received from the various sensory organs such as eyes, ears, nose, tongue, skin, joints and the internal organs. These received sensations are then rerouted to the corresponding primary sensory cortices. The interpretation of these received stimuli is called perception. Perception is a higher cortical function of the brain involving various regions and is more complex than reception [49].

8. Cognitive dysfunction

Among all the factors portending a negative outcome, cognitive dysfunction has been described as the most potent [59, 60]. It has been suggested in recent studies that cognitive impairment and dementia may be reduced by satisfactory control of hypertension and by using drugs such as acetylcholinesterase inhibitors commonly used in Alzheimer's disease (donepezil, galantamine, rivastigmine) [61, 62]. A step forward in the pharmaceutical approach to post-stroke cognitive impairment, mainly related to language function, fluency and repetition, has been a randomized, placebo-controlled, double-blind study with levodopa which reported positive results [63].

9. Sphincter dysfunction

Usually, transient up to 20% of patients report persistence of urinary incontinence at discharge from rehabilitation [64, 65]. The commonest bladder dysfunction is the uninhibited bladder usually resolving with timed voiding training. Anticholinergic drugs such as tolterodine or oxybutynin may be indicated to relax the bladder. Sphincter recovery parallels and accompanies other functional recovery. Bladder unawareness in addition to lower limb weakness and cognitive impairment is a poor prognostic factor. Significant cognitive impairment may remain a lifelong disability [49]. Dual incontinence involving both bladder and bowel is much common than an isolated incontinence [65].

10. Other impairments and disabilities sequel to stroke

Many stroke survivors require tracheostomy, some permanently. This does increase the risk of pulmonary aspiration since laryngeal elevation during deglutition is impaired. Careful

selection of the texture of food and scrupulous monitoring during swallowing are essential to prevent aspiration in these patients [49]. Post-stroke depression is notable and has been postulated to be the main reason for suicide in these patients [66]. Morbidity in many clinical scenarios is considered a worse outcome than death, especially in neurological disorders in which the patient may be “alive but dependent” [67].

11. Role of dedicated rehabilitation services

Exercise, in general, has been shown to impart several favorable effects in neural recovery [68, 69]. Rehabilitation of stroke patients is increasingly demanding as far as the resources are considered. In general, most rehabilitation units have inadequate resources making the selection process an imperative component of the assessment [37]. Stroke care units that incorporate rehabilitation services generally claim better clinical outcomes in comparison to other models of stroke care units [70]. A decreased incidence of mortality, morbidity and dependency have been reported in stroke patients who undergo therapeutic training in an inpatient unit than those who receive general rehabilitation in a nondedicated unit [71]. Medically stable neurological patients need to be placed in the best possible unit for which several deliberations need to be considered [11]. On termination of a course of inpatient rehabilitation, further therapy may be instituted on an outpatient basis or an extended functional training at home may be considered [11].

12. Conclusion

The overall outcome of the SICH patients depends on access to acute care facilities, availability and affordability of post-acute care and rehabilitation services. The provision of stroke rehabilitation services has received considerable attention in recent years. There is a large amount of literature that support the rehabilitation of acute and subacute phase of SICH that has potential for improvement in the functional outcome of these patients. However, more studies are needed to further define and compare different methods for rehabilitation in patients with SICH.

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References

- [1] Caplan LR. Intracerebral haemorrhage. *The Lancet*. 1992;**339**:656
- [2] Qureshi AI, Tuhim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. *New England Journal of Medicine*. 2001;**344**:1450-1460
- [3] Sacco S, Marini C, Toni D, Olivieri L, Carolei A. Incidence and 10-year survival of intracerebral hemorrhage in a population-based registry. *Stroke*. 2009;**40**:394-399
- [4] Vermeer SE, Algra A, Franke CL, Koudstaal PJ, Rinkel GJE. Long-term prognosis after recovery from primary intracerebral hemorrhage. *Neurology*. 2002;**59**:205-209
- [5] Fogelholm R, Murros K, Rissanen A, Avikainen S. Long term survival after primary intracerebral haemorrhage: A retrospective population based study. *Journal of Neurology, Neurosurgery & Psychiatry*. 2005;**76**:1534-1538
- [6] Fogelholm R, Nuutila M, Vuorela AL. Primary intracerebral haemorrhage in the Jyväskylä region, central Finland, 1985-89: Incidence, case fatality rate, and functional outcome. *Journal of Neurology, Neurosurgery & Psychiatry*. 1992;**55**:546-552
- [7] Broderick J, Brott T, Tomsick T, Leach A. Lobar hemorrhage in the elderly. The undiminished importance of hypertension. *Stroke*. 1993;**24**:49-51
- [8] Zahuranec DB, Gonzales NR, Brown DL, et al. Presentation of intracerebral haemorrhage in a community. *Journal of Neurology, Neurosurgery & Psychiatry*. 2006;**77**:340-344
- [9] Morgenstern LB, Hemphill JC, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke*. 2010;**41**:2108-2129
- [10] Hårdemark HG, Wesslén N, Persson L. Influence of clinical factors, CT findings and early management on outcome in supratentorial intracerebral hemorrhage. *Cerebrovascular Diseases*. 1999;**9**:10-21
- [11] Saulle MF, Schambra HM. Recovery and Rehabilitation after Intracerebral Hemorrhage. *Seminars in Neurology*. 2016;**36**:306-312
- [12] Moon J-S, Janjua N, Ahmed S, et al. Prehospital neurologic deterioration in patients with intracerebral hemorrhage. *Critical Care Medicine*. 2008;**36**:172-175
- [13] Diring MN, Edwards DF. Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. *Critical Care Medicine*. 2001;**29**:635-640
- [14] Hemphill JC, Greenberg SM, Anderson CS, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;**46**:2032-2060
- [15] Alberts MJ, Latchaw RE, Selman WR, et al. Recommendations for comprehensive stroke centers: A consensus statement from the brain attack coalition. *Stroke*. 2005;**36**:1597-1616

- [16] Lyden PD, Shuaib A, Lees KR, et al. Safety and tolerability of NXY-059 for acute intracerebral hemorrhage. *Stroke*. 2007;**38**:2262-2269
- [17] Takahata H, Tsutsumi K, Baba H, Nagata I, Yonekura M. Early intervention to promote oral feeding in patients with intracerebral hemorrhage: A retrospective cohort study. *BMC Neurology*. 2011;**11**:6
- [18] Peurala SH. Rehabilitation of Gait in Chronic Stroke Patients: University of Kuopio, 2005.
- [19] Auriat AM, Wowk S, Colbourne F. Rehabilitation after intracerebral hemorrhage in rats improves recovery with enhanced dendritic complexity but no effect on cell proliferation. *Behavioural Brain Research*. 2010;**214**:42-47
- [20] Hays SA, Rennaker RL, Kilgard MP. Targeting plasticity with vagus nerve stimulation to treat neurological disease. *Progress in Brain Research*. 2013;**207**:275
- [21] Furmaga H, Carreno FR, Frazer A. Vagal nerve stimulation rapidly activates brain-derived neurotrophic factor receptor TrkB in rat brain. *PLoS One*. 2012;**7**:e34844
- [22] Follesa P, Biggio F, Gorini G, et al. Vagus nerve stimulation increases norepinephrine concentration and the gene expression of BDNF and bFGF in the rat brain. *Brain Research*. 2007;**1179**:28-34
- [23] Yang Y-R, Wang R-Y, Wang PS-G. Early and late treadmill training after focal brain ischemia in rats. *Neuroscience Letters*. 2003;**339**:91-94
- [24] Rand D, Eng JJ. Predicting daily use of the affected upper extremity 1 year after stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2015;**24**:274-283
- [25] Lee KB, Kim JS, Hong BY, Kim YD, Hwang BY, Lim SH. The motor recovery related with brain lesion in patients with intracranial hemorrhage. *Behavioural Neurology*. 2015;**2015**:
- [26] Xue M, Del Bigio MR. Intracerebral injection of autologous whole blood in rats: Time course of inflammation and cell death. *Neuroscience Letters*. 2000;**283**:230-232
- [27] Gong C, Hoff JT, Keep RF. Acute inflammatory reaction following experimental intracerebral hemorrhage in rat. *Brain Research*. 2000;**871**:57-65
- [28] Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: Mechanisms of injury and therapeutic targets. *The Lancet Neurology*. 2012;**11**:720-731
- [29] Donovan FM, Pike CJ, Cotman CW, Cunningham DD. Thrombin induces apoptosis in cultured neurons and astrocytes via a pathway requiring tyrosine kinase and RhoA activities. *Journal of Neuroscience*. 1997;**17**:5316-5326
- [30] Carmichael ST, Vespa PM, Saver JL, et al. Genomic profiles of damage and protection in human intracerebral hemorrhage. *Journal of Cerebral Blood Flow & Metabolism*. 2008;**28**:1860-1875
- [31] Xue M, Del Bigio MR. Intracortical hemorrhage injury in rats: Relationship between blood fractions and brain cell death. *Stroke*. 2000;**31**:1721-1727

- [32] Daverat P, Castel JP, Dartigues JF, Orgogozo JM. Death and functional outcome after spontaneous intracerebral hemorrhage. A prospective study of 166 cases using multivariate analysis. *Stroke*. 1991;**22**:1-6
- [33] Barber M, Roditi G, Stott DJ, Langhorne P. Poor outcome in primary intracerebral haemorrhage: Results of a matched comparison. *Postgraduate Medical Journal*. 2004;**80**:89-92
- [34] Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Intracerebral hemorrhage versus infarction: Stroke severity, risk factors, and prognosis. *Annals of Neurology*. 1995;**38**:45-50
- [35] Lipson DM, Sangha H, Foley NC, Bhogal S, Pohani G, Teasell RW. Recovery from stroke: Differences between subtypes. *International Journal of Rehabilitation Research*. 2005;**28**:303-308
- [36] Kelly PJ, Furie KL, Shafqat S, Rallis N, Chang Y, Stein J. Functional recovery following rehabilitation after hemorrhagic ischemic stroke. *Archives of Physical Medicine and Rehabilitation*. 2003;**84**:968-972
- [37] Katrak PH, Black D, Peeva V. Do stroke patients with intracerebral hemorrhage have a better functional outcome than patients with cerebral infarction? *PM&R*. 2009;**1**:427-433
- [38] Schepers VPM, Ketelaar M, Visser-Meily AJM, de Groot V, Twisk JWR, Lindeman E. Functional recovery differs between ischaemic and haemorrhagic stroke patients. *Journal of Rehabilitation Medicine*. 2008;**40**:487-489.
- [39] Paolucci S, Antonucci G, Grasso MG, et al. Functional outcome of ischemic and hemorrhagic stroke patients after inpatient rehabilitation. *Stroke*. 2003;**34**:2861-2865
- [40] Mestriner RG, Miguel PM, Bagatini PB, et al. Behavior outcome after ischemic and hemorrhagic stroke, with similar brain damage, in rats. *Behavioural Brain Research*. 2013;**244**:82-89
- [41] Chae J, Zorowitz RD, Johnston MV. Functional outcome of hemorrhagic and nonhemorrhagic stroke patients after in-patient rehabilitation. *American Journal of Physical Medicine & Rehabilitation*. 1996;**75**:177-182
- [42] Ween JE, Alexander MP, D'Esposito M, Roberts M. Factors predictive of stroke outcome in a rehabilitation setting. *Neurology*. 1996;**47**:388-392
- [43] Hemphill JC, Farrant M, Neill TA. Prospective validation of the ICH score for 12-month functional outcome. *Neurology*. 2009;**73**:1088-1094
- [44] Rost NS, Smith EE, Chang Y, et al. Prediction of functional outcome in patients with primary intracerebral hemorrhage: The FUNC score. *Stroke*. 2008;**39**:2304-2309
- [45] Coughlan AK, Humphrey M. Presenile stroke: Long-term outcome for patients and their families. *Rheumatology*. 1982;**21**:115-122
- [46] Goto A, Okuda S, Ito S, et al. Locomotion outcome in hemiplegic patients with middle cerebral artery infarction: The difference between right-and left-sided lesions. *Journal of Stroke and Cerebrovascular Diseases*. 2009;**18**:60-67

- [47] Fink JN, Frampton CM, Lyden P, Lees KR. On behalf of the VI. Does hemispheric lateralization influence functional and cardiovascular outcomes after stroke?: An analysis of placebo-treated patients from prospective acute stroke trials. *Stroke*. 2008;**39**:3335-3340
- [48] Howard G, Till JS, Toole JF, Matthews C, Truscott BL. Factors influencing return to work following cerebral infarction. *Journal of the American Medical Association*. 1985;**253**:226-232
- [49] Kim C-T, Han J, Kim H. Pediatric stroke recovery: A descriptive analysis. *Archives of Physical Medicine and Rehabilitation*. 2009;**90**:657-662
- [50] Mosch SC, Max JE, Tranel D. A matched lesion analysis of childhood versus adult-onset brain injury due to unilateral stroke: Another perspective on neural plasticity and recovery of social functioning. *Cognitive and Behavioral Neurology*. 2005;**18**:5-17
- [51] Jehkonen M, Ahonen JP, Dastidar P, et al. Predictors of discharge to home during the first year after right hemisphere stroke. *Acta Neurologica Scandinavica*. 2001;**104**:136-141
- [52] Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Recovery of walking function in stroke patients: The Copenhagen stroke study. *Archives of Physical Medicine and Rehabilitation*. 1995;**76**:27-32
- [53] Hardwick RM, Rottschy C, Miall RC, Eickhoff SB. A quantitative meta-analysis and review of motor learning in the human brain. *NeuroImage*. 2013;**67**:283-297
- [54] Horovitz SG, Gallea C, Najee-ullah MA, Hallett M. Functional anatomy of writing with the dominant hand. *PLoS One*. 2013;**8**:e67931
- [55] Planton S, Jucla M, Roux F-E, Démonet J-F. The “handwriting brain”: A meta-analysis of neuroimaging studies of motor versus orthographic processes. *Cortex*. 2013;**49**:2772-2787
- [56] Boudrias M-H, McPherson RL, Frost SB, Cheney PD. Output properties and organization of the forelimb representation of motor areas on the lateral aspect of the hemisphere in rhesus macaques. *Cerebral Cortex*. 2010;**20**:169-186
- [57] de Nap Shelton F, Reding MJ. Effect of lesion location on upper limb motor recovery after stroke. *Stroke* 2001;**32**:107-112.
- [58] Titianova EB, Pitkänen K, Pääkkönen A, Sivenius J, Tarkka IM. Gait characteristics and functional ambulation profile in patients with chronic unilateral stroke. *American Journal of Physical Medicine & Rehabilitation*. 2003;**82**:778-786
- [59] Patel MD, Coshall C, Rudd AG, Wolfe CDA. Cognitive impairment after stroke: Clinical determinants and its associations with long-term stroke outcomes. *Journal of the American Geriatrics Society*. 2002;**50**:700-706
- [60] Barker-Collo S, Feigin VL, Parag V, Lawes CMM, Senior H. Auckland stroke outcomes study part 2: Cognition and functional outcomes 5 years poststroke. *Neurology*. 2010;**75**:1608-1616

- [61] Narasimhalu K, Effendy S, Sim CH, et al. A randomized controlled trial of rivastigmine in patients with cognitive impairment no dementia because of cerebrovascular disease. *Acta Neurologica Scandinavica*. 2010;**121**:217-224
- [62] Rojas-Fernandez CH, Moorhouse P. Current concepts in vascular cognitive impairment and pharmacotherapeutic implications. *Annals of Pharmacotherapy*. 2009;**43**:1310-1323
- [63] Seniów J, Litwin M, Litwin T, Leśniak M, Członkowska A. New approach to the rehabilitation of post-stroke focal cognitive syndrome: Effect of levodopa combined with speech and language therapy on functional recovery from aphasia. *Journal of the Neurological Sciences*. 2009;**283**:214-218
- [64] Wilson DAN, Lowe D, Hoffman A, Rudd A, Wagg A. Urinary incontinence in stroke: Results from the UK National Sentinel Audits of stroke 1998-2004. *Age and Ageing*. 2008;**37**:542-546
- [65] Kovindha A, Wattanapan P, Dejpratham P, Permsirivanich W, Kuptniratsaikul V. Prevalence of incontinence in patients after stroke during rehabilitation: A multi-centre study. *Journal of Rehabilitation Medicine*. 2009;**41**:489-491
- [66] Brønnum-Hansen H, Davidsen M, Thorvaldsen P. Long-term survival and causes of death after stroke. *Stroke*. 2001;**32**:2131-2136
- [67] Solomon NA, Glick HA, Russo CJ, Lee J, Schulman KA. Patient preferences for stroke outcomes. *Stroke*. 1994;**25**:1721-1725
- [68] Ke Z, Yip SP, Li L, Zheng X-X, Tong K-Y. The effects of voluntary, involuntary, and forced exercises on brain-derived neurotrophic factor and motor function recovery: A rat brain ischemia model. *PLoS One*. 2011;**6**:e16643
- [69] Pilc J. The effect of physical activity on the brain derived neurotrophic factor: From animal to human studies. *Journal of Physiology and Pharmacology*. 2010;**61**:533-541
- [70] Chan DKY, Cordato D, O'Rourke F, et al. Comprehensive stroke units: A review of comparative evidence and experience. *International Journal of Stroke*. 2013;**8**:260-264
- [71] Langhorne P, Duncan P. Does the organization of postacute stroke care really matter? *Stroke*. 2001;**32**:268-274