



Monitoring cerebral ischemia during carotid endarterectomy and stenting

Jian Li¹, Ahmed Shalabi², Fuhai Ji¹, Lingzhong Meng^{2,✉}

¹Department of Anesthesiology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu 215006, China;

²Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, CA 94143, USA.

Abstract

Current therapy for carotid stenosis mainly includes carotid endarterectomy and endovascular stenting, which may incur procedure-related cerebral ischemia. Several methods have been employed for monitoring cerebral ischemia during surgery, such as awake neurocognitive assessment, electroencephalography, evoked potentials, transcranial Doppler, carotid stump pressure, and near infrared spectroscopy. However, there is no consensus on the gold standard or the method that is superior to others at present. Keeping patient awake for real time neurocognitive assessment is effective and essential; however, not every surgeon adopts it. In patients under general anesthesia, cerebral ischemia monitoring has to rely on non-awake technologies. The advantageous and disadvantageous properties of each monitoring method are reviewed.

Keywords: cerebral ischemia monitoring, carotid endarterectomy, carotid artery stenting

Introduction

Stroke is the second leading cause of death, responsible for about 10% of all deaths per year in the world^[1]. Carotid artery stenosis is responsible for 20% of strokes in the adult population^[2]. It is typically caused by atherosclerosis at the bifurcation of the common carotid artery and the internal or external carotid artery^[3]. Carotid endarterectomy (CEA) and carotid artery stenting (CAS) is the mainstay of therapy, with the aim of relieving stenosis and preventing thromboembolism. Both carotid clamping during CEA and balloon insufflation during stenting can lead to complete stoppage of the blood flow *via* an already

stenotic carotid artery. The perfusion of the brain ipsilateral to the side of procedure relies on the collateral flow when carotid clamping or balloon insufflation are applied. The ipsilateral brain undergoes ischemia if the collateral flow is inadequate. Moreover, ruptured atherosclerotic plaque and/or surgical debris can result in distal embolic stroke if they are accidentally washed into the cerebral circulation. Therefore, the brain is prone to cerebral ischemia during CEA and CAS.

However, not every episode of cerebral ischemia leads to stroke. The outcome of cerebral ischemia depends on the severity, duration, and location of the ischemic insult^[4]. The incidence of cerebral ischemia in the perioperative period of CEA and CAS is lacking

✉ Corresponding author: Lingzhong Meng, MD, Department of Anesthesia and Perioperative Care, University of California San Francisco, 500 Parnassus Avenue, Box 0648, San Francisco, CA 94143, USA. Tel: 415-502-2297. E-mail: meng.lingzhong@gmail.com

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however, the incidence of stroke has been reported. The rate of ipsilateral ischemic stroke from the time of randomization to 30 days after the procedure was reported to be 6.51% with CAS and 5.14% with CEA in the Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial that studied 1,200 patients^[5]. The periprocedural rate of stroke was reported to be 4.1% in the CAS group and 2.3% in the CEA group ($P=0.01$); however, after this period, the incidences of ipsilateral stroke with stenting and with endarterectomy were similarly low (2.0% and 2.4%, respectively, $P=0.85$) in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) that recruited 2,502 patients^[6]. A systematic review of 32 studies found that the incidences of the diffusion-weighted imaging (DWI) identified lesions, suggestive of ischemic nature, are 37% after carotid angioplasty and stenting and 10% after CEA, respectively^[7]. On the other hand, cerebral hyperperfusion syndrome may also occur with an incidence of 0–3% after CEA^[8].

Therefore, it is crucial to continuously monitor cerebral perfusion in order to timely reverse cerebral ischemia during CEA and CAS given the nature of these procedures and high incidence of cerebral blood flow disturbance. The aim of this paper is to specifically review cerebral hemodynamic monitoring during CEA and CAS, with a focus on the advantages and disadvantages of each monitoring modality.

Keeping patient awake

The most reliable monitoring of cerebral ischemia is to directly and continuously assess neurocognitive function in an awake patient given brain sensitivity to even a very brief period of cerebral ischemia and hypoxia^[9-10]. The wellbeing of neurocognitive function is by all means the end point of cerebral perfusion monitoring and management. The successful conduction of CEA or CAS will have to rely on loco-regional anesthesia (LRA) in order to have the patient awake while accomplishing the intended procedure. Superficial cervical plexus block with or without deep cervical plexus block is the common LRA technique during CEA while local anesthetic infiltration of the area used for vascular access is normally used for CAS. The neurocognitive function that is commonly assessed during procedure includes mental status, orientation, language, motor and muscle strength, sensation, and calculation.

In a cohort study involving 314 patients undergoing CEA, intraoperative direct neurologic monitoring of the awake patients was shown to be the most sensitive and specific method of identifying patients requiring shunt placement compared to electroencephalography (EEG)

and stump pressure (SP)^[11]. The potential disadvantages of LRA include patients' agitation or distress, airway obstruction, and injury to nearby structures during nerve block^[12-13]; for example, 4.4% of patients under LRA suffered from injuries related to the nerve block needle in the GALA trial^[12]. Importantly, the GALA trial failed in defining outcome differences including quality of life, length of hospital stay, stroke, myocardial infarction and death between LRA and general anesthesia (GA) during CEA^[12]. However, the GALA trial found that fewer shunts are used in the LRA group than the GA group (14% vs. 43%)^[12].

Overall, the primary advantages of direct neurocognitive monitoring in awake patients are its specificity and sensitivity^[11,14-15]. However, the available evidence in relevance to patients' outcome does not bestow superiority to LRA (awake approach) over GA.

Electroencephalography

EEG is determined by the summated neuronal electrical activity in the cerebral cortex and has been used for more than 40 years for cerebral ischemia detection during carotid surgery^[16]. When affected by ischemia, EEG waveform shows up as ipsilateral slowing, attenuation, even a loss of signal^[17]. In a retrospective study of 1,411 patients undergoing CEA, selective shunting group guided by EEG showed a lower rate of perioperative stroke than the routine shunting group (1% vs. 4%, $P=0.04$)^[18]. A meta-analysis including a total of 742 measurements of EEG monitoring during CEA reported a sensitivity of 70% and specificity 96%^[15]. This study also showed the diagnostic odds ratio of 65.3 (95% CI: 20.5–207.7) for EEG increased with the number of channels used ($P=0.03$) and suggested use of a high number of channels^[15]. In the prospective study involving 314 patients undergoing awake CEA, ischemic EEG changes were observed only in 19 of 32 (59.4%) patients requiring shunt placement, with a false-positive rate of 1.0% and a false-negative rate of 40.6%^[11]. EEG monitoring has advantages of directly assessing cerebral electrical activity and being continuous. However, both hypothermia and almost all anesthetic agents affect EEG tracing^[19]. Therefore, maintaining a stable core temperature and anesthetic depth is a prerequisite of using EEG to monitor cerebral ischemia. Furthermore, EEG only reflects the processes in cerebral cortex, does not detect electrical activity in deeper brain structures, and may be affected by a previous stroke^[20]. The complexity of interpretation of raw data also limits the wide use of EEG in clinical care.

Bispectral index (BIS) monitoring is currently widely used to monitor the depth of anesthesia. Its ability to detect cerebral ischemia was also tested in

several studies. In a study of 52 patients undergoing awake CEA, 6 patients showed clinical signs of cerebral ischemia; however, only one patient showed a decrease of BIS value from 92-98 down to 38^[21]. In another study of CEA under GA, BIS values were reported as increase, decrease, or being stable during carotid cross clamping^[22]. Therefore, the available evidence does not support the use of BIS monitoring in detecting cerebral ischemia during carotid procedures.

Somatosensory and motor evoked potential

Somatosensory evoked potential (SSEP) measures cerebral response to peripheral stimulations *via* somatosensory pathways. Therefore, compared to EEG, SSEP monitors neurological function of deeper brain structures^[23]. A reduction of SSEP's amplitude of over 50% and/or prolongation of its latency of more than 10% is considered clinically significant^[24]; however, the cause of these changes needs to be determined in the clinical context. The SSEP's ability to detect cerebral ischemia has been tested during carotid procedures. In a study of 64 patients undergoing CEA under GA, the sensitivity and specificity in predicting postoperative neurologic deficits were 100% and 94% for SSEP in comparison to 50% and 92% for EEG^[25]. In another study of 156 patients, SSEP predicted intraoperative cerebral infarction in two cases without false negatives or false positives, while EEG yielded one false negative result^[23]. However, SSEP only covers sensory pathways/regions of the brain, which leaves the rest of the neurological system unmonitored^[26]. Similar to EEG, various anesthetic agents affect SSEP monitoring to certain degrees depending on the agent and dose being used^[19].

Previous studies also tested the use of transcranial motor evoked potential (tcMEP) to monitor cerebral ischemia during CEA. The criteria used for diagnosing cerebral ischemia vary, with some studies using a reduction of tcMEP's amplitude of > 50%^[27] while others using presence-or-loss of tcMEP^[28-29] as clinically significant. All of these studies concluded that tcMEP is a useful adjunct to other monitoring modalities^[27-29]. Similar to SSEP, tcMEP only monitors the function of motor pathway/region of the neurological system; therefore, it does not monitor the area that it does not cover. At present, there is no evidence to advocate the use of tcMEP as the sole monitor of cerebral ischemia during carotid procedures.

Transcranial Doppler (TCD)

Transcranial Doppler (TCD) measures the blood flow velocity in major cerebral arteries such as the middle

cerebral artery (Vmca). Its application in detecting cerebral ischemia during clamping and hyperperfusion after declamping has been tested in patients undergoing CEA^[30]. A reduction of Vmca suggests a decrease of cerebral blood flow. However, different studies have proposed different thresholds, from 50% to 90%, for shunting placement^[31-32]. The meta-analysis by Guay *et al.* reports a sensitivity of 81% and specificity of 92% using TCD to detect cerebral ischemia in CEA patients^[15]. Most perioperative strokes are due to solid and gaseous microemboli^[33] and the TCD's ability to detect microemboli signal in CEA patients has been demonstrated^[33-35]. At present, TCD is the only monitor that is capable of continuously monitoring cerebral blood flow and the only technology that is capable of detecting microemboli^[36]. The limitations of TCD monitoring are that it cannot be applied in about 10% to 20% of patients due to the lack of acoustic window^[37], its bulky design prevents it from being applied in certain head/neck procedures, it requires skilled operators for consistent result^[36], and it monitors flow velocity, not mass flow in the major cerebral artery being insonated.

Carotid stump pressure

Carotid stump pressure (SP) is measured at the distal end of the carotid artery being clamped during CEA. It reflects the adequacy of the collateral flow that originates from the posterior circulation and contralateral anterior circulation and perfuses the territory covered by the ipsilateral internal carotid artery *via* the circle of Willis. The SP threshold used for selective shunting varies from 25 to 70 mmHg in different studies^[38-41], and extreme values (< 25 or > 50 mmHg) may be more useful indicators during CEA procedure^[42]. The overall sensitivity and specificity of SP is 75% and 88% for evaluating cerebral perfusion^[15]. SP approach is featured by easy application and low cost. However, the available evidence failed in showing its validity of predicting the need for shunt placement during CEA^[43].

Cerebral oximetry

Cerebral oximetry based on near-infrared spectroscopy (NIRS) measures hemoglobin oxygen saturation in mixed arterial, capillary and venous blood (SctO₂) in the frontal tissue bed illuminated by near-infrared light. SctO₂ monitored on the ipsilateral forehead decreases if carotid artery clamping or balloon occlusion leads to a decrease of the ipsilateral cerebral perfusion and oxygen delivery^[44-45]. The SctO₂ reduction was shown to correlate with changes in EEG^[46], TCD^[47], SP^[45] and postoperative neurologic deficits^[44-48]. Several studies showed varying sensitivity

(30%-80%) and specificity (77%-98%) using cerebral oximetry for brain ischemia detection in CEA patients under LRA^[44-49] and GA^[50], while other studies consider it reliable with high sensitivity (100%) and specificity (82.83%-96%) under LRA^[51] and GA^[45]. At present, there is no consensus on the cut-off SctO₂ value for predicting cerebral ischemia, with a relative decrease of 11.7%-25% from baseline being adopted in previous studies^[44-45,49-51]. Cerebral oximetry has advantages of being non-invasive, continuous, and easy to interpret. However, it only monitors a superficial area of the frontal lobe when it is applied on the forehead that leaves the areas such as the parietal lobe, the area likely most prone to ischemia during CEA, uncovered^[49]. The signal contamination by the scalp is another limitation; however, the newer algorithm of cerebral oximetry is able to minimize this interference.

Other techniques

In a study of 48 patients undergoing awake CEA, arterial-jugular venous lactate content difference (AJDL) was found to have a sensitivity of 67% and specificity of 86%, while jugular bulb venous blood oxygen saturation (SjvO₂) having a sensitivity of 75% and specificity of 83%, in detecting cerebral hypoperfusion^[52]. Xenon-133 washout technique was also tested in CEA patients^[53]. It is able to assess the global cerebral perfusion; however, it is expensive, complicated to operate and interpret, and does not offer continuous monitoring^[54].

Summary

Due to the high risk of cerebral ischemia, continuous and reliable monitoring of cerebral ischemia is crucial during carotid procedures including CEA and CAS. Direct assessment of neurocognitive function in awake patients has high sensitivity and specificity in detecting cerebral ischemia; however, its beneficial effect on the overall outcome has not yet been proven. In patients undergoing GA, the monitoring of cerebral ischemia during carotid procedures has to rely on modalities including EEG, evoked potentials, cerebral oximetry, TCD and SP. Each modality has its advantages and disadvantages in monitoring cerebral ischemia during CEA and CAS and at present, no one shows clear superiority over others. As a result, combining different monitoring modalities for the purpose of better detection of cerebral ischemia in these high-risk procedures is well advised, especially in patients whose neurocognitive function cannot be directly assessed due to GA.

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References

- [1] Feigin VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010[J]. *Lancet*, 2014, 383(9913):245-254.
- [2] Linfante I, Andreone V, Akkawi N, et al. Internal carotid artery stenting in patients over 80 years of age: single-center experience and review of the literature[J]. *J Neuroimaging*, 2009,19(2):158-163.
- [3] Beebe HG, Clagett GP, DeWeese JA, et al. Assessing risk associated with carotid endarterectomy. A statement for health professionals by an Ad Hoc Committee on Carotid Surgery Standards of the Stroke Council, American Heart Association[J]. *Circulation*, 1989,79(2):472-473.
- [4] Bramlett HM, Dietrich WD. Pathophysiology of cerebral ischemia and brain trauma: similarities and differences[J]. *J Cereb Blood Flow Metab*, 2004,24(2):133-150.
- [5] Ringleb PA, Allenberg J, Bruckmann H, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial[J]. *Lancet*, 2006,368(9543):1239-1247.
- [6] Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis[J]. *N Engl J Med*, 2010,363(1):11-23.
- [7] Schnaudigel S, Groschel K, Pilgram SM, et al. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature[J]. *Stroke*, 2008,39(6):1911-1919.
- [8] van Mook WN, Rennenberg RJ, Schurink GW, et al. Cerebral hyperperfusion syndrome[J]. *Lancet Neurol*, 2005,4(12):877-888.
- [9] Moritz S, Kasprzak P, Arlt M, et al. Accuracy of cerebral monitoring in detecting cerebral ischemia during carotid endarterectomy: a comparison of transcranial Doppler sonography, near-infrared spectroscopy, stump pressure, and somatosensory evoked potentials[J]. *Anesthesiology*, 2007,107(4):563-569.
- [10] Ali AM, Green D, Zayed H, et al. Cerebral monitoring in patients undergoing carotid endarterectomy using a triple assessment technique[J]. *Interact Cardiovasc Thorac Surg*, 2011,12(3):454-457.
- [11] Hans SS, Jareunpoon O. Prospective evaluation of electroencephalography, carotid artery stump pressure, and neurologic changes during 314 consecutive carotid endarterectomies performed in awake patients[J]. *J Vasc Surg*, 2007,45(3):511-515.

- [12] Lewis SC, Warlow CP, Bodenham AR, et al. General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial[J]. *Lancet*, 2008,372(9656):2132-2142.
- [13] Quigley TM, Ryan WR, Morgan S. Patient satisfaction after carotid endarterectomy using a selective policy of local anesthesia[J]. *Am J Surg*, 2000,179(5):382-385.
- [14] Stoneham MD, Knighton JD. Regional anaesthesia for carotid endarterectomy[J]. *Br J Anaesth*, 1999,82(6):910-919.
- [15] Guay J, Kopp S. Cerebral monitors versus regional anesthesia to detect cerebral ischemia in patients undergoing carotid endarterectomy: a meta-analysis[J]. *Can J Anaesth*, 2013,60(3):266-279.
- [16] Jordan KG. Emergency EEG and continuous EEG monitoring in acute ischemic stroke[J]. *J Clin Neurophysiol*, 2004,21(5):341-352.
- [17] Arnold M, Sturzenegger M, Schaffler L, et al. Continuous intraoperative monitoring of middle cerebral artery blood flow velocities and electroencephalography during carotid endarterectomy. A comparison of the two methods to detect cerebral ischemia[J]. *Stroke*, 1997,28(7):1345-1350.
- [18] Woodworth GF, McGirt MJ, Than KD, et al. Selective versus routine intraoperative shunting during carotid endarterectomy: a multivariate outcome analysis[J]. *Neurosurgery*, 2007,61(6):1170-6; discussion 1176-1177.
- [19] Sloan TB. Anesthetic effects on electrophysiologic recordings[J]. *J Clin Neurophysiol*, 1998,15(3):217-226.
- [20] Green RM, Messick WJ, Ricotta JJ, et al. Benefits, shortcomings, and costs of EEG monitoring[J]. *Ann Surg*, 1985,201(6):785-792.
- [21] Deogaonkar A, Vivar R, Bullock RE, et al. Bispectral index monitoring may not reliably indicate cerebral ischaemia during awake carotid endarterectomy[J]. *Br J Anaesth*, 2005,94(6):800-804.
- [22] Bonhomme V, Desiron Q, Lemineur T, et al. Bispectral index profile during carotid cross clamping[J]. *J Neurosurg Anesthesiol*, 2007,19(1):49-55.
- [23] Rowed DW, Houlden DA, Burkholder LM, et al. Comparison of monitoring techniques for intraoperative cerebral ischemia[J]. *Can J Neurol Sci*, 2004,31(3):347-356.
- [24] Nwachuku EL, Balzer JR, Yabes JG, et al. Diagnostic Value of Somatosensory Evoked Potential Changes During Carotid Endarterectomy: A Systematic Review and Meta-analysis[J]. *JAMA Neurol*, 2015,72(1):73-80.
- [25] Lam AM, Manninen PH, Ferguson GG, et al. Monitoring electrophysiologic function during carotid endarterectomy: a comparison of somatosensory evoked potentials and conventional electroencephalogram[J]. *Anesthesiology*, 1991,75(1):15-21.
- [26] De Vleeschauwer P, Horsch S, Matamoros R. Monitoring of somatosensory evoked potentials in carotid surgery: results, usefulness and limitations of the method[J]. *Ann Vasc Surg*, 1988,2(1):63-68.
- [27] Uchino H, Nakamura T, Kuroda S, et al. Intraoperative dual monitoring during carotid endarterectomy using motor evoked potentials and near-infrared spectroscopy[J]. *World Neurosurg*, 2012,78(6):651-657.
- [28] Malcharek MJ, Kulpok A, Deletis V, et al. Intraoperative multimodal evoked potential monitoring during carotid endarterectomy: a retrospective study of 264 patients[J]. *Anesth Analg*, 2015; 120(6):1352-1360.
- [29] Malcharek MJ, Ulkatan S, Marino V, et al. Intraoperative monitoring of carotid endarterectomy by transcranial motor evoked potential: a multicenter study of 600 patients[J]. *Clin Neurophysiol*, 2013,124(5):1025-1030.
- [30] van der Schaaf IC, Horn J, Moll FL, Ackerstaff RG. Transcranial Doppler monitoring after carotid endarterectomy[J]. *Ann Vasc Surg*, 2005,19(1):19-24.
- [31] Ackerstaff RG, Moons KG, van de Vlasakker CJ, et al. Association of intraoperative transcranial doppler monitoring variables with stroke from carotid endarterectomy[J]. *Stroke*, 2000,31(8):1817-1823.
- [32] McCarthy RJ, McCabe AE, Walker R, Horrocks M. The value of transcranial Doppler in predicting cerebral ischaemia during carotid endarterectomy[J]. *Eur J Vasc Endovasc Surg*, 2001,21(5):408-412.
- [33] Skjelland M, Krohg-Sorensen K, Tennoe B, et al. Cerebral microemboli and brain injury during carotid artery endarterectomy and stenting[J]. *Stroke*, 2009,40(1):230-234.
- [34] Jansen C, Ramos LM, van Heesewijk JP, Moll FL, van Gijn J, Ackerstaff RG. Impact of microembolism and hemodynamic changes in the brain during carotid endarterectomy[J]. *Stroke*, 1994,25(5):992-997.
- [35] Horn J, Naylor AR, Laman DM, et al. Identification of patients at risk for ischaemic cerebral complications after carotid endarterectomy with TCD monitoring[J]. *Eur J Vasc Endovasc Surg*, 2005,30(3):270-274.
- [36] Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care[J]. *Br J Anaesth* 2004,93(5):710-724.
- [37] Howell SJ. Carotid endarterectomy[J]. *Br J Anaesth*, 2007,99(1):119-131.
- [38] Whitley D, Cherry KJ, Jr. Predictive value of carotid artery stump pressures during carotid endarterectomy[J]. *Neurosurg Clin N Am*, 1996,7(4):723-732.
- [39] Calligaro KD, Dougherty MJ. Correlation of carotid artery stump pressure and neurologic changes during 474 carotid endarterectomies performed in awake patients[J]. *J Vasc Surg*, 2005,42(4):684-689.
- [40] Gnanadev DA, Wang N, Comunale FL, et al. Carotid artery stump pressure: how reliable is it in predicting the need for a shunt?[J]. *Ann Vasc Surg*, 1989,3(4):313-317.
- [41] Boulard G, Nicod J, Oca C, et al. Anesthesia for carotid surgery with clamping under residual carotid pressure control[J]. *Ann Fr Anesth Reanim*, 1982,1(3):301-305.
- [42] Cherry KJ Jr, Roland CF, Hallett JW Jr, et al. Stump pressure, the contralateral carotid artery, and electroencephalographic changes[J]. *Am J Surg*, 1991,162(2):185-8; discussion 188-189.
- [43] Belardi P, Lucertini G, Ermirio D. Stump pressure and transcranial Doppler for predicting shunting in carotid endarterectomy[J]. *Eur J Vasc Endovasc Surg*, 2003,25(2):164-167.
- [44] Rigamonti A, Scandroglio M, Minicucci F, et al. A clinical evaluation of near-infrared cerebral oximetry in the awake patient to monitor cerebral perfusion during carotid endarterectomy[J]. *J Clin Anesth*, 2005,17(6):426-430.
- [45] Pedrini L, Magnoni F, Sensi L, et al. Is Near-Infrared Spectroscopy a Reliable Method to Evaluate Clamping Ischemia during Carotid Surgery?[J]. *Stroke Res Treat*, 2012,2012:156975.
- [46] Shang Y, Cheng R, Dong L, et al. Cerebral monitoring during carotid endarterectomy using near-infrared diffuse

- optical spectroscopies and electroencephalogram[J]. *Phys Med Biol*, 2011,56(10):3015-3032.
- [47] Pugliese F, Ruberto F, Tosi A, et al. Regional cerebral saturation versus transcranial Doppler during carotid endarterectomy under regional anaesthesia[J]. *Eur J Anaesthesiol*, 2009,26(8):643-647.
- [48] Giustiniano E, Alfano A, Battistini GM, et al. Cerebral oximetry during carotid clamping: is blood pressure raising necessary?[J]. *J Cardiovasc Med (Hagerstown)*, 2010,11(7):522-528.
- [49] Samra SK, Dy EA, Welch K, et al. Evaluation of a cerebral oximeter as a monitor of cerebral ischemia during carotid endarterectomy[J]. *Anesthesiology*, 2000,93(4):964-970.
- [50] Mille T, Tachimiri ME, Klersy C, et al. Near infrared spectroscopy monitoring during carotid endarterectomy: which threshold value is critical?[J]. *Eur J Vasc Endovasc Surg*, 2004,27(6):646-650.
- [51] Ritter JC, Green D, Slim H, et al. The role of cerebral oximetry in combination with awake testing in patients undergoing carotid endarterectomy under local anaesthesia[J]. *Eur J Vasc Endovasc Surg*, 2011,41(5):599-605.
- [52] Moritz S, Kasprzak P, Woertgen C, et al. The accuracy of jugular bulb venous monitoring in detecting cerebral ischemia in awake patients undergoing carotid endarterectomy[J]. *J Neurosurg Anesthesiol*, 2008,20(1):8-14.
- [53] Zampella E, Morawetz RB, McDowell HA, et al. The importance of cerebral ischemia during carotid endarterectomy[J]. *Neurosurgery*, 1991,29(5):727-730; discussion 730-731.
- [54] Latchaw RE, Yonas H, Hunter GJ, et al. Guidelines and recommendations for perfusion imaging in cerebral ischemia: A scientific statement for healthcare professionals by the writing group on perfusion imaging, from the Council on Cardiovascular Radiology of the American Heart Association[J]. *Stroke*, 2003,34(4):1084-1104.

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