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## 小骨窗开颅血肿清除术与微创血肿碎吸术治疗高血压脑出血的临床疗效比较\*

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**摘要目的:**观察和比较小骨窗开颅血肿清除术与微创血肿碎吸术治疗高血压脑出血的临床疗效和安全性。**方法:**选择2014年9月-2017年6月在我院接受手术治疗的60例高血压脑出血患者,随机分为对照组和研究组,每组各30例。对照组行小骨窗开颅血肿清除术,研究组行微创血肿碎吸术手术,比较两组血肿清除率、残余血肿量、再出血发生率、手术时间、住院时间、术中失血量及术后并发症发生率。**结果:**两组患者术后48h及7d血肿清除率、残余血肿量相比差异均无统计学意义( $P>0.05$ )。对照组再出血发生率与研究组,但差异无统计学意义( $P>0.05$ )。研究组的手术时间和住院时间与对照组相比显著缩短( $P<0.05$ ),术中失血量及术后并发症发生率较对照组显著下降( $P<0.05$ )。术后3个月及6个月,两组患者日常生活能力显著改善( $P<0.05$ ),且研究组ADL评分显著高于对照组( $P<0.05$ )。两组术后NFD评分逐渐降低,与术前比较差异具有统计学意义( $P<0.05$ ),在术后1个月与3个月,研究组NFD评分均显著低于对照组( $P<0.05$ )。**结论:**采用微创血肿穿刺碎吸术治疗高血压脑出血的创伤小,疗效显著,可有效改善患者日常生活能力,降低神经功能损伤

**关键词:**小骨窗开颅血肿清除术;微创血肿碎吸术;高血压脑出血;疗效

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## Comparison of the Curative Effect of Hematoma Evacuation by Small Bone window Craniotomy and Minimally Invasive Hematoma Aspiration on the Hypertensive Intracerebral Hemorrhage\*

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**ABSTRACT Objective:** To observed and compare the curative effect and safety between hematoma evacuation by small bone window craniotomy and minimally invasive hematoma aspiration for hypertensive intracerebral hemorrhage. **Methods:** 60 cases of patients with hypertensive intracerebral hemorrhage treated in our hospital from September 2014 to June 2017 were selected as research subjects and randomly divided into the control group and the study group, 30 cases in each group. The control group was given craniotomy with small bone window craniotomy. The study group was given minimally invasive hematoma aspiration surgery. The incidence of hematoma clearance, residual hematoma, rehemorrhage rate, operation time, hospital stay, intraoperative blood loss and postoperative complication rate of two group were compared. **Results:** The 48h and 7d hematoma clearance rates and the amount of residual hematoma showed no statistically difference between the two groups ( $P>0.05$ ). There was no significant difference in the rehemorrhage rate between the two groups after operation ( $P>0.05$ ). Compared with the control group, the operation time and hospitalization time were significantly shortened ( $P<0.05$ ). The amount of peroperative hemorrhage in control group was significantly higher in the study group ( $P<0.05$ ). And the incidence of postoperative complications was significantly lower in the study group than that of the control group ( $P<0.05$ ). Before surgery, the ADL score showed no significant difference between the two groups ( $P>0.05$ ). At 3 months and 6 months after treatment, the ability of daily life of two groups of patients were significantly improved ( $P<0.05$ ), and the ADL score of study group was significantly higher than that of the control group ( $P<0.05$ ). Compared with before surgery, the NFD score of two groups were significantly decreased after surgery ( $P<0.05$ ), at 3 months and 6 months after treatment, the NFD scores of study group were significantly lower than those of the control group ( $P<0.05$ ). **Conclusions:** Minimally invasive hematoma aspiration had minor injuries and remarkable curative effect on the hypertensive intracerebral hemorrhage, which improved the ability of daily living and reduced the impairment of function of the extensor nerve.

**Key words:** Hematoma evacuation by small bone window craniotomy; Minimally invasive hematoma aspiration; Hypertensive intracerebral hemorrhage; Curative effect

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## 前言

高血压患者脑内易出现血管梗阻、硬化、坏死及病变引起血管破裂导致患者颅内出血<sup>[1]</sup>。高血压性脑出血是中老年高血压病严重并发症之一,属于神经系统急、重病症<sup>[1,2]</sup>,病死率高达50%,同时60%以上存活患者表现不同程度残疾<sup>[3-5]</sup>。随着社会经济的发展,我国人口老龄化愈演愈烈,高血压性脑出血发病率持续上升,尤其是50岁以上的高血压患者,严重威胁中老年人生命健康<sup>[6]</sup>。

目前,高血压脑出血的治疗主要有保守治疗和手术治疗。但高血压脑出血对患者最大的威胁是血肿对脑组织压迫及继发性神经损伤,内科治疗并不能解决根本问题,尤其是脑出血严重血肿较大的患者<sup>[8]</sup>。因此,临床常采用外科手术,常用的手术方法有大骨瓣开颅血肿清除术、小骨窗开颅血肿清除术及微创血肿碎吸术等<sup>[9-11]</sup>。本研究选择2014年9月-2017年6

月在我院接受小骨窗开颅血肿清除术或微创血肿碎吸术手术治疗的60例高血压脑出血患者,比较两种手术的治疗效果及预后恢复情况,旨在为高血压脑出血的临床治疗提供参考。

## 1 资料与方法

### 1.1 一般临床资料

选择2015年9月-2017年6月在我院接受治疗的60例高血压脑出血患者,均符合高血压脑出血CT影像特征<sup>[12]</sup>,包括男39例,女21例,年龄40~80岁,平均年龄为 $56.79 \pm 14.66$ 。纳入标准:符合脑出血诊断标准<sup>[13]</sup>;具有高血压病史;出血量在20-85 mL;患者及家属知情并签署知情同意书。排除标准:颅内动脉瘤;动静脉畸形;外伤性出血;脑疝形成及具有手术禁忌的患者。将所有患者根据手术习惯及家属要求随机分为对照组和研究组,两组的一般资料对比差异无统计学意义( $P > 0.05$ ),具有可比性,见表1。

表1 两组患者的一般资料比较

Table 1 Comparison of the general data between two groups

	Control(n=30)	Study(n=30)	P
Age	58.24± 12.18	56.94± 13.56	0.697
Sex(Male/Female)	19/11	20/10	0.787
Hemorrhage position(n)			
Lobe	6	7	0.754
Thalamo	10	11	0.787
Basal ganglia	14	12	0.602
Amount of hemorrhage(mL)	54.22± 14.91	57.19± 14.46	0.437
GCS (grade)	9.48± 2.59	8.98± 3.01	0.493

### 1.2 手术方法

所有患者在发病12h内开展手术治疗,根据患者病情尽早安排手术:

对照组:选择小骨窗开颅血肿清除术,手术前,在头颅CT扫描下确定血肿位置,行全麻插管,在血肿最大位置做倒U形切口或直切口,避开功能区,小骨窗开颅,显微镜下在皮质无血管区电凝切开皮质进入血肿腔,行血肿清除。发现活动性出血,采用小电流双极电凝止血,用生理盐水冲洗血肿腔至清亮后,放置引流管引流。

研究组:选择微创血肿碎吸术,行局部麻醉,术前通过在头颅CT扫描下确定血肿位置,明确穿刺点位置;选择适当长度的碎吸针。取平卧位,穿刺点做小切口钻口,待碎吸针穿过硬脑膜后停止进针,插入针芯,并在侧管上连接引流管,行血肿清除,抽吸过程中注意力度,随时用生理盐水冲洗针芯。抽吸部分血肿达到减压即可。

### 1.3 术后处理

手术治疗后两组患者均给予吸氧、抗感染、预防并发症、持续心电监护等对症治疗,并在术后48h做头部CT复查,检测血肿残留情况。另外研究组术后给予生理盐水持续冲洗,术后8h给予2~4万U尿激酶及3mL生理盐水注入血肿腔,关闭引流管3h后打开。

### 1.4 观察指标

术后48h、7d做头部CT复查,计算血肿残留及血肿清除率,统计两组术后再出血发生率,统计并记录两组手术时间,住院时间,颅内感染,术后并发症。根据ADL评估量表<sup>[14]</sup>和神经功能缺损(NFD)量表对两组患者治疗前、治疗后3个月及治疗6个月日常生活能力及神经功能缺损程度进行评估。

### 1.5 统计学分析

本研究采用SPSS20.0软件进行数据整理及统计学分析,计量资料以均数标准差( $\bar{x} \pm s$ )表示,组间比较行t检验;计数资料以百分比表示,组间比较行 $\chi^2$ 检验,以 $P < 0.05$ 表示差异具有统计学意义。

## 2 结果

### 2.1 两组治疗后残余血肿量及血肿清除率的比较

两组患者术后48h及7d血肿清除率、残余血肿量相比差异无统计学意义( $P > 0.05$ ),对照组再出血发生率为6.67%,略高于研究组,但差异无统计学意义( $P > 0.05$ )。见表2。

### 2.2 两组手术时间、住院时间及术后并发症发生情况的比较

与对照组相比,研究组的手术时间和住院时间显著缩短( $P < 0.05$ )。对照组的术中失血量显著高于研究组( $P < 0.05$ )。研究组的术后并发症发生率显著低于对照组( $P < 0.05$ )。见表3。

表 2 两组治疗后残余血肿量及血肿清除率的比较

Table 2 Comparison of the residual hematoma and hematoma clearance rate between two groups after treatment

Groups	Hematoma Clearance Rate(%)		Residual Hematoma(mL)	RehemorrhageRate[n(%)]
	After 48h	After 7d		
Control group(n=30)	90.02%	92.04%	7.31± 3.47	2(6.67%)
Study group(n=30)	88.64%	91.31%	8.98± 4.22	1(3.33%)
<i>P</i>	0.818	0.8	0.099	0.554

表 3 两组手术时间、住院时间、术中出血量及术后并发症发生情况的比较

Table 3 Comparison of the operation time, hospitalization time, peroperative hemorrhage amount and incidence of postoperative complications between two groups

Groups	Operation time(min)	Hospitalization time(d)	Amount of Peroperative hemorrhage	Postoperative complications [n(%)]
Control group(n=30)	167.18± 34.21	17.53± 4.74	231.48± 47.81	10(33.33%)
Study group(n=30)	128.56± 42.17	12.88± 3.38	184.79± 39.29	3(10.00%)
<i>P</i>	0.000	0.000	0.000	0.028

2.3 两组治疗前后 ADL 评分和 NFD 评分的比较

高( $P<0.05$ ),且研究组 ADL 评分均显著高于对照组( $P<0.05$ )。见

两组患者术前 ADL 评分比较差异无统计学意义( $P>0.05$ )。表 4。

术后 3 个月及 6 个月, 两组患者 ADL 评分均较治疗前显著升

表 4 两组治疗前后 ADL 评分的比较

Table 4 Comparison of the ADL score before and after treatment between two groups

Groups	ADL scores			<i>P</i>
	Before treatment	At 1 month after treatment	At 3 months after treatment	
Control group(n=30)	77.43± 15.68	80.16± 10.37	88.71± 5.27	0.001
Study group(n=30)	76.21± 13.99	91.02± 8.91	94.14± 4.88	0.000
<i>P</i>	0.752	0.000	0.000	

研究组和对照组术后 NFD 评分与术前比较均显著降低, NFD 评分均显著低于对照组( $P<0.05$ )。见表 5。

差异具有统计学意义( $P>0.05$ ),且术后 1 个月与 3 个月,研究组

表 5 两组治疗前后 NFD 评分的比较

Table 5 Comparison of the NFD score before and after treatment between two groups

Groups	NFD score			<i>P</i>
	Before treatment	At 1 month after treatment	At 3 months after treatment	
Control group(n=30)	27.08± 8.32	17.24± 4.27	14.42± 3.11	0.000
Study group(n=30)	26.74± 7.94	13.87± 5.21	9.80± 3.49	0.000
<i>P</i>	0.872	0.008	0.000	

3 讨论

高血压脑出血指由高血压引起的原发性颅内出血,中老年为高发人群,且男性发病率高于女性<sup>[5]</sup>。脑出血后除出血造成患者的原发损害外,会出现早起血肿增大,形成占位效应,血肿对脑组织毒性作用等继发损害。损害因素超过药物治疗范畴及脑组织本身的代偿能力时,须降低颅内压、清除血肿,恢复受压的神经细胞,防止、减少出血等一系列继发性的病理变化,降低致残率,挽救患者生命。初期高血压脑出血采用内科保守治疗,但其治疗后病死率高达 60%以上<sup>[6]</sup>,随着医疗水平的发展,高

血压脑出血治疗主要依靠外科手术,通过清除血肿降低血肿对周围神经组织或功能的压迫,降低颅内压,改善脑组织水肿,提高患者生存几率,改善患者生活质量<sup>[7]</sup>。常见治疗高血压脑出血手术方法有:传统小骨窗开颅血肿清除术,大骨瓣开颅血肿清除术,小骨窗开颅血肿清除术,微创血肿穿刺吸碎术等<sup>[18-20]</sup>。其中,小骨窗开颅血肿清除术是传统小骨窗开颅血肿清除术的改良,近几年临床治疗主要应用小骨窗开颅血肿清除术<sup>[21,22]</sup>。由于微创血肿穿刺吸碎术具有创伤小、恢复快、治疗效果佳等优点被广泛应用。

本研究主要探讨了小骨窗开颅血肿清除术与微创血肿碎

吸术手术治疗高血压脑出血患者的效果。结果显示两组患者术后 48h 及 7d 残余血肿量相比差异无统计学意义,对照组再出血发生率略高于研究组,但差异无统计学意义,提示微创血肿穿刺吸碎术与小骨窗开颅血肿清除术血肿清除能力相当。同时,与对照组相比,研究组的手术时间和住院时间显著缩短( $P < 0.05$ ),对照组的术中失血量显著高于研究组,这与王浩<sup>[23]</sup>等研究结果一致。

高血压脑出血患者术后死亡的主要危险因素为术后并发症。因此,减少术后并发症的发生可以有效提高患者治疗效果,降低高血压脑出血患者的病死率<sup>[24-26]</sup>。本研究中,研究组的术后并发症发生率为 10.00%,显著低于对照组。两组患者术前 ADL 评分差异无统计学意义。术后 3 个月及 6 个月,两组患者日常生活能力显著改善,且研究组 ADL 评分显著高于对照组,提示微创血肿穿刺吸碎术可有效改善患者生活能力并降低对神经功能的伤害,与以往研究结果一致<sup>[27-29]</sup>。

综上所述,采用微创血肿穿刺吸碎术治疗高血压脑出血创伤口小,疗效显著,可有效改善患者日常生活能力,减轻伸神经功能损伤。

#### 参考文献(References)

- [1] Kumar N S, Neeraja V, Raju C G, et al. Multiple spontaneous hypertensive intracerebral hemorrhages [J]. *Journal of Stroke & Cerebrovascular Diseases the Official Journal of National Stroke Association*, 2015, 24(1): e25
- [2] Chen G, Ping L, Zhou S, et al. Early prediction of death in acute hypertensive intracerebral hemorrhage [J]. *Experimental & Therapeutic Medicine*, 2016, 11(1): 83
- [3] Xu H, Chen W, Wang M, et al. CT Perfusion Imaging Predicts One-Month Outcome in Patients with Acute Spontaneous Hypertensive Intracerebral Hemorrhage [J]. *Advances in Computed Tomography*, 2013, 02(3): 107-111
- [4] Qureshi A I, Palesch Y Y, Barsan W G, et al. Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage [J]. *Cjem*, 2017, 375(11): 1
- [5] Charidimou A, Pasi M, Fiorelli M, et al. Leukoaraiosis, Cerebral Hemorrhage, and Outcome After Intravenous Thrombolysis for Acute Ischemic Stroke: A Meta-Analysis (v1) [J]. *Stroke; a journal of cerebral circulation*, 2016, 47(9): 2364
- [6] Zheng J, Li H, Guo R, et al. Minimally invasive surgery treatment for the patients with spontaneous supratentorial intracerebral hemorrhage (MISTICH): protocol of a multi-center randomized controlled trial[J]. *Bmc Neurology*, 2014, 14(1): 206
- [7] Weihua L I, Gao J, Wei S, et al. Application values of clinical nursing pathway in patients with acute cerebral hemorrhage [J]. *Experimental & Therapeutic Medicine*, 2016, 11(2): 490
- [8] Ziai W, Nyquist P, Hanley D F. Surgical Strategies for Spontaneous Intracerebral Hemorrhage[J]. *Seminars in Neurology*, 2016, 36(3): 261
- [9] Wang W H, Hung Y C, Hsu S P C, et al. Endoscopic hematoma evacuation in patients with spontaneous supratentorial intracerebral hemorrhage[J]. *Journal of the Chinese Medical Association*, 2015, 78(2): 101-107
- [10] Vega M B, Hamamoto Filho P T, Machado C J, et al. Traumatic brain injury presenting with bilateral basal ganglia hemorrhage [J]. *Neurologia I neurochirurgia Polska*, 2015, 49(6): 456-459
- [11] Wang W, Zhou N, Wang C. Minimally invasive surgery for hypertensive intracerebral hemorrhage patients with large hematoma volume: a retrospective study[J]. *World Neurosurgery*, 2017, 9(105): 348-358
- [12] Schindlbeck K A, Santaella A, Galinovic I, et al. Spot Sign in Acute Intracerebral Hemorrhage in Dynamic T1-Weighted Magnetic Resonance Imaging[J]. *Stroke; a journal of cerebral circulation*, 2016, 47(2): 417
- [13] Yang G, Shao G F. Elevated serum IL-11, TNF- $\alpha$ , and VEGF expressions contribute to the pathophysiology of hypertensive intracerebral hemorrhage (HICH)[J]. *Neurological Sciences Official Journal of the Italian Neurological Society & of the Italian Society of Clinical Neurophysiology*, 2016, 37(8): 1-7
- [14] Zhang Y S, Cheng G, Fan L, et al. Effect of residue hematoma volume on inflammation factors in hypertensive intracranial hemorrhage[J]. *Medical Journal of Chinese Peoples Liberation Army*, 2016, 41(9): 763-766
- [15] Akhigbe T, Zolnourian A. Role of surgery in the management of patients with supratentorial spontaneous intracerebral hematoma: Critical appraisal of evidence [J]. *Journal of Clinical Neuroscience*, 2017, 39(5): 35-38
- [16] Zheng J, Li H, Guo R, et al. Minimally invasive surgery treatment for the patients with spontaneous supratentorial intracerebral hemorrhage (MISTICH): protocol of a multi-center randomized controlled trial[J]. *Bmc Neurology*, 2014, 14(1): 206
- [17] Xu X, Yi Z, Chen X, et al. Comparison of endoscopic evacuation, stereotactic aspiration and craniotomy for the treatment of supratentorial hypertensive intracerebral haemorrhage: study protocol for a randomised controlled trial[J]. *Trials*, 2017, 18(1): 296
- [18] Kumar N S, Neeraja V, Raju C G, et al. Multiple spontaneous hypertensive intracerebral hemorrhages [J]. *Journal of Stroke & Cerebrovascular Diseases the Official Journal of National Stroke Association*, 2015, 24(1): e25
- [19] Sato S, Carcel C, Anderson C S. Blood Pressure Management After Intracerebral Hemorrhage [J]. *Current Treatment Options in Neurology*, 2015, 17(12): 49
- [20] Fargen K, Mocco J. Novel Device and Technique for Minimally Invasive Intracerebral Hematoma Evacuation in the Same Setting of a Ruptured Intracranial Aneurysm: Combined Treatment in the Neurointerventional Angiography Suite COMMENTS [J]. *Neurosurgery*, 2015, 11(1): 50-50
- [21] Deng X, Yang C, Gan J, et al. Long-Term Outcomes After Small-Bone-Window Posterior Fossa Decompression and Duraplasty in Adults with Chiari Malformation Type I [J]. *World Neurosurgery*, 2015, 84(4): 998
- [22] Jeswani S, Nuño M, Wu A, et al. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study[J]. *Journal of Neurosurgery*, 2016, 124(3): 627
- [23] Fujita T, Nishino A, Mori K, et al. Simultaneous bilateral hypertensive intracranial hemorrhage treated by endoscopic surgery [J]. *Nosotchu*, 2016, 38(5): 336-339

(下转第 559 页)

- [4] Srisomboon J, Kietpeerakool C, Suprasert P, et al. Survival and prognostic factors comparing stage IB 1 versus stage IB 2 cervical cancer treated with primary radical hysterectomy [J]. *Asian Pacific journal of cancer prevention*, 2011, 12(7): 1753-1756
- [5] 张芳真, 郑苍尚, 邓永强. 1320 例唇腭裂患者临床统计分析[J]. *口腔医学研究*, 2008, 24(1): 82-84
- [6] Murray JC. Gene/environment causes of cleft lip and/or palate [J]. *Clinical genetics*, 2002, 61(4): 248-256
- [7] Yimin Sun, Yongqing Huang, Aihua Yin, et al. Genome-wide association study identifies a new susceptibility locus for cleft lip with or without a cleft palate[J]. *Nature Communication*, 2015, 6(2): 1-7
- [8] Lai AH, Brett MS, Chin WH, et al. A submicroscopic deletion involving part of the CREBBP gene detected by array-CGH in a patient with Rubinstein-Taybi syndrome[J]. *Gene*, 2012, 499(1): 182-185
- [9] Mattina T, Palumbo O, Stallone R, et al. Interstitial 16p133 microduplication: case report and critical review of genotype-phenotype correlation[J]. *European journal of medical genetics*, 2012, 55(12): 747-752
- [10] Tajir M, Fergelot P, Lancelot G, et al. Germline mosaicism in Rubinstein-Taybi syndrome[J]. *Gene*, 2013, 518(2): 476-478
- [11] Petrij F, Giles RH, Dauwerse HG, et al. Rubinstein-Taybi syndrome caused by mutations in the transcriptional co-activator CBP [J]. *Nature*, 1995, 376(6538): 348-351
- [12] Van Belzen M, Bartsch O, Lacombe D, et al. Rubinstein-Taybi syndrome (CREBBP, EP300)[J]. *European journal of human genetics* : *EJHG*, 2011, 19(1): preceding 118-120
- [13] Kim SR, Kim HJ, Kim YJ, et al. Cryptic microdeletion of the CREBBP gene from t (1;16) (p362;p133) as a novel genetic defect causing Rubinstein-Taybi syndrome [J]. *Annals of clinical and laboratory science*, 2013, 43(4): 450-456
- [14] Hennekam RC. Oral aspects of Rubinstein-Taybi syndrome [J]. *American journal of medical genetics. Supplement*, 1990, 6: 42-47
- [15] Richman LC, Eliason MJ. Reading disability in children with clefts [J]. *The Cleft palate journal*, 1988, 25(1): 21-25
- [16] Richman LC. Do the reading disabilities of children with cleft fit into current models of developmental dyslexia [J]. *The Cleft palate-craniofacial journal: official publication of the American Cleft Palate-Craniofacial Association*, 2003, 40(2): 154-157
- [17] Wang B, Zhou Y, Leng S, et al. Genetic polymorphism of nonsyndromic cleft lip with or without cleft palate is associated with developmental dyslexia in Chinese school-aged populations [J]. *Journal of human genetics*, 2017, 62(2): 265-268
- [18] Ding L, Zhang S, Qiu W, et al. Novel mutations of PKD1 gene in Chinese patients with autosomal dominant polycystic kidney disease [J]. *Nephrol Dial Transplant*, 2002, 17(1): 75-80
- [19] 张殿勇, 张树忠, 汤兵, 等. 利用 PCR-SSCP 技术检测中国汉族人 PKD2 基因的突变[J]. *第二军医大学学报*, 2002, (4): 413-416
- [20] Sah VP, Attardi LD, Mulligan GJ, et al. A subset of p53-deficient embryos exhibit exencephaly[J]. *Nature genetics*, 1995, 10(2): 175-180
- [21] Beaty TH, Taub MA, Scott AF, et al. Confirming genes influencing risk to cleft lip with/without cleft palate in a case-parent trio study[J]. *Human genetics*, 2013, 132(7): 771-781
- [22] Xu S, Yin X, Li S, et al. Genomic dissection of population substructure of Han Chinese and its implication in association studies [J]. *American journal of human genetics*, 2009, 85(6): 762-774
- [23] Jin L. Natives or immigrants: modern human origin in east Asia[J]. *Nature reviews. Genetics*, 2000, 1(2): 126-133
- [24] Leite IC. Oral clefts, consanguinity, parental tobacco and alcohol use: a case-control study in Rio de Janeiro, Brazil [J]. *Brazilian oral research*, 2009, 23(1): 31-37
- [25] Beaty TH, Ruczinski I, Murray JC, et al. Evidence for gene-environment interaction in a genome wide study of nonsyndromic cleft palate[J]. *Genetic epidemiology*, 2011, 35(6): 469-478
- [26] Jia ZL, Shi B, Chen CH, et al. Maternal malnutrition, environmental exposure during pregnancy and the risk of non-syndromic orofacial clefts[J]. *Oral diseases*, 2011, 17(6): 584-589

(上接第 505 页)

- [24] Chen G, Ping L, Zhou S, et al. Early prediction of death in acute hypertensive intracerebral hemorrhage [J]. *Experimental & Therapeutic Medicine*, 2016, 11(1): 83
- [25] Li Q, Zhang G, Huang Y J, et al. Blend Sign on Computed Tomography: Novel and Reliable Predictor for Early Hematoma Growth in Patients With Intracerebral Hemorrhage [J]. *Stroke*, 2015, 46(8): 2119
- [26] Turner R D, Vargas J, Turk A S, et al. Novel Device and Technique for Minimally Invasive Intracerebral Hematoma Evacuation in the Same Setting of a Ruptured Intracranial Aneurysm: Combined Treatment in the Neurointerventional Angiography Suite [J]. *Neurosurgery*, 2015, 11 Suppl 2(Issue): 43
- [27] Mori R, Yuki I, Kajiwara I, et al. Hybrid Operating Room for Combined Neuroendovascular and Endoscopic Treatment of Ruptured Cerebral Aneurysms with Intraventricular Hemorrhage [J]. *World Neurosurgery*, 2016, 89(727): e9-727.e12
- [28] Yang G, Shao G. Clinical effect of minimally invasive intracranial hematoma in treating hypertensive cerebral hemorrhage [J]. *Pakistan Journal of Medical Sciences*, 2016, 32(3): 677
- [29] Nong S D, Lu M X, Li T Y, et al. Effect of minimally invasive intracranial hematoma drainage on inflammatory factors, serum ferritin and serum P substance in patients with hypertensive cerebral hemorrhage [J]. *Journal of Hainan Medical University*, 2017, 23(1): 113-116