麻醉与监护论坛

Forum of Anesthesia and Monitoring

中华医学会麻醉学分会
Chinese Society of Anesthesiology

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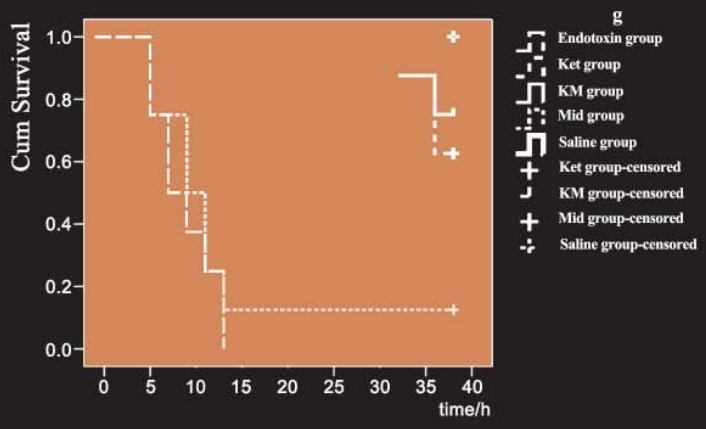
Fig 2 Survival rates. All rats in endotoxin group died within 13 hours after endotoxin injection, and all the rats in saline group (without endotoxin)survived. The shortest survival time of rats in either Ket group or KM group was 32 hours. Survival rates in Ket, KM and Mid groups were, respectively, 62.5%, 75% and 12.5%. The survival rate for ten days was the same as in forty hours.



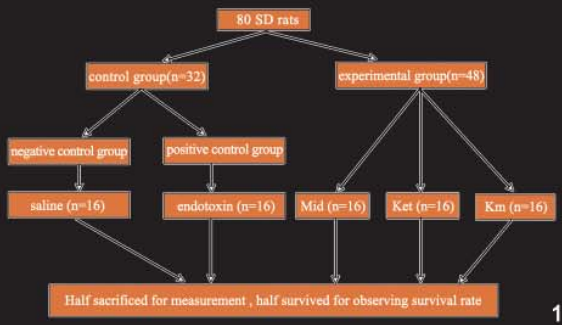


Fig 1 Derivation of the five groups

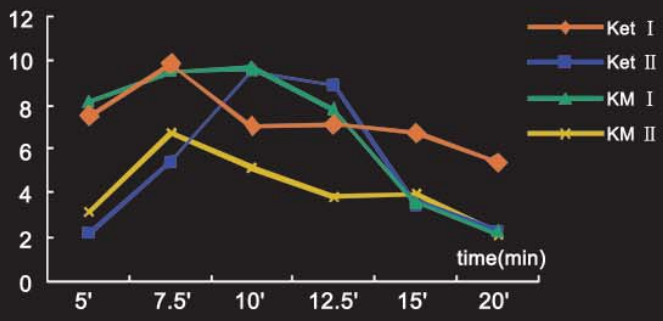


Fig 3 The plasma concentration of initial (i.e. ketamine 80mg/kg) and supplemental administration of ketamine (i.e. ketamine 40 mg/kg) was measured at time of 5', 7.5', 10', 12.5', 15' and 20' minutes. The plasma concentration of initialadministration and supplemental administration of ketamine was from 2.27±1.35 mg/L to 9.9±0.57 mg/L and 2.07±1.02 to 9.56±1.01 mg/L, respectively.

Ket Ⅰ = initial (i.e. ketamine 80mg/kg) administration of ketamine)
Ket Ⅱ = supplemental administration of ketamine (i.e. ketamine 40mg/kg)
KM Ⅰ = initial (i.e. ketamine 80mg/kg) administration of ketamine)
KM Ⅱ = supplemental administration of ketamine (i.e. ketamine 40mg/kg)

Ketamine improved survival rates of septic rats. Increase of myocardial HSP70 expression, inhibition of TNF-α production and upregulation of myocardiac cAMP may be involved in it's underlying mechanisms.

Figure related to "Ketamine Improves Septic Shock Survival"
by Hong Xiao, Lan Zhang, David T. Wong, Quan-Yun Wang, Ren Liao, Jin Liu ,pp.20.

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辛卯年 吉祥 2011

主编寄语

新年祝辞

老虎呼啸远去，兔子蹦跳而来。在新的一年开始之际，我谨代表《麻醉与监护论坛》杂志全体编委和编辑部工作人员，向奋战在全国各地的广大麻醉科、重症医学科、疼痛科的工作人员，致以最衷心的问候。

在过去的一年里，《麻醉与监护论坛》完成了改版工作，成为中华医学会麻醉学分会的机关刊物。新的编辑方针也已确定，就是从过去的全中文刊物，逐步转为中英文混编刊物，最终要成为全英文、SCI收录的杂志。一年来，在全国广大同道的热情支持下，在编辑部工作人员的认真努力下，在学会的大力扶持和帮助下，杂志无论是在论文的学术质量上，在内容的安排上，还是在编辑与装帧的质量上，都比以往上了一个台阶，达到了改版的初期目的，也受到读者们的热烈欢迎和鼓励。

在取得更好成绩的同时，我们也应清醒地看到，杂志距离我们所设定的目标，还有很远的路要走。首先，由于全国同道们的学术水平和英文写作水平的不断提高，中国学者在SCI杂志上所发表的论文逐年增多。以麻醉学科为例，2009年发表的SCI论文还只有99篇，而到2010年底为止，麻醉学科已发表论文231篇，呈现爆炸式的增长。这一方面说明，中国学者正在大踏步地走向世界，是一件大好事；但另一方面，也给杂志的英文组稿带来了困难，使杂志的英文稿件来源更为紧张。对此，我们只能寄希望于各位编委，在发表SCI论文的同时，也能对学会的刊物予以支持，以使我们能早日实现跻身国际SCI引用杂志的目标。其次，在新的一年里，杂志希望能进一步弱化杂志的学术性，淡化不同学科间的争论。应当明白，医疗的根本任务是救死扶伤，为病患解除痛苦。谁能更好地为病员解除病患，谁就拥有了学术上的发言权。因此，杂志不仅希望广大麻醉学科的同道能积极投稿，也希望广大从事ICU和疼痛诊疗的同道能踊跃投稿，以使杂志能更全面地反映这几个学科的进步与成长。

国家医改工作的基调是“保基本、强基层、建机制”。我以为，与我们关联更为密切的是建机制。这不仅反映在建立新的医疗联合体这种不同层次医院间联合的机制，以至更高层次的建立新的养老机制、支付机制等国家层面的行动；也应包含在医院内部，如何根据医疗市场的发展规律来建立各科室间新的协作关系的机制。随着医院管理的不断现代化，各种新的学科组合模式将不断涌现，必将冲击我们现有的医疗模式。因此，我们也希望，不同学科的学科带头人和广大同道，能根据自己学科的发展特点和认识，积极总结本学科的发展经验，并对其它学科的发展提出自己的看法。

2011年是兔年。兔子温顺可爱，做事又谨慎敏捷，所求甚少，却贡献更多，尤其是在医学实验领域，兔子为人类的健康做出了突出的贡献，我们应该感谢它们。最后，让我们大家共同努力，为更好地服务于广大患者而做出我们应有的贡献。

The year of the tiger is gone while the year of the rabbit is coming. In the beginning of this year, I, onbehalf of all the editing staff in department of the “Forum of Anesthesia and Monitoring”, express all-hearted greetings to all the nationwide staff in the fields of Anesthesia, Intensive Care and Pain Treatment.

In the past year, “Forum of Anesthesia and Monitoring” has finished our revision and become the official magazine of the anesthesiology subranch of Chinese Medical Association. The new editorial policy is made to transform gradually from the chinese edition to bilingual edition and finally become an English only magazine recruited by SCI. During the past year, with the warm help of the nationwide fraternity, the great effort of all editorial staff, the enormous support of the Chinese Society of Anesthesiology, our magazine has moved forward to a new stage and achieved our initial goal, which gained warm wellcome and encouragement from the reader, not only on the academic level, but also on the content management and the printing quality.

While gaining great success, we also realize that we still have a long way to go to achieve the prestablished aim. Firstly, the chinese scholars publish more and more thesises on the SCI with their growth on academic study and English writing. Taking anesthetization for example, the recruited thesises on SCI by the chinese are 99 in 2009, but in the end of 2010, the number has jumped to 231, at an explosive rate of growth. On one hand, this shows that the chinese scholars have come to an international level, which is a good thing, but on the other hand, it brings trouble to the edition work making narrow resource of original English thesises. Therefore we can only hope our editorial board that you can support us while you publish the thesises on SCI, and help us to achieve our goal earlier to become a cited magazine by SCI. Secondly, in the new year, our magazine hopes to strengthen the academic atmosphere and desalt the department dispute. We should know that the core mission of our medical staff is to save and cure people and remove pain for the illness. Whoever better removes the pain for the illness has the right to speak. Therefore, our magazine not only hopes that all the anesthetization staff can contribute your thesis to us but also the ICU and pain treatment staff can contribute your thesis to us in order that our magazine can reflect the development of these subjects more comprehensively.

The national medical transformation’s main key is to guarantee the fundamental need, to emphasize the basic level and to establish a system. To establish a system is more intimate to us. We not only need to establish a joint system by the integration of diverse hospitals, a more advanced retirement system and payment system, but also a cooperative system between different departments. With the modernization of hospital management, various subject integration model will appear which’ll certainly lash the present medical model. So we hope that the academic pace-maker and other fellow can sum up your experience and put forward your opinion on other subjects according to your knowledge on the development of your subject.

2011 is the year of the rabbit. Rabbits are tender and lovely, discreet and agile. They ask less but contribute more. Especially in the medical field, rabbits contribute a lot to the human health, for which we should thank them. At last, let’s work hard together to further contribute to all the illness.

于布为 **Bu-wei Yu**
中华医学会麻醉学分会第十届委员会主任委员
President, Chinese Society of Anesthesiologists
《麻醉与监护论坛》主编
"Form of Anesthesia and Monitoring"Editor-in-Chief
2011年2月 February,2011


谢荣

祝大家新年快乐，事业上取得新的成就！

《麻醉与监护论坛》杂志顾问　谢荣


罗爱伦

一元复始，万象更新。值此新春佳节，借《麻醉与监护论坛》一方宝地，希望与全国麻醉界同道一起努力，共同把我国麻醉事业发展推向新的高峰！

北京协和医院麻醉科教授、中华医学会理事、中华医学基金会副理事长
杨森科学委员会主任委员、《麻醉与监护论坛》杂志名誉主编　罗爱伦


王恩真

怀着共同的理想；紧跟学科前沿的动向；传递飞速发展的医学信息；展现《麻醉与监护论坛》杂志的进取与领航！衷心祝愿新的一年我们的杂志再创辉煌！

教授，主任医师，博士研究生导师
《中华麻醉学杂志》栏目编委、《麻醉与监护论坛》杂志顾问
中华医学会、北京医学会医疗事故鉴定专家
首都医科大学麻醉系及北京麻醉质控中心聘任专家　王恩真


吴新民

2010年我们在北京成功召开了第十二届国际心胸血管麻醉学术会议和全国麻醉学术年会，我国麻醉学已经步入了快速发展的大好时机，让我们更加努力、携手共进，为我国麻醉学的发展做出我们应有的贡献！

中华医学会麻醉分会前任主任委员
《麻醉与监护论坛》杂志名誉主编　吴新民

排名不分先后


刘进

猛虎长啸去，玉兔呈吉祥。

值此新春佳节来临之际，祝愿读者们在新的一年里幸福安康！愿我们共同为中国的麻醉事业创造更大的价值，做出更大的贡献！

四川大学华西医院麻醉科主任、中华医学会麻醉学会副主任委员
中国麻醉学医师协会卸任会长、四川省危重病医学分会主任委员
《麻醉与监护论坛》常务副主编　刘进


陈德昌

麻醉学是围手术期医学的基础和重要组成部份。为适应新世纪发展，需要培养更多的麻醉医师成为围手术期医学专业人才。

祝麻醉学会在学科建设方面更上一层楼！

北京协和医院外科教授
亚太危重病医学联合会理事　陈德昌


刘大为

给全国的同道们拜年！祝大家心情愉快，身体健康！

北京协和医院加强医疗科主任
中华医学会重症医学分会主任委员
《麻醉与监护论坛》杂志副主编　刘大为

新年快乐

辛卯年 2011

Happy New Year

希望我们《麻醉与监护论坛》快速发展，早日成为SCI刊物。

北京三博脑科医院医疗院长、麻醉学科首席专家、主任医师
首都医科大学附属北京天坛医院麻醉学教授、中国医师协会麻醉学医师分会常委
国家标准委员会委员、亚洲神经外科麻醉和重症治疗学会副会长
中华医学会麻醉学会神经外科麻醉专业组组长、北京麻醉专业委员会副主任委员
北京市国外来华行医甄查考核麻醉专业主任委员、首都医科大学麻醉学系副主任
北京市临床麻醉和疼痛治疗质量控制和改进中心主任、《麻醉与监护论坛》副主编

王保国

岳云

祝《麻醉与监护论坛》成为中华医学会麻醉学分会官方杂志后，能尽快进入世界舞台。在不远的将来成为麻醉学界的国际品牌杂志，中国麻醉学的SCI。

北京首都医科大学麻醉学系副主任
首都医科大学附属北京朝阳医院麻醉科主任
中华医学会麻醉学分会常务委员兼秘书长
北京医学会麻醉学专业委员会副主任委员
《麻醉与监护论坛》副主编

祝全国麻醉同道新年快乐，祝《麻醉与监护论坛》，越来越出色！

第四军医大学西京医院副院长兼麻醉科主任
世界麻醉医师学会常务理事
世界麻醉医师联合会亚澳区副主席
中华医学会麻醉学分会常委
陕西省麻醉学会主任委员、《麻醉与监护论坛》副主编

熊利泽

倪家骧

祝愿全国麻醉同仁们，新年快乐，身体健康，事业更上一层楼！

首都医科大学宣武医院疼痛诊疗中心主任，麻醉科副主任
首都医科大学疼痛生物医学研究所副所长
中华医学会疼痛学分会常务委员，癌症疼痛学组组长
北京市康复医学会疼痛分会副会长、《麻醉与监护论坛》副主编

倪家骧

排名不分先后

新年伊始，气象更新，祝愿全国麻醉业的同仁们，新年快乐，在新的一年里，能够更上一层楼！

中华医学会麻醉分会全国常委
中华医学会北京麻醉学分会主任委员
北京市临床麻醉和疼痛治疗质量改进中心管理委员会副主任委员
《麻醉与监护论坛》常务编委

叶铁虎

叶铁虎

杜斌

致全国危重病医学界同仁

祝大家在新的一年里，工作顺利，事业有成，家庭和睦，好运兔U！

北京协和医院教授、内科ICU主任
中国病理生理学为重医学专业委员会秘书长
中华医学会重症医学专业委员会全国委员
北京医学会危重病学专业委员会副主任委员
《麻醉与监护论坛》专栏主编

因新春组稿时间紧迫，如未刊登，敬请谅解

《麻醉与监护论坛》编辑部敬上

薛富善

祝愿各位同道在2011年里，所有的希望都能如愿，所有的梦想都能实现，所有的期待都能出现，所有的付出都能兑现。新年快乐。

薛富善

《麻醉与监护论坛》专栏主编
北京市临床麻醉和疼痛治疗质量控制和改进中心委员
国家自然科学基金评委、北京市疼痛学会委员
中华口腔学会麻醉学会委员、美国纽约科学院和科学进展学会会员

俞卫锋

祝我国的麻醉学事业乐驰千里马，更上一层楼！祝麻醉同道事业正当午，身体壮如虎，金钱不胜数，干活不辛苦，悠闲像老鼠，浪漫似乐谱！

俞卫锋

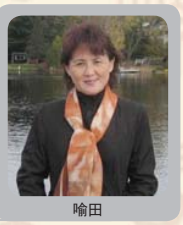
第二军医大学东方肝胆外科医院麻醉科主任、教授博导
中国医师协会麻醉学医师分会副会长、中华医学会麻醉学分会常委兼副秘书长
中国药理学会麻醉药理分会常委兼副秘书长、上海医学会麻醉专科分会副主任委员
全军麻醉与复苏专业委员会常委、《麻醉与监护论坛》专栏主编

徐建国

认识自己，明确目标，专心规划，执着努力，而且心中乐观着、善良着、微笑着、坚信着，做一个高超的医生，正直的好人，坦荡的君子！

徐建国

中华医学会麻醉学分会常委、《临床麻醉学》杂志主编
江苏省医学会麻醉学分会主委、上海第二军医大学及南京大学、山东大学教授
博士生导师、南京军区南京总医院博士后站导师
《麻醉与监护论坛》常务编委



喻田

值此玉兔迎春之际，诚挚的祝福麻醉同仁们，新春快乐，万事如意！为我们共同的事业——给力！

喻田

遵义医学院副院长、麻醉学系主任
中华医学会麻醉专业委员会全国委员
中国医师协会全国麻醉学分会委员
省麻醉专业委员会主任委员
《麻醉与监护论坛》专栏主编

排名不分先后

姚尚龙

当祝我国麻醉事业兔年蒸蒸日上，再展宏图；全国麻醉工作者身体健康，合家欢乐。

姚尚龙

任中华医学会麻醉学会常委、湖北省麻醉学会副主任委员
武汉市麻醉学会主委、湖北省急救中心副主任
华中科技大学同济医学院附属协和医院麻醉学教研室主任、ICU主任
《麻醉与监护论坛》专栏主编

李文志

祝全国的麻醉同仁们兔年吉祥，祝《麻醉与监护论坛》杂志，越来越好”！

李文志

哈尔滨医科大学附属二院副院长
哈医大二院麻醉科主任、中华麻醉学会委员
中国医师协会麻醉学分会常务委员
省医学会常务理事、省麻醉学会主任委员
《麻醉与监护论坛》专栏主编

董振明

值此新春来临之际，河北董振明给全国的麻醉界同仁拜年，祝愿大家新春快乐，身体健康，万事如意！

董振明

河北医科大学第二医院麻醉科主任、中华医学会麻醉分会委员
河北省医学会麻醉分会主任委员
河北省医师协会麻醉医师分会主任委员
《麻醉与监护论坛》常务编委

新年快乐

辛卯年 2011 Happy New Year

虎辞旧岁看江山如画，兔贺新春喜盛世繁华！

充满希望的2011年已迎面走来。在这辞旧迎新的喜庆的时刻，向辛勤工作在全国麻醉学临床、教学和科研战线上的各位同道们致以崇高的敬意和新年祝福！向《麻醉与监护论坛》的所有工作人员表示衷心的感谢和良好的祝愿！作为麻醉学学术交流的工具、科技信息的载体，《麻醉与监护论坛》杂志亦迎来了广阔的发展空间，使命在肩。有一批国内一流的编委专家，有一批活跃在科研和临床实践中的读者群体，有多名训练有素的编辑人员，相信《麻醉与监护论坛》杂志会百尺竿头，更进一步！

特此，衷心祝愿同道们平安喜乐，身体健康，工作顺利，万事胜意！

中国医师协会麻醉学医师分会副主任委员
广东省麻醉学会副主任委员、中山大学附属第一医院麻醉科主任
全国卫生专业技术资格考试专家委员会委
《麻醉与监护论坛》专栏主编

黄文起

黄文起

郭曲练

过去的一年,论坛办得内容丰富、有声有色，为全国麻醉学同道提供了宝贵的精神食粮，感谢你们辛勤的工作，同时祝愿全国麻醉学同道兔年蹦得更高!成绩取得更大!

中华麻醉学会常务委员、中国麻醉医师协会常务委员
湖南省麻醉学专业委员会主任委员、中南大学湘雅医学院麻醉学系主任
中南大学湘雅医院麻醉科主任、《麻醉与监护论坛》专栏主编

尊敬的各位麻醉同仁和其他同道朋友们：

新年的钟声激荡神州大地，岁月的航船开启崭新航程。在辞旧迎新的美好时刻，我们要感谢《麻醉与监护论坛》为麻醉事业所做的贡献，也要携手支持《麻醉与监护论坛》的全英文改版和成为SCI收录的期刊，并为其做出努力。

新的一年，我们要把握机遇，开拓进取，积极、创新、务实，共创麻醉事业的美好未来！祝朋友们新春快乐、身体健康、工作顺利、幸福安康！

温州医学院麻醉系主任、温州医学院附属第二医院副院长
中华医学会麻醉分会委员、中华医学会疼痛学会常务委员
中国医师协会麻醉医师分会常务委员
《麻醉与监护论坛》常务编委

连庆泉

值此2011年新春来临之际，衷心祝愿全国麻醉同道以及《麻醉与监护论坛》杂志读者新春愉快，阖家幸福，工作顺利。相信杂志在于布为主编的领导之下，《麻醉与监护论坛》杂志的明天将更加辉煌！

王天龙

首都医科大学宣武医院麻醉科主任、教授、主任医师，博士研究生导师
中华麻醉学模拟教育培训基地（宣武医院）负责人、中华麻醉学会全国委员
中华麻醉学会神经外科学组副组长、世界疼痛医师学会中国分会常委
北京麻醉学会常委兼秘书、《中华麻醉学大查房（电子版）》总编辑
《中华麻醉学杂志》编委、《国际麻醉学与复苏杂志》编委
《麻醉与监护论坛》杂志编委、《医学参考报-麻醉学频道》编委
《中华医学杂志》审稿人等

在新年来临之际，借《麻醉与监护论坛》之平台，祝福麻醉界的同仁平安、快乐、幸福！祝愿你心中永远都有首快乐的歌，兔年快乐！

首都医科大学第六临床学院麻醉学教研室主任
首都医科大学附属北京安贞医院麻醉科主任
世界疼痛医师协会中国分会常务委员
中华医学会北京分会麻醉专业委员会委员

卿恩明

因新春组稿时间紧迫，如未刊登，敬请谅解

《麻醉与监护论坛》编辑部敬上

排名不分先后


米卫东

瑞虎辞旧岁，金兔迎新春。恭祝全国麻醉同仁们新春吉祥、阖家幸福、万事如意。

解放军总医院麻醉手术中心副主任、主任医师、教授、博士生导师
中华医学会麻醉学分会常委、中国医师协会麻醉学医师分会常委
北京医学会麻醉专业委员会 副主任委员、全军麻醉与复苏专业委员会常委兼秘书长
《中华麻醉学杂志》、《临床麻醉学杂志》、《国际麻醉学与复苏杂志》
《解放军军医进修学院学报》和《麻醉与镇痛》中文版等杂志编委
《麻醉与监护论坛》常务编委


徐礼鲜

金虎辞岁啸九岳;玉兔祥瑞麻坛春;
麻醉监护人气旺;聚气给力步步高!

第四军医大学第三附属医院(口腔医院)麻醉科主任、中华口腔医学会麻醉组副主任委员
陕西省医学会麻醉学分会副主任委员、陕西省医学会疼痛学分会副主任委员
全军麻醉与复苏专业委员会常委、中华麻醉学会临床学组委员
陕西省麻醉学临床质量控制中心委员、陕西省医学会医疗事故鉴定专家库成员
《麻醉与监护论坛》专栏主编

徐礼鲜


郭政

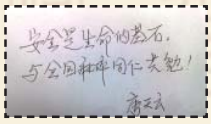
尊敬的各位麻醉学同仁，郭政祝贺大家通过不懈的努力在过去的一年中所取得的成绩和获得的进步。让我们继续在科学与艺术的4D空间里拼搏、生活：在医疗中体现能力，让病人更安全治疗更顺利；在科研中发挥想象力，让学说更新颖成果更富有影响力；在教学中更具有感染力，让知识传授更有动力；在生活中辐射魅力，让生活更加丰富、和谐、绚丽。

山西医科大学麻醉学教授、麻醉学系主任
山西医科大学第二医院麻醉科主任、兼任中国医师协会麻醉学医师分会常委
中华医学会麻醉学分会委员、中华医学会疼痛学专科委员会委员
中国高等医学教育学会理事、中华医学会山西分会副会长、山西省麻醉学会主任委员
山西省麻醉医师协会会长、《中华麻醉学杂志》、《临床麻醉学杂志》
《国际麻醉学与复苏杂志》《Anesthesia & Analgesia》中文版，编委
Neuroscience、Neuroscience Letters、International Journal of Cardiology杂志审稿专家
《麻醉与监护论坛》编委

郭政

排名不分先后

安全是生命的基石
与全国麻醉同仁共勉。




唐天云

南省第一人民医院麻醉科主任医师/教授、昆明医学院教授、成都医学院教授
美国麻醉医师协会(ASA)会员、美国匹兹堡大学医学院医学中心(UPMC)国际访问学者
中华医学会云南省麻醉学分会委员、中华医学会云南省疼痛学分会委员
中国中西医结合灾害医学专业委员会院内救治专家委员会常委
云南省医师资格实践技能考试考官、云南省/昆明市医疗事故鉴定委员会专家

唐天云


张达颖

祝各位同道身体健康，事业生活顺心遂愿！
祝杂志越办越好！

南昌大学医学院第一附属医院麻醉科副主任，疼痛科主任
中华医学会疼痛学分会副主任委员、中华医学会麻醉学分会青年委员
江西省医学会疼痛学会主任委员、中国医师学会麻醉分会委员

祝所有的麻醉同仁们兔年行大运，祝《麻醉与监护论坛》杂志，越办越好！


王俊科

中国医科大学第一附属医院
中华医学会那最分会常务委员
辽宁省医学会麻醉分会主任委员

新年快乐

辛卯年 Happy New Year 2011

新的一年，新的开始；心的祝福，心的起点。

全国麻醉学界的同仁们，在你们繁忙的工作中请接受我及安徽省立医院麻醉科全体医护人员最真挚的问候和祝福：

愿我们的祝福消除大家工作上的疲劳！愿我们的祝福像高高低低的风铃，给大家带去叮叮铛铛的快乐！愿我们的祝福每分每秒都带给大家健康、好运！

祝愿大家在新的一年里事业蒸蒸日上，幸福和快乐伴随着每个人生活、工作的每一天。

安徽省立医院麻醉科主任、博士研究生导师、中华医学会麻醉学分会第十届委员会委员
中国医师协会麻醉医师分会第二届委员会常委、国家科学技术奖励评审委员会专家
中华口腔医学会口腔麻醉专业委员会常务委员、安徽医科大学学位评定委员会省立医院分委会委员
安徽省医学会第九届理事会理事、安徽省麻醉学会第六届委员会副主任委员
《中华麻醉学杂志》编委、《临床麻醉学杂志》编委、《国际麻醉学与复苏杂志》编委
《麻醉与监护论坛》杂志编委、《实用疼痛学杂志》编委、《中国药理学通报》杂志编委
《安徽医学》杂志编委、《安徽医药》杂志编委、《医学参考报麻醉学频道》报刊编委

方才

方才

钱燕宁

拜年了，祝大家在新的一年里身体健康！祝我国麻醉事业蓬勃向上！让我们在《麻醉与监护论坛》的平台上常见面、多交流，呵护“论坛”茁壮成长！

博士，教授，博士生导师
南京医科大学第一附属医院麻醉科研究室主任兼南医大外科学总论教研室副主任
中华医学会麻醉学分会第十届委员会委员、江苏省麻醉学会副主任委员
中国医师协会麻醉分会常委、中国医师协会疼痛分会常委
《临床麻醉学杂志》常务编委；《中华麻醉学杂志》、《Anesthesia & Analgesia》(中文版)
《国际麻醉与复苏杂志》、《南京医科大学学报》编委、《麻醉与监护论坛》杂志编委

钱燕宁

郑宏

真诚的感谢一路上有您的支持与信任，值此新年来临之际，谨向麻醉届的同胞们献上最诚挚的祝福！

新疆医科大学麻醉医学系主任、新疆医科大学第一附属医院麻醉科主任
新疆临床麻醉质量控制中心主任、新疆临床麻醉研究所所长
自治区有突出贡献的专家、为《中华医学会麻醉学分会》常务委员
《中国医师协会.麻醉学医师分会》常务委员、《新疆医学会麻醉专业委员会》主任委员
《麻醉与监护论坛》常务编委

郑宏

祝胜美

在这辞旧迎新、吉祥喜庆的时刻，我谨代表浙江省医学会麻醉学分会，向辛勤工作在全国麻醉医学战线上的各位同仁致以崇高的敬意和新年祝福！向关心和支持浙江省医学会麻醉学分会的各界人士表示衷心的感谢和良好的祝愿！让我们携手并肩努力为在新的一年取得更辉煌的成就，为麻醉医学事业更上一层楼而努力！祝大家在新的一年里，身体健康，工作顺利，阖家欢乐，万事如意！

浙江大学医学院麻醉学位点负责人、浙江大学医学院附属第一医院麻醉科主任
浙江省医学会麻醉学分会第七届主任委员、中华医学会麻醉学分会委员
世界疼痛医师协会中国分会常务委员、中华医学会疼痛学分会委员
中国医师协会麻醉学医师分会委员、浙江省麻醉学分会疼痛诊疗学组组长
《麻醉与监护论坛》杂志编委

祝胜美

排名不分先后

李天佐

把新春的祝福给所有的朋友，愿《麻醉与监护论坛》的成长又好又快！

首都医科大学附属北京同仁医院麻醉科主任医师
首都医科大学附属北京同仁医院麻醉科主任
中华医学会北京分会麻醉专业委员会副主任委员
全国麻醉学会委员、北京医师协会麻醉专业专家委员会委员
《麻醉与监护论坛》杂志编委

李天佐

林财珠

虎岁刚饮祝捷酒，兔年又放报春花。新年新气象，祝大家在新的一年里，万事如意，身体健康。

福建医科大学附属第一医院麻醉科主任
中华医学会麻醉学分会委员
福建麻醉学会主任委员、省麻醉质控中心主任
《麻醉与监护论坛》杂志编委

林财珠

因新春组稿时间紧迫，如未刊登，敬请谅解

《麻醉与监护论坛》编辑部敬上

GOLDWAY

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G60
病人监护仪
国食药监械（准）字2010第3211276号

UT6000C
病人监护仪
粤食药监械（准）字2009第2210381号

G40
病人监护仪
国食药监械（准）字2009第3210890号

UT4000Fpro
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Ketamine Improves the Survival Rates in Rats with Septic Shock and the Underling Mechanism Involved

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Introduction

SEPTIC shock is a critical situation in clinical practice and is associated with many pathophysiological alterations, including hypotension and end-stage organ damage. It has been reported that these changes were induced by endotoxin (lipopolysaccharide, LPS)[1, 2]. Researches have shown that the administration of ketamine after endotoxin-induced septic shock improves survival rates in the rat model[3, 4]. The mechanisms involved may be multifactorial, among which, the production of cytokines may play an important role in endotoxin-induced septic shock[5, 6]. Meanwhile, tumor necrosis factor - α (TNF- α) has been implicated as the earliest appearing and the most prominent cytokine in septic shock[1,7]. It may cause myocardial contractile dysfunction by inhibiting myocardial β -adrenergic receptor-adenylcyclase-cAMP (β AR-AC-cAMP) signal transduction[8,9]. Research based on myocardial cell culture has shown that ketamine suppresses TNF- α -induced cAMP reduction and other proinflammatory cytokines[10]. However, whether ketamine has the similar effect in vivo is unknown.

Heat shock protein70 (HSP70) is a stress protein which may function as a molecular chaperon and thereby maintains the self-stabilization system of cell protein and exerts self-protection against injury. It shows myocardial protection in animals subjected to ischemic injuries[11, 12]. Furthermore, it was also reported that ketamine has brain-protective effect by stimulating the expression of HSP70[13]. However, no researches have demonstrated that whether or not HSP70 is involved in the anti-inflammation and up-regulation process of cAMP caused by ketamine in septic shock. Our hypothesis is that serum TNF- α , myocardiac cAMP and the expression of HSP70 constitute underlying mechanisms for the improved survival rates of rats with endotoxin-induced septic shock.

Methods and Materials

Animals

All experimental protocols and procedures conducted in this investigation were approved by the Institutional Animal Care and Use Committee of Sichuan University (Sichuan, China). Healthy and mature Sprague-Dawley rats of both sexes weighing 250–300g were used in the present study. All rats had free access to food and water and were individually housed under a 12-h light/dark cycle and were kept under controlled condition of temperature (22°C ±2°C) 1 week before experiments.

Experimental Protocols

Eighty rats were randomly distributed into two control groups and three experimental groups, (n=16 each). Two control groups included one negative control group (saline group) and one positive control group (endotoxin group). Three experimental groups contained Endotoxin-Midazolam Group (Mid Group), Endotoxin-Ketamine Group (Ket Group), and Endotoxin-Ketamine-Midazolam Group (KM Group).(Fig 1). All the rats except those in saline group had Lipopolysaccharide (LPS) of Salmonella minnesota injection intraperitoneally (Sigma Chemical, St. Louis, MO, USA). Twenty min prior LPS injection, the rats in experimental groups received midazolam 0.5mg/kg by intraperitoneal injection (ip), ketamine 80mg/kg ip, ketamine 80mg/kg +midazolam 0.5 mg/kg ip respectively while equal volume of saline were given in two control groups. Half of the initial doses of ketamine, midazolam were repeated in the experimental groups at 1 hour after

their first administration. The dosage of ketamine used in this study was decided according our pilot study（table1）, in which rats survival rates improved significantly. In this study, the plasma concentration of ketamine was measured (see fig.3).

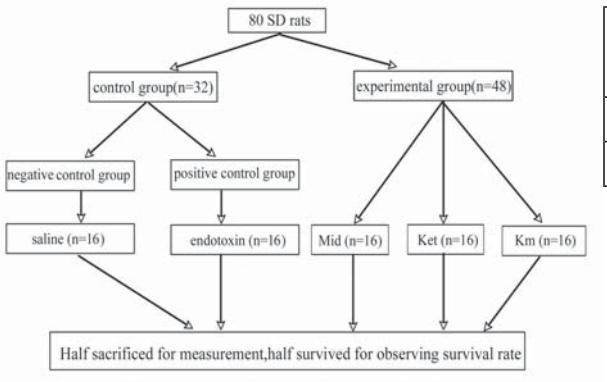
Intestinal perforation and other complications caused by intraperitoneal injection were visually examined after the rats were sacrificed by neck dislocation.

Half of the rats in three experimental groups (24 rats) were sacrificed by neck dislocation two hours after the administration of LPS and the plasma concentration of epinephrine, norepinephrine, TNF-α, myocardial cAMP and HSP70 expression were measured afterwards. For the purposes of comparison, half of the rats in the control groups (16 rats) were sacrificed at the same time. The other half in all groups was used to observe the survival rate which was determined by counting the number of the surviving rats in each group on the tenth day .

Measurements

After the exposure of endotoxin for 2 hours, the arterial blood from the common iliac artery was taken in the sacrificed rats in five groups (saline, endotoxin, Mid, Ket and KM) to measure the plasma concentration of epinephrine, norepinephrine, and TNF-α. The blood sample of 0.3 ml was collected from angular vein for the plasma concentrations of ketmine measurements at 5', 7.5', 10', 12.5', 15' and 20' min followed the initial and supplemental administration.Additionally, myocardium sample was harvested from the rats in these groups to examine cAMP and HSP70 level. The blood for epinephrine, norepinephrine, and TNF-α measurements was centrifuged at 3,000g for 10 min (Kendro laboratory product, GMBH Post1563, D-63405 Hanace/Germany)) at 4℃. Serum was decanted and stored at-70℃ (refrigerator :MDF-3821, SANYO, Japan). TNF-α and cAMP were measured using radioimmunoassay.(TNF-α :Beijing Chemiclin Biotech, Co,Ltd, Beijing, China; cAMP: Sigma Chemical, St. Louis, MO, USA). High performance liquid chromatograpy (Model Angilent 1100, Palo Alto, CA, USA) was applied to measure the plasma concentration of epinephrine, norepinephrine with YQC-C18 column while the plasma concentration of Ketamine with YMC-ODS column（250×4.6mm 5um）. All of these measurements for biochemical analysis (ie., TNF-α, cAMP epinephrine, norepinephrine and plasma concentration of ketamine) were duplicated. The level of HSP70 expression was measured using immunohistochemistry. Half of the hearts of each scarified rat were removed and postfixed for 12 hours in 4% paraformaldehyde and then embedded in paraffin. Five micrometer coronal sections were cut via microtome. Sections were deparaffinised, rehydraged and then incubated (37°C) for 2 hours with the primary HSP70 antibody (monoclonal antibody of HSP70: Monoclonal anti-heat shock protein70 clone BRM-22, Sigma; SPTM kit:SP-9002 Mo SP kit,ZYMGD, USA) diluted 1:2000 in HS-PBS. After three PBS washes, sections were incubated (30min) at room temperature with anti-mouse antibody (biotinylated anti-mouse IgG (Vector Labs, Burlingame, CA) and then incubated for 30min in an avidin-horseradish peroxidase solution prepared from an ABC kit (Vector Labs, Burlingame, CA). The complex was detected by diaminobenzidine (0.015% in PBS, Sigma Chemical, St. Louis, MO, USA) and 0.001% hydrogen peroxide, which produced a dark brown end product. Sections were then triple washed in PBS and mounted on slides.

Figure 1: Derivation of the five groups.



TABEL 1.The effect of different dose of ketamine on TNF-α and Survival rate in the pilot study

	Endotoxin 20mg/kg Mean (SE) 95%CI	KTM1 (20mg/kg) Mean (SE) 95%CI	KTM2 (40mg/kg) Mean (SE) 95%CI	KTM3 (60mg/kg) Mean (SE) 95%CI	KTM4 (80mg/kg) Mean (SE) 95%CI	KTM5 (100mg/kg) Mean (SE) 95%CI	KTM6 (120mg/kg) Mean (SE) 95%CI
TNF-α (ng/ml)	2.18(±0.04) 2.26,2.10	1.5(±0.01)* 1.52,1.48	1.2(±0.01)* 1.22,1.18*	0.9(±0.03)* 0.96, 0.84*	0.67(±0.07)* 0.80,0.53*	0.53(±0.003)** 0.54,0.52**	0.51(±0.004)** 0.52,0.50**
urvival rate(%)	0	25	25	50	75*	50	50

Note: All groups on which the above calculations are based consisted of 4 rats.

Endotoxin=endotoxin 20mg/kg,(i.p) , KTM1=ketamine 20mg/kg,(i.p), KTM2=ketamine 40mg/kg,(i.p) , KTM3=ketamine 20mg/kg,(i.p) KTM4=ketamine 40mg/kg,(i.p) KTM5=ketamine 60mg/kg,(i.p) KTM6=ketamine 60mg/kg,(i.p).

*=P<0.05 as compared with group endotoxin **=P<0.05 as compared with groupKTM4

All ketamine groups received ketamine 20 minute before endotoxin exposure

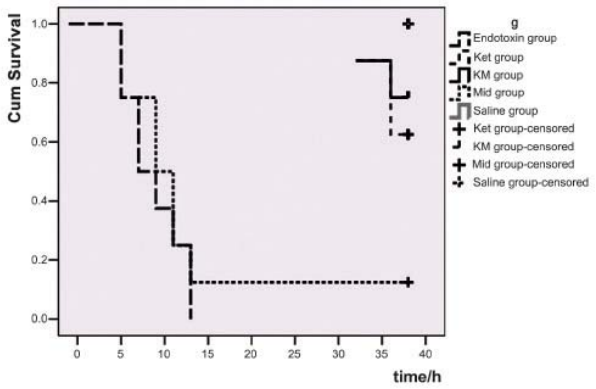
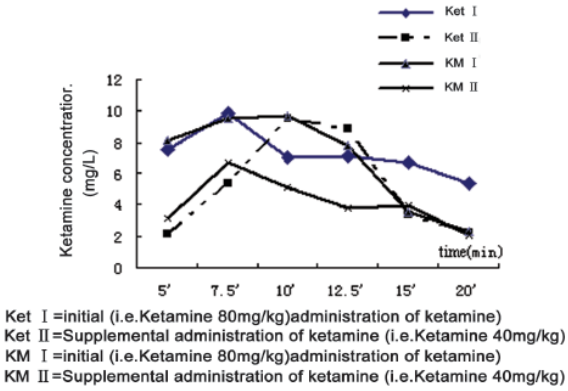


Figure 2: Survival rates. All rats in endotoxin group died within 13 hours after endotoxin injection, and all the rats in saline group (without endotoxin)survived. The shortest survival time of rats in either Ket group or KM group was 32 hours. Survival rates in Ket, KM and Mid groups were, respectively, 62.5%, 75% and 12.5%. The survival rate for ten days was the same as in forty hours.



Ket Ⅰ=initial (i.e.Ketamine 80mg/kg)administration of ketamine)
Ket Ⅱ=Supplemental administration of ketamine (i.e.Ketamine 40mg/kg)
KM Ⅰ=initial (i.e.Ketamine 80mg/kg)administration of ketamine)
KM Ⅱ=Supplemental administration of ketamine (i.e.Ketamine 40mg/kg)

Figure 3: The plasma concentration of initial (i.e. ketamine 80mg/kg) and supplemental administration of ketamine (i.e. ketamine 40 mg/kg) was measured at time of 5', 7.5', 10', 12.5', 15' and 20' minutes. The plasma concentration of initialadministration and supplemental administration of ketamine was from 2.27±1.35 mg/L to 9.9±0.57 mg/L and 2.07±1.02 to 9.56±1.01 mg/L, respectively.

Sections were viewed via a light microscope (Olympus BX-60 microscope, OLYMPUS Co., Ltd. Tokyo, Japan.) and gray value was measured with an image analysis system (Mias-2000 image analyzer, Chengdu, China) to determine the expression of HSP70. The lower the HSP70 gray value is, the higher expression of HSP70 exists, so the reciprocal of the gray value (i.e., 1/HSP70 gray value) was chosen to represent the level of HSP70 expression in the correlation analysis. Grey values of six sequential visual sights from each section were measured and the average from five sections of one heart was calculated. The mean grey value of each group was determined by 8 animals from the same group.

Statistical Analysis

Comparisons among survival rates of the groups were made with the Kaplan Meier and Fisher's exact test. Differences of other measurements among groups were analyzed using one-way analysis of variance (ANOVA) and followed by post hoc tests. The correlation between HSP70 , survival rate, TNF- α and cAMP were determined by linear correlation analysis. Statistical analyses were performed using SPSS software (Version 13.0, SPSS Inc, Chicago, IL, USA) Statistical significance was defined as $P < 0.05$.

Results

All the rats in endotoxin group died within 13 hours after endotoxin injection, and all the rats in saline group survived. Survival rates of the ketamine treated groups (Ket and KM Groups) were 62.5% and 75% , which were significantly higher than that of endotoxin group (0%) ($P<0.05$). The survival rates of KM group (75%) was higher than that of Mid group (12.5%) ($P<0.05$). There were no differences in survival rates between Ket(62.5%) and KM (75%)groups, as well as Mid(12.5%) and endotoxin group(0%) ($P>0.05$) (fig.2)

The plasma concentration of initial (i.e. ketamine 80mg/kg) administration and supplemental administration of ketamine (i.e. ketamine 40mg/kg) was from 2.27±1.35 mg/L to 9.9±0.57 mg/L and 2.07±1.02 to 9.56± 1.01 mg/L respectively (fig.3) .

Epinephrine, norepinephrine, TNF- α , cAMP, and HSP70 were measured in all groups (data in Table 2). Epinephrine and norepinephrine were significantly higher in endotoxin, Mid, Ket and KM groups compared to the saline group ($P<0.01$). There was no substantial difference in plasma concentration of epinephrine and norepinephrine among endotoxin, Mid, Ket and KM groups ($P>0.05$).

TNF- α was lower, and cAMP and HSP70 expression were higher in Ket and KM groups compared to Mid, and endotoxin groups. Specifically, TNF- α in endotoxin group was 7.5 times higher than that in saline group and the cAMP in endotoxin group was 3.7 times lower ($P<0.01$) (see Table 2, columns 1as compared with columns2). TNF- α and cAMP in Ket and KM groups were, respectively,

almost 3.6 times lower and higher than Mid, and endotoxin groups (P<0.01) (see Table2, columns1,2, and3 as compared with columns 4 and 5). There was no difference in TNF- α , cAMP and HSP70 between Ket and KM groups or Mid, and endotoxin groups (P>0.05).

As shown in table 2, the increased expression of HSP70 produced three effects: a decrease in TNF- α , an increase in cAMP , and a significant improvement in survival rates. There was a significant positive correlation between survival rate and the expression of HSP70 (R^2=0.956, P<0.05) (see Fig 4), cAMP and the expression of HSP70 (R^2=0.984, P<0.05) (see Fig. 5) and a significant negative correlation between TNF- α and the expression of HSP70 (R^2=0.903, P<0.05) (see Fig. 6) .

Discussion

The main findings of this study are: 1.The rats treated with endotoxin all died within 13 hours and the rats without endotoxin all survived, 2. Ketamine improved the survival rates of rats with septic shock, and 3. The combined use of ketamine-midazolam did not cooperate with ketamine in improving survival rates.

Cytokines produce notable effects on the mechanism of endotoxin-induced septic shock.[5, 6]TNF- α responds to septic shock earlier and more prominently than other cytokines, it would induce a myocardial contractile dysfunction and also promote the release of other cytokines, such as IL-1, IL-6 and IL-8. Consequently, a cascade of events may ensue, beginning with an imbalance of proinflammatory and anti-inflammatory cytokines that destroy the defense function of the immune system and ultimately culminate in septic shock[14, 15]. Levitzki describes β AR-AC-cAMP(β -adrenergic receptor-adenylylcyclase-cAMP) signal transduction in the myocardium[16]. The increased intracellular accumulation of cAMP may result in an increased heart rate and force of cardiac contraction [6], and TNF- α along with other proinflammatory cytokines may suppress this signal transduction. This may cause the reduction of cardiac contraction and other effects such as heart failure [7]. Meanwhile, endotoxin (LPS) induced myocardial dysfunction was shown to stimulate myocardial TNF- α production.[17]. The results of the current study support these previously published findings in which septic shock were partly attributed to the influence of these cytokines and second messenger system. In our study, we found that TNF- α in endotoxin group was 7.5 times higher than that in negative control group and the cAMP in endotoxin group was 3.7 times lower . We also found that, compared with both the Med and endotoxin groups, TNF- α decreased and cAMP increased in Ket and KM groups. ketamine may inhibit the endotoxin-induced TNF- α release and increases cAMP in myocardium. Other studies, both in vitro and in vivo, support our explanation[3, 4, 18, 19]. Thus, consistent with our explanation and findings from other studies, ketamine-suppressed TNF- α production and ketamine-induced cAMP accumulation may be a mechanism of the ketamine to improve the survival rate of septic shock rats.

We have shown from the β AR-AC-cAMP signal transduction, catecholamine level is directly related

Figure 4: Relativity of the expression of HSP70 with survival rate. With the increasing expression of HSP70, survival rates increased, showing a positive correlation , R^2=0.956. The lower the HSP70 gray value is, the higher expression of HSP70 exists, so the reciprocal of the gray value (i.e., 1/HSP70 gray value) was chosen to represent the expression of HSP70.

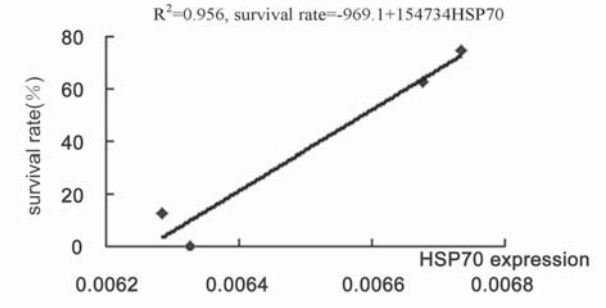
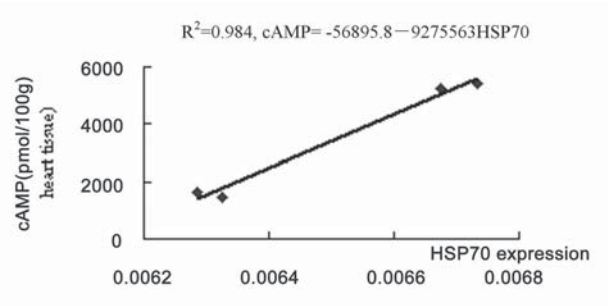


Figure 5: Relativity of the expression of HSP70 with cAMP. With the increasing expression of HSP70, cAMP increased, showing a positive correlation , R^2=0.984. The reciprocal of the gray value (i.e., 1/HSP70 gray value) was chosen to represent the expression of HSP70.



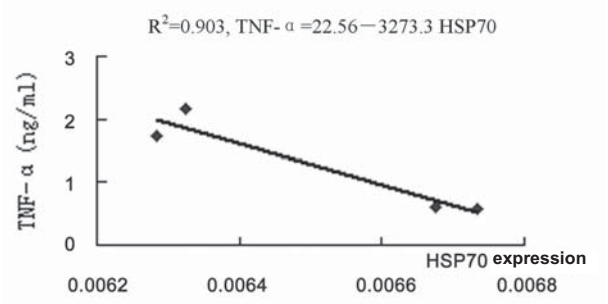


Figure 6: Relativity of the expression of HSP70 with TNF-α. With the increasing expression of HSP70, the TNF-αdecreased, showing a negative correlation, R^2=0.903. The reciprocal of the gray value (i.e., 1/HSP70 gray value) was chosen to represent the expression of HSP70.

to the concentration of cAMP. However, compared with endotoxin group, we did not find an increase in epinephrine and norepinephrine level in Ket and KM groups. The implication is that the catecholamine level is not involved in either the increase or decrease of cAMP in endotoxin, Mid, Ket and KM groups ,.

Of particular interest in our study is HSP70. This is a protein largely conserved throughout animal evolution, and its major function is to aid in the proper folding of proteins so that they are configured to be molecular chaperons. Consequently, HSP70 protects cells from injuries including the toxicity of hydrogen peroxide, light damage, and ischemia-reperfusion damage[20, 21]. In our study, both the level of HSP70 expression and survival rates were higher in Ket and KM groups than in groups endotoxin and Mid, and, as shown in figure 4, we found a robust correlation between survival rates and the level of HSP70 expression (R^2=0.956). Our study, then, suggests that HSP70 protected against endotoxin-induced injury, and ketamine bolstered this effect. As shown in figures 5 and 6, we found a robust negative correlation between TNF- α and HSP 70 (R^2=0.903), and a robust positive correlation between cAMP and HSP70 (R^2=0.984).

According to the previous study , the mechanism of endotoxin(LPS) inducing myocardiac dysfunction is partly by stimulating myocardial TNF- α production[17]. The release process of TNF- α was as following described: LPS binds to LPS-binding protein(LBP), after several transduction events, transcription factor for tumor necrosis factor (NF κ β) translocates to nucleus after its inhibitory subunit(κ β) is phosphorylated and dissociated. In nucleus, nuclear factor- κ β binds to tumor necrosis factor promoter site and induces myocardial tumor necrosis factor production[22]. HSP70 thus may disrupt the signal cascade of endotoxin binding to nuclear factor- κ β , which would prevent the translocation of this process to the nucleus. Furthermore, other studies have shown a transient attenuation of cAMP accumulation following heat shock but, with the expression of HSP70, it was restored to control levels. If Quercetin, an inhibitor of heat shock factor, is administered, it functioned to inhibit the restoration of cAMP[23]. The heat shock probably affects configurations of the membrane receptors such as β AR, G protein and/or adenylate cyclase , and, as discussed above, HSP70 functions as a molecular chaperon in the re-folding and re-assembling of proteins that restore the signal transduction of myocardial β AR-AC-cAMP .

Ketamine has been recommended for anesthesia induction and sedation in patients with circulatory failure because it increases sympathetic nervous system activity. This in turn aids to maintain blood pressure and preserve cardiovascular function[24]. Some investigators have suggested that these cardiovascular effects are due to the anti-inflammatory effects of ketamine, rather than its sympathomimetic properties and, accordingly, they have

TABEL 2.Epinephrine , Norepinephrine, TNF-α, cAMP Values in the Five Study Groups

	Group Saline Mean (SE) 95%CI	Group Endotoxin Mean (SE) 95%CI	Group Mid Mean (SE) 95%CI	Group Ket Mean (SE) 95%CI	Group KM Mean (SE) 95%CI
E(ng/L)	657(±6.94) 643.4，670.6	1315 (±23.27)* 1269.4，1360.6*	1217 (±6.79)* 1203.6，1230.3*	1119 (±22.70)* 1074.5，1163.5*	1125 (±23.47)* 1079.0，1171.0*
NE(ng/L)	465(±5.36) 454.5，475.5	821± (12.86)* 795.8，846.2*	701 (±10.61)* 680.2，721.8*	777 (±9.85)* 757.7，796.3*	724 (±15.30)* 694.0，754.0*
TNF-α(ng/ml)	0.29 (±0.01) 0.270，0.310	2.17± (0.05)* 2.07，2.26*	1.72 (±0.02)* 1.68，1.76*	0.60 (±0.02) ** 0.57，0.63**	0.59 (±0.03) ** 0.54，0.64**
cAMP (pmol / 100g heart tissue)	5533.1 (±1061) 5512.2，5553.9	1477.1±(29.13)* 1420.0，1534.19*	1644.3(±33.42)* 1578.8，1709.8*	5253.2 (±145.31) ** 4968.4，5538.0**	5392.6 (±60.67) ** 5273.7，5511.5**
HSP70 gray value	166.1 (±0.53) 165.1，167.13	158.1±(0.56)* 157.0，159.2*	159.11 (±0.25)* 158.6，159.60*	149.8 (±0.50) ** 148.9，150.7**	148.5 (±0.51) ** 147.5，149.5**

Note: All groups on which the above calculations are based consisted of 8 rats. Additionally, another 8 rats from each group were not sacrificed at the same time as those above in order to observe their survival rates.

* = P<0.01 as compared with saline group ; ** P<0.01 as compared with Endotoxin groups and group Mid

Group Saline=negative control Group); Groups Endotoxin= positive control Group; Group Mid= First experimental group; Group Ket= Second experimental group; Group KM= Third experimental group

E=plasma epinephrine; NE=plasma norepinephrine; TNF-α=serum tumor necrosis factorα; cAMP=myocardiac cAMP.

suggested that, given its anti-inflammatory properties, the conservative use of ketamine may be advantageous as an anesthetic agent in endotoxemia [25-28]. However, as is well recognized, ketamine stimulates the limbic system of the brain and may cause undesirable side effects unless it is combined with other anesthetics. For this reason, ketamine is often administered in combination with midazolam. However, no differences were found between ketamine group and the ketamine-midazolam combined group in all values measured, such as the survival rate, TNF-α, cAMP and HSP70. The possible implications for clinical practice are notable: the combined use of ketamine and midazolam may not affect the character of ketamine in septic shock.

We chose 80 mg/Kg ketamine according to our preliminary studies. It is of potential clinical importance that the improved survival of infected animals and the lower TNF-α was achieved despite the fact that the cumulative dose of ketamine in the present study was more than some authors used previously (80 mg/kg versus 10 mg/kg, respectively) . In the present study, the plasma concentrations of ketamine within 20 minutes were measured. The plasma concentration was from 2.27±1.35 mg/L to 9.9±0.57 mg/L after initial administration and from 2.07±1.02 to 9.56± 1.01 mg/L after supplemental administration. These plasma concentrations of ketamine measured in this study were similar to those measured in clinical settings. Idvall J reported[29] the peak plasma concentration of ketamine after intravenously injection of 2mg/kg in human was 60μmol/L(14.22mg/L), and the maintaining concentration was 7～10μmol/L(1.4～2.37mg/L) . Domino EF reported[30] that patient intravenously received ketamine in a dose between 2.0 and 2.2 mg/kg, showing plasma levels of ketamine varied from 9,000 to 25,800 ng/ml (9-25.8mg/L) and approximately 1,000 ng/ml (1mg/L) when the patients began to recover consciousness. Recently some authors [31]also reported that 70mg/kg ketamine (we used 80mg/kg) has the inhibitory action on cytokines such as TNF-α .

In our study, we found ketamine improved survival rates , inhibited serum TNF-α , enhanced myocardiac cAMP . One of the underlying mechanisms for its effects may due to stimulating the expression of myocardial HSP70. Some other mediators such as NO and adenosine may be involved. Inducible NO synthase (iNOS) has been implicated as a mediator of endotoxin-induced tissue injury[32]. Ketamine was reported to attenuate LPS– induced upregulation of iNOS mRNA and protein during endotoxemia in a rat model[33]. In another research, ketamine administration in mice was associated with a surge of adenosine in serum and peritoneal fluid at 20–35 min. The adenosine receptor agonist mimicked the effect of ketamine in peritonitis, whereas the receptor antagonists blocked its anti-inflammatory effects[27].

We conducted a randomized controlled experiment on rats, and the extent to which findings may be extended to humans is obviously unknown. Similar studies on different animal models are necessary to validate the safety of our conclusions on ketamine. Once these studies are conducted, extrapolation from animal to humans may be contemplated. And in our study, we just proved the involvement of the cAMP in the septic shock, we extrapolate the secondary effect of myocardium by the β AR-AC-cAMP signal transduction in the myocardium. We did not measure the haemodynamics and the cardiac function. This is the limitation of this study.

In summary, ketamine improved survival rates of septic rats. Increase of myocardial HSP70 expression, inhibition of TNF-α production and upregulation of myocardiac cAMP may be involved in it's underlying mechanisms.

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摘要

在体外循环（cardiopulmonary bypass，CPB）心脏直视手术后，患者常常发生伴有甲状腺激素血清水平严重降低的正常甲状腺病态综合征。然而，是否应该给实施CPB心脏直视手术的患者常规应用外源性甲状腺激素，以减轻手术中的心肌缺血-再灌注损伤和防治手术后正常甲状腺病态综合征的发生，目前尚无一致意见。本文综述正常甲状腺病态综合征及其相关不良影响、CPB心脏直视手术对甲状腺激素血清水平的影响和CPB心脏直视手术患者应用外源性甲状腺激素治疗等内容。

关键词：甲状腺激素；正常甲状腺病态综合征；心肌保护；心脏直视手术；体外循环

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甲状腺激素在体外循环心脏直视手术患者的应用

Application of Thyroid Hhormones in Patients Undergoing open Heart Surgery with Cardiopulmonary Bypass

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Abstract

After open heart surgery with cardiopulmonary bypass (CPB), the patients often present (euthyroid sick syndrome, ESS) with significantly decreased serum levels of thyroid hormones. However, there is still controversy regarding on whether exogenous thyroid hormones should be routinely used in the patients undergoing open heart surgery with CPB to attenuate the myocardial ischemia/reperfusion injury during surgery and prevent occurrence of postoperative ESS. This article reviews the occurrence of ESS and its adverse effects, effects of open heart surgery with CPB on serum levels of thyroid hormones, supplemental administration of exogenous thyroid hormones in the patients undergoing open heart surgery with CPB, etc.

Key Words: Thyroid Hormones; Euthyroid Sick Syndrome; Cardioprotection; Open Heart Surgery; Cardiopulmonary Bypass

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众所周知，甲状腺激素作用广泛并具有强大的生理功能，其中对心脏的作用是其主要的生理功能之一。研究发现，在体外循环（cardiopulmonary bypass,CPB）心脏直视手术后，患者常常发生伴有甲状腺激素血清水平严重降低的正常甲状腺病态综合征（euthyroid sick syndrome，ESS），并对患者的预后具有明显的影响。本文就正常甲状腺病态综合征及其不良影响、CPB心脏直视手术对甲状腺激素血清水平的影响以及CPB心脏直视手术患者补充性应用甲状腺激素的研究现状等内容进行综述。

一、正常甲状腺病态综合征

1. 正常甲状腺病态综合征[1]

ESS是指在一些严重的急性和（或）慢性非甲状腺疾病患者中出现甲状腺激素血清水平降低，而促甲状腺激素血清水平正常或降低，并且临床上无甲状腺功能减退表现的一组综合征。许多严重的非甲状腺疾病均可引起甲状腺激素血清水平降低而发生ESS。

2. ESS的分型[2]

根据患者甲状腺激素血清水平的改变，ESS被分为两型：其中最常见的是总T_3和游离T_3（Free T_3，FT_3）血清水平降低而促甲状腺激素（Thyroid stimulating hormone，TSH）和T_4血清水平基本正常，被称为I型ESS；在许多危重症患者，除T_3血清水平降低之外，T_4血清水平亦可出现降低，被称之为II型ESS或低T_4综合征。一般认为，ESS的发生是因为促进T_4转化为T_3的5'-脱碘酶（D1）活性降低导致T_3生成减少和无生物学活性的反T_3生成增多所致。

3. ESS与危重病患者病情的关系

ESS是一种病理学表现，T_3血清水平降低的程度实际上是与患者病情的严重程度密切相关，即：一旦危重病患者同时出现T_3和T_4血清水平减低，常常预示病情严重和预后不佳。Rothwell等[3]在ICU成年患者中发现，与急性生理及慢性健康评分II（acute physiologic and chronic health evaluation II，APACHE II）相比，患者入住ICU时的甲状腺激素血清水平是预测患者预后更准确的指标。另外，其他研究证实，在APACHE II评分基础上加入甲状腺激素血清水平变化能够更准确地预计ICU患者的死亡率[4]。

已经证实，与伴发I型ESS的患者相比，伴发II型ESS危重症患者的死亡率和并发症发生率明显增高。De Groot通过对四篇文献中报道的160例危重症患者（包括烧伤、急性心肌梗死等）进行综合分析发现，当T_4血清水平低于4μg/dl时，患者的死亡率为50%；当T_4血清水平降低至2μg/dl时，患者的死亡率可高达80%以上[5]。

二、ESS和CPB心脏直视手术

1. CPB心脏直视手术与ESS的关系

Velissaris等[6]发现，与实施CPB冠状动脉搭桥手术的患者相比，实施非CPB冠状动脉搭桥手术的患者在手术后同样可发生ESS。但是，与实施无CPB的心脏直视手术患者相比，CPB心脏直视手术患者手术后发生ESS的几率显著增加，并可伴有甲状腺激素血清水平更严重的降低[7]。

2. CPB影响甲状腺激素血清水平的途径

一般认为，CPB主要是通过以下几个途径影响甲状腺激素血清水平。

CPB期间可发生甲状腺组织细胞缺氧和血流灌注不足，从而导致1型5'-单脱碘酶（D1）合成和甲状腺摄碘能力降低，进而造成甲状腺激素合成减少[8]。

CPB心脏直视手术可导致机体严重的应激反应，在应激状态下甲状腺球蛋白(thyroglobulin)合成减少和消耗增加，从而甲状腺激素合成随之减少[9]。另外，应激状态亦可使甲状腺素结合球蛋白（thyroid binding globulin，TBG）合成减少，而作为将T_4转运至循环血液的主要载体，TBG减少可直接引起T_4血清水平降低[10]。

实施CPB心脏直视手术的患者，手术后常常发生全身炎症反应综合征。在炎症反应时，体内众多的炎症细胞因子，例如白介素-1（interleukin-1，IL-1）、IL-6、肿瘤坏死因子-α（tumor necrosis factor-α，TNF-α）和干扰素-γ等生成增多，可抑制促甲状腺激素释放激素（thyrotropin-releasing hormone，TRH）、TSH和TBG的合成，从而引起T_3和TSH血清水平降低[11]。

肝脏和肾脏中的D1是一种含硒蛋白，是促进T_4向T_3转化的关键酶，而且T_4向T_3转化是机体T_3的主要来源。Holzer等[12]在59例实施CPB心脏直视手术的小儿观察了不同时间点的血清硒浓度。结果表明，与麻醉诱导时相比，手术后48h时患儿的硒血清浓度显著降低，这提示CPB心脏直视手术后患儿的硒血清浓度可显著降低，进而导致D1活性降低和T4转化为T_3的数量减少。这可能是小儿CPB心脏直视手术发生ESS的重要原因。

Buket等[13]在30例冠状动脉搭桥手术患者发现，与CPB转流期间应用非搏动性血流灌注的患者相比，应用搏动性血流灌注患者手术后2h和24h时的T_3和FT3血清水平显著升高，提示CPB期间应用非搏动性血流灌注可影响下丘脑-垂体-甲状腺轴功能。然而，目前在CPB转流期间大多是采用非搏动性血流灌注，可导致丘脑-垂体-甲状腺轴调节机制失调，进而影响TRH、TSH和甲状腺激素的分泌及功能。

在CPB心脏直视手术期间常常应用多种拟交感神经药物，其中多巴胺是最常用的药物之一，它可作用于垂体前叶的抑制性多巴胺受体而直接抑制腺垂体的分泌功能，导致TSH释放减少，进而使甲状腺激素合成降低，从而诱导或加重ESS[14]。

三、甲状腺激素心肌保护的作用机制

虽然甲状腺激素对心肌缺血-再灌注损伤的保护作用在动物实验和临床研究中均已得到证实，并且有些研究也证实部分信号转导通路以及与心肌保护相关的蛋白在甲状腺激素的心肌保护作用机制中具有一定的地位，但是关于甲状腺激素心肌保护作用的确切机制目前尚不完全清楚，相关研究主要是集中在以下几方面：

1. 蛋白激酶C

Rybin等[15]发现，切除大鼠甲状腺可显著降低甲状腺素血清水平，并提高心肌细胞内蛋白激酶C（protein kinase C，PKC）含量。Light等[16]在兔心室肌细胞采用单通道膜片钳技术观察了心肌细胞内PKC含量对线粒体ATP敏感性钾离子通道（KATP通道）开放的影响，结果发现，心肌细胞内PKC浓度增高可导致线粒体KATP通道对ATP的敏感性降低，使线粒体KATP通道在细胞内ATP浓度相对较高的情况下仍可保持开放状态，并发挥心肌保护作用。

2. 丝裂原活化蛋白激酶途径

丝裂原活化蛋白激酶（mitogen activated protein kinases，MAPK）途径是由细胞内的一类丝氨酸和(或)苏氨酸蛋白激酶组成的信号传导链，是应激和损伤反应的主要信号途径之一。Pantos等[17]在大鼠的研究中发现，与对照组相比，每天皮下注射左旋甲状腺素钠25μg/100g体重14天后，大鼠离体心脏经历全心缺血后，反映心肌收缩力的指标左室发展压明显升高，并且心肌组织的p38MAPK和JNKs表达显著减弱，提示MAPK途径激活受到抑制。Pantos等[18]在新生大鼠心室肌细胞的进一步研究发现，与对照组相比，在心室肌细胞培养液中加入100nM的T_3 48h可使心室肌细胞形状显著拉长（分离前细胞形状呈条状，而对照组心室肌细胞呈球形），提示T3处理有助于心肌细胞更好地保持其原有形状。该研究还发现，与对照组相比，T_3处理后心肌细胞内磷酸化ERK的表达水平升高了1.9倍，但是磷酸化AKt和磷酸化p38MAPK水平无显著差异；并且ERK信号转导通路抑制剂—PD98059可消除T_3对心肌细胞形态的影响。据此，Pantos等[18]认为T_3诱导的心肌细胞形态学改变与ERK信号转导通路有关。

3. 热休克蛋白70

正常条件下，细胞内主要是表达结构型热休克蛋白70（heat shock protein70，HSP70），并且在应激情况下结构型HSP70的表达仅略有增加；而诱导型HSP70是仅在细胞应激时才出现表达。目前研究认为，HSP70抗缺血-再灌注损伤的作用主要是通过诱导型HSP70介导的。Marber等[19]曾比较性观察了转基因技术和直接热休克法诱导小鼠心肌组织HSP70表达情况的差别以及HSP70表达水平与心肌保护效果的关系。结果发现，与单纯热休克（在体加热至42℃保持15min）组相比，转基因技术处理组心肌组织的HSP72表达显著增强，并且缺血-再灌注后心肌梗死面积降低40%，冠脉流出液内的CK-MB活性降低50%。这些研究结果提示HSP70表达水平增高可获得心肌保护作用。Jayakumar等[20]通过转基因技术将HSP72基因转染到大鼠心肌4天后，观察了离体心脏耐受低温（4℃）缺血（停跳）4h的能力，结果发现：与正常大鼠相比，HSP72转基因大鼠心脏恢复再灌注（复跳）1h后的各项心功能指标显著改善，并且冠脉流量显著增加和冠脉流出液中的心肌酶含量显著降低，提示通过转染HSP72基因不仅可改善缺血-再灌注损伤后的心脏功能，而且可保护冠脉血管内皮的功能。此

外，该研究还发现，心肌组织的HSP72表达显著增加，进一步提示HSP70家族表达增强可获得显著的心肌保护作用。Okubo等[21]发现，将诱导型HSP70基因转染到兔左心室4天后，可显著增强心肌耐受长时间缺血的能力，与对照组相比，HSP70基因转染组的心肌梗死面积显著降低（24.5% vs.41.9%），并且诱导型HSP70表达增强亦可获得显著的心肌保护作用。这些研究结果说明，不同干预措施均可通过增强心肌组织HSP70家族蛋白的合成而获得心肌保护作用，并且心肌组织HSP70表达增强的程度与心肌保护效果密切相关。

已经证实，多种非致死性应激均可诱导HSP70表达增强，然后通过以下途径发挥其心肌保护作用[22]：①HSP70可发挥“分子伴侣”作用，与新生的、未折叠的、错折叠或聚集的蛋白质相结合，帮助需要折叠的蛋白正确折叠。②HSP70有助于维持某些肽链的伸展状态，以利于其跨膜转运，以便在线粒体和内质网等不同区域内发挥作用。③HSP70能够促进某些变性蛋白的降解和清除，减少其对机体的不利影响。④HSP70能够维持机体生物酶的生物学活性，以维护细胞的正常功能。

Pantos等[23]曾经在大鼠离体心脏缺血-再灌注模型观察了预先应用甲状腺激素的心肌保护效果。他们发现，实验前应用左旋甲状腺素钠25μg/100g体重14天可显著改善再灌注后的血流动力学指标，并且心肌组织的HSP70表达显著增强。作者认为甲状腺激素可引起心肌组织的氧化应激反应，进而诱导心肌组织HSP70表达增强。

四、甲状腺激素在体外循环心脏直视手术患者的应用

多年来，甲状腺激素一直是在CPB心脏直视手术后作为正性肌力药物使用，而不是CPB心脏直视手术中的常规用药。目前在实施CPB心脏直视手术患者应用甲状腺激素的临床研究主要是集中在其安全性和有效性两方面。

1. CPB心脏直视手术中应用甲状腺激素的安全性

1990年Mullis等[24]在170例实施冠状动脉搭桥手术的患者发现，手术后即刻静脉输注T_3（首次负荷剂量为0.1μg/kg，随后在6h内再缓慢静脉输注0.1μg/kg）的81例患者均未发生不良反应，而且与对照组的89例患者相比，治疗组的81例患者对起搏器的使用显著减少（14%vs.25%）。1995年Klemperer等[25]在142例实施冠状动脉搭桥手术患者进行了一项随机双盲对照临床研究，在开放主动脉后治疗组患者首次应用负荷剂量的T_3 0.8μg/kg，随后以0.113μg/kg/h的速率持续静脉输注6h，结果显示：与安慰剂组患者相比，治疗组患者的心排血量显著增加和外周血管阻力显著降低，并且治疗组患者手术后心律失常的发生率与安慰剂组患者相比无显著差异。因此，他们认为在实施冠状动脉搭桥手术期间应用该甲状腺激素补充方案是安全的。2006年Magalhães等[26]在实施CPB心脏直视手术的成年患者观察了口服T_3的效果，在手术前1天开始给患者经胃肠道应用$T_3$25μg，每日3次，直至手术后24h；结果显示：与未应用T_3的对照患者相比，治疗组患者手术后甲状腺激素血清水平降低的程度显著减轻，并且对血流动力学参数无显著影响。

既往在实施CPB心脏直视手术的小儿亦曾进行过类似研究。1999年Chowdhury等[27]曾经对6例在CPB下实施复杂先天性心脏病（包括肺动脉闭锁、二尖瓣闭锁和三尖瓣闭锁）矫正手术的小儿（年龄4天到3.5岁）进行了研究，在手术后检测到小儿甲状腺激素血清水平降低时，通过静脉持续补充T_3使其血清水平恢复到正常范围。2001年Chowdhury等[28]又在75例于CPB下实施复杂先天性心脏病矫正手术（年龄为4天到18岁）的小儿进行了一项系列观察，手术后每天测定小儿的甲状腺激素血清水平，一旦T_3血清水平降低至40ng/dL（或新生儿的T_3血清水平低于60ng/dL），即以0.05～0.15μg/kg/h的速率静脉输注T_3，直至甲状腺激素血清水平恢复到正常范围。Chowdhury等的两项临床研究均表明，对于在CPB下实施复杂先天性心脏病矫正手术的小儿，手术后应用T_3治疗可显著改善血流动力学指标，并且不导致明显的副作用。Bettendorf等[29]在40例实施CPB心脏直视手术的小儿研究了手术后补充T_3的治疗效果，他们将小儿分为两组，治疗组小儿手术后每日静脉注射T_3一次（第1天为2μg/kg，以后每天1μg/kg，直至手术后第12天）。结果发现，与未补充T_3的对照组小儿相比，治疗组小儿手术后的甲状腺激素血清水平显著升高、心指数显著增加和手术后监护时间显著缩短，并且未出现明显的不良反应。Carrel等[30]在心脏直视手术后出现严重低心排血量且常规治疗无效的7例小儿观察了静脉注射T_3的治疗效果，首次应用的T_3负荷剂量是（2±1.5）μg，随后以0.4±0.3μg/h的速率持续静脉输注，连续用药48±12h，结果显示，与治疗前相比，小儿的血流动力学趋于稳定，正性肌力药物需要量减少，并且未出现不良反应。

Portman等[31]曾对7例年龄小于1岁、实施室间隔缺损和Fallot四联症修复的小儿进行了研究，他们分别在CPB转流前和开放主动脉时静脉应用$T_3$0.4μg/kg，与对照组相比，治疗组小儿应用T_3后出现心率短暂升高，但是收缩压却未出现降低，并且手术后T_3血清水平降低的幅度显著小于对照组。Mackie等[32]在22例年龄小于1岁、实施左心室发育不良矫正手术和主动脉弓中断伴室间隔缺损行双心室修复手术的新生儿发现，在CPB结束后以0.05μg/kg/h的速率持续静脉应用T_3 72h，除2例患儿分别因高血压和频发性房性早搏停药之外，其余新生儿均未出现严重不良反应，并且治疗组小儿的心指数和收缩压均显著高于对照组，但是心率和舒张压在治疗组和对照组之间无显著差异。

总之，到目前为止，无论是在成年人还是在小儿，CPB心脏直视手术后应用T_3或T_4治疗ESS均被证明是安全的，至今尚无因补充应用甲状腺激素制剂而发生严重副作用的相关研究报道。

2. CPB心脏直视手术中应用甲状腺激素的有效性

实施CPB心脏直视手术的患者，在开放主动脉后静脉补充性应用T_3可减少手术后心房纤颤的发生。Kokkonen等[33]在46例65岁以上实施非急症心脏直视手术的患者，分别是在手术前、手术后第4天和手术后3个月时检测患者的甲状腺激素血清水平，结果发现43%的患者手术后发生了心房纤颤，并且发生心房纤颤患者的T_3血清水平显著降低，从而作者认为T_3

血清水平降低与心脏直视手术后心房纤颤的发生密切相关。Klemperer等[34]采用随机双盲研究方法将142例实施冠状动脉搭桥手术的左室功能不全患者分为两组，治疗组患者在开放主动脉后单次静脉注射$T_3$0.8μg/kg，然后以0.05μg/kg/h的速率持续静脉输注$T_3$6h，结果显示，与未应用T_3的对照组患者相比，治疗组患者心房纤颤的发生率显著降低（24%vs.46%）。

在实施CPB心脏直视手术的患者，在开放主动脉后静脉补充性应用T_3可显著改善手术后心脏功能。Mullis等[24]将170例实施冠状动脉搭桥手术患者随机分为两组，治疗组（n=81）患者在开放主动脉后单次静脉注射$T_3$0.4μg/kg，然后以0.1μg/kg/h的速率持续静脉输注$T_3$6h，结果显示：与对照组相比，治疗组的心指数显著增高、正性肌力药物需要量显著减少、心肌缺血发生率（通过心电图诊断）显著降低（4%vs.18%）和起搏器的使用率显著降低（14%vs.25%）。

实施CPB心脏直视手术的患者，在开放主动脉后静脉补充性应用T_3可显著减少血管扩张剂的使用。Vavouranakis等[35]将30例实施冠状动脉搭桥手术的患者随机分为两组，治疗组患者在主动脉开放后1min单次静脉应用$T_3$0.15μg/kg，并在CPB结束时以及CPB结束后4h、9h和14h单次静脉应用$T_3$0.1μg/kg，结果显示：手术后22h时，治疗组的FT3血清水平显著高于对照组，并且血管扩张剂的使用量显著低于对照组，但是两组的血流动力学指标无显著差异。

Chowdhury等[27]在6例实施复杂先天性心脏病矫正手术的小儿发现，当手术后出现T_3血清水平降低时，补充性应用T_3可使体循环血管阻力降低25%和心排血量增加20%。另外，小儿的代谢性酸中毒亦被减轻或纠正，并且使3例小儿的结性心律转变为了窦性心律。Portman等[31]在14例实施室间隔缺损或法乐氏四联症矫正手术的婴儿发现，与对照组相比，在CPB前即刻和开放主动脉后分别静脉应用$T_3$0.4μg/kg的治疗组（n=7），手术后T_3血清水平显著升高，心肌氧耗和心脏功能储备明显改善。

但是也有研究表明，实施CPB心脏直视手术的患者，在开放主动脉后静脉补充性应用甲状腺激素并不显著改善患者的血流动力学指标，甚至可导致心率增快、血压升高和频发房性早搏等副作用[32]。

总之，根据目前现有的研究结果，仍然不能就在CPB心脏直视手术中（开放主动脉后）静脉补充性应用甲状腺激素制剂能否改善患者手术后的血流动力学指标和预后做出最终的结论。另外，是否应该在CPB心脏直视手术后常规应用甲状腺激素制剂以纠正ESS目前也存在着很大的分歧。因此，尚需进行大量的临床和动物实验研究来证实这些问题。

五、小结

综上所述，实施CPB心脏直视手术的患者，手术后常常出现甲状腺激素血清水平严重降低。部分研究表明，通过补充甲状腺激素制剂可获得明确的心肌保护作用，并能防止ESS的发生，提示该干预措施在CPB心脏直视手术中具有较高的临床应用价值。然而，现有的文献资料尚不能对CPB心脏直视手术患者补充甲状腺激素制剂的时机、剂量和用药时间等一系列问题做出肯定结论。因此，为了进一步明确补充性应用甲状腺激素制剂在实施CPB心脏直视手术患者中的价值，诸如其对手术中心肌缺血-再灌注损伤的保护作用及其对手术后ESS的预防作用，今后尚需进行更多的动物实验和临床研究。

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Lighted Stylet (Trachlight) Enhances the Success of LMA-Classic™ Placement

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Abstract

LMA-Classic™ placement is difficult for some patients in our clinical practice. In this study, we have tested the feasibility of using lighted stylet to guide LMA-Classic™ placement. We then further assessed cuff location with bronchofibroscopy and compared to those controls with LMA-Classic™ being placed in classic approach in a randomised study of 100 patients. The successful insertion rate of the first attempt in the lighted stylet group was higher than that the control group. The effective airway establishing time was shorter in the lighted stylet group and the average cuff pressure required without leaking was significantly lower. The fibreoptic score of the LMA-Classic™ cuff location assessment was significantly better in the lighted stylet group. The present study demonstrates that LS guided LMA-Classic™ placement was feasible, associated with less placement time, a lower leak intro-cuff pressure and a higher FOB score, compared to conventional technique of LMA-Classic™ placement.

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Since the advent of the Laryngeal Mask Airway (LMA-Classic™) in the early 1990s, it has been utilized in millions of patients with an excellent record in safety and efficacy. LMA-Classic™ has been used both as a primary airway and as a rescue device in "cannot intubate cannot ventilate" events in recent years[1-4].

Successful LMA-Classic™ placements can be achieved in the majority of patients by the conventional approach (technique suggested by the manufacturer). However, LMA-Classic™ insertion has been found to be difficult or impossible for some individuals because of the backplate impacting against the posterior pharyngeal wall[5]. Alternative insertion techniques such as by using laryngoscope[6], self-made intra-tube introducers[7-10] and Bosworth introducers[11] were attempted to facilitate insertion. Apart from insertion difficulties, malposition of the LMA-Classic™ cuff is frequently seen. A number of complications may result from clinically unrecognized LMA-Classic™ cuff malposition such as ventilation insufficiency, inhalational anesthetic leakage, gastric insufflations and aspiration[12]. Bronchoscopic visualization of LMA-Classic™ cuff position has been shown to reduce malposition[12, 13].

Lighted stylet (Trachlight ®, Laerdal Medical Inc., Armonk, NY) is a simple and inexpensive device used to direct endotracheal tube into trachea by utilizing the principle of transillumination. It is an effective and safe intubating technique[14], and has been recommended as an alternative way of endotracheal intubation[1, 2]. When lighted stylet (LS) was used for tracheal intubation via the intubating LMA, it helped visualize the position of the LMA cuff in the hypopharynx[15, 16] and improved the success of tracheal intubation[17].

The purpose of this study was to test if the lighted stylet (Trachlight) enhances the success of LMA-Classic™ placement.

Methods

The study has been approved by the Sichuan University research ethics committee and 100 consecutive patients with written informed consents were recruited in this trial. Patients from West China Hospital (from October 2007 to February 2008) ranging in age from 18 to 65 yr, ASA grades I or II, Mallampati scores I, undergoing general anesthesia for elective surgeries of less than two hour duration were candidate for inclusion in the study. Those with edentulous,

overbite, obese/thick neck, known difficult airways or a history of regurgitation were excluded from this study

Participants were randomly assigned according to computer-generate lists by SPSS 12.0 to the LMA (for conventional technique of LMA-Classic™ placement, n = 51) or LS (for trachlight assisted LMA-Classic™ placement, n = 49) group. The opaque, sealed, and sequentially numbered envelopes were designed for each patient, with additional containing allocation lists and document recording tables. The data-analyst collected the envelopes and analyzed the data.

In the operating room, the routine monitoring and a standard anesthesia protocol was applied to both groups. Intravenous fentanyl 1.0 $\mu g.kg^{-1}$ was given, a face mask was applied and oxygen was administered. Two minutes later, anesthesia was induced with propofol 3.0 $mg.kg^{-1}$ injected within 30 seconds and maintained with oxygen and 1-2% sevoflurane via a circle anesthesia breathing system with a fresh gas flow of 3L/min. No muscle relaxant was used during the anesthesia procedure. LMA-Classic™ was inserted after loss of consciousness and the relaxation of the jaw muscles (jaw thrust is a reliable clinical test to assess the adequate depth of anesthesia for insertion of the laryngeal mask[18]) about 1 min after the initial injection of propofol. If required, additional bolus of $1mg.kg^{-1}$ propofol was given. The size of LMA-Classic™ was chosen based on the patient's weight according to the guideline offered by manufacture: size 3 for individuals weighing 30–50kg, size 4 for individuals weighing 50–70kg, and size 5 for individuals weighing >70kg. The LMAs deflated partially for insertion in both groups.

In the LS group, the LMA-Classic™ was prepared before the insertion. The lighted stylet were lubricated with water soluble lubricant, and then inserted the lighted stylet through the LMA-Classic™ until the bulb at the distal end of stylet was lined up with the LMA aperture bars (Fig.1). Then, the LMA-Classic™ was locked to the clamp lever of the LS and the entire unit was bent to about 90 degree curve (Fig 2). For the shaft of the LMA-Classic™ might be too short to match the stylet, we prolonged the shaft by using a section of tracheal tube (Fig 2). The nondominated hand lifted the jaw; the unit was hold by the other hand and advanced along the midline until it passed downward into the lower pharynx. When finished insertion, the room light was dimmed and the lighted stylet was turned on, the distinct central glow above the thyroid prominence was the evidence that the cuff was placed around the pharyngeal inlet. If transillumination described above was not seen, the unit was repositioned under the guidance of transillumination[15]. When the ideal tranillumination was obtained, the lighted stylet was extracted and the LMA-Classic™ cuff was inflated. Ventilation parameter was set to deliver a volume-controlled 8ml.kg-1 tidal volume and a flow of 2l/min of fresh gas. Minimum intro-cuff pressure was measured by the cuff inflator manometer which deflated the cuff when the tide volume maintained at the set level.

For the LMA group, the LMA-Classic™ was inserted by the conventional technique[19]. LMA-Classic™ cuff position was confirmed clinically by the attending physician by auscultating both lung fields to ensure symmetrical air entry, by the absence of leak at airway pressures less than 20 cmH_2O and no signs of airway obstruction. Otherwise, the LMA-Classic™ was repositioned by up-down maneuver[20], lateral movement or head positioning until the above conditions were met. The minimum intro-cuff pressure was measured the same way as the LS group. Minimum intro-cuff pressure was measured the same as the LS group.

For both groups, an attempt was deemed a failure if the insertion of the LMA-Classic™ was not successful or LMA-Classic™ cuff position adjustment was not completed in two minutes, or a capnograph waveform was failed to obtain after the insertion and reposition or oxygen desaturation fell below 89%. Between attempts, face mask ventilations were allowed. All LMA-Classic™ placements were initially performed by the same junior anesthesia resident who was experienced with more than 50 LMA-Classic™ placements. Two attempts of insertion for each patient were allowed by the resident and one more attempt was given by the attending physician. After the third failed attempt, tracheal intubation by direct laryngoscopy was performed.

The total LMA-Classic™ placement time is the period from the lift of the jaw to the establishment of satisfactory ventilation after LMA-Classic™ placement. The score of fibreoptic bronchoscope (FOB) examination was done within approximately 5 min of final placement by an anesthesiologist who was not present during the placement

of LMA-Classic™. A fibreoptic scope was inserted through the LMA-Classic™ to a position 1 cm proximal to the distal portion of the LMA-Classic™[21]. An established scoring system (Keller's fibreoptic scoring system[19]) was used to grade the fibreoptic bronchoscopy view: Score IV, only vocal cords visible; Score III, vocal cords plus posterior epiglottis visible; Score II, vocal cords plus anterior epiglottis visible; Score I, vocal cords not seen. A Keller's FOB score of IV represents ideal position, and decreasing scores represent progressively less well position conditions.

Primary outcomes included the overall successful rate of LMA placement, the successful rate of the first insertion attempt, the total LMA-Classic™ placement time, the score of bronchoscope examination, the intra-cuff pressure. The baseline values of heart rate (HR) and blood pressure (BP) were documented and they were measured immediately followed the placement of LMA in both groups. When the surgeries were completed, LMA was removed and the blood stainings were examed and documented which was used to assess soft tissue injury of LMA placements. Patients were questioned about the presence/absence of sore throat and hoarseness 10h postoperatively by an independent physician observer who was blinded to the whole placement process.

Statistical analysis

Data was analyzed with SPSS 12.0 statistical software (SPSS, Chicago, Ill). Student t test was used for age, weight, heart rate, blood pressure, insertion time, LMA-Classic™ cuff pressure and peak airway pressure, and categorical data (ie, the successful rate LMA placement) was analyzed using Fisher's analysis. Ordinal data (ie, fibreoptic bronchoscopy score) were analyzed by using the Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

Results

One hundred patients were studied and analyzed with 49 in the lighted stylet group and 51 in the control group. There were no significant differences between the two groups in age, weight and ASA grades (Table 1). In the LS group, 48 patients out of 49 (97.9%) were successful on the first attempts which was higher than that in the control group (44 patients out of 51, 86.2%) ($p > 0.05$). All the LMA placements were successfully accomplished by the resident except one by both the trainee attending physicians in the LS group.

Patients who was unsuccessful inserted were excluded from data analysis. On the first attempts, the position of LMA cuff required further adjustments (repositioning) in 15 patients (34.1%) in the control group versus 6 (12.5%) in the LS group. In the control group, seven LMA-Classic™ placements (13.8%) were failed by the resident and four of them (7.9%) were successfully completed by the attending physician and three of them failed by both the trainee and attending physicians. The overall successful rate of LMA-Classic™ placements in the control group was 94.1% versus 97.9% in the LS group ($p >0.05$). Moreover, the average time of the LMA-Classic™ establishment of the first attempt in the LS group was much shorter than that in the control group (30.8±4.1s versus 24.9±2.1s, $p =0.007$) (table 2).

The baseline values of heart rate and blood pressure before the LMA-Classic™ placements were similar in both groups ($p>0.05$). After the placement of LMA-Classic™, the heart rate and blood pressure dropped significantly compared to the baseline values in both groups ($p<0.05$). However, there were no significant differences between the two groups ($p>0.05$).

LMA-Classic™ cuff position was assessed by fiberoptic bronchoscopy. The total fiberoptic score in the LS group was higher than that in the LMA group (52.95 versus 39.15,

TABEL 1. Basic data of the patients

	LMA* (N=51)	LMA-LS* (N=49)
Age; years	38±2.0	38±1.8
Sex; M:F	28:23	13:36
Weight; kg	62.9±1.4	57.8±1.3
ASA Grade:		
1	30 (58.8%)	30 (61.2%)
2	21 (41.2%)	19 (38.8%)
LMA Size		
3	6 (11.7%)	7 (14.2%)
4	38 (74.5%)	37 (75.5%)
5	7 (13.8%)	5 (10.3%)

Values are mean±SD or number (proportion).

* LMA = control group; LMA-LS= lighted stylet group.

p=0.008) (table 2). Ideal position (score IV) under the fiberoscope in the LS group was 65% versus 34% in the LMA group (p<0.05, table 3). However, the incidence of score I was almost the same (LS: 10% and LMA: 15%, p>0.05).

The mean intro-cuff pressure was lower in the LS group (15.7±2.5 cmH_2O versus 28.0±3.4 cmH_2O, p=0.044) (Table 2). There were 5 LMA cuffs had little blood staining in each groups. And one patient complained sore throat postoperatively in LS group and four in the LMA group.

Discussions

In this study, we found that the LS was an effective locating device which enhanced successful LMA placement. The results showed the improved insertion success rates, shorter insertion time, better fiberoptic position of the airway and lower intra-cuff pressure when the LMA-Classic™ placement was guided by the LS.

LMA-Classic™ has been used both as a primary airway device during anesthesiology and as a rescue device in emergency airway control in recent years. However, the overall successful rate of LMA-Classic™ establishment is about 68-98% according to literature[22]. Failure is either due to difficulty in LMA-Classic™ insertion or the LMA-Classic™ cuff position. In this study, we attempted to improve the success of LMA-Classic™ placement with the LS originally designed for endotracheal intubation. The results demonstrated that LS increased the successful rate of LMA-Classic™ establishment on the first attempt and the overall successful rate, however, there was no significant difference. We postulated that the possible mechanism is the rigid stylet and the angle created change the insertion from the art of applying the correct amount of force and in the right direction to a simple wrist motion; and the clamp lever of the LS provided a better control of LMA-Classic™ than the other single rigid stylet. The LS light also helped the LMA-Classic™ advancing towards midline possibly and adjusting LMA cuff position in the lower pharynx under the guidance of the transillumination. For the conventional technique of LMA-Classic™, the shaft is malleable and it may stop advancement by laryngeal soft tissues under some circumstances and the cuff adjustment in the conventional technique is blind to the operator. This is why we have more patients inserted more than one attempt and adjusted longer time.

Insertion of the LMA-Classic™ is usually smooth, atraumatic, and successful on the first attempt. However, some insertion of a LMA-Classic™ is clearly not as easy as expected and takes more than one attempt. Less frequently, a bloody LMA tip is seen as the result of the excessive force used to push the LMA into position. In this study, we had most of the LMA-Classic™ placement accomplished on the first attempt in the LS group. The shaped LMA-Classic™ by the lighted can be advanced the lower pharynx anatomically, which may have the potential benefits of reducing the tissue injury by repeated attempts with conventional techniques. However, we did not reduce the incidence of the bloody LMA tip related to LMA insertion in LS group. We think this may correlated with proficiency of this technique by the operator.

Besides the airway trauma during insertion, the incidence of postoperative sore throat may be correlated

TABEL 2. Comparisons of data in the first placements between two groups

	LMA* (n=44)	LMA-LS* (n=48)	P -value
Placement Time	30.8±4.1	24.9±2.1	0.007
Cuff Pressure; cmH_2O	28.0±3.4	15.7±2.5	0.044
Sfob*	52.95	39.15	0.008
Blood contaminated	5	5	
Sore throat	4	1	

Values are mean±SD or number (proportion).

*LMA = control group; LMA-LS= lighted stylet; T= time from lift the jaw to satisfactory ventilation; VT=tide volume; Sfob= fibreoptic assessment score.

TABEL 3. Comparasion of fibreoptic score between the two groups in the first placements

*Fibreoptic score	Ⅳ	Ⅲ	Ⅱ	Ⅰ
LMA; patients	15 (34.1%)	6 (13.6%)	16 (36.4%)	7 (15.9%)
LMA-LS; patients	31(64.6%)	6 (12.5%)	6 (12.5%)	5 (10.4%)
P	<0.05	>0.05	<0.05	>0.05

*Fibreoptic score: Ⅳ=only vocal cords visible, Ⅲ=vocal cords plus posterior epiglottis, Ⅱ=vocal cords plus anterior epiglottis, score Ⅰ= vocal cords not seen.

with the intracuff pressure during the operation. LS guided LMA-Classic™ placement improves LMA-Classic™ cuff position and maintains good ventilation with lower intracuff pressure needed. The complaint of postoperative sore throat happened fewer in the LS group, though both group had the same patient with the bloody LMA tip. The good LMA-Classic™ cuff position also can reduce the occurrence of ventilation inadequacy and potential disaster of aspiration. The lighted stylet-guided technique may be particularly useful in the emergency LMA-Classic™ placement in hospital or pre-hospital settings where there is difficult airway encountered.

The average FOB assessment scores were significantly higher in lighted stylet group than those in the control group. This indicated that lighted stylet improves LMA-Classic™ cuff positioning substantially. It was noticed that a number of patients who had very low score (score 1) associated with improper location even though with the help of lighted stylet. However, the mean intra-cuff pressure remained much lower in lighted stylet group than that in the controls. Although the lighted stylet approach can not avoid some cuff malpositions, ventilation still appeared normal in these patients. Therefore, examination LMA-Classic™ cuff position with FOB after lighted stylet guided placements may be useful to further reduce the malpositions.

The LS designed for tracheal intubation was used in this study. As we described in the method, the shaft of the LMA-Classic™ for small size LMA is too short to match the wand. The shaft had to be artificially prolonged to secure it the connnector of lighted stylet handle. It would be much more convenient if there is a LS specially made for LMA-Classic™ placement in the future.

This study has some limitations. Firstly, this study was carried out on Chinese patients，which may not be able to extrapolate to other ethic groups. Secondly, the LS group is non-uniform with almost 3:1 females to males, and may contribute to bias in the results.

The present study demonstrates that LS guided LMA-Classic™ placement was feasible, associated with less placement time, a lower leak intro-cuff pressure and a higher FOB score, compared to conventional technique of LMA-Classic™ placement. This technique may be used as an adjunct to improve success rate and optimal positioning of LMA in patients.

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摘要

脓毒血症具有高发病率和高死亡率的特点。脓毒血症的治疗强调综合治疗，包括多脏器支持治疗、抗炎治疗、液体复苏、强化胰岛素治疗等治疗方法。因为病理生理机制方面的研究进展较少，脓毒血症的治疗也没有取得较大的突破。Ghrelin是最近发现的一种脑肠肽，同时也是生长激素促分泌受体的一种内源性配体。研究发现ghrelin能够在盲肠结扎穿孔所致的大鼠脓毒血症模型中减弱炎症反应、器官损伤和降低死亡率。本文主要关注ghrelin在脓毒血症中的作用机制，为ghrelin将来在脓毒血症中的应用提供线索。

关键词：Ghrelin;脓毒血症;盲肠结扎穿孔

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Ghrelin在脓毒血症中的作用机制研究进展

Development on Mechanism of The Role of Ghrelin in Sepsis

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Abstract

Sepsis manifests a high morbidity and high mortality. Comprehensive treatments including multiple organ support therapy, anti-inflammatory therapy, fluid resuscitation, intensive insulin therapy were emphasized to treat sepsis. Since the research on the pathophysiology of sepsis made slow progress, treatment of sepsis achieved little breakthrough. Ghrelin, an endogenous ligand of growth hormone secretagogue receptor, is a recently discovered brain-gut peptide. It was found that ghrelin could attenuate inflammatory response, organ injure and mortality in sepsis caused by cecal ligation and puncture rat model. In this review, we describe the mechanisms of ghrelin in treating sepsis and lay the foundation for ghrelin as a potential therapy for sepsis.

Key Words: ghrelin, sepsis, cecal ligation and puncture

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脓毒血症和脓毒性休克一直是ICU的首要致死疾病，具有高发病率和高死亡率的特点。美国每年严重脓毒症的发病人数估计有75,0000人，并且每年增加1.5%[1]。大约40-70%的死亡率与严重的脓毒症和脓毒性休克有关[2]。随着免疫抑制病人增多、侵入性治疗检查的增加、微生物耐药、老年人口的增长和人们对脓毒症认识与诊断水平的提高，目前脓毒症的发病率呈上升趋势。尽管对其治疗给予巨大的投资，严重脓毒症的死亡率还是呈上升的趋势。脓毒症的治疗强调综合治疗，包括多脏器支持治疗、抗炎治疗、液体复苏、强化胰岛素治疗等治疗方法。因为在脓毒血症的病理生理机制方面的研究进展较少，脓毒血症的治疗至今没有取得较大的突破。

一、Ghrelin在脓毒血症中的作用

1999年，日本科学家Kojima等人首先在《Nature》杂志上报道从大鼠的胃内用免疫组化的方式提取到ghrelin，并对其生物学活性及结构做了一定的阐述[3]。研究发现它在大鼠和人类有较强的刺激生长激素分泌的功能。Ghrelin是生长激素促分泌受体(growth hormone secretagogue receptor-1a，GHSR-1a)的内源性配体，能通过结合在GHSR-1a上而产生作用。同时也发现ghrelin是一种潜在的血管舒张肽。在健康的人类志愿者血管内注射ghrelin可以在不显著增加心率的情况下引起显著的外周血管阻力下降和心输出量的增加[4]。

Ghrelin的血管舒张的特性可能与ghrelin以及其受体GHSR-1a在脓毒血症的心血管反应中发挥的作用有关。Wu等研究发现在CLP后5小时和20小时ghrelin水平下降，GHSR-1a mRNA的表达则在早期脓毒症显著上升。Ghrelin导致的血管舒张也在脓毒症早期显著增加但晚期没有变化。这些结果提示在脓毒症的高动力循环阶段GHSR-1a的表达上调以及血管对ghrelin刺激的敏感性增加[5]。有研究发现血浆ghrelin水平在动物的内毒素血症时显著下降。

很多研究结果表明ghrelin有抗炎作用，可抑制活化的T细胞、单核细胞、内皮细胞及脓毒症大鼠释放促炎细胞因子[6]。同时，研究发现在盲肠结扎穿孔模型所致的脓毒血症后5小时和15小时后注射ghrelin能显著减少TNF-α、IL-6和外周腹膜液的量，这些效应可能是由ghrelin刺激迷走神经和抑制交感神经导致的[7]，也有可能与ghrelin改善脓毒症大鼠血流动力学变化、降低乳酸、增加组织灌注相关[8]。此外，ghrelin可以减轻脓毒症导致的急性肺损伤，且可降低脓毒症大鼠的死亡率[9]。这些研究结果为ghrelin作为脓毒血症的有效的治疗药物提供了证据。

二、Ghrelin在脓毒血症中的作用机制

近年来，尽管很多文献报道ghrelin有下调细胞因子的作用，但具体的作用机制尚不清楚。Ghrelin对脓毒症的保护机制可能是多种途径的。Alejo等发现ghrelin可以抑制脓毒症小鼠高迁移率族蛋白1（high mobility box 1，HMGB1）的释放并且能产生杀菌作用[10]。Chen等的研究则发现ghrelin可以通过增加一氧化氮的产生进而减弱脂多糖（lipopolysaccharide,LPS）诱导的急性肺部炎症和促炎性细胞因子的产生[11]。Ghrelin的作用是否通过其巨噬细胞的

受体还不知道。为了验证这个假说，Wu等用LPS刺激Kupffer细胞和腹腔巨噬细胞，当用LPS单独刺激这些细胞的时候，TNF-α和IL-6显著上升。相反，用ghrelin和LPS同时处理细胞的话，TNF-α和IL-6上升的幅度和LPS单独处理组一致。这些结果提示ghrelin在脓毒血症中的下降细胞因子的作用不是通过其巨噬细胞上面的受体其作用的[7]。

脓毒血症期间细胞因子上调引起的的肝功能的紊乱部分是因为交感激活从而导致肠释放去甲肾上腺素。在盲肠结扎穿孔(cecal ligation and puncture,CLP)引起的脓毒血症后2小时去甲肾上腺素和TNF-α的显著上升，静脉注射ghrelin显著降低了CLP后2小时的去甲肾上腺素和TNF-α，而在假手术组血浆去甲肾上腺素和TNF-α都没有明显的变化。另外，脑室内注射ghrelin显著降低了CLP后2小时循环中的去甲肾上腺素，而脑室内注射GHSR-1α拮抗剂可完全阻断ghrelin对血浆去甲肾上腺素的抑制作用，并部分阻断ghrelin对TNF-α水平的抑制作用。ghrelin处理显著增加脓毒症大鼠丝裂原活化蛋白激酶及其磷酸酶-1(mitogen-activated protein kinase phosphatase-1, MKP-1)mRNA水平和蛋白水平的表达，提示ghrelin对脓毒症时的TNF-α的抑制作用可能是通过MKP-1来调节的[12]。这些结果说明ghrelin在脓毒血症中降低TNF-α的保护作用至少部分是通过抑制交感神经激活来实现的。

大量的证据表明ghrelin是通过调控中枢和外周受体分布来调节其生理功能的，GHSR的广泛分布提示ghrelin作用的多种通路。其中一个研究发现结状神经节的传入神经存在GHSR，提示ghrelin信号是通过迷走传入神经传导到大脑的[13]。近期的研究发现在大鼠注射LPS后电刺激迷走神经可预防巨噬细胞的TNF-α的释放[14]。同时也发现对麻醉的大鼠中枢注射ghrelin可以刺激迷走传出神经。这些研究都发现迷走神经在ghrelin生理功能中的重要作用。

为了证实迷走神经是否与ghrelin在脓毒血症中的作用相关，研究者在脓毒血症5小时后行膈下迷走神经切断术观察ghrelin对脓毒血症动物TNF-α和IL-6的影响[7]。晚期脓毒症期间，迷走神经切断后立即注射ghrelin可完全预防ghrelin对循环中TNF-α和IL-6的抑制作用。相反，如果在迷走神经未切除的动物使用ghrelin则产生抗炎的作用。另外，迷走神经切断完全预防对腹腔液的TNF-α和IL-6的水平。而在迷走神经未切断的大鼠ghrelin显著降低腹腔液的细胞因子的水平。迷走神经切断术也消除了ghrelin对脓毒症导致的器官功能指标（如谷草转氨酶、谷丙转氨酶和乳酸）的保护作用。这些结果都提示ghrelin在脓毒血症中的作用是通过迷走神经来实现的。总结这些结果，ghrelin在脓毒血症中抑制炎症因子的保护作用可能通过激活迷走神经和抑制交感神经系统联合实现。

三、Ghrelin对脓毒症中年龄相关炎症的作用机制

脓毒血症的发病率和死亡率与年龄有正相关性。老年人免疫功能有下降，导致免疫反应的不足而引起发病率和死亡率上升[15]。然而，老年的免疫功能的损害可能与失控的炎症反应导致的过度的促炎性因子如TNF-α和IL-6的产生有关。年龄加强了内毒素血症中促炎症反应并加剧组织损伤[16]。研究发现血浆的ghrelin水平在老年大鼠显著上升，内毒素在老年大鼠相比年轻大鼠导致的ghrelin更多的下降。而老年大鼠相比年轻大鼠在背侧迷走神经复合体的基因和蛋白水平的ghrelin表达显著减少。但是注射ghrelin没有成功地保护内毒素的老年大鼠。

研究发现ghrelin通过刺激垂体GHSR-1a从而引起生长激素的释放。在人类，生长激素水平在25岁之后每10年下降约15%。生长激素随着年龄增长而下降，会引起诸多不良事件。基于此，Jacob等发现在老年大鼠相比于年轻大鼠血浆的生长激素水平显著下降。当用生长激素处理这些大鼠的时候，背侧迷走神经复合体ghrelin受体基因和蛋白的表达在老年大鼠显著增加[16]。然而，生长激素处理并不改变内毒素血症老年大鼠的细胞因子的水平和器官损伤标记物，这提示生长激素不能单独预防老年大鼠的高炎症状态[16]。相反，合用ghrelin和生长激素能显著下降老年大鼠的炎症反应和器官损伤，这提示因为生长激素下降引起的ghrelin低反应性与脓毒血症期间年龄相关的高炎症状态有关。

四、回顾与展望

Ghrelin对动物模型脓毒血症的治疗作用已经得到了肯定，它的出现为脓毒血症的治疗带来了新的思路，作为小分子活性肽，其抗炎的作用机理和常规抗生素完全不同，而且ghrelin的许多作用尚未完全开发。尽管ghrelin的发现给脓毒血症的治疗带来了新的思路，但其潜在的临床价值，仍有待进一步研究。

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Effect of Body Positioning on Intra-abdominal Pressure Measurement and Prognosis in Critically Ill Patients

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Abstract

Background: The current literatures confirm the widespread and frequent development of both intra abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) among the critically ill with a significant associated risk of organ failure and increased mortality. The occurrence of intra abdominal hypertension (IAH) during the intensive care unit stay was an independent outcome predictor. The Consensus Conference proposes intra-abdominal pressure (IAP) should be measured in the complete supine position, However, the supine position of ICU patients (＜30° of bed increase) presents a significant risk factor for ventilator-associated pneumonia. The potential contribution of head of bed (HOB) position in elevating IAP should be considered. The purpose of this study was to evaluate the effect of body positioning on intra-abdominal pressure measurement and the effect of IAP at different body positioning on prognosis in critically ill patients.

Methods: A prospective, cohort study to investigate the effect of patient positioning on IAP and prognosis was conducted on critically ill patients admitted to a medical–surgical intensive care unit (ICU). On admission, epidemiologic data and risk factors for intra-abdominal hypertension were studied; then, daily maximal intra-abdominal pressures (IAPmax), abdominal perfusion pressure, filtration gradient, Acute Physiology and Chronic Health Evaluation (APACHE) II score and sequential organ failure assessment (SOFA) score, were registered. IAPs were recorded through a bladder catheter every 4 hrs in first day. IAP was measured in a range of patient HOB increases from 0° to 45°. Intra-abdominal hypertension was defined as IAP >12 mm Hg. Abdominal compartment syndrome was defined as IAP >20 mm Hg plus >1 new organ failure. Main outcome measure was hospital mortality.

Results: The main results of this study are the high incidence of IAH (27.8%) in a prospective cohort of consecutive ICU patients; a significant and independent relationship between IAP and HOB increases. Considering the absolute numbers of IAP, the differences for 10° and 20° were small, whereas the differences for 30° and 45° become clinically relevant; APACHE II and SOFA scores, abdominal perfusion pressure (APP) and filtration gradient (FG) at each body position differed significantly between survivors and non-survivors; length of mechanical ventilation, length of ICU stay, APACHE II,SOFA scores, APP and FG at HOB increases of 30° and 45° differed significantly between MODS group and Non-MODS group; there are significant correlations between APP or FG and APACHE II, SOFA, Length of Mechanical ventilation, Length of ICU stay.

Conclusions: Our study expands previous knowledge in several ways. First, it provides a prospective, well-documented approach to the epidemiology and the risk factor of IAH in a heterogeneous ICU population. Second, there is a significant and independent relationship between IAP and HOB positioning in critically ill patients, whereas the differences for 30° and 45° become clinically relevant. Third, APP and FG are associated with a higher rate of multiple organ failure and mortality. The potential contribution of body position in elevating IAP should be considered in patients with the risk factor for IAH and ACS in critically ill patients.

Key words:Abdominal compartment syndrome; Intra-abdominal hypertension; Intra-abdominal pressure measurement; body positioning; prognosis; abdominal perfusion pressure and filtration gradient

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Intra-abdominal pressure (IAP) is increasingly considered to be an important physiologic parameter in critically ill patients. The current literatures confirm the widespread and frequent development of both intra abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) among the critically ill with a significant associated risk of organ failure and increased mortality[1,2]. The occurrence of intra abdominal hypertension (IAH) during the intensive care unit stay was an independent outcome predictor[3,4]. This second installment from the 2004 International ACS Consensus Conference proposes Definition and treatment guidelines for the Definition, diagnosis, management, and prevention of IAH and ACS as well as recommendations for future clinical investigation[5,6]. Both of these documents highlight the significant need for well-designed, prospective clinical trials to clarify the many questions and issues that remain unanswered with respect to IAH and ACS[6].

As IAP measurement techniques have evolved, several key questions have arisen including the optimal intravascular saline instillation volume, the proper zero reference position for transducer placement (symphysis

pubis, mid-axillary, or phlebostatic axis), and the proper body position for IAP measurements. Although previous studies have provided answers to the first two questions, this study addresses this last and very important question. The purpose of this study was to evaluate the effect of body positioning on intra-abdominal pressure measurement and the effect of IAP at different body positioning on prognosis in critically ill patients.

METHODS

Study Design

A prospective, cohort study to investigate the effect of patient positioning on IAP was conducted on critically ill patients admitted to the Peking University Third Hospital medical–surgical ICU after approval by the Institutional Ethics Board.

Patient Selection

Patients were included in the study if they were aged ≥18 years, sedated and on mechanical ventilation, and demonstrated at least one risk factor for IAH or ACS. Either written informed consent or a waiver of informed consent, as determined by the study site's institutional review board, was also required. Patients were excluded if they were unable to tolerate changes in body position (because of spinal precautions, intracranial hypertension, hemodynamic instability, etc) or intravascular pressure measurements were contraindicated (such as recent bladder surgery, injury or pregnancy).

TABEL 1.Patient demographics

Patients	54
Age (yrs)	66.17 ± 13.69
Male gender (%)	57.4%
Etiology of critical illness (%)	
Medical	32
Surgical	68
Severity of illness scores	
APACHE II	14.11 ± 9.30
SOFA	7.26 ± 3.37
Intra-abdominal hypertension (%)	27.8
Abdominal compartment syndrome (%)	1.8
Abdominal decompression (%)	0
Pulmonary aspiration	0
Length of Mechanical ventilation (hours)	159.59 ± 310.76
Length of ICU stay (days)	8.19 ± 14.05
Survival to intensive care unit discharge (%)	90.7

Data Collection

On admission, age, sex, clinical/surgical status, diagnoses, antecedent of trauma, presence of IAH risk factors, Acute Physiology and Chronic Health Evaluation (APACHE) II score[7], expected mortality, and Sequential Organ Failure Assessment (SOFA) score were recorded[8]. Use and length of mechanical ventilation, and of ICU stay, were calculated. Patient survival to intensive care unit discharge was recorded.

Measurements

Intra-abdominal pressure was measured in millimeters of mercury through a Foley bladder catheter (the bladder technique). The aspiration port was attached to a short 18-G catheter with three stopcocks connected to an intravenous infusion set, a syringe for flushing and draining the tubing system, and a pressure transducer. After clamping the tube leading to the collection bag, 25 ml of saline was injected into the bladder[9] and IAP was measured at end expiration at each body position (supine, 10°, 20°, 30°, 45° head of bed elevation) and with the transducer zeroed at the level of the midaxillary line at the iliac crest[10]. The procedure was repeated after 3 mins, and the mean of the two measurements was used for calculations. IAP was recorded every 4 hrs (8:00 a.m., 12:00 p.m., 4:00 p.m., 8:00 p.m., 0:00 a.m., and 4:00 a.m.) in first day, the highest daily value was considered for main analysis. Mean arterial pressure was recorded simultaneously, abdominal perfusion pressure (APP) and filtration gradient (FG) were calculated simultaneously. All measurements were performed by two of the researchers.

TABEL 2.Risk factors for intra-abdominal hypertension/ abdominal compartment syndrome

Mechanical ventilation (%)	100
Positive end-expiratory pressure (%)	100
Fluid resuscitation (%)	71
Abdominal surgery (%)	50
Hypotension	37
Sepsis (%)	30
Acidosis (%)	20
Abdominal infection (%)	19
Respiratory failure(%)	18
Coagulopathy (%)	15
Gastroparesis/ileus (%)	11
Polytransfusion (%)	2

TABEL 3.The comparisons of IAP among body position

body position	SE	95% CI	t	p
0° versus 10°	0.0446	-0.16 — 0.0155	-1.659	0.103
0° versus 20°	0.0613	-0.33 — -0.0807	-3.322	0.002
0° versus 30°	0.24	-4.46 — -3.50	-16.583	0.000
0° versus 45°	0.35	-7.05 — -5.83	-18.446	0.000
10° versus 20°	0.0532	-0.24 — -0.023	-2.438	0.018
10° versus 30°	0.22	-4.34 — -3.47	-18.022	0.000
10° versus 45°	0.33	-7.13 — -5.80	-19.468	0.000
20° versus 30°	0.24	-4.26 — -3.30	-15.814	0.000
20° versus 45°	0.35	-7.03 — -5.63	-18.163	0.000
30° versus 45°	0.19	-2.93 — -2.18	-13.717	0.000

Statistical Analysis

SPSS 10.0 software was used to process the data. All data were expressed as mean ± standard deviation (SD). A student's t test was used for evaluating statistical significance. Linear correlation analysis was used for correlation analysis. A P value less than 0.05 was considered as a significant difference between the values compared.

RESULTS

Patient enrollment occurred from March 1, 2009 to August 31, 2009. During the study period, 292 patients were admitted to the ICU and 233 were excluded from the protocol for the following reasons: six were ＜18 yrs, eleven were pregnant or lying-in women, 74 were spinal precautions, 52 had bladder or renal surgery, 16 patients were unable to tolerate the 30° and 45° head of bed elevation position of measurements due to their critical illness. 67 were in weaning during ICU stay first 24 hrs, and seven did not require urinary catheterization. Fifty-nine patients fulfilled the inclusion criteria for IAP measurement. The entire protocol of IAP measurements was completed in 54 patients (91%). A total of 432 IAP measurements were performed.

Demographics and risk factors for IAH/ACS

Patient demographics and severity of illness are presented in Table 1. The prevalence of IAH and ACS are 27.8% and 1.8% respectively, only one patient developed ACS. The risk factors for IAH that justified patient enrollment are listed in Table 2. 9.3 percent of the study patients died due to the following reasons: multiple system organ failure, 60%; severe sepsis, 20%; and cardiogenic shock, 20%.

IAP measurements for each body position were

TABEL 4.The comparison of survivors vs nonsurvivors in all the study population

Variable	Survivors	Nonsurvivors	t	p
APACHE II	12.88±8.56	26.20±8.07	-3.328	0.002
SOFA	6.73±3.07	12.40±1.14	-4.072	0.000
Length of Mechanical ventilation (hours)	142.57±314.69	326.40±229.95	-1.267	0.211
Length of ICU stay (days)	7.73±14.36	13.60±9.58	-0.089	0.378
IAP0°	9.57±3.45	10.00±5.70	-0.249	0.804
IAP10°	9.65±3.55	10.00±5.70	-0.197	0.845
IAP20°	9.78±3.74	10.20±6.10	-0.228	0.821
IAP30°	13.57±3.83	15.00±4.30	-0.787	0.435
IAP45°	16.12±4.32	18.20±4.09	-1.029	0.308
APP0°	77.98±13.19	53.40±6.43	4.092	0.000
APP10°	76.43±12.33	51.00±6.71	4.517	0.000
APP20°	73.53±12.44	46.80±6.53	4.712	0.000
APP30°	71.27±12.77	41.80±3.96	11.587	0.000
APP45°	67.43±14.08	38.40±3.21	11.747	0.000
FG0°	68.41±14.40	43.40±7.64	3.806	0.000
FG10°	65.65±13.37	41.00±7.87	4.030	0.000
FG20°	61.47±13.93	36.60±7.96	3.904	0.000
FG30°	57.78±14.51	26.80±5.50	4.706	0.000
FG45°	51.14±16.33	20.20±4.09	10.440	0.000

compared

The data for effect of HOB elevation on bladder pressure measurements are summarized in Table 3. HOB increase was found to be significantly associated with IAP, with stronger correlations at HOB increases of 30° and 45°.

The comparison of survivors vs nonsurvivors in all the study population

When analyzing all patients, nonsurvivors exhibited higher APACHE Ⅱ and SOFA scores, higher IAP and lower APP and FG at each body position than survivors. Briefly, APACHE Ⅱ and SOFA scores, APP and FG at each body position differed significantly between survivors vs nonsurvivors (Table 4).

The comparison of MODS group vs Non-MODS group in all the study population

When analyzing all patients, MODS group exhibited Longer length of mechanical ventilation and length of ICU stay, higher APACHE Ⅱ and SOFA scores, higher maximal IAP and lower APP and FG at each body position than Non-MODS group. Briefly, length of mechanical ventilation, length of ICU stay, APACHE, SOFA scores, APP and FG at HOB increases of 30° and 45° differed significantly between MODS group and Non-MODS group (Table 5).

The correlations between IAP measurements and prognosis

There isn't any significant correlation between IAP measurements and APACHE II, SOFA, Length of Mechanical ventilation, Length of ICU stay. However, there are significant correlations between APP or FG and APACHE II, SOFA, Length of Mechanical ventilation, Length of ICU stay (Table 6).

DISCUSSION

IAP measurements are essential to the diagnosis and management of both IAH and ACS. Given the prevalence of elevated intra-abdominal pressure (IAP) as well as earlier detection and appropriate therapeutic management of IAH and ACS, significant decreases in patient morbidity and mortality have been achieved[2]. Increased recognition of elevated IAP prevalence, combined with recent advances in the diagnosis and management of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) has resulted in significantly improved

TABEL 5.The comparison of MODS group vs Non-MODS group in all the study population

Variable	Non-MODS group	MODS group	t	p
APACHE II	10.42±4.38	28.55±9.50	6.163	0.000
SOFA	6.12±2.17	11.73±3.58	4.969	0.000
Length of Mechanical ventilation (hours)	66.00±126.67	525.45±509.45	2.968	0.014
Length of ICU stay (days)	4.02±5.14	24.91±23.44	2.938	0.014
IAP0°	9.40±3.82	10.45±2.77	0.860	0.394
IAP10°	9.47±3.91	10.55±2.88	0.856	0.396
IAP20°	9.60±4.15	10.64±3.01	0.772	0.443
IAP30°	13.37±4.12	15.00±2.28	1.257	0.214
IAP45°	15.79±4.49	18.36±2.77	1.807	0.077
APP0°	77.49±14.56	68.73±12.96	-1.818	0.075
APP10°	75.65±13.67	67.91±14.26	-1.662	0.103
APP20°	73.12±13.76	63.00±14.09	-2.166	0.035
APP30°	70.56±14.64	60.64±14.01	-2.022	0.048
APP45°	66.74±16.04	56.91±13.13	-1.875	0.048
FG0°	68.09±15.81	58.27±12.95	-1.899	0.063
FG10°	65.12±14.80	56.55±13.22	-1.749	0.086
FG20°	61.09±15.02	51.64±14.58	-1.874	0.067
FG30°	57.28±16.49	45.64±14.03	-2.148	0.036
FG45°	50.72±18.38	38.73±13.30	-2.026	0.048

TABEL 6.The correlations of IAP measurements and prognosis

IAP measurements	APACHE II	SOFA	Length of Mechanical ventilation	Length of ICU stay
IAP0°	0.127	0.077	0.019	0.028
IAP10°	0.126	0.072	0.013	0.024
IAP20°	0.116	0.059	0.025	0.031
IAP30°	0.213	0.191	0.004	0.013
IAP45°	0.264	0.194	0.074	0.094
APP0°	-0.385*	-0.418*	-0.195*	-0.202*
APP10°	-0.412*	-0.142*	-0.143*	-0.142*
APP20°	-0.424*	-0.424*	-0.143*	-0.145*
APP30°	-0.398*	-0.398*	-0.123*	-0.130*
APP45°	-0.341△	-0.341*	-0.118*	-0.137*
FG0°	-0.387*	-0.387*	-0.185*	-0.194*
FG10°	-0.411*	-0.411*	-0.126*	-0.129*
FG20°	-0.411*	-0.411*	-0.089*	-0.091*
FG30°	-0.407*	-0.407*	-0.113*	-0.121*
FG45°	-0.353*	-0.353*	-0.109*	-0.133*

△ $P<0.05$, *$P<0.01$

patient survival[11].

The main results of this study are the high incidence of IAH in a prospective cohort of consecutive ICU patients; a significant and independent relationship between IAP and HOB increases. Considering the absolute numbers of IAP, the differences for 10° and 20° were small, whereas the differences for 30° and 45° become clinically relevant; APACHE II and SOFA scores, APP and FG at each body position differed significantly between survivors vs nonsurvivors; Length of mechanical ventilation, length of ICU stay, APACHE II, SOFA scores, APP and FG at HOB increases of 30° and 45° differed significantly between MODS group and Non-MODS group; there are significant correlations between APP or FG and APACHE II, SOFA, Length of Mechanical ventilation, Length of ICU stay.

Epidemiology of Intra-abdominal Hypertension

The prevalence of IAH (27.8%) and ACS (1.8%) are lower than previously published trials. Malbrain et al[2] and Cheatham et al[12] found the prevalence of IAH was 58.8% and 46% in their study, respectively. We considered specific medical procedures to reduce IAP for the patient with risk factor for IAH/ACS in our ICU might play a role, for example, sedation, nasogastric decompression, enemas, fluid restriction, colloid, etc. Given the significant associated morbidity and mortality, IAP should be monitored in any patient who demonstrates risk factors for IAH/ACS. No patient developed aspiration as a result of being placed supine during the study.

The effect of body positioning on IAP measurement

The Consensus Conference proposes IAP should be measured in the complete supine position[5,6], However, the supine position of ICU patients (<30° of bed increase) presents a significant risk factor for ventilator-associated pneumonia[13]. Changes in body position (i.e., supine, prone, head of bed elevated) and the presence of both abdominal and bladder muscle contractions have also been demonstrated to impact upon the accuracy of IAP measurements[14]. Prone positioning for acute lung injury has also been demonstrated to significantly increase IAP[15]. As a result supine IAP measurements may underestimate the true IAP if the patient's head of bed is being elevated between measurements.

McBeth et al[16] demonstrated there is a significant, positive association between IAP and HOB positioning in critically ill patients. However, the study used a continuous IAP technique that is not widely used and for which the residual fluid volume within the bladder cannot be standardized. Vasquez et al[17] proposed elevating HOB significantly increases bladder pressure measurement. Bladder pressure measurements in no supine positions may not provide valid interpretation for IAP, and more so in cases of increased body mass index. However, the study used a saline instillation volume of 50 ml, which exceeds the currently recommended volume and could potentially have resulted in erroneously high IAP measurements .This study also did not report the zero reference point used. Our study also demonstrated head of bed elevation results in clinically significant increases in measured IAP. Clinically relevant changes in IAP occur at HOB increases>20°.So, the potential contribution of body position in elevating IAP should be considered in patients with moderate to severe IAH or ACS in critically ill patients. Furthermore, we suggested studies that involve IAP measurements should describe the patient's body position so that these values may be properly interpreted.

The effect of IAP at different body positioning on prognosis

Reduced organ perfusion pressure and interference with cardiopulmonary interactions account for the harmful effects of IAH. Several clinical scores not including IAP measurements have been proposed as independent predictors of mortality in critically ill patients. However, in liver transplant recipients an IAP＞25 mmHg and in trauma patients an IAP＞25 mmHg with at least one organ failure (i.e., defined as the abdominal compartment syndrome, ACS) were associated with a higher rate of multiple organ failure and mortality[18,19,20,21]. Regueira et al[22] demonstrated Septic shock patients have a very high incidence of IAH, which seems to be associated with the severity of shock and could be related to the development of organ dysfunctions, particularly renal dysfunction. Cheatham[23] showed that abdominal perfusion pressure (APP) (i.e., the mean arterial blood pressure minus the IAP) was a better resuscitation end point compared with the only single measurement of the arterial blood pressure. Our study also showed APACHE II and SOFA scores, APP and FG at each body position differed significantly between survivors vs nonsurvivors, although IAP at each body position didn't differ significantly between two groups; length of mechanical ventilation, length of ICU stay, APACHE II, SOFA scores, APP and FG at HOB increases of 30° and 45° differed significantly between MODS group and Non-MODS group, although IAP at each body position didn't differ significantly between two groups; There are significant correlations between APP or FG and APACHE II, SOFA, Length of Mechanical ventilation, Length of ICU stay. Therefore, there is a strong physiological basis for considering IAP and derived variables as "vital signs" to monitor in the critically ill and to be added eventually to predictive scores. This validation, however, should be performed in prospective, multiple-center, and preferably international studies.

CONCLUSIONS

Our study expands previous knowledge in several ways. First, it provides a prospective, well-documented approach to the epidemiology and the risk factor of IAH in a heterogeneous ICU population. Second, there is a significant and independent relationship between IAP and HOB positioning in critically ill patients, whereas the differences for 30° and 45° become clinically relevant. Third, APP and FG are associated with a higher rate of multiple organ failure and mortality. The potential contribution of body position in elevating IAP should be considered in patients with the risk factor for IAH and ACS in critically ill patients.

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Lithium Chloride Inhibited Neuronal Apoptosis and Glycogen Synthase Kinase -3β Activities in Hippocampal CA1 Area After Middle Cerebral Artery Occlusion and Reperfusion in Rats

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Abstract

Background: Lithium pretreatment has been proved to be neuro-protective. Post-ischemia conditioning attracted more and more attention during the last years. This study was designed to observe the effect of lithium post-treatment on neuron apoptosis and glycogen synthase kinase(GSK)-3βin rats after middle cerebral artery occlusion(MCAO).

Methods: The right middle cerebral artery was occluded with a nylon suture for 90 mins. Rats were randomly divided into NO group, SH group，IR group，Li1 group（1mmol/kg）, Li2 group（2mmol/kg）, and Li3 group（3mmol/kg）. Animals in each group were killed 6 hours, 1 day, 3day, or 7days after cerebral ischemia, with six rats in each time point. Neuron apoptosis in the CA 1 region were examined by Hoechst staining. The expression and distribution of GSK-3βand p-GSK-3β(Ser9）was examined by immunofluorescence analysis.

Results: The apoptotic nuclei was detected significantly in IR groups compared with SH group(P<0.01), which peaked one day later and then declined gradually in all groups. Compared with IR group, the number of apoptotic nuclei reduced in groups treated with lithium chloride dose dependently (P<0.01).

There was no visible difference in the total amounts of GSK-3beta between any of the two groups or between any of the two time point (P>0.01) .

The amounts of P-GSK-3β（Ser9）seemed increased with the time and they were higher in IR groups than those in SH groups (P<0.01). Lithium post-treatment reinforced this tendency dose-dependently (P<0.01).

Conclusion: Lithium chloride can dose-dependently (1～3 mmol/kg) suppress neuron apoptosis and GSK-3βafter MCAO/ reperfusion injury.

Key words: apoptosis；lithium chloride；glycogen synthase kinase -3β；middle cerebral artery occlusion

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INTRODUCTION

Lithium, a major drug used for bipolar mood disorder, has been proved to have neuroprotective properties in recent decades. Though the underlying mechanism remains unclear, increasing evidence from both in vitro and in vivo studies have confirmed that lithium can antagonize the neuronal apoptosis caused by multiple factors[1-3]. The neuroprotective mechanisms of lithium are complex, likely involving multiple mechanisms such as inactivation of N-methyl-D-aspartate (NMDA) receptors, changes in the expression of pro-apoptotic and anti-apoptotic genes as well as activation of cell survival factors[1, 2, 4], super-induction of heat shock protein 70 (HSP70)[5], but inhibition of ischemia-induced up-regulation of Bax and caspase-3[6]. Our previous research also demonstrated that the long-term lithium pretreatment on cerebral ischemia in gerbils indeed had a protective effect, which might be related to the down-regulation of pro-apoptotic p53, but up-regulation of anti-apoptotic Bcl-2 and heat shock protein 70 (HSP70) in the CA1 hippocampal area of ischemic gerbil[7].

During the last years, ischemia postconditioning got more and more attention and lithium post-treatment was proven to be effective in decreasing cerebral ischemic injury in the rat ischemia model of stroke using middle cerebral artery occlusion(MCAO)[5, 6, 8]. The neuroprotective mechanism of lithium post-treatment involve super-induction of heat shock protein 70 (HSP70)[5], but inhibition of ischemia-induced up-regulation of Bax and caspase-3[6].

Glycogen synthase kinase-3β (GSK-3β),the phosphorylation kinase of glycogen synthase (Glycogen Synthase, GS)[9],had recently been found to play very important roles in many physiological and pathological

processes. Inactivated GSK-3 β promotes self-renewal of murine embryonic stem cells[10]. GSK-3 β reduce phosphorylation of tau, which had been certificated play an important role in suppressing Alzheimer's disease[11, 12]. GSK-3beta inhibitors could obliterated proinflammatory NF-kappaB[13] activation and inflammatory injury in chronic renal allograft disease[14]. Furthermore, inhibition of glycogen synthase kinase 3 β could suppress proliferation and survival of some cancer cells[15-19].

GSK-3 β has also been found to play important role in regulation of apoptosis, such as Activation of p53 gene[9] and inhibition of heat shock factor 1 (HSF1)[20]. GSK-3 β was proven to be downstream regulatory factor of protein kinase B[21, 22], but little information is available on the effects of lithium to GSK-3 β in the rat ischemia model of middle cerebral artery occlusion. Vulnerable to cerebral ischemia, the hippocampus CA1 area was selected. The objective of this study was to investigate the effects of lithium post-treatment on the GSK-3 β induced by cerebral ischemia, as well as apoptosis in the CA1 area of the rat hippocampus.

MATERIALS AND METHODS

Rats and grouping

One hundred and twenty-six male Sprague-Dawley rats of specific pathogen Free, weighing 280-320g , aging 18-22 weeks, were randomly divided into normal group (NO group, n=6), sham-operation group (SH group, n=24), ischemia-reperfusion group (IR group, n=24), lithium chloride 1mmol/kg treatment group (LI1 group, n=24), lithium chloride 2mmol/kg treatment group (LI2 group, n=24), lithium chloride 3mmol/kg treatment group (LI3 group, n=24). Except for the normal group, the others were further divided into four sub-groups by different observation time points (6hours, 1day, 3days, and 7days after MCAO), with 6 rats in each sub-group. No treatments were given to the rats of normal group. The appropriate dose (1mmol/kg, 2mmol/kg, 3mmol/kg) of lithium chloride were given to the rats of lithium chloride treatment groups intraperitoneally immediately after reperfusion. Then, the same dose of lithium chloride was repeated to all rats of Li groups every 24 hours till the rats were killed. The rats in ischemia-reperfusion group and sham operation group were intraperitoneally injected of an equal volume of 0.9% saline.

Middle cerebral artery occlusion

Rats were anaesthetized with 0.25ml/100g body weight 2% sodium pentobarbital intraperitoneally. The rats' body temperature was maintained at 37° C with an infrared heat lamp and a heating pad.

The basic surgical procedure, introduced by Longa, E.Z. et al[23], consisted of blocking blood flow into the middle cerebral artery (MCA) with an intraluminal suture introduced through the extracranial internal carotid artery (ICA). Under the operating microscope, the right common carotid artery (CCA) was exposed through a midline incision; a selfretaining retractor was positioned between the digastric and sternomastoid muscles, and the omohyoid muscle was divided. The occipital artery branches of the external carotid artery (ECA) were then isolated and coagulated. Next, the superior thyroid and ascending pharyngeal arteries were dissected and coagulated. The ECA was dissected further distally and coagulated along with the terminal lingual and maxillary artery branches, which were then divided. The ICA was isolated and carefully separated from the adjacent vagus nerve. Further dissection identified the ansa of the glossopharyn geal nerve at the origin of the pterygopalatine artery; this posteriorly directed extracranial branch of the ICA was ligated with 7-0 nylon suture close to its origin. At this point, the ICA is the only remaining extracranial branch of the CCA. A small hole was made on the stump of the right ECA carefully after the right ICA and CCA were clamped by vascular clamps. Single-strand nylon suture of 3-0 was inserted in MCA through the right external carotid artery stump. Then, the vascular clamps were relaxed and the nylon line continued to be pushed forward to cranium till a slight feeling of resistance. The length of the nylon suture in the internal carotid artery was about 20±3mm from the carotid artery bifurcation. The middle cerebral artery blood flow was blocked in this way. The removal of nylon after 90 minutes meaned reperfusion. Except the filament depth of nylon sutures were less than 15mm, the other surgical procedure of rats in sham-operated group were the same as that of rats in ischemia-reperfusion group.

Specimen collection

Rats in each group were deeply anesthetized with sodium pentobarbital at the scheduled time points. Then its' chests were incised and its' hearts were revealed. Special blunt thick needles were inserted through the left ventricle from the apex of the ascending aorta infusion line. The right atrial appendage were incised. About 150ml normal saline (37℃) was perfused quickly into the left ventricle through the needle, in order to break through all of the blood. Then about 500ml of 4% paraformaldehyde phosphate buffer solution (4℃,0.1mol/L, PH=7.4) was perfused to fix the brain for 2 hours. The brains were taken out and thrown into the paraformaldehyde phosphate buffer solution. After 2~4hours, the brains were transferred to 30% sucrose for 3~5days. Coronal slices of 10 μm were cuted from the fixed brains in frozen slicer. Six slices of hippocampal dentate gyrus plane , that is 1.7mm-4mm behind optic chiasma of every brain were randomly selected for observation.

Immunofluorescence staining of GSK-3βand p-GSK-3β

Slices were placed in 24-well plate. After washed by PBS solutions, slices were mixed with 10% normal goat serum in the plate for an hour. Then the goat serum was discarded. Thereafter, polyclonal goat anti-p-GSK-3 β (Ser9) and polyclonal goat anti-GSK-3 β , both diluted to1:100 by 0.01M PBS dilution, were added in the plate. The plates were placed in refrigerator (4℃) for one night. The next day, slices were washed by PBS for three times in the plate, and 5 minutes for each time. Then, the anti-goat IgG-FITC (diluted to 1:200 by PBS) and anti-rabbit IgG-Cy3 (diluted to 1:1000 by PBS) were placed in the plate at 37℃ for 1 hour. Last slices were again washed by PBS for three times in the plate, and 5 minutes for each time.

Hoechst staining

After the above process, slice continued to be stained with Hoechst33258 according to kit instructions in 24-well plate. Slices were washed by PBS for 2 times in the plate, and 3 minutes for each time. After PBS solution was removed, 0.5ml of Hoechst33258 was added in the plate to stain the slices. Five minutes later, Slices were washed again by PBS for 2 times in the plate, and 3 minutes for each time. Last, the stained slices were carefully moved to slide, and were sealed with anti-fluorescence quenching liquid. Three randomly chosen high power field of vision (× 400) of each slice were observed and took photographs in the red, green, and blue of fluorescence under Fluorescence microscopy.

TABEL 1.the number of apoptotic cells in hippocampal CA1 area of each group at different time points ($\bar{x}\pm s$, n=6, 0.05mm^2)

	MCAO6h	MCAO1d	MCAO3d	MCAO7d
NO	0.7±0.8	--	--	--
SH	0.7±0.8	0.5±0.6	0.7±0.8	0.8±0.8
IR	14.3±1.0^{**++}	21.8±0.7**	16.6±0.8^{**++}	12.3±0.8^{**++}
Li1	8.6±0.8$^{**\#\#}$	15.2±0.8$^{**\#\#}$	9.8±0.8$^{**\#\#}$	9.3±1.0$^{**\#\#}$
Li2	6.2±0.8$^{**\#\#\blacktriangle\blacktriangle}$	12.5±1.1$^{**\#\#\blacktriangle\blacktriangle}$	8.2±0.8$^{**\#\#\blacktriangle}$	6.8±0.8$^{**\#\#\blacktriangle\blacktriangle}$
Li3	6.0±0.9$^{**\#\#\blacktriangle\blacktriangle}$	10.5±0.6$^{**\#\#\blacktriangle\blacktriangle\triangledown\triangledown}$	6.5±0.6$^{**\#\#\blacktriangle\blacktriangle\triangledown}$	5.7±0.8$^{**\#\#\blacktriangle\blacktriangle\triangledown}$

Compared with the SH group, **P<0.01; Compared with the IR group, $^{\#\#}$P<0.01; Compared with the Li1 group, $^{\blacktriangle}$P<0.05, $^{\blacktriangle\blacktriangle}$P<0.01; Compared with the Li2 group, $^{\triangledown}$P<0.05, $^{\triangledown\triangledown}$P<0.01; Compared with the MCAO1d, $^{++}$P<0.01

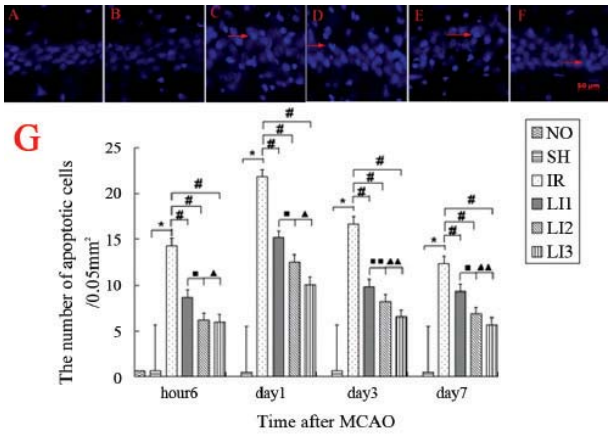

Figure 1: Lithium post-treatment decreases the apoptotic cells of CA1 areas in rats following middle cerebral artery occlusion. Hoechst staining, Magnification = 400, Scale = 50μm. Arrow points densely stained apoptotic nuclei. The Hoechst staining of CA1 region in groups NO(A), group SH(B), group IR(C), group LI1(D), group LI2(E) and group LI3(F) on day 1 after MCAO of rats. The number of compact fluorescent particles blocks can be observed obviously in hippocampal CA1 area 6 hours after the onset of ischemia, and reached it's peak on day 1 after the onset of ischemia, which was followed by a gradual decline at day 3 and day 7. Lithium post-treatment dose-dependently reduced the number of apoptosic cells in the dose range of 1 ~ 3mmol/kg after the onset of ischemia(G). Comparison with SH group,*P<0.01; comparison with IR groups, #P<0.01; comparison with LI1 groups, ■P<0.01, ■■P<0.05; comparison with LI2 groups, ▲P<0.01, ▲▲P<0.05..

Statistical methods

All photos were treated and analyzed with imageJ1.36b software. All data were expressed in the form of mean ± standard deviation. One-way ANOVA analysis was down by STATA 8.2, scheffe method was used to do pairwise comparison. P <0.05 was considered to be significant.

RESULTS

Detection of Apoptosis

Hoechst staining was employed to assess apoptosis in hippocampal CA1 area of rats following ischemic insult. Chromatin in apoptotic cells was dyed into compact fluorescent particles block by Hoechst33258. There were few compact fluorescent particles blocks in hippocampal CA1 area of rats in normal group or shame operation group. However, compact fluorescent particles blocks were abundant in the CA1 area of the IR group, and the blocks was robustly decreased by lithium treatment after ischemia. The number of apoptotic cells in Li2 group was less than that in Li1 group. The number of apoptotic cells in Li3 group was less than that in Li2 group. (Tab.1, Fig.1)

Detection of Phospho- Glycogen synthase kinase-3β

The expression and distribution of p-GSK-3 β (Ser9) in the cell was examined by indirect immunofluorescence staining. Marked with fluorescein isothiocyanate(FITC), p-GSK-3 β (Ser9) was dyed green. Only a few green particles appeared in the cytoplasm of the hippocampal CA1 area in SH and NO groups. Ischemia-reperfusion increased the p-GSK-3 β (Ser9) expression, especially in the nucleus. After the application of lithium chloride, p-GSK-3 β (Ser9) expression continued to rise. The number of p-GSK-3 β (Ser9) positive particles in Li2 group was less than that in Li1 group. The number of p-GSK-3 β (Ser9) positive particles in Li3 group was less than that in Li2 group. (Tab.2, Fig .2)

Detection of Glycogen synthase kinase-3β

Stained with Cy3, Glycogen synthase kinase-3 β was dyed red in indirect immunofluorescence staining. There was no statistic difference in the number of GSK-3 β positive particles in hippocampal CA1 area of rat in each group. There were more Cy3 positive reactions in the cytoplasm, but less in nucleus in NO group and SH groups. A large number of Cy3 positive granules in the nucleus could be seen in IR groups and Li groups. The distributions of GSK-3 β -positive particles in cells were similar in each

TABEL 2.The number of p-GSK-3β (Ser9) positive particles in hippocampal CA1 area of each group at different time point（$\bar{x}\pm s$，n=6, 0.05mm²）

	MCAO6h	MCAO1d	MCAO3d	MCAO7d
NO	24.0±8.3	--	--	--
SH	27.5±8.9	27.2±8.9	25.5±8.0	27.2±7.9
IR	87.5±7.5**	113.3±8.2**	154.0±11.4**	201.0±9.9**
Li1	124.7±13.7**##	160.5±10.8**##	204.0±12.5**##	235.8±5.2**##
Li2	151.3±12.7**##▲▲	185.3±12.6**##▲▲	235.5±10.8**##▲▲	256.3±12.1**##▲
Li3	181.7±8.6**##▲▲▽▽	215.3±4.2**##▲▲▽▽	257.8±9.8**##▲▲▽	280.2±11.9**##▲▲▽▽

Compared with the SH group，**P<0.01；Compared with the IR group，##P<0.01；Compared with the Li1 group，▲P<0.05，▲▲P<0.01；Compared with the Li2 group，▽P<0.05，▽▽P<0.01

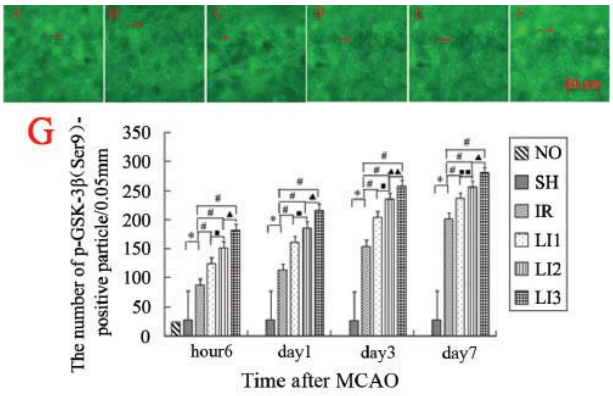

Figure 2: Lithium post-treatment dose dependently increased the expression of p-GSK-3β (Ser9) in hippocampal CA1 areas after MCAO. Immunofluorescence staining, Magnification = 400, Scale=50m. Arrow points p-GSK-3β(Ser9)-positive particles. Immunofluorescence staining of p-GSK-3β (Ser9) by FITC of CA1 region in groups NO(A), group SH(B), group IR(C), group LI1(D), group LI2(E) and group LI3(F) on day 1 after MCAO of rats. P-GSK-3β(Ser9)-positive particles within the nucleus increased gradually from A to F. The number of p-GSK-3β(Ser9)-positive particles in 0.05mm2 of corresponding areas was calculated(G). The amounts of p-GSK-3β(Ser9)-positive particles in CA1 areas of rats in IR goups were significantly higher than that in the respective SH groups, but were significantly lower than that in the respective LI groups. compared with SH group ,* p <0.01; compared with the respective IR group ,* p <0.05; comparison with LI1 groups,■P<0.01, ■■P<0.05; comparison with LI2 groups,▲P<0.01, ▲▲P<0.05..

TABEL 3.The number of GSK-3β positive particles in hippocampal CA1 area of each group at different time point （$\bar{x}$±s，n=6, 0.05mm²)

	MCAO6h	MCAO1d	MCAO3d	MCAO7d
NO	626.3±38.7	--	--	--
SH	633.7±41.4	615.3±22.6	616.2±58.3	638.7±32.2
IR	619.2±36.7	609.2±36.2	648.8±46.5	630.3±26.2
Li1	607.0±36.1	626.2±44.6	641.0±50.1	617.0±34.6
Li2	623.8±34.9	656.3±39.0	596.5±31.4	595.0±45.2
Li3	628.8±19.3	613.5±23.5	627.7±47.1	623.0±36.7

IR and Li group.(Tab.3, Fig 3)

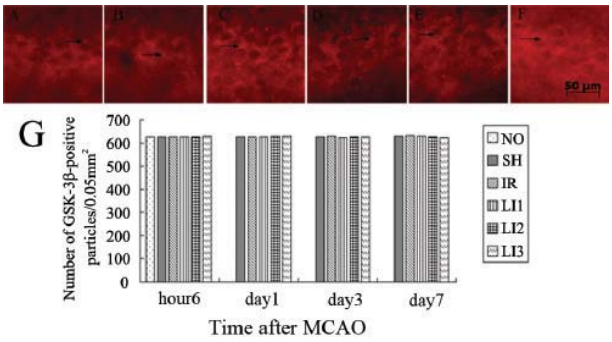

Figure 3: Lithium post-treatment did not affect the amount of GSK-3β. Immunofluorescence staining, Magnification = 400, Scale=50m. Arrow points GSK-3β-positive particles. Immunofluorescence staining of GSK-3β by Cy3 of CA1 region in groups NO(A), group SH(B), group IR(C), group LI1(D), group LI2(E) and group LI3(F) on day 1 after MCAO of rats. GSK-3β-positive particles within the nucleus increased after the onset of ischemia and lithium post-treatment. The number of GSK-3β-positive particles in 0.05mm² of corresponding areas has no statistical difference in each groups(G).

DISCUSSION

MCAO model is a commonly used focal cerebral ischemia model in experimental study. This model does not require craniotomy, and has a high success rate[23]. Most of the occurrence of cerebral ischemia is unpredictable, and the effective treatment comes usually after the reperfusion. So we blocked the right middle cerebral artery of Sprague-Dawley rats to established focal cerebral ischemia model, and give lithium chloride after reperfusion to observe the therapeutic effect of lithium.

According to Ren M, et al[5], the therapeutic dose of lithium should not exceed 3mmol/Kg, due to the toxic effects of neurons of lithium. Therefore, 1, 2 and 3mmol/Kg of lithium chloride were adopted to explore the effects of different doses of lithium chloride on the apoptosis and GSK-3β expression in this study. Hippocampal CA1 area, vulnerable area to the ischemia, was selected to observe the pathological changes caused by ischemia in this study.

There was significant apoptosis in ischemic hippocampal CA1 area of IR groups as early as 6 hour after ischemia. The number of apoptotic cells in hippocampal CA1 region of the lithium chloride treatment groups were significantly less than those in IR groups at the same point time, but still more than those in SH groups. And the dose of lithium chloride increased, the number of apoptotic cells reduced. These results suggested that lithium post-treatment still had a dose-dependent anti-neuronal apoptosis role after reperfusion .

The number of GSK-3β-positive granules in hippocampal CA1 areas of rats had no significant difference in each group. GSK-3β-positive granules were mainly distributed in the cytoplasm, and less in the nucleus in NO group and the SH group. While, there were a large number of GSK-3β in the nucleus of IR groups and LI groups. The number and the distribution of GSK-3β positive particles had no significant difference among the IR groups and LI groups at the same time points. So we can say that, MCAO-reperfusion did not alter the amount of GSK-3β, but the distribution of GSK-3β in the cells. In other words, GSK-3β transferred from the cytoplasm to the nucleus after MCAO-reperfusion. And lithium chloride had no effect on this kind change of GSK-3β. After its transferred to the nucleus, GSK-3β may participate in the following ways to regulate apoptosis: negative regulation of the transcription and expression of p53[24] and HSF1[20] gene, reduction of the expression of Bcl-2[25], modulation of survivin in subcellular redistribution[16].

P-GSK-3β (Ser9), the phosphate of GSK-3β on Ser9 site, was the inactivation form of GSK-3β. So the amount of P-GSK-3β (Ser9) were used to measure the activity of GSK-3β [24, 25]. Before ischemia, only a small amount of p-GSK-3β (Ser9) could be found in the cytoplasm of cells in the hippocampus ca1 areas. After ischemia, the number of P-GSK-3β (Ser9) was significantly increased,

especially in the nucleus. It was indicated that the activity of GSK-3 β was inhibited through the phosphorylation on ser9 site in order to reduce neuronal apoptosis. From this study, we can also see that lithium chloride post-treatment had dose-dependently promoted the phosphorylation of GSK-3 β in the hippocampus CA1 areas after ischemia-reperfusion. The mechanism of Lithium in promoting phosphorylation of GSK-3 β was still unclear, probably including the following several paths. (1)Lithium could activate phosphatidylinositol -3 kinase (PI-3K), which in turn activate protein kinase B (Akt)[22, 28] or protein kinase C (PKC)[27]. Then Akt and PKC phosphorylate GSK-3 β on site Ser9. (2) Lithium phosphorylate GSK-3 β on site Ser9 directly[29].

Our results suggested that the way that lithium inhibited GSK-3 β was not to affect the synthesis of GSK-3 β , but was to promote the phosphorylation on Ser9 sites of GSK-3 β in hippocampal CA1 area of rats after MCAO. This may be one of the mechanisms of lithium to resistant neuronal apoptosis.

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摘要

目的：探讨预注射氟比洛芬酯用于妇科腹腔镜手术超前镇痛的作用。方法：ASAI—II级择期妇科腹腔镜手术60例，随机分为治疗组和对照组各30例，对照组缝皮前不用任何镇痛药，治疗组缝皮前10—15min静脉注射氟比洛芬酯50mg，分别于术后1h(T1)，4h(T2)，8h(T3)对切口疼痛采用BCS评分标准，分为5分，当评分0分时给予哌替啶100mg肌肉内注射镇痛，记录两组术后使用哌替啶的时间，例数及次数，咽喉疼痛发生率等不良反应。结果：治疗组术后1，4，8小时疼痛评分均低于对照组(P＜0.01)，术后使用哌替啶的时间，例数及次数均低于对照组(P＜0.01)，治疗组和对照组咽喉疼痛发生率分别为15%和60%(P＞0.05)，两组的不良反应除恶心呕吐外差异无显著性(P＞0.05)。结论：氟比洛芬酯超前镇痛用于妇科腹腔镜手术，能有效缓解术后切口疼痛，减轻炎症反应，减少术后镇痛药的使用和不良反应，且术后苏醒迅速安全。

关键词：氟比洛芬酯，超前镇痛，妇科腹腔镜手术

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氟比洛芬酯超前镇痛在妇科腹腔镜手术中的应用

Flurbiprofen Ester Preemptive Analgesia in Gynecologic Laparoscopic Surgery

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Abstract

Objective: To study the preemptive analgesia of flurbiprofen ester in gynecological laparoscopic surgery.

Methods: 60 patients (ASAI-II) under elective gynecologic laparoscopic surgery were randomly divided into treatment group and control group (n=30). Control group without any pre-analgesic treatment; Treatment group: intravenous injection of flurbiprofen ester 50mg 10-15min before sewing leather. Score the pain level after 1h (T1), 4 h(T2), 8 h(T3) using the standard BCS, once patients at 0 score, intramuscular injection 100mg pethidine, recorded the time and frequency of each group, as well as the incidences of throat pain and other adverse reactions.

results: Pain scores of treatment group at 1,4,8 hours were lower than the control group(P＜0.01). The number and frequency of pethidine injection were lower in treatment group than control group(P＜0.01). The incidence of sore throat were 15%(treatment group) and 60% (control group) (P＞0.05). There were no significant difference of other adverse events between two groups except nausea and vomiting (P＞0.05).

Conclusion: Flurbiprofen ester pre-emptive treatment in gynecologic laparoscopic surgery can effectively relieve postoperative incisional pain, reducing inflammation reaction

Key Words: esters of flurbiprofen, preemptive analgesia, gynecologic laparoscopic surgery

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氟比洛芬酯(商品名凯纷，北京泰德制药有限公司生产)是静脉注射的非甾体类抗炎药(NSAIDS)，具有起效快，镇痛效果明显，持久，无呼吸抑制，胃肠道不良反应轻等优点。2009年6-12月通过预注射氟比洛芬酯用于妇科腹腔镜手术超前镇痛60例，观察其对术后切口痛的影响及不良反应，探讨其疗效及安全性。

一、资料与方法

1. 临床资料

ASAI-II级择期妇科腹腔镜手术60例，年龄25-54岁，体重45-68kg，卵巢囊肿剥离术12例，陈旧性宫外孕(病灶清除术)10例，粘膜下子宫肌瘤18例，子宫全切20例，随机分为治疗组和对照组各30例。排除支气管哮喘史，消化道溃疡史，严重的肝，肾及血液系统疾病。

2. 麻醉方法

麻醉诱导前静脉注射阿托品0.3-0.5mg，静吸复合麻醉，入室后开放外周静脉，诱导前输注8-10ml/kg复方乳酸钠林格液，常规监测生命体征。麻醉诱导用药咪达唑伦0.02-0.03mg/kg，芬太尼20-30ug/kg，丙泊酚1.5-2mg/kg，阿曲库铵0.3-0.4mg/kg诱导快速气管内插管，麻醉维持以1-1.5%异氟醚吸入，瑞芬太尼，丙泊酚持续微量泵泵入，必要时追加阿曲库铵5-10mg。术毕前30min停用异氟醚，缝皮前10-15min停止瑞芬太尼，丙泊酚，停药后随即予以治疗组静脉缓慢注射氟比洛芬酯50mg，对照组则不用任何镇痛药，手术结束5-10min后患者呼吸恢复，清醒后拔管。

3. 观察指标

术中常规监测血压(BP)，心率(HR)，心电图(ECG)，血氧饱和度(SPO_2)和呼气末二氧化碳分压($PetCO_2$)，术毕拔管送回病房观察。分别于术后1h(T_1)，4h(T_2)，8h(T_3)对切口疼痛采用BCS(Bruggmann Comfort Scole)评分标准，分为5分，当评分0分时给予哌替啶100mg肌肉内注射镇痛，记录两组患者术后使用哌替啶的时间，例数及次数，咽喉疼痛发生率等。并于术后第二天复查血常规，肝肾功能，凝血功能等指标。观察术后不良反应如恶心，呕吐，呼吸抑制，异常出血等。

4. 统计学方法

所有数据以均数±标准差(x±s)表示，采用SPSS11.0统计软件进行检验和检验，P＜0.05为差异有显著性。

二、结果

治疗组术后1，4，8小时疼痛评分明显低于对照组，术后初次使用哌替啶的时间，例数及次数均低于对照组(P＜0.01)，不良反应:咽喉疼痛，治疗组4例（15%），对照组11例(60%)(P＜0.05)，恶心呕吐发生情况:治疗组2例(6%)，对照组15例(50%)(P＜0.05)，头昏呼吸抑制的发生率对照组虽然增加趋势，但两组差异无显著性(P＞0.05)，治疗组术后第二天血常规，凝血功能，肝肾功能等各项指标均在正常值范围内与术前相比差异无显著性。

表1 一般资料(x±s)

组别	例数	年龄(岁)	体重(kg)	卵巢肿瘤	子宫肌瘤	宫外孕	子宫全切
治疗组	30	36.70±0.08	54.6±5.9	8	7	4	11
对照组	30	37.25±0.00	53.7±5.0	4	11	6	9

*P＞0.05

表2 术后各时点BCS评分及镇痛药应用情况(x±s)

手术后各时点BCS评分					手术后应用哌替啶情况		
组别	例数	T1	T2	T3	初次使用时间	例数	次数
治疗组	30	3.61±0.08	3.75±0.09	3.77±0.10	14.3±2.8	4	7
对照组	30	1.48±0.05*	1.66±0.07*	2.01±0.09*	4.2±0.7*	13*	21*

*P＜0.05

表3 术后咽喉疼痛及不良反应发生率(x±s)

		咽喉疼痛	恶心呕吐	头晕嗜睡	呼吸抑制	出血量
组别	例数	例	例	例	例	ml
治疗组	30	4(13.3%)	2(6.67%)	1(3.33%)	0(0.0%)	52.0±4.5
对照组	30	1(36.7%)*	15(50.0%)*	3(10.0%)	3(10.0%)	48.0±5.5

*与对照组比较，P＜0.05

三、讨论

妇科腹腔镜手术因其创伤小，术后恢复快而被临床广泛应用，二氧化碳气腹导致患者术后出现的肩部酸痛和膈下，腹部胀痛以及腹腔创伤后引起的局部炎症反应痛等全身性疼痛(腹腔镜术后疼痛综合症)，虽属中等度疼痛，仍是影响患者住院时间及手术恢复程度的重要因素。近年来疼痛治疗中提出了超前镇痛这一概念，即在伤害性刺激作用于身体之前采取一定措施防止中枢神经系统敏感化，从而消除或减轻术后疼痛。

阿片类，非甾体类，局麻药等都是超前镇痛的常用药物，但所有的阿片类镇痛药均存在呼吸抑制作用，还可能导致过度镇静，恶心呕吐，肠蠕动减少，增加胆道内压等不良反应而限制其应用。而传统非甾体类镇痛药大多为口服剂，易引起胃肠功能紊乱，出血等不良反应，而且在治疗术后疼痛时多数无法口服药物。与之相比，经过脂微球这一新型的药物载体系统包裹的氟比洛芬酯静脉注射液有以下4个方面的优势，1)靶向性:脂微球可在体内特异性分布，靶向聚集在手术切口及炎症部位，提高药物局部有效浓度，直接抑制前列腺素合成，产生强力速效的镇痛作用。2)抢先性:通过升高痛阈，降低神经末梢痛觉传导，减轻中枢敏化，延长和扩散术后疼痛达到超前镇痛的目的。3)缓释性:氟比洛芬酯通过脂微球的包裹和保护作用，避免了在体内被迅速代谢而达到长效，减少用药次数，改变药物峰谷现象。4)舒适性:不会引起恶心呕吐，呼吸抑制，依赖性等不良反应，较传统胃肠道的安全性提高，对血小板影响轻微，不影响出凝血时间。

本研究结果提示，缝皮前10-15分钟静脉注入氟比洛芬酯50mg能明显减轻腹腔镜术后的切口性疼痛，术后使用哌替啶的例数，次数明显减少(P＜0.01)，患者能更早下床活动，增加了对手术的满意度，未见胃肠道紊乱及出血倾向，提高术后镇痛质量，降低术后麻醉性镇痛药用量的50%，并降低全麻术后躁动的发生率。说明预注氟比洛芬酯超前镇痛能有效延长和减少术后阿片类药物的使用，避免了相关不良反应。

本研究显示氟比洛芬酯超前镇痛用于妇科腹腔镜手术，能有效缓解术后切口疼痛，减轻炎症反应，减少术后镇痛药的使用和不良反应，且术后苏醒迅速安全，值得临床推广。

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书讯

复旦大学附属肿瘤医院麻醉科陈志扬著的《临床麻醉难点解析》一书，已由人民卫生出版社出版，书中阐述了临床麻醉医生经常遇到的难点，如困难气管插管、硬膜外阻滞进展、双腔管原则、麻醉禁忌症（停手术）、麻醉与催眠术、心肺复苏失败的原因、把植物人唤醒、手术后猝死、癌痛治疗等。30元/本，汇款至200032，上海市徐汇区东安路270号复旦大学肿瘤医院麻醉科 陈志扬收

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摘要

目的：探讨七氟烷后处理减轻大鼠局灶性脑缺血-再灌注(I/R)损伤中黄嘌呤氧化酶（xanthine oxidase，XO）含量变化的意义。方法：40只SD大鼠，随机入假手术(Sham)组、缺血-再灌注(I/R) 组、七氟烷后处理（PostS）组、IR+别嘌醇(Adenock A，I/R+A）组，各10只。大脑中动脉线栓(MCAO)法建立大鼠局灶性脑缺血损伤模型，观察缺血前、再灌注后各组血清XO、超氧化物岐化酶（SOD）活性、丙二醛（MDA）含量及脑组织Na^+-K^+-ATP酶（Na^+-K^+-ATPase）活性变化。实验结束后，处死大鼠，取脑组织经HE、TTC染色，观察各组脑组织梗死体积。结果：再灌注24h末，Sham组血清XO活性、MDA含量低于其它三组（$p<0.05$），SOD及脑组织Na^+-K^+-ATPase活性高于其它三组（$p<0.05$）；I/R组与PostS组、I/R+A组比较，XO活性升高（$p<0.05$），MDA含量增加（$p<0.05$），SOD、Na^+-K^+-ATPase活性降低（$p<0.05$）；S组SOD、XO以及Na^+-K^+-ATPase活性均高于IR+A组（$p<0.05$），MDA含量低于IR+A组（$p<0.05$）。结论：下调XO活性，可能是七氟烷后处理有效减轻大鼠脑缺血-再灌注损伤重要途径之一。

关键词：黄嘌呤氧化酶；缺血-再灌注损伤；七氟烷；后处理

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七氟烷后处理减轻大鼠局灶性脑缺血-再灌注损伤与黄嘌呤氧化酶

The Effect of Xanthine Oxidase in Post-conditioning of Sevoflurane on Cerebral Infarction Volume in Focal Cerebral Ischemia/Reperfusion Rat Mode

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Abstract

Objective：To explore the significance of change in xanthine oxidase content in rat's focal cerebral ischemia/reperfusion injury, that was treated with sevoflurane post-conditioning.

Method：40 healthy SD rats, with either sex, were randomly divided into 4 groups：shame group,ischemia/reperfusion injury (I/R) group, postcondition with sevoflurane (PostS) group, I/R plus Adenock(A) (I/R+A) group, 10 in each. Focal cerebral ischemia/reperfusion model was established in wistar with suture method. The activities of superoxide dismutase(SOD)、xanthine oxidase (XO) 、malondialdehyde(MDA) and sodion-potasium ion-dependant triphophade adenosin enzyme (Na^+-K^+-ATPase) were measured, volume of cerebral infarction determined with dyeing by hematoxylin eosin (HE) and triphenyltetrazolium staining(TTC) at the end of reperfusion.

Result：The activities of XO, MDA, SOD and Na^+-K^+-ATPase are much higher in sham group than that of I/R, PostS and I/R+A groups（$p<0.05$）at the end of reperfusion. The volume of cerebral infarction is much less in PostS than that of I/R+A group（$p<0.05$）.

Conclusion：Post-conditioning with sevoflurane can attenuate ischemia/reperfusion injury in rat's focal cerebral infarction，descending the activity of XO maybe one of the important ways.

Key Words：xanthine oxidase; cerebral ischemia /reperfusion injury; sevoflurane; post-conditioning

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脑组织对缺血缺氧极其敏感，麻醉手术中，蛛网膜下隙出血、严重颅脑外伤、控制性降压等均有潜在脑缺血可能，加强麻醉手术期间脑功能监测和脑保护倍受关注。七氟烷是一种临床应用广泛的新型挥发性麻醉药，研究表明，大鼠脑在经历缺血-再灌注损伤前，预先给予一定浓度的七氟烷吸入（预处理）可有效降低由缺血后再灌注引发的脑细胞凋亡[1]。也有文献证明七氟烷的预处理及后处理可通过诱导体内多种酶活性水平上或下调、激活线粒体KATP通道、减轻神经元线粒体内钙超载、抗细胞内氧化作用等，减轻脑缺血-再灌注损伤[2-3]。黄嘌呤氧化酶（XO）是细胞代谢过程中重要的限速酶，作为细胞内电子传递的载体，对于调控细胞内多种氧化还原反应至关重要。本文观察OX活性动态变化，探讨七氟烷后处理对大鼠局灶性脑缺血-再灌注损伤的保护作用，探讨XO活性变化与七氟烷后处理其的关系，为七氟烷脑保护临床应用提供实验基础。

一、材料与方法

1. 主要仪器与试剂

Drāger Fabius2000型麻醉机（中德合资）、Vamos多功能气体监护仪（德国）自制吸入麻醉箱（有机玻璃材料，箱底置2cm厚去粉尘钠石灰，表面铺1cm厚细木屑，一侧箱体下部设新鲜气体入口，与麻醉机相连接。对侧箱壁上部设废气出口，标准接口可串接麻醉气体监测仪，后接延长管道通至室外）、眼科手术剪刀、文氏止血钳、尼龙线（大脑中动脉

栓塞用）。试剂包括七氟烷（喜保福宁，雅培药业公司），XO、SOD、MDA、Na^+-K^+-ATPase检测试剂盒（武汉博士德公司），别嘌呤醇（美国Cardiome公司）。

2. 实验动物分组与模型建立

40只健康SD大鼠（北京军事科学院生物研究所提供），雌雄不拘，体质量280～320g，随机分为4组，各10只。按文献[4]的方法建立局灶性脑缺血-再灌注模型（MCAO）。Sham组，仅分离血管，不留置线栓。I/R组，线栓大脑中动脉2h后，经24h再灌注；IR+A组，缺血前5min，腹腔注射别嘌呤醇130mg/kg，再灌注24h；PostS组，缺血2h后，再灌注同时，将大鼠放入自制麻醉箱（箱内预充1.5MAC（2.6%）七氟烷）。纯氧流量4L/min，麻醉机挥发罐刻度调至3.5%。麻醉箱废气排放出口接Vamos连续监测，保持出气口七氟烷浓度1.5MAC，维持30min。

3. 标本采集及检测方法

再灌注末24h，从大鼠心脏取血2ml，硫代巴比妥法测定MDA含量，黄嘌呤氧化酶法测定SOD活性，酶法分批测定Na+-K+-ATPase活性，辣根过氧化物酶分光光度法测定XO活性。

4. 脑组织HE染色、TTC染色

HE染色：试验结束后，取各组一半大鼠立即断头处死。取部分脑组织切片后投入4%甲醛液中固定，浸蜡包埋、切片、贴片后，经酒精、二甲苯脱水透明，脱蜡染色。TTC染色：各组余下大鼠于再灌注24h后断头处死，去掉小脑及低位脑干、视交叉前后部分脑组织，余部分脑组织制成2mm 厚的冠状脑片，置于氯化三苯基四氮唑（TTC）溶液中，移入37℃水浴箱内避光孵育30min，待显色完全后，再移入10%甲醛溶液中固定24h。存活组织内的线粒体过氧化氢酶能够氧化TTC，组织着色染为深红色，坏死组织不着色，呈苍白色。染色后，用数码相机（品牌）给每片组织拍照，记录结果输入计算机，用Scion Image图像分析软件对不显色部分分析后，计算梗死面积，各组脑切片梗死面积之和乘以厚度(2mm)即脑梗死总体积。

5. 统计学处理

应用SPSS11.0统计学软件，所有计量资料以均数±标准差($\bar{x}\pm s$)表示。组间比较采用单因素方差分析，组间两样本均数的比较采用q检验（SNK法），$p<0.05$为差异有统计学意义。

二、结果

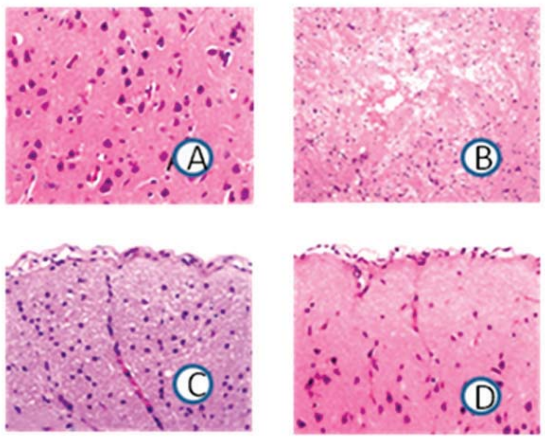
1. XO、SOD、Na^+-K^+-ATPase活性及MDA含量变化

再灌注24h末，Sham组血清XO活性、MDA含量低于其它三组（$p<0.05$），SOD及脑组织Na^+-K^+-ATPase活性高于其它三组（$p<0.05$）；与PostS和I/R+A组比较，I/R组大鼠XO活性及MDA含量明显升高（$p<0.05$），SOD、Na^+-K^+-ATPase活性明显降低（$p<0.05$）；PostS组SOD、脑组织Na^+-K^+-ATPase活性高于IR+A组（$p<0.05$），XO活性及MDA含量降低（$p<0.05$）见表1。

2. 各组HE染色结果

Sham组大鼠脑组织神经元形态基本正常，胞体无明显肿胀，胞质均匀透明，胞浆内尼氏小体清晰可见。细胞核居中，血管周围无明显炎细胞浸润（图A）；I/R组鼠大脑皮质神经元数量明显减少，结构模糊，胞体肿胀，广泛的细胞核固缩、核深染、核溶解现象。胞浆着色变浅，尼氏小体减少或消失，呈中～重度变性、坏死改变，血管周围炎细胞浸润明显（图B）；PostS组与I/R+A组虽可见神经元轻度变性、坏死，但正常神经元数量明显多于I/R组（图C、D）。

图1 各组脑皮质HE染色光镜图像（HE，×400）



A. Sham组；B. I/R组；C. PostS组；D. I/R+A组

3. TTC染色

TTC染色结果：Sham组大鼠脑组织未见明显梗死区；I/R组与I/R+A组、PostS组均可见明显的白色梗死灶，主要集中在额、顶区皮质，壳核与尾核背外侧。I/R组大鼠脑梗死体积及梗死体积百分比均大于I/R+A、PostS组，三者比较有显著差异($p<0.01$)；I/R+A组脑梗死体积及梗死体积百分比大于PostS组（$p<0.01$）见表2。

表1 各组血清XO、Na^+-K^+-ATPase、SOD活性及MDA含量(n=10, $\bar{x}\pm s$)

组别	XO(U/g prot)	SOD(μg/L)	Na^+-K^+-ATPase(μg/L)	MDA(μmol/L)
Sham	9.65±0.33	84±6	4.2±0.3	5.9±1.3
I/R	14.54±0.24*	59±4*	1.2±0.3*	10.7±0.9*
PostS	10.21±0.31*▲	75±5*▲	3.3±0.3*▲	6.8±1.1*▲
I/R+A	12.32±0.28*▲	64±3*▲	2.7±0.2*▲	7.7±0.8*▲

与I/R组比较，*$p<0.05$；与Sham组比较，▲$p<0.05$

表2 各组脑梗死体积及百分比的比较(n=10, $\bar{x}\pm s$)

组别	脑体（mm^3）	脑梗死体积（mm^3）	脑梗死体积百分比（%）
Sham	1379±36	0	0
I/R	1368±37	278±32	19.8±3.2
PostS	1376±44	132±26#	10.2±2.5#
I/R+A	1359±41	135±21#★	12.1±2.7#★

与IR组比较，#$p<0.01$；与PostS组比较，★$p<0.01$

三、讨论

在体动物模型具有重现性好、价格低廉、某种程度上可直接借鉴到临床等优点。研究表明脑缺血-再灌注损伤病理生理过程复杂。脑组织经历一定时间的缺血，恢复灌注后，会发生神经元损伤和功能障碍，触发一系列复杂的级联反应，

包括多种酶活性改变、钙平衡失调、过量自由基生成、脂质过氧化增强、线粒体功能障碍等。

血清中XO、SOD活性及MDA含量，脑组织中Na^+-K^+-ATPase活性变化作为脑损伤生化标志物已被广泛接受。本文通过观察七氟烷后处理（七氟烷浓度选择参照文献[1]）上述指标变化，间接反映脑损伤程度。HE染色结果表明急性脑缺血梗死模型建立成功，TTC染色直观表明了脑梗死体积。结果显示，I/R+A组和PostS组脑组织在经历缺血-再灌注后与I/R组比较，血清XO活性显著下调，脑梗死体积明显缩小，一定意义上证明XO参与了脑缺血-再灌注损伤过程，抑制XO活性，具有脑保护作用，XO活性下调可能是七氟烷后处理发挥脑保护作用的重要信号转导因子之一。

XO前身是黄嘌呤脱氢酶（XD），两种酶主要存在于毛细血管内皮细胞内。正常时只有10％以XO形式存在，90％为XD。ATP是脑细胞最重要的能量来源，脑组织Na^+-K^+-ATPase活性水平是细胞有效利用ATP的前提条件。本试验发现，IR组Na^+-K^+-ATPase活性较其它三组明显降低，表明经历缺血－再灌注损伤后， IR组大鼠脑组织中可利用的ATP水平明显降低。I/R+A组Na^+-K^+-ATPase活性变化，证明XO活性抑制，即XO活性下调，同时有Na^+-K^+-ATPase活性上调。Zhong等[5]发现，脑组织缺血时，由于ATP减少，膜泵功能障碍，$Ca2^+$进入细胞，激活$Ca2^+$依赖性蛋白水解酶，使XD变构，转变为XO；同时不能有效利用ATP，堆积的ATP有磷酸二酯酶参与，依次降解为ADP、AMP和次黄嘌呤，故次黄嘌呤在脑组织内大量堆积。再灌注时，大量氧分子随血液进入缺血区域，缺血期梗死灶周围暂时失活组织复苏，XO催化次黄嘌呤转变为黄嘌呤，产生大量氧自由基，也可成为造成脑损伤重要原因。MDA是脂质过氧化产物，是一种重要的交联因子，可导致神经细胞能量产生、利用障碍。再灌注末，I/R组脑组织MDA含量显著高于PostS和I/R+A组。Abramov等[6]发现脑组织经历缺血-再灌注损伤过程中，产生大量氧自由基同时，并存氧自由基清除系统功能降低或丧失，氧自由基可引发脂质过氧化，使膜受体、膜蛋白酶、离子通道和膜转运系统等的脂质微环境发生变化，同时生成MDA，表现为细胞的呼吸链活性、细胞膜上离子泵受损，脑组织细胞内钙离子超载，甚至导致脑组织发生不可逆损伤。SOD一定程度上可防御氧自由基攻击生物膜，减轻内环境损伤。本文再灌注末PostS、I/R+A两组SOD活性明显高于I/R组，表明XO活性下调可能是七氟烷后处理抗脑组织缺血-再灌注损伤，发挥脑保护作用通路中一个重要的信号因子。

综上所述，七氟烷后处理具有较明确的脑保护效果，XO活性下调可能是减轻脑缺血-再灌注损伤的重要信号因子之一。

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中华医学会麻醉学分会

2010年12月

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摘要

目的：观察咽喉粘膜表面麻醉、气管粘膜表面麻醉、导管外涂乳膏表面麻醉三种不同方式的应用，对全麻插管应激反应及耐管性影响的临床研究。方法 选取90例ASAⅠ～Ⅱ级择期全麻手术气管插管病人，随机分为三组(n=30)，A组为三重表麻组、B组为双重表麻组、C组为对照组。记录三组在喉镜显露声门即刻（T_0），插管后1min（T_1）、3min（T_2）、5min（T_3）的平均动脉压（MAP）和心率（HR）数值以及意识恢复后，患者对导管的耐受程度。结果：同对照组比较，三重表麻组和双重表麻组的MAP和HR均明显低于对照组（P<0.01）。在耐管性方面，三重表麻组明显高于双重表麻组和对照组（P<0.05）。结论：三种表麻方法序贯应用能有效预防喉镜置入和气管插管引起的心血管应激反应，并明显提高导管耐受程度。

关键词：表面麻醉；乳膏表面麻醉；应激反应；耐管性；

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不同表面麻醉方式对全麻插管应激反应及导管耐受性影响的研究

Influence of Different Surface Anesthesia on Stress Reaction during induction and Tolerance of Tube during Recovery

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Abstract

Objective: Three ways of surface anesthesia:Throat mucosa, trachea mucosa, and Emulsifiable paste, which applied in general anesthestia with different combination, to investigate the influence on stress reaction during induction and also the tolerance of tube during recovery.

Methods: 90 ASAI-II patients with general anesthesia were randomly divided into 3 groups(n=30):A: apply with all three surface anesthesia; B: Throat and trachea mucosa surface anesthesia; C: Control, without any anesthesia. Recorded the mean blood pressure(MAP)and heart rate(HR) at intubation （TO），1 min（T_1）、3min（T_2）、5min（T_3）after intubation, as well as the tolerance of tube after recovery.

Rusults: Compared with Control group, MAP and HR in A and B groups were much lower（P<0.01）. A group had the highest tolerance of tube than group B and C（P<0.05）.

Conclusion: Combination with all three surface anesthesia can effectively prevent the stress reaction of intubation, and increase the tolerance of the tube.

Key Words: Surface anesthesia, Emulsifiable paste anesthesia, Stress Reaction, Tolerance of Tube

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全麻气管插管和拔管期间，由于对咽、喉、气管粘膜的机械刺激使交感-肾上腺素系统的活性增强，体内儿茶酚胺释放增加，导致BP上升、HR增快或心律失常。此种心血管反应虽是一过性的，但对合并高血压、颅内高压、心脏病等病人则可产生严重影响[1]。目前，在临床麻醉中，已有多种预防全麻插管应激反应和提高导管耐受性方法、并取得一定效果。本研究采用咽喉粘膜表麻、气管粘膜表麻+导管外涂乳膏表麻三种方法不同应用，观察气管插管应激反应及对导管耐受性的影响，现报道如下。

一、临床资料

1. 一般资料

选择90例择期全麻手术病人，ASAⅠ～Ⅱ级，男44例,女46例,年龄36-58岁,体重50-80公斤,随机分成三组，每组30例。A组为咽喉粘膜表面麻醉+气管粘膜表面麻醉+导管外涂乳膏表面麻醉；B组为咽喉粘膜表面麻醉+气管粘膜表面麻醉；C组为对照组，无任何表面麻醉。

A组（三重表麻组）、B组（双重表麻组）和C组（对照组）三组患者年龄、体重、性别构成比、手术时间、手术种类差异均无显著性（P>0.05），见表1。

表1 患者一般资料比较($\bar{x}\pm s$，n=30)

组别	年龄（岁）	性别（男/女）	体重（kg）	手术时间（h）	手术种类（乳腺/胃/肠/其他）
A组	46.7±6.2	16/14	58.2±10.3	2.1±0.63	11/9/4/6
B组	44.7±5.2	18/12	60.2±11.3	2.0±0.83	9/9/4/8
C组	47.5±8.4	13/17	61.6±11.2	2.0±0.78	13/8/3/6

2. 表麻方法

三组病人入室后开放静脉，咪哒唑仑0.05mg/kg静脉滴入，持续监测HR、BP、ECG、SpO_2、$PETCO_2$等参数。A组和B组诱导前分别用利多卡因气雾剂（上海信谊制药总厂生产）循序分3次定量喷雾，每喷约4.5mg。首先对准舌背后半部及软腭喷雾2-3次，再隔1-2分钟后嘱病人张嘴，同时发“啊”长声，将喷嘴对准咽壁及喉部喷雾2-3次，再隔1-2分钟，用喉镜片当压舌板轻轻提起舌根，将喷嘴对准喉头，在病人深吸气时揿压阀门2-3次，使咽喉部粘膜充分表面麻醉。诱导后，置入喉镜，暴露声门，将接有2%利多卡因2ml注射器经过喉麻管注入气管内，再面罩加压给氧1分钟行气管插管。A组插入导管前1/3涂有复方利多卡因乳膏（北京清华紫光制药厂生产）的气管导管，B组为普通导管插入。C组无任何表面麻醉。三组诱导用药及麻醉维持用药相同。

所有操作由专人负责，气管插管未能一次成功或时间超过15秒的病例不列入观察对象。

3. 观察指标与方法

入室后，连续监测ECG、BP、HR、SpO_2、$P_{ET}CO_2$。记录三组病例在插管即刻（T_0）、插管后1min（T_1）、3min（T_2）、5min（T_3）时平均动脉压（MAP）和心率（HR）数值。在意识恢复后，给套囊充放气，观察并记录屏气和呛咳情况。导管耐受评定标准：优：清醒时能耐受气管导管，对套囊放气和再充气刺激无呛咳和屏气反应。良：能耐受气管导管，气囊放气，但再充气时有呛咳。有效：能耐受气管导管，但放气和再充气均呛咳。无效：不能耐受气管导管，未刺激即有呛咳反应，放气和再充气均引起剧烈呛咳反应。

二、统计分析

所得数据用SPSS10.0统计软件进行统计学处理，计量资料以均数±标准差（$\bar{x}\pm s$）表示，比较采用配对t检验，计数资料比较采用X^2检验，P＜0.05为有统计学意义。

三、结果

三组患者诱导前各项监测项目比较均无差异。在插管即刻（T_0）、插管后1min（T_1）、插管后3min（T_2）插管后5min（T_3），A、B两组MAP和HR比较，P＞0.05，无统计学差异；A组与C组比较，B组与C组比较，组间MAP、HR数值变化均有显著统计学意义（P＜0.01）。见表2

表2 三组患者血液动力学改变（$\bar{x}\pm s$，n=30）

组别	时间点	MAP	HR
A组*△	T_0	79.0±13.6	71.44±11.32
	T_1	75.2±11.4	71.00±14.42
	T_2	74.1.±12.2	72.34±11.21
	T_3	77.2±12.3	73.42±12.12
B组*▲	T_0	82.3±10.5	73.14±10.62
	T_1	86.6±9.6	71.41±10.32
	T_2	77.3±10.2	74.23±13.31
	T_3	80.2±10.7	74.14±9.72
C组△▲	T_0	88.3±18.0	97.34±13.45
	T_1	89.4±13.3	93.53±15.31
	T_2	92.4±12.5	87.23±14.67
	T_3	91.5±14.6	88.12±15.12

注：A、B两组比较，*P＞0.05；A、C两组比较，△P＜0.01；B、C两组比较，▲P＜0.01

在麻醉苏醒期间，呼之能睁眼时，给导管套囊放气和充气，观察并记录患者呛咳和屏气等反应，并依据耐管评定标准进行评估。见表3。

表3 不同表麻方法耐管效果分布（$\bar{x}\pm s$，n=30）

N	优	良	有效	无效
A组*△	20	7	3	0
B组*▲	4	5	7	14
C组△▲	0	4	6	20

注：A、B两组比较，*P＜0.05；A、C两组比较，△P＜0.05；B、C两组比较，▲P＞0.05

四、讨论

全麻下喉镜置入和气管插管极易并发比较严重的心血管应激反应，表现为血压急剧升高，心率加快或心动过缓等循环反应，对心血管系统功能正常的人危害不大，但对有心血管疾患的病人则可能构成生命危险。近年来，喉镜置入及气管插管引起的心血管应激反应已受到普遍重视，有关预防措施的相关研究和报道甚多，方法不一[2,3]。

本研究结果提示，三重表麻和双重表麻在全麻插管期间，对减少血压、心率的波动方面有显著保护作用，A、B两组虽表麻方法不同，但无明显差异性。在麻醉苏醒期间，A组能明显提高导管耐受性，与B组和C组比较有明显差异性，B组与C组比较差异不明显，提示双重表麻并不能提高对导管的耐受性。而三重表面麻醉的序贯使用，除能最大限度减少全麻插管期间血压、心率的波动外，还能明显提高导管耐受程度。

咽喉粘膜表麻和气管粘膜表麻在插管期间即可减轻循环功能的波动[4]。在麻醉苏醒期间，由于导管外涂复方利多卡因乳膏对气管粘膜的长效麻醉作用，明显提高导管的耐受程度[5]。三重表麻联合使用，能在插管和拔管全过程提供完善的表面麻醉，对年龄大并伴有心脑血管疾病的手术患者，是较为理想的表麻方式。

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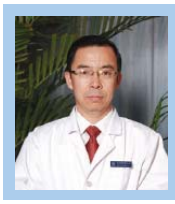

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第十届华东六省一市麻醉学会议暨2011年上海市医学会麻醉年会

为提高华东地区麻醉学术水平，交流国内外麻醉学的研究进展，同时也为提高基层临床医师对麻醉学的认识和诊治水平，促进多方合作，华东地区麻醉学协作委员会与上海市医学会麻醉分会定于2011年5月20日～5月22日在上海市联合召开“第十届华东六省一市麻醉学会议暨2011年上海市医学会麻醉年会”，会议将授上海市医学会继续教育项目Ⅱ类学分。会议将邀请国内知名的麻醉学专家教授与会作精彩演讲，同时进行大会学术交流和病例讨论。

征文要求：1、围绕上述征文范围及会议热点且未曾发表过的论文，附800字以内摘要，具有较强的科学性、先进性和实用性；2、按结构摘要撰写，顺序为文题、作者、单位、邮编、目的、方法、结果、结论；3、投稿一律采取电子邮件方式，请以附件形式将word文档发送至上海市医学会学术会务部，E-mail：huadongmazui@163.com。

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摘要

多种神经机能紊乱可导致急性全身性衰弱以致住院治疗，接受神经系统评估；神经肌肉系统的严重病变也见于ICU中的危重病人。呼吸肌常受累于多种病例中，可导致通气不足、高碳酸血症性呼衰，增加或延长呼吸机的使用。对于严密监测的有神经肌肉衰弱的病人来说，早期发现其呼吸衰竭征象并立即进行呼吸支持是很关键的；可能还需要对病人进行插管以维持气道通畅。插管时，病人有很高风险患肺炎等致死性的并发症。及时发现潜在的神经肌肉性病变有助于进行有效的治疗和预后判断，以及避免呼吸机的应用。当临床诊断不明确，或需要进一步评估预后情况时，选择性地进行肌电图（EMG）、神经/肌肉等辅助检查是很有帮助的。

关键词：神经肌肉性呼吸衰竭

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神经肌肉性呼吸衰竭与ICU

Neuromuscular respiratory failure in ICU

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Abstract

A wide variety of neurologic disorders cause acute generalized weakness precipitating hospital admission and neurologic evaluation; serious dysfunction of the neuromuscular system also occurs in critically ill patients in the intensive care unit. Respiratory muscles are commonly affected in either case, leading to hypoventilation, hypercapnic respiratory failure, and the need for (or prolongation of) mechanical ventilation (MV).Closely monitoring patients with neuromuscular weakness is critical in recognizing early signs of respiratory failure and guiding the need for prompt ventilatory support; patients may also need to be intubated for airway protection. While intubated, these patients are at high risk for complications such as pneumonia that contribute to mortality. The proper recognition of the underlying neuromuscular disorder allows appropriate management and discussion of prognosis, including weaning from MV.Selective use of ancillary testing, such as EMG and nerve/muscle biopsy, may help when the clinical diagnosis is unclear and further assist with estimating recovery.

Key Words：Neuromuscular respiratory failure（NMRF）

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一、病因及表现

神经肌肉性呼吸衰竭（NMRF）的主要病因，根据神经系统病变的位置进行分类，并把那些于入院治疗之前就出现症状的病人和那些由于其他危重病而进入ICU之后才有症状的病人区别开来（表1）。然而，左边一栏的几乎所有病变都只在已经进入ICU的病人中才被首诊。这可能是由于呼吸衰竭的迅速恶化（如格林-巴利综合症，GBS），慢性病的急性恶化，由间发的疾病或新的治疗所导致的未被发现的症状（如重症肌无力，MG），某种最初无神经系统症状的多系统紊乱（如脉管炎，卟啉病），或者已因为其他疾病而住院的病人所表现出来的这些紊乱中的一种。

表1 神经肌肉性呼吸衰竭（NMRF）的主要病因

疾病的位置	ICU前发病	ICU后获得性疾病
肌肉	炎症性肌病	危重病性肌病
	酸性麦芽糖酶缺乏	急性坏死性肌病
	线粒体性肌病	横纹肌溶解症
	肌强直性营养不良	电解质紊乱(低磷，低钾)
	周期性麻痹	
	重症肌无力	神经肌肉性阻断延长
	Labert-Eaton综合征（LEMS）	
神经肌肉接头	肉毒杆菌中毒	高镁血症
	有机磷中毒	
	格林-巴利综合症 多病灶性神经病变	
	脉管炎，卟啉病	
	Charcot-Marie-Tooth病	危重病性多发性神经病
	重金属中毒	
外周神经、神经根	HIV，白喉，莱姆病(Lyme)	膈神经损伤
	病变蛋白血症	
	副癌综合症	
前角细胞	肌萎缩侧索硬化(ALS)	
	脊髓灰质炎	
中枢神经（脊髓，脑）	急性脊髓病（缺血性、	脊髓缺血（如术后）
	压迫性、炎症性）	硬膜外脓肿
	脑干梗塞	中桥脑脱髓鞘

以膈肌为主、包括肋间肌在内的呼吸肌衰弱，可导致通气受影响、咳嗽及清除呼吸道分泌物能力下降。辅助性呼吸肌，包括胸锁乳突肌和斜角肌，在某种程度上有代偿作用，但高碳酸血症性呼吸衰竭是由于进展性衰弱所致。由于肺不张以及充气不足的肺内气体交换率下降，低氧血症也会发生。而且，快动眼阶段睡眠期中枢呼吸驱动和辅助性呼吸肌的活动性都降低，这就加剧了呼吸功能的下降，并导致低氧血症、高碳酸血症的发生率。端坐呼吸经常发生，这是由于病人平卧时膈肌上抬。同时伴发如肺炎，或呼吸需要量增加（如发热）也可以导致有神经肌肉性衰弱的病人发生急性呼吸失代偿。

NMRF伴发的疾病中大多数都表现有四肢轻瘫的症状，尽管这个症状因为并存的脑病、镇静或医源性不安定的存在而显得很轻微或经常被忽略。少数情况下，呼吸机衰弱也会单独出现，比如在一些ALS病人尚未卧床不起时，呼吸衰竭就出现了。辨认清楚衰弱的类型有助于将潜在的病变局限化。MG中最初的眼球症状包括早期的眼睑下垂和复视，随着呼吸症状的日趋明显，吞咽困难的症状也加剧；四肢易疲劳的症状可能比较轻微，尽管伴有呼衰。一种相似的遗传性的衰弱

类型是典型的肉毒杆菌中毒，但无反应的瞳孔将之与MG区别开来。瞳孔放大也见于有机磷酸酯类致胆碱能神经中毒。相反，GBS的典型症状表现为初期的近端下肢衰弱，逐渐发展为手臂、颈部、两侧面部肌肉的衰弱；然而，许多变异的类型不表现为这种逐渐上行的现象。颈部肌肉（尤其是屈曲肌）的受累、冈下肌的衰弱都和膈神经受累及膈肌麻痹的关联最大。咽肌、喉肌的衰弱及舌头活动的受限表明管理分泌物和保护气道的能力受损。这些病人会被要求或观察其咳嗽情况，因为肋间肌的衰弱会严重影响到咳嗽反射，这一反射可清除分泌物和避免肺萎陷。

详细询问病史可发现一些感染的前驱症状，新的治疗方案，毒物接触史，全身性症状如发烧、疹，家族史，或之前是否有过相似的发作。对于自主神经元、神经肌肉接头、肌肉的病变来说，感知觉的检查可以省去，在自主性、主要的神经病（如GBS或卟啉病）的客观检查中，感觉会受到轻微影响。肌痛见于特定的（炎症性或坏死性）肌肉肌病中，而四肢或根部疼痛正是神经性疾病的重要表现。尽管GBS中背痛常见，但对于双侧衰弱及背痛的病人来说，MRI拍摄脊柱图像时十分有用的，它可以检查出压迫性脊髓病变如赘生物、血肿，在感觉水平或肠、膀胱功能障碍中表现的尤为明显。自主神经功能障碍，如体位性低血压、尿潴留、或异常出汗，可能和神经性疾病相伴随，但也见于LEMS或肉毒杆菌中毒。肌痉挛后的深部腱反射（DTRs）表明了突触前的神经肌肉接头性肌病如LEMS。

对ICU病人进行详细检查是很有挑战性但收益不大的事。脑病或使用了镇静剂的病人不能配合进行精确的肌力检查或感觉功能的评估，耐心观察病人的本能反应和对刺激的反应。深部腱反射和音调可被评估，萎缩和肌束震颤的测验可被监测设备和伤口所阻碍。四肢水肿会导致感觉测验不可信，即使是意识清醒的病人，并能掩盖萎缩的症状。

二、预测神经肌肉性呼衰

对于有进展性全身衰弱表现的病人来说，尽早发现呼吸衰弱的征象并在急性失代偿发生之前预测插管术或呼吸机的使用是极为关键的。插管的延误会导致误吸的发生并加剧肺炎的发展。而且，对呼吸功能的下降坐视不管是很危险的，会增加肺部疾病的死亡率。早期进行积极的肺部护理，包括使用刺激性肺量测定法以避免肺不张、按需要进行胸部理疗来打开气道并清除分泌物，都可以减少并发症的发生。然而，对于通气不足和气道不受保护的NMRF的治疗中，唯一有限制性的治疗手段就是插管和机械通气。

一些呼吸衰弱的临床标记可能会引起注意并且表明了进行插管的需要（表2）。这些在GBS病人身上得到了最好的研究，却可以应用于NMRF的所有病例中。急进性的衰弱是进行严密观察的指征，而无法将头从床上移开是膈肌衰弱恶化的早期征象。交谈时不能说出整句，或一次呼吸内不能数到20的病人可能有呼吸功能的受累。他们会有如下主诉：呼吸困难，无法平卧位，焦躁不安，心跳过速，发汗以及用辅助肌呼吸以代偿膈肌的麻痹。

表2 神经肌肉性呼吸衰竭即将发生的指征

指征	危险信号
临床	
进行性四肢轻瘫	四肢瘫痪，头部无法从床上移开
延髓受累	吞咽困难，声音无力，双侧面部衰弱
咳嗽虚弱	清除分泌物困难，湿罗音
呼吸功能主诉	
呼吸困难	主诉：呼吸疲劳
呼吸急促	无法说整句或不能一口气数到20
端坐呼吸	夜间低氧血症，喜坐位
应用辅助性呼吸肌	使用颈部、腹部肌肉呼吸
腹部反常运动	吸气时腹部向内运动
监测	
肺活量（VC）测定（床边）	VC<15ml/kg~20ml/kg
动脉血氧饱和度	低氧血症（晚期征象）
动脉血气分析（$PaCO_2$）	高碳酸血症=通气不足（晚期征象）
胸部X片	肺不张，肺炎

对VC进行连续监测是预测NMRF的最佳辅助工具。每天应进行2～4次呼吸量测定，视危急状况和病人最近的病情趋势而定；应避免检查过于频繁，以免导致呼吸肌的疲劳。每次试验结果可能有很大出入，这取决于病人和操作者，以及二者的配合程度和检测设备的精密度，这些都影响监测结果的可信度。如果双侧面部衰弱，使用口罩可能产生一些影响，会导致空气泄漏、检测结果偏低；大小很合适的口周的面罩可能会提高此装置的可信度。监测应一直持续进行直到病情改善或需要进行插管。当病人使用呼吸机时，应每天进行肺参数的测定，有助于计划撤掉呼吸机的试验和做好插管的准备。也应进行仰卧位的试验，因为卧位后VC下降>15%意味着膈肌的衰弱。

VC下降时严密监测的指征，尤其对于像ICU这样可以立即进行气管插管的地方更有价值。VC值低于30ml/kg提示呼吸功能已受影响，与咳嗽衰弱有关，会增加肺不张的范围。一旦VC降至20ml/kg以下，为了维持气体交换，则会导致通气不足。负性吸气力（NIF），也叫最大吸气压（MIP）的测定，可作为VC测定的补充，压力下降提示膈肌受损。最大呼气压力（MEP）也可以被测定并与减少咳嗽有关。以20/30/40的标准作为VC,MIP,MEP用来预测NMRF的水准应该提高。表3总结了这些床边检查的正常值和重要阈值。

表3 神经肌肉性呼衰的肺功能检查

检查	正常值	插管	撤掉呼吸机	拔去插管
肺活量	≥60ml/kg	<20ml/kg	≥7ml/kg~10ml/kg	15~20ml/kg
最大吸气压	<-70cmH$_2$0	>-30cmH$_2$0	<-20cmH$_2$0	-30~-50cmH$_2$0
最大呼气压	≥100cmH$_2$0	<40cmH$_2$0	≥40cmH$_2$0	50cmH$_2$0

监测动脉血氧饱和度和血气分析不能早期发现急性呼吸功能障碍。随着肺不张的发生可出现轻度缺氧，所以即使是需氧量的轻度升高，也应该立即重新评估病人的肺部和神经肌肉状况。然而，单纯低氧血症和高碳酸血症很少出现，除非已经到达VC降至10ml/kg以下的终末期，相当于急性失代偿期的一部分，应该全力避免。

另外，一些病人从未出现过需要使用呼吸机的通气障碍却仍然需要插管，以保护气道、排除分泌物。延髓功能下降、咳嗽虚弱、不能控制分泌物等症状的出现使插管成为必要，以防止误吸发生。这就强调了床边评估病人病情的重要

性，而不能仅仅认为，稳定的VC值就能保证病人的稳定。

早期进行电生理测验也有助于预测GBS病人是否需要进行机械通气，远端到近端腓侧复合肌活动潜在（CMAP）比率的降低（≤55.5%）可作为一个有用的预测因素。膈神经反应性的测定可作为评估膈肌是否受累的直接方法。可以在胸锁乳突肌后缘的双侧锁骨上窝处刺激膈神经，用放置于剑突和第7、第8肋缘处的表面电极测量膈神经的反应性。因为典型GBS的潜伏期会延长，伴随着振幅的下降，一些病人需要使用MV，但不是所有病人。膈神经的研究对于评估ICU中撤掉呼吸机失败有多大比例是因为神经肌肉功能紊乱所导致的具有很大帮助，单侧异常有助于对其同侧膈神经损伤的诊断。反复的神经刺激（RNS）在神经肌肉接头功能紊乱的情况下可表现为异常。

膈的EMG可通过在腋前线与锁骨中线之间的肋骨边缘处向肋间隙插入一种可以记录的穿刺针而获得。随着每次呼吸，呼吸运动的暴发就会被观察到，所以，要想评估自主运动（作为去神经的标致），施行插管后的病人就要安置一个可以测定自主呼吸模式，例如CPAP。这种穿刺术禁忌应用于因COPD所致的肺过度充气、肠梗阻或出血体质的病人。

三、气管插管和机械通气

神经肌肉阻滞剂（NMBs）禁用于神经肌肉性呼衰的病人。使用琥珀胆碱可导致致死性的高钾血症，尤其当去神经存在时，非去极化的NMBs可延长MG病人的麻痹。尽管鼻腔插管舒服很多、也可使口腔得到更好的护理，但目前仍多采用口腔插管法，因其可避免鼻腔插管法并发的鼻窦炎、鼻中隔坏死和穿孔的风险。

一旦呼吸肌衰弱导致必须使用MV时就必须对通气进行适当的支持，以确保病人呼吸肌不再继续疲劳。使用辅助性通气模式可确保这一点，至少在通气次数上，或者可以确保每次通气都能在固定的容量之上而不需要病人额外的花力气。对于严重虚弱或疲劳的病例来说，更加建议使用辅助性可控的通气模式以提供完整的通气支持，直到通气功能开始恢复为止。为避免肺不张，对于患有NMRF且无其他肺部疾病的病人来说，此装置每次的潮气量应控制在较大水平（理想体重者应在10ml/kg或更多）。当对有一定程度慢性高碳酸血症和高碳酸氢盐的患者（常发生于亚急性呼吸衰竭中）施行辅助通气时，应避免过度通气和完全将提高的CO2分压规格化，因为这样会导致代谢性碱中毒，而且导致以后想撤掉呼吸机更加困难。将最初的通气率设定在10即可避免此种情况发生。可检测动脉血气以评估通气是否充足。

相反，如果病人插管只是为了保护气道、而没有明显的呼吸肌衰弱，可以用压力支持通气(PSV)的CPAP作为最初的通气模型。对于清醒且可自主呼吸的病人来说，这是个更舒服、更容易同步化的模型。PSV水平应该设定在5～25cmH_2O以达到适当的潮气量（目标是＞6～8ml/kg）和≤30的通气比率。如果病人的衰弱程度随即加剧，比如在一个设定的PSV内潮气量的下降，可以考虑换一个辅助通气模型。

通气的过程应包括正呼气末压力，以避免出现肺不张。这就避免了呼气末肺泡塌陷的发生，而且可在肺不张致氧气不足时逐渐上调通气量。但也要避免过高的正呼气末压力，因为胸内压过高会影响静脉回流及心输出量，这对于自主神经功能紊乱（如GBS）的患者来说是十分危险的。然而，也不应该低于一个最低水平（如5mmHg），以避免肺不张；这对于预防呼吸机相关性肺炎来说也比较严重。对肺不张患者进行积极的物理疗法可预防气体交换情况的恶化、避免肺炎发生风险的提高。

四、双相正性气道压力的使用

非侵袭性通气，例如双相正性气道压力（BiPAP），为通气衰竭提供了正性压力辅助而不需要气管插管。此法已成功应用于许多呼吸衰竭的患者，包括慢性神经肌肉衰弱（如ALS）的患者。尽管它为衰弱导致的通气不足提供了通气支持，但BiPAP不用于呼吸中枢功能障碍和气道分泌物多。事实上，对于意识模糊、无法保护气道的病人来说，此种方法应该禁用；而且，如果出现了呕吐，使用全面罩而发生误吸的风险就更高。

自从出现了病人突然恶化、需进行紧急插管的报道以来，对GBS患者使用BiPAP的热情有所缓和；这会短暂的掩盖衰弱病情的进展。对MG的研究则有较大价值，因为应用BiPAP作为MG病人的气管内通气手段很有效。最初应用BiPAP时，24例病人中有14例需避免插管，缩短MV使用时间。BiPAP的失败会伴发使用BiPAP初期CO_2分压超过45mmHg，但没有肺活量的下降，这通常出现于24小时内；BiPAP在这些病人中平均应用4天。这对于MG患者来说是一个新的选择，因为它可以较迅速的逆转神经肌肉衰弱（与GBS相比，病情迅速进展的风险更小），这使得非侵袭性的通气成为更先进的方法出现之前的一个过渡的桥梁。

五、气管切开术

每天监测肺指数可以显示出插管后是否有病情的改善，因为增加了免疫疗法之后病情通常会改善。Lawn和Wijdicks（2000）已经为GBS插管病人制定了一套肺功能评分方案，将VC、MIP、MEP三者相加得到总和，如果第12天的得分没有比插管当天高，病人很可能需要3周以上的机械通气。此评分法有助于判断哪些病人需要行气管切开术，气管切开术需在插管后的最初3周之内进行。一些人曾建议更早施行气管切开术，因为可以对口腔进行更好的护理、对肺部盥洗、病人更加舒适、而且可能会更快撤去呼吸机。目前还没有实验性研究论证对NMRF病人应用此策略的可行性，尽管回顾性研究已经证明了延迟的气管切开术（插管后14天或更久）有更高风险伴发呼吸机相关性肺炎。然而，早期进行气管切开术的益处还需要针对病人的个体情况进行谨慎的权衡，以避免早期判断到底谁需要延长机械通气的过程（例如在2～3周内就可拔除插管的病人中进行此操作）和困难的风险。我们发现，最严重的GBS患者总是需要长期的机械通气，而且能从早期气管切开术中获益最大。但是，我们还是建议，当最终确定施行这种方案之前，能再观察一下是否有巨大的好转。因为MG患者机械通气的持续时间有变短的趋势，且对于治疗的反应可能更迅速，所以只有不到半数的危重病人需要进行气管切开术。

六、撤呼吸机和拔除插管

随着神经肌肉功能的恢复，呼吸容量将得到改善、可以撤去呼吸机。可否撤去呼吸机取决于肺参数的改善，如VC或NIF，尽管肌力的改善在临床中更容易观察。患有GBS或MG的四肢瘫痪病人至少要手臂可以活动，能转头，最理想的是能在成功撤掉呼吸机之前可以将头部从床上移开。也要在撤掉呼吸机、不需机械通气之前能够进行氧合作用，不患肺炎等常见的肺部并发症；病人应该能够维持充足的血氧饱和度和一个正常的O_2分压，氧气供应不低于一个最低值（$FiO_2 \leq 0.5$），呼气末正压也不低于一个最低值（≤5mmHg）。液体负荷量不过大，充足营养，戒断镇静剂，纠正贫血都能够增加病人呼吸机撤机的耐受力。

三种常用的撤掉呼吸机的方案是：（1）将病人的辅助控制变为间断的强制性通气（这可以使自主呼吸在设定频率之上，并可以在设定的PSV水平上评估潮气量），并逐渐撤去间断的强制性通气率，因为病人肌力恢复，所以从病人设想的每分通气量的角度来说，这些将使工作负荷日益增多。最终，一旦呼吸支持频率率低于4次，病人必然会自主性呼吸，可被CPAP所替代。(2)直接将病人变为CPAP并逐步增加PSV以实现充足的潮气量，然后根据病人的可耐受情况将呼吸支持的水平逐渐下降直至10cmH_2O（如果是靠气管切开呼吸的就降至5cmH_2O）。（3）自主呼吸的试验可以进行，该试验中，病人的呼吸支持从一个较高水平降低至最低水平，CPAP及最低的PSV（5～10cmH_2O）。一个自主性呼吸试验是所有撤掉该疗法的最后一道关卡；所不同的是达到这个目的的途径（以间断的强制性通气来逐渐降低频率，CPAP中PSV的逐渐降低，或快速降到最低支持）。

尽管第三条方案被证明通常是针对ICU的最好方法，但它是否适于NMRF患者尚不清楚。还没有做好自主呼吸准备的病人若向SBT转变的太快可以加剧肌肉疲劳和病人的焦虑。另外，虽然一开始就让有膈肌衰弱和疲劳的病人休息对于恢复是有益的，但让这样的病人长时间持续使用可控制的呼吸机实际上可能导致呼吸肌萎缩，并减缓康复进程。如果病人表现出一些好转的征象，可以自主的用力呼吸但没有成功，我们会使用第一和第二条方案，然后一旦出现VC进一步改善和明显好转，再快速的转换。

抛开应用的方案不管，病人撤机械通气还需要对SBT的耐受力。这需要在病人休息一夜之后早期开始，且那一夜必须进行了严密的照顾、确保病人可以耐受撤掉呼吸支持的尝试。呼吸专科医生，护士，临床医师应该在SBT刚开始时就守护在床边。试验进行过程中，必须评估自主潮气量的大小，检测为实现舒适的每分通气量而需要达到的呼吸率，记录终末潮气CO_2水平的增高以评估肺泡充气不足或高碳酸血症。一些人提倡使用快速浅呼吸指数，即呼吸率与潮气量的比率。该指数的理想值是30～60之间，不大于105。与之同样重要的还有评估病人是否舒适的指征，例如呼吸困难的视觉指征、出汗、心动过速、血压上升或下降、心率失常。如果这些指数发生了巨大变化，SBT则应该中止，将病人恢复到之前呼吸支持的可耐受水平。若低氧血症的指征出现，也应该中止SBT，并重新评估病人的肺和神经状况。一些已恢复的NMRF病人因为撤掉呼吸机而产生了巨大焦虑，可通过抗焦虑剂和镇痛药得到缓解、使自主呼吸变得更加轻松。

任何可耐受SBT的插管病人都可以考虑拔除插管。但我们建议，对于PSV10mmHg的施行CPAP的NMRF患者，在拔除插管之前应该再保留插管24小时。这种预防措施可以检测到延长的自主性呼吸所致的肌肉疲劳、并预测拔除插管的失败。动脉血气分析中CO_2动脉血分压若没有升高，则是一个较好的征象。若GBS患者的NIF较强（少于-50cmH_2O）、VC有所升高（拔管时与插管之前相比），则可以预测拔除插管会成功。在一项对严重肌无力患者的相似的研究中显示，只有56%的病人能成功拔管，而且拔管的病人中有26%又需要重新再插管。肺不张、拔管时VC值低于插管前都是拔管失败的指征。

除了SBT通过，NMRF病人还必须能够在拔管之前保护气道、管理肺部分泌物生成。这可根据咳嗽的力度、分泌物的量、意识的程度进行评估。一个清醒的病人如果能自主咳嗽、将分泌物推入气管内，他应该能够耐受拔管。但临床标致也不能被忽略。对于衰弱病情尚未稳定、经GBS或MG治疗后尚未好转的病人，不能考虑拔除插管。头部、颈部、舌头的力度正常，表示延髓功能有所改善。

表4 神经肌肉性呼吸衰竭主要病因的比较（NCS=神经传导研究）

特征	危重性多发性神经病	危重性肌病	格林-巴利综合征	肌无力	运动神经元障碍	中枢神经
衰弱类型	全身性	全身性	全身性 上行性	近端肌肉疲劳	不对称性	锥形
颅神经受累	无受累	通常无受累	通常受累	眼球和延髓受累	延髓受累	无受累（脊髓除外）
感觉受累	通常轻微	无	通常轻微痛感	无	无	感觉平面受累（脊髓除外）
自主功能障碍	无	无	常见	无	无	反射异常（后期）
深肌腱反射	迟钝/无 部分保留	保留（可变）	无	保留	可变（反射迟钝/亢进）	亢进（早期迟钝）
临床背景	脓毒症 全身系统炎症反应（SIRS） 脑病多器官功能衰竭（MOF）	类固醇激素/神经肌肉阻滞剂（如哮喘） 器官移植	先驱疾病（上呼吸道疾病，腹泻）	医源性 感染	西尼罗河病毒感染	背痛
血清肌酸激酶	正常	上升（50-85%）	正常	正常	正常（轻度升高）	正常
脑脊液（CSF）	正常	正常	蛋白升高（少量白细胞）	正常	正常	炎症（脊髓炎）
复合肌肉活动电位	幅度下降 无减慢或传导阻滞（轴突）	幅度下降 ±延长期	潜伏期延长，减速±传导阻滞(中枢脱髓鞘)	正常	节段性下降	正常
感觉神经活动电位	幅度下降	正常	下降/缺失	正常	正常	正常
自主性（肌电图）	存在（去神经）	存在（可变）	晚期存在（轴突退化）	无	存在	无
运动单元形（肌电图）	大，延长（后期）	小，多相短周期	正常（后期增大）	正常（不稳定）	大，多区域延长	正常
补充性（肌电图）	下降	早期迅速	下降	正常	下降	正常（活动性差）
反复神经 刺激递减	不会	不会	不会	会	不会	不会
直接肌肉刺激	正常	无反应	正常	正常	正常	正常
肌肉活检	神经性疾病	粗级丝缺失	神经性疾病	正常	神经性疾病	废用性萎缩

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摘要

血管外肺水（EVLW）与肺水肿的发生发展密切相关，因此对EVLW进行动态观察和定量监测，已成为肺水肿基础与临床研究的热点。本文对现今使用的EVLW监测方法及其原理进行综述。

关键词：血管外肺水，肺水肿，监测

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血管外肺水监测进展

Research Progress on Measurements of Extravascular Lung Water

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Abstract

Extravascular lung water can be considered a relevant parameter that contributes to the development of pulmonary edema.The dynamic and quantitative estimation of changes in extravascular lung water forms an intriguing field of pulmonary edema during different experimental and clinical conditions.This article reviews the measurements of extravascular lung water used today and the principles.

Key Words：Extravascular lung water;Pulmonary edema;Measurement

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重症病人常因各种原因导致血管外肺水增多或急性肺水肿，病情凶险，变化快，病死率高。据统计，约有10%的各种病例在死亡前并发肺水肿，因此及时正确的治疗对改善患者预后十分重要。以往临床上主要通过氧合指数（PaO_2/FiO_2）、中心静脉压（CVP）、肺动脉楔压（PAWP）等指标来间接判断肺水肿的发生和严重程度。近来EVLW作为一种新的监测指标，因其具有更高的特异性和灵敏度，逐渐被临床关注。

一、EVLW

EVLW是指分布于肺血管外的液体，包括细胞内液、肺间质液和肺泡液。由于细胞内液一般变化不大，所以EVLW的变化主要反映肺间质液和肺泡液的改变。EVLW的改变和肺水肿的程度具有很好的相关性，是研究肺水肿的定量监测指标，可以早期，灵敏地对肺水肿的程度进行动态监测，并及时指导治疗，改善病人预后。

1. EVLW的产生机制

$EVLW=\{Kf[(P_{mv}-Pp_{mv})-\delta f(\pi_{mv}-\pi p_{mv})]\}-Flymph$，其中$Kf=SA\times Lp$，为液体滤过系数，SA为滤过面积，Lp为水流体静水传导率，P_{mv}为肺毛细血管静水压，Pp_{mv}为肺间质静水压，π_{mv}为肺毛细血管胶体渗透压，πp_{mv}为肺间质胶体渗透压，δf为反射系数，Flymph为淋巴引流量。正常情况下，经微血管净滤过的液体将经淋巴管回流到循环系统。因此，肺EVLW含量的多少决定于经微血管净滤过生成的组织液量与经淋巴管回流的重吸收量的平衡状态。目前对EVLW正常值的界定仍有分歧，大部分人认为小于7ml/kg，也有人认为小于10ml/kg[1]。

2. EVLW的调节

正常情况下人体通过其解剖和生理机制保持着渗出和回流的平衡，以保证肺间质的水分趋于稳定。①肺血管上皮的屏障和抗渗漏作用；②肺泡表面活性物质降低肺泡表面张力以对抗血管外液体的渗出；③肺泡上皮主动转运清除血管外液体和大量淋巴液回流对肺间质的吸引。

二、EVLW的监测方法

EVLW的理想测量方法应当是无创，定量，简便，经济，精确且能连续监测。而现在所用的大部分监测方法，无论从精确度还是特异性上，还不能很好地反映EVLW的生成和清除[2]。其中常见的监测方法有称重法，胸片，CT，超声扫描术，PET，电生物阻抗技术，双指示剂热稀释法和单指示剂热稀释法。现综述如下：

1. 称重法

称重法主要用于动物实验，具体方法为：动物全身肝素化，抽取动脉血称重备用。饱和氯化钾（KCL）处死动物，迅速开胸，扎闭双侧肺门，以防肺血丢失。切取两完整肺组织，称重后加入同重量的蒸馏水，搅拌器充分搅拌形成肺匀浆。取10ml匀浆，高速离心（5000r/min,5min）后放置于5℃1小时，取上清液。采用WHO推荐分光光度计比色法分别测定动脉血，肺组织匀浆和上清液血红蛋浓度。另取动脉血，肺组织匀浆和上清液，80℃干燥72小时以上，分别计算含水百分比。根据下列公式计算可得出EVLW：

肺匀浆血红蛋白浓度=上清液血红蛋白浓度×（匀浆含水百分比/上清液含水百分比）

肺血重=匀浆重×匀浆中血红蛋白浓度/血液血红蛋白浓度

肺血液中水重=肺血重×血液含水百分比

肺脏中总的水含量=匀浆含水百分比×肺匀浆重-附加水（蒸馏水）

EVLW=肺脏中总的水含量-血液中水重

称重法于1965年由Pearce等人[3]第一次使用，是测定EVLW的经典方法。因其结果可靠，常将其作为判断其他方法准确性的金标准[4]。但因其创伤太大，多用于动物实验和尸检。

2. 胸片

胸片是比较广泛用于临床的判断肺水肿及其演变的手段。肺水肿典型的X线表现是肺纹理增粗，紊乱和重分布。间质性肺水肿肺野呈磨玻璃样并伴有小粟粒影，并可见肺小叶间隔线，即Kerley’s A、B线；肺泡性肺水肿主要表现为斑片状模糊阴影，其中中央型具有典型的“蝴蝶状”或“蝙蝠翼状”的特殊形态。当EVLW增加30%以上时，才可观察到X线检查异常。胸片具有无创，经济，可重复，适于床旁操作等优点，并可直接观察肺水肿的分布情况，有利于推断压力性肺水肿和通透性肺水肿。但X线检查不能定量和连续监测，相对病情发展有一定的延迟性，并且胸片结果也易受很多因素的影响，如：肺的充气状态，摄片的质量，医师的经验等。在检查过程中患者还会接受大量放射线。甚至有学者认为X线与EVLW无相关性[5]。总之，从灵敏度和准确度上考虑，胸片都不是最佳监测方法，只可用于辅助诊断。

3. CT

CT作为另一种影像学方法，较之胸片有较高的分辨率和良好的组织对比度。断层相消除了组织结构重叠的影响，更易发现肺水肿的存在，甚至早于CVP等血流动力学指标的变化[6]。近年高分辨CT的应用，更能清楚的显示EVLW和肺实质的情况，从而使不同类型的肺水肿得以鉴别[7]。如静水压性肺水肿主要表现为血管充血，支气管血管袖口征等，而渗透性肺水肿则以肺实质密度改变为主要表现。所以不论从精确度还是灵敏度来讲，CT都是监测肺水肿的不错选择[8]。但因其设备庞大，操作复杂，不宜用于床旁监测，用于危重病人监测有其局限性。

4. 超声

在正常情况下，胸膜下小叶间隔厚度约为0.10-0.15mm，大部分小于超声分辨力（1ml），故正常情况下肺部超声检查多为肺泡内气体强回声所包绕而不能显示。当肺部充血或肺间隙液体积聚时，小叶间隔增厚，与周围肺泡内气体的阻抗差异很大，产生多重反射即混响声影，即彗星尾征。其特征是自强回声界面开始的逐渐内收并减速弱的多条平行强回声线。

临床上可以根据彗星尾数和对EVLW进行半定量估计，并且比氧合指数等血流动力学指标能更早发现肺水肿的发生[9]。Vicki E.Noble等[10]对45例肺水肿患者进行血液透析治疗，并在透析前中后三个时间点分别做胸部超声，结果显示超声检查能及时发现水肿液的变化。Qureshi和Gleeson[11]的研究结果表明超声对微量的EVLW的增加（>5ml）也很敏感。Zoltan Jambrik等[12]认为超声监测的结果与金标准的肺称重法有良好的相关性（r=0.91,P<0.001）。

胸部超声作为一种监测EVLW的有效方法，具有敏感准确，简单，无创，床旁检查等优势。但超声检查范围可能达不到深部的肺组织，而且超声不能区别小叶间的液体积聚是水还是血液，所以该方法还需要更多动物和临床的研究。

5. PET

（1）PET显像是一种用正电子核素进行的放射性示踪显像技术，根据显像剂按其化学性质特性能够选择性地浓缩于某一器官组织的特点，将能发射正电子的放射性核素或所标记的化合物导入人体内。然后探测人体内发出的放射性信号，采集三维数据，再将三维数据重组成二维数据，最后再经二维重建得到各断层图像。以解剖形态方式显示活体组织器官内生物化学物质的浓度及其随时间的变化。

（2）PET临床应用多集中于神经，心脏及肿瘤性疾病的诊断。对肺疾病的诊断也可提供很好的临床依据。PET可用于测量整体及局部的肺水积聚情况。方法为：将两种同位素序贯给入，一般是用O_2-15标记的H_2O静脉注入，几分钟后当与体液达到平衡之后，摄胸片可反映整体肺水的量。第二步再静注一种留于血管内的同位素示踪剂，如标记的血浆蛋白，再重复胸片，可反映肺血管内容积。将第二步的影像密度从第一步的影像密度减影，即可确定EVLW的积聚颁。虽然测量结果会低估10%-20%，但仍与称重法的相关性高（r=0.93）[13]，且能监测到1mlEVLW的增加[14]。PET在肺疾病的研究中有巨大的潜力，但因该技术的高昂费用以及将重症病人移至检查室的不便，使PET的发展受到了限制。

6. 生物电阻抗技术

生物电阻抗技术是利用生物组织与器官的电特性及其变化提取与人体生理，病理状况相关的生物医学信息的一种无操作检测技术。

（1）原理：人体内各组织的电特性是由该组织所含水分的多少决定的。如血液，肌肉对电的传导性要比骨和脂肪组织好[15]。对于肺来说，正常状态下肺内充满气体，电流传导性低，而当肺部发生水肿时，肺部血液循环，组织液含量以及通气状况等发生改变，这将引起肺部阻抗的相应变化。借助于体表的电极系统向检测对象送入一微小的交流电流和电压，检测相应的电阻抗及其变化情况，可推断出肺部的相应病变。现对监测EVLW有研究价值的有经胸电阻抗（Transthoracie Electrical Bio-impedance,TEB）技术和电阻抗断层成像（Electrical Impedance Tomogrphy,EIT）技术。

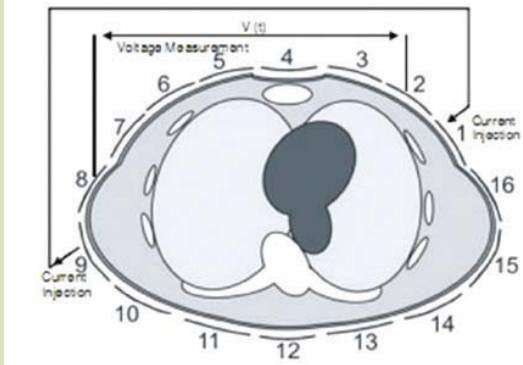
（2）检测方法

TEB的检测方法：分别将6只电极置于前额，左膝下，两侧颈根部，胸部剑突水平左右腋中线，测出颈围（颈根部放置电极的周径），胸围（胸部放置电极的周径），胸长（颈部电极至胸部电极的垂直距离），将以上的数据和红细胞压积，体重，身高，心率，收缩压以及舒张压输入监测仪，所有电极连于生物阻抗计算机上，给予2.5mA电流，频率为70KHz，通过电阻率测量获得相应的结果。

EIT与TBE检测方法大致。不同的是，EIT可以通过在动物体某一断面进行阻抗测量，根据外加信号与被测量信号的关系，按照一定的算法计算这一断面内电阻率或其变化的颁，并以数字图像的形式加以表述。

此种方法最大的特点就是无创，简单，可连续监护，实时显示。Arad M等对压力性肺水肿的患者用EIT法进行监测得出此法对EVLW的变化的敏感性高[15]。而因临床普遍认为此法的准确性受电极位置影响，Lisa Beckmann等[16]针对最佳电极置放位置做了研究，发现在8或16点给予电流，在9或15点接受信号时，此法准确性最高（图1）。但目前为止，此法的准确性仍受到置疑，需要进一步的研究证实其可行性。

图1 围绕胸廓的16个电极位置



7. 双指示剂稀释法

双指示剂稀释法是将温度稀释法和染料稀释法相结合的方法。

（1）方法：通过颈内静脉或锁骨下静脉放置中心静脉导管，外接温度探头。自中心静脉同时注入两种指示剂。热稀释指示剂（常用冰的生理盐水）和染料稀释指示剂（常用白蛋白结合的吲哚绿）。股动脉置管，放置一根尖端带有热敏电阻丝的导管检测并绘制热稀释曲线。根据各自的稀释曲线分别得出稀释曲线的平均变化时间，计算出CO。

（2）原理：当冰生理盐水和ICG染料被同时注入右心房时，冰水作为可弥散的指示剂（血管外指示剂），可在肺血管内外自由地与肺组织进行热能量交换而分布至全肺。所以冰水所流经的所有容积为EVLW和胸腔内血容量（intratheraeic blood volume,ITBV）的总和，即胸腔内热容量（intrathoracic thermal volume,ITTV）。而染料指示剂流经的所有容积量为心脏舒张末期容积（global end-diastolic volume,GEDV）和肺血管内容量（pulmonary blood volume,PBV）的总和，即胸腔内血容量（intratheraeic blood volume,ITBV）。

根据公式：V=CO×MTT，可得：

ITTV=CO×MTT（热稀释指示剂）

ITBV=CO×MTT（染料指示剂）

EVLW=ITTV-ITBV

MTT：平均传输时间，即指示剂从注射点到测量点的平均时间；V：指示剂所流经的所有容积；CO：心输出量

（3）该方法准确敏感，特异地对EVLW做定量测定，甚至有人将它可作为临床上测量EVLW的金标准[17]。但Eisenbergt等[18]提出用液体为介质测量EVLW可能会加速EVLW的清除而影响结果，Milchell等[19]则用实验证实了这个观点。除此之外，此法操作复杂，费用昂贵，近年来已很少用于临床。然而它是监测EVLW的一大进步，并且为单指示剂稀释法的发展奠定了基础。

8. 单指示剂稀释法

单指示剂稀释法是现今测量EVLW最经典的方法之一，是由双指示剂稀释法演变而来。临床上常用PICCO仪通过热指示剂来监测EVLW，CO，MTT。

（1）方法：与双指示剂法基本相同。置入中心静脉导管和装有热探头的股动脉导管，从中心静脉导管注入8℃的冷生理盐水，冷水的量由患者的体表面积决定，一般为10-20ml。由股动脉的热探头可得到热稀释曲线。

（2）原理：心脏和肺可看成是由一系列贯而独立的容积腔组成，股动脉导管检测到的热稀热曲线可看成是多个容积腔稀释曲线的组合，稀释曲线中最长衰变曲线对应的是其中最大的容积腔。将热稀释曲线取对数后进行标记，可得到稀释曲线的指数波形下降时间（DSt）。根据公式：

ITTV=CO×MTT（热稀释指示剂）

PTV=CO×DSt（热稀释指示剂）

GEDV=ITTV-PTV（ml）

ITBV=（1.25×GEDV）-28.4（ml）[20]

EVLW（ml/kg）=ITTV-ITBV（ml）

（3）Katzenelon R等[21]用狗做实验得出单指示剂稀释法与称重法的相关系数为0.97，Fernandez-Mondejar E等[22]的研究结果显示单指示剂稀释法能检测出EVLW10%-20%的变化，这对于判断病情，确定治疗方案有重要意义。单指示剂稀释法还具有床旁连续监测，操作简单，结果可靠等优点而逐渐被临床所关注使用。北京大学附三医院也报道了他们用单指示剂稀释法监测EVLW，指导治疗2名H1N1引起ARDS的病例[23]，该技术目前已在国内广泛应用于临床。

但这种技术仍存在一些缺点。如不能反映局部肺组织EVLW的情况，需要借且影像学。Benjamin Maddison等[24]以双指示剂稀释法作为金标准，得出单指示剂稀释法与其相关性不令人满意。现在普遍认为肺栓塞，肺损伤，肺切除术后的病人，EVLW的监测结果低于实际值。这是因为此方法要求热指示剂必须通过肺所有区域进行热交换，如果肺灌注不足，热指示剂不能通过血流达到相应的肺组织，从而导致该区EVLW不易测出，即实测值低于实际值。然而相对于液体指示剂而言，气体指示剂的扩散速度快且容易，它可通过灌注好的区域扩散到灌注不良的区域，这一特点在一定程度上弥补了单指示剂稀释法的误差[2]。

总之，作为一种较新的监测EVLW的技术，单指示剂稀释法具有深入研究的价值。

三、EVLW监测的价值

EVLW能直接反映肺水肿的严重程度，比CAP、氧合指数等更有利于反映血流动力学情况，可作为一个独立的评价指标[25]，对于早期预防治疗提供了依据。Sakka等[26]的临床实验调查发现，高EVLW患者的病死率显著高于低EVLW患者。

Martin等[27]发现，EVLW和氧合指数，机械通气时间以及住院病死率均显著相关，提示EVLW对判断危重患者的病情及预后有重要价值。监测EVLW还可指导液体治疗，呼吸机支持治疗，并可对治疗肺水肿的新方法作出评估。

四、结论

EVLW可作为临床诊断、治疗肺水肿的一个独立、重要的指标。对EVLW进行早期、连续、定量的监测也显示得至关重要。X线，B超作为最基本的方法有很多不确定性；CT，PET能提供精确的诊断，但不适于危重病人；电阻抗法是无创测量中较理想的方法，但其准确性仍不确定，影响因素多；[23]指示剂法尤其是单指示剂稀释法能提供早期，连续，定量的监测，但作为一种新的技术，仍需更多的研究去证明和改进它的可靠性。

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中华医学会第五届全国老年呼吸病学术大会

“中华医学会第五届全国老年呼吸病学术大会暨中国老年学学会第二届全国老年呼吸和危重病学术大会”将于2011年5月在北京召开。本届大会由中华医学会老年分会呼吸病学组、中国老年学学会老年医学委员会呼吸和危重病专家委员会和解放军总医院南楼呼吸科共同主办，北京协和医院、北京大学第一临床医院协办。

一、征文内容：

1.老年肺部感染；2.呼吸危重症临床救治；3.机械通气临床实践；4.老年肺癌治疗；5.气道阻塞性疾病；6.肺部疾病的介入治疗；7.其他与老年呼吸病和危重病相关的临床实践与实验研究

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（1）未在国内公开发行刊物上发表的论文和综述等，写作格式参照《中华结核和呼吸杂志》投稿须知，论文不超过3500字，综述限制在4000字以内；

（2）提供非结构式摘要一份,800字以内，编排顺序为：题目、单位、邮编、姓名、正文；

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摘要

小儿发热是围麻醉手术期的常见问题之一，如处理不当甚至会危及患儿生命。本文报道我院近1年遇到的3例先心病小儿术中发热病例，分析小儿术中高热的原因及预防处理措施，探讨先心病小儿围术期的体温监测，预防高热发生及积极治疗的有效方法，旨在为小儿临床麻醉积累相关经验。

关键词：小儿；高热；先心病；麻醉

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先心病小儿术中高热的治疗与分析

Treatment and analysis of high fever during operation about children with congenital heart diseases

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Abstract

The high fever during operation about children is a difficult question, it's very terrible if we couldn't treatment it correctly. This paper report 3 children cases of high fever during operation with congenital heart diseases, and discuss temperature monitoring, take precautions against high fever and treatment it effectively in operating room.

Key Words: Children; High fever; Congenital heart diseases; Anesthesia

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我们于2009年6月至2010年7月在临床工作中遇到3例先心病患儿麻醉后高热的病例，2例抢救成功，1例死亡，现分析报道如下。

例1，男，9岁，19kg。因间断胸闷、气短1年入院。术前诊断先天性心脏病，房间隔缺损(Ⅱ孔型，多孔)。麻醉诱导采用咪唑安定2mg、芬太尼0.1mg及维库溴铵2mg静脉注射，气管插管顺利，R24次/分，P100次，BP102/60mmHg，吸入七氟醚麻醉维持。麻醉诱导后经桡动脉和颈内静脉置管行有创动脉压和中心静脉压监测，行鼻温和肛温监测，鼻温:38.9℃、肛温:39.1℃，未预处理，经与外科医生讨论后暂停手术，维库溴铵1mg和芬太尼0.1mg静注后送回胸外科ICU，行呼吸机辅助呼吸、心电监测，生命体征:R:24次/分、P:120次/分、BP:99/54mmHg，急查血常规:WBC12.05×109/L、中性粒细胞比率0.84淋巴细胞比率0.11。采用50%酒精擦浴，肌肉注射安痛定、非那根等退热药物和物理降温等措施，患儿体温渐降至37℃～36.8℃，手术医生与麻醉医生讨论后一致认为此时手术风险较大，当日手术取消，继续抗炎及降温治疗，严密观察病情变化。经过11天治疗，患儿体温及血常规检验恢复正常后再次手术，麻醉诱导采用咪唑安定1.5mg、芬太尼0.2mg、依托咪酯6mg及维库溴铵2mg静脉注射，吸入七氟醚，间断辅以芬太尼和维库溴铵及依托咪酯维持麻醉，术中监测体温波动在36.7℃～37.8℃，手术过程顺利，术后随访未见麻醉相关并发症，经治疗后患儿痊愈出院。

例2，男，5个月，8.5kg。因感冒后出现咳嗽、咳痰伴气短一月余入院。术前诊断先天性心脏病，房间隔缺损(Ⅱ孔型)，右心扩大，三尖瓣关闭不全(中度)，肺动脉高压(38mmHg)。给予氯胺酮10mg后行桡动脉穿刺建立有创动脉压监测，R30次/分，P120次，BP80/50mmHg，麻醉诱导采用咪唑安定0.5mg、芬太尼0.04mg及维库溴铵1mg静脉注射，气管插管顺利，行鼻温和肛温监测后，示鼻温:38.0℃、肛温:38.9℃，肛门塞入消炎痛栓1/8粒，在腋窝、腹股沟、颈部置以冰块行物理降温治疗，近1小时后患儿体温下降至鼻温:36.6℃、肛温:37.4℃，行颈内静脉穿刺建立中心静脉压监测。间断辅以芬太尼和维库溴铵及依托咪酯维持麻醉，开始手术。术中监测体温在正常范围，手术过程顺利，术后随访未见麻醉相关并发症，经术后康复治疗后患儿痊愈出院。

例3，女，1.5岁，7kg。因感冒后出现胸闷气短一周余入院。术前诊断先天性心脏病、室间隔缺损、肺动脉高压(65mmHg)。给予氯胺酮45mg肌肉注射后行桡动脉穿刺置管建立有创动脉压及体温监测，T39.6℃，R30次/分，P120次，BP90/60mmHg。约10分钟后患儿出现面色潮红，面部肌肉抽搐，呼吸急促，R48次/分，HR190次/分，心律齐，双肺未闻及湿性啰音。立即给予面罩加压吸氧，酒精擦浴，腋窝、腹股沟、颈部置以冰块行物理降温治疗。30分钟后患儿T达41℃以上，面色紫绀，四肢抽搐，呼吸加深加快，50～60次/分，P180～200次/分，节律不齐。急送胸外ICU，患儿体温仍维持在41℃以上，症状无缓解，20分钟后呼吸心跳停止，经积极抢救无效，临床死亡。

讨论

在全麻中，多数病人出现低体温，然而在小热麻醉中高热的发生率相对较高[1]。小儿恶性高热报道多见，而小儿术中高热报道不多但临床并不少见。体温变化会影响心律、心率、血压及呼吸等生命体征，并影响循环和呼吸功能及基础

代谢，给机体带来急性损伤甚至危及生命，并直接影响到手术效果。对小儿来说，其机体各组织器官系统尚未完全发育成熟，体温自身调节能力较差，相同环境下易发生体温改变。因此，对小儿麻醉中体温的有效监测和调控值得临床注意观察和探讨[2]。

小儿时期正常体温可波动于一定范围，正常小儿腋下体温一般在36.0℃～37.0℃之间。临床上根据体温的高低可分为：低热：<38℃；中热：38.0℃～39.0℃；高热：39.0℃～41.0℃；超高热：>41℃[3]。术中高热可致小儿心率加快，心脏负荷加重，颅内压升高和大脑皮质过度兴奋，出现烦躁、头痛或高热惊厥，严重者可出现瞻望、昏迷、呕吐和脑水肿，持续的高热还可出现神经系统紊乱、恶心、呕吐、苍白、皮肤厥冷、大汗、心动过速，低血压等。小儿术中一旦发生高热应及时处理，采取相应的降温措施。可以降低室温，体表敷以冰袋，还可给予适量的冬眠合剂，此外，解热镇痛药物、糖皮质激素和利尿剂的应用也有助于降温。

3例患儿均在麻醉用药后出现了高热，导致了手术的停止或暂缓。由于小儿发热受多种因素的影响，当出现体温增高时，临床医生首先考虑器官炎症或感染控制不佳，临床上其他疾病如甲状腺危象、麻醉机发生故障引起的重复吸入、嗜铬细胞瘤、吸收热、药物反应、过敏、电击造成多脏器（肝、肾）功能损伤、下丘脑脑干等中枢功能障碍等均能引起高热。小儿腺体分泌旺盛，术前抗胆碱能药物的剂量相对较大，可兴奋高位中枢神经引起基础代谢率增高。同时可抑制下丘脑的功能，抑制皮肤粘膜腺体分泌，呼吸道粘膜干燥，使机体产热增多而散热减少，导致体温升高。目前认为一些麻醉药物及肌松药有可能诱发恶性高热(Malignant Hyperthermia，MH），易于诱发MH最常见的药物是氟烷和琥珀胆碱,此外,甲氧氟烷、氨氟醚、异氟醚、地氟醚、七氟醚、乙醚、环丙烷、三氯乙烯、三碘季铵酚、右旋筒箭毒碱、利多卡因和甲哌卡因等也可诱发[4]。这些麻醉药物在临床应用当中也都可引起机体发热。本文例2，例3中均使用了氯胺酮，经查阅文献亦有相似的报道。氯胺酮为分离麻醉剂，其主要作用部位为丘脑及大脑皮质层，体温中枢正位于丘脑下部，有可能氯胺酮在发生麻醉作用的同时，亦使体温调节中枢出现暂时的功能紊乱，导致体温升高[5]。因而，氯胺酮用于小儿麻醉时需连续监测体温、血氧饱和度，遇到原因不明的高热时，应立即行血气分析，查血K^+、Ca^{2+}、CPK及监测$P_{ET}CO_2$，以便排除和早期确诊MH，对遗传性骨骼肌疾病及经常感冒发烧的患儿，应慎用氯胺酮[6]。全身麻醉下由于意识消失和肌松药的应用，体温调节中机体的行为调节减弱甚至消失，而所有麻醉药均可显著损碍体温的自动调节机制，患者体温因产热和散热的不平衡而发生被动性变化出现发热。小儿体温还可受麻醉操作的影响，在全身麻醉下气管导管过细而又未作控制呼吸，患儿用力呼吸以克服呼吸道阻力，产热增加，使体温升高。使用循环紧闭式麻醉，钠石灰可以产热，如钠石灰失效或更换不及时，能通过呼吸道使体温升高。患儿在手术中出现心率过快、$P_{ET}CO_2$升高时，除插管过深、麻醉深度过浅、容量不足等原因，还应考虑小儿高热的可能性[7]。

小儿麻醉中发热对小儿的循环和呼吸系统的影响甚大，尤其是先心病小儿更应积极治疗，早期预防。其处理仍以物理降温为主，辅以解热剂，但需要值得注意的是慢性先心病的小儿慎用扑热息痛和布洛芬，以避免加重心血管的负荷[8],可考虑使用心血管副作用较小的对乙酰氨基酚[9]。必要时予以不同剂量的鲁米那镇静及抗惊厥，同时注意补充液体及维持电解质平衡，尽量缩短麻醉时间，选择安全的麻醉药物，减少麻醉药物的摄入量，减轻创伤，都可减少或减轻发热的发生。有研究认为：阿片类药物呈剂量依赖性抑制发热，在小儿发热中可以考虑使用一些小剂量芬太尼和阿芬太尼[10-11]。此外，小儿病人在接受麻醉前要接受一个有效的上呼吸道感染和体温的评估，可以减少麻醉和手术的风险[12]。

综上所述，关于先心病小儿术中高热的治疗先心病小儿麻醉中的体温监测、临床治疗及发热的机制都尚需进行深入的基础和临床研究。

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2011年天坛·国际神经外科麻醉论坛（TiNAS2011）

由首都医科大学附属北京天坛医院、首都医科大学麻醉学系和北京医学会麻醉学分会主办的“2011年天坛·国际神经外科麻醉论坛（TiNAS2011）”将于2011年6月3-5日在北京隆重举行！

2011年，我们以“探索，合作，进步”为主题，以更新的视角、更丰富的内容、更高质量的学术研究和创新的组织形式，全面展示神经外科麻醉其崭新的学术理念与高新技术。届时，我们将围绕脑外伤与麻醉、脑血管病与麻醉、术中神经功能监测与麻醉、唤醒麻醉技术以及神经外科麻醉恢复期管理等专题的进行交流与探讨。为促进与国际接轨，大会特邀欧洲专家亲临现场，与国内知名专家零距离对话，共同聚焦国际热点话题。

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摘要

目的：探讨小儿腹股沟区手术麻醉安全便利的麻醉方法。方法：小儿腹股沟部手术40例，随机分成二组，Ⅰ组20例以氯胺酮肌注后行髂腹下及髂腹股沟神经阻滞；Ⅱ组20例以氯胺酮肌注后行骶管阻滞麻醉。监测Bp、P、R、SpO_2变化，及术毕清醒时间、术中不良反应。结果：平均年龄、手术时间两组无统计学意义（P>0.05），所有病例均较好地完成手术。两组生命体征、清醒时间无明显差异；切皮时Ⅱ组有4例出现肢体躁动；处理疝囊及牵拉精索时Ⅰ组中有4例出现肢体躁动；Ⅱ组有4例经多次穿刺成功，1例局部血肿。结论：作者认为髂腹下及髂腹股沟神经阻滞操作简单，穿刺引起的并发症及危险性少，麻醉效果与骶麻相似，可作为小儿腹股沟部手术的麻醉方法之一，特别是骶管阻滞困难时。

关键词：神经阻滞、骶麻、腹股沟区、小儿手术

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髂腹下及髂腹股沟神经阻滞用于小儿腹股沟区手术

IIliohypogastric and Ilioinguinal Nerve Block Applied in Pediatric Groin Surgery

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Abstract

Objective: To discuss the safe and convenient method of pediatric anesthesia in groin surgery.

Methods: 40 children who would undergo groin surgery were divided into two groups randomly. 20 cases of Group Ⅰ underwent the illiohypogastric and ilioinguinal nerve block after intramuscular injection of ketamine; the other 20 cases of Group Ⅱ underwent caudal block after intramuscular injection of ketamine. Monitor the changes of Bp、P、R、SpO_2, waking time after surgery, and adverse reaction during surgery.

Results: There was no statistical significance in mean age and operation time（P>0.05）. All operations of children were completed well. 4 patients of Group Ⅱ occurred physical agitation during incision; 4 patients of Group Ⅰ occurred physical agitation during treating the hernia sac and tracting spermatic cord; There was no statistical significance in Bp、P、SpO_2 and waking time during the whole surgery; 4 cases of Group Ⅱ underwent multiple successful puncture, and 1 case occurred hematoma.

Conclusions: I believe that the illiohypogastric and ilioinguinal nerve block is simple, and the puncture cause less complications and risks. The anesthetic effect of illiohypogastric and ilioinguinal nerve block is similar with the caudal anesthesia. It can be one of the pediatric anesthesia in groin surgery, especially when the caudal block is difficult.

Key Words: nerve block; caudal; block; groin; pediatric surgery

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小儿腹股沟区手术是小儿常见手术，该部位麻醉方法有多种选择，但都有一定缺陷，为探讨安全便利的麻醉方法，我们以髂腹下及髂腹股沟神经阻滞，用于腹股沟区手术麻醉，取得较好的效果。

一、一般资料及方法

1. 一般资料

小儿腹股沟部手术40例，年龄9月—5岁，ASA-Ⅰ级，随机分成二组，Ⅰ组20例以氯胺酮肌注后行髂腹下及髂腹股沟神经阻滞；Ⅱ组20例以氯胺酮肌注后行骶管阻滞麻醉。

2. 麻醉方法

患儿常规术前禁食，入室前肌注氯胺酮4-6mg/kg，与父母分离无哭闹时抱入手术室，静脉输液后注阿托品0.01mg/Kg；Ⅰ组以0.25%的罗哌卡因1ml/kg，行髂腹下及髂腹股沟神经阻滞，Ⅱ组以0.25%的罗哌卡因1ml/kg行骶管麻醉；术中面罩吸氧，密切观察并保持呼吸道通畅；监测Bp，P，R，SpO_2并采集切皮时、术中、及术毕时Bp，P，SpO_2数据，及术毕清醒时间、术中不良反应。患儿肢体躁动时，吸入七氟醚或静注1mg/kg氯胺酮。

3. 统计学分析

计量资料以（$\bar{x}\pm s$）表示，应用SPSS 13.0统计学软件处理数据，组间比较采用t检验，计数资料采用x^2检验。以P<0.05为差异有显著性。

二、结果

Ⅰ组平均年龄（2.66±1.56）y，Ⅱ组平均年龄（2.68±1.52）y，两组无统计学意义（P>0.05）；手术时间Ⅰ组（45.8±21.6）min，Ⅱ组平均（44.6±19.4）min，两组无统计学意义（P>0.05），所有病例均较好地完成手术。切皮时Ⅰ组中有2例，Ⅱ组有4例出现肢体躁动；处理疝囊及牵拉精索时Ⅰ组中有4例，Ⅱ组有2例出现肢体躁动，经追加1mg/kg氯胺酮或吸入七氟醚后好转；缝皮时各有1例出现肢体躁动（见表1）。各手术段采集的Bp、P、SpO_2两组无明显变化（见表2）。两组清醒时间Ⅰ组平均

（20.6±10.6）min，Ⅱ组平均（19.3±12.2）min，两组都未发生不良反应；Ⅱ组有4例多次穿刺成功，1例局部血肿。

表1 各手术阶段肢体躁动情况[例（%）]

	切皮时	处理疝时	缝皮时
Ⅰ组 （20例）	2（10）	4（20）	1（5）
Ⅱ组 （20例）	4（20）*	2（10）*	1（5）*

注：与Ⅰ组相比较，*P>0.05(卡方检验)

表2 各时间段生命体征的变化（$\bar{x}\pm s$）

		基础值	切皮时	处理疝时	缝皮时
MAP(mmHg)	Ⅰ组	68.6±11.2	74.2±14.6	76.6±22.6	72.5±16.4
	Ⅱ组	66.4±13.6*	76.4±16.2*	74.8±18.4*	70.9±14.7*
HR(次/min)	Ⅰ组	126.8±16.6	136.4±20.4	140.2±16.6	132.8±14.7
	Ⅱ组	124.3±15.8*	138.6±22.6*	136.8±18.3*	134.4±12.9*
SPO_2(%)	Ⅰ组	99.0±0	98.7±0.66	98.6±0.68	98.9±0.31
	Ⅱ组	99.0±0*	98.4±0.82*	98.5±0.69*	98.8±0.36*

注：与Ⅰ组相比较，*P>0.05

三、讨论

小儿腹股沟部手术是综合医院小儿常见手术之一，各院根据习惯麻醉方法颇多，但多有不理想之处，基础麻醉加骶管麻醉是较多用的方法之一。因骶管变异性大，有的穿刺困难阻滞失败、效果不佳；以及穿刺部位损伤致骶骨骨膜周围血肿，引起术后疼痛；穿刺进入静脉或骨髓可能致空气栓塞、局麻药中毒[1]。Cunter对119家儿童医院150000例骶管阻滞，严重灾难性并发症发生率为1：[2]40000；对非儿童专科麻醉医生而言，技术要求高，有5%穿刺困难阻滞失败且有一定危险性。[3]而髂腹下及髂腹股沟神经阻滞操作简单，相对安全。骶管阻滞要注意药量，观测麻醉平面，切皮时Ⅱ组有4例出现肢体躁动，可能麻醉药扩散不够，而Ⅰ组起效快切皮时效果较好；但处理疝囊有牵拉时Ⅰ组出现肢体躁动较Ⅱ组多，此时要求手术医生动作轻柔，避免过度牵拉组织，出现肢体躁动时吸入七氟醚或小剂量氯胺酮可使患儿安静。

作者认为髂腹下及髂腹股沟神经阻滞操作简单，麻醉效果与骶麻相似，可作为小儿腹股沟部手术的麻醉方法之一，特别是骶管阻滞困难时。髂腹下及髂腹股沟神经阻滞还可用于腹股沟部手术后镇痛，效果同骶管阻滞。

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第十届华东六省一市麻醉会议暨2011年上海市医学会麻醉年会

为提高华东地区麻醉学术水平，交流国内外麻醉学的研究进展，同时也为提高基层临床医师对麻醉学的认识和诊治水平，促进多方合作，华东地区麻醉学协作委员会与上海市医学会麻醉分会定于2011年5月20日～5月22日在上海市联合召开"第十届华东六省一市麻醉学会议暨2011年上海市医学会麻醉年会"，会议将授继续教育项目Ⅱ类学分。会议将邀请国内知名的麻醉学专家教授与会作精彩演讲，同时进行大会学术交流和病例讨论。

一、会议主题：团结协作，促进华东地区麻醉学科和谐发展。

二、征文范围：

1、近年来临床麻醉、重症监测和疼痛诊治新方法、新技术及新进展；

2、麻醉药物和方法的多中心研究结果、经验及体会；

3、麻醉科罕见的病案报导；

4、麻醉科基础研究的新成果。

三、会议热点：

1、国内外麻醉学科建设动态；

2、可视技术在麻醉学领域的应用；

3、高危病人围手术期处理；

4、产科麻醉的发展与展望；

5、病理性神经痛诊治进展；

6、新药的临床。

四、征文要求：

1、围绕上述征文范围及会议热点且未曾发表过的论文，附 800 字以内摘要，具有较强的科学性、先进性和实用性；

2、按结构摘要撰写，顺序为文题、作者、单位、邮编、目的、方法、结果、结论；

3、投稿一律采取电子邮件方式，请以附件形式将 word 文档发送至上海市医学会学术会务部，

E-mail：huadongmazui@163.com。

五、截稿日期：2011年3月15日

六、本通知为大会第一轮征文通知，会议确切时间、地点、日程安排将在2011年3月下旬发出第二轮会议正式通知。

张晶 翻译 卢家凯 卿恩明 审校
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接受抗栓或溶栓治疗患者的区域麻醉指南

美国区域麻醉与疼痛医学协会循症指南（第3版）

Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy

American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition)

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许多研究探讨了正在进行抗凝治疗的患者接受椎管内麻醉和疼痛治疗的安全性。对这类患者的管理重点是：掌握好抗凝药应用时间与椎管内穿刺及导管拔出时机。在对影响凝血药物了解的基础上，这些研究包括服用抗凝药后接受椎管内麻醉的临床研究以及发生了椎管内血肿的个案，都将为临床医生的临床决策给予指导。

随着预防围术期静脉血栓医疗标准的出现，接受抗凝治疗患者施行椎管内阻滞的管理出现了新挑战。同样，随着更有效的抗凝以及抗血小板药物投入临床使用，临床管理也更加复杂化。基于患者安全考虑，美国区域麻醉与疼痛医学协会（ASRA）召开了以区域麻醉与抗凝治疗为主题的第3次共识会议。本文的部分内容是曾发表的1997年与2002年ASRA共识会议的会议记要更新内容，1－6并加入了自发表以后报道中的更新数据。其中的变更是否可接受取决于责任麻醉医生的自我判断。本共同声明的目的是提高患者的安全性和临床处理质量，但并不为某一特定临床结局提供保证。声明会根据认识和临床实践的发展进行及时更新。

这些建议主要关注在手术室、重症监护治疗病房、术后外科病房、产房、普通病房或疼痛门诊接受椎管内阻滞和周围神经阻滞治疗的患者，并为麻醉医生、其他专科医生和医疗机构实施椎管内阻滞和周围神经阻滞麻醉/镇痛时使用，也可为进行类似操作（比如脊髓造影，腰椎穿刺）的医疗机构提供参考。

原文发表在Regional Anesthesia and Pain Medicine（Reg Anesth Pain Med 35:64－101）上，其内容来源于第32届区域麻醉年会以及2007年4月19－22日温哥华研讨会，它提供了透彻理解共识会议中所涉及临床问题的背景。

一、应用抗凝药防治静脉血栓栓塞

1. 根据美国胸科医师协会的指南，我们建议对于每一个抗凝治疗药物，临床医生应按照说明书推荐的剂量使用。（1C级）

二、接受溶栓治疗患者的麻醉管理

应用纤溶或溶栓药物的患者有发生严重出血事件的风险，尤其是正在接受有创治疗的患者。这些建议是基于药物对止血的显著影响、肝素和/或抗血小板药的同时使用（这将进一步增加出血风险）以及使用这些药物后出现椎管内自发性出血的潜在危险而给出的。

1. 对计划接受溶栓治疗的患者，我们建议通过详细询问和仔细阅读病历以发现是否有近期接受过腰椎穿刺、腰麻或椎管内麻醉或椎管内注射类固醇激素，根据以上资料为患者选择适当的监测。指南详细介绍了应用溶栓药的禁忌症并建议避免在不可压迫血管部位进行穿刺后的10天内使用溶栓药。（1A级）。

2. 我们建议除非极特殊情况，对应用纤溶或溶栓药物的患者，禁止施行腰麻或硬膜外麻醉（1A级）。停用这些药物多长时间才能行椎管内穿刺尚无资料依据。

3. 对正在或近期接受溶栓和抗栓治疗的患者施行椎管内麻醉，我们建议一段时间内行持续神经功能监测，每次行神经功能监测的间隔不超过2小时。如果行椎管内阻滞的同时行纤溶或溶栓治疗，并且经硬膜外导管持续输注给药，我们建议输注对感觉和运动影响小的药物，以利于判断神经功能（1C级）。

4. 在通过硬膜外导管输注同时又需使用纤溶或溶栓药物的患者，对于拔除硬膜外导管的时机，目前尚无确切建议。我们建议监测纤维蛋白原水平（代表最后一个凝血因子恢复）来评估残留的溶栓作用以及合适的拔管时机（2C级）。

三、应用普通肝素（UFH）患者的麻醉管理

肝素化患者的麻醉管理方法最初是在20年前建立的。早期的建议是在深入的病例总结、椎管内血肿的个案报道以及美国麻醉医生协会受理索赔方案的基础上提出的。近期血栓预防指南认为有更多患者需要接受每日3次皮下注射肝素，这一治疗使出血风险明显增加并促使了以往ASRA指南内容的改进。

1. 我们建议每日都要检查患者的用药记录，确定药物的同时使用是否会对患者凝血机制中其他成分造成影响。这些药物包括：抗血小板药物、低分子肝素（LMWH）以及口服抗凝药物（1B）。

2. 对接受每日2次5000U普通肝素皮下注射预防血栓的患者，椎管内穿刺技术并非禁忌。推迟肝素的注射时间直到阻

滞完成后使用，可降低椎管内出血的风险，但对于体弱且肝素治疗时间较长的患者，出血风险可能增加（1C级）。

3.对每日接受普通肝素剂量超过10000U或超过每日2次注射的患者接受椎管内阻滞是否安全尚未确定。虽然每日使用3次普通肝素可能导致手术相关出血的风险性增加，但还不清楚是否会增加椎管内血肿发生的风险。我们建议每日3次普通肝素的风险与利益要个体化评估，并且运用易于监测新发或者进展性神经损伤的技术（先进的神经系统功能监测技术和使用对感觉和运动影响最小的神经阻滞溶液）（2C级）。

4.因为应用肝素可发生肝素诱导的血小板减少症，我们建议使用肝素超过4天的患者需在椎管内穿刺或导管拔除前测定血小板计数（1C级）。

5.对血管手术围术期需应用肝素的患者来说，若遵循以下建议，则施行椎管内穿刺是可行的（1A级）。

（1）避免为合并有其他凝血病的患者施行椎管内穿刺。

（2）穿刺后1小时再给予肝素。

（3）末次肝素给予后2～4小时后方可拔除留置导管并评估患者凝血状态，导管拔除后1小时再次肝素化。

（4）术后密切监测以早期发现运动阻滞，应考虑使用最小浓度的局麻药提高早期发现椎管内血肿的可能性。

（5）虽然出血或穿刺困难会增加风险，但并无数据支持因此原因而强制性停手术。与外科医生直接交流后，作出个体化的风险利益判断。

（6）目前，尚无充足数据与经验确定心脏手术患者使用全量抗凝时施行椎管内阻滞技术，是否会增加椎管内血肿的风险。我们建议术后监测神经系统功能，并选择运用对感觉和运动功能阻滞程度最小的药物，确保能早期发现新出现或进展性的神经损伤（2C级）。

四、应用低分子肝素患者的麻醉管理

北美的麻醉医生可借鉴欧洲的经验，制定自己的使用低分子肝素患者接受椎管内或蛛网膜下腔阻滞围术期管理实践指南。所有的共识声明都与美国食品与药品管理局（FDA）所推荐的低分子肝素用药方法一致。虽然我们不可能提出建议完全消除椎管内血肿风险，然而以往的共识性建议似乎对结局有改善作用。我们仍然关注一些较大剂量用药患者的情况，这些病例持续使用了治疗剂量的抗凝药物。

1.Xa抗体水平并不能预测出血风险。我们建议不要常规监测Xa抗体水平（1A级）。

2.抗血小板药或口服抗凝药物与低分子肝素联合运用会增加椎管内血肿的风险。对所有治疗团队进行教育，避免治疗中使抗凝效果增强是非常必要的。我们建议不要在不了解低分子肝素给药方案情况下联合使用影响凝血功能的药物，如抗血小板药，普通肝素或右旋糖苷（1A级）。

3.穿刺或置管过程中出血并无必要推迟手术。我们建议在这种情况下，术后低分子肝素开始使用时间应在与外科医师商榷后推迟24小时（2C级）。

4.术前应用低分子肝素

（1）术前应用低分子肝素预防血栓形成的患者存在凝血功能改变。对这些患者，我们建议至少在给予低分子肝素后10－12小时再行穿刺（1C级）。

（2）对接受较大剂量（治疗需要）低分子肝素患者，如依诺肝素每12小时1mg/kg，每日1.5mg/kg依诺肝素，达肝素每12小时120U/kg，每日200U/kg达肝素或每日175U/kg亭扎肝素，我们建议在这些药物使用24小时后并确保凝血功能正常情况下方可行穿刺（1C级）。

（3）术前2小时使用低分子肝素的患者（普外科手术），我们建议不要施行椎管内穿刺，因此时正值抗凝作用达峰（1A级）。

5.术后应用低分子肝素

对术后应用低分子肝素预防血栓的患者施行单次阻滞或置管连续阻滞都是安全的。这类患者管理取决于每日低分子肝素总量，术后运用低分子肝素的时机及给药方案（1C级）。

（1）每日两次。这种方案增加椎管内血肿风险。无论施行何种麻醉方法，确切的外科止血前提下，术后至少应24小时后给予低分子肝素。术后留置导管应在开始低分子肝素预防血栓治疗前拔除。若应用连续阻滞技术，椎管内导管可留置一晚，但须在术后使用低分子肝素前拔除。导管拔除2小时后再使用低分子肝素。

（2）每日一次。首次低分子肝素应术后6－8小时使用。第二次应首次后至少24小时使用。置入导管可安全的留置。导管应在末次低分子肝素使用后至少10－12小时拔除。导管拔除后至少2小时再应用低分子肝素。不能由于追求更好的抗凝效果而增加影响凝血药物的剂量。

五、口服抗凝药物患者的区域麻醉管理

围术期服用华法林患者的管理仍存争议。目前建议是在华法林的药理学、临床相关的维生素K依赖凝血因子的水平或不足、一系列临床病例以及这些患者中发生了椎管内血肿的个案报道的基础上提出的。以下网站可指导临床医生使用华法林(www.WarfarinDosing.org)。

1.近期刚停止长期华法林治疗的患者接受椎管内阻滞要格外注意。停止华法林治疗第1－3天，尽管此时国际标准化比值（(INR;代表VII因子功能的恢复)已缩短，但机体凝血功能（主要反映在II 和X因子水平）尚未恢复正常。直到国际标准化比值恢复到正常参考值范围内，才有充足的II、VII、IX及X因子存在。我们建议椎管内阻滞前，停止抗凝治疗（最理想的时间间隔为4－5天）并监测国际标准化比值（1B级）。

2.我们建议不要同时使用其他影响凝血机制的药，可能会增加已口服抗凝血药患者出血风险，却不影响国际标准化比值。这些药包括：阿司匹林以及其他的非甾体类抗炎药（NSAIDs），噻氯匹定以及氯吡格雷，普通肝素以及低分子肝素（1A级）。

3.对药物高敏的患者，我们建议减少用药剂量。目前已设计出结合预期效果、患者因素及外科因素来计算合适的华法林剂量的公式来指导医生给药。这些公式对华法林高敏的患者非常有用（1B级）。

4.对术前已服用华法林的患者，若首次服用超过24小时和/或第2次抗凝药已服用，椎管内阻滞前需检测国际标准化

比值（2C级）。

5. 硬膜外镇痛期间接受低剂量华法林治疗的患者，建议必须每日监测国际标准化比值（2C级）。

6. 接受华法林治疗的硬膜外镇痛患者，必须每日常规监测感觉及运动功能。为便于评估神经系统功能，建议使用对感觉和运动功能阻滞程度最小的镇痛药物溶液（1C级）。

7. 对应用华法林预防血栓的患者，建议椎管内导管应在国际标准化比值小于1.5时拔除。研究显示，当国际标准化比值达到此值时，相关凝血因子活动水平大于40%。对这些患者，建议在导管拔除后至少24小时内应连续监测神经系统功能（2C级）。

8. 对国际标准化比值在1.5和3之间的患者，建议拔除导管时要格外小心，仔细回顾是否有使用其他影响凝血功能但不影响国际标准化比值的用药记录（例如NSAIDs、噻氯匹定、氯吡格雷、普通肝素及低分子肝素）（2C级）。我们同样建议导管拔除前做神经系统功能评估并持续到国际标准化比值稳定在所期望预防性水平。（1C级）。

9. 国际标准化比值大于3时，建议留置硬膜外导管的患者华法林剂量维持不变或减量（1A级）。在通过硬膜外导管输注同时又应用治疗剂量抗凝药物的患者，拔除硬膜外导管的时机，目前尚无确切建议。（2C级）。

六、应用抗血小板药患者的麻醉管理

抗血小板药包括NSAIDs、噻吩吡啶类（噻氯匹定及氯吡格雷）以及血小板糖蛋白（GP）IIb/IIIa受体拮抗剂（阿昔单抗、依替巴肽、替罗非班）对血小板功能产生不同影响。由于药理作用不同，我们无法推测椎管内阻滞时药物之间的反应。目前没有一个包括出血时间在内的完全让人接受的检验，来指导抗血小板治疗。术前仔细评估患者健康状况的变化至关重要，这些改变可能导致出血。这些情况包括有易发生瘀血或大量出血的病史、女性患者和高龄。

1. 非甾体类抗炎药物似乎不增加接受硬膜外或蛛网膜下腔麻醉患者椎管内血肿的风险。NSAIDs类药物（包括阿司匹林）不会产生影响椎管内阻滞操作的风险，使用这些药的患者，无论使用单次或连续椎管内阻滞，我们对风险发生与NSAIDs药物剂量、术后监测以及导管拔除时机的相关性无确切建议（1A级）。

2. 服用NSAIDs类药的患者，我们建议同时使用其他影响凝血机制的药时不要施行椎管内阻滞，如：口服抗凝药物、普通肝素或低分子肝素，推测这些药物在术后早期会增加出血等并发症发生的风险。环氧合酶-2抑制剂对血小板功能影响最小，可考虑用于接受抗凝治疗同时又需抗炎治疗的患者（2C级）。

3. 服用噻氯匹定、氯吡格雷以及血小板糖蛋白（GP）IIb/IIIa受体拮抗剂发生椎管内血肿的实际风险未知。这类患者的管理主要基于药品说明书上的注意事项和外科、介入性心脏病学及放射科的一些经验（1C级）。

（1）基于外科和药品说明书上的观点，建议在停止服用噻氯匹定14天后，氯吡格雷7天后方可施行椎管内阻滞。若停用氯吡格雷后5－7天施行椎管内阻滞，应有血小板功能正常化的结果。

（2）血小板糖蛋白（GP）IIb/IIIa受体拮抗剂对血小板聚集功能产生深远影响。服用阿昔单抗24－48小时后血小板聚集功能才可恢复正常，而依替巴肽，替罗非班则需4－8小时。椎管内阻滞需在血小板功能恢复正常后方可施行。虽然血小板糖蛋白（GP）IIb/IIIa受体拮抗剂在手术四周内禁止使用，如需术后服用（椎管内阻滞后），建议服药同时密切监测神经系统功能。

七、接受中草药治疗患者的麻醉管理

接受椎管内或蛛网膜下腔阻滞的患者，服用中草药本身似乎并不增加椎管内血肿的风险。这个发现非常重要，很多准备手术的患者会在术前或术后改变使用的药物。

1. 中草药并不产生影响椎管内阻滞效果的风险。我们建议不强制服用中草药的患者停药或拒绝为其施行区域麻醉（1C级）。

八、应用凝血酶抑制剂[地西卢定、来匹卢定（重组水蛭素）、比伐卢定及阿加曲班]患者的麻醉管理

1. 接受凝血酶抑制剂治疗的患者，我们建议不要施行椎管内阻滞（2C级）。

九、应用戊聚糖钠患者的麻醉管理

应用戊聚糖钠发生椎管内血肿的实际风险并不了解。共识声明是基于持续及不可逆的抗血栓作用、术后早期给药和最初临床试验报道的椎管内血肿病例而制定的。仔细阅读手术出血相关危险因素的临床文献，对患者的风险评估与管理有帮助。

1. 在进一步临床经验获取之前，椎管内穿刺只能使用经临床试验验证的方法（单针穿刺，使用无创穿刺针，避免椎管内置管）。如果这些都不可行，需要考虑其他预防方法。

十、接受抗凝治疗产妇的麻醉管理

1. 随着大量防治深静脉血栓产妇需行椎管内阻滞情况的出现，我们建议ASRA指南（主要来自手术患者）同样适用于这类产妇（2C级）。

十一、神经丛或周围神经阻滞患者的麻醉管理

1. 对接受深部神经丛或周围神经阻滞的患者，我们认为椎管内阻滞的建议同样适用（1C级）。

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临床麻醉管理的新思路

A New Way of Clinical Anesthesia

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在体现医院步入国际先进水平的高、新、尖技术发展的今天，医疗安全仍是各家医院、各个专业的立足之本。作为高风险的麻醉专业医生，在当今复杂的医疗环境中，承担了保障手术患者术中乃至术后的医疗安全重任。如何做好我们的日常工作？不断提高麻醉质量，使我们的工作得到患者及术者的肯定？同时又能够保护好医护人员免遭不必要的医疗纠纷？经过8年“安全麻醉三阶梯管理规范技术”的临床实践，确保了31300余例心血管、胸外科手术患者的手术安全，培养了50人次的临床医生，科室整体临床麻醉水平及教学能力明显提高。现将经验总结交流如下。

一、统一思想，明确目标

首先明确麻醉医生在围术期的主要作用：一是要保障患者在“安全、无痛、舒适”地度过围术期；二是要为手术医生提供静息的手术野。所谓的“静”即是制动：包括肌肉松弛、单肺通气、心脏停止（体外循环）等技术支持；“息”即清晰：包括血压的控制、凝血功能的调控等技术来维持术野的清晰，便于手术止血操作。麻醉医生要做好手术医生的后盾，能够使手术医生在进入手术室后安心专注于尽快完成手术而不是经常性地关注监护仪及患者的生理指标。

“安全、无痛、舒适”作为科室共同的安全麻醉管理理念深入人心。简单的六个字，不能颠倒的次序，分阶梯实施，决定了麻醉处理的原则和针对不同患者个体化方案的统一。“安全”有客观的指标，“无痛、舒适”的主体是患者，因此，要提高麻醉质量的工作必须开始于麻醉前，术前有效的沟通、耐心的解答、适宜的心理疏导，可以增进医患双方的互信，减轻患者的焦虑，也可让患者及家属在术后即便有轻微并发症时对医护人员理解而避免产生纠纷。做好术前沟通、术后随访是麻醉工作顺应医学模式从单纯的生物医学向“生物-心里-社学医学”模式转化的需要。

二、安全麻醉三阶梯管理规范技术的内涵与实施

1.“安全麻醉三阶梯管理规范技术”包含两大块内容

第一部分：确保该技术实施的规章制度、标准操作规程(SOP)及应急预案。

第二部分：支撑安全麻醉三阶梯管理规范技术实施的一系列专业技术。在众多的专业技术中，最为主要的是呼吸管理、循环管理和精确给药技术。

2. 规章制度、标准操作规程(SOP)及应急预案

涉及到具体科室的管理、学科建设是确保该项技术实施的必要条件，也是安全麻醉管理规范技术的基础与核心。在制度与SOP、抢救预案制定过程中必须是根据自身科室的特点，可执行并能够在实践中不断完善、与时俱进，日积月累，从而形成科室的文化，变强制的执行为自觉的习惯性行为。

3. 保障安全的概念

麻醉安全不仅仅是监护仪上的数据，临床麻醉管理的目标是维持机体接近生理状态。建议：

必须根据患者的病情（即病理生理的改变）做好术前准备与评估；

药理学基础——已掌握的与不断更新的知识是麻醉用药的前提；

严密的观察（要使监护仪成为医生的第三只眼睛而不是替代了医生的眼睛），看到的信息必须汇总成综合判断与随机应变（知识与经验的积累）的能力；

选用适合不同患者的麻醉方法与药物治疗（经验医学与循证医学的结合）。

4. 抓住关键的问题——即呼吸、循环的管理

麻醉中千头万绪，要使复杂的问题简单化，最为关键的是抓住呼吸、循环的管理。因为只有保证呼吸、循环的功能：①才能保障脏器的氧与营养成分的供给、CO_2和代谢产物的排出，才能维持生命；②才能保护其它脏器的功能（肾脏、肝脏、胃肠、血液等等可以有时间去处理）。理想处理是在麻醉中不仅要发挥麻醉药的阻滞、抑制作用，还要发挥麻醉药的脏器调控、保护作用。

为了便于记忆及在麻醉中能够快速查找呼吸、循环功能的问题，我们将呼吸和循环看成两个相连接的平面，且每个平面均有三条腿（即三大要素）来支撑。

实现呼吸功能的三大要素：

①气道（即呼吸道）：从口鼻至肺泡是沟通肺泡与外界的通道，需保持通畅；

②肺泡：是气体与血液交换的场所，在这一层面使呼吸

与循环功能紧密扣在一起，必须维持V/Q比相匹配，增高或降低均可导致PaO_2的下降；

③呼吸动力系统：呼吸运动有赖于自主神经调控、呼吸肌的活动、胸壁的完整性等等。在全身麻醉过程中，呼吸运动受控于麻醉医生调控的机械通气，而在全麻恢复期及硬膜外麻醉过程中这是必须考虑的问题。麻醉药对呼吸中枢的抑制、肌肉松弛药对于呼吸肌的影响等等均可影响正常的呼吸运动。

麻醉中呼吸功能障碍的表现之一是：SpO_2或PaO_2下降、$PaCO_2$上升。如果这些指标异常即应从上述三个方面查找原因；同时必须考虑到呼吸与循环是紧密相扣在一起的，不能忽略循环的问题，肺栓塞在麻醉中最为典型的是$PaCO_2$的突然下降。

实现正常循环功能的三大要素

①心脏（泵功能）：心脏有次序地协调的收缩与舒张是实现心泵功能的必要条件。

心脏正常的心律、正常的收缩与舒张功能、正常的自身血供与营养是维持心泵功能正常的前提，随着循环功能监测的进步，心脏泵功能异常是较容易发现的问题。

②血容量：是循环系统内的物质基础（量和质），必须有适宜的容量来维持一定的前负荷。

③血管：血管与心脏是构成循环系统的解剖基础，血管必须保持其完整性及与血容量相匹配的正常的舒、缩功能（后负荷）才能维持血液在心脏泵功能的驱动下在循环系统内流动。毛细血管的通透性是麻醉中应予以关注的问题，通透性增大，相当于血管的完整性遭到破坏，可引起明显的血容量不足，如过敏性修可时。麻醉中应注意避免可使毛细血管通透性增大的缺氧、酸中毒、过多炎性介质的释放等，对严重创伤、烧伤、中毒性休克晚期、缺血再灌注损伤等要考虑已经存在毛细血管通透性的增大。

以心脏泵功能、血管、血容量三者之间的平衡来调节循环功能，以达到满足机体灌注之需求的循环目的。血压是反映循环功能的综合指标，血压降低应迅速从心泵、血管、血容量这三者之间找出问题，对因处理。

5. 支撑安全麻醉实施的关键技术（基本技术）

（1）掌握新型气管插管工具，确保患者气道安全

建立通畅的气道是麻醉医生的基本功。麻醉科医生不仅要有保持气道通畅（如手法托下颌、应用口、鼻咽通气道或喉罩）、快速进行气管插管的能力，而且要掌握几种新型气管插管技术，如可视喉镜、视可尼、光棒、Airtraq喉镜和支气管镜引导插管等，以解决不同情况的困难插管，至今尚无一种方法可以解决所有的困难气道，故必须要有安全的成本，准备各种气管插管工具，并储备掌握工具的麻醉医生。对于繁琐的气道评估程序，我们简化为6步，口诀方式加强记忆：一看（改良M氏评分、牙列）、二张（张口度）、三测量（甲颏距离）、四伸（咬唇试验）、五动（颈部活动度）六再量（颈围）。对于改良M氏III或IV、牙列不齐或缺齿、张口度<3指，甲颏距离<6.5cm、咬唇试验不能咬住上唇、颈部活动受限、颈围>41cm患者要做好困难插管准备。对于预测失败，普通喉镜暴露GradeIII或IV级，按照困难插管预案流程，必须在保证通气的情况下，准备工具，借助新型气管插管工具完成气管插管，记录并在术后告知患者。

（2）目标导向的循环管理

以疾病所致的循环系统病理生理的改变为依据，设定血流动力学的调控目标，并以此目标对血流动力学的紧急变化作出预测和及时处理，维持心脏-血管-血容量三者的平衡。该技术为建立在对血流动力学监测理解的基础上，可以迅速发现问题，使患者避免长时间低血压和高血压的危害。通过经常性观察SpO_2和/或IBP波形，获取心脏收缩力、血管张力、血容量的信息及时调整。有创动脉压监测在心、胸外科手术中尤为重要，可以在电刀干扰ECG的情况下及时发现心脏骤停及时处理复苏。在麻醉中应用血管活性药物调整循环功能应在麻醉用药的基础上，不能为了维持血压让患者处于“浅麻醉”状态中。强调控制，消除不良反应，设立预定的目标管理范围，走在手术操作的前面适时加深麻醉。

（3）精确给药技术

鉴于麻醉过浅、过深对患者潜在的不利影响，建议适度麻醉。BIS等麻醉深度监测仪为适宜麻醉提供了保障，但现有条件不能普及至每例麻醉，可以利用TCI靶控精确给药技术以达到适宜麻醉之目的。通过BIS或其他麻醉深度监测仪监测下的TCI麻醉或其他麻醉培训，掌握不同靶浓度与BIS的相关性，使更多的医生做到适宜麻醉。

（4）不断知识更新、技术更新的学习与提高

对于提高麻醉安全的新知、新技术要用于学习与掌握。

①其他需要注意的问题

（1）对于不同手术、不同的患者，在呼吸、循环管理的基础上应结合手术特点、患者特点，关注其特殊问题，制定个体化麻醉方案，如对于一个颈动脉狭窄的患者，麻醉中应保持足够的血液流通，血压宜维持在较高水平，避免脑缺血、脑梗死的发生。

（2）重视术中保温；有利于组织灌注，有利于止血、凝血。

（3）强化麻醉全程管理：重视麻醉恢复室的工作、常规开展多模式（不同给药途径、不同给药方式）、全程术后镇痛、预防开胸手术后并发症。

（4）关注患者的心灵感受：术前心理辅导舒缓紧张情绪，术后随访、总结。

三、不断总结、知识更新、掌握新技术

要有勇于承担责任的气魄，严格按照规章制度、SOP执行，实施免责意外事件登记报告讨论制度。事件的发生要追寻是个人的原因？还是系统（科室）的原因？集体分析、学习经验、吸取教训，改进工作，不断提高麻醉质量。

倡导认真履行住院医生培训制度及医师终身继续医学教育和继续职业发展教育以保持医护人员的专业技能水平不断完善、与时俱进。

基金项目：上海市级医院适宜技术联合开发推广项目
编号：12010222

任重道远，学无止境

——第一届国际继续医学教育大会纪要

深秋的北京正是气候风景最迷人的季节，第一届中国国际继续医学教育大会于11月13和14日在首都的国际会议中心召开了。

此次会议由卫生部科教司全国继续教育委员会、北京大学、复旦大学、浙江大学、中华医学会和中国继续医学教育杂志社共同主办，并得到世界医学教育联合会（WFME），国际继续医学教育联盟（ACME），美国继续医学教育认证委员会（ACCEM）、亚洲医学教育学会（AMEA）的支持指导。

麻醉学、肝病学、心律学、消化内镜学四个临床学科，成为首届会议的首批学科年度进展报告编制试点学科，相应学科的“2009-2010年度进展报告”也与大会同期发布。这是中国首次主办的集全球知名继续教育领导者、卫生保健官员、临床医学教育者和多学科的临床一线医生共同参与的国际大聚会。也是全球继续医学教育领域一次极具深远意义的交流盛会。它的召开，不仅将对国际继续医学教育理论与实践的创新产生深远影响，也将促进我国继续医学教育工作和卫生事业的发展。尤其在国家深化医药卫生改革的大形势下，麻醉科作为首批参与的众多学科之一，共同参与此次盛会的组织工作，充分说明了麻醉学科的发展已经得到国家卫生主管部门的重视。同时，麻醉学科还邀请知名专家编撰了《2009-2010麻醉学科年度进展报告》，更新知识面，缩短与国际先进水平的差距，提高麻醉医生的专科素养，提供了很好的参考资料。这一活动对引领学科的建设与发展，进一步提高继续医学教育质量，必将发挥重要的作用，。

此次会议的主题是：继续医学教育在医药卫生体制改革中的机遇与使命。而会议的宗旨：构建国际交流平台、提升继续医学教育质量、推进继续医学教育创新、服务卫生事业发展，必将对中国医疗事业的发展产生深远的影响。

开幕式由北京大学常委副校长柯杨主持，并代表全国人大副委员长韩启德——大会的名誉主席致辞，大会主席卫生部副部长刘谦、中国工程院院士巴德年，WFME主席Stefen Lindgren 等分别致辞。他们都对此次大会的意义给予了充分的肯定，并预祝会议的圆满成功。

在开幕式后，四个学科分别进行了分会场的学术报告和交流。麻醉学会不仅进行了学术报告交流专场，还以Workshop的形式，通过实践操作，直观的将临床麻醉进展带给与会成员。

麻醉学科学术讲座专场由上海瑞金医院张富军教授、上海胸科医院徐美英教授主持，中华医学会麻醉学分会主任委员于布为教授致辞。他再次提到：医学职业的特殊性，使医学教育具有终身制的重要意义，需要紧跟时代步伐，掌握最新、最有效的医疗手段，服务于患者。他深有感触的提起：医学这项非常规工作不能“吃老本”，年资越高，越要广泛学习，与时俱进。而且医学知识和技能是日积月累的，并非一蹴而就。麻醉学科在30年前，仍是静脉普鲁卡因麻醉，但现在其在医学、以及在现代医院中的作用和地位已经越来越显著，此次作为首批入选的临床骨干学科，参与到卫生部医政司的继续教育大会，就是全国麻醉同仁努力被认可的体现。

中华麻醉学会新一届的困难气道学组组长田鸣教授和副组长左明章教授亲自担任此次Workshop 的指导教师，希望通过这样一个平台，使与会同仁在麻醉理论和临床技能上都有所收获。Workshop的现场气氛热烈，得到了与会者的踊跃参与和高度好评。

同样，在学术报告会场，与会者分别从全麻药物机制新解——SUMU化；术中知晓；器官保护——血液保护、机械通气肺损伤保护及脓毒血症；新进展——心血管麻醉进展、阿片类药物进展、小儿麻醉进展、急性疼痛管理进展、模拟教育进展等麻醉学科的热点论题进行了全面深入的探讨。尤其在讨论时段，云集了包括于布为教授、黄宇光教授、岳云教授、姚尚龙教授、左云霞教授、徐美英教授、方向明教授、安建雄教授、王天龙教授、赵砚丽教授、徐铭军教授等在内的麻醉界“大师级”与会者们的热烈讨论。他们从基础医学到临床医学；从医学实践到医学教育；从医学、生物学、物理学到哲学、社会学，乃至东西方文化的差异等进行了长足深入、积极热烈的探讨和交流，使与会同仁们进行了一次麻醉界高层次的 “智慧之旅”，圆满实现了会议主旨：更新知识面，提高麻醉医生的专科素养，引领学科的建设与发展，并最终是服务于人类健康。

中华医学会麻醉学分会
Chinese Society of Anesthesiology

學會與征文

Welcome Message of CSM 2011 Shanghai Satellite Meeting — 'East Meets West——Anesthesiologist Talks Today'

In order to better promote the solidarity, cooperation, friendship and academic achievement of CSM2011, the Chinese Society of Anesthesiology will hold the satellite meeting with the theme of "East Meets West——Anesthesiologist Talks Today" from May 19th to May 20th, 2011, in Kerry Hotel Pudong, Shanghai (No.1388 Hua Mu Road, Pudong, Shanghai, 201204, China). This Satellite Meeting will comprise of a one-and-a-half day programme commencing on the afternoon of 19 May with hospital visits. Kerry Hotel Pudong, Shanghai is the first of a new luxury hotel brand of the Shangri-La group located in the heart of Pudong. Within easy reach of the Shanghai New International Expo Centre, and downtown. This Satellite Meeting will provide an invaluable opportunity for delegates to meet with specialists in China, visit local hospitals and sample the wonderful history and culture of Shanghai.

Shanghai is located 1300km (2 ½ hours flying time) from Hong Kong, on China's Eastern coast, and at the mouth of the Yangtze River. It is the most populous city in the world and one of the most prosperous cities in China. It has a fascinating history and rich cultural heritage, welcoming people and an abundance of tourism resources. It is regarded as a centre of commerce between East and West and has become a multinational hub of finance and business. The city is renowned for its historical landmarks such as the Bund and City God Temple, and its modern and ever-expanding Pudong skyline including the Oriental Pearl Tower.

When you come, you will see the great achievements that have been made in the 30 years since China adopted the opening policy and get a feeling for the on-going development and progress of Mainland China for yourself. We sincerely invite you to come to Shanghai and join us in working with the Chinese Society of Anesthesiology to make the satellite meeting of CSM2011a great success.

We are looking forward to meeting you at the event.

●Meeting Chairman

Yu Buwei M.D., Ph.D.

President, Chinese Society of Anesthesiology (CSA)

Chair, Department of Anesthesiology, Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai, China

Chief Editor, Forum of Anesthesia & Monitoring

●Meeting Executive Chairman

Yu Weifeng M.D.,Ph.D.

Vice Secretary-General & Member of Standing Committee, Chinese Society of Anesthesiology (CSA)

Professor, Department of Anesthesia & Intensive Care, Eastern Hepatobiliary Surgery Hospital, the Second Military Medical University

Website: http://www.csaol.cn; http://www.ehbhane.com

2011联合麻醉科学会议上海卫星会会议通知

受澳大利亚新西兰新麻醉学会和香港麻醉医师协会委托，中华医学会麻醉学分会主办的以“中西交融---醉给力（East meets West---Anesthesiologist Talks Today）”为主题的联合麻醉科学会议（Combined Scientific Meeting，CSM2011）上海卫星会将于2011年5月19-20日在中国上海浦东花木路1388号上海浦东嘉里大酒店举行。

此前，由澳新麻醉学会（The Australian and New Zealand College of Anaesthetists, ANZCA）及其疼痛医学分部（The Faculty of Pain Medicine, FPM）、香港麻醉医师协会（The Hong Kong College of Anaesthesiologists, HKCA）合办的联合麻醉科学会议（CSM2011）于2011年5月14日-17日在香港举行，会后与会代表将移师上海参加本次卫星会。

本次会议旨在促进中西方麻醉科学家的大联合，加强彼此间的交流与合作，推动麻醉、疼痛和危重病等学科方面的发展。会议将邀请了国际麻醉领域的知名专家做学术报告，届时仅与会的外方代表将超过200人，来自澳大利亚人、新西兰和香港的麻醉专家还将参观上海市10家大医院，与大陆的麻醉同道共同交流和分享麻醉与疼痛学的热点话题。

上海素有“东方明珠”之美誉。正焕发迷人的风采，既怀旧又摩登，既富东方神韵又有西方风味，更是一座极具现代化而又不失中国传统特色的海派文化都市，五月的上海春意盎然，一定会以海纳百川的热情欢迎和款待来自五湖四海的麻醉同道。

●大会主席：于布为教授（中华医学会麻醉学分会主任委员，交通大学医学院附属瑞金医院麻醉科主任， 麻醉与监护论坛主编）

●大会执行主席：俞卫锋教授（中华医学会麻醉学分会常委兼副秘书长，第二军医大学附属东方肝胆外科医院麻醉与危重病科主任）

大会网址：http://www.csaol.cn; http://www.ehbhane.com

中华医学会麻醉学分会
Chinese Society of Anesthesiology

學會與征文

Welcome Message of the 1st Global Conference of Chinese Anesthesiologists（GCCA）in Shanghai, 2011

In order to better promote the solidarity, cooperation, friendship and academic achievement of global Chinese anesthesiologists, the Chinese Society of Anesthesiology (CSA) will hold the first Global Conference of Chinese Anesthesiologists (GCCA) with the theme of "Innovation Decides Tomorrow----Anesthesiologist Talks Today" from May 19th to May 20th, 2011, in Kerry Hotel Pudong, Shanghai (No.1388 Hua Mu Road, Pudong, Shanghai, 201204, China).

Looking at the development of modern anesthesia, Chinese and ethic Chinese anesthesiologists have made remarkable academic achievements and an indelible contribution. The goals of this conference are to promote the development of anesthesia, pain and critical care medicine, enhance the friendship of fellow Chinese anesthesiologists, further improve their research capabilities and clinical services, and ultimately benefit their patients.

Shanghai, also known as the Pearl of the Orient, is one of the best examples where East meets West. When you come, you will see the great achievements that have been made in the 30 years since China adopted the opening policy and get a feeling for the on-going development and progress of Mainland China for yourself. You will also have the opportunity to enjoy the beauty of Shanghai, its long history and unique Shanghai culture, a combination of Chinese and Western elements. We sincerely invite you to come to Shanghai and join us in working with the Chinese Society of Anesthesiology to make the first Global Conference of Chinese Anesthesiologist a great success.

We are looking forward to meeting you at the event.

●1st Global Conference of Chinese Anesthesiologists Chairman

Yu Buwei M.D., Ph.D.

President, Chinese Society of Anesthesiology (CSA)

Chair, Department of Anesthesiology, Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai, China

Chief Editor, Forum of Anesthesia & Monitoring

●1st Global Conference of Chinese Anesthesiologists Executive Chairman

Yu Weifeng M.D.,Ph.D.

Vice Secretary-General & Member of Standing Committee, Chinese Society of Anesthesiology (CSA)

Professor, Department of Anesthesia & Intensive Care, Eastern Hepatobiliary Surgery Hospital, the Second Military Medical University

Website: http://www.csaol.cn; http://www.ehbhane.com

2011首届全球华人麻醉大会（GCCA）通知

为了更好地宣扬华人麻醉同道的学术成就，构筑一个相互交流和联系的国际化学术平台，由中华医学会麻醉学分会主办的以“创新凝聚未来——醉·给力”为主题的首届全球华人麻醉大会（1st Global Conference of Chinese Anesthesiologists，GCCA）将于2011年5月19-20日在中国上海浦东花木路1388号上海浦东嘉里大酒店举行。

综观现代麻醉学的发展，华人、华裔同道做出了不可磨灭的贡献。华人麻醉学家的学术成就也为世人所瞩目。召开全球华人麻醉大会旨在促进海内外麻醉界华人科学家的大联合，加强彼此间的交流与合作，推动麻醉、疼痛和危重病等学科方面的发展。

上海素有“东方明珠”之美誉。正焕发迷人的风采，既怀旧又摩登，既富东方神韵又有西方风味，更是一座极具现代化而又不失中国传统特色的海派文化都市，五月的上海春意盎然，一定会以海纳百川的热情欢迎和款待来自五湖四海的华人麻醉同道。2011年首届全球华人麻醉会议诚邀全球华裔麻醉学家热情参与，积极奉献。

●**大会主席**：于布为教授

●**大会执行主席**：俞卫锋教授

大会网址：http://www.csaol.cn; http://www.ehbhane.com

现将学术论文征文有关事项通知如下：

一、征文内容及分类：1、麻醉学基础研究；2、临床麻醉与研究；3、疼痛治疗与研究；4、重症监测治疗与研究；5、麻醉相关新技术、新业务进展；6、其它。

二、征文要求：1、凡报送参加年会交流的论文，均提交论文摘要一份（800～1000字以内），并请在稿件左上角按上述征文分类注明论文类别（请自留底稿，恕不退稿）。

2、格式要求：论文摘要一律4号字体，A4版面，文稿顺序为题目、单位、邮编、作者姓名、摘要内容。

3、凡已在学术会议上或公开发行的刊物上发表过的论文，不予受理。

4、论文需经所在单位审查后方可电邮；请在电邮题目注明“2011全球华人麻醉会议”字样。

三、投稿方式：本次会议只接受网上征文，不接受信件等纸质投稿，投稿邮箱ehbhane@126.com；

四、截稿日期：2011年3月16日；过期恕不受理。与个人邀请外宾来参加会议并拟进行学术交流者，也请通知俞卫锋教授并在上述截稿日期前交来论文摘要，以便统一安排。

五、有其它相关事宜，请联系大会学术秘书组，杨立群副教授（021-81875235，15921969001）

2011年中华医学会全国麻醉学术年会
征 文 通 知（草案）

医学术便函（2010）第0号

各省、自治区、直辖市医学会：

各有关医疗单位：

中华医学会麻醉学分会拟定于2011年9月7—10日在济南召开“2011年中华医学会全国麻醉学术年会”，本次会议是中华医学会一类学术会议，麻醉分会各专业学组年会将同时并会召开，因此是2011年度的重要学术盛会。年会将设各专业学组分会场、专题板块和学术论文报告相结合的形式进行学术交流；现将会议学术论文征文的有关事项通知如下：

一、征文内容及分类：

1. 麻醉学基础研究；
2. 临床麻醉与研究；
3. 疼痛治疗与研究；
4. 重症监测治疗与研究；
5. 麻醉相关新技术、新业务进展；
6. 特殊病例报告；
7. 其它。

二、征文要求：

（一）、年会征文：

1. 凡报送参加年会交流的论文，均提交论文摘要一份（800——1000字以内），并请在稿件左上角按上述征文分类注明论文类别（请自留底稿，恕不退稿）。

2. 格式要求：论文摘要请用Microsoft Word2000或2003编辑，页面设置请用4号字体，A4纸，文稿顺序为题目、单位、邮编、作者姓名、联系电话、摘要内容。

3. 凡已在全国性学术会议上或全国公开发行的刊物上发表过的论文，不予受理。

4. 本次年会仍将进行中青年优秀论文评选，参评条件为1966年9月1日以后出生（投稿时请将身份证复印件扫描成图片格式粘贴在文章的首页）。凡申请参加中青年优秀论文评选的论文，均需提交中、英论文摘要各一份（800--1000字以内）及中文全文一份，论文一律用word文档撰写（请网上投稿）；征文要求同上；并请在稿件右上角注明“中青年优秀论文评奖”字样。评选设一等奖1名，二等奖3名，三等奖5名（具体参评要求届时见有关会议通知）；获奖者将获得临床科研奖金。

5. 各专业学组征文也按年会要求一并投稿，学科管理学组、疼痛学组、ICU学组、儿科麻醉学组、神经外科麻醉学组、心胸外科麻醉学组、气道管理学组、器官移植麻醉学组、产科麻醉学组及青年委员会，都将在年会期间组织学术活动。

（注：年会还将继续进行2011年度SCI论文奖评选；获奖者将获得优秀论文奖金；具体评选办法请登录年会网址查询）。

三、投稿方式：

1. 网上征文与报名：年会网址：http://www.csaol.cn/；

2. 书面邮寄：“北京东四西大街42号中华医学会麻醉学分会办公室白雪同志收（邮编：100710；投寄的论文请在信封上注明“2011年麻醉年会征文”字样）。联系电话010-85158614，传真：010—85158753；邮箱：csa2011@live.cn）；（请尽量采用网上投稿；以保证投稿和注册的准确性；二种方式只选一种）。

四、截稿日期：

年会：2011年3月31日

五、凡个人邀请外宾来参加全国年会并拟进行学术交流者，请与麻醉学分会办公室白雪同志联系（联系方式同上）。

联系人：白雪　中华医学会麻醉学分会办公室

联系电话：010-85158614；传真：010-85158753；

第五届北京三博国际神经科学论坛（第一轮通知）

主办单位：首都医科大学第十一临床医学院北京三博脑科医院

会议地点：北京裕龙国际酒店（北京市海淀区阜成路40号，010-68468479）

报到时间：2011年4月28日（周四）9:00至21:00

会议时间：2011年4月29日（周五）至4月30日（周六）

大会主席：王晓民/栾国明/于春江/石祥恩/王保国/刘兴洲

大会执行主席：王保国

组织委员会主席：张阳/闫长祥/吴斌

组织委员会：周健/张宏伟/张永力/范涛/陈述花/王双燕/袁宏勋/张云馨/张伯君/刘彬/吴涛/苏晗/刘菲/廖中玉/李欣雨/孙艳/艾海玲

学术委员会：（排名不计先后）

国内：蔡立新/陈彪/陈述花/陈小兵/陈昭燃/陈忠平/丁成赟/丁玎/窦万臣/范涛/樊碧发/冯华/富壮/焦保华/江涛/姜玉武/金丽日/李路明/李田昌/李文滨/李勇杰/李佑祥/李云林/廖利民/凌峰/刘晓燕/刘兴洲/凌至培/卢德宏/栾国明/马斌/毛颖/倪家骧/秦炯/石祥恩/宋来君/宋明/史锡文/孙伯民/孙炜/王保国/王贵怀/王丽华/王立文/王伟民/王献清/王玉平/王运杰/万新华/吴斌/吴立文/肖江喜/许佰男/徐如祥/闫长祥/杨金庆/杨学军/于春江/邹丽萍/赵世光/赵英/张国君/张宏伟/张建党/张建国/张建宁/张新中/张月华/张俊平/张俊廷/张玉琪/张世忠/周健/周忠清/周忠蜀/朱明旺/佟小光

国外：杨少华（美国南德克萨斯大学）

施炯（Barrow Neura Surgical Institute）

Yongqing Li (Harvard University)

Ronald Wender (Cedars-Sinai Medical Center)

Yong-Jian Lin (Pain Center, Cedars-Sinai Medical Center)

Chuck Tong (Wake Forest University)

吴坤（美国YALE大学）

沙志一（美国）

李天富（美国）

自2006年北京三博国际神经科学论坛举办以来，已经成功举办了四届，逐渐成为有影响的品牌学术会议。第五届北京三博国际神经科学论坛将于2011年4月28日至4月30日在北京召开。本次大会诚邀国内外从事神经科及相关领域的专家学者，共聚一堂，就神经科学的基础研究、神经科疾病的个性化治疗及进展等进行学术交流。

大会的专题讲座包括神经科学基础研究进展、脑功能监测进展、疼痛基础和临床研究进展、脑保护研究进展、癫痫手术进展、神经肿瘤治疗进展、脑血管病治疗进展、神经调控技术在功能神经外科进展、神经变性及修复研究进展等。疑难病例讨论专场将围绕特殊病例进行病因、发病机制、临床表现特点、治疗方法、预后等进行讨论。

本次会议为北京市级继续医学教育项目（I类学分6分）。会议免收注册费，食宿及资料费用自理。真诚欢迎相关领域的同道们光临研讨！

一、会议征稿：

本次论坛将面向全国神经外科、神经内科、麻醉学、疼痛医学、ICU、神经护理、神经生物学、神经康复和干细胞神经修复等领域广泛征稿。

投稿要求：提交论文的内容应具有科学性、实用性，论点明确、资料可靠。综述和讲座不超过4000字。研究成果摘要800字。要求未在国内外公开发表过。来稿使用word编辑，正文4号字，采用单倍行距，请务必提供电子版。

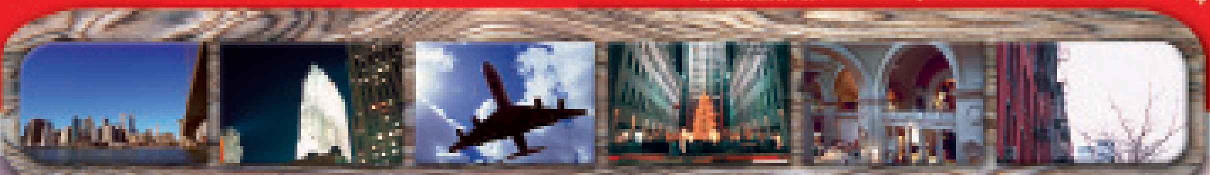
投稿方式（截止日期：2011年4月10日）：

1. E-mail：shsbnk@sina.com

2. 邮寄地址：（需附电子版光盘）北京市海淀区香山一棵松50号北京三博脑科医院1号楼302室 苏晗收 邮编：100093

二、报名方式：

1. 邮箱报名：shsbnk@sina.com；2. 电话报名：010-62856766，联系人：苏晗；3. 传真报名：010-62856902



国内会议信息

第十三届全军麻醉与复苏学术会议
时　　间：2011–04–22 至 2011–04–24日
地　　点：北京
主办单位：中国人民解放军医学科学技术委员会麻醉与复苏专业委员会
联 系 人：吴冬
电　　话：010–66938152
邮　　箱：301mz@163.com

中华医学会第五届全国老年呼吸病学术大会
时　　间：2011年5月
地　　点：北京
主办单位：中华医学会老年分会呼吸病学组
联 系 人：周继宏 王艺燕
电　　话：13901310681 13611071328

第48届世界传统医学大会
时　　间：2011–05–07 至 2011–05–09
地　　点：四川 成都
主办单位：国际补充医学研究学会
联 系 人：王老师
电　　话：010–67534765/15300094072
邮　　箱：yxhy1742@163.com

2011北医麻醉学论坛
时　　间：2011–05–13 至 2011–05–15
地　　点：北京
主办单位：北京大学医学部麻醉学系
联 系 人 ：张超 郭敏敏
电　　话：010–81458365/15712954537

第十届华东六省一市麻醉学会议暨2011年上海市医学会麻醉年会
时　　间：2011–05–20 至 2011–05–22
地　　点：上海
主办单位：华东地区麻醉学协作委员会
　　　　　上海市医学会麻醉分会
邮　　箱：huadongmazui@163.com

2011年天坛·国际神经外科麻醉论坛
时　　间：2011–06–03 至 2011–06–05
地　　点：北京
主办单位：首都医科大学附属北京天坛医院
　　　　　首都医科大学麻醉学系
　　　　　北京医学会麻醉学分会
联 系 人：董老师
电　　话：010–59046396

2011全国青年麻醉学科医师学术论坛
时　　间：2011–06–03 至 2011–06–05
地　　点：安徽合肥
主办单位：中华医学会麻醉学分会青年委员会
联 系 人：张野
电　　话：13966768081

2011年第十六次长江流域麻醉学术会议、2011年中国西部十一省麻醉学术年会、2011青海省麻醉学年会
时　　间：2011–06–17 至 2011–06–19
地　　点：青海西宁市
主办单位：青海省医学会麻醉学分会
联 系 人：俞文军/靳晓红
电　　话：13327641112/13709738734

中华医学会第五次重症医学大会
时　　间：2011–05–26 至 2011–05–30
地　　点：北京
主办单位：中华医学会重症医学分会
电　　话：010–85158128
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第17届世界灾难及急救医学学术会议暨第14次全国急诊医学会学术年会
时　　间：2011–05–30 至 2011–06–03
地　　点：北京
主办单位：世界灾难与急救医学学会授权
　　　　　中华医学会
　　　　　中华医学会急诊医学分会
联 系 人：李清敏
电　　话：010–85158149

第四届首都急诊医学高峰论坛
时　　间：2011–08–27 至 2011–08–28
地　　点：北京
主办单位：首都医科大学急诊医学系
联 系 人：王老师
电　　话：15300094072
邮　　箱：yxhy2021@163.com

2011年中华医学会全国麻醉学术年会
时　　间：2011–09–07 至 2011–09–10
地　　点：济南
主办单位：中华医学会麻醉学分会
联 系 人：白雪
电　　话：010–85158614

国内展会信息

2011年国际医疗仪器设备展览会
时　　间：2011–03–25 至 2011–03–27
地　　点：北京国家会议中心
主办单位：中国人民解放军总后勤部卫生部
联 系 人：付 芳/雷 明
电　　话：13714515535/13510905486
传　　真:0755—23938426
邮　　箱:cmffok@163.com

2011第三届中国北京抗体和疫苗大会暨展览会
时　　间：2011–03–23 至 2011–03–25
地　　点：北京
主办单位：中国医药生物技术协会
联 系 人：杨妮
电　　话：13624084306

2011第四届蛋白质和多肽大会暨生命科学仪器展览会
时　　间：2011–03–23 至 2011–03–25
地　　点：北京
主办单位：中国医药生物技术协会
联 系 人：唐小姐
电　　话：0411–84795469

2011中西部（昆明）医疗器械展览会
时　　间：2011–03–24 至 2011–03–26
地　　点：昆明国际会展中心
主办单位：全国医药技术市场协会
联 系 人：王德
电　　话：0871–8369572

2011年中国东北第十三届国际口腔器材展览会暨学术交流会
时　　间：2011–04–01 至 2011–04–04
地　　点：辽宁 沈阳
主办单位：北方工商业展览有限公司
电　　话：024–23914926
传　　真：024–23922432
网　　址： www.bfexpo.com.cn

第二届中国大连国际DNA和基因组活动周
时　　间：2011–04–25 至 2011–04–29
地　　点：大连
主办单位：国家外国专家局国外人才信息研究中心
联 系 人：李梦思
电　　话：0411–84799609–826

第十一届中国国际家庭医疗保健、康复器械及健康用品（北京）展览会
时　　间：2011–05–07 至 2011–05–09
地　　点：北京
主办单位：中国医疗保健国际交流促进会
　　　　　美国国际健康产品协会
联 系 人：徐良
电　　话：13167331017/13810331731

2011安徽省医疗器械展览会
时　　间：2011–05–12 至 2011–05–14日
地　　点：安徽芜湖
主办单位：中国国际贸易促进委员会
联 系 人：许沛东
电　　话：13205532761

2011第九届中国上海国际医疗器械展览会
时　　间：2011–06–27 至 2011–06–29
地　　点：上海
主办单位：中国医促会
联 系 人：杨浩
电　　话：13795367353

2011第九届中国（上海）家用医疗用品展览会
时　　间：2011–06–27 至 2011–06–29
地　　点：上海
主办单位：中国医促会
联 系 人：杨浩
电　　话：137953673532/021–54175192

2011中国（上海）检验医学及输血用品展览会
时　　间：2011–06–27 至 2011–06–29
地　　点：上海
主办单位：中国医促会
联 系 人：杨浩
电　　话：13795367353

2011第十二届（上海）国际营养健康产业博览会
时　　间：2011–08–22 至 2011–08–24
地　　点：上海
主办单位：中国保健营养理事会
联 系 人：田振（经理）
电　　话：13691567172

第二十届中国国际医用仪器设备展览会暨技术交流会
时　　间：2011–11–08 至 2011–11–20
地　　点：北京国家会议中心
主办单位：中国卫生部
联 系 人：马冉/南易/张珍桢
电　　话：010–88393925/88393927
传　　真：010–88393924
邮　　箱：info@chinahospeq.com

国际展会信息

印度国际医疗展
时　　间：2011–03–25 至 2011–03–27
地　　点：印度新德里迈丹国际展览中心
联 系 人：刘春
电　　话：13978693330
传　　真:0771–2848731
邮　　箱:liu–chun2007@163.com

2011年第17届杜塞尔多夫（印度）国际医疗展国际诊断、医疗设备及技术专业展览
时　　间：2011–03–25 至 2011–03–27
地　　点：印度新德里迈丹国际展览中心
主办单位：德国杜塞尔杜夫展览集团公司
联 系 人：周鹏
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稿約

《麻醉与监护论坛》

MANUSCRIPT STANDARD

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[1] [illegible] 0876 [illegible] 163, 65-

[2] Lacoumants S, YeoTH, Burrin JM, et al. Fentanyl and β-endophin, ACTH and glucoregulatory hormonal response to surgery. Br J Anaesth, 1987, 59:713-716.

[3] [illegible] 0883-165, 2/5

[4] Tamsen A. Comparison of patient-controlled analgesia with constant infusion and intermittent intramuscular regimes. In: Harmer M, Rose M, Vickens MD, eds. Patient-controlled analgesia .2nd eds. London: Blackwell Scientific, 1985. 111-125.

[illegible] lyelectron@yahoo.com.cn; fam@medicalinfo.cc

[illegible]

E-Mali: lyelectron@yahoo.com.cn

famttyy@sina.com

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