

## • 论著 •

# 限制性液体复苏对多发性骨折合并创伤失血性休克患者免疫功能和炎症介质的影响

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**【摘要】目的** 观察限制性液体复苏(LFR)对多发性骨折合并创伤失血性休克患者免疫功能和炎症介质的影响。**方法** 选择2014年1月至2016年6月宁波大学医学院附属医院收治的102例多发性骨折合并创伤失血性休克患者,按随机数字表法分为LFR组及早期充分常规液体复苏(RFR)组,每组51例。两组入院后均对患者创面进行包扎止血,并做好术前准备。RFR组患者实施早期充分RFR,LFR组患者实施LFR。观察两组患者复苏后4 h 血细胞比容(HCT)、血小板计数(PLT)、凝血酶原时间(PT)、血乳酸、免疫细胞、炎症介质及微小RNA-155(miR-155)等的变化。**结果** 与RFR组比较,LFR组复苏时间(h:  $3.67 \pm 1.45$  比  $5.14 \pm 1.61$ )、PT(s:  $11.43 \pm 2.21$  比  $15.73 \pm 2.52$ )、血乳酸(mmol/L:  $3.35 \pm 0.15$  比  $3.81 \pm 0.25$ )、肿瘤坏死因子- $\alpha$  [TNF- $\alpha$  (ng/L):  $14.10 \pm 3.39$  比  $16.28 \pm 3.47$ ]、白细胞介素[IL-10(ng/L):  $31.43 \pm 10.51$  比  $40.09 \pm 13.23$ , IL-6(ng/L):  $490.10 \pm 55.13$  比  $610.30 \pm 63.15$ ]、内皮素-1[ET-1(pg/L):  $183.35 \pm 30.51$  比  $250.01 \pm 31.23$ ]含量均明显降低(均  $P < 0.01$ ), PLT( $\times 10^9/L$ :  $134.58 \pm 28.13$  比  $108.12 \pm 30.35$ )、HCT( $\times 10^{-2}$ :  $0.34 \pm 0.04$  比  $0.24 \pm 0.05$ )、miR-155( $0.15 \pm 0.02$  比  $0.08 \pm 0.02$ )、CD4 $^+$ CD25 $^+$ 调节性T细胞[CD4 $^+$ CD25 $^+$ Treg( $\times 10^{-2}$ ):  $2.28 \pm 0.47$  比  $2.10 \pm 0.39$ ]均明显升高(均  $P < 0.01$ )。**结论** LFR在抢救多发性骨折合并创伤失血性休克患者时能有效缩短复苏时间,调节患者凝血功能,减少不必要的液体过多输注,改善机体免疫状态和炎症反应程度。

**【关键词】** 创伤; 骨折; 失血性休克; 限制性液体复苏; 炎症反应

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**Effects of limited fluid resuscitation on immune function and inflammatory mediators in patients with multiple bone fractures complicated with traumatic hemorrhagic shock Tang Hualin, Wang Liang, Liu Zhenxin, Zuo Rongyue**

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**【Abstract】Objective** To observe the effects of limited fluid resuscitation (LFR) on immune function and inflammatory mediators in patients with multiple bone fractures complicated with traumatic hemorrhagic shock.  
**Methods** One hundred and two patients with multiple bone fractures complicated with traumatic hemorrhagic shock admitted to the Affiliated Hospital of Medical College of Ningbo University from January 2014 to June 2016 were enrolled, and they were divided into a LFR group and a early sufficient routine fluid resuscitation (RFR) group by random number table, each group 51 cases. After admission, the patients in the two groups underwent bandaging and hemostasis at the traumatic sites and preoperative management was prepared. The patients in RFR group were treated with early sufficient RFR, while LFR group was treated with LFR. The changes of hematocrit (HCT), blood platelet count (PLT), prothrombin time (PT), blood lactic acid and immune cells, inflammatory mediators and micro RNA-155 (miR-155) were observed in patients of the two groups at 4 hours after resuscitation. **Results** Compared with RFR group, the resuscitation time (hours:  $3.67 \pm 1.45$  vs.  $5.14 \pm 1.61$ ), levels of PT (s:  $11.43 \pm 2.21$  vs.  $15.73 \pm 2.52$ ), serum lactic acid (mmol/L:  $3.35 \pm 0.15$  vs.  $3.81 \pm 0.25$ ), tumour necrosis factor- $\alpha$  [TNF- $\alpha$  (ng/L):  $14.10 \pm 3.39$  vs.  $16.28 \pm 3.47$ ], interleukin [IL-10 (ng/L):  $31.43 \pm 10.51$  vs.  $40.09 \pm 13.23$ , IL-6 (ng/L):  $490.10 \pm 55.13$  vs.  $610.30 \pm 63.15$ ] and endothelin-1[ET-1(pg/L):  $183.35 \pm 30.51$  vs.  $250.01 \pm 31.23$ ] in LFR group were significantly decreased (all  $P < 0.01$ ), while PLT ( $\times 10^9/L$ :  $134.58 \pm 28.13$  vs.  $108.12 \pm 30.35$ ), HCT ( $\times 10^{-2}$ :  $0.34 \pm 0.04$  vs.  $0.24 \pm 0.05$ ), miR-155 ( $0.15 \pm 0.02$  vs.  $0.08 \pm 0.02$ ) and CD4 $^+$ CD25 $^+$  regulatory T cell [CD4 $^+$ CD25 $^+$ Treg ( $\times 10^{-2}$ ):  $2.28 \pm 0.47$  vs.  $2.10 \pm 0.39$ ] in LFR group were obviously increased (all  $P < 0.01$ ). **Conclusions** Using LFR in the emergency treatment of patients with multiple bone fractures complicated with traumatic hemorrhagic shock can effectively shorten the resuscitation time, regulate the patients' coagulation function, reduce the unnecessary excessive liquid infusion, improve immune status and decrease the degree of inflammatory reaction.

**【Key words】** Trauma; Bone fracture; Hemorrhagic shock; Limited fluid resuscitation; Inflammatory response

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多发性骨折是骨科及急诊科常见的严重疾病,主要由于交通事故、高处坠落、暴力撞击、机器损

伤、生活伤等导致的严重创伤,创伤失血性休克是最常见且最紧急的并发症<sup>[1-2]</sup>。液体复苏是多

发性骨折急救的重点,临幊上常采用大量液体复苏快速恢复患者生命体征,尽早进行液体复苏能有效提高患者的存活率,降低并发症发生率。有研究显示,液体复苏会增加创伤失血患者全身炎症反应的发生率<sup>[3-4]</sup>。限制性液体复苏(LFR)又称低压复苏,是指机体处于有活动性出血的创伤失血性休克时,在手术彻底止血前限制液体的输入量,只维持机体的基本需求,直至彻底止血<sup>[5]</sup>。LFR不仅能降低血栓破坏及再出血风险,也避免了患者的稀释性凝血功能障碍,但对LFR多发性骨折合并创伤失血性休克患者炎症反应及免疫功能的影响并不清楚。本研究观察LFR对多发性骨折合并创伤失血性休克患者免疫功能和炎症介质的影响,现报告如下。

## 1 资料与方法

**1.1 病例选择:**选取2014年1月至2016年6月在本院骨科及急诊室治疗的102例多发性骨折合并创伤失血性休克患者。

**1.1.1 纳入标准:**①经CT或磁共振成像(MRI)检查,患者均发生两个或两个以上部位骨折;②均符合创伤失血性休克标准<sup>[6]</sup>,入院首次收缩压≤90 mmHg(1 mmHg=0.133 kPa);③创伤指数(Ts)≥10,损伤严重程度评分(ISS)≥16分;④患者及其家属知情同意并签署知情同意书。

**1.1.2 排除标准:**①合并高血压;②有心、肺、肾严重损伤;③入院濒死或入院24 h死亡。

**1.1.3 伦理学:**本研究符合医学伦理学标准,经本院医学伦理委员会批准,取得患者或家属知情同意。

**1.2 一般资料:**102例患者中男性66例,女性36例,年龄24~67岁,平均(44.6±4.1)岁。病因:交通事故伤53例,高处坠落伤28例,暴力撞击伤16例,机器损伤5例;肝、脾破裂为主18例,胸部创伤为主27例,四肢、骨盆骨折为主48例,颅脑损伤为主6例,其他3例。

**1.3 分组及治疗方法:**将患者按随机数字表法分为LFR组及早期充分常规液体复苏(RFR)组。两组患者入院后均进行紧急救治,并快速开放气道,保证患者呼吸道通畅,建立两条有效的静脉通道进行快速输液;均进行心电监护、血压监测及血氧饱和度监测,对创面进行包扎止血,做好术前准备。

**1.3.1 RFR组:**实施早期充分RFR,及时快速给予补液,输入足量7.5%高渗生理盐水、平衡液、羟乙基淀粉及血液,快速扩充血容量,尽量维持收缩压≥90 mmHg,舒张压60~80 mmHg。

**1.3.2 LFR组:**实施LFR,早期给予250 mL 7.5%

高渗生理盐水,根据患者病情,必要时在30 min后重复输入(控制输入生理盐水量<350 mL),同时输入平衡液、羟乙基淀粉及血液。当患者收缩压为70~90 mmHg或舒张压为50~60 mmHg时适当减速,控制输液量,观察患者病情并做好相关检查。

**1.4 观察指标及方法:**①检测两组患者复苏后4 h血小板计数(PLT)、血细胞比容(HCT)、凝血酶原时间(PT)、血乳酸;②检测两组患者的炎症介质肿瘤坏死因子-α(TNF-α)、白细胞介素(IL-10、IL-6)、内皮素-1(ET-1)和微小RNA-155(miR-155)以及免疫功能指标CD4<sup>+</sup>CD25<sup>+</sup>调节性T细胞(CD4<sup>+</sup>CD25<sup>+</sup>Treg)水平。

**1.5 统计学方法:**使用SPSS 17.0软件进行统计分析,符合正态分布的计量资料以均数±标准差( $\bar{x}\pm s$ )表示,采用t检验,计数资料采用 $\chi^2$ 检验, $P<0.05$ 为差异有统计学意义。

## 2 结果

**2.1 两组患者一般资料比较(表1):**两组性别、年龄及休克程度、受伤原因、损伤部位患者数等比较差异均无统计学意义(均 $P>0.05$ ),说明两组资料均衡,有可比性。

表1 两组患者一般资料比较

组别	例数 (例)	性别[例(%)]		休克程度[例(%)]		
		男性	女性	(岁, $\bar{x}\pm s$ )	轻度	中度
RFR组	51	35	16	44.9±3.7	9(17.65)	27(52.94)
LFR组	51	31	20	45.6±3.8	7(13.72)	35(68.63)
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组别	例数 (例)	受伤原因[例(%)]				<hr/>
		交通事故伤	高处坠落伤	暴力撞击伤	机器损伤	
RFR组	51	30(58.82)	10(19.61)	8(15.69)	3(5.88)	<hr/>
LFR组	51	23(45.10)	18(35.29)	8(15.69)	2(3.92)	<hr/>
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组别	例数 (例)	损伤部位[例(%)]				
		肝、脾破裂 为主	胸部创伤 为主	四肢、骨盆 骨折为主	颅脑 损伤为主	其他
RFR组	51	8(15.69)	14(27.45)	25(49.02)	2(3.92)	2(3.92)
LFR组	51	10(19.61)	13(25.49)	23(45.10)	4(7.84)	1(1.96)

**2.2 两组患者复苏效果比较(表2):**LFR组复苏时间明显短于RFR组( $h:3.67\pm 1.45$ 比 $5.14\pm 1.61$ ),LFR组PLT、HCT均明显高于RFR组,PT、血乳酸明显低于RFR组(均 $P<0.05$ )。

表2 两组患者PLT、HCT、PT、血乳酸水平比较( $\bar{x}\pm s$ )

组别	例数 (例)	PLT ( $\times 10^9/L$ )	HCT ( $\times 10^{-2}$ )	PT (s)	血乳酸 (mmol/L)
RFR组	51	108.12±30.35	0.24±0.05	15.73±2.52	3.81±0.25
LFR组	51	134.58±28.13	0.34±0.04	11.43±2.21	3.35±0.15

注:与RFR组比较, $^aP<0.05$

**2.3** 两组患者炎症介质和miR-155及免疫功能指标比较(表3):LFR组TNF- $\alpha$ 、IL-10、IL-6、ET-1均明显低于RFR组,miR-155、CD4 $^+$ CD25 $^+$ Treg水平平均明显高于RFR组(均P<0.05)。

**表3** 两组患者炎症介质和miR-155及免疫功能指标比较( $\bar{x} \pm s$ )

组别	例数 (例)	TNF- $\alpha$ (ng/L)	IL-10 (ng/L)	IL-6 (ng/L)
RFR组	51	16.28 $\pm$ 3.47	40.09 $\pm$ 13.23	610.30 $\pm$ 63.15
LFR组	51	14.10 $\pm$ 3.39 <sup>a</sup>	31.43 $\pm$ 10.51 <sup>b</sup>	490.10 $\pm$ 55.13 <sup>b</sup>
组别	例数 (例)	ET-1 (pg/L)	miR-155	CD4 $^+$ CD25 $^+$ Treg ( $\times 10^{-2}$ )
RFR组	51	250.01 $\pm$ 31.23	0.08 $\pm$ 0.01	2.10 $\pm$ 0.39
LFR组	51	183.35 $\pm$ 30.51 <sup>b</sup>	0.15 $\pm$ 0.02 <sup>b</sup>	2.28 $\pm$ 0.47 <sup>a</sup>

注:与RFR组比较,<sup>a</sup>P<0.05,<sup>b</sup>P<0.01

### 3 讨论

多发性骨折的出血点数量多、部位隐匿,加之出血空间大,造成有些部位无法有效加压止血,易出现很多并发症,其中创伤失血性休克是主要的并发症及重要的高病死率原因。创伤失血性休克是一种常见的临床急危重症,由于组织灌注不足和病原微生物等的刺激,IL-10、TNF- $\alpha$ 、巨噬细胞、中性粒细胞等迅速浸润、扩散使组织损伤更为严重<sup>[7]</sup>。创伤死亡者中有1/3是由创伤失血性休克引起,临床急救治疗中常应用液体复苏使血容量尽快恢复,将收缩压尽量控制在90 mmHg以上,使组织的血流灌注稳定,以避免缺血、缺氧症状的出现<sup>[8]</sup>。

RFR和LFR是目前临幊上常用的液体复苏方式,RFR是在短时间内大量输注高渗液体升压,而LFR则根据患者实际情况将血压控制在安全范围内。本研究显示,LFR组复苏时间、PT、血乳酸含量均明显低于RFR组,PLT、HCT均明显高于RFR组,这也提示LFR抢救多发性骨折合并创伤失血性休克患者疗效明确,能有效缩短复苏时间,保护患者的凝血功能,避免缺血、缺氧状况的出现。

在早期止血中,液体复苏能改善患者预后,但不恰当地选择液体会造成患者凝血功能障碍、组织水肿、肾功能损害及机体免疫抑制等不良后果。本研究复苏液体均选用高渗液,高渗液扩容能力强,不仅能降低血液黏稠度、增强心肌收缩功能,还能刺激血管运动中枢及兴奋循环系统。有研究显示,高渗液在抑制IL-6、TNF- $\alpha$ 等方面也起着重要作用<sup>[9]</sup>。LFR旨在寻求平衡点,使液体复苏适当恢复组织器官的血流灌注同时,减少对机体内环境和代偿功能的干扰<sup>[10-11]</sup>。体液复苏引起的再灌注损害会对患

者免疫功能产生一定影响,但并不是引起失血性休克及复苏后免疫功能改变的主要原因,早期快速大量液体复苏可加重组织缺血/再灌注损伤,激活炎症免疫反应<sup>[12]</sup>。本研究结果显示,LFR组TNF- $\alpha$ 、IL-10、IL-6、ET-1均明显低于RFR组,miR-155、CD4 $^+$ CD25 $^+$ Treg水平明显高于RFR组,表明RFR与LFR均能加重多发性骨折合并创伤失血性休克患者的全身炎症反应,但LFR组炎症反应程度明显较轻,这提示LFR可明显抑制全身促炎细胞因子的释放,从而提高抗炎细胞因子水平。与相关研究<sup>[13-15]</sup>结果一致,LFR可有效降低失血性休克患者循环中机体ET-1水平,减少组织损伤和休克恶化程度。

综上所述,LFR在抢救多发性骨折合并创伤失血性休克患者时,能有效缩短复苏时间,保护患者的凝血功能,减少不必要液体过多的输注,改善机体免疫功能和炎症反应程度。

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