

早期肠内营养对静脉 - 动脉体外膜肺氧合患者预后的影响

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【摘要】目的 观察静脉 - 动脉体外膜肺氧合(VA-ECMO)患者早期肠内营养(EEN)的可行性及相关的临床结果。**方法** 选择2012年1月至2017年12月入住宁波市医疗中心李惠利医院重症医学科(ICU)使用VA-ECMO治疗的34例患者作为研究对象。所有患者均在排除禁忌证后积极实施EEN,按照 $104.65 \text{ kJ} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ ($25 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$)计算目标热卡量,按照 $1.2 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ 计算目标蛋白量,以1周内是否达到上述目标量的80%将患者分为达标组和非达标组,观察两组患者入ICU时急性生理学与慢性健康状况评分系统Ⅱ(APACHEⅡ)评分、多器官功能障碍综合征(MODS)评分、ECMO治疗至开始EN的时间、EN达标时间、VA-ECMO持续时间、ICU住院时间、总住院时间及住院病死率,并记录EN中断的原因,分析VA-ECMO患者EEN对预后的影响。**结果** 非达标组入ICU时APACHEⅡ评分、MODS评分均高于达标组[APACHEⅡ评分(分): 25.50 ± 5.62 比 19.91 ± 8.53 , MODS评分(分): 11.08 ± 3.26 比 6.73 ± 2.05 , 均 $P < 0.05$],且达标组的住院病死率更低[40.9%(9/22)比83.3%(10/12), $P < 0.05$]。两组ECMO治疗至开始EN时间、EN达标时间、VA-ECMO治疗时间、ICU住院时间、总住院时间比较差异无统计学意义(均 $P > 0.05$)。高胃残余量是喂养中断最主要的原因。**结论** 接受VA-ECMO的危重患者能否在1周内达到目标喂养量,与疾病的危重程度相关,疾病危重者较难达到目标喂养量,进而可能影响患者的预后。

【关键词】 肠内营养; 静脉 - 动脉体外膜肺氧合; 预后

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【Abstract】Objective To observe the feasibility of early enteral nutrition (EEN) in adult patients during veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and its related clinical results. **Methods** Thirty-four patients admitted to the Intensive Care Unit (ICU) of Ningbo Medical Center Li Huili Hospital from January 2012 to December 2017 to receive VA-ECMO treatment were selected as the study objects. All patients received EEN after exclusion of contraindications; the target calories were calculated by using $104.65 \text{ kJ} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ ($25 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$) and according to $1.2 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$, the target protein requirements were calculated. Within one week of EN energetic treatment, if the feeding amount reached 80% or over of the above calculated targets, the EN administration was fulfilling the standard, thus the patients were divided into a standard group and a non-standard group. After ICU admission, the acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) score, multiple organ dysfunction syndrome (MODS) score, the time from the beginning of ECMO to the start of EN, time reaching feeding standard, VA-ECMO persistent days, ICU days of stay, total hospitalization days, hospital mortality, and reasons for feeding interruptions were recorded, and the effects of EEN on prognosis of patients during VA-ECMO were analyzed in the two groups. **Results** The APACHE Ⅱ score and MODS score of the non-standard group were higher than those of the standard group on admission of ICU (APACHE Ⅱ score: 25.50 ± 5.62 vs. 19.91 ± 8.53 , MODS score: 11.08 ± 3.26 vs. 6.73 ± 2.05 , both $P < 0.05$), and the hospital mortality was lower in the standard group than that in non-standard group [40.9% (9/22) vs. 83.3% (10/12), $P < 0.05$]. The comparisons of differences in time from the beginning of ECMO to the start of EN, time of reaching feeding standard, VA-ECMO treatment days, ICU days of stay, hospitalization days between the two groups were of no statistical significance (all $P > 0.05$). The most common reason for interruption of feeding was high gastric residual volume (GRV). **Conclusion** Whether a critically ill patient receiving VA-ECMO can reach the target feeding amount in a week or not is related to the degree of disease severity; it is difficult for a seriously ill patient to reach the target amount of feeding, that may affect their prognosis.

【Key words】 Enteral nutrition; Veno-arterial extracorporeal membrane oxygenation; Prognosis

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体外膜肺氧合(ECMO)是采取人工心肺支持技术对危重患者进行有效呼吸循环支持的方法,

目前在成人难治性心力衰竭(心衰)和呼吸衰竭(呼衰)的治疗中使用越来越广泛^[1-2], ECMO辅助

治疗大大提高了患者的生存率^[3-4]。目前重症医学科(ICU)危重症患者营养不足极为常见,且使病死率显著增加^[5-7]。美国肠外肠内营养学会(ASPEN)指南推荐,重症患者24~48 h内开始早期肠内营养(EEN),且肠内营养(EN)是首选途径,提供EEN可以维持肠道完整性,调节全身免疫反应,减轻疾病严重程度,缩短住院时间^[8]。连续EN可最大限度地减少充血性心衰患者的全身和心肌耗氧量^[9]。然而,很多危重疾病患者不能很好地耐受EN^[10]。目前尚无关于ECMO期间相关的营养指南,因此研究这类患者的营养支持非常有意义。

本研究观察宁波市医疗中心李惠利医院近6年来实施静脉-动脉ECMO(VA-ECMO)辅助治疗患者EEN的可行性及相关的临床结果。

1 资料和方法

1.1 研究对象:采用回顾性研究方法,选择2012年1月至2017年12月本院ICU收治的严重心衰需要接受VA-ECMO治疗34例患者。

1.1.1 纳入标准:①年龄≥18岁;②行72 h以上VA-ECMO支持;③入ICU后行常规治疗,包括维持水、电解质和酸碱平衡,感染者给予抗菌药物,呼衰者行机械通气等各项器官功能支持治疗;④VA-ECMO辅助后循环趋于稳定能耐受EN。

1.1.2 排除标准:①胃肠道活动性出血;②胃肠道穿孔;③完全机械性肠梗阻或持续麻痹性肠梗阻;④腹腔内高压(IAH),腹内压>20 mmHg(1 mmHg=0.133 kPa);⑤腹腔感染导致的严重胃肠功能障碍。

1.2 研究分组:按照104.65 kJ·kg⁻¹·d⁻¹计算目标热卡量,1.2 g·kg⁻¹·d⁻¹计算目标蛋白量^[8],以1周内是否达到上述目标量的80%将患者分为达标组和非达标组。

1.3 营养支持方法:所有患者营养风险筛查(NRS)评分均≥3分,在ECMO支持后24~48 h内,血流动力学指标趋于稳定(血管活性药物减量,乳酸<4 mmol/L)、胃潴留量<100 mL时,排除EN禁忌证积极实施EEN,采用华瑞制药有限公司生产的EN制剂瑞代和瑞能,EN输注速率从20 mL/h开始,24 h逐渐增加到目标速率。每4 h监测1次胃残余量,若胃残余量>250 mL,则使用促胃肠动力疗法,给予胃复安10 mg静脉推注(静推),然后降低喂养频率。如果高胃残余量仍存在并超过48 h,除外禁忌证后考虑采用空肠营养管喂养。VA-ECMO后1周EN未达到目标量的80%为未达标,则加用肠外营

养(PN)。

1.4 资料收集:记录两组患者入ICU时急性生理学与慢性健康状况评分系统Ⅱ(APACHEⅡ)评分^[11]、多器官功能障碍综合征(MODS)评分^[12]、ECMO治疗至开始EN时间、EN达标时间、VA-ECMO治疗持续时间、ICU住院时间、总住院时间以及住院病死率。收集喂养中断的原因,例如高胃残余量、腹泻、呕吐、胃肠道出血等。以EN中断患者数最多的原因定义为主要原因。

1.5 统计学方法:使用SPSS 18.0统计软件分析数据,符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,组间比较采用t检验;计数资料以例(率)表示,采用 χ^2 检验。所有统计分析采用双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者一般情况:共纳入34例患者,其中男性24例,女性10例;年龄18~68岁,平均(48.00±12.33)岁。入ICU时APACHEⅡ评分(21.88±8.01)分,MODS评分(8.26±3.27)分,ECMO治疗至开始EN时间(12.56±3.30)h。EN达标时间3~9 d,平均(4.94±1.58)d,ECMO持续时间(9.15±3.39)d,ICU住院时间(14.47±5.25)d,总住院时间(21.21±6.34)d,住院病死率55.9%(19例)。VA-ECMO原因:心脏术后心衰25例(73.5%),重症病毒性心肌炎9例(26.4%)。ECMO期间最常用的EN途径是经胃28例(82.4%),其次是经空肠6例(17.6%)。达标与未达标两组患者性别、年龄、VA-ECMO原因患者数比较差异均无统计学意义(均 $P > 0.05$;表1),说明两组一般资料均衡,有可比性。

表1 EN达标与未达标两组患者一般资料比较

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)	VA-ECMO原因(例)	
		男性	女性		心脏术后	重症病毒性心衰
达标组	22	15	7	46.23±13.47	15	7
未达标组	12	9	3	50.92±9.69	10	2

2.2 1周内EN是否达标两组患者疾病严重程度、EN情况及临床结果比较(表2):与EN达标组比较,未达标组入ICU时APACHEⅡ评分、MODS评分均明显升高,住院病死率明显增加,差异均有统计学意义(均 $P < 0.05$)。两组ECMO治疗至开始EN时间、EN达标时间、ECMO持续时间、ICU住院时间、总住院时间比较差异均无统计学意义(均 $P > 0.05$)。

表2 1周内EN是否达标两组患者疾病严重程度、EN情况及临床结果比较

组别	例数 (例)	APACHE II (分, $\bar{x} \pm s$)	MODS (分, $\bar{x} \pm s$)	ECMO治疗至开始 EN时间(h, $\bar{x} \pm s$)	EN达标时间 (d, $\bar{x} \pm s$)	ECMO持续时 间(d, $\bar{x} \pm s$)	ICU住院时间 (d, $\bar{x} \pm s$)	总住院时间 (d, $\bar{x} \pm s$)	住院病死率 [% (例)]
达标组	22	19.91±8.53	6.73±2.05	12.23±3.74	4.67±1.68	8.82±3.51	14.05±4.08	20.95±4.97	40.9(9)
未达标组	12	25.50±5.62 ^a	11.08±3.26 ^a	13.17±2.29	5.45±1.29	9.75±3.19	15.25±7.07	21.67±8.55	83.3(10) ^a

注:与达标组比较,^aP<0.05

2.3 喂养中断原因:29例患者发生了喂养中断,胃肠道不耐受17例,其中高胃残余量是最主要的原因,为11例(32.4%),呕吐[2例(5.9%)];腹泻[4例(11.8%)];其他原因还包括胃肠道出血[1例(2.9%)];手术或检查操作禁食[8例(23.5%)],需拔除气管插管禁食1例,未记录中断原因2例。

3 讨 论

营养不良会增加危重患者的病死率。越来越多的人认识到EN可使危重患者获益^[13]。2016年ASPEN重症患者营养指南推荐在24~48 h内开始EEN^[8]。研究表明,EEN可作用于胃肠道神经-内分泌免疫轴,刺激机体的免疫应答,维持患者的胃肠道黏膜屏障保护功能^[14],调节炎症反应,促进一些消化酶和免疫球蛋白的分泌,有效预防肠源性感染的发生^[15]。ECMO患者往往病情危重,常伴有心、肺等其他器官基础疾病,特别是VA-ECMO患者。2016年ASPEN指南建议血流动力学不稳定的患者待血管活性药物剂量减少、血流动力学稳定后再启用EN^[8]。另外因VA-ECMO本身的作用,可能会减少肠道灌注和胃排空,进而影响胃肠道运动,导致患者能量和蛋白质摄入不足,最终出现营养不良。也有研究表明,使用ECMO设备也可能会增加蛋白质分解代谢和炎症反应,增加营养需求^[16],因此,EEN对ECMO患者有重要意义。

本研究19例患者在最初12 h内接受了EN,并且所有患者在72 h内接受了EN,大部分患者在VA-ECMO治疗1周内实现了营养达标,VA-ECMO患者入ICU时APACHE II评分(21.88±8.01)分,MODS评分(8.26±3.27)分,提示这些患者病情极其危重,有重大的循环功能障碍,多合并多器官功能障碍,并接受血管活性药物和大剂量镇静剂治疗导致器官血流灌注不足,肠道完整性被破坏,易发生细菌移位和脓毒症。疾病严重程度越重越容易导致胃潴留的发生,提示这些患者较普通患者更易发生营养摄入不足。研究表明,EN是大多数VA-ECMO患者唯一的营养来源^[17]。未达标组入ICU时APACHE II评分、MODS评分均高于达标组,本结果与一项静脉-静脉ECMO(VV-ECMO)

研究结果^[18]相似,提示疾病的严重程度可能会影响ECMO患者的EN达标情况,病情越重越难以达到目标喂养量。同时本研究也显示胃肠道耐受差的患者往往提示疾病危重。本研究显示,达标组住院病死率较未达标组降低,有研究观察到危重患者达到80%的营养目标60 d的病死率较低^[19],也提示胃肠功能良好的危重患者早期EN的达标可能改善预后。

一项澳大利亚的多中心前瞻性研究表明,VA和VV-ECMO患者EN中断的原因中高胃残余量占22%^[7],本研究显示,更高比例的患者出现高胃残余量(32.4%),其可能原因是VA-ECMO较VV-ECMO患者血流动力学障碍更显著,导致肠道血流灌注不足和胃排空减慢。其他EN中断原因还有呕吐、腹泻等胃肠道不耐受表现,ECMO患者通常是平卧,抬高床头有限,这也可能引起更高的胃残余量和肠内吸收减少。有研究显示,大部分患者EN至少中断1次,使用PN比例相对较低,最常见应用PN的原因是EN不能耐受^[20-21]。解决胃肠道不耐受患者的方法包括使用促胃运动药物^[22]、留置鼻空肠管、减少镇静剂的使用,密切观察胃肠动力情况,精细化医护管理等。本研究有1例患者出现胃肠道出血,考虑原因可能是接受ECMO的患者要常规接受治疗性肝素化抗凝,易于出血所致。但也可能与患者疾病严重程度或本身基础疾病有关。但本研究病例数较少,具有一定的局限性,需要进一步行前瞻性研究。

综上所述,接受VA-ECMO的危重患者能否在1周内达到目标喂养量,与其疾病的危重程度有关,病情更严重的患者较难达到目标喂养量,进而可能影响患者的预后。EN是VA-ECMO患者最主要的营养方式,高胃残余量是EN中断的最主要原因。

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