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结直肠癌患者急诊手术后口服营养补充剂的临床效果

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• 临床研究 •

结直肠癌患者急诊手术后口服营养补充剂的临床效果

刘发强¹, 路晓林², 常迎彬²**Clinical Effect of Oral Nutritional Supplements in Patients with Colorectal Cancer After Emergency Surgery**LIU Faqiang¹, LU Xiaolin², CHANG Yingbin²

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Abstract: Objective To assess the clinical effect of oral nutritional supplements in patients with colorectal cancer after emergency surgery. **Methods** Based on a retrospective comparative analytic design, 38 CRC patients undergoing emergency surgery were divided into two groups according to nutrition support methods: TPN and PN+ONS groups. We collected the clinical data of two groups, including the number of blood lymphocyte and albumin before surgery and on the 1st and 7th postoperative day, postoperative complication, total length of stay and postoperative length of stay. **Results** The age, gender, operation time and the amount of operative blood loss volume did not show statistically significant difference between two groups ($P>0.05$). PN+ONS group had lower postoperative infection rate and complication rate and shorter total length of stay, but the difference was not statistically significant between two groups ($P>0.05$). **Conclusion** The application of ONS may be helpful to reduce postoperative complications and shorten the length of stay in CRC patients after emergency surgery.

Key words: Colorectal cancer; Nutritional support; Oral nutritional supplements; Total parenteral nutrition

摘要: 目的 评价添加口服营养补充剂对结直肠癌患者急诊手术后康复的影响。**方法** 回顾性对比分析2008年6月—2018年1月间进行急诊手术的38例结直肠癌患者,按营养支持方法分为TPN组和PN+ONS组,收集两组患者术前、术后第1天、术后第7天的血淋巴细胞数及白蛋白等指标,同时结合病历记载,获取患者并发症发生情况、总住院时间、术后住院时间等数据。**结果** 两组患者一般资料(包括年龄、性别、手术时间、术中失血量(ml))等指标差异无统计学意义;PN+ONS组术后总并发症发生率和术后感染率及总住院时间短,但两组间差异无统计学意义。**结论** 结直肠癌患者急诊手术后适当添加口服营养补充剂,可能有利于减少患者的术后并发症、缩短住院时间。

关键词: 结直肠癌; 营养支持; 口服营养补充剂; 全胃肠外营养

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0 引言

结直肠癌发病率呈逐渐升高趋势,全球预测每年新发约180万例,我国2015年新发病例约37.63万^[1-2]。研究表明,约30%的结直肠癌患者初次发病时需急诊处理,包括肠梗阻、穿孔及出血等情况,其中肠梗阻多达70%。与择期手术相比,结直

肠癌急诊手术的住院时间较长,术后并发症与死亡率较高^[3]。有超过20%的结直肠癌急症患者需急诊手术,并可获得与择期手术相同的淋巴结清扫效果(至少12枚淋巴结)^[3-4]。

恶性肿瘤患者存在较高的营养不良患病率,根据肿瘤位置不同,介于20%~80%之间,其中需手术或放化疗的胃肠道恶性肿瘤患者比例较高,营养干预可降低此类患者的术后并发症与死亡率^[5]。口服营养补充剂(oral nutritional supplements, ONS)作为额外能量的补充,如达到130 kcal/d,即可满足维持体重的基本需求^[6],部分研究提示,富含各种营养素的ONS虽然不能有效改变肿瘤转归与提

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高总生存率,但可改善患者的部分临床症状,提高生活质量^[7]。目前关于ONS对术后康复的影响研究较多,但缺乏结直肠癌急诊术后应用的相关研究。本研究结合临床实际,回顾性分析了结直肠癌患者急诊术后全胃肠外营养支持(total parenteral nutrition, TPN)与PN联合ONS(PN+ONS)之间的临床效果异同,探索ONS对此类患者术后康复的影响。

1 资料与方法

1.1 临床资料

回顾性分析民航总医院普通外科2008年6月—2018年1月因肠梗阻、出血、穿孔等原因行急诊开腹手术的结直肠恶性肿瘤患者,根据科室开展术后添加ONS时间,按营养支持方法不同分为TPN组和PN+ONS组。其中2014年12月31日之前的患者术后仅采用TPN,属TPN组;自2015年1月起此类患者术后开始添加ONS,属PN+ONS组。病例纳入标准:(1)年龄>18岁;(2)术前营养风险筛查2002(nutrition screening risk 2002, NRS 2002)评分 ≥ 3 分;(3)术前无重要脏器功能障碍;(4)术前无严重内分泌和代谢性疾病;(5)初次发现肿瘤;(6)伴发肠梗阻、出血或穿孔等急症,保守治疗无效者;(7)术后病理结果明确诊断为结直肠癌者。共收集符合条件的结直肠癌患者38例,其中TPN组23例,PN+ONS组15例。两组患者住院期间均行肿瘤一期切除吻合术。

临床资料包括:(1)一般资料:年龄、性别等;(2)实验室化验结果:术前、术后第7天(7th postoperative day, 7th POD)的白蛋白等指标以及血淋巴细胞等免疫指标;(3)临床数据:手术时间、手术出血量等;(4)循证医学临床结局指标:总住院时间(total length of stay, t-LOS)及术后住院时间(postoperative length of stay, postop-LOS)、术后患病率、死亡率等。

患者出院时符合营养出院指数^[8],即三个客观指标:(1)无发热;(2)无静脉通路;(3)能独立如厕。

本研究入组65岁以上患者22例,占57.9%。考虑老年性疾病可能对结果产生较大影响,在筛选病例时,根据病历记载,若因合并老年性疾病而延长住院时间,或者需转入内科继续诊疗者,均未纳入本研究范围。

1.2 营养不良风险筛查

民航总医院普通外科长期坚持对需急诊手术可疑肿瘤患者进行NRS2002评分,评分 ≥ 3 分者术

后给予营养支持治疗。因临床实际所限,急诊患者多数为平车推入病房,无法准确测量当时体重,仅根据其家属所述估计体重,易造成研究误差,本研究决定舍弃体重指数评价指标。同时因当时条件所限,所有患者缺乏人体测量指标、营养相关实验室指标等,这将在后续系统研究中补充。

1.3 营养支持

2014年12月31日之前,对NRS2002评分 ≥ 3 分者,给予TPN。按前期研究结果,患者均按热量25 kcal/(kg·d)和氮0.16 s/(kg·d)标准从术后第1天开始接受营养支持^[9]。

2015年1月之后,科室引进ONS,PN+ONS组患者于术后第1天开始口服温开水,若无恶心、呕吐、严重腹胀等,当天即开始添加ONS,口服肠内营养剂安素(total protein, TP),并保证每日最低热量130 kcal/d。本研究入组患者从第1天开始口服250 ml安素(6平勺安素+200 ml温水),热量约250 kcal,根据患者耐受性,从早到晚啜饮或分多次口服完成。PN按总热量减去TP已给予的热量及氮。

术后第8天若未出现需禁食水的严重并发症,则开始停用TPN或PN,均开始口服流食,剩余热量通过静脉输注葡萄糖提供,逐渐增加进食量至出院。

1.4 统计学方法

用SPSS24软件进行统计分析。计数资料采用卡方检验(Chi-Square Test, χ^2 检验)。计量资料先行单样本K-S检验(One-Sample Kolmogorov-Smirnov Test)验证正态分布,服从正态分布者,在F检验基础上(齐/异方差)进行两个独立样本单尾T检验;不服从正态分布者,进行两个独立样本非参数Mann-Whitney检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 病例特征

38例患者被纳入研究,中位年龄75岁(42~92岁)。TPN组23例,PN+ONS组15例。两组的计量资料(包括年龄、肿瘤大小、术中出血量、实验室化验结果等)和计数资料(包括性别、术后总并发症发生率、术后感染率、术后死亡率等)指标差异均无统计学意义,见表1、2。

15例PN+ONS组患者中仅有1例术后伴发肠梗阻,经保守治疗后缓解。23例TPN组患者术后发生中心静脉导管感染1例,术后1周出现低白蛋白血症伴大量胸腹水1例,肺部感染及切口感染1例,单纯切口感染2例。围手术期输血情况:PN+ONS组患者中有3例,TPN组患者中有5例均接

表1 TPN和PN+ONS组病例特征指标比较 (计量资料)
Table1 Comparison of colorectal cancer patients' characteristics between TPN and PN+ONS groups (measurement data)

Characteristics	TPN group (n=23)	PN+ONS group (n=15)	P
Age (years)	68.9±12.5	67.7±11.6	0.7836
Tumor size (cm)	5.6±2.1	5.8±2.4	0.7808
Surgical time (min)	160.4±32.4	172.2±43.7	0.3607
Blood loss (ml)	197.0±214.6	483.3±749.8	0.1015

Notes: TPN: total parenteral nutrition; PN: parenteral nutrition; ONS: oral nutritional supplements

表2 TPN和PN+ONS组病例特征指标比较 (计数资料)
Table2 Comparison of colorectal cancer patients' characteristics between TPN and PN+ONS groups (enumeration data)

Characteristics	TPN group (n=23)	PN+ONS group(n=15)	P
Gender (Male/Female)	14/9(60.9%/39.1%)	8/7(53.3%/46.6%)	0.6456
Postoperative complication(%)	7/23(30.4%)	1/15(13.3%)	0.0790
Postoperative infection(%)	4/23(17.4%)	0/15(0%)	0.0877
Postoperative mortality(%)	0	0	

受了不同量的输血, 包括红细胞或(和)血浆。

两组间的实验室化验结果, 包括术前、术后第7天(7th postoperative day, 7th POD)血淋巴细胞(blood lymphocyte)、血清白蛋白(serum albumin, ALB)等差异均无统计学意义, 见表3。

表3 TPN和PN+ONS组患者术前、术后第7天的血淋巴细胞、血清白蛋白比较

Table3 Comparison of blood lymphocyte and ALB before operation and on 7th POD between TPN and PN+ONS groups

Groups	n	Lymphocyte(×10 ⁹)		ALB(g/L)	
		Before operation	7 th POD	Before operation	7 th POD
TPN	23	1.22±0.54	1.16±0.32	34.3±2.9	32.9±3.2
PN+ONS	15	1.17±0.52	0.92±0.21	35.4±2.8	34.1±5.1

Notes: 7th POD: 7th postoperative day; ALB: serum albumin

2.2 住院时间

两组总住院时间和术后住院时间比较差异均无统计学意义, 见表4。

表4 TPN和PN+ONS组患者的住院时间比较

Table4 Comparison of LOS between TPN and PN+ONS groups

LOS(d)	TPN group (n=23)	PN+ONS group(n=15)	P
Total LOS	31.2±14.7	23.9±7.1	0.0912
Postoperative LOS	21.3±14.0	16.6±5.2	0.2280

Notes: LOS: length of stay

3 讨论

营养不良或营养不良风险状态可增加胃肠道肿瘤患者术后并发症发生率, 或(和)延长住院时间^[10-11]。临床实践提示, 合并肠梗阻、穿孔或

出血需急诊手术的此类患者, 因肿瘤进展及普遍存在的喂养困难, 术前几乎均合并有营养不良或营养不良风险^[12-14]。本研究入组病例均存在营养不良风险, 验证了此类患者的这一特征。以往研究表明, 合理的围手术期营养支持能在一定程度上减低结直肠癌术后患病率, 缩短住院时间^[5,14]。检索文献, 目前尚缺乏需急诊手术的结直肠癌患者围手术期营养支持研究, 可能与此类患者干扰因素较多, 影响预后因素繁杂有关, 不利于有效开展工作。

结直肠癌患者急诊手术前情况复杂: (1) 术前多数合并有不良症状, 如发热、食欲下降及慢性体重减轻、贫血、低蛋白血症等^[4,13]; (2) 在术前均无法彻底行肠道准备, 术中肠道内容物较多, 或因机械性肠梗阻引起近端肠道严重扩张, 伴发肠道菌群失调或全身炎症反应综合征(systemic inflammatory response syndrome, SIRS)、中毒症状等; (3) 由于细菌及炎性介质的作用, 普遍存在肠黏膜屏障功能受损^[15]。

因需术前充分的肠道准备, 以及预防术后吻合口瘘的发生, 结直肠癌患者术后普遍存在恢复进食较晚、广泛采用TPN促进恢复的现象^[16]。但越来越多的研究表明, 围手术期实时添加肠内营养, 尤其术后早期肠内营养(early enteral nutrition, EEN)具有保护肠道屏障功能、降低SIRS发生率、减少术后患病率、缩短住院时间等优势^[17-19]。

ONS作为肠内营养的一种方式, 是指正常食物之外的, 可经口摄入, 能够补充日常饮食不足的特殊医学用途(配方)食品^[20]。系统的研究表明, ONS作为TPN、PN及管饲营养的有力补充, 能够改善因慢性疾病引起的生长迟缓, 预防肿瘤患者的体重丢失, 改善各种原因引起的恶液质等作用, 具有良好的成本效果优势^[21-22]。结直肠癌患者围手术期添加一定剂量的ONS, 不仅有较好的依从性, 而且能够有效降低术后患病率, 缩短住院时间, 达到快速康复的目的^[5,23]。加速康复外科更多采用ONS帮助患者康复^[23]。本研究入组患者术后添加ONS后, 术后总并发症发生率、患病率低于TPN组, 总住院时间略有缩短, 但差异缺乏统计学意义。受回顾性研究所限, 无法获取部分患者住院时间较长的真实原因, 只能根据病程记录或者医嘱内容推测, 具有一定的主观性。

ONS具有良好优势的机制可能与以下因素有关: (1) 刺激消化道生理功能的恢复, 维持胃肠道相关的神经内分泌系统正常运转; (2) 能够保护或改善肠黏膜屏障功能, 避免肠道细菌移位, 减少术后感染概率; (3) ONS便于添加部分具有

抗氧化、提高免疫能力的特殊营养剂，如L-肉碱和牛磺酸等，抑制SIRS的发生^[24-26]。

值得进一步研究的是，结直肠癌急诊手术患者多数病情危急，术前常合并慢性消耗性贫血或急性失血性贫血，术中术后需要输血的概率较大，可能会对结果产生一定的影响。本研究纳入的病例，共有8例患者术中术后接受了不同量的输血，包括红细胞或（和）血浆，可能对营养指标及白蛋白水平产生较大影响。对仅能提供部分热量的ONS作用产生一定的干扰。本研究未能深究输血对结果产生的潜在影响，需进一步增加例数，减少对结果偏倚的影响。

由于围手术期诊疗过程较为复杂，结直肠癌急诊手术患者的术后康复影响因素较多，术后短时间添加ONS的作用有限。但本研究结果显示，对于合并营养不良风险的此类患者尽早进行营养干预，仍然是减少术后并发症、缩短住院时间，进而减少经济开支的重要保障。

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