

强直性脊柱炎患者消化功能的影响因素分析及临床意义

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【摘要】目的:评估强直性脊柱炎(ankylosing spondylitis, AS)患者的消化功能,探讨其消化功能紊乱的影响因素及临床意义。**方法:**2014年7月~2015年4月,101例AS患者纳入本研究,其中门诊患者84例、住院患者17例。收集患者年龄、病程、服用非甾体类抗炎药(NSAIDs)和抗风湿药(DMARD)情况、烟酒嗜好、合并症等临床资料,记录红细胞沉降率(ESR)、C反应蛋白(CRP)等检查结果,在X线片上测量脊柱最大后凸 Cobb 角(global kyphosis, GK)。采用食品效益评估调查问卷(FBA)和功能性消化不良生存质量量表(FDDQL)评估患者消化功能。根据 GK 将患者分为轻度后凸组($GK < 60^\circ$, 67例)和重度后凸组($GK \geq 60^\circ$, 34例)。采用 Spearman 相关性分析和多元线性回归分析探讨 AS 患者消化功能的影响因素。**结果:**101例患者 FBA 评分为 63.2 ± 13.5 分, FDDQL 评分为 77.4 ± 13.1 分, ESR 26.6 ± 20.2 mm/h, CRP 32.0 ± 22.7 mg/L, GK $52.1^\circ \pm 23.5^\circ$, 48例有服用 NSAIDs 药物史, 23例有服用 DMARD 药物史, 52例有吸烟嗜好, 40例有饮酒嗜好, 3例合并有贫血。除了 FDDQL“疾病控制”维度外, 两组患者消化功能评分差异无统计学意义($P > 0.05$)。Spearman 相关分析显示, 轻度后凸组 FBA 总分与患者年龄、CRP 和饮酒相关(均 $P < 0.05$), FDDQL 总分与 CRP 呈负相关($P < 0.05$); 重度后凸组 FBA 总分与各影响因素均无相关性(均 $P > 0.05$), FDDQL 总分与 GK 和贫血呈负相关(均 $P < 0.05$); 101例 AS 患者 FBA 总分与年龄、服用 NSAIDs 和饮酒相关(均 $P < 0.05$), 而与病程、ESR、CRP、GK、吸烟、服用 DMARD、贫血无相关性(均 $P > 0.05$); FDDQL 总分与 GK、服用 NSAIDs、服用 DMARD 和贫血呈负相关(均 $P < 0.05$), 而与年龄、病程、ESR、CRP、吸烟和饮酒无相关性(均 $P > 0.05$)。101例 AS 患者多元线性回归分析显示服用 NSAIDs 和饮酒致 FBA 总分减少; 服用 NSAIDs 和贫血致 FDDQL 总分减少。**结论:**轻、重度胸腰椎后凸畸形 AS 患者消化功能无明显差异。AS 患者消化功能下降与年龄、脊柱最大后凸 Cobb 角、服用 NSAIDs、服用 DMARD、饮酒和贫血有关, 而与病程、炎症活动程度和吸烟无相关性, 服用 NSAIDs、饮酒和贫血是 AS 患者消化功能紊乱的重要因素。

【关键词】强直性脊柱炎; 消化功能; 影响因素

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Influence factors and clinical significance of digestive disturbance in ankylosing spondylitis patients/ZHANG Yunpeng, QIAN Bangping, QIU Yong, et al/Chinese Journal of Spine and Spinal Cord, 2015, 25(9): 799-804

【Abstract】Objectives: To investigate the digestive disturbance in ankylosing spondylitis(AS) patients, and to analyze its influence factors and clinical significance. **Methods:** From July 2014 to April 2015, 101 AS patients were included in this study, consisting of 84 outpatients and 17 inpatients. The parameters of patients, including age, disease duration, history of taking non steroidal anti inflammatory drugs(NSAIDs) and disease modifying anti rheumatic drugs(DMARD), smoking and alcohol history, comorbidities, erythrocyte sedimentation rate(ESR), C reactive protein(CRP) and global kyphosis(GK) were collected. Digestive function was assessed by the Food and Benefits Assessment(FBA) and Functional Digestive Disorders Quality of Life(FDDQL) question-

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naires. The patients were divided into mild kyphosis group($GK < 60^\circ$, $n=67$) and severe kyphosis group($GK \geq 60^\circ$, $n=34$). Correlations of FBA, FDDQL with the influencing factors were calculated by the Spearman coefficients of correlations. Multiple regression analysis was used to investigate the influence factors which impaired digestive function of AS patients. **Results:** The score of FBA and FDDQL was 63.2 ± 13.5 and 77.4 ± 13.1 . The average GK of patients was $52.1^\circ \pm 23.5^\circ$. Additionally, the ESR and CRP were 26.6 ± 20.2 mm/h and 32.0 ± 22.7 mg/L. History of smoking, alcohol, taking NSAIDs and DMARD were found in 52, 40, 48 and 23 patients, respectively. Among them, 3 patients were companied with anemia. There was no significant difference between two groups in questionnaire scores except for the score of coping with disease domain of FDDQL questionnaire. Spearman correlation analysis revealed that FBA was significantly correlated with age, CRP and alcohol($P < 0.05$), while FDDQL was significantly related to anemia($P < 0.05$) in mild kyphosis group. Moreover, in severe kyphosis group, no significant correlation was found between FBA and influence factors, and FDDQL was significantly associated with GK and anemia($P < 0.05$). For all 101 AS patients, significant correlations were observed between FBA and age, NSAIDs as well as alcohol history($P < 0.05$). Similarly, FDDQL significantly correlated with GK, NSAIDs, DMARD, and anemia($P < 0.05$). Multiple regression analysis revealed that NSAIDs and alcohol history resulted in lower FBA score, while NSAIDs and anemia led to lower FDDQL score. **Conclusions:** There is no significant difference between AS patients with mild and severe kyphosis in digestive function. The digestive function of AS patients is impaired, which is related to age, GK, NSAIDs, DMARD, alcohol and anemia. Digestive disturbance is not correlated with disease duration, ESR, CRP and smoking. Among them, NSAIDs, alcohol and anemia are the most important factors impairing the digestive function in AS patients.

[Key words] Ankylosing spondylitis; Digestive disturbance; Influencing factors

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强直性脊柱炎(ankylosing spondylitis, AS)是一种慢性炎症性疾病,主要累及脊柱与骶髂关节,严重者可出现脊柱畸形和关节强直。AS 胸腰椎后凸畸形患者躯干塌陷,腹腔容积减小,甚至出现肋骨边缘压迫内脏,影响其呼吸和消化功能^[1,2]。AS 也是一种系统性疾病,可合并不同程度的其他脏器或组织受累,消化系统也会受到影响。研究表明,10%的 AS 患者有明显的炎症性肠病,70%的 AS 患者可并发末端回肠炎,而且从基因和免疫学角度上讲,AS 和克罗恩病有内在联系^[3]。长期慢性疼痛影响患者的生活质量,而疼痛的治疗主要是通过口服非甾体类抗炎药(NSAIDs)和抗风湿药(DMARD)。NSAIDs 和 DMARD 的不良反应,特别是对胃肠道的损害值得重视^[4,5]。国内对 AS 患者消化功能影响因素未见报道,明确 AS 患者消化功能的影响因素,改善其消化功能,有助于增强患者治疗的依从性,从而提高治疗效果。本研究评估 AS 患者的消化功能,并探讨其影响因素和临床意义。

1 资料与方法

1.1 研究对象

选取 2014 年 7 月~2015 年 4 月南京鼓楼医院收治的 AS 患者。纳入标准:(1)符合 1984 年 AS 的纽约分类标准^[6];(2)有站立位全脊柱正侧位 X 线片;(3)有红细胞沉降率(erythrocyte sedimentation rate, ESR)、C 反应蛋白(C reactive protein, CRP)检查结果;(4)完整填写食品效益评估调查问卷(Food and Benefits Assessment questionnaire, FBA)和功能性消化不良生存质量量表(Functional Digestive Disorders Quality of Life questionnaire, FDDQL)^[7,8]。排除标准:(1)有脊柱手术史;(2)脊柱病理性骨折及假关节;(3)既往有消化道溃疡、炎症性肠病、克罗恩病等消化系统疾病史。符合上述标准的 101 例 AS 患者(门诊 84 例,住院 17 例)最终纳入本研究。

1.2 一般资料

101 例患者中,男 93 例,女 8 例;年龄 19~58 岁(33.7 ± 9.0 岁);病程 1~30 年(10.0 ± 6.3 年);ESR $2 \sim 94$ mm/h (26.6 ± 20.2 mm/h);CRP $1.7 \sim 89.6$ mg/L (32.0 ± 22.7 mg/L);脊柱最大后凸 Cobb 角(global kyphosis, GK)^[9] $11^\circ \sim 110^\circ$ ($52.1^\circ \pm 23.5^\circ$);48 例有服

用 NSAIDs 药物史;23 例有服用 DMARD 药物史;52 例有吸烟嗜好;40 例有饮酒嗜好;3 例合并贫血(表 1)。

1.3 消化功能评估及病例分组

采用 FBA^[7]和 FDDQL^[8]评定,由专门的医师采用相同的方法向患者阐述每个因子的含义,患者在最符合自己情况的项目上打勾。FBA 共 41 个项目,7 个维度组成,分别是零食、活力、幸福、审美、外观、疾病不适和疾病预防。FDDQL 共 43 个项目,8 个维度组成,分别是日常活动、忧虑、饮食、睡眠、不适、健康感觉、疾病控制和压力。各部分计分采用百分制,分值越高表示消化功能越好。各维度平均分为量表总分。

根据 GK^[10]将患者分为轻度后凸组(GK<60°, 67 例)和重度后凸组(GK≥60°, 34 例)(表 1),比较两组患者 FBA 和 FDDQL 评分。轻度后凸组中 6 例、重度后凸组中 11 例接受了截骨矫形术。

1.4 统计学方法

应用 SPSS 19.0 统计软件进行分析,近似正态分布的计量资料以 $\bar{x} \pm s$ 表示。轻度和重度后凸组患者消化功能的比较采用成组设计资料 t 检验。各因素和消化功能间的相关性采用 Spearman 相关性分析。筛选影响 AS 患者消化功能的影响因素采用多元线性回归分析。以 $P<0.05$ 为差异有

统计学意义。

2 结果

2.1 消化功能评分

轻度后凸组、重度后凸组和总体(101 例)患者的 FBA 评分和 FDDQL 评分结果见表 2。101 例患者 FBA 评分总分为 39.2~100 分,患者消化功能紊乱在 7 个维度上均有所表现。101 例患者

表 2 AS 患者消化功能评分
Table 2 Digestive function of AS patients

量表 Questionnaire	轻度后凸 组(n=67) Mild kyphosis group	重度后凸 组(n=34) Severe kyphosis group	总体 (n=101) All patients
FBA 评分 FBA score			
零食 Snacking	65.7±17.0	64.3±16.9	65.2±16.9
活力 Vitality	60.3±17.2	57.9±15.5	59.5±16.6
幸福 Well-being	65.7±17.9	61.5±17.5	64.3±17.7
审美 Aesthetics	62.0±18.8	62.4±16.9	62.1±18.1
外观 Physical appearance	63.6±23.6	60.5±24.6	62.5±23.9
疾病不适 Digestive comfort	75.1±15.7	73.4±20.9	74.5±17.5
疾病预防 Disease prevention	54.3±23.1	53.1±24.6	53.9±23.5
总分 Total score	63.8±13.3	61.9±13.9	63.2±13.5
FDDQL 评分 FDDQL score			
日常活动 Activities	81.0±17.2	79.9±17.5	80.6±17.2
忧虑 Anxiety	87.6±14.1	82.0±20.0	85.7±16.4
饮食 Diet	86.8±13.7	85.9±16.4	86.5±14.6
睡眠 Sleep	86.3±17.4	84.1±17.1	85.6±17.2
不适 Discomfort	85.7±12.1	82.9±15.0	84.7±13.1
健康感觉 Health perceptions	54.7±23.2	48.8±23.2	52.7±23.2
疾病控制 Coping with disease	71.9±25.9	60.5±27.0 ^①	68.1±26.7
压力 Impact of stress	76.4±25.2	73.8±22.7	75.5±24.3
总分 Total score	78.8±13.1	74.7±12.8	77.4±13.1

注:FBA 食品效益评估调查问卷;FDDQL:功能性消化不良生存质量量表;①与轻度后凸组比较 $P<0.05$

Note: FBA, food and benefits assessment questionnaire; FDDQL, functional digestive disorders quality of life questionnaire;
①Compared with mild kyphosis group $P<0.05$

表 1 AS 患者一般临床资料

Table 1 Clinical characteristics of AS patients

	轻度后凸 组(n=67) Mild kyphosis group	重度后凸 组(n=34) Severe kyphosis group	总体 (n=101) All patients
年龄(岁) Age	34.0±9.9	33.3±7.5	33.7±9.0
病程(年) Duration	8.2±6.0	12.7±5.8	10.0±6.3
血沉(mm/h) ESR	31.2±23.0	19.1±11.3	26.6±20.2
C反应蛋白(mg/L) CPR	35.4±23.8	26.4±20.1	32.0±22.7
胸腰椎最大后凸 Cobb角(°) Global kyphosis	37.0±12.1	77.6±15.2	52.1±23.5
吸烟(是/否) Smoking(yes/no)	37/30	15/19	52/49
饮酒(是/否) Drinking(yes/no)	24/43	16/18	40/61
非甾体类抗炎药 (是/否) NSAIDs(yes/no)	34/33	14/20	48/53
抗风湿药(是/否) DMARD(yes/no)	19/48	4/30	23/78
贫血(是/否) Anemia(yes/no)	1/66	2/32	3/100

FDDQL 评分总分为 39.0~100 分,患者消化功能紊乱主要表现在健康感觉、疾病控制、压力 3 个维度。轻度和重度胸腰椎后凸畸形患者 FBA 总分及各维度评分的差异无统计学意义 ($P>0.05$); FDDQL 除“疾病控制”维度 ($P=0.043$) 外,其他维度评分及总分的差异无统计学意义 ($P>0.05$)。

2.2 Spearman 相关性分析

AS 患者消化功能评分与各因素的相关性分析结果见表 3。轻度后凸组 FBA 总分与患者年龄、CRP 和饮酒相关 (均 $P<0.05$),而与病程、ESR、GK、吸烟、服用 NSAIDs、服用 DMARD 和贫血无相关性 (均 $P>0.05$); FDDQL 总分与 CRP 呈负相关 ($P<0.05$),而与年龄、病程、ESR、GK、吸烟、饮酒、服用 NSAID、服用 DMARD 和贫血无相关性 (均 $P>0.05$)。

重度后凸组 FBA 总分与各因素均无相关性 (均 $P>0.05$); FDDQL 总分与 GK 和贫血呈负相关 (均 $P<0.05$),而与年龄、病程、ESR、CRP、吸烟、饮酒、服用 NSAIDs 和服用 DMARD 无相关性 (均 $P>0.05$)。

101 例 AS 患者 FBA 总分与年龄、服用 NSAIDs 和饮酒呈正相关 (均 $P<0.05$),而与病程、ESR、CRP、GK、吸烟、服用 DMARD 和贫血无相关性 (均 $P>0.05$); FDDQL 总分与 GK、服用 NSAIDs、服用 DMARD 和贫血呈负相关 (均 $P<0.05$),而与年龄、病程、ESR、CRP、吸烟和饮酒无相关性 (均 $P>0.05$)。

2.3 多元回归分析

多元线性回归分析表明,在 101 例 AS 患者中,服用 NSAIDs 和饮酒是 FBA 总分减少的危险因素;服用 NSAIDs 和贫血是 FDDQL 总分减少的危险因素 (表 4)。

3 讨论

3.1 AS 患者消化功能紊乱的病因

AS 是血清反应阴性、包含很多与炎症相关症状的脊柱关节病 (spondyloarthropathies, SpA),而 NOD2/CARD15 的多态性使 SpA 患者更容易患有肠道疾病^[11]。AS 患者肠道通透性增加且容易合并肠道炎症^[12]。Dany 等^[13]的研究发现一些基因与 AS

表 3 AS 患者消化功能评分与各因素的相关性分析

Table 3 Correlation between digestive function and factors of AS patients

	FBA 评分 (FBA score)						FDDQL 评分 (FDDQL score)					
	轻度后凸组 (n=67) Mild kyphosis group		重度后凸组 (n=34) Severe kyphosis group		总体 (n=101) All patients		轻度后凸组 (n=67) Mild kyphosis group		重度后凸组 (n=34) Severe kyphosis group		总体 (n=101) All patients	
	r	P	r	P	r	P	r	P	r	P	r	P
年龄 Age	0.345	0.037	0.060	0.786	0.265	0.041	0.227	0.177	-0.177	0.420	0.107	0.417
病程 Duration	0.010	0.955	-0.025	0.909	-0.025	0.852	-0.078	0.648	-0.206	0.345	-0.166	0.204
血沉 ESR	-0.293	0.078	-0.041	0.852	-0.201	0.124	-0.204	0.225	0.061	0.781	-0.069	0.602
C反应蛋白 CRP	-0.354	0.032	0.191	0.383	-0.161	0.220	-0.389	0.017	0.321	0.136	-0.094	0.477
脊柱最大后凸 Cobb角 Global kyphosis	0.006	0.970	-0.397	0.060	-0.107	0.415	0.006	0.973	-0.764	0.000	-0.255	0.049
吸烟 Smoking	-0.278	0.095	0.118	0.592	-0.118	0.371	-0.074	0.663	0.039	0.858	-0.023	0.861
饮酒 Drinking	-0.386	0.018	-0.344	0.108	-0.356	0.005	-0.300	0.071	-0.304	0.158	-0.241	0.064
非甾体类抗炎药 NSAIDs	-0.264	0.114	-0.385	0.069	-0.307	0.017	-0.310	0.062	-0.289	0.181	-0.324	0.012
抗风湿药 DMARD	-0.187	0.269	-0.398	0.060	-0.247	0.057	-0.230	0.171	-0.277	0.201	-0.256	0.049
贫血 Anemia	-0.187	0.267	-0.116	0.597	-0.157	0.232	-0.234	0.163	-0.491	0.047	-0.311	0.015

注: FBA, 食品效益评估调查问卷; FDDQL, 功能性消化不良生存质量量表

Note: FBA, food and benefits assessment questionnaire; FDDQL, functional digestive disorders quality of life questionnaire

表 4 101 例 AS 患者消化功能与各影响因素的多元回归分析

Table 4 Multiple regression analysis between digestive function and influencing factors in 101 AS patients

变量 Variables	FBA评分(FBA score)			FDDQL评分(FDDQL score)		
	回归系数 Coefficient	t值 t value	P值 P value	回归系数 Coefficient	t值 t value	P值 P value
非甾体类抗炎药 NSAIDs	-8.364	-3.458	0.001	-8.092	-2.745	0.007
饮酒 Drinking	-8.416	-3.390	0.001	—	—	—
贫血 Anemia	—	—	—	-24.612	-3.329	0.001
常数 Constant	48.565			77.843		

注:FBA,食品效益评估调查问卷;FDDQL,功能性消化不良生存质量量表

Note: FBA, food and benefits assessment questionnaire. FDDQL, functional digestive disorders quality of life questionnaire

和炎症性肠病共同相关,尤其是在白介素 13 通路中的一些因子,如信号转导与转录激活因子 3 (STAT3)、白介素 23 受体等。研究表明,AS 患者(尤其是人类白细胞抗原 B27 阳性患者)血清中的克雷伯氏菌的含量比正常人高^[14]。最新的研究表明,AS 患者较高的 IgA 抗克雷伯氏菌抗体与肠道炎症的程度相关^[3]。

此外,疲劳、疼痛、长期的疾病困扰、日常活动障碍、焦虑情绪及生活质量降低等也会导致 AS 患者消化功能紊乱^[15,16]。其他因素,如长期服用 NSAIDs^[17]及晚期 AS 胸腰椎后凸畸形患者的躯干塌陷等也会影响其消化功能。本组 101 例 AS 患者 FBA 评分 63.2 ± 13.5 分,在 FBA 的 7 个维度上消化功能紊乱均有所体现;FDDQL 评分 77.4 ± 13.1 分,消化功能紊乱主要表现在健康感觉、疾病控制、压力 3 个维度上。

3.2 AS 患者消化功能的影响因素

有研究表明,NSAIDs 的并发症之一是 NSAIDs 相关性胃肠病,轻者粘膜充血、水肿、糜烂以及一过性浅表溃疡形成,重者造成大面积溃疡合并消化道出血、穿孔甚至危及生命^[18]。DMARD 的不良反应也主要表现为胃肠道反应。此外,有研究^[19,20]表明,酗酒为不明原因消化不良的危险因素。AS 伴胸腰椎后凸畸形患者腹腔容积减小,内脏受压,胃肠道容量和胃动力降低,消化功能受到影响;最新研究结果显示,通过截骨矫形术能有效改善 AS 患者内脏受压情况,患者消化功能得到改善^[21-23]。

本研究 Spearman 相关分析发现,101 例 AS 患者消化功能紊乱主要与年龄、GK、服用 NSAIDs、服用 DMARD、饮酒和贫血相关,而与病

程长短、ESR、CRP、吸烟无相关性,表明 AS 患者消化功能与疾病的病程、炎症活动程度无关。然而,Spearman 相关分析发现,67 例轻度后凸的 AS 患者消化功能紊乱主要与年龄、CRP 和饮酒相关,34 例重度后凸的 AS 患者消化功能紊乱主要与 GK、贫血相关。因此,对于轻度后凸的 AS 患者,在炎症活动期也需要密切关注其消化功能;对于重度后凸的 AS 患者,胸腰椎后凸畸形进展的同时,消化功能紊乱也会进一步恶化。多元回归分析发现,服用 NSAIDs 和饮酒是 FBA 总分降低的危险因素;服用 NSAIDs 和贫血是 FDDQL 总分降低的危险因素。

3.3 AS 患者消化功能评估的临床意义

AS 患者的治疗及康复锻炼是综合性的,而改善 AS 患者的消化功能可提高患者的依从性。尽管 AS 患者消化功能的影响因素很多,但本研究发现,101 例 AS 患者消化功能的下降与年龄、GK、服用 NSAIDs、服用 DMARD、饮酒和贫血有关,服用 NSAIDs、饮酒和贫血是患者消化功能紊乱的主要影响因素。因此,在对长期口服 NSAIDs、DMARD 的患者应注意其消化功能的损害情况,口服一段时间后予以停药或更换其他药物以控制炎症;同时对饮酒和合并贫血的 AS 患者,应注意其消化功能情况,嘱其戒酒和治疗贫血。对于轻度后凸的 AS 患者,在炎症活动期要加强胃肠功能的保护;对于重度后凸的 AS 患者,在评估患者畸形严重程度的同时,也需要关注患者合并的内科疾病以及患者的消化功能,以减少截骨矫形术围手术期并发症。

本研究的不足之处在于,样本中女性患者所占比例较小,未探讨 AS 消化功能与性别的相关

性;另外,本研究未区分 AS 静止期与活动期、未评估患者全身营养状态以及未设立正常对照组,需进一步大样本对照研究,以更深入探讨 AS 患者消化功能紊乱的影响因素。消化功能紊乱是 AS 患者的常见问题,与患者年龄、GK、服用 NSAIDs、服用 DMARD、饮酒和贫血有关,与疾病的病程、炎症活动程度和吸烟无关。服用 NSAIDs、饮酒和贫血是 AS 患者消化功能紊乱的重要因素。

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