

doi: 10.13241/j.cnki.pmb.2023.19.017

不同病因肝硬化患者临床特征及其预后影响因素分析 *

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摘要 目的:探讨不同病因肝硬化患者临床特征及其预后影响因素。**方法:**回顾性选择2017年1月至2020年12月来我院诊治的具有完整资料,同时明确诊断为肝硬化,病因为乙肝后肝硬化(78例)、酒精性肝硬化(42例)。分析两组患者的一般资料、并发症发生情况、合并疾病情况,分析乙肝后肝硬化、酒精性肝硬化的预后影响因素。**结果:**两组患者在性别、职业、临床表现(黄疸、黑便、呕血、蜘蛛痣、脾脏增大)、肝脏体积缩小、并发症(上消化道出血、肝性脑病)、合并疾病(脂肪肝、糖尿病、胰腺炎、胆结石)方面有统计学意义($P<0.05$)。乙肝后肝硬化组的疾病进展发生率明显较酒精性肝硬化组高($P<0.05$)。单因素分析结果表明,临床表现(乏力、食欲减退、皮肤瘙痒、腹痛、腹胀、呕血、黑便、腹水)、Child-Pugh分级、并发症(上消化道出血、肝性脑病)是影响乙肝后肝硬化患者预后的因素($P<0.05$)；Logistic回归分析结果表明,Child-Pugh分级在B、C级、存在上消化道出血与肝性脑病是影响乙肝后肝硬化患者预后的危险因素($P<0.05$)。单因素分析结果表明,临床表现(黄疸)、Child-Pugh分级、并发症(上消化道出血、肝性脑病、感染)是影响酒精性肝硬化患者预后的因素($P<0.05$)；Logistic回归分析结果表明,Child-Pugh分级为C级、存在上消化道出血肝性脑病、感染是影响酒精性肝硬化患者预后的危险因素($P<0.05$)。**结论:**乙肝后肝硬化与酒精性肝硬化的差异主要体现在性别、职业、临床表现、并发症与合并疾病中,影响乙肝后肝硬化预后的危险因素为Child-Pugh分级在B、C级、存在上消化道出血与肝性脑病,影响酒精性肝硬化预后的危险因素为Child-Pugh分级为C级、存在上消化道出血、肝性脑病、感染,需防治并发症,以改善患者预后。

关键词:肝硬化；临床特征；预后

中图分类号:R575.2 文献标识码:A 文章编号:1673-6273(2023)19-3683-07

Analysis of Clinical Features and Prognostic Factors of Patients with Cirrhosis of Different Etiology*

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ABSTRACT Objective: To investigate the clinical characteristics and prognostic factors of patients with cirrhosis of different etiology.
Methods: Complete data of patients who came to our hospital from January 2017 to December 2020 were retrospectively selected. At the same time, they were diagnosed as cirrhosis, which was caused by posthepatitis B cirrhosis (78 cases) and alcoholic cirrhosis (42 cases). The general data, complications and diseases of the two groups were analyzed, and the prognostic factors of patients with posthepatitis B cirrhosis and alcoholic cirrhosis were analyzed. **Results:** There were statistical significance in gender, occupation, clinical manifestations (jaundice, black stool, hematemesis, spider naevi, spleen enlargement), liver size reduction, complications (upper digestive tract hemorrhage, hepatic encephalopathy), and concomitant diseases (fatty liver, diabetes, pancreatitis, gallstones) of the two groups ($P<0.05$). The incidence of disease progression was significantly higher in the posthepatitis B cirrhosis group than in the alcoholic cirrhosis group ($P<0.05$). The incidence of disease progression was significantly higher in the posthepatitis B cirrhosis group than in the alcoholic cirrhosis group ($P<0.05$). The results of single factor analysis showed that clinical manifestations (fatigue, loss of appetite, pruritus, abdominal pain, abdominal distension, hematemesis, black stool, ascites), Child-Pugh grade, complications (upper digestive tract hemorrhage, hepatic encephalopathy) were the factors affecting the prognosis of patients with posthepatitis B cirrhosis ($P<0.05$). Logistic regression analysis showed that Child-Pugh grades in B and C, the presence of upper gastrointestinal bleeding and hepatic encephalopathy were risk factors for the prognosis of patients with posthepatitis B cirrhosis ($P<0.05$). Unifactorial analysis showed that clinical manifestations (jaundice), Child-Pugh grade, complications (upper gastrointestinal bleeding, hepatic encephalopathy, infection) were the prognostic factors of alcoholic cirrhosis ($P<0.05$). Logistic regression analysis showed that Child-Pugh grade C, the presence of upper gastrointestinal bleeding hepatic encephalopathy and infection were the risk factors affecting the prognosis of patients with alcoholic cirrhosis ($P<0.05$). **Conclusion:** The

* 基金项目:甘肃省自然科学基金科技计划项目(22JR5RA739)

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(收稿日期:2023-02-13 接受日期:2023-03-10)

differences between posthepatitis B cirrhosis and alcoholic cirrhosis are mainly reflected in gender, occupation, clinical manifestations, complications and co-diseases. The risk factors affecting prognosis of posthepatitis B cirrhosis are Child-Pugh grade B and C, the presence of upper gastrointestinal bleeding and hepatic encephalopathy. The risk factors affecting the prognosis of alcoholic cirrhosis are Child-Pugh grade C, the presence of upper gastrointestinal bleeding, hepatic encephalopathy, infection, complications need to be prevented to improve the prognosis of patients.

Key words: Cirrhosis of the liver; Clinical features; Prognosis

Chinese Library Classification(CLC): R575.2 Document code: A

Article ID: 1673-6273(2023)19-3683-07

前言

肝硬化是一种进行性的慢性肝病，也是多种慢性肝病发展的晚期阶段，病理上特征为再生结节、肝脏弥漫性纤维化、假小叶，而引起肝硬化有多种病因^[1-2]。流行病学统计显示，目前我国每年因肝硬化导致的死亡人数超过10万人^[3]。导致患者出现肝硬化的疾病病因较多，最常见的是长期大量饮酒引起的酒精性肝硬化与肝炎病毒感染引起的肝炎后肝硬化^[4-5]。我国是乙肝大国，目前在我国每年约有2.1%乙肝患者会进展为乙肝后肝硬化^[6-7]。同时随着社会交往活动的日益频繁，酒精性肝硬化发病率不断升高。以上两种肝硬化患者的主要特征为门静脉高压、肝功能进行性减退，而两者表现不尽相同^[8-9]。如果可以分析肝硬化的疾病病因、疾病特征、预后转归等分析，给患者制定合理的治疗方案，提高其生存质量，延长其生存时间，对于晚期的肝病防治有重要意义^[10-12]。既往对乙肝后肝硬化、酒精性肝硬化的并发症、临床表现、合并疾病等方面等综合性分析较少。因此本研究回顾性分析了120例肝硬化患者的临床资料，以提高对两种疾病的诊断与鉴别，分析两者治疗上的不同侧重点，进而为患者提供有效防治。

1 资料与方法

1.1 一般资料

回顾性选择2017年1月至2020年12月来我院诊治的具有完整资料，同时明确诊断为肝硬化，病因为乙肝后肝硬化组（78例）、酒精性肝硬化组（42例）。

纳入标准：乙肝后肝硬化^[13]：既往有乙肝病毒抗原抗体标记(HBsAg)阳性，或HBsAg阴性、抗-HBc阳性，且有明确的慢性HBV感染史（既往HBsAg阳性>6个月），并除外其他因素和（或）存在慢性乙肝病史或乙肝病毒DNA为阳性；临幊上存在门静脉高压、肝功能减退表现，影像学检查支持患者的肝硬化改变；除药物性、酒精性、自身免疫性、胆汁性等类型的肝硬化。

酒精性肝硬化诊断标准^[14]：根据中华医学会肝脏病学分会中肝硬化和酒精性肝病学组提出的关于酒精性肝病的疾病诊疗指南：大量、长期饮酒史，每日酒精摄入量>40g，同时饮酒时间超过5年；患者存在门静脉高压或肝功能减退的情况，同时影像学出现肝硬化改变；既往肝炎病毒标记物为阴性且无肝炎病史；排除其他因素引起的肝硬化。

排除标准：酒精性、乙肝病毒感染因素外其他原因造成的肝硬化，例如药物、心源性肝硬化、非就进行脂肪肝肝病引起的肝硬化、毒物引起的肝硬化、隐源性肝硬化等；满足以上标准同

时存在导致其他肝硬化的病因者、病例资料不全的患者等。

1.2 观察指标

1.2.1 分析两组患者的一般资料 包括性别、年龄、职业。临床特征包括食欲减退、乏力、腹痛、皮肤瘙痒、肝掌、浮肿、腹胀、蜘蛛痣、脾脏肿大、肝脏体积增大或缩小、黑便、呕血、发热。记录患者入院时的Child分级，其中肝脏大小、脾脏大小、肝腹水数据来源患者入院后的腹部CT、B超及体格检查。

1.2.2 分析两组患者的并发症发生情况 包括上消化道出血、肝性脑病、自发性腹膜炎、肝肾综合征、感染。

1.2.3 分析两组患者的合并疾病情况 包括脂肪肝、糖尿病、胰腺炎、胆结石、弥漫性结缔组织病（包括系统性红斑狼疮、原发性干燥综合征、系统性硬化病、类风湿关节炎、皮肌炎、多肌炎等）、甲状腺疾病。

1.2.4 分析120例患者的疾病进展与未进展情况 通过电话、门诊等方式随访，记录患者2年的预后，随访截止时间为2022年12月。根据其是否出现了肝硬化失代偿情况，将患者分为无进展组（无肝硬化失代偿）与进展组（合并肝硬化失代偿）。并分析乙肝后肝硬化、酒精性肝硬化的预后影响因素。

1.3 统计学方法

SPSS23.0软件，计数资料频数表示，卡方检验分析，计量资料 $\bar{x}\pm s$ 表示，t检验对比分析，使用Logistic回归分析， $P<0.05$ 为差异统计学意义。

2 结果

2.1 分析两组患者的一般资料

两组患者在性别、职业、临床表现（黄疸、黑便、呕血、蜘蛛痣、脾脏增大）、肝脏体积缩小、并发症（上消化道出血、肝性脑病）、合并疾病（脂肪肝、糖尿病、胰腺炎、胆结石）方面有差异（ $P<0.05$ ）。

2.2 分析两组患者的疾病进展情况

乙肝后肝硬化组的疾病进展发生率明显较酒精性肝硬化组高（ $P<0.05$ ）。

2.3 分析乙肝后肝硬化预后影响因素

单因素分析结果表明，临床表现（乏力、食欲减退、皮肤瘙痒、腹痛、腹胀、呕血、黑便、腹水）、Child-Pugh分级、并发症（上消化道出血、肝性脑病）是影响乙肝后肝硬化患者预后的因素（ $P<0.05$ ）；Logistic回归分析结果表明，Child-Pugh分级在B、C级、存在上消化道出血与肝性脑病是影响乙肝后肝硬化患者预后的危险因素（ $P<0.05$ ）。

2.4 分析酒精性肝硬化患者预后的影响因素

单因素分析结果表明，临床表现（黄疸）、Child-Pugh分级、

并发症(上消化道出血、肝性脑病、感染)是影响酒精性肝硬化患者预后的因素($P<0.05$);Logistic 回归分析结果表明,Child-Pugh 分级为 C 级、存在上消化道出血肝性脑病、感染是影响酒精性肝硬化患者预后的危险因素($P<0.05$)。

表 1 分析一般资料
Table 1 The general data were analyzed

Groups	Items	Posthepatitis B cirrhosis group(n=78)	Alcoholic cirrhosis group(n=42)	χ^2/t	P
Gender	Male	54	42	16.154	0.000
	Female	24	0		
Age(Year)		51.25± 8.89	51.03± 9.12	1.023	0.452
Occupation	Farmer	39	4	33.873	0.000
	Worker	16	6		
	Cadre	7	20		
	Merchant	8	9		
	Others	8	3		
Clinical picture	fatigue	37	20	0.002	0.964
	Anorexia	38	21		
	Jaundice	9	12		
	Itchy skin	3	1		
	Abdominal pain	19	8		
	Bloating	39	22		
	Liver palm	8	6		
	Hematemesis	44	6		
	Puffiness	12	7		
	Spider nevus	1	4		
	Black stool	40	9		
	Ascites	42	25		
	Splenomegaly	62	25		
	Fever	8	4		
Child-Pugh grade	A grade	18	8	4.874	0.087
	B grade	40	15		
	C grade	20	19		
Liver volume reduction		40	9	10.071	0.002
Complications	Upper gastrointestinal hemorrhage	43	11	9.237	0.002
	Hepatic encephalopathy	6	10		
	Hepatorenal syndrome	1	0		
	Infection	19	10		
Concomitant disease	Fatty liver	1	7	10.385	0.001
	Diabetes	7	11		
	Pancreatitis	0	3		
	Gallstone	15	15		
Diffuse connective tissue disease		6	3	0.012	0.913
	Thyroid disease	2	4		

表 2 两组患者的疾病进展情况(n)
Table 2 Disease progression in both groups(n)

Groups	n	Progress	No progress	χ^2	P
Posthepatitis B cirrhosis group	78	27	51	10.503	0.001
Alcoholic cirrhosis group	42	8	34		

表 3 分析乙肝后肝硬化预后单因素影响分析(n=78)
Table 3 To analyze the influence of single factor on prognosis of posthepatitis B cirrhosis

Groups	Items	n	Progress(n=27)	No progress(n=51)	χ^2/t	P
Gender	Male	54	17	37	0.422	0.516
	Female	24	10	14		
Age(Year)			51.05±7.58	51.45±9.43	1.002	0.478
Occupation	Farmer	39	15	24	1.080	0.897
	Worker	16	6	10		
	Cadre	7	2	5		
	Merchant	8	2	6		
	Others	8	2	6		
Clinical picture	Fatigue	37	20	17	11.752	0.000
	Anorexia	38	22	16	17.743	0.000
	Jaundice	9	5	4	1.971	0.160
	Itchy skin	3	3	0	5.893	0.015
	Abdominal pain	19	11	8	6.014	0.014
	Bloating	39	25	14	29.965	0.000
	Liver palm	8	5	3	3.062	0.080
	Hematemesis	44	24	20	17.715	0.000
	Puffiness	12	7	5	3.525	0.060
	Spider nevus	1	1	0	1.913	0.167
	Black stool	40	25	15	28.207	0.000
	Ascites	42	27	15	35.395	0.000
Child-Pugh grade	Splenomegaly	62	21	41	0.074	0.786
	Fever	8	5	3	3.062	0.080
	A grade	18	0	18	33.596	0.000
	B grade	40	10	30		
	C grade	20	17	3		
Liver volume reduction		40	25	15	28.207	0.000
Complications	Upper gastrointestinal hemorrhage	43	22	21	11.593	0.000
	Hepatic encephalopathy	6	6	0	12.278	0.000
	Hepatorenal syndrome	1	1	0	1.913	0.167
	Infection	19	10	9	3.602	0.058
Concomitant disease	Fatty liver	1	1	0	1.913	0.167
	Diabetes	7	5	2	4.605	0.312
	Pancreatitis	0	0	0	-	-
	Gallstone	15	5	10	0.013	0.909
	Diffuse connective tissue disease	6	3	3	0.680	0.410
	Thyroid disease	2	0	2	1.087	0.297

表 4 Logistic 回归分析乙肝后肝硬化预后影响因素(n=78)

Table 4 Logistic regression analysis of the prognostic factors of posthepatitis B cirrhosis(n=78)

Factors	B	SE	Wald	P	OR	95%CI
Fatigue	0.856	0.412	2.874	0.062	2.304	0.856~4.125
Anorexia	0.896	0.358	1.859	0.125	2.156	0.756~2.998
Itchy skin	0.756	0.412	1.896	0.102	2.256	0.743~3.526
Abdominal pain	0.841	0.389	1.523	0.256	2.758	0.695~3.589
Bloating	0.856	0.412	1.485	0.312	3.125	0.745~5.126
Hematemesis	0.712	0.445	1.231	0.356	2.158	1.235~4.126
Black stool	0.699	0.412	1.102	0.415	2.156	1.025~3.895
Ascites	0.702	0.359	1.253	0.395	2.415	1.002~4.124
Child-Pugh grade	0.452	0.184	6.201	0.011	1.574	1.102~2.289
Upper gastrointestinal hemorrhage	0.649	0.315	4.242	0.035	1.598	1.102~2.275
Hepatic encephalopathy	0.691	0.278	6.185	0.012	1.956	1.152~3.452

表 5 分析酒精性肝硬化预后单因素影响分析(n=42)

Table 5 To analyze the influence of single factor on the prognosis of alcoholic cirrhosis(n=42)

Groups	Items	n	Progress(n=8)	No progress(n=34)	χ^2/t	P
Gender	Male	42	8	34	-	-
	Female	0	0	0		
Age(Year)		72.12±15.12	50.10±8.52	5.125	0.012	
Occupation	Farmer	4	1	3	0.782	0.941
	Worker	6	1	5		
	Cadre	20	3	17		
	Merchant	9	2	7		
	Others	3	1	2		
Clinical picture	Fatigue	20	2	18	2.027	0.155
	Anorexia	21	4	17	0.000	1.000
	Jaundice	12	5	7	5.574	0.018
	Itchy skin	1	1	0	2.856	0.152
	Abdominal pain	8	2	6	0.227	0.634
	Bloating	22	5	17	0.406	0.524
	Liver palm	6	2	4	0.926	0.336
	Hematemesis	6	2	4	0.926	0.336
	Puffiness	7	2	5	0.494	0.482
	Spider nevus	4	1	3	0.102	0.749
	Black stool	9	3	6	1.516	0.218
	Ascites	25	7	18	3.210	0.719
Child-Pugh grade	Splenomegaly	24	7	17	3.719	0.054
	Fever	4	0	4	1.040	0.308
	A grade	8	0	8	7.275	0.026
	B grade	15	1	14		
	C grade	19	7	12		
Liver volume reduction		9	2	7	0.075	0.784
Complications	Upper gastrointestinal hemorrhage	11	6	5	12.179	0.000

	Hepatic encephalopathy	10	6	4	14.275	0.000
	Hepatorenal syndrome	0	0	0	-	-
	Infection	10	5	5	8.155	0.004
Concomitant disease	Fatty liver	7	2	5	0.494	0.482
	Diabetes	11	3	8	0.654	0.419
	Pancreatitis	3	0	3	0.760	0.383
	Gallstone	15	4	11	0.878	0.349
	Diffuse connective tissue disease	3	0	3	0.760	0.383
	Thyroid disease	4	0	4	1.040	0.308

表 6 Logistic 回归分析酒精性肝硬化预后影响因素(n=42)

Table 6 Logistic regression analysis of prognostic factors of alcoholic cirrhosis(n=42)

Factors	B	SE	Wald	P	OR	95%CI
Jaundice	0.759	0.443	1.589	0.210	1.598	0.730~4.125
Child-Pugh grade	0.435	0.195	5.854	0.020	1.625	1.115~2.789
Upper gastrointestinal hemorrhage	0.462	0.185	6.125	0.014	1.352	0.854~3.415
Hepatic encephalopathy	0.475	0.196	5.523	0.026	1.452	1.023~3.895
Infection	0.412	0.210	7.152	0.008	1.985	1.452~4.521

3 讨论

肝硬化是一种常见的慢性疾病,患者的肝脏合成能力会降低。酒精性肝硬化、乙肝后肝硬化患者逐渐增多,主要是因为乙型肝炎病毒、酒精性肝炎是导致患者出现肝硬化的主要原因^[15-17]。基于当地居民的饮酒习惯,酒精性肝硬化的发生率显著较高,因此本文分析了乙肝后肝硬化与酒精性肝硬化两种患者的临床表现及其预后影响因素,以为其鉴别、诊断、改善患者的预后提供依据。

本文结果表明,两组患者在性别、年龄、职业方面有统计学意义。表明酒精性肝硬化患者均为男性,其与乙肝后肝硬化在性别上有差异,可能与本地的女性饮酒者较少有关。两组的年龄对比无统计学意义,酒精性肝硬化发病年龄高发期在30~45岁,乙肝后肝硬化发病高发期在40~60岁,本研究发现酒精性肝硬化组中患者均超过30岁,其原因为:酒精性肝硬化发展为肝硬化是一个过程,因此该疾病的年龄均超过30岁^[18-20];乙肝后肝硬化疾病因为乙肝病毒感染,其可通过幼年感染或母婴传播,因此降低了基础年龄,但是随着疫苗的开展及相关知识的普及,乙肝后肝硬化会大大降低^[21,22]。两组疾病在职业中无差异,乙肝后肝硬化多在低收入人群或体力劳动者中,与职业特点相关。

本研究发现两组在黄疸、黑便、呕血、蜘蛛痣、脾脏增大有差异,患者出现黑便、呕血原因为门脉高压性胃病、食管胃底曲张静脉破裂出血、应激性溃疡出血,因此临幊上对于乙肝肝硬化患者需对上消化道出血进行积极预防^[23,24]。此外脾脏增大会出现血小板等降低,易诱发出血、感染,因此乙肝后肝硬化患者需定期检查血常规,观察脾功能的亢进情况,预防疾病出现。酒精性肝硬化患者的蜘蛛痣发生率较高,可能是由于就进行会影

响肝脏芳香化酶活性,增加雌激素^[25,26]。两组的黄疸发生率有统计学意义,可能是由于酒精性肝硬化患者会出现血清总胆红素增加、胆汁淤积的情况,而乙肝后肝硬化的代偿期肝功能检查仅会出现轻度酶学异常,总胆红素升高的必要条件是肝脏储备功能降低明显^[27,28]。

两组肝脏体积缩小对比有统计学意义,是因为乙肝病毒引起肝脏内细胞出现广泛变性、坏死,改建血液循环途径及结构,从造成肝脏变形、变硬,体积缩小^[29]。两组上消化道出血有统计学意义,乙肝后肝硬化组的消化道出血比例高与其黑便、呕血、脾脏增大比例高趋势相同;酒精性肝硬化组患者长期大量饮酒,血液中酒精浓度升高,氧供降低,在出现肝功能恶化的同时脑细胞也明显缺氧,出现昏迷,因此其肝性脑病发病率较高^[30]。

两组脂肪肝、糖尿病、胰腺炎、胆结石对比有统计学意义,可能上由于乙醇导致肝损害,会使得肝细胞变形,病理学改变为大泡性为主伴小泡性混合的肝脂肪细胞变性,因此其脂肪肝占比较高;此外长期饮酒会损伤内分泌器官,使得胰腺、内分泌出现紊乱,因此诱发糖尿病;其胰腺炎及胆结石占比较高可能与患者长期大量饮酒导致胰液蛋白沉淀阻塞胰管、引起营养障碍有关。

乙肝后肝硬化组的疾病进展发生率明显较酒精性肝硬化组高,表明乙肝后肝硬化患者的预后较酒精性肝硬化差,可能是由于乙肝肝硬化患者的肝功能受损更严重,而酒精性肝硬化患者预后与其是否饮酒明显相关,若患者长期戒酒,会明显改善其预后。

Logistic 回归分析结果表明,Child-Pugh 分级在 B、C 级、存在上消化道出血与肝性脑病是影响乙肝后肝硬化患者预后的危险因素 Child-Pugh 分级为 C 级、存在上消化道出血肝性脑病、感染是影响酒精性肝硬化患者预后的危险因素,主要是由

于临幊上多采用 Child-Pugh 分级评估肝硬化预后、肝功能储备及其手术风险,本研究发现,Child-Pugh 分级较高时,患者会出现消化道出血、黄疸、感染甚至肝性脑病等多种并发症,均增加了患者的肝硬化进展发生率,因此 Child-Pugh 高分级、存在上消化道出血、肝性脑病、感染是影响患者预后的危险因素。

总之,乙肝后肝硬化与酒精性肝硬化的差异主要体现在性别、职业、临床表现、并发症与合并疾病中,影响乙肝后肝硬化预后的危险因素为 Child-Pugh 分级在 B、C 级、存在上消化道出血与肝性脑病,影响酒精性肝硬化预后的危险因素为 Child-Pugh 分级为 C 级、存在上消化道出血肝性脑病、感染,需防治并发症,以改善患者预后。

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