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肺结核患者治愈后复发危险因素分析及耐药状况调查*

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摘要 目的:研究肺结核患者治愈后复发危险因素以及耐药状况。**方法:**回顾性分析我院于2015年5月~2017年12月期间收治的1000例肺结核患者的临床资料。对所有患者均进行为期2年的随访观察,统计复发情况。将所有患者按照治愈后复发与否分成复发组58例以及无复发组942例,比较两组患者基线资料情况,包括年龄、性别、耐药、吸烟、职业类型、居住情况以及空洞,并对影响肺结核患者治愈后复发的因素作多因素 Logistic 回归分析,对所有治愈后复发患者的耐药情况进行检验,分析其耐单药、耐2药、耐3药、耐4药人数的占比情况。**结果:**1000例肺结核患者治愈后复发58例,复发率为5.80%。肺结核患者治愈后是否复发与性别、年龄、吸烟无关($P>0.05$),复发组耐药、体力型工作、流动人口、空洞患者的比例高于未复发组($P<0.05$)。经多因素 Logistic 回归分析可得:耐药、体力型工作、流动人口、空洞均是肺结核患者治愈后复发的独立危险因素。58例患者中发生耐药例数27例,耐药率为46.55%;其中耐单药、耐2药、耐3药、耐4药人数分别为8、10、7、2例,相应占比为13.79%、17.24%、12.07%、3.45%。**结论:**肺结核患者治愈后复发的风险较高,尤其应注意耐药、体力型工作、流动人口、空洞的患者,以降低疾病复发,且肺结核复发患者的耐药情况不容乐观。

关键词:肺结核;复发;危险因素;耐药;多因素 Logistic 回归分析

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Risk Factors Analysis and Drug Resistance Status Investigation of Pulmonary Tuberculosis Patients after Cure*

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ABSTRACT Objective: To study the risk factors and drug resistance of pulmonary tuberculosis patients after cure. **Methods:** A retrospective analysis was performed on 1000 tuberculosis patients who were admitted to our hospital from May 2015 to December 2017. All patients were followed up for a period of 2 years, and the recurrence was counted. All the patients were divided into the relapse group 58 cases and the non-relapse group 942 cases according to whether they had relapsed or not after cure. The baseline data of the two groups were compared, mainly including age, gender, drug resistance, smoking, occupation type, residence status and void. The factors influencing the recurrence of pulmonary tuberculosis after cure were analyzed by multivariate Logistic regression analysis. The drug resistance of all patients with relapse after cure were tested, and the proportion of patients with single drug resistance, 2 drugs resistance, 3 drugs resistance and 4 drugs resistance were analyzed. **Results:** 58 cases recurrence after the cure of 1000 cases of tuberculosis, the recurrence rate was 5.80%. There was no correlation between relapse and gender, age and smoking ($P>0.05$). The proportion of drug resistance, physical work, floating population and cavity patients in relapse group were higher than those in non-relapse group ($P<0.05$). According to the multivariate logistic regression analysis, drug resistance, physical work, floating population and air pollution were the independent risk factors for relapse of pulmonary tuberculosis patients. Among the 58 patients, 27 were resistant, the resistant rate was 46.55%. Among them, 8, 10, 7 and 2 cases were resistant to single drug, 2, 3 and 4 respectively, accounting for 13.79%, 17.24%, 12.07% and 3.45% respectively. **Conclusion:** Tuberculosis patients have a higher risk of recurrence after cure, especially should pay attention to drug resistance, physical work, the floating population, cavity patients, in order to reduce the recurrence of disease. And the tuberculosis relapses patient's resistance condition is not optimistic.

Key words: Tuberculosis; Recurrence; Risk factors; Drug resistance status; Multivariate Logistic regression analysis

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前言

肺结核是一种可经由呼吸道传染的慢性疾病,主要是由结核分枝杆菌所致,在结核菌侵入人体后往往不会立即出现相关

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临床症状,而是在潜伏一段时间后,于患者机体免疫力下降时引发结核病^[1,2]。尽管首次涂阳肺结核患者具有较高的临床治愈率,然而因受多种因素的共同作用,复发率较高,且复治效果不佳,极易成为结核病重要的持续性传染源^[3,4]。由此可见,如何有效降低肺结核患者治愈后的复发率显得至关重要,而明确肺结核复发的相关影响因素在此过程中发挥着极其重要的作用,有助于临床医师制定相关干预措施,继而达到降低复发率的目的^[5,6]。另有研究报道表明^[7,8],结核杆菌具有较高的耐药性,可能使得患者对异烟肼、利福平、链霉素以及乙胺丁醇等药物产生耐药性,继而增加了临床治疗的难度,不利于患者预后,且迄今为止临床上尚无针对复发肺结核的统一治疗方案。鉴于此,本研究主要分析肺结核患者治愈后复发的危险因素以及耐药状况,旨在为临床防治提供参考依据,现作以下报道。

1 资料与方法

1.1 一般资料

回顾性分析我院于2015年5月~2017年12月期间收治的1000例肺结核患者的临床资料。其中男性患者556例,女性患者444例,年龄24~78岁,平均年龄(46.33±10.26)岁;耐药情况:有235例,无765例;吸烟573例,不吸烟427例;职业类型:体力型718例,非体力型282例;居住情况:常住人口798例,流动人口202例;空洞:有226例,无774例。纳入标准:(1)所有研究对象均经影像学检查确诊为肺结核;(2)均经临床治疗后痊愈;(3)年龄≥18周岁;(4)无临床病历资料缺失。排除标准:(1)合并其他肺部疾病者;(2)意识障碍或伴有精神疾病者;(3)研究过程中因各种原因退出者。纳入对象均在知情同意书上签字,并获批于医院伦理委员会。

1.2 研究方法

(1)基线资料调查:采用我院自制的患者基线资料调查问

卷表完成基线资料的统计、记录,主要内容有年龄、性别、耐药、吸烟、职业类型、居住情况以及空洞等。(2)痰结核菌培养与药物敏感试验:主要是参照中国结核病防治规划实施工作指南(2008年版)^[9]完成相关操作。分别对异烟肼、利福平、链霉素以及乙胺丁醇进行耐药性检验。

1.3 观察指标

分析1000例肺结核患者治愈后复发情况,比较复发组与未复发组的基线资料,采用多因素Logistic回归分析肺结核患者治愈后复发的危险因素,统计、记录肺结核患者治愈后复发的耐药情况。

1.4 评价标准

(1)肺结核治愈^[10]:连续2次及以上痰涂片检查结果均显示为阴性,且至少有1次在治疗末检查。(2)复发^[11]:肺结核治愈后2年时间内,痰涂片出现至少1次阳性或经影像学检查发现恶化。

1.5 统计学方法

数据的分析借助SPSS20.0软件完成,计数资料以[n(%)]表示,予以 χ^2 检验。肺结核患者治愈后复发与各项因素的关系予以多因素Logistic回归分析。 $P<0.05$ 表示差异具有显著性。

2 结果

2.1 肺结核复发情况

1000例肺结核患者治愈后均进行为期2年的随访,复发58例,复发率为5.80%。

2.2 两组患者基线资料对比

肺结核患者治愈后是否复发与性别、年龄、吸烟无关($P>0.05$),复发组耐药、体力型工作、流动人口、空洞患者的比例高于未复发组($P<0.05$),见表1。

表1 两组患者基线资料对比例(%)
Table 1 Comparison of baseline data between the two groups n(%)

Baseline data		Relapse group (n=58)	Non-relapse group (n=942)	χ^2	P
Gender	Male	34(58.62)	522(55.41)	0.228	0.633
	Female	24(41.38)	420(44.59)		
Age (years)	> 5	42(72.41)	610(64.76)	1.412	0.235
	≤5	16(27.59)	332(34.24)		
Drug resistance	Yes	27(46.55)	208(22.08)	18.199	0.000
	No	31(53.45)	734(77.92)		
Smoking	Yes	33(56.90)	540(57.32)	0.004	0.949
	No	25(43.10)	402(42.68)		
Professional types	Physical	51(87.93)	667(70.81)	7.913	0.005
	Non-physical	7(12.07)	275(29.19)		
Living situation	Permanent population	34(58.62)	764(81.10)	17.134	0.000
	Floating population	24(41.38)	178(18.90)		
Cavity	Yes	25(43.11)	201(21.34)	14.797	0.000
	No	33(56.89)	741(78.66)		

2.3 肺结核患者治愈后复发的多因素 Logistic 回归分析

以治愈后复发为因变量,赋值为复发=0,未复发=1。以耐药、职业类型、居住情况、空洞为自变量,赋值如下:耐药=0,无耐药=1;职业类型为体力型=0,非体力型=1;居住情况为流动

人口=0,常住人口=1;空洞有=0,无=1。经多因素 Logistic 回归分析可得:耐药、体力型工作、流动人口、空洞均是肺结核患者治愈后复发的独立危险因素($P<0.05$),见表2。

表2 肺结核患者治愈后复发的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis of pulmonary tuberculosis patients after cure recovery

Influence factors	β	Wald χ^2	P	OR	95%CI
Drug resistance	0.890	0.494	0.000	1.304	1.044~4.021
Physical work	0.601	0.346	0.024	1.482	1.149~2.874
Floating population	0.677	0.391	0.013	2.084	1.793~4.518
Cavity	0.821	0.452	0.000	1.873	1.425~6.023

2.4 58 例肺结核患者治愈后复发的耐药情况分析

耐单药、耐2药、耐3药、耐4药人数占比见表3。

58 例患者中发生耐药例数 27 例,耐药率为 46.55%;其中

表3 58 例肺结核患者治愈后复发的耐药情况分析

Table 3 Analysis of drug resistance in 58 patients with pulmonary tuberculosis after cure

Drug resistance situation	n	Accounting(%)
Single drug resistance	8	13.79
2 drugs resistance	10	17.24
2 drugs resistance	7	12.07
4 drugs resistance	2	3.45
Total	27	46.55

3 讨论

肺结核患者临床治愈后的复发现象是目前国内外临床防治肺结核的重点难题,亦是肺结核发病率高的主要原因之一^[12,13]。相关研究学者认为^[14],肺结核复发的主要原因有内源性、外源性再感染,内源性再感染主要是指正常生理状态下致病菌寄生在体内,在患者机体免疫力下降时引发疾病,外源性再感染主要是指宿主之外的病原菌所导致的感染。我国是全球范围内结核病高负担国家之一,肺结核发病率以及病死率位居各类传染病之首^[15-17]。且有相关调查数据表明,2001~2010 年,我国发现以及治疗的肺结核患者便突破 800 万的大关,其中复治肺结核的患者占比 16%,且有 25%左右的复治肺结核患者具有多药耐药风险^[18-20]。由此可见,我国在防治肺结核方面尚有较长的路要走。目前,国内外已有不少研究分析了肺结核复发的流行状况以及相关影响因素,然而,由于不同地区、不同人群的肺结核复发原因和相关因素存在一定程度的差异^[21-23],因此,为了掌握本地区肺结核复发情况和相关影响因素,本研究分析了本院近几年的肺结核患者基线资料,以期了解肺结核复发的危险因素。

本研究结果发现,1000 例肺结核患者治愈后共有 58 例复发,复发率为 5.80%。邓翔^[24]等人的研究报道显示,800 例肺结核患者复发率为 5.75%,这与本研究结果相近,但这与我国肺结核复发率水平相比略高,其中主要原因可能和本地区属于肺结核高发区域有关。此外,经多因素 Logistic 回归分析可得,耐

药、体力型工作、流动人口、空洞均是肺结核患者治愈后复发的独立危险因素。分析原因,从事体力型劳动患者往往劳动强度大,收入低,居住与饮食条件不佳,缺乏相关抗肺结核知识,因此复发率较高^[25]。流动人口有流动性强的特点,且往往为外出打工人员,其居住条件普遍较差、收入较低、劳动强度大,因此抵抗力相对较低,易引起内源性再感染,加之居住拥挤,增加了外源性再感染的风险。耐药则是临床公认的肺结核复发危险因素,随着耐药的发生,会导致肺结核患者临床治疗效果大打折扣,继而增加了复发风险。空洞会导致病灶出现广泛纤维化,在机体免疫力出现下降时,空洞病灶修复、吸收和恶化、进展相互交替,继而进展成为慢性纤维空洞型肺结核,导致肺结核的复发^[26-28]。另外,58 例患者中发生耐药例数 27 例,耐药率为 46.55%;其中耐单药、耐2药、耐3药、耐4药人数占比分别为 13.79%、17.24%、12.07%、3.45%。这提示在临床工作中应考虑合理调整抗结核药物的应用,从而提高治疗效果。相关研究报道表明^[29,30],一线抗结核药物的耐药频率较高,二线抗结核药物则普遍价格昂贵。因此,为了有效减轻缓和患者的经济负担,同时降低耐药性出现的风险,政府部门应考虑按照医生的建议,逐渐将更多抗结核药物纳入医保药物目录,从而保障患者的合理治疗,降低肺结核复发的几率。

综上所述,肺结核患者治愈后存在一定的复发风险,且从事体力型工作、流动人口以及发生耐药、空洞的肺结核患者具有较高的复发风险。此外,肺结核复发患者存在较高的耐药性,值得临床关注。

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