

肝癌患者经系统治疗后甲胎蛋白变化对预后的影响

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摘要 目的 探讨肝癌患者经系统治疗后甲胎蛋白(AFP)变化对患者预后的影响。方法 对 53 例肝癌患者于入院后和系统治疗后分别于不同时间点测定血清 AFP 值后,将入院时 AFP 值作为基线,以变化 50%作为标准分组,并进行无疾病进展生存时间(PFS)和总生存时间(OS)分析。结果 9 例患者血清 AFP 值下降超过 50%(A 组),28 例患者 AFP 值升高超过 50%(B 组),而 AFP 值变化小于 50%(C 组)的为 16 例。和 C 组相比,A 组患者 PFS 明显延长($P<0.05$),B 组 PFS 明显缩短($P<0.05$)。B 组 OS 短于 C 组($P<0.01$),而 A 组和 C 组间 OS 无明显差别($P>0.05$)。结论 肝癌系统治疗前后的 AFP 值变化可作为临床上预后判断的标志之一。

关键词 肝癌;系统治疗;甲胎蛋白;预后

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Prognostic Influence of Changes of Alpha-Fetoprotein in Patients receiving Systemic Therapy with Hepatocellular Carcinoma

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ABSTRACT Objective: To explore the prognostic influence of the changes of alpha-fetoprotein in patients receiving systemic therapy with hepatocellular carcinoma. **Methods:** Serum AFP was collected at baseline and at different time points after admission receiving systemic therapy in 53 patients with hepatocellular carcinoma. Patients were separated into different groups based on a 50% change in serum AFP from baseline. Overall survival (OS), progression-free survival (PFS) were compared between groups. **Results:** Nine patients experienced a >50% AFP decline(Group A), 28 patients had a >50%AFP increase(Group B), and 16 patients had a <50% change in serum AFP in either direction (Group C). Compared with Group C, Group A had a longer PFS time ($P<0.05$), whereas Group B had a shorter PFS time ($P<0.05$). Group B had a shorter OS time than Group C ($P<0.01$), whereas Group A was not associated with a significant difference in OS ($P>0.05$). **Conclusion:** Serum AFP change may serve as a useful marker for clinical outcome and prognostic influence in patients with hepatocellular carcinoma receiving systemic therapy.

Key words: Hepatocellular carcinoma; Systemic therapy; Alpha-fetoprotein; Prognosis

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肝癌^[1]是死亡率仅次于胃癌、食道癌的常见恶性肿瘤之一,初期症状并不明显,晚期主要表现为肝痛、乏力、消瘦、黄疸、腹水等症状,在我国诱因主要是感染乙丙型肝炎病毒和肝硬化^[2-4]。临床上一般采取手术、放化疗与中药结合疗法,但治愈率极低。而对进展期的肝癌,也只有系统治疗才有最低程度的有效^[5]。甲胎蛋白(alpha-fetoprotein, AFP)是一种糖蛋白^[6-10]。正常情况下,这种蛋白主要来自胚胎的肝细胞,胎儿出生约两周后甲胎蛋白从血液中消失,而 AFP 可以在大约 80%的肝癌患者血清中升高。本研究旨在探讨肝癌系统治疗后甲胎蛋白变化,以揭示其对预后的影响的意义。

1 对象与方法

1.1 研究对象

临床资料所有病例均为 2007 年 3 月~2010 年 12 月在我

院住院的肝癌患者,其中男 36 例,女 17 例。年龄 38~77 岁。根据 2001 年中国抗癌协会肝癌专业委员会制定的分期标准^[11]对患者进行分期,其中 I 期 14 例,IIa+IIb 期 39 例。分别于不同时间点测定血清 AFP 值后,将入院时 AFP 值作为基线,以变化 50%作为标准,分为 AFP 值降低超过 50%组(A 组),AFP 值升高超过 50%组(B 组)和 AFP 值变化 50%以内组(C 组)。

1.2 研究方法

于患者入院治疗前后分别于不同时间点测定血清 AFP 值后,将入院时 AFP 值作为基线,以变化 50%作为标准,分为 AFP 值降低超过 50%组(A 组),AFP 值升高超过 50%组(B 组)和 AFP 值变化 50%以内组(C 组)。分别统计并比较 3 组之间的无疾病进展生存时间(progression-free survival, PFS)和总生存时间(overall survival, OS),均自入院后第一天治疗开始计算。采用 SPSS17.0 统计软件进行统计分析,比较采用 log-rank 检验, $P<0.05$ 表示差异有统计学意义。

2 结果

9 例患者血清 AFP 值下降超过 50%(A 组),28 例患者

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AFP 值升高超过 50%(B 组),而 AFP 值变化小于 50%(C 组) B 组 PFS 明显缩短($P<0.05$)。B 组的 OS 明显短于 C 组($P<0.01$) ,而 A 组和 C 组间 OS 无明显差别($P>0.05$)(Table 1)。

表 1 不同组别的无疾病进展生存时间和总生存时间
Table 1 PFS and OS results in different groups

Group	Total cases	PFS	OS
		(median μ m)	(median μ m)
Group A	9	17.8	13.2
Group B	28	2.6	6.6
Group C	16	6.2	11.8

3 讨论

肝癌是死亡率仅次于胃癌、食道癌的常见恶性肿瘤之一，初期症状并不明显 晚期主要表现为肝痛、乏力、消瘦、黄疸、腹水等症状，在我国诱因主要是感染乙丙型肝炎病毒和肝硬化。临床上一般采取手术、放化疗与中药结合疗法 但治愈率极低。因此，对其治疗的预后评价就成为临床上工作的主要难点之一。AFP 是一种糖蛋白，主要在胎儿肝脏中合成，分子量 6.9 万。在胎儿 13 周 AFP 占血浆蛋白总量的 1/3。在妊娠 30 周达最高峰，以后逐渐下降，出生时血浆中浓度为高峰期的 1%左右 约 40mg/L 在周岁时接近成人水平(低于 30 μ mg/L)^[6-10]。正在成人 AFP 可以在大约 80%的肝癌患者血清中升高，被公认为是诊断原发性肝癌的特异性肿瘤标志物，具有确立诊断、早期诊断、鉴别诊断的作用。尽管 AFP 被发现已有超过半个世纪，但我们在临床上对它的认识还停留在作为血清中肿瘤标志物的地位。关于如何应用和解释该标志物的意义一直有较大争论。一些研究表明其对预后有很重要的价值^[10,12,13]。同样 AFP 还被证明其可用于监测外科切除手术和介入手术后的反应，术后几天内 AFP 的下降可以反映出个体对手术的良好反应^[14]。然后，有关 AFP 值作为标志对肝癌系统治疗的反应却很少提及。

我们的研究将 AFP 作为最有潜力预测肝癌经过系统治疗后预后效果的评价指标，其有以下特点：我们对 AFP 升高和降低对临床结果的影响均做分析。此外，我们发现 AFP 值的变化对系统治疗后 PFS 的影响明显超过 OS。在我们的实验中，血清 AFP 值下降超过 50%组患者的 PFS 明显超过 AFP 值变化小于 50%组，而 AFP 值升高超过 50%组 PFS 明显缩短。在 OS 的结果统计时发现，AFP 值升高超过 50%组的 OS 明显短于其他两组组，而 AFP 值下降超过 50%组和 AFP 值变化小于 50%组间无明显差别。Chan 等^[15]的新近研究将 20%作为血清中 AFP 变化的研究标准。他们发现经过治疗 AFP 下降超过 20%的患者其 OS 明显超过 AFP 变化小于 20%和升高者。因为肝癌患者合并肝硬化和肝炎会对 AFP 测定值的波动有较大影响，所以我们将相对较高的 50%作为标准以发现肝癌患者的真正变化，而最大程度的减少其他因素的影响，Vora 等^[16]的研究也支持这一点。

综上所述，我们的实验表明血清 AFP 变化可用来对肝癌患者接收系统治疗后的反应和临床预后结果做非常有效的评价。常规 AFP 检测对此类患者的病情发展和 OS 的监测很有价值。

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