

doi: 10.13241/j.cnki.pmb.2017.18.041

脾多肽注射液对原发性肝癌患者超声学改变及 AFP 水平的影响 *

徐兰英¹ 杨国春² 王艳丽¹ 黄 茜¹ 刘胜玉¹

(1 沈阳市第七人民医院电诊科 辽宁 沈阳 110003; 2 中国医科大学附属第一医院超声科 辽宁 沈阳 110010)

摘要 目的:探讨脾多肽注射液对原发性肝癌患者超声学改变及 AFP 水平的影响。**方法:**选取我院肿瘤科收治的原发性肝癌患者 168 例,随机分为对照组和研究组,每组 84 例。对照组患者予以经导管动脉化疗栓塞术(TACE)治疗,研究组在对照组基础上予以脾多肽注射液治疗。观察并比较两组患者治疗前后肿瘤血供情况、血清肿瘤标志物水平、外周血免疫细胞水平、临床疗效及不良反应发生率。**结果:**研究组治疗有效率高于对照组,差异具有统计学意义($P < 0.05$);与对照组比较,研究组治疗后肿瘤内动脉、肿瘤周边动脉血流分级水平较低,肿瘤周边门脉血流分级水平较高,治疗后血清 AFP、CA19-9、GGT、AFU 水平较低,治疗后外周血 NK 细胞、CD4⁺、CD4⁺/CD8⁺ 比值水平较高,CD8⁺T 淋巴细胞水平较低($P < 0.05$);研究组恶心呕吐、食欲不振、白细胞减少、发热、乏力疲劳等不良反应的发生率低于对照组($P < 0.05$)。**结论:**脾多肽注射液能够有效减少原发性肝癌患者肿瘤组织的血供,降低 AFP、CA19-9、GGT、AFU 水平,减轻免疫抑制,提高临床疗效,降低不良反应的发生率。

关键词:原发性肝癌;脾多肽注射液;彩超;AFP;疗效

中图分类号:R735.7 文献标识码:A 文章编号:1673-6273(2017)18-3574-05

Effects of Lial Polypeptide Injection on Ultrasound Changes and Serum Levels of AFP in Patients with Primary Liver Cancer*

XU Lan-ying¹, YANG Guo-chun², WANG Yan-li¹, HUANG Qian¹, LIU Sheng-yu¹

(1 Department of Electrical Diagnosis, the Seventh People's Hospital, Shenyang, Liaoning, 110003, China;

2 The First Affiliated Hospital of China Medical University, Shenyang, Liaoning, 110010, China)

ABSTRACT Objective: To investigate the influence of lial polypeptide injection on ultrasound and serum levels of AFP in patients with primary liver cancer. **Methods:** 168 patients with primary liver cancer who were treated in our hospital were selected and divided into the control group and the experiment group, with 84 cases in each group. The patients in the control group were treated with transcatheter arterial chemoembolization (TACE), while the patients in the experiment group were treated with lial polypeptide injection on the basis of the control group. Then the tumor blood supply, serum tumor marker levels, peripheral blood immune cell levels, the clinical effect and the incidence of adverse reactions in the two groups were observed and compared before and after the treatment. **Results:** The effective rate in the experiment group was higher than that of the control group, and the difference was statistically significant ($P < 0.05$); Compared with the control group, the blood flow classification levels of intra tumor artery and peripheral tumor artery were lower, blood flow classification level of tumor peripheral portal vein was higher, serum levels of AFP, CA19-9, GGT and AFU were lower, peripheral blood NK cell, CD4⁺T lymphocyte and CD4⁺/CD8⁺ ratio levels were higher, and CD8⁺T lymphocyte level was lower in the experiment group after treatment ($P < 0.05$); The incidence of adverse reactions including the nausea and vomiting, loss of appetite, leukopenia, fever and fatigue in the experiment group was lower than that of the control group ($P < 0.05$). **Conclusion:** Lial polypeptide injection can significantly reduce the blood supply of tumor tissue in patients with primary liver cancer, reduce the levels of AFP, CA19-9, GGT, AFU, reduce the inhibitory on immune functions, improve the clinical effect, and reduce the incidence of adverse reactions.

Key words: Primary liver cancer; Lial polypeptide injection; Color doppler; AFP; Clinical effect

Chinese Library Classification(CLC): R735.7 **Document code:** A

Article ID: 1673-6273(2017)18-3574-05

前言

原发性肝癌(PHC)是我国临床上常见的恶性肿瘤之一,病理分型主要包括肝细胞癌、肝内胆管癌以及混合型癌等^[1]。PHC 男性较女性多发,我国 PHC 患病率约为 29.9/10 万,病死率达

27.7/10 万,居于恶性肿瘤引起死亡的第三位^[2]。经导管动脉化疗栓塞术(TACE)成为目前临床上治疗 PHC 的主要方法^[3],但 TACE 治疗时使用化疗药物,不可避免的对正常细胞、组织等造成损伤,影响预后。脾多肽注射液是由健康小牛脾脏提取物制成的免疫调节剂,能够调节机体免疫机能,辅助化疗减少不

* 基金项目:辽宁省科技厅计划项目(2013226012)

作者简介:徐兰英(1977-),女,本科,主治医师,研究方向:超声诊断等

(收稿日期:2017-01-08 接受日期:2017-01-26)

良反应,在非小细胞肺癌、胰腺癌等恶性肿瘤化疗中取得较好疗效^[4,5]。本次主要探讨脾多肽注射液对 PHC 患者超声学改变及 AFP 水平的影响,现报告如下:

1 资料与方法

1.1 临床资料

选取自 2014 年 5 月到 2016 年 8 月来我院肿瘤科治疗的原发性肝癌患者 168 例作为研究对象,患者临床症状、体征及影像学检查结果均符合中华人民共和国卫生部制订的《原发性肝癌诊疗规范(2011 年版)》^[6]关于原发性肝癌的诊断标准,并经病理组织学或细胞学检查确诊,TNM 分期为 II-IV 期,患者存在可测量病灶;经我院伦理委员会审核通过,排除存在经导管动脉化疗栓塞术(TACE)禁忌症的患者,排除预计生存期<3 个月的患者,近期接受手术、局部治疗、放化疗或免疫治疗的患者除外,已经存在肝外远处转移的患者除外,恶性腹水、肝性脑病患者除外,排除门静脉完全性阻塞患者,合并严重心脑血管疾病患者除外,对脾多肽过敏的患者除外;患者本人或家属签订知情同意书。按随机数字表法分组,对照组 84 例予以 TACE 手术治疗,男性 55 例,女性 29 例,年龄 37~74 岁,平均年龄(56.73±7.25)岁;肿瘤分期:II 期 18 例,III 期 37 例,IV 期 29 例;研究组 84 例在对照组基础上给予脾多肽注射液治疗,男性 56 例,女性 28 例,年龄 35~72 岁,平均年龄(56.32±7.11)岁;肿瘤分期:II 期 19 例,III 期 38 例,IV 期 27 例。两组间性别、年龄、肿瘤分期等临床资料具有可比性($P>0.05$)。

1.2 治疗方法

对照组患者予以 TACE 手术治疗,采用 Seildinger 技术,对患者右股动脉进行穿刺,利用导丝放置 5F 肝动脉导管鞘及 5F 导管,对腹腔干动脉进行造影检查,观察肿瘤的解剖位置、体积、数目和肿瘤供血血管情况;采用同轴微导管技术造影确定供血血管后,向血管内灌注注射用丝裂霉素(日本 Kyowa Hakko Kirin Co.,Ltd.,注册证号:H20100695)16 mg+氟尿嘧啶注射液(哈药集团三精制药股份有限公司,国药准字 H23021689)1.0g+顺铂注射液(江苏豪森药业股份有限公司,国药准字 H20010743)80 mg,之后缓慢注入碘化油造成血管栓塞。对患者生命体征进行密切观察,无异常则常规结束手术。术后给予止痛、保肝、抑酸等药物对症处理。研究组在对照组基础上给予脾多肽注射液(吉林丰生制药有限公司,国药准字 H22026498)10 mL,溶于 500 mL 的 0.9%氯化钠注射液中,1 次/d,静脉滴注,连续用药两周。

1.3 观测指标

1.3.1 临床疗效评价 参照 RECIST《实体瘤治疗疗效评价标准》^[7]制定临床疗效判定标准:完全缓解(CR):肿瘤完全消失,

且 1 个月内未再发;部分缓解(PR):肿瘤组织的最大直径缩小 50%及以上;稳定(SD):肿瘤组织的最大直径缩小不足 50%或增大 25%以下;进展(PD):肿瘤组织的最大直径增加 25%以上,或有新发病灶出现。有效率=(CR+PR)例数/总例数×100%。

1.3.2 彩超观察肿瘤血供情况 采用飞利浦 IU22 彩色多普勒超声诊断仪(美国飞利浦股份有限公司),采用 2.5-5.0MHz 频率观察肿瘤内动脉血流、肿瘤周边动脉血流以及肿瘤周边门脉血流情况,并对血流情况进行分级:无血流为 0 级,可见少量动脉血流为 1 级,可见中量动脉血流为 2 级,可见大量动脉血流为 3 级;计算治疗前后各动脉血流分级的平均值并进行比较。

1.3.3 血清肿瘤标志物水平检测 治疗前后空腹采集 5 mL 肘静脉血,3000 r/min 离心分离血清后保存备用。采用美国贝克曼库尔特 UniCel DxI800 全自动化学发光免疫分析仪,通过化学发光法检测血清甲胎蛋白(AFP)、糖类抗原 19-9(CA19-9)水平;采用瑞士罗氏 Modular 全自动生化分析仪,检测血清 γ -谷氨酰转肽酶(GGT)、 α -L 岩藻糖苷酶(AFU)水平。

1.3.4 外周血免疫细胞水平检测 治疗前后空腹采集 5 mL 肘静脉血,置于含有抗凝剂的抗凝管中。采用 CytoFLEX 流式细胞仪(美国贝克曼库尔特有限公司产品)检测外周血 NK 细胞、CD4⁺、CD8⁺T 淋巴细胞水平,并计算 CD4⁺/CD8⁺ 比值。

1.3.5 不良反应发生率 检测患者血、尿、便常规进行,观察患者恶心呕吐、食欲不振、白细胞减少、发热、乏力疲劳等不良反应的发生情况,计算不良反应发生率。

1.4 统计学分析

采用 SPSS 17.0 软件包进行分析,符合正态性的计量资料采用均数±标准差表示,两组患者治疗前后肿瘤血供情况、血清肿瘤标志物水平、外周血免疫细胞水平对比予以配对样本 t 检验,两组间肿瘤血供情况、血清肿瘤标志物水平、外周血免疫细胞水平对比予以独立样本 t 检验,临床疗效及不良反应发生率采用百分率(%)表示,予以 R×C 卡方检验, $P<0.05$ 存在统计学意义。

2 结果

2.1 两组患者临床疗效对比

对照组治疗有效率为 46.43%(39/84),研究组治疗有效率为 61.91%(52/84),研究组明显高于对照组,具有统计学意义($P<0.05$)。见表 1。

2.2 两组患者治疗前后肿瘤血供对比

治疗前肝脏肿瘤组织内部及周边红、蓝血流包绕,可见较多分支血管,血供丰富(见图 1);治疗后肿瘤内部及肿瘤周边动脉血流信号减弱,肿瘤周边门脉血流信号增强(见图 2)。与

表 1 两组患者临床疗效对比

Table 1 Comparison of the clinical efficacy between the two groups (cases,%)

Groups	n	CR	PR	SD	PD	Total effective rate
Control group	84	5(5.95%)	34(40.48%)	26(30.95%)	19(22.62%)	46.43%
Study group	84	12(14.29%)	40(47.62%)	22(26.19%)	10(11.90%)	61.91%
χ^2	-	-	-	-	-	4.052
P	-	-	-	-	-	0.044

治疗前比较,对照组患者治疗后肿瘤内动脉、肿瘤周边动脉血流分级水平降低,肿瘤周边门脉血流分级水平增高,研究组患者治疗后肿瘤内动脉、肿瘤周边动脉血流分级水平明显降低,肿瘤周边门脉血流分级水平显著增高,研究组患者治疗后肿瘤内动脉、肿瘤周边动脉血流分级水平低于对照组,肿瘤周边门脉血流分级水平高于对照组($P<0.05$)。见表2。

表2 两组患者治疗前后肿瘤血供对比

Table 2 Comparison of intra arterial blood flow classification, peripheral arterial blood flow grade of tumor between the two groups ($\bar{x}\pm s$, N=84)

Groups		Intra - arterial blood flow classification	Peripheral arterial blood flow grade	Peripheral blood flow grade of tumor
Control group	Before treatment	2.76± 0.38	2.63± 0.34	1.53± 0.18
	After treatment	1.85± 0.25*	1.92± 0.27*	2.14± 0.24*
Study group	Before treatment	2.73± 0.36	2.61± 0.29	1.55± 0.19
	After treatment	1.32± 0.16**	1.46± 0.18**	2.81± 0.36**

Note: compared with before treatment, * $P<0.05$; compared with the control group after treatment, ** $P<0.05$.

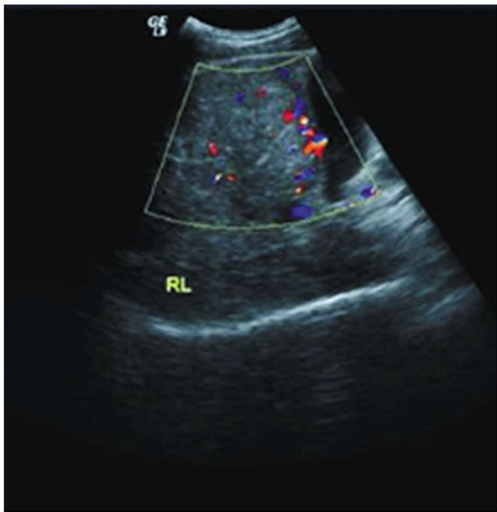


图1 治疗前肝脏肿瘤血供

Fig.1 Right liver multiple nodular liver cancer before treatment

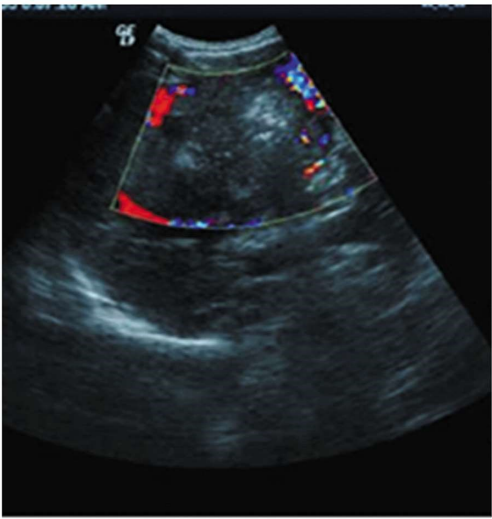


图2 治疗后肝脏肿瘤血供

Fig.2 Right liver multiple nodular liver cancer after treatment

2.3 两组患者治疗前后肿瘤标志物水平对比

与治疗前比较,对照组患者治疗后血清 AFP、CA19-9、GGT、AFU 水平均下降,研究组患者治疗后血清 AFP、CA19-9、GGT、AFU 水平均下降,研究组患者治疗后血清 AFP、CA19-9、

GGT、AFU 水平均明显下降,研究组患者治疗后血清 AFP、CA19-9、GGT、AFU 水平低于对照组($P<0.05$),见表3。

表3 两组患者治疗前后肿瘤标志物水平对比

Table 3 Comparison of serum levels of AFP, CA19-9, GGT and AFU between the two groups($\bar{x}\pm s$, N=84)

Groups		AFP($\mu\text{g/L}$)	CA19-9(ng/mL)	GGT(U/L)	AFU(U/L)
Control group	Before treatment	281.45± 27.46	54.32± 6.25	243.78± 21.24	57.97± 7.49
	After treatment	41.28± 4.82*	26.68± 3.24*	64.17± 7.73*	28.74± 3.29*
Study group	Before treatment	281.57± 27.15	54.58± 6.12	243.67± 41.84	57.23± 7.17
	After treatment	29.83± 2.43**	15.11± 1.96**	40.07± 5.16**	17.44± 2.23**

Note: compared with before treatment, * $P<0.05$; compared with the control group after treatment, ** $P<0.05$.

2.4 两组患者治疗前后外周血免疫细胞水平对比

与治疗前比较,对照组患者治疗后外周血 NK 细胞、CD4⁺、CD4⁺/CD8⁺ 比值水平明显降低,CD8⁺T 淋巴细胞水平显著升高,研究组患者治疗后外周血 NK 细胞、CD4⁺、CD4⁺/CD8⁺ 比值水平降低,CD8⁺T 淋巴细胞水平升高,研究组患者治疗后外周血 NK 细胞、CD4⁺、CD4⁺/CD8⁺ 比值水平高于对照组,CD8⁺T 淋

巴细胞水平低于对照组($P<0.05$),见表4。

2.5 两组患者不良反应发生率对比

研究组恶心呕吐、食欲不振、白细胞减少、发热、乏力疲劳等不良反应的发生率明显低于对照组,具有统计学意义 ($P<0.05$)。见表5。

3 讨论

表 4 两组患者治疗前后外周血免疫细胞水平对比

Table 4 Comparison of CD4⁺, CD8⁺ T lymphocytes and CD4⁺/CD8⁺ ratio in the peripheral blood between the two groups before and after treatment ($\bar{x} \pm s$, N = 84)

Groups		NK cell(%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Control group	Before treatment	20.05± 2.15	33.47± 3.21	27.73± 3.07	1.21± 0.16
	After treatment	13.25± 1.63*	25.17± 3.13*	35.47± 4.31*	0.71± 0.09*
Study group	Before treatment	20.11± 2.06	33.52± 3.19	27.69± 3.12	1.22± 0.15
	After treatment	17.11± 2.12*#	29.38± 3.08*#	30.22± 3.51*#	0.97± 0.13*#

Note: compared with before treatment, *P<0.05; compared with the control group after treatment, #P<0.05.

表 5 两组患者不良反应发生率对比

Table 5 Comparison of the incidence of adverse reactions between the two groups (cases,%)

Groups	n	Nausea and vomiting	Loss of appetite	Leukopenia	Fever	Fatigue fatigue
Control group	84	56(66.67%)	67(79.76%)	27(32.14%)	23(27.38%)	64(76.19%)
Study group	84	40(47.62%)*	53(63.09%)*	15(17.86%)*	11(13.10%)*	49(58.33%)*
χ^2	-	6.222	5.717	4.571	5.309	6.082
P	-	0.013	0.017	0.033	0.021	0.014

Note: compared with the control group, *P<0.05.

原发性恶性肿瘤(PHC)是病死率仅次于肺癌和胃癌的常见消化系统恶性肿瘤,具有恶性程度高、起病隐匿、进展快、易复发转移、预后差的特点^[8,9],给患者带来很大痛苦。PHC 的发生与乙肝、丙肝病毒感染、饮酒、感染黄曲霉素、糖尿病、寄生虫感染、肥胖等危险因素有关,发病机制尚未完全明确。对于无法进行手术治疗的 PHC 患者,通常采用化疗、放疗、生物治疗、TACE 等治疗手段,其中 TACE 最为常用且疗效较好,可是这些治疗手段特异性不高,治疗过程中产生的毒副作用较多,对免疫功能损害较大,已经成为限制其疗效的主要问题。本次研究在 TACE 治疗的基础上加用脾多肽注射液,脾多肽注射液为健康小牛脾脏提取物,主要含多肽、核糖、游离氨基酸等有效成分^[10-12],具有纠正免疫功能紊乱、抗肿瘤、提高造血功能、抑制氧自由基产生、保护细胞和脏器等作用,临床上联合化疗治疗大肠癌、晚期胃癌等消化系统恶性肿瘤,均发挥了提高疗效、减低毒副作用的作用^[13]。本研究结果显示,研究组患者治疗后肿瘤内动脉、肿瘤周边动脉血流分级水平低于对照组,肿瘤周边门脉血流分级水平高于对照组,治疗有效率明显高于对照组,表明脾多肽能够增强 TACE 对于肿瘤组织内外血液供应的阻断作用,改善门静脉循环,提高抗肿瘤效果。

肿瘤标志物是肿瘤相关的特异性物质,其水平与肿瘤的发生发展密切相关。AFP 是分化紊乱的细胞基因产物,为 PHC 高特异性、高灵敏度诊断指标之一^[14];CA19-9 属于一种肿瘤细胞相关糖抗原,为消化道肿瘤标志物;GGT 是质膜结合糖蛋白的一种,在多种组织中存在,PHC 发生时,肿瘤细胞释放 GGT,同时患者肝内阻塞,可以刺激肝细胞释放过多 GGT;AFU 是促进含岩藻糖苷酶的糖脂、糖蛋白等分解的一种水解酶^[15],PHC 患者肝细胞功能下降,无法正常降解 AFU,造成 AFU 水平上升;AFP、CA19-9、GGT、AFU 联合检测可以作为预测 PHC 患者预后的指标^[16,17]。本研究结果显示,研究组患者治疗后血清 AFP、CA19-9、GGT、AFU 水平低于对照组,表明脾多肽注射液能够降低 AFP 等肿瘤标志物水平,改善患者预后。

机体细胞免疫为主的免疫功能下降在恶性肿瘤的发生发展过程中起到重要作用^[14],TACE 手术、放疗等治疗能够进一步抑制免疫功能,对患者预后产生不良影响。NK 细胞属于非特异性免疫细胞,抗肿瘤作用广泛,可直接杀伤肿瘤细胞,发挥早期抗肿瘤效应;T 淋巴细胞则为特异性免疫细胞,主要分为 CD4⁺和 CD8⁺T 淋巴细胞两种亚群,CD4⁺T 淋巴细胞为辅助性 T 细胞,可释放多种细胞因子发挥抗肿瘤作用,CD8⁺T 淋巴细胞为细胞毒性 T 细胞,CD4⁺/CD8⁺ 比值则与细胞免疫状态稳定程度正相关。本研究结果显示,研究组患者治疗后外周血 NK 细胞、CD4⁺、CD4⁺/CD8⁺ 比值水平高于对照组,CD8⁺T 淋巴细胞水平低于对照组,提示脾多肽注射液能够减轻 TACE 治疗对机体免疫功能的损伤,提高抗肿瘤能力,这可能与脾多肽注射液激活和增强机体非特异性免疫功能的作用有关^[18-20]。不良反应研究结果显示,研究组恶心呕吐、食欲不振、白细胞减少、发热、乏力疲劳等不良反应的发生率明显低于对照组,表明脾多肽注射液能够有效降低不良反应发生率,提高治疗安全性。

综上所述,脾多肽注射液能够有效减少原发性肝癌患者肿瘤组织的血供,降低 AFP、CA19-9、GGT、AFU 水平,减轻 TACE 治疗对免疫功能的抑制作用,提高临床疗效,降低不良反应的发生率。

参考文献(References)

- [1] Lepage C, Capocaccia R, Hackl M, et al. Survival in patients with primary liver cancer, gallbladder and extrahepatic biliary tract cancer and pancreatic cancer in Europe 1999-2007: Results of EURO-CARE-5[J]. European Journal of Cancer, 2015, 51(51): 2169-2178
- [2] Bester L, Meteling B, Boshell D, et al. Transarterial chemoembolisation and radioembolisation for the treatment of primary liver cancer and secondary liver cancer: a review of the literature [J]. Journal of Medical Imaging and Radiation Oncology, 2014, 58(3): 341-352

- [3] Xue T C, Zhang L, Xie X Y, et al. Prognostic Significance of the Neutrophil-to-Lymphocyte Ratio in Primary Liver Cancer: A Meta-Analysis[J]. Plos One, 2014, 9(5): e96072
- [4] Chen Q, Cheng C, Hao C, et al. Effectiveness and Complications of Ultrasound Guided Fine Needle Aspiration for Primary Liver Cancer in a Chinese Population with Serum α -Fetoprotein Levels ≤ 200 ng/ml - A Study Based on 4,312 Patients [J]. Plos One, 2014, 9(8): e101536-e101536
- [5] McGlynn K A, Hagberg K, Jie C, et al. Statin Use and Risk of Primary Liver Cancer in the Clinical Practice Research Datalink [J]. JNCI: Journal of the National Cancer Institute, 2015, 107(4): 993-996
- [6] 中华人民共和国卫生部.原发性肝癌诊疗规范(2011年版)摘要[J].中华肝脏病杂志, 2012, 20(6): 419-426
Ministry of Health of the People's Republic of China. Diagnosis and treatment of primary liver cancer (2011 Edition)[J]. Chinese Journal of Hepatology, 2012, 20(6): 419-426
- [7] 杨学宁, 吴一龙. 实体瘤治疗疗效评价标准 -RECIST[J].循证医学, 2004, 4(2): 85-90, 111
Yang Xue-ning, Wu Yi-long. Criteria for Evaluation of Therapeutic Efficacy of Solid Tumors - RECIST [J]. Journal of Evidence-Based Medicine, 2004, 4(2): 85-90, 111
- [8] Hagberg K W, McGlynn K A, Sahasrabudhe V V, et al. Anti-diabetic medications and risk of primary liver cancer in persons with type II diabetes[J]. British Journal of Cancer, 2014, 111(9): 1710-1717
- [9] Chen B B, Murakami T, Shih T T, et al. Novel Imaging Diagnosis for Hepatocellular Carcinoma: Consensus from the 5th Asia-Pacific Primary Liver Cancer Expert Meeting (APPLE 2014) [J]. Liver Cancer, 2015, 4(4): 215-227
- [10] Chen B B, Murakami T, Shih T T, et al. Novel Imaging Diagnosis for Hepatocellular Carcinoma: Consensus from the 5th Asia-Pacific Primary Liver Cancer Expert Meeting (APPLE 2014) [J]. Liver Cancer, 2015, 4(4): 215-227
- [11] Jianyuan Meng, Jianhong Zhong, Hanguang Zhang, et al. Pre-, Peri-, and Postoperative Oral Administration of Branched-Chain Amino Acids for Primary Liver Cancer Patients for Hepatic Resection: A Systematic Review[J]. Nutrition & Cancer, 2014, 66(3): 517-522
- [12] Konfortion J, Coupland V H, Kocher H M, et al. Time and deprivation trends in incidence of primary liver cancer subtypes in England [J]. Journal of Evaluation in Clinical Practice, 2014, 20(4): 498-504
- [13] 韩鲁军, 张红欣, 许会军, 等. 奥沙利铂联合参芪扶正注射液对原发性肝癌患者 AFP 与 GP73 水平的影响及临床疗效[J]. 现代生物医学进展, 2016, 16(22): 4289-4291, 4366
Han Lu-jun, Zhang Hong-xin, Xu Hui-jun, et al. Effects of Oxaliplatin and Shenqi Fuzheng Injection on Serum Levels of AFP and GP73 in Patients with Primary Liver Cancer and its clinical Efficacy [J]. Progress in Modern Biomedicine, 2016, 16(22): 4289-4291, 4366
- [14] Yan W, Man L, Jiang L, et al. Clinical significance of increased expression of Nijmegen breakage syndrome gene (NBS1) in human primary liver cancer [J]. Hepatology International, 2014, 8 (2): 250-259
- [15] Liu Y, He Y, Li T, et al. Risk of primary liver cancer associated with gallstones and cholecystectomy: a meta-analysis[J]. Plos One, 2014, 9 (10): e109733-e109733
- [16] Huang L Y, Chang C C, Lee Y S, et al. Inhibition of Hec1 as a novel approach for treatment of primary liver cancer [J]. Cancer Chemotherapy and Pharmacology, 2014, 74(3): 511-520
- [17] Li Q Y, Zhao N M, Wang L C, et al. Individuals having variant genotypes of cytochrome P450 2C19 are at increased risk of developing primary liver cancer in Han populations, without infection with the hepatitis virus[J]. Tumor Biology, 2014, 35(9): 9023-9026
- [18] Michikawa T, Inoue M, Sawada N, et al. Plasma isoflavones and risk of primary liver cancer in Japanese women and men with hepatitis virus infection: A nested case-control study[J]. Cancer Epidemiology Biomarkers & Prevention, 2014, 24(3): 532-537
- [19] Huang G, Tang B, Tang K, et al. Isoquercitrin inhibits the progression of liver cancer in vivo and in vitro via the MAPK signalling pathway [J]. Oncology Reports, 2014, 31(5): 2377-84
- [20] Li D, Kang J, Madoff D C. Locally ablative therapies for primary and metastatic liver cancer [J]. Expert Review of Anti-infective Therapy, 2014, 14(8): 931-945

(上接第 3560 页)

- [25] Ghobadi H, Fouladi N, Beukaghazadeh K, et al. Association of High Sensitive CRP Level and COPD Assessment Test Scores with Clinically Important Predictive Outcomes in Stable COPD Patients[J]. Tanaffos, 2015, 14(1): 34-41
- [26] 李向欣, 赵鹏程. 老年慢性阻塞性肺疾病急性加重期血清降钙素原 \C-反应蛋白检测的临床意义[J]. 中国实验诊断学, 2014, 18(6): 909-911
Li Xiang-xin, Zhao Peng-cheng. The clinical implications of serum procalcitonin and high-sensitivity C-reactive protein in elderly acute exacerbations of chronic obstructive pulmonary disease [J]. Chinese Journal of Laboratory Diagnosis, 2014, 18(6): 909-911
- [27] Akpınar EE, Hoşgü n D, Doğanay B, et al. Should the cut-off value of D-dimer be elevated to exclude pulmonary embolism in acute exacerbation of COPD[J]. J Thorac Dis, 2013, 5(4): 430-434
- [28] Pfortmueller CA, Lindner G, Funk GC, et al. Role of D-Dimer testing in venous thromboembolism with concomitant renal insufficiency in critical care[J]. Intensive Care Med, 2017, 43(3): 470-471
- [29] Matsuo H, Nakajima Y, Ogawa T, et al. Evaluation of D-Dimer in Screening Deep Vein Thrombosis in Hospitalized Japanese Patients with Acute Medical Diseases/Episodes [J]. Ann Vasc Dis, 2016, 9(3): 193-200
- [30] Liu BH, Sun MX, Zhou N, et al. Detection and study of plasma D-dimer change in patients with acute exacerbation of chronic obstructive pulmonary disease[J]. J Biol Regul Homeost Agents, 2016, 30(3): 839-845