

doi: 10.13241/j.cnki.pmb.2014.33.034

肿瘤和非肿瘤患者合并肺栓塞的临床分析

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摘要 目的:探讨肿瘤和非肿瘤患者合并肺栓塞的临床特点及危险因素。**方法:**收集 2009 年 1 月至 2013 年 12 月我院收治的影像学确诊肺栓塞患者 78 例,按是否合并恶性肿瘤分为肿瘤组(n=42)和非肿瘤组(n=36),分析两组的临床特点、危险因素及实验室指标。**结果:**肺癌是最容易发生肺栓塞的恶性肿瘤,腺癌是最常见的病理类型。肿瘤组肺栓塞 50%发生在肿瘤确诊的 3 个月内,肿瘤组血清 D-Dimer 水平($3195.12 \pm 4835.28 \mu\text{g/L}$)高于非肿瘤组($1338.39 \pm 1320.16 \mu\text{g/L}$),两组间具有统计学差异($\chi^2=2.172, P=0.03$)。非肿瘤组中冠心病、慢性肺病、糖尿病及高脂血症和脑梗塞与肿瘤组有显著性差异($P<0.01$)。不明原因的呼吸困难 50 例(64.10%)是肺栓塞患者的主要症状,两组之间无明显差异;27 例(34.6%)患者合并下肢静脉血栓,右下肢静脉血栓高于左下肢,影像学肺栓塞的类型以右肺动脉主干及其分支受累多见共 39 例(50.0%),影像学表现在两组间无明显差异。**结论:**肿瘤组和非肿瘤组的临床症状无明显差异,一旦确诊采取积极的抗凝溶栓治疗可以取得很好的疗效。

关键词:恶性肿瘤;肺栓塞;D-二聚体

中图分类号:R563.5;R734 文献标识码:A 文章编号:1673-6273(2014)33-6527-05

Clinical Analysis of Tumor and Non-tumor Patients Complicated with Pulmonary Embolism

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ABSTRACT Objective: To analyze the differences of the clinical characteristics and risk factors between tumor and non-tumor complicated with pulmonary embolism. **Methods:** A retrospective analysis was conducted on 78 patients with pulmonary embolism who were treated in our hospital from January 2009 to December 2013 and were divided into tumor group (n=42) and non-tumor group (n=36) according to the pathological types of tumors. The relevant characteristics, the risk factors and the laboratory results were assessed and compared between two groups. **Results:** Lung cancer was prone to pulmonary embolism in malignant tumors and adenocarcinoma was the commonest pathological type. 50% of pulmonary embolism in patients with tumor occurred within 3 months after tumor was diagnosed. The level of serum D-dimer in tumor group was higher than that in non-tumor group ($3195.12 \pm 4835.28 \mu\text{g/L}$ vs $1338.39 \pm 1320.16 \mu\text{g/L}$), with a significant statistical difference ($\chi^2=2.172, p=0.03$). Coronary heart disease, chronic lung disease, diabetes, hyperlipemia and cerebral infarction were significantly different ($P<0.01$). Unexplained dyspnea (50/78, 64.10%) was the main symptom of pulmonary embolism without significant difference ($P>0.05$). 27 patients (34.6%) were detected the deep venous thrombosis of lower limb, and the right lower limb was more than the left. Right main pulmonary artery and its branches embolism were seen in 39 cases (50%) without significant difference ($P>0.05$). **Conclusion:** There is no obvious and significant difference existed in clinical symptoms between tumor and non-tumor patients complicated with pulmonary embolism. Using of anticoagulant and thrombolytic therapy can obtain good curative effect upon diagnosis.

Key words: Malignant tumor; Pulmonary embolism; D-dimer

Chinese Library Classification(CLC): R563.5; R734 **Document code:** A

Article ID: 1673-6273(2014)33-6527-05

前言

肺栓塞(pulmonary embolism, PE)是由各种内源性或外源

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(收稿日期:2014-06-16 接受日期:2014-07-10)

性栓子,如血栓、癌栓等阻塞肺动脉系统,引起肺循环障碍而导致的一种综合征,具有发病率、死亡率及漏诊率高的特点^[1,2]。它包括肺动脉血栓栓塞(pulmonary thromboembolism, PTE)、脂肪栓塞、羊水栓塞、空气栓塞、异物栓塞和肿瘤栓塞等,其中 PTE 最为常见^[3,4]。肺栓塞的临床表现主要为急性肺心病、肺梗死、不明原因的呼吸困难、慢性反复性肺血栓栓塞等^[5]。肺栓塞的危险因素有很多,年龄、性别、血栓性静脉炎、静脉曲张、心肺疾病、

手术、肿瘤、妊娠及肥胖等均可引起肺栓塞。据报道,肿瘤患者肺栓塞的发病率是正常人群的 3-4 倍^[6-8]。在我国肺栓塞患者中,因肿瘤而发生肺栓塞的占 35%,远高于国外的 6%。我们回顾性分析了 2009 年 1 月至 2013 年 12 月我院肺栓塞患者的临床资料,对其临床特征进行分析,结果如下:

1 材料与方法

1.1 一般资料

研究对象来自 2009 年 1 月 1 日至 2013 年 12 月 31 日本院收治的影像学确诊的肺栓塞患者 78 例,按是否合并恶性肿瘤分为肿瘤组和非肿瘤组。肿瘤组 42 例(男/女=23/19),非肿瘤组 36 例(男/女=18/18);肿瘤组中位年龄为 58 岁(范围:12 岁-84 岁),非肿瘤组中位年龄为 62 岁(范围:28 岁-84 岁),恶性肿瘤的具体类型见表 1。

表 1 肿瘤组原发肿瘤的类型

Table 1 Tumor types of patients with malignancies

Tumor location	Tumor types	n	Ratio(%)
Respiratory system	Squamous cell carcinoma of lung	2	4.8
	Adenocarcinoma of lung	14	33.3
	Small cell lung cancer	4	9.5
	Large cell lung cancer	1	2.4
	Pulmonary neuroendocrine tumor	1	2.4
	Total	22	52.4
Digestive system	Gastric cancer	2	4.8
	Peritoneal carcinoma	1	2.4
	Pancreatic cancer	1	2.4
	Total	4	9.5
Central nervous system	Meningioma	1	2.4
	Glioblastoma	1	2.4
	Total	2	4.8
Breast cancer	Breast cancer	3	7.1
Gynecological tumor	Ovarian cancer	2	7.1
	Endometrial carcinoma	1	4.8
	Total	3	2.4
Blood system tumors	Leukemia	5	11.9
	Lymphoma	3	7.1
	Total	8	19.0

1.2 诊断标准

所有的恶性肿瘤患者均经过组织病理学或细胞学检查证实。PE 的诊断标准如下:①患者存在肺栓塞的危险因素;②存在呼吸困难、胸痛及咯血等临床症状和相关体征;③心电图、X 线胸片、动脉血气分析等基本检查提示肺栓塞;④螺旋 CT、肺动脉造影或核素肺 V/Q 显像等任一项检查阳性可确诊^[9,10]。

1.3 研究方法

收集 78 例患者的临床资料,包括:患者年龄及性别、是否吸烟、基础疾病(高血压、冠心病、慢阻肺、糖尿病、脑梗塞、高脂血症)、肿瘤类型、肺栓塞距离肿瘤确诊的时间,是否合并四肢静脉血栓及血栓类型,患者血红蛋白(hemoglobin, Hb)和血小板计数(blood platelet count, PLT)、动脉血氧分压(PaO₂)和动脉血二氧化碳分压(PaCO₂),血浆 D-二聚体(D-Dimer)和 B 型钠酸酐(BNP)水平及影像学表现;肺栓塞的临床表现及治疗转归等进行分析。

1.4 统计学方法

采用 SPSS13.0 统计软件进行分析。计量资料应用均数 ± 标准差($\bar{x} \pm s$)表示,统计方法采用 t 检验;计数资料表示为

(%),采用 χ^2 检验进行单因素结果分析,结果 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 肿瘤组原发肿瘤的分布

42 例患者中肺癌 22 例(52.4%),其次是血液系统肿瘤 9 例(19.0%)、消化系统肿瘤 4 例(9.5%)、乳腺和妇科肿瘤各 3 例(7.1%)。3 例患者肺栓塞发生在肿瘤确诊前,7 例与原发性肿瘤同时确诊,32 例发生在肿瘤确诊后:其中 11 例在肿瘤确诊后 3 个月发生,5 例发生在 3~6 月,3 例发生在 6~12 个月,13 例发生在 12 个月以后,中位肺栓塞发生时间是在确诊后 6 个月。42 例肿瘤患者中 36 例为 IV 期患者,30 例患者在放疗过程中诊断肺栓塞。

2.2 两组患者的风险因素

两组患者的年龄、性别、是否吸烟、是否合并高血压均无显著性差异,但两组中是否合并冠心病、慢性肺病、糖尿病及高脂血症和脑梗塞有显著性差异($P < 0.01$),见表 2。

表 2 两组患者肺栓塞的风险因素

Table 2 Risk factors of PE patients in the two groups

Items	Tumor	Non-tumor	t/ χ^2	P
Age	57.97± 2.32	62.36± 2.45	1.295	0.199
Sex	23	18	0.176	0.820
Smoking	11	9	0.067	1.000
Hypertension	11	16	2.26	0.160
Coronary heart disease	6	15	7.38	0.010
COPD	4	16	12.398	0.001
Hyperlipemia and cerebral infarction	3	14	11.462	0.001
Diabetes mellitus	5	10	9.002	0.004

2.3 两组肺栓塞患者的主要症状

者以晕厥起病(5.12%),无症状者(12.82%),临床症状在两组之

间无显著性差异($P>0.05$),见表 3。

两组患者中原因不明的呼吸困难共 50 例(64.10%),胸痛 19 例(24.35%),具有典型的三联征的仅有 4 例(5.12%),4 例患

表 3 两组患者肺栓塞的临床表现

Table 3 Clinical symptoms of patients with PE in two groups

Items	Tumor	Non-tumor	χ^2	P
Dyspnea	28	22	0.26	0.643
Chest pain	7	7	0.412	0.657
Syncope	1	3	1.412	0.88
No symptom	6	4	0.175	0.745

2.4 两组患者实验室指标的差异

瘤组,具有统计学差异($P=0.03$),而其它指标包括 Hb、PLT、

分别对两组患者的 Hb、PLT、D-Dimer、BNP、PaO₂ 和 PaCO₂ BNP、PaO₂ 和 PaCO₂ 在两组间无显著性差异($P>0.05$),见表 4。

指标进行比较,结果显示肿瘤组的 D-Dimer 水平显著高于非肿

表 4 两组患者实验室指标的比较

Table 4 Comparison of laboratory markers of patients with PE in two groups

Items	Tumor	Non-tumor	χ^2	P
Hb(g/L)	118.75± 23.59	128.37± 25.09	-1.72	0.090
PLT(10 ⁹ /L)	226.97± 125.86	223.17± 85.5	0.152	0.88
D-Dimer(ug/L)	3195.12± 4835.28	1338.39± 1320.16	2.172	0.030
BNP(pg/mL)	2401.75± 3310.31	3666.57± 7421.05	-4.3	0.471
PaO ₂ (mmHg)	64.15± 17.74	56.96± 13.47	1.719	0.09
PaCO ₂ (mmHg)	34.20± 6.41	37.98± 8.56	-1.84	0.070

2.5 影像学检查

本研究中 78 例肺栓塞患者均进行了血管超声的检查,结果显示 27 例(34.6%)患者存在四肢静脉血栓,其中左下肢 8 例,右下肢 13 例,双下肢 5 例,左锁骨上静脉血栓 1 例;78 例患者中 76 例进行了肺血管造影检查,2 例肿瘤患者进行了核素肺 V/Q 显像。中央型肺栓塞是指肺段以上的肺血管栓塞,周围型肺栓塞是指段以下的肺血管栓塞。结果 42 例(53.85%)中央型肺栓塞,36 例(46.15%)周围性肺栓塞;两组相比没有统计学差异。此外右肺动脉主干及其分支栓塞 39 例(50.0%),左肺动脉主干及其分支栓塞 10 例(12.8%),双侧均累及的 29 例(37.2%)。

2.6 不同治疗与转归

本组 68 例非大面积肺栓塞患者(血压正常和右室运动正

常)给予低分子肝素钙、华法林抗凝治疗,其中 1 例行下腔静脉滤网植入术,术后给予抗凝治疗;10 例大面积肺栓塞患者中 9 例行尿激酶溶栓治疗,其中 4 例在肺动脉造影下进行;5 例行静脉尿激酶溶栓治疗。本组患者死亡 9 例(11.5%),其中 1 例症状出现后未行治疗而猝死;3 例溶栓后再栓塞致死亡,5 例合并全身衰竭,导致感染而死亡。9 例患者溶栓治疗过程中 2 例(22.2%)出血,无大出血发生。

3 讨论

目前,临床对于 PTE 误诊和漏诊的情况较为严重,肺栓塞发病率和死亡率逐年增加,这引起国内外学者的重视^[11,12]。本研究发现,年龄、性别、吸烟史及是否伴有高血压在两组间无显著性差异,而是否患有冠心病、高血脂症、慢性阻塞性肺疾病及糖

尿病在两组间具有显著性差异,尤其是合并慢性肺部 COPD 的患者是非肿瘤患者罹患肺栓塞的主要基础疾病。肺栓塞的主要临床表现在肿瘤组和非肿瘤组间无显著性差异。结合本研究,具有典型的肺栓塞三联征(呼吸困难,胸痛和咯血)表现的患者仅有 4 例(5.12%),以晕厥起病 4 例(5.12%),均为大面积肺栓塞,无明显诱因的呼吸困难 50 例(64.10%)。因此,对不明原因的呼吸困难的患者要高度警惕肺栓塞的发生。在临床实践中,对于存在发生肺栓塞的危险因素、尤其是同时存在数种容易发生肺栓塞危险的患者,应积极作好预防工作,根据病情积极行溶栓或抗凝治疗改善患者预后^[21]。

恶性肿瘤使机体血液处于高凝状态,易引起肺栓塞的发生。癌症晚期、静脉血栓、多周期化疗和放疗均为恶性肿瘤患者继发肺栓塞的危险因素。肺癌和血液系统肿瘤是引起肺栓塞的主要因素,而静脉血栓很可能是隐匿性恶性肿瘤的一个首发症状^[13,14]。本组有 50% 的患者肺栓塞发生在肿瘤确诊前或确诊后 3 个月内。Geerts^[15]等报道全身化疗可以使患者发生血栓的风险增加,考虑可能为化学药物、手术等直接损伤患者的血管内皮细胞,导致内外源性凝血途径的激活。本组肿瘤患者 36 例(85.7%)为 IV 期患者,30 例患者在放化疗过程中诊断肺栓塞。我们分析原因认为,晚期肿瘤患者在对症治疗过程中使用的细胞因子类药物,如 EPO、G-CSF 及 TPO 等可导致患者出现高凝状态,导致肺栓塞发生率增高^[16,17]。Bajaj N^[18]报道伴有肺栓塞的患者深静脉血栓的发生率为 29%。本组 78 例 PE 患者中,恶性肿瘤组的比例高达 53.85%,高于 Bajia 的报道的 27%,考虑与我院收治的病例数 60% 左右为恶性肿瘤有关。

按照肺栓塞指南 D-Dimer 水平低于 500 $\mu\text{g/L}$ 是肺栓塞的排除标准^[19]。本组共 11 例患者的血浆 D-Dimer 水平低于 500 $\mu\text{g/L}$,其中 4 例有肺栓塞病史,6 例有下肢静脉血栓,经低分子肝素和或华法林抗凝治疗均为非大面积肺栓塞,预后较好。肿瘤组患者的 D-Dimer 水平高于非肿瘤组,考虑 D-Dimer 是纤维蛋白的降解产物,除了血栓外也与肿瘤分泌的一些因子及抗凝治疗等多种因素相关。尽管 D-Dimer 水平低于 500 $\mu\text{g/L}$ 的患者预后较好,但亦应引起医生的关注^[20]。BNP 可以体现心功能的水平,由于肺栓塞会引起右室系统的改变,BNP 水平的增高也会间接提示肺栓塞的可能性^[21]。

本研究中,27 例患者(34.6%)合并四肢静脉血栓,以右下肢血栓多见。对于合并下肢静脉血栓的患者要认识到发生肺栓塞的可能性,应给予积极的重视。影像学检查提示,肺栓塞的类型以右肺动脉主干或分支栓塞为主,考虑与右肺血管走行有关。肺栓塞患者接受抗凝和溶栓治疗后,仅有 3 例发生治疗相关性死亡,其余患者均得到治愈或缓解。

综上所述,肿瘤患者合并肺栓塞的机率较高,且容易漏诊。因此,临床实践中应采取有效的预防措施,早期诊断并及时治疗以减少肺栓塞的发病率。

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