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·临床研究·

肿瘤患者导管相关性血栓的会诊与治疗体会

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摘　要

背景与目的：经外周穿刺中心静脉导管（PICC）为需要长时间输注化疗药物的肿瘤患者提供了一条安全的静脉治疗通道，然而，随着PICC在临床上的普及，血栓、感染、静脉炎、导管脱落、移位等相关并发症也越来越多，尤其是PICC导管相关性血栓（CRT），严重干扰肿瘤相关科室的诊疗活动，同时影响患者的预后。本研究通过回顾性分析肿瘤患者CRT的会诊意见及处理结果，探讨肿瘤患者CRT的处理策略。

方法：回顾性分析2014年4月23日—2020年1月10日由海南省人民医院血管外科会诊的92例放疗科CRT患者的临床资料。所有患者均由彩超检查明确诊断，其中无症状74例（80.4%），感染症状9例（9.8%），血栓症状9例（9.8%）。会诊的主要问题包括：拔管时机及能否续用；是否进行抗栓治疗；是否需要制动等。

结果：48例（52.2%）建议直接拔除导管（无症状者43例、感染症状者3例、血栓症状者2例）；30例（32.6%）建议继续使用导管（无症状者23例、感染症状者3例、血栓症状者4例）；14例（15.2%）建议延迟拔管并暂停使用导管（无症状者8例、感染症状者3例、血栓症状者3例）。32例（34.8%）建议行抗凝和（或）抗血小板等的抗栓治疗（无症状者20例、感染症状者4例、血栓症状者8例），另外60例（62.5%）未建议受抗栓治疗。共4例（4.3%）建议行患肢制动（感染症状者1例，血栓症状者3例），余88例（95.7%）未建议患肢制动或会诊中未提及。所有92例患者遵照会诊意见处理，无症状性或致死性肺栓塞发生，无血栓新发或加重事件等发生。在74例无症状患者中分析显示，是否行抗栓治疗以及患肢是否制动均对该类患者肺栓塞的发生无明显影响（均χ^2=0，P>0.05）。

结论：无症状CRT患者可直接拔管或继续使用导管，并适当活动患肢，抗栓治疗无明显临床获益。合并感染患者应个体化处理，感染较重者，可适当抗凝、制动；感染较轻，不推荐抗凝，并可适当活动患肢。症状性CRT患者建议按上肢深静脉血栓的诊疗规范及相关指南行规律抗凝及制动等处理。

关键词　血栓形成；导管插入术，外周；血栓溶解疗法；肺栓塞

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Experience in consultation and treatment of cancer patients with catheter-related thrombosis

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Abstract

Background and Aims: The peripherally inserted central catheter (PICC) provides a safe therapeutic venous access for cancer patients requiring long-term infusions of chemotherapeutic agents. However, with the widespread use of PICC in clinical practice, the PICC-related complications such as thrombosis, infections, phlebitis, and catheter disconnection or displacement have substantially increased, especially the catheters related thrombosis (CRT) in PICC, which seriously interferes the patient management activities of the cancer care departments, and also affects the prognosis of patients. Therefore, this study was performed to investigate the treatment strategies for CRT in cancer patients through a retrospective analysis of the consultation opinions for these patients and their treatment results.

Methods: The clinical data of 92 cancer patients with CRT who were consulted by the physicians in the Department of Vascular Surgery of Hainan Provincial People's Hospital from April 23, 2014 to January 10, 2020 were retrospectively analyzed. All patients were definitively diagnosed by color ultrasound examination. Of the patients, 74 cases (80.4%) were asymptomatic, 9 cases (9.8%) had infection symptoms, and 9 cases (9.8%) had symptoms of thrombosis. The consultation questions mainly included that the timing of extubation or feasibility of maintaining intubation, requirement of antithrombotic therapy, and necessity of immobilization.

Results: Direct extubation was recommended in 48 patients (52.2%, 43 cases without symptoms, 3 cases with infection symptoms and 2 cases with symptoms of thrombosis); continuous intubation was advised in 30 cases (32.6%, 23 cases without symptoms, 3 cases with infection symptoms and 4 cases with symptoms of thrombosis); delayed extubation and discontinuation of PICC were suggested in 14 patients (15.2%, 8 cases without symptoms, 3 cases with infection symptoms and 3 cases with symptoms of thrombosis); antithrombotic therapy with anticoagulation and (or) antiplatelet medications were considered in 32 case (34.8%, 20 cases without symptoms, 4 cases with infection symptoms and 8 cases with symptoms of thrombosis), and the other 60 cases（62.5%）were not prescribed antithrombotic therapy; 4 cases were found requiring immobilization of the affected limb (4.3%, 1 case with infection symptoms and 3 cases with symptoms of thrombosis), and the remaining 88 cases (95.7%) were not requested for immobilization or immobilization for them was not mentioned during the specialist consultation. All the 92 patients underwent treatment following the consultation opinions, and no symptomatic or fatal pulmonary embolism, and events of newly developed thrombosis or thrombosis aggravation occurred. Analysis among the 74 asymptomatic patients showed that whether performing antithrombotic therapy or immobilization exerted no significant influences on the occurrence of pulmonary embolism in this type of patients (both χ^2=0, P>0.05).

Conclusion: For asymptomatic CRT patients, direct extubation or continuous intubation can be considered, proper movement of the affected limb is recommended, and antithrombotic therapy yield no obvious clinical benefit. For those combined with infection, treatment should be individualized, appropriate anticoagulation and immobilization are feasible for the severe cases, while anticoagulation is not recommended but proper movement of the affected limb is helpful for the mild cases. For symptomatic CRT patients, the standard antithrombotic treatment and immobilization according to the management protocol and relevant guidelines for the upper extremity deep venous thrombosis are recommended.

Key words　Thrombosis; Catheterization, Peripheral; Thrombolytic Therapy; Pulmonary Embolism

CLC number: R654.3

经外周穿刺中心静脉导管（peripherally inserted central catheter，PICC）指的是将1条能经放射显影的导管由外周静脉（贵要静脉、肘正中静脉、头静脉、肱静脉等）穿刺，沿静脉送入，使其末端送达上腔静脉（superior vena cava，SVC）下1/3或SVC与右心房连接处。相比其他静脉留置导管，PICC的留置时间更长[1]，血液系统感染率低[2]，极少出现出血及气胸等并发症，能降低药物对外周血管的刺激，目前PICC已广泛应用于临床，是目前肿瘤患者化疗的主要静脉通道[3]。然而，随着PICC的广泛应用，相关并发症也逐渐增多[4-6]，如导管相关血流感染、静脉炎、导管脱出、异位等，特别是占上肢深静脉血栓70%的PICC导管相关性血栓（catheter-related thrombosis，CRT）[7]得到越来越多的关注和研究，有文献[8-9]报道，CRT的发生率为0.11~0.49/千插管日，还有报道[10-11]，CRT的发生率为1.6%~66.0%，严重干扰肿瘤相关科室的诊疗活动，同时影响患者的预后。本研究通过回顾性分析肿瘤患者PICC导管相关性血栓的会诊意见，拟探讨肿瘤患者PICC导管相关性血栓的处理策略，现将结果报告如下。

1 资料与方法

1.1 一般资料

本研究回顾性分析2014年4月23日—2020年1月10日，海南省人民医院血管外科会诊的92例放疗科PICC导管相关性血栓患者的病例资料，包括年龄、性别、置管手臂、置管静脉、血栓堵塞范围、受累静脉、临床症状等。导管均由美国巴德公司生产，其中男性73例，女性19例；年龄27~78岁，平均年龄（53.57±11.01）岁；PICC留置时间1~14个月，平均（4.64±2.31）个月；鼻咽癌75例，食管癌5例，子宫癌3例，肺癌2例，乳腺癌2例，下咽癌1例，口咽癌1例，舌癌1例，喉癌1例，肘肉瘤1例。92例患者中左上肢置管33例，右上肢置管59例；置管静脉包括贵要静脉88例，头静脉2例，肱静脉2例。血管堵塞包括：管腔闭塞40例，管腔狭窄19例，附壁血栓33例；共有59例血栓累及上肢深静脉（锁骨下静脉、腋静脉等），33例仅累及上肢浅静脉（贵要静脉、头静脉、肱静脉等）；按临床表现分为血栓症状者（整条患肢肿胀、皮温及张力升高）9例（9.78%）；非血栓症状者：无症状74例，感染症状（置管穿刺处周围红肿热痛、脓液）9例，共83例（90.22%）（表1）。

表1 92例CRT患者一般情况及临床特征

Table 1 General conditions and clinical characteristics of the 92 CRT patients

因素	数值
年龄（岁，$\bar{x}\pm s$）	53.57±11.01
性别[n(%)]	
男性	73(79.3)
女性	19(20.7)
PICC留置时间（月，$\bar{x}\pm s$）	4.64±2.31
置管手臂[n(%)]	
左上肢	33(35.8)
右上肢	59(64.1)
置管静脉[n(%)]	
贵要静脉	88(95.6)
头静脉	2(2.2)
肱静脉	2(2.2)
血栓堵塞情况[n(%)]	
闭塞	40(43.5)
狭窄	19(20.7)
附壁血栓	33(35.8)
受累静脉[n(%)]	
含深静脉	59(64.1)
仅浅静脉	33(35.9)
临床症状[n(%)]	
无症状	74(80.4)
感染	9(9.8)
血栓症状	9(9.8)

1.2 判断标准

彩色多普勒超声对于上肢静脉血栓的诊断，其灵敏度78%~100%，特异度为82%~100%[12-13]，通过血管多普勒超声诊断上肢深静脉血栓，标准为：血管腔内出现低回声伴血流信号消失，超声探头对血管加压后无改变。如果血栓发生在PICC导管走行静脉内被认为是导管相关性上肢深静脉血栓。

1.3 会诊及处理方案

所有92例患者均由彩超检查明确诊断，随后请血管外科会诊，会诊的主要问题包括：能否直接拔管、能否续用、指导抗栓、是否制动等。

1.4 统计学处理

计量资料以均数±标准差（$\bar{x}\pm s$）表示，计数资料以例数（百分率）[n（%）]表示，肺栓塞发生率的比较采用χ^2检验，P<0.05为差异有统计学意义。

2　结　果

2.1　会诊结果

48 例（52.2%）患者建议直接拔除导管，其中无症状者 43 例、感染症状者 3 例、血栓症状者 2 例；30 例（32.6%）建议继续使用导管，其中无症状者 23 例、感染症状者 3 例、血栓症状者 4 例；14 例（15.2%）建议延迟拔管并暂停使用导管，其中无症状者 8 例、感染症状者 3 例、血栓症状者 3 例；共计 32 例（34.8%）建议接受抗凝和（或）抗血小板等的抗栓治疗，其中无症状者 20 例、感染症状者 4 例、血栓症状者 8 例，另外 60 例（62.5%）未建议接受抗栓治疗；共 4 例（4.3%）建议患肢制动，包括感染症状者 1 例，血栓症状者 3 例，余 88 例（95.7%）未建议患肢未制动或会诊中未提及（表 2）。

表 2　CRT 患者会诊后处理方案 [*n*（%）]

Table 2　Treatment recommendations for the CRT patients after consultation [*n* (%)]

处理方案	例数（*n*）	无症状（*n*=74）	感染症状（*n*=9）	血栓症状（*n*=9）
导管去留				
直接拔管	48	43(58.1)	3(33.3)	2(22.2)
继续使用	30	23(31.1)	3(33.3)	4(44.4)
延期拔管	14	8(10.8)	3(33.3)	3(33.3)
抗栓治疗				
无	60	54(72.9)	5(55.6)	1(11.1)
利伐沙班	25	15(20.2)	3(33.3)	7(77.8)
低分子肝素	3	3(4.1)	0(0.0)	0(0.0)
华法林	1	1(1.4)	0(0.0)	0(0.0)
阿司匹林	1	1(1.4)	0(0.0)	0(0.0)
低分子肝素+利伐沙班	1	0(0.0)	0(0.0)	1(11.1)
利伐沙班+阿司匹林	1	0(0.0)	1(11.1)	0(0.0)
患肢活动				
制动	4	0(0.0)	1(11.1)	3(33.3)
活动	41	40(54.1)	1(11.1)	0(0.0)
未提及	47	34(45.9)	7(77.8)	6(66.7)

2.2　处理结果

所有 92 例患者遵照我科会诊意见处理，均得到妥善处理，无症状性或致死性肺栓塞发生，无血栓新发或加重事件等发生。在 74 例无症状患者中分析，结果显示，是否行抗栓治疗以及患肢是否制动均与肺栓塞发生无关（均 χ^2=0，P>0.05）。

3　讨　论

PICC 给临床上需要长期留置导管进行输液，特别是肿瘤化疗患者带来了巨大的福音，然而，随着 PICC 在临床的普及，其相关并发症也不可避免地暴露出来，而在 PICC 导管相关并发症中，CRT 是最常见也是最严重的并发症之一。CRT 是指 PICC 置管后，由穿刺或导管刺激血管壁导致的血管内膜损伤以及患者自身状态等多种因素作用使导管所在的血管内壁及导管附壁形成血凝块。据文献[14-16]报道，CRT 的发生率在 5%~20% 不等。

静脉壁损伤、血液流速缓慢和血液凝固性增加是造成静脉血栓形成的 3 大要素。PICC 导管的穿刺和留置均可造成对血管壁的损伤，从而引起局部血管内膜反应性炎症；其次，导管在血管内的留置在一定程度上减缓了血流速度；与此同时，由患者自身疾病（如肿瘤）而造成的血液黏稠度改变，都有利于血栓的形成，因此，PICC 带管患者易受到并发症 CRT 的困扰。大量研究[17-22]表明影响 CRT 形成的危险因素有：患者年龄、性别、体质量指数（body mass index，BMI）、D- 二聚体水平、所患疾病（如恶性肿瘤、糖尿病、血栓史及中心静脉导管置管史）等，此外，化疗药物种类[23]、长期卧床、营养不良[20, 24]及导管的材质类型[25-26]等也会增加 CRT 形成的风险。

现阶段，很多学者围绕着 CRT 患者的临床特征、影响因素及风险评估模型的构建、并发症预

防等方面进行了研究[27-30]，但是对于血栓形成后如何处理的研究并不多见。

目前对于血栓后导管能否续用，是否拔除，什么时候拔除导管尚无统一的意见。本研究92例患者置管均超过2周，由血管外科会诊拔管后无症状性或致死性肺栓塞发生，笔者认为：(1) 通过对74例无症状CRT患者的分析，认为此类患者如置管超过2周，可直接拔管或续用导管；(2) CRT合并感染者主要症状为置管口周围的皮肤潮红、发热、触痛、脓性分泌物等，对于此类患者，如果化疗结束，建议尽早拔管，去除感染灶；轻症感染者如感染能够控制，也可续用，但续用期间如感染不能控制，甚至出现全身感染症状，建议尽早拔管；(3) 症状性CRT是在彩超证实血栓的基础上伴有患肢肿胀、皮温高、张力高、深静脉系统局部压痛等。由于深静脉血栓在急性期及没有经过系统抗凝等治疗之前，血栓有脱落而致肺栓塞的可能，故对于症状性CRT，不推荐直接拔管及续用导管，建议延迟拔管并暂停使用，规律抗凝治疗2周后，再酌情拔管或续用。

随着医疗水平的不断提高，深静脉血栓形成的治疗越来越多样化[31-33]，使用抗血小板药物如阿司匹林、氯吡格雷可能有获益[5]，但依然缺乏大量数据的支持。抗凝虽为基本治疗[34]，但目前国内外指南[35-36]中并未推荐中心静脉置管的肿瘤患者常规进行预防性抗凝治疗，故本研究中所有患者均未预防性抗凝。发现血栓后，25例（78.1%，25/32）使用新型口服抗凝药，包括带管抗栓、拔管后抗栓。所有92例患者均未出现新发血栓症状及原有血栓症状加重的现象。笔者认为：(1) 对于无症状CRT患者，不推荐抗凝等抗栓治疗，并推荐拔管后适当活动患肢，促进静脉回流，避免血栓事件；(2) CRT合并感染患者建议个体化处理，感染较重者，为避免感染扩散，宜适当制动，并适当抗凝，视感染控制情况，一般2周左右。感染较轻，不推荐抗凝，可适当活动患肢；(3) 症状性CRT患者建议按上肢深静脉血栓的诊疗及相关指南[34, 37]行规律抗凝及制动等处理。

本研究CRT患者其血栓堵塞情况包括管腔闭塞40例，管腔狭窄19例，附壁血栓33例；而血栓累及范围有59例累及上肢深静脉，33例仅累及上肢浅静脉，上肢深静脉常有两支，且吻合支丰富，代偿能力强，笔者认为虽然血栓导致血管堵塞程度、受累静脉不同，暂建议仍以是否出现患肢肿胀、疼痛等血栓性症状为主要参考意见，进行相对应的处理。

综上，无症状CRT，可以直接拔管或继续使用导管，并适当活动患肢，抗栓治疗无明显临床获益。但本研究病例数较少，未能进行分组分析。对于血栓堵塞情况、受累静脉不同如何影响诊疗方案需进一步开展研究分析，以期更好地为CRT患者提供临床诊疗帮助。

利益冲突：所有作者均声明不存在利益冲突。

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