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血栓弹力图指导食管癌患者临床输血的价值及其与常规凝血实验检测指标的相关性分析*

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摘要 目的:探讨血栓弹力图(TEG)指导食管癌患者临床输血的价值及其与常规凝血实验检测指标的相关性。**方法:**选取2017年1月-2019年3月在我院收治的食管癌手术治疗需输血的99例患者作为研究对象,将99例患者随机分为常规凝血功能检测组和TEG组,常规凝血功能检测组采用常规凝血实验检查结果指导输血,TEG组采用TEG检查结果指导输血,对比两组输血前后的常规凝血实验检测指标以及临床输血量,对比TEG组输血前后的TEG指标,分析TEG指标与常规凝血实验检测指标的相关性。**结果:**两组患者输血前凝血四项和血小板计数(PLT)差异无统计学意义($P>0.05$),输血后两组活化凝血酶时间(APTT)、凝血酶原时间(PT)、凝血酶时间(TT)、纤维蛋白原(FIB)均有不同程度的改善($P<0.05$),TEG组PT、TT较常规凝血功能检测组低($P<0.05$);输血后,TEG组患者凝血反应时间(R值)、血凝块形成时间(K值)较输血前降低,最大血凝块强度(MA值)、凝血综合指数(CI值)升高,凝血形成速率(Angle角)增大,差异有统计学意义($P<0.05$);Pearson相关性分析结果显示,R值与APTT呈正相关($P<0.05$),K值与PLT呈负相关,与FIB呈正相关($P<0.05$),Angle角、MA值、CI值与FIB、PLT呈正相关($P<0.05$);TEG组新鲜冰冻血浆、冷沉淀输注量少于常规凝血功能检测组,差异有统计学意义($P<0.05$)。**结论:**TEG能更好地指导食管癌手术患者各种血液成分的合理输注,有效改善凝血异常情况,减少输血用量,TEG指标与常规凝血实验检测指标存在一定的相关性。

关键词:血栓弹力图;常规凝血功能检测;食管癌;临床输血

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The Value of Thromboelastography in Guiding the Clinical Blood Transfusion of Esophageal Cancer Patients and the Correlation between Thromboelastography and Routine Blood Coagulation Test*

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ABSTRACT Objective: To explore the value of thromboelastography (TEG) in guiding clinical blood transfusion in patients with esophageal cancer and its correlation with routine blood coagulation test. **Methods:** 99 patients who needed blood transfusion for surgical treatment of esophageal cancer who were admitted to our hospital from January 2017 to March 2019 were selected as subjects. 99 patients were randomly divided into the conventional coagulation function test group and the TEG group. The conventional coagulation function test group used the results of conventional coagulation tests to guide blood transfusion, and the TEG group used the results of TEG tests to guide blood transfusion. The conventional coagulation test indicators and clinical blood volume before and after blood transfusion in the two groups were compared. TEG indexes before and after blood transfusion in TEG group were compared. The correlation between TEG and routine coagulation test was analyzed. **Results:** There was no significant difference in coagulation four and platelet counts (PLT) between the two groups ($P>0.05$). After blood infusion, the thrombin time (APTT), prothrombin time (PT), and thrombin time (TT), Fibrinogen (FIB) were improved in different degrees ($P<0.05$). The PT and TT in the TEG group were lower than those in the conventional coagulation function test group ($P<0.05$). After blood transfusion, the coagulation reaction time (R value) and blood clot formation time (K value) in TEG group were lower than those before blood transfusion, the maximum clot intensity (MA value) and the comprehensive clotting index (CI value) were increased, the coagulation formation rate (Angle) were increased, and the differences were statistically significant ($P<0.05$). Pearson correlation analysis showed that R value was positively correlated with APTT ($P<0.05$). K value was negatively correlated with PLT, and positively correlated with FIB ($P<0.05$), while Angle, MA value and CI value were positively correlated with FIB and PLT ($P<0.05$). The amount of fresh frozen plasma and cryoprecipitate infusion in the TEG group was less than that in the conventional coagulation test group, and the differences were statistically significant ($P<0.05$). **Conclusions:** TEG can bet-

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ter guide the reasonable transfusion of various blood components in patients with esophageal cancer surgery, it can effectively improve the abnormal situation of blood coagulation, reduce the amount of blood transfusion. There is a certain correlation between TEG and conventional coagulation test indicators.

Key words: Thromboelastography; Routine blood coagulation test; Esophageal cancer; Clinical blood transfusion

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前言

食管癌是常见的消化道恶性肿瘤,具有较高的发病率和死亡率。美国研究显示,从 1973 年到 2010 年,美国食管癌的发病率以 7.5 倍速率显著增长^[1],在我国,食管癌的发病率、死亡率位居各类肿瘤第 5 位、第 4 位^[2]。在恶性肿瘤疾病发展的各个时期因凝血功能障碍影响凝血、炎症、血栓形成、病程进展,增加治疗难度,增加患者的死亡风险。手术切除仍是目前食管癌主要的治疗方法^[3]。对凝血情况进行快速准确评估,明确患者的失血量和输血量,临床输血合理,可使围手术期手术风险降低,减少血液资源浪费以及输血不良反应的发生,减少术后切口感染率和延迟愈合率。临床上,评估恶性肿瘤患者凝血功能状态和指导制定输血方案的常用手段是常规凝血功能检测,但越来越多的研究证实常规凝血功能检测在临床的应用上具有一定的单一性和局限性^[4],其检测通常只能反映凝血机制中的某些阶段或组成成分,而不能完整、真实地反映出患者体内凝血状况,不能准确地预测凝血病和弥散性血管内凝血的发生发展。近年来,血栓弹力图(Thrombelastogram, TEG)检测逐渐发展起来,体外模拟血液样本在人体内凝血状态的全局图像,动态监测从凝血到纤溶的全局效应,同时提供凝血、纤溶属性、动态相关的资料,可以更直观、更全面、更精准并及时地检测患者凝血功能状态及分析凝血功能异常^[5,6]。TEG 在创伤复苏、监测患者高凝状态、外科及循环系统手术中监测围术期凝血功能、冠脉支架术后抗血小板聚集、指导临床成分输血、指导个体化抗血小板治疗方面均体现出了其技术优势^[7-9]。本研究探讨 TEG 指导食管癌凝血异常患者临床输血的价值,分析常规凝血实验检测指标与 TEG 指标的相关性,为 TEG 应用于食管癌围手术期的有效性、安全性提供参考依据。

1 资料与方法

1.1 临床对象

选取 2017 年 1 月-2019 年 3 月在我院收治的 99 例食管癌手术治疗需输血的患者作为研究对象,术后经病理学检查明确诊断为食管癌。纳入标准:(1)术前未行放疗、化疗或其他抗癌治疗者;(2)患者临床资料完整者;(3)所有患者知情且签署同意书;(4)预计中位生存时间 ≥ 6 个月。排除标准:(1)既往有严重胸膜炎或胸廓畸形病史导致手术难度明显增大的患者;(2)二次复发病例;(3)2 周内接受过抗凝治疗者。本研究已获我院伦理委员会批准进行。将 99 例患者随机分为常规凝血功能检测组和 TEG 组,常规凝血功能检测组 50 例,其中男 32 例,女 18 例,年龄 27-66 岁,平均年龄(48.25 $\pm$ 4.53)岁,TEG 组 49 例,其中男 33 例,女 16 例,年龄 28-68 岁,平均年龄(50.14 $\pm$ 5.44)岁。两组一般资料比较无差异($P>0.05$)。

1.2 检测方法及观察指标

两组输血前、后均空腹抽取静脉血液行常规凝血检测,TEG 组输血前、后空腹抽取静脉血液行 TEG 检查。凝血功能检测:应用日本希森美康 CA1500 全自动血凝仪检测活化凝血酶时间(Activated partial thromboplastin time, APTT)、纤维蛋白原(Fibrinogen, FIB)、凝血酶原时间(Prothrombin time, PT)、凝血酶时间(Thrombin time, TT)等凝血四项检测。迈瑞 BC-2600 血细胞分析仪检测血小板计数(Platelet, PLT)。TEG 检查:应用美国唯美 Haemonetics TEG[®] 5000 血栓弹力图仪检测凝血反应时间(R 值)、最大血凝块强度(MA 值)、凝血形成速率(Angle 角)、血凝块形成时间(K 值)、计算凝血综合指数(CI 值)。

1.3 输血治疗

常规凝血检测组根据患者临床症状、常规凝血检测及 PLT 指导输血。TEG 组根据患者临床症状、TEG 结果指导输血。血液制品输注指征按《临床输血技术规范》要求进行。常规凝血功能检测组 PT、FIB、APTT 低于正常值时输注新鲜冰冻血浆, FIB<1.5 g/L 时输注冷沉淀; PLT<50 $\times 10^9$ /L 时输注机采血小板; TEG 组患者出血且 K 值>3 min, Angle 角<53 $^\circ$ 补充冷沉淀, R 值>10 min 输注新鲜冰冻血浆, MA 值<50 mm 输注血小板。

1.4 统计学方法

数据应用 SPSS20.0 统计软件分析。计量资料符合正态分布,以($\bar{x}\pm s$)表示,应用 t 检验,计数资料应用 χ^2 检验,数据的相关性分析采用 Pearson 相关性分析,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 输血前后凝血四项和 PLT 比较

输血前两组凝血四项和 PLT 比较无差异($P>0.05$),输血后两组 APTT、PT、TT、FIB 均有不同程度的改善($P<0.05$),TEG 组 PT、TT 较常规凝血功能检测组低($P<0.05$),输血后两组 PLT 比较无差异($P>0.05$)。见表 1。

2.2 TEG 组输血前、后 TEG 指标比较

输血后,TEG 组患者 R 值、K 值较输血前降低,MA 值、CI 值较输血前升高,Angle 角较输血前增大,差异有统计学意义($P<0.05$)。见表 2。

2.3 TEG 指标与常规凝血实验检测指标的相关性

Pearson 相关性分析结果显示, R 值与 APTT 呈正相关($P<0.05$), K 值与 PLT 呈负相关, 与 FIB 呈正相关($P<0.05$), Angle 角、MA 值、CI 值与 FIB、PLT 呈正相关($P<0.05$)。见表 3。

2.4 两组临床用血量

TEG 组新鲜冰冻血浆、冷沉淀输注量少于常规凝血功能检测组($P<0.05$),而两组血小板输注量比较无差异($P>0.05$)。见表 4。

表 1 输血前后凝血四项和 PLT 比较($\bar{x} \pm s$)Table 1 Comparison of four items of coagulation and PLT before and after blood transfusion($\bar{x} \pm s$)

Groups	Time	PT(s)	APTT(s)	TT(s)	FIB(g/L)	PLT($\times 10^9/L$)
Conventional coagulation function test group (n=50)	Before blood infusion	17.83 $\pm$ 4.15	41.24 $\pm$ 8.59	26.13 $\pm$ 4.63	1.37 $\pm$ 0.51	110.36 $\pm$ 67.25
	After blood infusion	14.12 $\pm$ 3.76 [#]	35.17 $\pm$ 7.35 [#]	22.03 $\pm$ 4.24 [#]	2.52 $\pm$ 0.78 [#]	119.35 $\pm$ 58.18
TEG group(n=49)	Before blood infusion	18.02 $\pm$ 4.77	40.85 $\pm$ 8.13	25.93 $\pm$ 5.26	1.39 $\pm$ 0.46	112.37 $\pm$ 64.86
	After blood infusion	11.21 $\pm$ 3.16 ^{**}	33.83 $\pm$ 7.17 [#]	19.26 $\pm$ 4.19 ^{**}	2.76 $\pm$ 0.85 [#]	117.33 $\pm$ 62.93

Note: compared with before blood infusion, [#] $P<0.05$; compared with conventional coagulation function test group, ^{*} $P<0.05$.

表 2 TEG 组输血前、后 TEG 指标比较(n=49, $\bar{x} \pm s$)Table 2 Comparison of TEG indexes before and after blood transfusion in TEG group(n=49, $\bar{x} \pm s$)

Time	R value(min)	K value(min)	MA value(mm)	Angle Angle(°)	CI value
Before blood infusion	7.23 $\pm$ 1.26	4.31 $\pm$ 0.86	46.23 $\pm$ 11.16	55.12 $\pm$ 10.86	-2.75 $\pm$ 0.77
After blood infusion	5.83 $\pm$ 0.84	3.15 $\pm$ 0.73	57.03 $\pm$ 10.64	64.85 $\pm$ 11.65	1.48 $\pm$ 0.47
t	6.472	7.198	4.903	4.276	30.024
P	0.000	0.000	0.000	0.000	0.000

表 3 TEG 指标与常规凝血实验检测指标的相关性

Table 3 Correlation between TEG index and conventional coagulation test index

Indexes	R value		K value		Angle		MA value		CI value	
	r	P	r	P	r	P	r	P	r	P
PT	0.245	0.072	-0.075	0.763	0.168	0.926	0.121	0.753	0.249	0.791
APTT	0.327	0.035	-0.158	0.694	0.073	0.686	0.135	0.146	-0.224	0.635
TT	-0.319	0.184	0.163	0.547	-0.035	0.653	-0.094	0.563	-0.158	0.073
FIB	0.273	0.096	0.183	0.026	0.327	0.028	0.336	0.014	0.234	0.021
PLT	-0.152	0.586	-0.386	0.002	0.472	0.000	0.461	0.000	0.347	0.016

表 4 两组临床用血量比较($\bar{x} \pm s$)Table 4 Comparison of clinical blood volume of two groups($\bar{x} \pm s$)

Groups	Fresh frozen plasma(ml)	Cryoprecipitate(u)	Platelet transfusion volume(u)
Conventional coagulation function test group(n=50)	164.23 $\pm$ 41.64	4.43 $\pm$ 1.23	5.43 $\pm$ 2.14
TEG group(n=49)	135.23 $\pm$ 38.17	3.17 $\pm$ 1.02	4.94 $\pm$ 1.93
t	3.610	5.542	1.196
P	0.000	0.000	0.235

3 讨论

研究证实^[10],恶性肿瘤细胞可分泌、释放一些组织因子、促凝物质及凝血活性物质,激活凝血系统,导致血小板活化,凝血活性增高,纤溶活性的改变等。手术损伤血管内皮细胞,激活人体的凝血系统,最终导致血细胞聚集、并释放促凝物质,凝血因子大量消耗,使机体凝血功能发生改变,成血液高凝状态^[11-13]。恶性肿瘤患者长时间的镇痛镇静、制动卧床、化疗、靶向治疗引

起的血管内皮受损等均可导致血液高凝及血栓形成^[14-16]。新辅助治疗期间和随后的围手术期静脉血栓栓塞很常见,20%的胰腺导管腺癌患者在术后 90 天内发生了 VTE^[17-19]。与健康成人相比,食管癌患者的凝血功能呈显著高凝状态,主要表现在各种内、外源性凝血因子的浓度增加、抗凝血酶含量的减少、FIB 和血小板功能相对增强、纤维蛋白功能亢进、纤溶相对抑制,患者存在血栓风险,患者的高凝状态促进肿瘤的转移和复发^[20]。

对于凝血功能异常的食管癌患者而言,纠正围术期失血及

其引起的凝血功能障碍,及时确定输血量与成分,及时指导成分输血,有助于控制其手术风险。TEG 是用来监测患者凝血功能及指导临床合理输血的重要工具^[21-23]。TEG 能对出血原因如凝血因子、血小板等引发进行准确快速判断,从而指导成分血输注种类、时间及剂量^[24,25]。应用 TEG 监测制定输血方案可以及时纠正凝血功能异常,减少输血量,减少由输血引起的相关并发症。本文研究中,输血后两组 APTT、PT、TT、FIB 均有不同程度的改善 ($P<0.05$),TEG 组 PT、TT 低于常规凝血功能检测组,TEG 组 R 值、K 值较输血前低,Angle 角、MA 值、CI 较输血前高,提示 TEG 不仅对凝血因子、FIB 的活性进行测定,还能够准确测定血小板的功能和纤维蛋白溶解情况,能在较短的时间内反映患者身体凝血功能异常,在评估食管癌患者异常凝血功能和指导临床输血方具有优势。输血后,TEG 组患者 R 值、K 值较输血前降低,MA 值、CI 值较输血前升高,Angle 角较输血前增大,TEG 能准确反映机体的凝血状态,有针对性的指导食管癌患者围术期输血,与徐秀凤等^[26]研究一致。

本研究结果显示,TEG 组 R 值与 APTT 呈正相关($P<0.05$),K 值与 PLT 呈负相关,与 FIB 呈正相关,MA 值、Angle 角、CI 值与 FIB、PLT 呈正相关($P<0.05$),更进一步证实 TEG 能对食管癌的发展进行动态监测,与常规凝血检测指标相关。Moore 等^[27]招募 100 例接受胰腺切除术的患者作为研究对象,术前 TEG 的使用有助于外科医师和麻醉师充分掌握患者凝血功能,并能指导临床治疗、给予针对性的凝血调节干预和判断预后。Wang 等^[28]研究结果显示,前列腺癌患者 TEG 预测出血和血栓形成的敏感性和特异性高于常规检测组。

本研究显示,TEG 组冷沉淀输注量、新鲜冰冻血浆较常规凝血功能检测组少,血小板输注量少于常规凝血功能检测组($P>0.05$),提示 TEG 可以明确检测出哪种血液成分活性降低导致的凝血功能降低,指导临床合理输注成分血与输血量,提高临床疗效,同时减少血液制品使用量,节约了医疗资源。常规凝血功能检测关注的是根据血小板数量决定血小板输注,TEG 检查更关注的是准确测定血小板功能来评估血小板输注,TEG 显示血小板功能正常时,可继续观察决定是否输注血小板制剂,减少血栓的风险,相应血液成分输注疗效更佳。在重症创伤患者中使用 TEG 指导的输血可以节省血液制品的利用率,并减少手术输血量^[29]。接受心脏手术的成年患者接受 TEG 指导的输血策略,血液输注的使用量显著降低,失血量和输血率明显减少,且未增加出血、再出血以及病死率^[30]。

综上所述,食管癌患者围术期多表现为高凝血状态,TEG 与常规凝血检测指标存在一定的相关,应用 TEG 制定输血方案,可显著降低食管癌患者围术期输血量。

参考文献(References)

- [1] Rosemurgy A, Wilfong C, Craig D, et al. The Evolving Landscape of Esophageal Cancer: A Four-Decade Analysis [J]. Am Surg, 2019, 85(9): 944-948
- [2] Arnold M, Soerjomataram I, Ferlay J, et al. Global incidence of oesophageal cancer by histological subtype in 2012[J]. Gut, 2015, 64(3): 381-387
- [3] Asombang AW, Chishinga N, Nkhoma A, et al. Systematic review and meta-analysis of esophageal cancer in Africa: Epidemiology, risk factors, management and outcomes [J]. World J Gastroenterol, 2019, 25(31): 4512-4533
- [4] Tur Martínez J, Petrone P, Axelrad A, et al. Comparison between thromboelastography and conventional coagulation test: Should we abandon conventional coagulation tests in polytrauma patients? [J]. Cir Esp, 2018, 96(7): 443-449
- [5] Pandey CK, Prakash K, Karna ST, et al. Detection of Coagulopathy in Chronic Renal Disease using Thromboelastography and its comparison with Conventional Tests [J]. J Assoc Physicians India, 2019, 67(4): 34-37
- [6] 禹梅, 李娜, 寇长元, 等. 血栓弹力图评估胃癌患者围手术期凝血状态的应用研究[J]. 现代生物医学进展, 2017, 17(14): 2721-2724
- [7] Li Y, Chang H, Ni L, et al. Analysis of thrombelastogram-guide medication in patients with coronary heart disease after percutaneous coronary intervention[J]. Exp Ther Med, 2019, 17(4): 3047-3052
- [8] Connelly CR, Van PY, Hart KD, et al. Thrombelastography-Based Dosing of Enoxaparin for Thromboprophylaxis in Trauma and Surgical Patients: A Randomized Clinical Trial [J]. JAMA Surg, 2016, 151(10): e162069
- [9] Schmidt AE, Israel AK, Refaai MA. The Utility of Thromboelastography to Guide Blood Product Transfusion [J]. Am J Clin Pathol, 2019, 152(4): 407-422
- [10] 辛士珍, 王燕. 恶性肿瘤与高凝状态[J]. 四川解剖学杂志, 2014, 22(3): 37-41
- [11] Guo JH, Xing GL, Fang XH, et al. Proteomic profiling of fetal esophageal epithelium, esophageal cancer, and tumor-adjacent esophageal epithelium and immunohistochemical characterization of a representative differential protein, PRX6[J]. World J Gastroenterol, 2017, 23(8): 1434-1442
- [12] Kitagawa YK, Takashi U, Oyama T, et al. Esophageal cancer practice guidelines 2017 edited by the Japan Esophageal Society: part 1 [J]. Esophagus, 2019, 16(1): 1-24
- [13] Deng HY, Lan XL, Zheng X, et al. The association between statin use and survival of esophageal cancer patients: A systematic review and meta-analysis[J]. Medicine (Baltimore), 2019, 98(29): e16480
- [14] Campello E, Ilich A, Simioni P, et al. The relationship between pancreatic cancer and hypercoagulability: a comprehensive review on epidemiological and biological issues [J]. Br J Cancer, 2019, 121(5): 359-371
- [15] Eric W, Tatiana A, Philip D, et al. The Tumor Microenvironment in Esophageal Cancer[J]. Oncogene, 2016, 35(41): 5337-5349
- [16] Liu WJ, Zhang YY, Chen M, et al. A genome-wide analysis of long noncoding RNA profile identifies differentially expressed lncRNAs associated with Esophageal cancer [J]. Cancer Med, 2018, 7(8): 4181-4189
- [17] Boone BA, Zenati MS, Rieser C, et al. Risk of Venous Thromboembolism for Patients with Pancreatic Ductal Adenocarcinoma Undergoing Preoperative Chemotherapy Followed by Surgical Resection[J]. Ann Surg Oncol, 2019, 26(5): 1503-1511
- [18] Sohda M, Kuwano H. Current Status and Future Prospects for Esophageal Cancer Treatment[J]. Ann Thorac Cardiovasc Surg, 2017, 23(1): 1-3
- [19] Zhang YJ, Zhang YX, Zhang L. Expression of cancer-testis antigens in esophageal cancer and their progress in immunotherapy [J]. J Cancer Res Clin Oncol, 2019, 145(2): 281-291

- [12] 李海军, 高晓嵘, 吴瑞, 等. 阿替普酶与巴曲酶治疗急性脑梗死的疗效比较及对患者血清 NSE、IL-6、TNF- α 、hs-CRP 水平的影响[J]. 现代生物医学进展, 2018, 18(7): 1330-1333
- [13] Cooke J, Maingard J, Chandra RV, et al. Acute middle cerebral artery stroke in a patient with a patent middle cerebral artery[J]. Neurol Clin Pract, 2019, 9(3): 250-255
- [14] Li Y, Zhong Z, Luo S, et al. Efficacy of Antihypertensive Therapy in the Acute Stage of Cerebral Infarction - A Prospective, Randomized Control Trial [J]. Acta Cardiol Sin, 2018, 34(6): 502-510
- [15] Ono H, Nishijima Y, Ohta S, et al. Hydrogen Gas Inhalation Treatment in Acute Cerebral Infarction: A Randomized Controlled Clinical Study on Safety and Neuroprotection [J]. J Stroke Cerebrovasc Dis, 2017, 26(11): 2587-2594
- [16] 孟佳雪, 贺帅, 谢惠芳, 等. 阿替普酶治疗急性脑梗死患者的出血不良反应影响因素分析 [J]. 中国临床药理学杂志, 2018, 34(14): 1595-1597
- [17] Kim JS, Kim YJ, Lee KB, et al. Low- versus Standard-Dose Intravenous Alteplase in the Context of Bridging Therapy for Acute Ischemic Stroke: A Korean ENCHANTED Study[J]. J Stroke, 2018, 20(1): 131-139
- [18] 王云, 刘定华, 吴伟. 阿替普酶治疗急性脑梗死的疗效[J]. 江苏医药, 2013, 39(16): 1923-1925
- [19] 秦文鹏, 朱慧芳. 阿替普酶静脉溶栓联合丁苯酞注射液治疗急性脑梗死的临床效果[J]. 河南医学研究, 2019, 28(6): 1056-1058
- [20] 熊文莉, 何晓英. 丁苯酞软胶囊联合长春西汀注射液治疗急性脑梗死的临床研究[J]. 中国临床药理学杂志, 2018, 34(23): 2686-2689
- [21] Niu H, Zhang Z, Wang H, et al. The impact of butylphthalide on the hypothalamus-pituitary-adrenal axis of patients suffering from cerebral infarction in the basal ganglia[J]. Electron Physician, 2016, 8(1): 1759-1763
- [22] Tang SC, Luo CJ, Zhang KH, et al. Effects of dl-3-n-butylphthalide on serum VEGF and bFGF levels in acute cerebral infarction [J]. Eur Rev Med Pharmacol Sci, 2017, 21(19): 4431-4436
- [23] 李克良, 耿直. 不同时间窗不同剂量阿替普酶治疗急性脑梗死的预后和安全性分析[J]. 现代仪器与医疗, 2018, 24(2): 24-27
- [24] 冯琮, 涂明义, 黄娟, 等. 丁苯酞联合阿替普酶治疗急性脑梗死的疗效观察[J]. 现代药物与临床, 2017, 32(10): 1876-1880
- [25] Helánová K, Patenica J, Jarkovský J, et al. S-100B protein elevation in patients with the acute coronary syndrome after resuscitation is a predictor of adverse neurological prognosis [J]. Vnitr Lek, 2012, 58(4): 266-272
- [26] Mao Y, Wang N, Yu F, et al. Simultaneous detection of carcinoembryonic antigen and neuron-specific enolase in human serum based on time-resolved chemiluminescence immunoassay [J]. Analyst, 2019, 144(16): 4813-4819
- [27] Schumacher H, Wenke NK, Kreye J, et al. IgA autoantibodies against native myelin basic protein in a patient with MS[J]. Neurol Neuroimmunol Neuroinflamm, 2019, 6(4): e569
- [28] 牛建平, 田红梅, 程鹤云, 等. 丁苯酞注射液联合阿替普酶治疗急性脑梗死的效果[J]. 河南医学研究, 2019, 28(7): 1241-1242
- [29] Wang Y, Bi Y, Xia Z, et al. Butylphthalide ameliorates experimental autoimmune encephalomyelitis by suppressing PGAM5-induced necroptosis and inflammation in microglia [J]. Biochem Biophys Res Commun, 2018, 497(1): 80-86
- [30] 刘阳, 马建斌. 低剂量与标准剂量阿替普酶治疗急性脑梗死的疗效比较[J]. 现代药物与临床, 2018, 33(11): 2822-2826

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- [20] 颜文龙, 卢兆桐, 王丽, 等. 食管癌患者血栓弹力图检测及临床意义[J]. 实用医学杂志, 2015, 31(4): 631-633
- [21] 梁春阳, 张强, 王斌, 等. 血栓弹力图和常规凝血试验在缺血性脑卒中凝血功能监测中的关联研究[J]. 中华神经医学杂志, 2018, 17(8): 790-795
- [22] Zhao SW, Wang YP, Xu LD, et al. The application of thromboelastogram in detection of indexes of antiplatelet therapy for coronary heart disease[J]. J Thorac Dis, 2016, 8(12): 3515-3520
- [23] Chandra K, Vandana S, Kumar G, et al. K time & maximum amplitude of thromboelastogram predict post-central venous cannulation bleeding in patients with cirrhosis: A pilot study[J]. Indian J Med Res, 2017, 145(1): 84-89
- [24] Kenneth N, Hiller. Clinically relevant exaggerated pharmacodynamic response to dual antiplatelet therapy detected by Thromboelastogram® Platelet Mapping™ [J]. J Anaesthesiol Clin Pharmacol, 2016, 32(1): 112-114
- [25] Lee KD, Wang TY, Lu CH, et al. The bidirectional association between oral cancer and esophageal cancer: A population-based study in Taiwan over a 28-year period [J]. Oncotarget, 2017, 8(27): 44567-4457
- [26] 徐秀凤, 柯靖兰, 吴越, 等. 血栓弹力图在肝癌患者术后临床输血中的应用价值[J]. 医疗装备, 2018, 31(17): 15-17
- [27] Moore HB, Paniccia A, Lawson PJ, et al. Utility of Viscoelastic Assays Beyond Coagulation: Can Preoperative Thrombelastography Indices Predict Tumor Histology, Nodal Disease, and Resectability in Patients Undergoing Pancreatectomy?[J]. J Am Coll Surg, 2018, 227(1): 55-62
- [28] Wang Z, Li J, Cao Q, et al. Comparison Between Thromboelastography and Conventional Coagulation Tests in Surgical Patients with Localized Prostate Cancer [J]. Clin Appl Thromb Hemost, 2018, 24(5): 755-763
- [29] Unruh M, Reyes J, Helmer SD, et al. An evaluation of blood product utilization rates with massive transfusion protocol: Before and after thromboelastography (TEG) use in trauma[J]. Am J Surg, 2019, 218(6): 1175-1180
- [30] Li C, Zhao Q, Yang K, et al. Thromboelastography or rotational thromboelastometry for bleeding management in adults undergoing cardiac surgery: a systematic review with meta-analysis and trial sequential analysis[J]. J Thorac Dis, 2019, 11(4): 1170-1181