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血栓弹力图评估胃癌患者围手术期凝血状态的应用研究

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摘要 目的:探讨血栓弹力图评估胃癌患者围手术期凝血状态的临床应用价值。**方法:**选择2013年8月至2016年8月在我院进行治疗的胃癌患者80例作为观察组,同时选择同期在我院治疗的胃部良性疾病患者80例作为对照组。采用TEG评估两组患者的凝血功能,并且与常规凝血检查比较,分析两种凝血评估方法的准确率。**结果:**I期胃癌患者的TEG各指标与对照组相比差异无统计学意义($P>0.05$),II期胃癌患者的R值、K值、MA值以及CI值与对照组比较差异显著,具有统计学意义($P<0.05$),III和IV胃癌患者的TEG各指标与对照组相比差异显著,具有统计学意义($P<0.05$);发生淋巴结转移的胃癌患者TEG各指标与对照组相比差异显著,具有统计学意义($P<0.05$),而没有发生淋巴结转移的患者与对照组相比差异无统计学意义($P>0.05$);进展期胃癌患者的TEG各指标与对照组比较差异显著,具有统计学意义($P<0.05$),而早期胃癌的TEG各指标与对照组差异不显著($P>0.05$);观察组患者治疗后,TEG检测血液发生低凝状态的检出率77.23%,常规检出率是46.15%;54例非出血患者中,TEG检出血液非凝状态的检出率为94.44%,常规检出率为77.78%。两种检测方法的检出率比较差异具有统计学意义($P<0.05$)。**结论:**胃癌患者的血液处于高凝状态,且高凝状态与病情发展的恶性程度呈正相关,TEG评估胃癌患者围术期的凝血状态较常规凝血检验更准确。

关键词:血栓弹力图;胃癌;凝血状态;准确率

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A Clinical Study on TEG for the Evaluation of Blood Coagulation State of Patients with Gastric Cancer during Perioperative Period

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ABSTRACT Objective: To explore the clinical value of thrombelastogram (TEG) for the evaluation of blood coagulation state of patients with gastric cancer during perioperative period. **Methods:** 80 gastric cancer patients were collected as study group in our hospital from January 2014 to January 2016, and 80 patients with benign gastric diseases for treatment in our hospital were enrolled as control group in the same period. The blood coagulation status of patients in two groups were evaluated with TEG, and the accuracy for assessment blood coagulation compared with the conventional blood coagulation detection. **Results:** No significant difference was found in the TEG parameters between I phase gastric cancer patients and control patients ($P>0.05$); Significant difference of TEG parameters including R, K, MA and CI was found between II phase gastric cancer patients and control patients ($P<0.05$). Significant difference of TEG parameters between III/IV phase gastric cancer patients and control patients was found ($P<0.05$); Significant difference of TEG parameters between gastric cancer patients with lymph node metastasis and control patients was observed ($P<0.05$), but no significant difference was found between patients with no lymph node metastasis and control patients ($P>0.05$). Significant difference of TEG parameters between advanced gastric cancer patients and control patients was found ($P<0.05$), but no significant difference was found between early gastric cancer patients and control patients ($P>0.05$). 26 cases of hemorrhage patients in the study group, the detection of hypercoagulable with TEG was 77.23%, and the conventional detection rate was 46.15% ($X^2=6.571$, $P=0.037$); 54 cases of no hemorrhagic patients in the study group, the detection of non-hypercoagulable with TEG was 94.44%, and the conventional detection rate was 77.78% ($P=0.047$). **Conclusions:** The blood state of gastric cancer patients was hypercoagulable, and the severity was positively related with the development of disease. To evaluate blood coagulation with TEG for patients with gastric cancer was more accuracy than conventional coagulation detection during perioperative period, which could effectively provide more accurate and useful data for clinical treatment, prevent the incurrence of adverse reaction induced by coagulation.

Key words: Thrombelastogram; Gastric cancer; Coagulation; Accuracy

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前言

近年来,凝血功能异常已成为临床治疗恶性肿瘤关注的热点之一,凝血功能异常的发生会引发静脉血栓的形成,严重者会导致患者发生重要脏器栓塞,影响患者的生命^[1,2]。目前,临床评估患者机体凝血功能状态主要以常规凝血功能检测联合血小板计数为主,常规凝血功能检测属于静态的终点检测凝血功能相关指标的实验技术,很难反映整个凝血过程,易错过预防血栓形成的最佳时机,给临床治疗带来很大的麻烦^[3]。1948年,Dr Hellmut Hartert 发明了血栓动力学(thrombelastogram, TEG)实验技术^[4],并于20世纪80年代逐渐应用于临床。TEG可以动态分析血小板、凝血因子、纤维蛋白原等血液成分之间的相互作用以及血凝块形成和纤维蛋白溶解的过程,并且以血栓弹性扫描图形象反应凝血动态的全部过程,是一项科学的动态监测血液凝固全部过程的实验技术^[5,6]。本研究以我院胃癌患者和胃部良性疾病患者为研究对象,与常规凝血检测比较,探讨TEG评估胃癌患者围术期凝血状态的作用,现将结果报道如下:

1 材料和方法

1.1 一般资料

选择2013年8月至2016年8月在我院进行治疗的患者,所有患者均经胃镜及病理检验确诊,收集并分析相应临床资料,胃癌组(观察组)患者80例,其中男性49例,女性患者31例,平均年龄66.1岁,均接受或全胃切除术、远端胃癌根治术或近端胃癌根治术。按照国际抗癌联盟TNM分期标准对胃癌组(观察组)患者进行分期:I期15例,II期18例,III期39例,IV期8例。按照淋巴结转移情况,胃癌组(观察组)中有29例无淋巴结转移情况,71例有转移。根据癌组织入侵的深度分为早期胃癌组12例,进展期胃癌组68例。排除标准:有严重心肝肾系统疾病患者;近期服用止血抗凝血药物患者;有严重糖尿病、高血压患者;治疗过程中接受输血患者等。胃部良性疾病组(对照组)患者80例作为对照组,包括胃炎、胃溃疡、胃多发溃疡等患者,其中男性45例,女性35例,平均年龄64.8岁。比较对照组和胃癌组患者的年龄、性别、体重等资料,通过统计分析,两组一般资料的差异不具有统计学意义,因此两组资料具有可比性。所有参与研究的患者均签署知情同意书并经医院伦理委员会通过。

1.2 方法

由专业护士对纳入研究的所有患者于清晨空腹抽取静脉血液8 mL,其中对照组患者治疗前采血,观察组患者于术前1 d采血。8 mL血液样本2 h内送检验科检验,其中2 mL做血常规检测,3 mL做常规凝血功能检验,3 mL做TEG检验。

1.3 观察指标

血常规检测血小板数量,即血小板计数(PLT);常规凝血功能指标包括5项,分别是纤维蛋白原(FIB)、凝血酶原时间(PT)、活化部分凝血酶原时间(APTT)、凝血酶时间(TT)、D-二聚体(D-D)等;TEG检测参数包括凝血反应时间(R)、凝血形成时间

(K)、Angle角、血栓最大振幅(MA)、总体凝血指数(CI)、血块稳定性(LY30)等。

1.4 统计学分析

采用SPSS17.0软件进行统计学分析,计量资料以均数±标准差($\bar{x} \pm s$)表示,组内比较采用重复测定数据的方差分析,组间比较采用t检验,计数资料采用 χ^2 检验分析,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 TEG评估两组患者凝血功能的基本情况

采用TEG评估两组患者的凝血功能,结果见表1。I期胃癌的TEG各指标与对照组相比差异无统计学意义($P > 0.05$),II期胃癌患者的R值、K值、MA值以及CI值与对照组比较差异具有统计学意义($P < 0.05$),III和IV胃癌患者的TEG各指标与对照组相比,差异具有统计学意义($P < 0.05$);发生淋巴结转移的胃癌患者TEG各指标与对照组相比差异具有统计学意义($P < 0.05$),而没有发生淋巴结转移的患者与对照组相比差异无统计学意义($P > 0.05$)。进展期胃癌患者的TEG各指标与对照组比较差异具有统计学意义($P < 0.05$),而早期胃癌的TEG各指标与对照组差异无统计学意义($P > 0.05$)。

2.2 常规凝血功能检查和TEG评估观察组患者凝血情况检出率的比较

观察组患者治疗后,按照是否发生出血分为出血患者26例,非出血患者54例,分别分析常规凝血功能检测和TEG检测评估凝血发生的准确率。如表3所示,出血患者中TEG检测血液发生低凝状态的检出率77.23%,常规检出率是46.15% ($\chi^2 = 6.571, P = 0.037$);非出血患者中,TEG检出血液非凝状态的检出率为94.44%,常规检出率为77.78% ($\chi^2 = 6.100, P = 0.047$),两种检测方法的检出率比较差异具有统计学意义($P < 0.05$)。

3 讨论

胃癌是发病率和病死率居高的一种消化道恶性肿瘤,在所有肿瘤中死亡率仅次于胰腺癌^[7],严重危害人类的生命健康。目前,临床治疗胃癌的方式以根治手术治疗为主^[8],而手术创伤对患者机体系统的影响会引发一系列复杂的病理生理改变,进而打破凝血和纤溶系统的平衡,导致血液高凝,引发血栓形成^[9]。有研究报道50%以上的恶性肿瘤患者存在凝血功能异常的现象,转移性恶性肿瘤发生凝血功能异常的概率更是高达90%^[10,11],肿瘤细胞在机体发生侵袭、转移的过程中常常通过分泌异常物质比如TNF- α 、IL-1 β 等影响人体正常的凝血功能^[12,13],致使血液处于高凝状态,从而引发静脉血栓,严重的静脉血栓可引发机体重要脏器栓塞,甚至导致患者死亡^[14]。因此,准确监测患者凝血功能的动态变化过程可以有效预防栓塞现象的发生,降低患者围术期不良现象的发生率,提高治疗效果。

临床检测患者凝血功能主要以常规凝血检测为主,以离心的血浆为检测样本,检测纤维蛋白原(FIB)、凝血酶原时间(PT)、活化部分凝血酶原时间(APTT)、凝血酶时间(TT)以及D-二聚

表 1 TEG 评估两组患者凝血功能的基本情况($\bar{x}\pm s$)Table 1 The basic conditions of coagulation function in two groups of patients detected by TEG($\bar{x}\pm s$)

		R/min	K/min	Angle	MA/mm	LY30/%	CI
TNM Phase	Control group	6.75± 1.98	1.92± 0.18	63.12± 4.89	54.78± 4.12	0.92± 0.56	-0.99± 1.12
	I phase	6.92± 1.87	1.78± 0.62	60.78± 4.67	56.96± 3.78	0.92± 0.53	-0.98± 1.11
	II phase	5.96± 1.35*	1.37± 0.32*	65.08± 5.12	70.11± 3.56*	0.85± 0.34	1.23± 0.72*
	III phase	5.14± 2.12*	1.05± 0.74*	68.97± 4.21*	75.26± 4.85*	0.79± 0.31*	1.62± 0.96*
	IV phase	4.18± 2.32*	0.78± 0.37*	75.14± 4.72*	75.63± 5.21*	0.71± 0.47*	2.03± 1.42*
Lymphon- odus	Non-metastasis	6.72± 2.32	1.63± 0.32*	64.14± 5.21	54.75± 4.21	0.89± 0.38	1.05± 0.57
	Metastasis	4.95± 1.78*	0.92± 0.41*	74.58± 4.76*	74.35± 3.54*	0.72± 0.36*	1.67± 0.87*
Invasion depth	Early gastric cancer	6.58± 1.26	1.36± 0.25*	64.23± 5.23	58.63± 3.75	0.87± 0.43	1.17± 1.35
	Advanced gastric cancer	4.69± 2.16*	0.98± 0.24*	73.58± 4.75*	74.64± 5.61*	0.76± 0.32*	1.79± 1.25*

Note: *P<0.05: compared with Control group.

表 2 常规凝血功能检查和 TEG 评估观察组患者凝血情况检出率的比较($\bar{x}\pm s$)Table 2 The comparison of coagulation detection rate in study group between TEG and routine coagulation test ($\bar{x}\pm s$)

			TEG	Routine coagulation
Hemorrhage (26)	Hypocoagulable	20	12	X ² =6.571,
	Hypercoagulability	3	3	P=0.037
	Non coagulation	3	11	
	Detection rate of hypocoagulable/%	77.23	46.15	
No hemorrhagic(54)	Hypocoagulable	3	11	X ² =6.100,
	Hypercoagulability	8	4	P=0.047
	Non coagulation	43	39	
	Detection rate of non-hypocoagulable/%	94.44	77.78	

体(D-D)等指标,然而离心的血浆恰恰忽略了对凝集素血小板的检测^[15],同时,常规凝血功能指标的检测只能反映血浆中某一阶段且无血小板参与的凝血状态,很难动态反映整个凝血过程并且难以评估血小板的作用和纤溶过程,易错过临床预防血栓发生的最佳时机,给临床治疗到来不可避免的麻烦^[16]。TEG 是以全血为研究对象,动态监测凝血功能的实验技术,可以从凝血因子活性、纤维蛋白原活性、血小板聚集功能、纤维蛋白溶解等指标的监测,真实反映凝血开始到血凝块形成以及纤维蛋白溶解的全部过程,综合评估患者凝血功能的综合状态^[17],最早用于心脏外科和肝脏移植等围术期患者凝血功能的监测^[18,19],为临床治疗提供依据,及早纠正凝血障碍。目前,TEG 用于评估胃癌患者围术期凝血功能的研究并不多,因此本研究主要探讨了 TEG 评估胃癌围术期凝血功能的状态。

TEG 实验技术涉及的参数有 20 多个,主要包括凝血反应时间(R 值)、凝血形成时间(K 值)、Angle 角、血栓最大振幅(MA)、总体凝血指数(CI)、血块稳定性(LY30),其中 R 值反应纤维蛋白凝块形成过程中凝血因子的作用,R 值延长,表示血液

低凝,R 值缩短,表示血液处于高凝状态,已形成血栓,需要提供抗凝治疗;K 值和 Angle 角可以反映纤维蛋白原的活性和水平,其活性升高,K 值缩短;MA 值主要反映血小板的聚集功能,其值越大,血小板功能越强;CI 值是评价整个凝血功能的指标,CI<3,血液低凝,CI>3,血液高凝。

本研究采用 TEG 分析了胃癌不同分期、淋巴结是否发生转移以及肿瘤入侵深度的血液凝结状态,结果提示随着胃癌的不断恶化(恶性胃癌、淋巴结发生转移或肿瘤发展进入进展期),患者 R 值逐渐缩短,提示患者病情越恶劣,血液高凝越明显。有研究报道肿瘤细胞在机体的生命代谢中通过分泌组织因子与凝血因子Ⅶ结合形成复合物,启动外源性凝血系统。除此之外,肿瘤组织/细胞还会诱导正常细胞比如内皮细胞、单核细胞等分泌组织因子,进一步打破机体凝血系统的平衡^[20]。此外,K 值随肿瘤的发展逐渐缩短,表明恶性胃癌患者血液中纤维蛋白原的活性升高,促进血凝过程。TEG 参数中 MA 直接反映了患者血小板的聚集功能,本研究结果显示胃癌病情越严重,MA 值越大,血小板功能越强。综合 TEG 检验的 6 个参数,可以分析

出胃癌患者随着病情的不断恶化,患者凝血反应时间和凝血形成时间越短,血小板功能越强,纤维蛋白原活性越高,血液高凝状态越明显。通过常规凝血功能检查和 TEG 检验评估胃癌患者治疗前后凝血状况的准确率,结果显示 TEG 动态监测患者凝血状态的准确率更高。

综上所述,胃癌患者的血液处于高凝状态,且病情越严重,高凝状态越显著;同时,TEG 评估胃癌患者围术期的凝血状态较常规凝血检验更准确,可有效预防凝血所引发的不良反应。

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