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乳腺癌手术前后凝血纤溶功能及血小板参数变化及意义

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摘要 目的:探讨乳腺癌患者手术前后凝血纤溶功能及血小板参数的变化情况及其意义。**方法:**收取2014年2月至2016年2月间于我院进行手术的乳腺癌患者90例作为研究对象进行回顾性分析,对其手术前一天及手术后凝血纤溶功能及血小板参数进行比较,另选择同期于我院进行体检的35例健康女性作为对照。**结果:**乳腺癌组手术前凝血纤溶功能各指标均显著高于对照组,手术后纤维蛋白原(FIB)、D-二聚体(D-D)均较术前明显升高,凝血酶原时间(PT)、活化部分凝血酶时间(APTT)明显降低,差异有统计学意义($P<0.05$)。乳腺癌组手术前血小板参数均显著高于对照组,手术后血小板压积(PCT)、平均血小板体积(MPV)、血小板分布宽度(PDW)均较术前明显升高,差异有统计学意义($P<0.05$)。肿瘤分期为I~II期的患者PT、APTT、FIB及D-D变化幅度均小于III期患者;无淋巴结转移的患者TT、APTT变化幅度小于有淋巴结转移的患者;HER-2受体阴性患者D-D变化幅度小于HER-2受体阳性患者,差异有统计学意义($P<0.05$)。肿瘤分期为I~II期的患者血小板计数(PLT)及MPV变化幅度小于III期患者;HER-2受体阴性患者PLT及MPV变化幅度小于HER-2受体阳性患者,差异有统计学意义($P<0.05$)。**结论:**乳腺癌患者凝血纤溶功能及血小板参数均较健康女性有较大改变,且术后患者血液高凝状态更加明显,机体存在更高的血栓风险,应加强围手术期管理。

关键词:乳腺癌;凝血纤溶功能;血小板参数;手术

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Variety and Value of Coagulation-fibrinolysis Function and Platelet Indexes before and after Surgery of Breast Cancer Patients

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ABSTRACT Objective: To explore the variety and value of coagulation-fibrinolysis function and platelet indexes before and after surgery of breast cancer patients. **Methods:** 90 breast cancer patients accepted in our hospital from February 2014 to February 2016 were retrospectively analyzed. The coagulation-fibrinolysis function and platelet indexes one day before surgery and after surgery were compared. And 35 healthy female underwent physical examination were selected as control. **Results:** The coagulation-fibrinolysis function of breast cancer group before surgery was obviously higher than that of control group. The expression levels of FIB, D-D after surgery were obviously higher than before, and PT, APTT were obviously lower than before with statistically significance ($P<0.05$). The platelet indexes of breast cancer group were obviously higher than that of control group, and the expression levels of PCT, MPV and PDW were all higher than before with statistically significance ($P<0.05$). The variety of PT, APTT, FIB and D-D of stage I~II breast cancer patients were less than stage III. The variety of TT and APTT of patients without lymph node metastasis were less than patients with lymph node metastasis. The variety of D-D of patients with HER-2 negative was less than patients with HER-2 positive. The differences above had statistically significance ($P<0.05$). The variety of PLT and MPV of stage I~II breast cancer patients were less than stage III. The variety of PLT and MPV of patients with HER-2 negative was less than patients with HER-2 positive. The differences above had statistically significance ($P<0.05$). **Conclusions:** The coagulation-fibrinolysis function and platelet indexes of breast cancer patients has great change with hypercoagulation after surgery compared to healthy female, which can improve the risk of thrombosis. It is very important to strengthen the management in the perioperative period.

Key words: Breast cancer; Coagulation-fibrinolysis function; Platelet indexes; Surgery

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前言

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乳腺癌是女性最为常见的恶性肿瘤之一,我国乳腺癌患者近年来也呈逐年升高趋势^[1]。研究报道显示,乳腺癌可打破机体凝血与抗凝之间的平衡,患者血液大多呈高凝状态,机体具有较高的血栓发生风险^[2]。手术治疗是乳腺癌重要的治疗方法,对于延长患者生存期、改善患者预后具有重要的意义^[3]。但其他恶性肿瘤的相关报道显示,手术可对患者围手术期凝血纤溶系统

造成一定影响,增加血栓形成等并发症发生风险,影响患者恢复^[4]。不少研究对乳腺癌患者的凝血纤溶功能及血小板参数进行了考察^[5-7],但关于手术前后乳腺癌患者血液状态的改变研究并不多见。本研究选取了近年来于我院进行手术的乳腺癌患者,对其手术前后凝血纤溶功能及血小板参数的变化情况进行考察,以期了解手术对乳腺癌患者血液状态改变,及可能对其产生影响的风险因素,现报道如下。

1 资料与方法

1.1 一般资料

本研究所收集样本为2014年2月至2016年2月之间于我院进行手术的乳腺癌患者,研究方式为回顾性分析。样本纳入标准为:①所有患者均于我院进行手术治疗,具有明确的病例结果证实为乳腺癌;②于手术前一天及手术后进行凝血纤溶功能及血小板参数检测,可于我科查询到完整的资料。样本排除标准为:①合并其他系统严重疾病或血液系统疾病等可能对凝血及纤溶功能产生影响的疾病;②术前经过任何其他形式的治疗,如手术治疗、放化疗等;③近期服用过影响凝血或血小板的药物。乳腺癌组共包含患者90例,年龄35~72岁,平均年龄(47.6±7.2)岁,按照手术方式的不同可分为单侧乳腺癌改良根治术68例,双侧乳腺癌改良根治术5例,单侧乳腺癌根治术7例。另选择同期于我院进行体检的35例健康女性作为对照,对照组年龄32~70岁,平均年龄(45.8±6.9)岁。两组患者年龄无显著差异,组间具有可比性(P>0.05)。

1.2 检测方法

乳腺癌组患者均于手术前一天以及手术后第一天清晨,体检者于体检当时采集患者静脉血5 mL加入枸橼酸钠抗凝管中,3000 r/min离心10 min收集血浆,使用西森美康CA1500全自动凝血分析仪和迈瑞CAL8000血液分析流水线检测凝血纤溶功能以及血小板参数。凝血纤溶功能指标包括凝血酶时间(TT)、凝血酶原时间(PT)、活化部分凝血酶时间(APTT)、国际标准化比值(INR)、纤维蛋白原(FIB)以及D-二聚体(D-D),血小板参数包括血小板参数(PLT)、血小板压积(PCT)、平均血小板体积(MPV)以及血小板分布宽度(PDW)。

1.3 统计学方法

本研究采用SPSS 18.0统计学分析软件处理数据,检测结果均为计量数据,以均数±标准差形式表示,组间比较选择独立样本t检验。以P<0.05为差异有统计学意义。

2 结果

2.1 两组凝血纤溶功能比较

比较乳腺癌患者及健康女性的凝血纤溶功能,结果显示,乳腺癌组手术前凝血纤溶功能各指标均显著高于对照组,手术后FIB、D-D均较术前明显升高,差异有统计学意义(P<0.05)。手术后PT、APTT均较术前明显降低,但仍高于对照组,差异有统计学意义(P<0.05)。手术前后TT、INR差异不显著(P>0.05)。见表1。

表1 两组凝血纤溶功能比较($\bar{x} \pm s$)

Table 1 Comparison of coagulation-fibrinolysis function of 2 groups ($\bar{x} \pm s$)

Groups	n	TT(s)	PT(s)	APTT(s)	INR	FIB(g/L)	D-D(g/L)
Breast cancer group	90						
Before surgery		12.42±2.16 ^a	14.63±1.38 ^a	32.61±6.01 ^a	0.94±0.13 ^a	3.15±0.72 ^a	0.36±0.14 ^a
After surgery		12.63±1.94 ^a	13.08±1.20 ^{ab}	30.14±5.68 ^{ab}	0.92±0.18 ^a	4.65±0.91 ^{ab}	0.48±0.22 ^{ab}
Control group	35	11.07±1.48 ^b	12.12±1.24 ^b	28.44±5.09 ^b	0.81±0.23 ^b	2.16±0.50 ^b	0.14±0.05 ^b

Note: Compared to control group, ^aP<0.05; Compared to before surgery, ^bP<0.05.

2.2 两组血小板参数比较

比较乳腺癌患者及健康女性的血小板参数,结果显示,乳腺癌组手术前血小板参数均显著高于对照组,手术后PCT、

MPV、PDW均较术前明显升高,差异有统计学意义(P<0.05)。手术前后PLT差异不显著(P>0.05)。见表2。

表2 两组血小板参数比较($\bar{x} \pm s$)

Table 2 Comparison of platelet indexes of two groups ($\bar{x} \pm s$)

Groups	n	PLT(10 ⁹ /L)	PCT(%)	MPV(fL)	PDW(fL)
Breast cancer group	90				
Before surgery		279.51±96.74 ^a	0.29±0.13 ^a	10.67±1.03 ^a	16.03±2.18 ^a
After surgery		268.40±87.91 ^a	0.34±0.18 ^{ab}	12.41±1.28 ^{ab}	16.39±2.54 ^{ab}
Control group	35	196.38±52.62 ^b	0.20±0.09 ^b	9.96±0.98 ^b	15.44±1.05 ^b

Note: Compared to control group, ^aP<0.05; Compared to before surgery, ^bP<0.05.

2.3 不同病理特征乳腺癌患者手术前后凝血纤溶功能变化情况比较

对不同病理特征乳腺癌患者手术前后凝血纤溶功能变化情况进行比较,以术后-术前计算各指标的差值。结果显示,肿

瘤分期为 I~II 期的患者 PT、APTT、FIB 及 D-D 变化幅度均小于 III 期患者;无淋巴结转移的患者 TT、APTT 变化幅度小于有淋巴结转移的患者;HER-2 受体阴性患者 D-D 变化幅度小于

HER-2 受体阳性患者,上述均具有统计学差异($P<0.05$)。其他指标变化情况比较差异不显著($P>0.05$)。见表 3。

表 3 不同病理特征乳腺癌患者手术前后凝血纤溶功能变化情况比较($\bar{x}\pm s$)

Table 3 Comparison of the variety before and after surgery of coagulation-fibrinolysis function of patients with different clinical features($\bar{x}\pm s$)

Items	n	Δ TT(s)	Δ PT(s)	Δ APTT(s)	Δ INR	Δ FIB(g/L)	Δ D-D(g/L)
Tumor stage							
Stage I~II	56	0.26 $\pm$ 0.04	-1.40 $\pm$ 0.19	-2.40 $\pm$ 0.22	0.02 $\pm$ 0.01	0.45 $\pm$ 0.09	0.08 $\pm$ 0.02
Stage III	34	0.23 $\pm$ 0.04	-1.96 $\pm$ 0.22	-2.63 $\pm$ 0.74	0.02 $\pm$ 0.01	0.68 $\pm$ 0.13	0.14 $\pm$ 0.03
P		>0.05	<0.05	<0.05	>0.05	<0.05	<0.05
Lymph node metastasis							
No	42	0.18 $\pm$ 0.03	-1.41 $\pm$ 0.18	-2.51 $\pm$ 0.45	0.02 $\pm$ 0.01	0.60 $\pm$ 0.12	0.12 $\pm$ 0.03
Yes	48	0.27 $\pm$ 0.06	-1.85 $\pm$ 0.24	-2.42 $\pm$ 0.31	0.01 $\pm$ 0.01	0.57 $\pm$ 0.13	0.10 $\pm$ 0.02
P		<0.05	<0.05	>0.05	>0.05	>0.05	>0.05
ER							
-	27	0.23 $\pm$ 0.05	-1.65 $\pm$ 0.30	-2.53 $\pm$ 0.40	0.01 $\pm$ 0.01	0.58 $\pm$ 0.20	0.11 $\pm$ 0.03
+	63	0.26 $\pm$ 0.04	-1.62 $\pm$ 0.26	-2.40 $\pm$ 0.29	0.02 $\pm$ 0.01	0.59 $\pm$ 0.16	0.12 $\pm$ 0.02
P		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
HER-2							
-	12	0.22 $\pm$ 0.04	-1.67 $\pm$ 0.42	-2.50 $\pm$ 0.37	0.02 $\pm$ 0.01	0.59 $\pm$ 0.22	0.08 $\pm$ 0.02
+	78	0.26 $\pm$ 0.04	-1.61 $\pm$ 0.31	-2.44 $\pm$ 0.41	0.01 $\pm$ 0.01	0.59 $\pm$ 0.24	0.12 $\pm$ 0.03
P		>0.05	>0.05	>0.05	>0.05	>0.05	<0.05

2.4 不同病理特征乳腺癌患者手术前后血小板参数变化情况比较

对不同病理特征乳腺癌患者手术前后血小板参数变化情况进行比较,以术后-术前计算各指标的差值。结果显示,肿瘤分期为 I~II 期的患者 PLT 及 MPV 变化幅度小于 III 期患者;HER-2 受体阴性患者 PLT 及 MPV 变化幅度小于 HER-2 受体阳性患者,上述均具有统计学差异($P<0.05$)。其他指标变化情况比较差异不显著($P>0.05$)。见表 4。

3 讨论

乳腺癌患者凝血纤溶功能及血小板的变化已被许多研究者证实,但手术前后乳腺癌患者的各项指标变化情况相关报道尚不多见^[8]。本研究在证实前人研究结果之外,通过对手术前后血液状态变化情况的考察,判断影响凝血纤溶功能及血小板变化的可能影响因素。本研究涉及到的检查指标包括凝血纤溶功能指标 TT、PT、APTT、INR、FIB、D-D 以及血小板参数包括 PLT、PCT、MPV、PDW。

本研究首先将手术前后乳腺癌患者与健康查体女性凝血纤溶功能进行了比较,结果显示,乳腺癌患者手术前凝血纤溶功能较健康女性就呈显著升高趋势。研究报道显示,乳腺癌患者的血液高凝状态不仅仅增加了血栓形成风险,同时也可参与肿瘤浸润及转移,即高凝状态与肿瘤进展相互促进,动态发展^[9,10]。后续一些研究对此现象进行了分析,认为血液处于高凝

状态时,纤维蛋白含量也显著升高。而纤维蛋白又是肿瘤微转移中重要的作用蛋白,可为微转移提供细胞生存和增殖的场所,同时可对其产生一定的保护作用,即避免肿瘤细胞被攻击破坏^[11-13]。接下来,我们对手术前后乳腺癌患者与健康查体女性血小板参数进行了比较,结果显示,乳腺癌患者手术前凝血功能较健康女性呈显著升高趋势。Bury 等研究报道显示,约有 60% 恶性肿瘤患者可合并 PLT 增多,本研究也观察到了这种现象,此外还观察到 PCT、MPV 以及 PDW 均产生了变化,提示血小板不仅仅在数量上发生改变,在形态上也逐渐呈现异常,影响正常功能^[14]。Lee 等研究认为,血小板可能通过与肿瘤细胞结合形成聚集体而参与肿瘤浸润及转移,此种聚集体可将肿瘤细胞包裹,从而逃避机体免疫防御,聚集体还可随血液流动至身体各处定植形成癌栓,造成血行转移^[15-17]。

本研究中,乳腺癌患者手术后 FIB、D-D 均较术前明显升高,PT、APTT 较术前明显降低,PCT、MPV 及 PDW 均较术前明显升高。分析该结果产生的原因,我们认为手术可对乳腺癌患者产生较大刺激,致使凝血纤溶功能发生更大程度的改变,加速肿瘤的亚临床转移。吕文远等对乳腺癌患者术前术后凝血指标进行了比较^[18],得到了与本研究相似的结果,即术前乳腺癌患者凝血系统已经发生改变,而术后与术前比较也有明显差别。在对结果的分析中,该研究称可能是由于肿瘤患者凝血系统处于相对脆弱的状态,而手术给机体造成巨大创伤,从本质上来讲是出血与止血的过程。该过程中可能涉及到多种凝血因

表 4 不同特征乳腺癌患者手术前后血小板参数变化情况比较($\bar{x} \pm s$)Table 4 Comparison of the variety before and after surgery of platelet indexes of patients with different clinical features($\bar{x} \pm s$)

Items	n	Δ PLT($10^9/L$)	Δ PCT(%)	Δ MPV(fL)	Δ PDW(fL)
Tumor stage					
Stage I ~ II	56	-6.28 $\pm$ 2.31	0.06 $\pm$ 0.03	1.45 $\pm$ 0.62	0.30 $\pm$ 0.07
Stage III	34	-18.37 $\pm$ 4.06	0.07 $\pm$ 0.02	2.36 $\pm$ 1.01	0.32 $\pm$ 0.10
P		<0.05	>0.05	<0.05	>0.05
Lymph node metastasis					
No	42	-9.92 $\pm$ 3.02	0.05 $\pm$ 0.02	2.00 $\pm$ 0.73	0.29 $\pm$ 0.08
Yes	48	-11.44 $\pm$ 3.17	0.07 $\pm$ 0.03	2.06 $\pm$ 0.69	0.32 $\pm$ 0.07
P		>0.05	>0.05	>0.05	>0.05
ER					
-	27	-10.66 $\pm$ 2.53	0.06 $\pm$ 0.03	1.98 $\pm$ 0.65	0.30 $\pm$ 0.09
+	63	-11.24 $\pm$ 2.61	0.06 $\pm$ 0.04	2.04 $\pm$ 0.68	0.33 $\pm$ 0.05
P		>0.05	>0.05	>0.05	>0.05
HER-2					
-	12	-5.30 $\pm$ 1.69	0.06 $\pm$ 0.02	1.50 $\pm$ 0.47	0.29 $\pm$ 0.04
+	78	-15.23 $\pm$ 2.76	0.07 $\pm$ 0.04	2.40 $\pm$ 0.75	0.32 $\pm$ 0.10
P		<0.05	>0.05	<0.05	>0.05

子、血小板及纤维蛋白原等物质的消耗,多方面综合作用使凝血系统产生较大改变^[18]。

本研究创新之处在于,并未使用手术前或手术后的检测结果对不同病理特征的乳腺癌患者进行比较,而是使用术后与术前凝血纤溶功能各项指标及血小板各参数之间的差值进行比较。有研究报道显示,病理分期越高,患者机体高凝状态越明显,各项指标表达水平也较低病理分期差异显著^[19,20]。采用差值比较,就是为了克服术前差异对术后结果产生的影响。本研究结果显示,肿瘤分期为 I ~ II 期、无淋巴结转移或 HER-2 受体阴性的患者,凝血纤溶功能及血小板参数的变化幅度均不及肿瘤分期较高、有淋巴结转移或 HER-2 受体阳性的患者。该结果产生的原因尚未可知,但必然与肿瘤进展造成的机体凝血纤溶功能紊乱有一定关系,因此可以观察到病情严重的患者变化幅度更大^[21]。

综上所述,乳腺癌患者凝血纤溶功能及血小板参数均较健康女性有较大改变,且术后患者血液高凝状态更加明显,机体存在更高的血栓风险,应加强围手术期管理。

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