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达芬奇机器人与腹腔镜手术治疗胰腺癌的近期疗效比较及对血清 CRP、PCT 及肿瘤标志物的影响*

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摘要 目的:探讨达芬奇机器人与腹腔镜手术治疗胰腺癌的近期疗效比较及对血清 C-反应蛋白(CRP)、降钙素原(PCT)及肿瘤标志物的影响。**方法:**选择 2019 年 1 月至 2020 年 1 月在我院接受治疗的 61 例胰腺癌患者,根据手术方法分为机器人组(n=26)和腹腔镜组(n=35)。腹腔镜组给予腹腔镜手术治疗,机器人组给予达芬奇机器人辅助治疗。比较两组围术期情况、CRP、PCT、糖类抗原 19-9(CA19-9)、糖类抗原 125(CA125)、术后恢复情况及并发症发生情况。**结果:**机器人组禁食时间及排气时间显著低于腹腔镜组,差异显著($P<0.05$);治疗前,两组血清 CA19-9、CA125 水平无明显差异;治疗后,两组血清 CA19-9、CA125 水平治疗后较治疗前均显著下降差异显著($P<0.05$);两组治疗后血清 CA19-9、CA125 水平比较无显著差异($P>0.05$);治疗前,两组 CRP、PCT 水平无明显差异;治疗后,两组 CRP、PCT 明显升高,且机器人组低于腹腔镜组差异显著($P<0.05$);机器人组和腹腔镜组术后下床活动时间、拔尿管时间、术后住院时间比较无显著差异;机器人组术后重症监护时间显著低于腹腔镜组,差异显著($P<0.05$);两组患者治疗期间并发症总发生率分别为 4.44%、6.67%,无显著差异($P>0.05$)。**结论:**达芬奇机器人辅助能够显著提高胰腺癌手术质量,且对血清 CRP、PCT 的影响较小,且对肿瘤标志物的影响与腹腔镜手术较为接近,为患者提供机器人微创治疗是未来临床的必然发展趋势。

关键词:达芬奇机器人;腹腔镜手术;胰腺癌;C-反应蛋白;降钙素原;糖类抗原 19-9;糖类抗原 125

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Comparison of Short-term Efficacy between da Vinci Robot and Laparoscopic Surgery in the Treatment of Pancreatic Cancer and its Effect on Serum CRP, PCT and Tumor Markers*

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ABSTRACT Objective: To study Comparison of short-term efficacy between da Vinci robot and laparoscopic surgery in the treatment of pancreatic cancer and its effect on serum C-reactive protein (CRP), procalcitonin (PCT) and tumor markers. **Methods:** 61 patients with pancreatic cancer who received treatment in our hospital from January 2019 to January 2020 were selected and divided into robotic group (n=26) and laparoscopic group (n=35) according to surgical methods. Laparoscopic surgery was given to the laparoscopic group, while Da Vinci robot assisted therapy was given to the robotic group. The perioperative conditions, CRP, PCT, carbohydrate antigen 19-9 (CA19-9), carbohydrate antigen 125 (CA125), postoperative recovery and complications were compared between the two groups. **Results:** The fasting time and exhaust time in the robot group were significantly lower than those in the laparoscopic group, the differences were significant ($P<0.05$). Before treatment, there was no significant difference in serum CA19-9 and CA125 levels between the two groups. After treatment, serum CA19-9 and CA125 levels in both groups were significantly decreased after treatment compared with before treatment ($P<0.05$). There were no significant differences in serum CA19-9 and CA125 levels between the two groups after treatment ($P>0.05$). Before treatment, there was no significant difference in CRP and PCT levels between the two groups. After treatment, CRP and PCT were significantly increased in the two groups, and the difference in the robot group was significantly lower than that in the laparoscopic group ($P<0.05$). There were no significant differences between the robot group and the laparoscopic group in the postoperative time of getting out of bed, catheter extraction time and postoperative hospitalization time. The duration of postoperative intensive care in the robot group was significantly shorter than that in the laparoscopic group ($P<0.05$). The total incidence of complications in 2 groups during treatment was 4.44% and 6.67%, respectively, with no significant difference($P>0.05$). **Conclusion:** Da Vinci robot assisted can significantly improve the surgical quality of pancreatic cancer, and has little effect on serum CRP and PCT, and its effect on tumor markers is close to that of laparoscopic surgery. Therefore, it is an inevitable clinical development trend to provide minimally invasive robotic treatment for patients in the future.

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前言

胰腺癌是临床常见恶性肿瘤,具有癌症之王的称号,早期无明显症状,肿瘤呈进行性生长,使大部分患者确诊时已是晚期,近年来其发病率和死亡率呈上升趋势,严重危及患者生命^[1-3]。目前对于胰腺癌的唯一有可能治愈的治疗方法为手术切除,近年来胰腺外科手术治疗措施越来越多样化,其中运用较多的为机器人与腹腔镜微创手术^[4]。腹腔镜下胰十二指肠切除术原来最有效的方法,具有创伤小、更加美观等特点,但在胰腺癌手术中由于胰腺血供丰富,且周围肠系膜上动静脉、胆总管、胃、十二指肠等重要组织器官与之毗邻,其解剖与周围血管关系复杂,导致其在胰腺手术中的应用难度大^[5-7]。达芬奇机器人手术是一种高级机器人平台,是通过微创的方法实施复杂的手术,能弥补腹腔镜手术存在的不足,被广泛用于外科手术中^[8]。有研究显示,CA19-9、CA125参与了胰腺癌的发生与发展,是目前诊断胰腺癌的标志物^[9,10]。本研究旨在探讨达芬奇机器人与腹腔镜手术治疗胰腺癌的近期疗效比较,并分析对血清CRP、PCT及肿瘤标志物的影响。

1 资料与方法

1.1 一般资料

选择2019年1月至2020年1月在我院接受治疗的61例胰腺癌患者进行研究。根据手术方法分为2组,机器人组26例,男16例,女10例,年龄45~72岁,平均(58.41±4.11)岁,其中病理分期:Ⅱ期14例,Ⅲ期12例;腹腔镜组35例,男19例,女16例,年龄46~71岁,平均(58.37±4.08)岁,其中病理分期:Ⅱ期19例,Ⅲ期16例。两组基线资料无显著差异($P>0.05$),可比较。

纳入标准:(1)符合《胰腺癌放射治疗专家共识》诊断标准^[11];(2)病理检查确诊;(3)肿瘤未侵犯门静脉;(4)知情同意。

排除标准:(1)合并其他恶性肿瘤患者;(2)意识障碍者;(3)合并泌尿系统疾病者;(4)合并高血压疾病者;(5)认知功能障碍者;(6)免疫功能低下者;(7)依从性较差者。

1.2 方法

腹腔镜组采用腹腔镜下胰十二指肠切除术:常规麻醉,脐下腹进行切口,置入观察孔及建立气腹,探查腹腔内情况,无明显腹水,无根治性手术禁忌症,按照动脉先行操作步骤,切断远端胃,暴露游离十二指肠,打通胰后隧道,切断胃,切除胆囊。离断肝总管。切断胰腺,移除肿瘤标本,完成后进行消化道重建,逐层关腹,结束手术。机器人组采用达芬奇机器人下胰十二指肠切除术:全麻后,完成插管,安装机器人操作臂。采用三臂法,探查腹腔内情况,无明显腹水,无根治性手术禁忌症,按照动脉先行操作步骤,切断远端胃,暴露游离十二指肠,打通胰后隧道,切除胆囊。离断肝总管。切断胰腺,移除肿瘤标本,完成后进行消化道重建,逐层关腹,结束手术。

1.3 观察指标

采集空腹静脉血5 mL,采用化学免疫分析测定CA19-9、CA125;双抗体夹心酶联免疫吸附法测定血清C-反应蛋白(CRP)、降钙素原(PCT)水平;随访记录患者康复情况;记录并发症发生情况。

1.4 统计学分析

以spss18.0软件包处理,计量资料均用均数±标准差($\bar{x}\pm s$)表示,组间比较使用独立样本t检验,计数资料以率表示, χ^2 检验, $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 机器人组与腹腔镜组围术期去对比

两组患者手术时间、术中出血量无差异($P>0.05$),机器人组禁食时间及排气时间显著低于腹腔镜组,差异显著($P<0.05$)见表1。

表1 机器人组与腹腔镜组手术时间、术中出血量、禁食时间及排气时间对比($\bar{x}\pm s$)
Table 1 Comparison of perioperative period between the machine group and the laparoscopic group($\bar{x}\pm s$)

Groups	n	The operation time (min)	Intraoperative blood loss(mL)	A fast time(d)	Exhaust time(d)
The machine set	26	374.16± 25.69	251.16± 30.26	4.12± 0.51	3.12± 0.71
Laparoscopic group	35	385.46± 24.18	264.25± 28.82	6.09± 0.37	4.56± 0.51
t value		1.758	1.717	17.497	9.225
P value		0.083	0.091	0.000	0.000

2.2 机器人组与腹腔镜组CRP、PCT水平比较

治疗前,两组CRP、PCT水平无明显差异;治疗后,两组CRP、PCT明显升高,且机器人组低于腹腔镜组,机器人组机器人组差异显著($P<0.05$),见表2。

2.3 机器人组与腹腔镜组血清CA19-9、CA125检查结果比较

治疗前,两组血清CA19-9、CA125水平无明显差异;治疗后,两组血清CA19-9、CA125水平治疗后较治疗前均显著下降差异显著($P<0.05$);机器人组两组治疗后血清CA19-9、CA125水平比较无显著差异($P>0.05$),见表3。

表 2 机器人组与腹腔镜组 CRP、PCT 水平比较($\bar{x} \pm s$, ng/mL)

Table 2 The levels of CRP and PCT in machine group and laparoscopic group were compared($\bar{x} \pm s$, ng/mL)

Groups	n	CRP(mg/L)		PCT(ng/mL)	
		Preoperative	Postoperative	Preoperative	Postoperative
The machine set	26	7.18± 2.71	10.25± 3.14	8.62± 1.13	9.32± 0.45
Laparoscopic group	35	7.56± 2.14	13.73± 3.78	8.75± 1.09	12.79± 0.93
t value		0.612	3.815	0.029	17.535
P value		0.543	0.000	0.977	0.000

表 3 机器人组与腹腔镜组血清 CA19-9、CA125 检查结果比较($\bar{x} \pm s$)

Table 3 Comparison of serum CA19-9 and CA125 between the machine group and the laparoscopic group($\bar{x} \pm s$)

Groups	n	CA19-9(U/mL)		CA125(U/mL)	
		Preoperative	Postoperative	Preoperative	Postoperative
The machine set	26	360.51± 47.18	74.56± 7.47	51.83± 18.61	12.57± 6.14
Laparoscopic group	35	361.08± 48.12	76.64± 7.15	52.05± 19.08	13.56± 5.89
t value		0.047	1.102	0.045	0.637
P value		0.963	0.275	0.964	0.526

2.4 机器人组与腹腔镜组术后恢复情况比较

后住院时间比较无显著差异;机器人组术后重症监护时间显著

机器人组和腹腔镜组术后下床活动时间、拔尿管时间、术

低于腹腔镜组,差异显著($P < 0.05$)见表 4。

表 4 机器人组与腹腔镜组术后恢复情况比较($\bar{x} \pm s, d$)

Table 4 Comparison of postoperative recovery between machine group and laparoscopic group($\bar{x} \pm s, d$)

Groups	n	Duration of postoperative	Postoperative activity	Postoperative	Duration of postoperative
		intensive care	time out of bed	catheterization time	hospital stay
The machine set	26	2.45± 0.54	3.30± 0.71	5.10± 0.56	20.12± 6.14
Laparoscopic group	35	4.07± 0.83	3.63± 0.75	5.18± 0.68	21.15± 8.78
t value		8.672	1.738	0.489	0.512
P value		0.000	0.087	0.627	0.611

2.5 机器人组与腹腔镜组术后并发症比较

无显著差异($P > 0.05$)见表 5。

两组患者治疗期间并发症总发生率分别为 4.44%、6.67%，

表 5 机器人组与腹腔镜组术后并发症比较[n(%)]

Table 5 Comparison of postoperative complications between machine group and laparoscopic group[n(%)]

Groups	n	Pancreatic fistula	Disordered gastric emptying	Abdominal cavity infection	The total incidence of
The machine set	26	1	1	0	2(4.44)
Laparoscopic group	35	1	0	2	3(6.67)
χ^2 value					0.001
P value					0.923

3 讨论

胰腺癌是一种恶性程度极高的肿瘤,在众多恶性肿瘤中被医学界称之为“癌症之王”,主要是由于胰腺比较隐蔽,生长在腹膜后位,包绕着门静脉及其他大血管,对胆总管胰腺段具有

较高的侵袭性,因此胰腺癌具有较高的侵袭性^[12-14]。胰腺癌发病率高,预后差,5 年生存率≤ 5%,据调查显示,欧美国家由胰腺癌引起的死亡排名是所有癌症中第 6 位,严重危及人们的生命^[15]。

手术是治疗胰腺癌的常用方法,但胰腺癌恶性程度高、预

后差,近年来随着医疗技术的飞速发展,微创手术具有创伤小的特点,被广泛应用各种外科手术中^[16,17]。腹腔镜手术是微创外科重要技术,能缩小手术切口、减轻对患者的创伤,但胰腺被后腹膜覆盖,位置深,分离裸化时较困难,导致胰腺外科的腹腔镜手术学习曲线较长^[18,20]。有研究显示,腹腔镜手术具有存在立体感差、操作视角不佳等缺点,在操作方面有一定劣势,因此应寻找新的治疗方法,为胰腺外科提供新思路^[21,22]。达芬奇机器人手术是一种全新的外科手术系统,机器人的机械臂取代了外科医生的手臂,为微创外科历史掀开了崭新的一页^[23]。有研究显示,达芬奇机器人手术是通过3D视野以及高度灵巧与精细的操作,在保留脾脏的胰体尾切除术中具有优势,被广泛用于胰腺体尾部良性肿瘤的手术治疗中^[24,25]。本研究结果显示,术中患者手术时间及术中出血量无明显差异,但使用达芬奇机器人手术的患者禁食时间及排气时间显著低于腹腔镜手术的患者,提示,达芬奇机器人与腹腔镜手术在胰腺癌中的治疗效果相当,不会影响术中出血量,仅能降低患者禁食时间及排气时间。同时在术后并发症无明显差异,提示,两种手术均具有较高的安全性,不会增加并发症发生率。分析其原因可能是因为达芬奇机器人手术具有高倍清晰视觉效果,可更清晰地辨别精细解剖结构,通过遥控操作手术器械,过滤手部震颤,灵活的器械臂对血管和组织的解剖等操作更精确,在手术中具有明显优势,因此降低患者禁食时间及排气时间。

有研究显示,癌症侵袭是细胞和组织驱动的过程,控制肿瘤细胞中细胞骨架动力学和细胞连接的转换,能启动和维持癌症侵袭^[26-30]。糖类抗原(CA)是细胞内恶性肿瘤的标志物,在恶性肿瘤中水平较高,CA19-9、CA125是血清肿瘤标志物,在多种肿瘤的发生和发展过程中扮演着重要的角色,目前已被证实与胰腺癌病情变化有关,对胰腺癌预后判断具有重要意义^[31,34]。本研究将血清CA19-9、CA125作为参与胰腺癌的重要指标,观察在手术期间各水平变化,结果显示,术后两组患者血清CA19-9、CA125水平明显降低,且两组术后血清CA19-9、CA125水平无显著差异,提示,达芬奇机器人手术同样可有效清除胰腺癌病灶,减少肿瘤标志物水平。分析其原因可能是因为使用达芬奇机器人手术时可为术者提供高清晰3D手术视野并使其放大10倍-15倍,使医师对解剖结构能进行更精确的辨认,清除患者体内肿瘤细胞。本研究结果还显示,治疗后患者血清CRP、PCT明显升高,且机器人组低于腹腔镜组,且给予达芬奇机器人手术的患者术后重症监护时间显著低于对照组,Popova A S^[35]等研究也显示,达芬奇机器人在外科手术中对患者创伤较小,不会增加患者感染发生率,与本研究结果相似。分析其原因可能是因为手术对患者机体创伤较大,产生强烈的应激反应,而达芬奇机器人手术具有较高的精准性与灵活性,减小了手术时其对血管等重要组织的损伤程度,减小创口,降低神经体液激活,从而对患者CRP、PCT影响较小。

达芬奇机器人辅助能够显著提高胰腺癌手术质量,且对血清CRP、PCT的影响较小,且对肿瘤标志物的影响与腹腔镜手术较为接近,为患者提供机器人微创治疗是未来临床的必然发展趋势。

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