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二次肿瘤细胞减灭术在铂类敏感的复发性卵巢上皮癌中的作用

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摘要 目的:探讨二次肿瘤细胞减灭术对铂类敏感的复发性卵巢上皮癌治疗的临床意义。**方法:**回顾性分析我院于2002年1月至2012年12月收治的115例铂类敏感的复发性卵巢上皮癌患者的临床及随访资料。**结果:**在115例铂类敏感的复发性卵巢上皮癌中,66例接受了二次肿瘤细胞减灭术(手术组),术后辅以铂类为基础的化疗。49例患者只接受了以铂类为基础的化疗(对照组)。两组患者肿瘤病理分型无统计学差异($P=0.485$)。与对照组相比,手术组FIGO分期IV期患者的比例少(15.2% VS 34.7%, $P=0.014$),低分化患者的比例少(71.2% VS 91.8%, $P=0.024$),多发复发灶患者的比例少(28.3% VS 49.0%, $P=0.027$)。平均随访30.2个月(6-48个月),Kaplan-Meier生存分析显示,手术组与对照组患者的中位生存期分别为35.0个月和27.0个月,差异有统计学差异(Log rank 7.9, $P=0.005$)。多因素Cox回归分析显示,校正了年龄、肿瘤病理类型、病理分级及FIGO分期后,不同治疗方案是复发上皮性卵巢癌患者远期生存率的独立影响因素。**结论:**二次肿瘤细胞减灭术可以改善铂类敏感的复发性卵巢上皮癌患者的临床预后。

关键词:肿瘤细胞减灭术;卵巢癌;复发;生存期

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Role of Secondary Cytoreductive Surgery for Patients with Platinum Sensitive Recurrent Epithelial Ovarian Cancer

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ABSTRACT Objective: To investigate the clinical benefit of secondary cytoreductive surgery for patients with platinum sensitive recurrent epithelial ovarian cancer. **Methods:** The clinical and follow-up data of 115 patients with recurrent epithelial ovarian cancer treated in our department between January 2002 and December 2012 were retrospectively analyzed. **Results:** 66 patients underwent secondary cytoreductive surgery assisted by platinum based chemotherapy (operation group), and other 49 patients were treated with chemotherapy only(control group). Patient's tumor pathological types of two groups were of no statistical difference($P=0.485$). Compared with the control group, FIGO clinical stage IV Patients were fewer in operation group (15.2% VS 34.7%, $P=0.014$), poorly differentiated carcinoma patients were fewer in operation group(71.2% VS 91.8%, $P=0.024$), multiple recurrent lesions patients were fewer in operation group (28.3% VS 49.0%, $P=0.0270$). All patients were followed up for the average follow-up of 30.2 months (range 6-48 months). Kaplan-Meier survival analysis showed that the median survival time was significantly different between the two groups (35 months VS 27 months, Log rank 7.9, $P=0.005$). Cox regression multivariate analysis showed that with adjustment for age, pathological type, pathological grading and FIGO clinical staging, different treatments were the independent predictors of recurrent epithelial ovarian carcinoma patients with long-term survival rate. **Conclusion:** The secondary cytoreductive surgery may improve the prognosis of patients with recurrent, platinum-sensitive epithelial ovarian carcinoma.

Key words: Cytoreductive surgery; Ovarian cancer; Recurrent; Survival

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前言

卵巢癌是女性中排名第7位的常见肿瘤,其世界范围内年

龄标化发病率为6.3/10万,死亡率为3.8/10万^[1-3]。由于缺乏有效的筛查手段,约70%的卵巢癌患者确诊时已属晚期。通过积极的手术治疗及铂类为基础的联合化疗,60%~80%患者在一 线治疗后能获得临床完全缓解^[4-6]。然而70%晚期卵巢癌患者将复发并需要接受挽救治疗^[7,8]。对于大多数复发患者,化疗是标准的治疗方法,但由于复发灶常存在耐药可能,化疗疗效欠佳。因此,二次肿瘤细胞减灭术(Secondary Cytoreductive Surgery, SCRS)成为重要的治疗方法^[9,10]。本文通过回顾性分析

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我院于 2002 年 1 月至 2012 年 12 月收治的 115 例铂类敏感的复发性卵巢上皮癌患者的临床及随访资料,探讨二次肿瘤细胞减灭术对铂类敏感的复发性卵巢上皮癌治疗的临床意义。

1 资料和方法

1.1 病例选择

筛选我院于 2002 年 1 月至 2012 年 12 月收治的铂类敏感的复发性卵巢上皮癌患者 115 例,均在首次肿瘤细胞减灭术后行 6 个疗程 PAC 或 PC 方案化疗,66 例接受 SCRS(手术组、A 组),术后继续原 PAC 或 PC 方案化疗,49 例仅采用顺铂及紫杉醇化疗 3-6 个疗程(对照组、B 组)。收集患者的以下临床资料:首次确诊卵巢癌的年龄,卵巢癌复发及接受 SCRS 的年龄,原发性肿瘤的组织学类型,肿瘤的临床及病理分期,复发肿瘤的部位及数量,SCRS 中残余瘤的存在与否及大小以及手术的相关并发症。

1.2 方法

(1)卵巢癌复发标准参考根据中华医学会妇产科学会妇科肿瘤学组制订的复发性卵巢癌的诊治规范(建议)^[10]。(2)随访:所有患者均经定期临床随访,包括全身及盆腔检查,盆腹腔 B 超、

CT 检查及血清 CA125 检查。(3)SCRS 方法及原则:遵循肿瘤细胞减灭术的原则,在全腹探查的基础上,决定手术范围,判断手术的可行性,尽可能切除盆腔或腹膜病灶,必要时切除部分肠管及泌尿道,行肠壁修补或肠吻合术,以达最佳减瘤术的目的。

1.3 统计处理

采用 PASW Statistics 18.0 软件包进行统计学处理。计量资料以均数±标准差表示,两组间比较用 t 检验。计数资料用百分数表示,两组间比较用卡方检验。采用 Kaplan-Meier 生存曲线 Log-rank 检验比较两组患者的中位生存期的差别,采用多因素 Cox 回归分析 SCRS 对复发性卵巢癌预后的影响,以 $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 手术组和对照组患者基线资料比较

手术组和对照组患者平均年龄差别无统计学意义($t=0.476, P=0.635$)。两组患者肿瘤病理分型无统计学差异($\chi^2=0.190, P=0.979$)。其余指标均差异有统计学意义。见表 1。

表 1 两组患者临床资料比较

Table 1 Comparison of clinical data between two groups

指标 Indexes		手术组(n=66) Operation group(n=66)	对照组(n=49) Control group(n=49)	t / χ^2 值	P
年龄(岁) Age(years)		56.5± 8.7	57.3± 9.2	0.476	0.635
病理类型[n (%)] Pathological type[n (%)]	浆液性 Serosity	43 (65.2)	30 (61.2)	0.190	0.979
	子宫内膜样 Endometrioid	12 (18.2)	10 (20.4)		
	粘液性 Mucinous	6 (9.1)	5 (10.2)		
	其它 Others	5 (7.6)	4 (8.2)		
FIGO 分期[n (%)] FIGO clinical staging[n (%)]	IIIC	56 (84.8)	32 (65.3)	5.978	0.014
	IV	10 (15.2)	17 (34.7)		
肿瘤细胞分化类型[n (%)] Tumor cell differentiation[n (%)]	高分化 Well-differentiated	5 (7.6)	1 (2.1)	7.478	0.024
	中分化 Moderately differentiated	14 (21.2)	3 (6.1)		
	低分化 Poorly differentiated	47 (71.2)	45 (91.8)		
复发病灶[n (%)] Recurrent lesions[n (%)]	单发 Single	47 (71.7)	25 (51.0)	4.898	0.027
	多发 Multiple	19 (28.3)	24 (49.0)		

2.2 手术组和对照组患者临床预后的比较

对所有患者进行定期随访,随访时间为(30.2± 10.2)个月(6-48 个月),失访 5 例(4.3%),手术组(A 组)与对照组(B 组)分别有 45 例和 39 例发生死亡。Kaplan-Meier 生存分析显示,手术组与对照组患者的中位生存期分别为 36.0 个月及 27.0 个月,两组之间差异有统计学差异(Log rank 7.9, $P=0.005$)。多因素 Cox 回归分析显示,校正了年龄、肿瘤病理类型、病理分级及 FIGO 分期后,不同治疗方案是复发上皮性卵巢癌患者远期生存率的独立影响因素。见图 1。

3 讨论

无论首次治疗是否有效,80%~90%的晚期卵巢癌患者会再次出现疾病进展^[12]。但对于复发性卵巢癌患者是否行再次肿

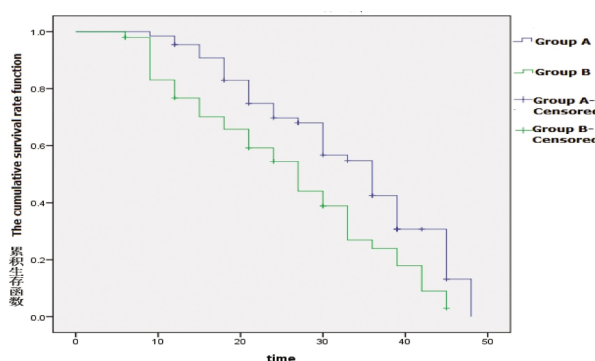


图 1 手术组与对照组累计生存曲线

Fig. 1 The cumulative survival curves of two groups

瘤细胞减灭术一直存在很大的争议^[13-15],二次肿瘤细胞减灭术

对生存的影响需要进一步证实。目前观点认为,二次肿瘤细胞减灭术是铂类敏感的复发性卵巢癌患者临床有益的治疗方案^[16],SCRS 对于二线化疗敏感、病灶限于盆腹腔内、估计手术及基本切除的复发性卵巢癌患者,具有一定效果^[17],许多研究也都证明了 SCRS 的有效性。Saladino 等^[18]将 SCRS 联合化疗(40 例)与单纯化疗(31 例)相比,中位生存期明显延长($P=0.03$),Cheng 等^[19]得出 SCRS 联合化疗(23 例)的中位生存期 41.7 个月,远长于行单纯化疗(23 例)的中位生存期 18.8 个月。

考虑到患者的临床预后因素,且大量临床实践表明,并非所有的复发性患者都适合再次手术且能获益于 SCRS。SCRS 施行的条件是患者达到临床缓解又复发,患者一旦术后出现并发症且病灶不能完全切除,化疗延后可能直接影响患者的临床预后,既往研究中完全切除率介于 9.4%~82.1%,且多在 50% 以内^[20]。

国外学者一致认为复发性卵巢癌的治疗是姑息性的,以延长患者生命、减轻痛苦、改善生活质量为目的^[7,18,20]。对复发性卵巢癌实施二次手术的目的在于切除明确的孤立病灶和解除肠梗阻,近年来一些研究表明,复发性卵巢癌经过理想的二次肿瘤细胞减灭术可以提高患者的生存期、改善生活质量。本文中复发的 115 例患者,手术组与对照组患者的中位生存期分别为 36.0 个月及 27.0 个月,两组之间差异有统计学差异(Log rank 7.9, $P=0.005$)。多因素 Cox 回归分析显示,校正了年龄、肿瘤病理类型、病理分级及 FIGO 分期后,不同治疗方案是复发上皮性卵巢癌患者远期生存率的独立影响因素

综上所述,及时、准确地诊断卵巢癌的复发、选择性的给予手术,并辅以适当化疗对提高患者生存质量、延长生存期具有重要作用。

参考文献(References)

- [1] Tomao F, Papa A, Strudel M, et al. Investigating Molecular Profiles of Ovarian Cancer: An Update on Cancer Stem Cells[J]. J Cancer, 2014, 5(5): 301-310
- [2] Yu Y, Zhang X, Hong S, et al. Epidermal growth factor induces platelet-activating factor production through receptors transactivation and cytosolic phospholipase A2 in ovarian cancer cells [J]. J Ovarian Res, 2014, 7(1): 39
- [3] Pu D, Jiang SW, Wu J, et al. Association between MTHFR Gene Polymorphism and the Risk of Ovarian Cancer: A Meta-analysis of the Literature[J]. Curr Pharm Des, 2014, 20(11): 1632-1638
- [4] Winarto H, Laihad BJ, Nuranna L, et al. Modification of Cutoff Values for HE4, CA125, the Risk of Malignancy Index, and the Risk of Malignancy Algorithm for Ovarian Cancer Detection in Jakarta, Indonesia[J]. Asian Pac J Cancer Prev, 2014, 15(5): 1949-1953
- [5] Lee JY, Kim HS, Song YS. Genistein as a Potential Anticancer Agent against Ovarian Cancer[J]. J Tradit Complement Med, 2012, 2(2): 96-104
- [6] Tang J, Liu DL, Shu S, et al. Outcomes and patterns of secondary relapse in platinum-sensitive ovarian cancer: implications for tertiary cytoreductive surgery[J]. Eur J Surg Oncol, 2013, 39(7): 786-791
- [7] Anwer K, Kelly FJ, Chu C, et al. Phase I trial of a formulated IL-12 plasmid in combination with carboplatin and docetaxel chemotherapy in the treatment of platinum-sensitive recurrent ovarian cancer [J]. Gynecol Oncol, 2013, 131(1): 169-173
- [8] Al Rawahi T, Lopes AD, Bristow RE, et al. Surgical cytoreduction for recurrent epithelial ovarian cancer [J]. Cochrane Database Syst Rev, 2013, 2: CD008765
- [9] Schorge JO, Garrett LA, Goodman A, et al. Cytoreductive surgery for advanced ovarian cancer: quo vadis[J]. Oncology, 2011, 25(10): 928-934
- [10] Puistola U, Leminen A. Treatment strategies in ovarian cancer Duodecim[J]. Duodecim, 2013, 129(18): 1917-1924
- [11] Monk BJ, Pujade-Lauraine E, Burger RA. Integrating bevacizumab into the management of epithelial ovarian cancer: the controversy of front-line versus recurrent disease. Ann Oncol [J]. Ann Oncol, 2013, 24(10): x53-x58
- [12] Eitan R, Fishman A, Meirovitz M, et al. Liposome-encapsulated doxorubicin citrate (Myocet) for treatment of recurrent epithelial ovarian cancer: a retrospective analysis [J]. Anticancer Drugs, 2014, 25(1): 101-105
- [13] Safra T, Asna N, Veizman A, et al. The combination of gemcitabine and carboplatin shows similar efficacy in the treatment of platinum-resistant and platinum-sensitive recurrent epithelial ovarian cancer patients[J]. Anticancer Drugs, 2014, 25(3): 340-345
- [14] Van de Laar R, Zusterzeel PL, Van Gorp T, et al. Cytoreductive surgery followed by chemotherapy versus chemotherapy alone for recurrent platinum-sensitive epithelial ovarian cancer (SOCceR trial): a multicenter randomised controlled study[J]. BMC Cancer, 2014, 14: 22
- [15] Nishio S, Ushijima K, Shimizu T, et al. Safety and efficacy of pegylated liposomal Doxorubicin and Carboplatin on platinum-sensitive recurrent epithelial ovarian cancer [J]. Gan To Kagaku Ryoho, 2013, 40(13): 2539-2543
- [16] Schorge JO, McCann C, Del Garmen MG. Surgical debulking of ovarian cancer: what difference does it make[J]. Rev Obstet Gynecol, 2010, 3(3): 111-117
- [17] Santillan A, Karam AK, Li AJ, et al. Secondary cytoreductive surgery for isolated nodal recurrence in patients with epithelial ovarian cancer [J]. Gynecol Oncol, 2007, 104(3): 686-690
- [18] Saladino E, Fleres F, Irato S, et al. The role of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the treatment of ovarian cancer relapse[J]. Updates Surg, 2013
- [19] Cheng X, Jiang R, Li ZT, et al. The role of secondary cytoreductive surgery for recurrent mucinous epithelial ovarian cancer (mEOC)[J]. Eur J Surg Oncol, 2009, 35(10): 1105-1108
- [20] Bristow RE, Puri I, Chi DS. Cytoreductive surgery for recurrent ovarian cancer: A meta-analysis[J]. Gynecol Oncol, 2009, 112(1): 265-274