

doi: 10.13241/j.cnki.pmb.2019.16.041

宫腔镜手术对子宫黏膜下肌瘤患者卵巢功能、免疫功能及炎症因子水平的影响*

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摘要 目的:探讨宫腔镜手术对子宫黏膜下肌瘤患者卵巢功能、免疫功能及炎症因子水平的影响。**方法:**选取2017年1月~2018年4月期间我院收治的子宫黏膜下肌瘤患者107例为研究对象。根据不同的手术治疗方式将患者分为腹腔镜组($n=55$,行腹腔镜子宫肌瘤切除术)和宫腔镜组($n=52$,行宫腔镜子宫肌瘤切除术),比较两组患者围术期指标;比较两组术前、术后3个月卵巢功能[促卵泡生长素(FSH)、雌二醇(E_2)、黄体生成素(LH)、窦卵泡数量(AFC)]、细胞免疫指标($CD3^+$ 、 $CD4^+$ 、 $CD8^+$)、体液免疫指标(IgG、IgA、IgM)水平;比较两组术前、术后7d炎症因子[白介素-2(IL-2)、白介素-6(IL-6)、C反应蛋白(CRP)]指标水平;记录两组术后并发症发生情况。**结果:**两组患者手术时间、术中出血量比较差异无统计学意义($P>0.05$);宫腔镜组术后下床时间、肛门排气时间、住院时间以及抗生素使用时间均短于腹腔镜组($P<0.05$)。两组患者术后3个月 E_2 、LH、AFC比较差异无统计学意义($P>0.05$);腹腔镜组术后3个月FSH水平高于术前及宫腔镜组($P<0.05$)。腹腔镜组患者术后3个月细胞免疫指标低于术前及宫腔镜组($P<0.05$),但体液免疫指标与术前比较差异无统计学意义($P>0.05$);宫腔镜组术后3个月各项免疫指标与术前比较差异无统计学意义($P>0.05$)。两组患者术后7d IL-2、IL-6以及CRP水平均升高,但宫腔镜组低于腹腔镜组($P<0.05$)。腹腔镜组术后并发症发生率为10.91%(6/55),与宫腔镜组的9.62%(5/52)比较差异无统计学意义($P>0.05$)。**结论:**宫腔镜子宫肌瘤切除术对子宫黏膜下肌瘤患者卵巢功能、免疫功能影响较轻,同时可降低炎症因子水平,未出现严重并发症,具有一定的临床应用价值。

关键词:宫腔镜;子宫黏膜下肌瘤;卵巢功能;免疫功能;炎症因子

中图分类号:R711.74;R713.4 文献标识码:A 文章编号:1673-6273(2019)16-3196-05

Effect of Hysteroscopic Surgery on Ovarian Function, Immune Function and Levels of Inflammatory Factors in Patients with Submucous Myoma of Uterus*

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ABSTRACT Objective: To investigate the effect of hysteroscopic surgery on ovarian function, immune function and inflammatory factors in patients with submucous myoma of uterus. **Methods:** 107 patients with submucous myoma were selected from January 2017 to April 2018. The patients were divided into laparoscopic group ($n=55$, laparoscopic surgery) and hysteroscopic group ($n=52$, hysteroscopic surgery). The perioperative indexes of the two groups were compared. The ovarian function [follicle growth hormone (FSH), estradiol (E_2), luteinizing hormone (LH) and the number of sinus follicles (AFC)], cellular immune index ($CD3^+$, $CD4^+$, $CD8^+$), humoral immune index (IgG, IgA, IgM) were compared before and 3 months after operation, and inflammatory factors [interleukin-2 (IL-2), interleukin-6 (IL-6), C-reactive protein (CRP)] before and 7 days after operation were compared between the two groups. The postoperative complications were recorded in the two groups. **Results:** There was no significant difference in operative time and intraoperative bleeding volume between the two groups ($P>0.05$), the time of getting out of bed, anal exhaust, hospitalization and antibiotic use in hysteroscopy group were shorter than those in laparoscopy group ($P<0.05$). There was no significant difference in E_2 , LH and AFC between the two groups at 3 months after operation ($P>0.05$); FSH in the laparoscopic group increased significantly at 3 months after operation, but that in the hysteroscopy group was lower than that in the laparoscopic group ($P<0.05$). The cellular immunity index of laparoscopic group was lower than that of preoperative group and hysteroscopy group at 3 months after operation ($P<0.05$), but there was no significant difference in humoral immunity index between preoperative group and laparoscopic group ($P>0.05$). The levels of IL-2, IL-6 and CRP were elevated 7 days after operation in both groups, but those in hysteroscopy group were lower than those in laparoscopy group ($P<0.05$). The incidence of postoperative complications in laparoscopic group was 10.91% (6/55), which was not significantly different from 9.62% (5/52) in hysteroscopy group ($P>0.05$). **Conclusion:** Compared with laparoscopic hysteromyomectomy, hysteroscopic hysteromyomectomy for submucous myoma has a faster recovery, less influence on ovarian function and immune function,

* 基金项目:新疆维吾尔自治区自然科学基金项目(2014C2347)

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(收稿日期:2018-11-24 接受日期:2018-12-19)

and can reduce the level of inflammatory factors, which has a certain clinical value.

Key words: Hysteroscopy; Submucous myoma of uterus; Ovarian function; Immune function; Inflammatory factors

Chinese Library Classification(CLC): R711.74; R713.4 **Document code:** A

Article ID: 1673-6273(2019)16-3196-05

前言

子宫肌瘤是育龄期女性最常见的良性肿瘤,多发于中年妇女,且随着患者年龄的增加,子宫肌瘤发病率呈现不断上升趋势^[1-3]。据相关报道数据显示,育龄期女性的子宫肌瘤发病率高达20%~25%,其中约有0.4%~0.8%的患者进展至恶性肿瘤,给我国育龄期女性健康及生活带来严重影响^[4]。临床上根据子宫肌瘤的解剖结构可分为子宫黏膜下肌瘤、肌壁间肌瘤以及浆膜下肌瘤,其中子宫黏膜下肌瘤发病比例最高^[5]。目前临床治疗子宫肌瘤患者的主要方式为手术治疗,以往多采取子宫切除术进行治疗,随着我国女性生育年龄的推迟,绝大多数患者均有保留子宫的意愿^[6],因此,子宫肌瘤切除术逐渐被应用。随着近年来微创技术的发展,宫腔镜子宫肌瘤切除术或者腹腔镜子宫肌瘤切除术已成为治疗该病的主要术式^[7,8],现临床有关上述两种术式对子宫黏膜下肌瘤患者卵巢功能、免疫功能及炎症因子水平影响的系统性报道并不多见,本研究就此展开探讨,以期临床术式选择提供参考。

1 资料与方法

1.1 一般资料

选取2017年1月~2018年4月期间我院收治的子宫黏膜下肌瘤患者107例为研究对象。纳入标准:(1)所有患者均符合2010版《妇产科学》^[9]中制定的有关子宫黏膜下肌瘤的相关诊断标准,并经病理实验证实;(2)均具备手术指征;(3)美国麻醉医师协会分级为II~III级;(4)患者及其家属知情本研究并签署知情同意书;(5)有配偶且性生活正常者。排除标准:(1)合并其他子宫疾病者;(2)合并双侧卵巢异常者;(3)妊娠及哺乳期妇女;(4)合并盆腔器官疾病者;(5)合并心肝肾等脏器功能异常者;(6)合并恶性肿瘤者。根据不同的手术治疗方式将患者分为腹腔镜组($n=55$)和宫腔镜组($n=52$),其中腹腔镜组年龄23~54岁,平均 (41.27 ± 3.59) 岁;肌瘤直径4.6~10.3 cm,平均 (6.12 ± 1.37) cm;肌瘤数量1~6枚,平均 (3.47 ± 0.45) 枚;子宫黏膜下肌瘤分型:0型19例,I型18例,II型18例。宫腔镜组年龄22~56岁,平均 (42.67 ± 4.03) 岁;肌瘤直径4.8~10.1 cm,平均 (5.93 ± 0.72) cm;肌瘤数量1~7枚,平均 (3.82 ± 0.62) 枚;子宫黏膜下肌瘤分型^[10]:0型17例,I型16例,II型19例。两组患者一般资料比较无差异($P>0.05$),存在可比性。本次研究获得我院伦理学委员会批准进行。

1.2 方法

腹腔镜组患者行腹腔镜子宫肌瘤切除术,具体操作如下:患者取截石位,采用全麻。常规消毒、铺无菌单,常规进行气腹穿刺,气腹压力控制在12~14 mmHg,于腹部处做4个穿刺孔,第一个穿刺孔为脐上缘处,置入腹腔镜,在腹腔镜观察下穿刺其余三个孔,往肌壁内注入稀释后的垂体后叶素6 μ g,采用单极电凝钩将瘤体纵向切开,同时使用大抓钳提拉肌瘤,分离后

取出,术毕清洗腹腔,取出器械,排出二氧化碳,随后采用3-0可吸收线对内膜层进行缝合,采用2-0可吸收线对子宫肌层进行缝合,采用1-0合成线带底对子宫创面行间断缝合。宫腔镜组患者行宫腔镜子宫肌瘤切除术,具体操作如下:患者取截石位,采用硬膜外麻醉,会阴处进行常规消毒,用宫颈扩张器将宫颈扩张为10~12 mm,采用膨宫液进行持续灌注,采用宫腔电切镜确认肌瘤的位置、大小以及数目,视肌瘤情况进行不同的切割术,有蒂黏膜下肌瘤,行表面切割,待瘤体缩小后将其用钳子取出,无蒂黏膜下肌瘤,切开子宫肌瘤包膜,并将子宫肌瘤切成碎片取出。手术完成后对宫腔进行检查,观察患者是否存在活动性出血,两组术后均给予常规促宫缩、抗炎治疗。所有患者手术均由同一组经验丰富的医师进行。

1.3 观察指标

观察两组患者手术时间、术中出血量、术后下床时间、抗生素使用时间、肛门排气时间以及住院时间。于术前、术后3个月采集患者清晨空腹静脉血6 mL,3000 r/min离心8 min,离心半径8 cm,取上清液,置于-80℃冰箱中待测。采用酶联免疫吸附试验检测促卵泡生长素(Follicular growth hormone,FSH)、雌二醇(Estradiol, E_2)、黄体生成素(Luteinizing hormone,LH)水平,试剂盒购自南京建成生物科技有限公司,严格遵守试剂盒操作进行。采用美国BD公司生产的FacScan流式细胞仪检测细胞免疫指标CD3⁺、CD4⁺、CD8⁺水平。采用美国贝克曼公司生产的ARRA Y360检测体液免疫指标免疫球蛋白G(immunoglobulin G,IgG)、免疫球蛋白A(immunoglobulin A,IgA)、免疫球蛋白M(immunoglobulin M,IgM)。采用阴道B超计算双侧卵巢中窦卵泡数量(Antral follicle count,AFC)。于术前、术后7 d采集患者清晨空腹静脉血4 mL,离心方法以及试剂盒同前文叙述一致。采用酶联免疫吸附试验检测白介素-2(Interleukin-2,IL-2)、白介素-6(Interleukin-6,IL-6)、C反应蛋白(C reactive protein,CRP)水平。记录两组患者术后并发症发生情况。

1.4 统计学方法

采用SPSS23.0统计学软件对研究数据进行处理。计量资料以 $(\bar{x} \pm s)$ 表示,行t检验;计数资料以[n(%)]表示,行 χ^2 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者围术期指标比较

两组患者手术时间、术中出血量比较差异无统计学意义($P>0.05$);宫腔镜组术后下床时间、肛门排气时间、住院时间以及抗生素使用时间均短于腹腔镜组($P<0.05$)。见表1。

2.2 两组患者手术前后卵巢功能比较

两组患者术前FSH、 E_2 、LH、AFC比较差异无统计学意义($P>0.05$);两组患者术后3个月 E_2 、LH、AFC比较差异无统计学意义($P>0.05$);腹腔镜组术后3个月FSH水平高于术前及宫腔镜组($P<0.05$)。见表2。

表 1 两组患者围术期指标比较($\bar{x} \pm s$)

Table 1 Comparison of perioperative indexes between two groups of patients($\bar{x} \pm s$)

Groups	Operation time (min)	Intraoperative blood loss(mL)	Postoperative out of bed time(h)	Anal exhaust time (h)	Time of hospitalization(d)	Antibiotic usage time(d)
Laparoscopic group (n=55)	58.47± 17.26	33.53± 8.87	39.37± 6.14	25.42± 6.21	11.53± 1.21	6.20± 0.96
Hysteroscopy group (n=52)	61.91± 19.63	36.45± 7.39	11.62± 3.75	14.15± 4.16	5.47± 0.67	2.19± 0.52
t	0.964	1.844	28.019	10.965	31.795	26.647
P	0.337	0.068	0.000	0.000	0.000	0.000

表 2 两组患者手术前后卵巢功能比较($\bar{x} \pm s$)

Table 2 Comparison of ovarian function before and after operation in two groups of patients($\bar{x} \pm s$)

Groups	FSH(U/L)		E ₂ (pg/L)		LH(U/L)		AFC(n)	
	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation
Laparoscopic group(n=55)	6.84± 0.95	7.51± 0.93*	43.67± 8.38	44.04± 7.26	7.33± 1.24	7.38± 1.26	43	41
Hysteroscopy group(n=52)	6.89± 0.87	7.05± 0.83	42.53± 7.19	43.83± 8.37	7.31± 1.18	7.40± 1.19	42	39
t/ χ^2	0.283	2.694	0.753	0.139	0.085	0.084	0.110	0.003
P	0.777	0.008	0.453	0.890	0.932	0.933	0.820	0.931

Note: compared with before operation, * $P < 0.05$.

2.3 两组患者手术前后免疫功能比较

两组患者术前 CD3⁺、CD4⁺、CD8⁺、IgG、IgA、IgM 比较差异无统计学意义 ($P > 0.05$); 腹腔镜组患者术后 3 个月 CD3⁺、CD4⁺、CD8⁺ 水平低于术前及宫腔镜组 ($P < 0.05$), 但 IgG、IgA、

IgM 水平与术前比较差异无统计学意义 ($P > 0.05$); 宫腔镜组术后 3 个月各项免疫指标与术前比较差异无统计学意义 ($P > 0.05$)。见表 3。

表 3 两组患者手术前后免疫功能比较($\bar{x} \pm s$)

Table 3 Comparison of immune function between two groups before and after operation($\bar{x} \pm s$)

Groups	IgG(g/L)		IgA(g/L)		IgM(g/L)		CD3 ⁺ (%)		CD4 ⁺ (%)		CD8 ⁺ (%)	
	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation	Before operation	3 month after operation
Laparo- scopic group (n=55)	13.26± 1.28	13.44± 1.33	2.24± 0.35	2.31± 0.23	1.66± 0.54	1.69± 0.73	66.82± 3.44	63.12± 4.19*	39.62± 3.02	35.73± 2.83*	29.94± 2.15	25.22± 3.93*
Hys- teroscopy group (n=52)	13.31± 1.30	13.41± 1.41	2.29± 0.37	2.33± 0.22	1.62± 0.61	1.70± 0.59	66.46± 3.51	67.06± 4.48	40.12± 4.24	39.86± 3.94	29.82± 3.24	29.16± 3.92
t	0.200	0.133	0.718	0.459	0.360	0.078	0.536	4.701	0.706	6.253	0.227	5.190
P	0.842	0.910	0.474	0.647	0.720	0.938	0.593	0.000	0.482	0.000	0.821	0.000

Note: compared with before operation, * $P < 0.05$.

2.4 两组患者炎症因子水平比较

两组患者术前 IL-2、IL-6 以及 CRP 比较差异无统计学意义 ($P > 0.05$); 两组患者术后 7 d 上述炎症因子水平均升高, 但腹腔镜组低于宫腔镜组 ($P < 0.05$)。见表 4。

腹腔镜组术后发生过性发热 5 例、低钠血症 1 例, 并发症发生率为 10.91%(6/55), 宫腔镜组术后发生过性发热 4 例、宫腔感染 1 例, 并发症发生率为 9.62%(5/52), 两组术后并发症发生率比较差异无统计学意义 ($\chi^2 = 0.049$, $P = 0.826$)。

2.5 两组患者术后并发症发生情况比较

表 4 两组患者炎症因子水平比较($\bar{x} \pm s$)Table 4 Comparison of inflammatory factors in two groups of patients($\bar{x} \pm s$)

Groups	IL-2(ng/mL)		IL-6(ng/mL)		CRP(mg/L)	
	Before operation	7 d after operation	Before operation	7 d after operation	Before operation	7 d after operation
Laparoscopic group (n=55)	26.42± 8.45	44.34± 7.52*	8.73± 2.25	55.36± 9.84*	8.91± 1.21	41.86± 8.25*
Hysteroscopy group (n=52)	25.26± 9.51	32.21± 6.45*	8.97± 2.13	31.26± 8.21*	8.84± 1.17	25.42± 9.14*
t	0.668	8.932	0.566	13.715	0.304	9.777
P	0.506	0.000	0.573	0.000	0.762	0.000

Note: compared with before operation, * $P < 0.05$.

3 讨论

子宫黏膜下肌瘤是子宫肌瘤中较为常见的一种类型,关于其发病形成机制,目前临床研究领域已较为明确,主要是由于患者肌瘤表明覆盖子宫内膜,增加子宫内膜面积,在宫腔内慢慢占位,导致经血排出^[11-13]。多数患者可伴有不同程度的月经量增多、周期紊乱等现象,同时由于肌瘤一直向宫腔内部发展,造成其邻近器官产生压迫,从而引发习惯性流产或者不孕,且当患者红色肌瘤变性时则可引发患者剧烈腹痛,因此,其发病的危害严重性逐渐受到临床医师的重视^[14-16]。目前子宫黏膜下肌瘤患者治疗方式分为药物治疗和手术治疗,然而药物治疗子宫黏膜下肌瘤临床疗效差、复发率高、不良反应多,限制了其临床应用价值,因此,手术治疗是现今治疗子宫黏膜下肌瘤主要方法^[17,18]。传统的子宫切除术或者开腹子宫肌瘤切除术手术视野佳,利于子宫肌瘤的完全切除,但是术后创伤大、康复时间长,尤其针对子宫切除术剥夺了女性的生育能力,临床应用依旧具有一定的局限性^[19,20]。腹腔镜、宫腔镜子宫肌瘤切除术是近年来新兴的微创术式,临床中已逐步取代传统的手术方式,现临床有关上述两种术式对子宫黏膜下肌瘤患者的系统性对比报道并不多见,就此展开探讨。

本次研究结果表明,宫腔镜组部分围术期指标情况优于腹腔镜组。提示子宫黏膜下肌瘤患者采用宫腔镜子宫肌瘤切除术,优势明显,这主要是因为宫腔镜手术操作难度较小,术式于阴道内完成,对腹腔内部环境影响较轻,加之无需在腹部打孔,减少创伤,加快患者术后康复时间,减少抗生素使用药量,缩短住院时间,提高治疗效果^[21]。本研究结果还显示,两组患者术后3个月卵巢功能指标比较无差异,腹腔镜组术后3个月FSH较术前明显上升。提示宫腔镜、腹腔镜子宫肌瘤切除术对患者卵巢功能影响均较轻,这主要是由于卵巢功能的血供维持主要来源于卵巢动脉和子宫卵巢动脉,上述两种术式均只对子宫浅层肌层造成一定的损害,对卵巢血供的影响则不明显,而腹腔镜组FSH术后存在一定波动可能是与短期的子宫损伤有关。另外本研究结果提示相较于腹腔镜术式,宫腔镜子宫肌瘤切除术对患者免疫功能无明显影响,而腹腔镜术式可对患者细胞免疫造成一定的影响,这可能是由于腹腔镜手术存在切口以及缝合等困难有关,而宫腔镜手术创伤相对较小,对机体刺激小。此外两组患者术后IL-2、IL-6以及CRP水平均升高,但宫腔镜组各

项炎症指标低于腹腔镜组,说明宫腔镜子宫肌瘤切除术在降低炎症反应效果中,优势明显,这与其不开腹、子宫无切口、术中实时监测肌瘤与子宫壁关系、利于控制切割深度有关。同时两组术后并发症发生率比较无差异,提示宫腔镜、腹腔镜子宫肌瘤切除术安全性相当,均未出现严重不良反应。

综上所述,子宫黏膜下肌瘤患者采用宫腔镜子宫肌瘤切除术,有利于优化部分围术期指标,且对患者卵巢功能、免疫功能无明显影响,同时可减轻机体炎性反应,安全性好,但宫腔镜子宫肌瘤切除术对手术医生的临床经验以及手术熟练程度要求较高,临床可根据患者实际情况选择术式。

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