

doi: 10.13241/j.cnki.pmb.2019.16.030

二尖瓣成形术与二尖瓣生物瓣置换术治疗 风湿性二尖瓣重度关闭不全的效果比较*

朱西安 高鲁方 胡大群 孙 鹏 向道康[△]

(贵州省人民医院心外科 贵州 贵阳 550002)

摘要 目的:探讨二尖瓣成形术(Mitral valve plasty,MVP)与二尖瓣生物瓣置换术(Mitral valve replacement,MVR)治疗风湿性二尖瓣重度关闭的临床疗效和安全性。**方法:**选择我院 2014 年 1 月至 2019 年 1 月收治的因风湿性二尖瓣重度关闭而行二尖瓣成形术或二尖瓣生物瓣置换术的患者 60 例,其中二尖瓣成形术组(MVP 组)27 例,二尖瓣生物瓣置换术组(MVR 组)33 例。比较两组患者的围手术期各项指标,治疗前后的心功能指标(左心室射血分数,左心房内径、左心室收缩末期内径、左心室舒张末期内径)及二尖瓣反流情况以及术后并发症的发生情况。**结果:**① MVP 组患者的手术时间、体外循环时间均明显长于 MVR 组($P<0.05$);而术中出血量、呼吸机使用时间、住院时间 MVP 组均显著低于 MVR 组($P<0.05$);② 术后,MVP 组的 LVEF 和 LVEDD 水平高于 MVR 组,而 LAD 和 LVESD 水平则低于 MVR 组($P<0.05$);③ 出院前及末次随访时,MVP 组二尖瓣反流发生率与 MVR 组相比差异均无统计学意义($P>0.05$)。④ MVP 组患者的术后并发症发生率低于 MVR 组($P<0.05$)。**结论:**二尖瓣成形术治疗风湿性二尖瓣重度关闭的临床疗效和安全性优于二尖瓣生物瓣置换术,但术者需严格掌控 MVP 的手术适应症。

关键词:二尖瓣关闭不全;二尖瓣成形术;生物瓣置换术

中图分类号:R654.2 **文献标识码:**A **文章编号:**1673-6273(2019)16-3150-05

Comparison of the Effect of Mitral Valve Plasty and Mitral Valve Replacement on the Severe Rheumatic Mitral Valve Insufficiency*

ZHU Xi-an, GAO Lu-fang, HU Da-qun, SUN Peng, XIANG Dao-kang[△]

(Department of Cardiac Surgery, Guizhou Provincial People's Hospital, Guiyang, Guizhou, 550002, China)

ABSTRACT Objective: To investigate the clinical efficacy and safety of mitral valve plasty (MVP) and mitral valve replacement (MVR) in the treatment of severe mitral valvular closure. **Methods:** 60 patients with mitral valve plasty or mitral valve biological flap replacement were selected in our hospital from January 2014 to January 2019 due to severe closure of rheumatic mitral valve. There were 27 patients in the group (MVP group) and 33 patients in the mitral valve biopsy group (MVR group). The perioperative indicators of the two groups were compared, and the cardiac function indexes (left ventricular ejection fraction, left atrium diameter, left ventricular systolic end diameter, left ventricular diastolic end diameter) and mitral valve reflux were detected before and after treatment, and the postoperative complications were compared. **Results:** The operation time and extracorporeal circulation time of MVP group were longer than that in the MVR group ($P<0.05$), while the intraoperative blood loss, ventilator use time and hospitalization time were lower than that in the MVR group ($P<0.05$). Before operation, there was no significant difference in cardiac function between the two groups ($P>0.05$). After operation, the LVEF and LVEDD levels in the MVP group were higher than that in the MVR group, while the LAD and LVESD levels were lower than that in the MVR group ($P<0.05$). The incidence of mitral valve reflux in the MVP group was not statistically significant compared with that in the MVR group before and at the last follow-up ($P>0.05$). The incidence of postoperative complications in the MVP group was lower than that in the MVR group ($P<0.05$). **Conclusion:** The clinical efficacy and safety of mitral valvuloplasty for the treatment of severe rheumatic mitral regurgitation is better than that of mitral valve bioprosthesis replacement, and the postoperative cardiac function and other indexes are better and have fewer complications. However, the surgeon must strictly control the surgical indications of MVP.

Key words: Mitral valve closure insufficiency; mitral valvuloplasty; mitral valve replacement

Chinese Library Classification(CLC): R654.2 **Document code:** A

Article ID:1673-6273(2019)16-3150-05

* 基金项目:国家自然科学基金项目(81760329)

作者简介:朱西安(1984-),男,硕士,主治医师,研究方向:心血管外科,电话:13985504402,

E-mail: zhuxian1805@163.com

[△] 通讯作者:向道康(1968-),男,博士,主任医师,研究方向:心血管外科,电话:13985173875,

E-mail: zhuxian1805@163.com

(收稿日期:2019-05-07 接受日期:2019-05-29)

前言

二尖瓣病变的原因复杂多样,主要分为五类:先天性、外伤性、感染性、风湿性、退行性心脏疾病。其中,风湿性二尖瓣关闭不全比较常见的是由风湿性心脏瓣膜病引发,临床上常与二尖瓣狭窄合并出现,如不及时进行治疗,很可能会造成患者心功能障碍,诱发房颤甚至心力衰竭等严重病理病变^[1-3]。

风湿性二尖瓣膜病变 (Rheumatic heart valvular disease, RHVD) 通常采用外科手术进行治疗,主要包括二尖瓣成形术(Mitral valvuloplasty, MVP)和二尖瓣生物瓣置换术(Mitral valve replacement, MVR)^[4,5]。有研究显示 MVP 保留了瓣膜及瓣下结构,对于维持患者的左心室形态及心脏功能具有重要意义,并且能有效降低手术的死亡率,降低术后长期抗凝的风险,因而正在逐渐被广泛应用到心外科的临床手术中^[6,7]。MVR 则保留了腱索和部分瓣叶,这种手术方式能有效降低左室破裂的风险,保护患者心功能,提高患者的生存率。两种手术方法均能对患者的病情进行有效缓解,但两种方法的临床疗效却各有利弊,临床治疗过程中需要结合患者的具体情况综合分析。本研

究主要对比了两种手术方式对风湿性二尖瓣重度关闭不全的临床疗效和安全性,现报道如下。

1 资料与方法

1.1 研究对象

选择我院于 2014 年 1 月至 2019 年 1 月收治的因风湿性二尖瓣重度关闭而行二尖瓣成形术或二尖瓣生物瓣置换术的患者 60 例,根据治疗方式分为二尖瓣成形术组(MVP 组)27 例和二尖瓣生物瓣置换术组(MVR 组)33 例。排除标准:① 同时进行主动脉瓣置换术;② 合并心肌病、恶性心律失常等严重器质性心脏病;③ 合并肝肾功能病变;④ 其他影响心脏结构及功能的疾病;所有患者均经食管超声心动图 (Transesophageal echocardiography, TEE)等临床诊断确诊为风湿性二尖瓣重度关闭不全,且无先天性心脏病。两组患者在性别、年龄、心功能分级、左心室射血分数(Left ventricular ejection fraction, LVEF)、左心室舒张末期内径 (Left ventricular end diastolic diameter, LVEDD)、二尖瓣反流面积、合并疾病等一般资料比较无差异 ($P>0.05$),具有可比性,详见表 1。

表 1 两组患者一般资料的比较

Table 1 Comparison of the general data between two groups of patients

Project	MVP(n=27)	MVR(n=33)	t/ χ^2	<i>P</i>	
Gender	Male [n(%)]	18(66.67)	18(54.55)	0.909	0.34
	Female [n(%)]	9(33.33)	15(45.45)		
Age /year		57.6± 7.2	60.4± 8.7	1.338	0.186
History of Hypertension [n(%)]		7(25.93)	9(27.27)	0.014	0.907
History of Diabetes mellitus [n(%)]		2(7.41)	2(6.06)	0.043	0.835
Myocardial infarction [n(%)]		6(22.22)	6(18.18)	0.152	0.697
NYHA>=III [n(%)]		21(77.78)	26(78.79)	0.009	0.925
Mitral valve Reflux Area(cm²)		11.1± 2.5	12.2± 3.2	1.458	0.15

Note: New York Heart Association (NYHA).

1.2 手术方法

两组患者均在全麻低温、体外循环下经胸骨正中切口,行二尖瓣成形术或二尖瓣生物瓣置换术。手术过程中经 TEE 再次查看二尖瓣结构及反流情况,再次确认二尖瓣反流的程度为重度。患者手术过程中,均接受经食管超声心动图监测,拟行 MVP 术的患者手术过程中及时检验修复效果,检查二尖瓣关闭不全是否得到纠正,如果仍然关闭不全,则应及时进行二尖瓣生物瓣置换术。手术完成后,确认二尖瓣无明显反流或仅轻微反流后关闭胸腔,完成手术。

1.3 观察指标

(1)两组患者围手术期情况:手术时间、出血量、体外循环时间、呼吸机使用时间、住院时间;(2)两组患者手术前后心功能指标:术前、术中、术后均采用超声心动图成像仪(型号:Philips IE33)测量 LVEF、左心房房内径(Left atrial diameter, LAD)、左心室收缩末期内径 (Left ventricular end-systolic dimension, LVESD)、LVEDD;(3)二尖瓣反流情况;(4)术后肺部感染、低心排出量、切口愈合不良等并发症发生情况。

1.4 统计学方法

采用 SPSS 19.0 软件进行数据分析。计量资料以($\bar{x}\pm s$)表示,组间比较采用 t 检验;计数资料以[例(%)]表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者围手术期情况的比较

MVP 组手术时间、体外循环时间均明显长于 MVR 组,而术中出血量、呼吸机使用时间、住院时间均显著低于 MVR 组 ($P<0.05$),详见表 2。

2.2 两组患者手术前后心功能的比较

两组患者在手术前心功能各项指标比较无明显统计学差异 ($P>0.05$);术后, MVP 组的 LVEF 和 LVEDD 水平高于 MVR 组, LAD 和 LVESD 水平则低于 MVR 组 ($P<0.05$),见表 3。

2.3 两组二尖瓣反流发生情况的比较

出院前及末次随访时, MVP 组二尖瓣反流发生率与 MVR 组比较差异无统计学意义 ($P>0.05$),见表 4。

表 2 两组患者围手术期情况比较($\bar{x} \pm s$)

Table 2 Comparison of the perioperative condition between two groups of patients ($\bar{x} \pm s$)

Groups	n	Operation time(min)	Volume of intraoperative bleeding(ml)	Extracorporeal circulation time(min)	Breathing time(h)	Duration of hospitalization(d)
MVP	27	252.51± 14.37	451.67± 40.31	101.47± 20.18	9.75± 0.48	12.84± 2.52
MVR	33	244.25± 15.24	490.35± 45.27	90.26± 19.87	11.62± 0.57	14.52± 3.24
t		2.143	3.457	2.159	13.557	2.203
P		0.036	0.001	0.035	<0.001	0.032

表 3 两组患者手术前后心功能指标的比较($\bar{x} \pm s$)

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

Groups	n	Time	LVEF(%)	LAD(mm)	LVESD(mm)	LVEDD(mm)
MVP	27	Before treatment	65.24± 7.02	53.42± 7.52	37.74± 6.54	56.93± 6.53
		After treatment	69.58± 8.36ab	40.16± 8.44 ab	30.18± 6.16 ab	49.88± 6.72 ab
MVR	33	Before treatment	66.22± 7.24	53.02± 7.47	36.57± 6.93	56.84± 6.42
		After treatment	62.04± 8.04 a	46.21± 8.84 a	33.68± 6.24 a	46.34± 6.55 a

Note: left ventricular ejection fraction (LVEF); Left atrium inner diameter, (LAD); Left ventricular contraction at the end of the inner diameter (LVESD); left ventricular end—diastolic dimension, (LVEDD); Compared with the same group before treatment, ^a $P<0.05$; Compared with control group at the same time, ^b $P<0.05$.

表 4 两组患者术后二尖瓣反流发生情况的比较[例(%)]

Table 4 Comparison of the incidence of mitral valve reflux after operation between two groups of patients [n(%)]

Groups	n	Time	Medium	Mild	Trace/None
MVP	27	Before discharge	0	3	24
		Last follow-up	1	6	20
MVR	33	Before discharge	0	2	31
		Last follow-up	0	8	25

表 5 两组患者术后并发症发生情况的比较[例(%)]

Table 5 Comparison of the incidence of postoperative complications between two groups of patients [n(%)]

Groups	n	Pulmonary infection	Low cardiac discharge	Poor incision healing	Total
MVP	27	1	2	1	3(11.1)
MVR	33	4	3	4	11(33.3)
χ^2			4.099		
P			0.043		

2.4 两组患者术后并发症发生情况比较

MVP 组患者的术后并发症的发生率显著低于 MVR 组 ($P<0.05$),见表 5。

3 讨论

二尖瓣关闭不全是由风湿性心脏瓣膜病所引发的疾病。研究表明风湿性二尖瓣膜病变 (Rheumatic mitral valve disease, RHVD)的病理过程为:心脏瓣叶出现纤维化,瓣叶缩短,面积变小,出现挛缩,瓣叶逐渐与腱索融合,伴随病情的继续进展,心脏瓣膜逐渐出现钙化、卷缩、硬化等改变,进而影响瓣膜的正常开合,从而引起机体出现瓣膜关闭不全^[8-10]。然而,单纯性的瓣

膜关闭不全比较少见,常伴随瓣膜的狭窄。随着我国外科医疗技术的快速发展,瓣膜材料及相关的技术工艺也得到了迅速发展,二尖瓣成形术与生物瓣置换术已成为临床常用的治疗二尖瓣关闭不全的两种手术治疗方式^[11]。然而,在手术方式的选择时,临床上却存在较大的争议。研究资料显示^[12]MVR 术后死亡率显著高于 MVP,但也有研究显示^[13]MVP 与 MVR 的术后死亡率无明显差异。

MVP 和 MVR 是临床中常用的两种手术治疗方式,其中 MVP 出现的比较早,技术也比较成熟。然而,MVP 具有自身的局限性,某些患者瓣膜无法采取 MVP 进行修复,而 MVR 的出现则很好的解决了这个问题,是不能采取 MVP 患者的最佳治

疗方法^[14,15]。MVR 的手术原理是采用人工瓣膜替换心脏原有的发生病变的瓣膜,使患者的心功能恢复正常。随着临床应用的增多,MVR 的弊端逐渐显现出来^[16]。患者置换人工瓣膜后需要持续使用抗凝药物,并且有研究显示 MVR 后患者出现室性早搏、栓塞、出血的概率呈上升趋势,可能会给患者造成严重的影响,尤其是术后患者需长期服用抗凝药物,严重影响患者的远期生存时间^[17,18]。本研究结果显示 MVR 组患者术中出血量、呼吸机使用时间、住院时间等围手术期指标显著高于 MVP 组,且术后并发症发生率也显著高于 MVP 组。

MVP 的手术原理^[19]是将患者瓣叶上出现病变的增生组织或钙化灶等剔除干净,由于 MVP 比 MVR 更好的保留了患者心脏腱索及乳头肌的功能^[20],能够最大限度的保留瓣叶与心室的联动,能恢复左心室的功能。MVP 采取物理性方法减少对心脏瓣叶的限制,使心脏瓣叶能基本恢复或者近似正常的完成开合的活动。此外,通过悬吊瓣环使心脏瓣叶的开放及重叠的面积增大,能更好的发挥心脏瓣膜的作用,从而解决患者血液循环动力不足的问题,改善患者受损的心脏功能^[21-22]。本研究结果提示术后 MVP 组 LVEF、LVESD 水平显著高于 MVR 组,而 LAD、LVESD 则显著低于 MVR 组,说明 MVP 组患者心脏功能的改善情况优于 MVR 组。但是 MVP 存在术后反流复发的风险,而这也是 MVP 的最大缺点。有研究报道二尖瓣成形术后二尖瓣反流复发率较高,术后 1 年为 30%,术后 5 年甚至超过 50%^[23-25]。本研究的结果虽然未发现 MVP 组术后二尖瓣反流显著高于 MVR 组,但 MVP 术后二尖瓣反流率过高是得到公认的^[26,27],其可能的原因一方面是患者术后左室重构的趋势难以逆转,乳头肌移位,瓣叶牵拉严重,致使二尖瓣出现反流;另一方面可能与 MVP 采取的单纯成形方式有关。因此,有研究^[28,29]认为在环缩术的基础上,结合患者左室的形态、瓣叶和瓣下结构病理情况修复受损瓣下结构以降低复发率。

本研究结果显示 MVP 组手术时间及体外循环时间均显著高于 MVR 组,这与相关研究结果一致,主要原因是手术过程中需要较长的时间进行阻断及手术修复。同时,由于 MVP 手术二尖瓣反流率较高,需要对 MVP 的手术指征进行严格掌控。结合本研究我们认为对于风湿性二尖瓣重度关闭不全的患者,MVP 的手术适应症为:① 病变瓣膜弹性尚可,病变主要是交界黏连;② 瓣膜特别是前瓣主要为轻度纤维性增生;③ 钙化面积小于瓣膜面积的 1/3;④ 病变瓣膜剔除钙化及增生后不影响其活动性,不存在僵硬状态;⑤ 手术前已经对风湿活动进行有效的控制。从病理角度来讲,MVP 不适合严重瓣膜病变患者,因为尽管可以通过手术尽可能修复病变瓣膜,但是手术后瓣膜仍旧不能避免变形、僵硬和活动受限的缺陷。本研究中,有 3 例患者在 MVP 术前术后瓣膜改善情况并不明显,影响了术后疗效。因此,需严格掌握 MVP 的手术指征,避免实施无效手术,加重患者的身心负担。

综上所述,对于风湿性二尖瓣重度关闭不全的治疗过程,采用 MVP 的临床疗效优于 MVR,MVP 能显著纠正二尖瓣的病理改变,心脏功能恢复较好,术后疗效确切,尤其是患者术后无需长期服用抗凝药物,避免了因此而产生的诸多副作用。术前需严格掌控适应症,术后预防和控制风湿活动。但 MVP 术二

尖瓣反流率略高,需继续改进手术方法以降低反流复发率。

参考文献(References)

- [1] Muller D W, Farivar R S, Jansz P, et al. Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation: A Global Feasibility Trial [J]. *Journal of the American College of Cardiology*, 2017, 69(4): 381-391
- [2] Duncan A, Daqa A, Yeh J, et al. Transcatheter Mitral Valve Replacement: Long-Term Outcomes of First-In-Man Experience with an Apically Tethered Device - A Case Series from a Single Centre[J]. *Eurointervention*, 2017, 13(9): e1047-e1057
- [3] Bourguignon T, Espitalier F, Pantaleon C, et al. Bioprosthetic mitral valve replacement in patients aged 65 years or younger: long-term outcomes with the Carpentier-Edwards PERIMOUNT pericardial valve[J]. *Eur J Cardiothorac Surg*, 2018, 54(2): 302-309
- [4] Van Hagen I M, Thorne S A, Taha N, et al. Pregnancy Outcomes in Women With Rheumatic Mitral Valve Disease: Results From the Registry of Pregnancy and Cardiac Disease[J]. *Circulation*, 2018, 137(8): 806-816
- [5] Kim D J, Joo H C, Lee S H, et al. Natural history of mild aortic valve disease untreated at the time of rheumatic mitral valve replacement[J]. *Interactive Cardiovascular & Thoracic Surgery*, 2018, 27(6): 828-835
- [6] Greene A, Russell C, Harris S, et al. Left Thoracotomy for Redo Mitral Valve Replacement in Giant Left Atrium and Severe Pectus Excavatum [J]. *Annals of Thoracic Surgery*, 2018, 4975 (18) 30492-30502
- [7] Regueiro A, Granada J F, Dagenais F, et al. Transcatheter Mitral Valve Replacement: Insights From Early Clinical Experience and Future Challenges[J]. *J Am Coll Cardiol*, 2017, 69(17): 2175-2192
- [8] Liu Y, Guo G L, Wen B, et al. Feasibility and effectiveness of percutaneous balloon mitral valvuloplasty under echocardiographic guidance only[J]. *Echocardiography*, 2018, 71(11): 1507-1511
- [9] Rastogi M, Sarkar S, Makol A, et al. Anti-endothelial cell antibody rich sera from rheumatic heart disease patients induces proinflammatory phenotype and methylation alteration in endothelial cells[J]. *Genes & Diseases*, 2018, 5(3): 275-289
- [10] Antunes M J. Repair for rheumatic mitral valve disease. The controversy goes on![J]. *Heart*, 2018, 104(10): 796-797
- [11] Berzingi C, Badhwar V, Alqahtani F, et al. Contemporary outcomes of isolated bioprosthetic mitral valve replacement for mitral regurgitation[J]. *Open Heart*, 2018, 5(2): 1-8
- [12] Zuern C S, Floss N, Mueller I I, et al. Galectin-3 is associated with left ventricular reverse remodeling and outcome after percutaneous mitral valve repair[J]. *Int J Cardiol*, 2018, 263: 104-110
- [13] Kumano H, Shuntoh K, Yamaguchi A. Beating Mitral Valve Replacement for Functional Mitral Regurgitation after Cardiac Resynchronization Therapy; Report of a Case [J]. *Kyobu Geka the Japanese Journal of Thoracic Surgery*, 2018, 71(3): 195-198
- [14] Reza M M, Hasan M K, Sarker R, et al. Electrocautery Maze for Chronic Atrial Fibrillation in Patients Undergoing Mitral Valve Replacement[J]. *University Heart Journal*, 2018, 13(2): 1-4
- [15] Ostovar R, Claus T, Hartrumpf M, et al. MitraClip for High-Risk Patients with Significant Mitral Insufficiency: Shall We Unreservedly Recommend It?[J]. *Thoracic & Cardiovascular Surgeon*, 2017, 65(1):

- S1-S110
- [16] Ejiofor J I, Hirji S A, Val R D, et al. Outcomes of Repeat Mitral Valve Replacement In Patients With Prior Mitral Surgery: A Benchmark For Transcatheter Approaches [J]. *Journal of Thoracic & Cardiovascular Surgery*, 2018, 156(2): 619-627
- [17] Matsunaga Y, Ishimura M, Nagata H, et al. Thrombotic microangiopathy in a very young infant with mitral valvuloplasty[J]. *Pediatrics & Neonatology*, 2018, 59(6): 595-599
- [18] Huang T T, Lin J H. Perinatal anticoagulation management of pregnant women with cardiac prosthetic valve replacement [J]. *Acta Metallurgica Sinica*, 2017, 33(7): 667-671
- [19] Prosnitz A R, Drogosz M, Marshall A C, et al. Early hemodynamic changes after fetal aortic stenosis valvuloplasty predict biventricular circulation at birth[J]. *Prenatal Diagnosis*, 2018, 38(4): 286-292
- [20] Gaspardone A, D'Errico F, Iamele M, et al. Single Transseptal Puncture for Left Atrial Appendage Closure and Mitral Valvuloplasty With Total Cerebrovascular Protection in a Patient With Acute Embolic Cerebral Ischemia [J]. *JACC: Cardiovascular Interventions*, 2018, 11(13): 1302-1306
- [21] Khalighi A H, Drach A, Gorman R C, et al. Multi-resolution geometric modeling of the mitral heart valve leaflets [J]. *Biomechanics & Modeling in Mechanobiology*, 2017, 17(4): 1-16
- [22] Yokoyama S, Kanemoto I, Mihara K, et al. Treatment of severe mitral regurgitation caused by lesions in both leaflets using multiple mitral valve plasty techniques in a small dog [J]. *Open Veterinary Journal*, 2017, 7(4): 328-331
- [23] De Bonis M, Lapenna E, Verzini A, et al. Recurrence of mitral regurgitation parallels the absence of left ventricular reverse remodeling after mitral repair in advanced dilated cardiomyopathy[J]. *Ann Thorac Surg*, 2008, 85(3): 932-939
- [24] Naruse H, Kawada N, Muramatsu K, et al. Huge Left Thrombosis after Mitral Valvuloplasty and Maze Procedure; Report of a Case[J]. *Kyobu Geka*, 2018, 71(3): 204-207
- [25] Crabtree T D, Bailey M S, Moon M R, et al. Recurrent of mitral regurgitation and risk factors for early and late mortality after mitral valve repair for functional ischemic mitral regurgitation [J]. *Ann Thorac Surg*, 2008, 85(5): 1537-1542
- [26] Gajjala O R, Durgaprasad R, Velam V, et al. New integrated approach to percutaneous mitral valvuloplasty combining Wilkins score with commissural calcium score and commissural area ratio[J]. *Echocardiography*, 34(9): 1284-1291
- [27] Kazemi S D. Early Outcomes, Complications and Hemodynamic results of 365 Cases of Percutaneous Transseptal Mitral Commissurotomy [J]. *Kowsar Medical Journal*, 2017, 22 (2): 2251-2259
- [28] Adhikari C M, Malla R, Koirala R, et al. Percutaneous transluminal mitral valvuloplasty in post Mitral valve repair and Aortic valve replacement patient[J]. *Egyptian Heart Journal*, 2017, 70(2): 57-58
- [29] Kim D, Chung H, Nam J H, et al. Predictors of Long-Term Outcomes of Percutaneous Mitral Valvuloplasty in Patients with Rheumatic Mitral Stenosis[J]. *Yonsei Medical Journal*, 2018, 59(2): 273-278

(上接第 3171 页)

- [18] 郑颖, 常新, 刘存明, 等. 塞来昔布对骨关节炎大鼠疼痛评分和 SP 表达的影响 [J]. *中华临床医师杂志 (电子版)*, 2013, 7(18): 8308-8311
- [19] Igonkina SI, Vetrile LA, Kukushkin ML. Effect of anti-norepinephrine antibodies on the development of neuropathic pain [J]. *Bull Exp Biol Med*, 2017, 162(6): 714-717
- [20] Malet M, Leiguarda C, Gastón G, et al. Spinal activation of the NPY Y1 receptor reduces mechanical and cold allodynia in rats with chronic constriction injury[J]. *Peptides*, 2017, 6(92): 38-45
- [21] 严长兰. 多巴胺受体阻滞剂联合吗啡术后镇痛的疗效观察[J]. *青海医药杂志*, 2017, 47(12): 14-17
- [22] Taylor AM, Becker S, Schweinhardt P, et al. Mesolimbic dopamine signaling in acute and chronic pain: implications for motivation, analgesia, and addiction[J]. *Pain*, 2016, 157(6): 1194-1198
- [23] Liu HF, Ren QM, Wang ZB, et al. Comparison of acute phase protein and hemodynamic variables in dogs undergoing video-assisted thoracoscopic vs. open pneumonectomy [J]. *Exp Ther Med*, 2017, 13 (5): 2391-2398
- [24] 颜姬, 何才, 戴珩, 等. 不同剂量纳布啡联合芬太尼对腹腔镜子宫肌瘤挖除术患者术后镇痛的效果分析 [J]. *第三军医大学学报*, 2018, 40(17): 1595-1598
- [25] Sikora M, Krol J, Nowak M, et al. The usefulness of uterine lavage and acute phase protein levels as a diagnostic tool for subclinical endometritis in Icelandic mares[J]. *Acta Vet Scand*, 2016, 58(1): 50
- [26] 刘辉, 李丕彬, 韩景田, 等. 硬膜外自控镇痛对老年髋关节置换术患者术后镇痛效果及 IL-6、IL-10 和 TNF- α 的影响[J]. *检验医学与临床*, 2017, 14(24): 3626-3628
- [27] Zangene M, Ashoori Barmchi A, Rezaei M, et al. The comparison between the serum level of interleukin-6 in women with acute ovarian torsion and other causes of lower abdominal pain [J]. *J Obstet Gynaecol*, 2017, 37 (2): 223-227
- [28] Zhou X, Li J, Deng S, et al. Ropivacaine at different concentrations on intrapartum fever, IL-6 and TNF- α in parturient with epidural labor analgesia[J]. *Exp Ther Med*, 2019, 17(3): 1631-1636
- [29] 黄传钟, 李洁羽, 陈淑萍, 等. IL-2、IL-4、IL-6、IFN- γ 、IL-17 A 在肝癌组织中表达及其与乙肝病毒感染的关系 [J]. *中国免疫学杂志*, 2015, 31(4): 527-530
- [30] Buchbinder EI, Dutcher JP, Daniels GA, et al. Therapy with high-dose Interleukin-2 (HD IL-2) in metastatic melanoma and renal cell carcinoma following PD1 or PDL1 inhibition [J]. *J Immunother Cancer*, 2019, 7(1): 49