

# 保肢与截肢治疗后骨肉瘤患者肢体功能及生活质量的 Meta 分析

罗明星<sup>1</sup>, 刘丙根<sup>1</sup>, 罗文礼<sup>1</sup>, 付有伟<sup>2</sup>, 庞清江<sup>2</sup>

(1. 浙江省宁波市杭州湾医院, 浙江 宁波 315010;

2. 浙江省宁波市第二医院, 浙江 宁波 315010)

**摘要 目的:**系统评价保肢与截肢治疗后骨肉瘤患者的肢体功能及生活质量。**方法:**以计算机检索 The Cochrane Library (2016 年第 12 期)、PubMed、Ovid、Spinger Link、Elsevier、CNKI、WanFang Data 1970 年 1 月 1 日至 2016 年 12 月 31 日所有有关比较保肢与截肢治疗后骨肉瘤患者肢体功能及生活质量的中、英文文献,同时手工检索纳入文献的参考文献。由 2 位研究人员独立进行文献检索、筛选,采用 Cochrane 协作网提供的 Revman5.0 软件进行 Meta 分析。**结果:**共检出文献 1301 篇,经筛选后最终纳入 10 篇文献,均为英文文献。总样本量 614 例,保肢治疗组 350 例、截肢治疗组 264 例。Meta 分析结果显示,2 组患者治疗后的多伦多保肢评分系统评分比较,差异无统计学意义 [ $WMD = -0.23, 95\% CI (-0.82, 0.36)$ ];保肢组的简明健康状况调查表评分高于截肢组 [ $WMD = -0.26, 95\% CI (-0.46, -0.06)$ ]。**结论:**与截肢治疗相比,采用保肢治疗后骨肉瘤患者的生活质量更高,但肢体功能与前者相当。

**关键词** 骨肉瘤;截肢术;保肢治疗;功能恢复;生活质量;Meta 分析;系统评价

## Comparison of limb salvage and amputation on limb function and life quality of patients with osteosarcoma: a meta analysis

LUO Mingxing<sup>1</sup>, LIU Binggen<sup>1</sup>, LUO Wenli<sup>1</sup>, FU Youwei<sup>2</sup>, PANG Qingjiang<sup>2</sup>

1. Hangzhou Bay Hospital of Ningbo City, Ningbo 315010, Zhejiang, China

2. The Second Hospital of Ningbo City, Ningbo 315010, Zhejiang, China

**ABSTRACT Objective:**To systematically review limb function and life quality of patients with osteosarcoma after limb salvage and amputation. **Methods:**All the Chinese and English articles about limb function and life quality of patients with osteosarcoma after limb salvage and amputation included from January 1, 1970 to December 31, 2016 were retrieved from the Cochrane Library (2016, No. 12), PubMed, Ovid, Spinger Link, Elsevier, China national knowledge internet and WanFang Data through computer. Meanwhile, all the references in the included articles were manual retrieved. The articles were searched and screened independently by two researchers. The articles were evaluated by using Cochrane system and a Meta-analysis was conducted by using Revman 5.0 software. **Results:**One thousand three hundred and one articles were searched out. After screening, 10 English articles (614 patients) were included in the final analysis, 350 patients in limb salvage group and 264 patients in amputation group. The result of Meta-analysis demonstrated that there was no statistical difference in posttreatment Toronto extremity salvage scores between the 2 groups ( $WMD = -0.23, 95\% CI (-0.82, 0.36)$ ) and the short form 36 health survey questionnaire (SF-36) scores were higher in limb salvage group compared to amputation group ( $WMD = -0.26, 95\% CI (-0.46, -0.06)$ ). **Conclusion:**The patients with osteosarcoma can obtain better life quality after limb salvage compared to amputation, while the two treatments are similar to each other in limb function.

**Key words** osteosarcoma; amputation; limb salvage; recovery of function; quality of life; Meta-Analysis; systematic review

骨肉瘤是儿童最常见的原发性恶性骨肿瘤,好发于血液循环丰富的干骺端<sup>[1]</sup>。以往骨肉瘤的治疗仅限于手术截肢,5 年总体生存率仅为 20% 左右<sup>[2]</sup>。近年来随着新辅助化疗药物的使用,骨肉瘤患者的 5 年

生存率大为提高,因此目前 80% ~ 90% 骨肿瘤患者,甚至是高度恶性骨肉瘤患者可以考虑选择保肢治疗<sup>[3]</sup>。有研究表明,与截肢治疗相比,保肢治疗骨肉瘤可部分保留患者肢体功能、改善生活质量<sup>[4-8]</sup>。但也有部分研究表明,2 种方式治疗后患者的生活质量无差异<sup>[9-10]</sup>。本研究通过收集保肢与截肢治疗骨肉

瘤的对比研究文献,运用循证医学的方法探讨了 2 种方式治疗后患者肢体功能和生活质量的差异。

## 1 资料与方法

**1.1 文献纳入标准** ①国内外公开发表的比较保肢治疗(保肢组)和截肢治疗(截肢组)的中文或英文文献;②研究对象为经 X 线、CT、MRI 及活检确诊的骨肉瘤患者;③有明确的结局数据;④观察指标中包括国际骨与软组织肿瘤协会(musculoskeletal tumor society, MSTs)评分<sup>[11]</sup>、多伦多保肢评分系统(Toronto extremity salvage score, TESS)评分<sup>[12]</sup>、简明健康状况调查表(short form 36 health survey questionnaire, SF-36)评分中的 1 种。

**1.2 文献排除标准** ①最终进行对比观察的病例数 < 4 例者;②未阐明研究结果者;③评分系统不标准者;④统计学处理方法不正确者。

**1.3 文献检索** 应用计算机检索 The Cochrane Library(2016 年第 12 期)、PubMed、Ovid、Spinger Link、Elsevier、CNKI、WanFang Data。检索时间为 1970 年 1 月 1 日至 2016 年 12 月 31 日。英文检索词包括 osteosarcoma、limb-salvage、amputation、quality of life、functional outcome;中文检索词包括骨肉瘤、保肢治疗、截肢治疗、功能结果、生活质量。同时手工检索纳入文献的参考文献。

**1.4 文献筛选及质量评价** 由 2 名研究人员分别独立进行文献检索及筛选,将各自筛选出的文献隐去标题、作者姓名及发表时间等信息后,再相互审核彼此的检索结果,出现争议时由第 3 名研究人员协助决定或集体讨论解决。采用纽卡斯尔-渥太华量表(the Newcastle-Ottawa scale, NOS)<sup>[13]</sup>对纳入文献的方法学质量进行评价,具体包括研究人群选择、可比性、暴露评价或结果评价,满分 9 分,剔除评分 ≤ 5 分的文献。

**1.5 数据统计分析** 使用 Cochrane 协作网提供的 RevMan 5.0 软件进行数据统计分析。先对各项研究结果进行同质性检验,若各研究结果之间具有同质性( $I^2 \leq 50\%$ )则采用固定效应模型 Meta 分析,若各研究结果之间不具有同质性( $I^2 > 50\%$ )则采用随机效应模型 Meta 分析。TESS 评分和 SF-36 评分均以 WMD 作为综合效应量。95% CI 的上下限均大于 0 或均小于 0 为差异有统计学意义,95% CI 包含 0 为差异无统计学意义。

## 2 结果

**2.1 文献检索及质量评价结果** 共检出文献 1301 篇,经筛选后最终纳入 10 篇文献<sup>[14-23]</sup>,均为英文文献。总样本量 614 例,保肢组 350 例、截肢组 264 例。纳入文献的基本特征见表 1。

表 1 纳入文献的基本特征

文献基本信息	样本量(例)		评价指标	NOS 评分
	保肢组	截肢组		
Mavrogenis 2012 <sup>[14]</sup>	23	19	MSTS 评分	7
Bekkering 2010 <sup>[15]</sup>	26	22	SF-36 评分	9
Robert 2010 <sup>[16]</sup>	33	24	TESS 评分	8
Yonemoto 2007 <sup>[17]</sup>	14	19	SF-36 评分	7
Renard 2000 <sup>[18]</sup>	22	18	MSTS 评分	8
Davis 1999 <sup>[19]</sup>	24	12	TESS 评分、SF-36 评分	7
Aksnes 2008 <sup>[20]</sup>	67	51	MSTS 评分、TESS 评分	8
Johansen 1998 <sup>[21]</sup>	89	58	MSTS 评分	8
Mason 2013 <sup>[22]</sup>	38	34	SF-36 评分	7
Akahane 2007 <sup>[23]</sup>	14	7	SF-36 评分	8

MSTS 为国际骨与软组织肿瘤协会;TESS 为多伦多保肢评分系统;SF-36 为简明健康状况调查表

## 2.2 Meta 分析结果

**2.2.1 MSTS 评分** 4 篇文献<sup>[14,18,20-21]</sup>记录了 2 组患者治疗后的 MSTS 评分,但数据均不完整(只有中位数,未提供均数和标准差),无法进行合并分析。

**2.2.2 TESS 评分** 3 篇文献<sup>[16,19-20]</sup>记录了 2 组患者治疗后的 TESS 评分,但文献[20]数据均不完

整(只有中位数,未提供均数和标准差),最终仅 2 篇文献纳入合并分析。2 项研究间<sup>[16,19]</sup>不具有同质性( $I^2 = 46\%$ ),故采用随机效应模型进行 Meta 分析。2 组患者治疗后的 TESS 评分比较,差异无统计学意义[WMD = -0.23, 95% CI(-0.82, 0.36)]。见图 1。

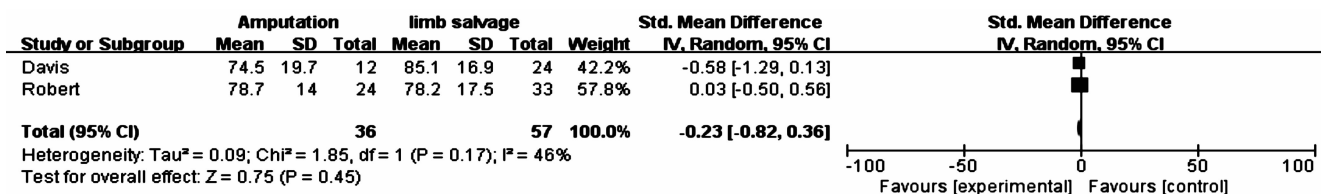


图 1 骨肉瘤患者保肢治疗和截肢治疗后多伦多保肢评分系统评分比较

2.2.3 SF-36 评分 5 篇文献[15,17,19,22-23]记录了 2 组患者治疗后的 SF-36 评分,各研究之间不具有同质性( $I^2 = 76\%$ ),故采用随机效应模型进行 Meta 分析。保肢组的 SF-36 评分高于截肢组 [ $WMD = -0.26, 95\% CI (-0.46, -0.06)$ ]。见图 2。

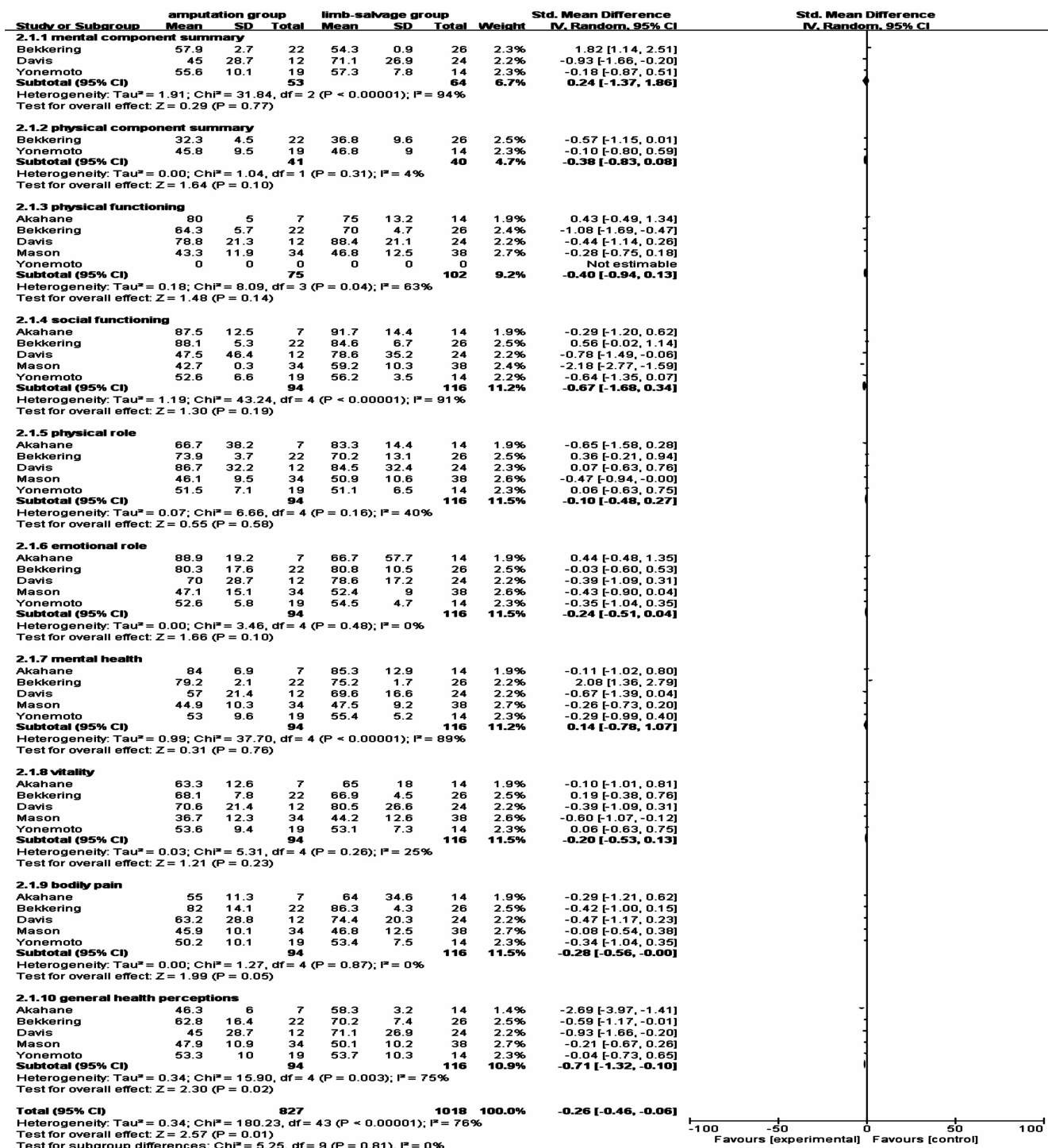


图 2 骨肉瘤患者保肢治疗和截肢治疗后简明健康状况调查表评分比较

**2.3 发表偏倚分析结果** 以 SF-36 量表中心体功能评分为效应指标的文献是合并纳入 Meta 分析数目最多的,故对其进行偏倚分析。漏斗图(图 3)显示各研究分布比较对称,提示本研究纳入的文献不存在发表偏倚。

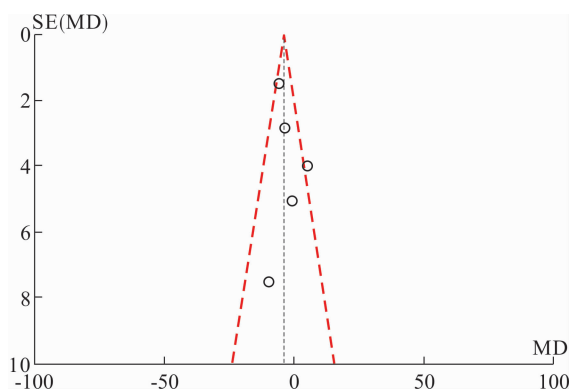


图 3 2 组骨肉瘤患者简明健康状况调查表中  
躯体功能评分的漏斗图

### 3 讨论

骨肉瘤是原发性恶性肿瘤中发病率最高的一种。20 世纪 70 年代以前,截肢是治疗骨肉瘤的唯一办法,化疗的应用显著提高了患者的生存率和保肢率。保肢治疗虽然能保留部分肢体功能,提高患者的生活质量,但治疗的过程相对漫长、花费巨大,而且可能需要多次手术。

对骨肉瘤的患者选择保肢治疗还是截肢治疗,往往涉及患者生存、生理、心理、生活质量、肢体功能等多方面复杂的因素。目前国内外许多学者认为保肢治疗已逐渐成为治疗骨肉瘤的首选方法,截肢治疗仅在骨肉瘤边界完全切除无法保证的情况下施行。截肢治疗后患者需要安装假肢,存在发生感染、出血、残肢生长过度、幻肢感等并发症的风险。安装假肢感染意味着患者可能失去全部肢体功能或需要进行二次截肢手术等。Aksnes 等<sup>[20]</sup>对 118 例接受保肢或截肢治疗的骨肉瘤患者进行了分析,术后随访 5 年发现截肢组患者中位 MSTS 评分低于保肢组,而 2 组的中位 TESS 评分并无显著差异。Eiser 等<sup>[24]</sup>研究发现,保肢与截肢治疗骨肉瘤患者术后的生活质量差异不明显,但保肢患者术后日常生活能力较强,行走时需要帮助的几率较低。Robert 等<sup>[16]</sup>研究发现,肢体功能康复效果越差,生活质量越低,而截肢手术本身并不影响生活质量。

目前的证据显示,与截肢治疗相比,采用保肢治疗后骨肉瘤患者生活质量更高,但肢体功能与前者相

当。本研究的不足在于:①收集到的文献数量较少,且均为回顾性研究;②纳入分析的文献中随访时间不一,也未能对不同随访时间肢体功能及生活质量进行亚组分析;③纳入文献的研究对象仅针对低度恶性骨肉瘤;④纳入文献中截肢组的手术方式包括了膝上、膝下、髌关节离断多种截肢术式,而不同水平的截肢术对患者术后的肢体功能和生活质量有一定影响。

### 4 参考文献

- [1] LUETKE A, MEYERS PA, LEWIS I, et al. Osteosarcoma treatment—where do we stand? A state of the art review[J]. Cancer Treat Rev, 2014, 40(4): 523–532.
- [2] JIANG F, SHI Y, LI GJ, et al. A meta-analysis of limb-salvage versus amputation in the treatment of patients with Enneking pathologic fracture osteosarcoma[J]. Indian J Cancer, 2015, 51(Suppl 2): e21–e24.
- [3] ABED R, GRIMER R. Surgical modalities in the treatment of bone sarcoma in children[J]. Cancer Treat Rev, 2010, 36(4): 342–347.
- [4] HOLZER LA, SEVELDA F, FRABERGER G, et al. Body image and self-esteem in lower-limb amputees[J]. PLoS One, 2014, 9(3): e92943.
- [5] PEIRANO AH, FRANZ RW. Spirituality and quality of Life in limb amputees[J]. Int J Angiol, 2012, 21(1): 47–52.
- [6] HAN G, WANG Y, BI WZ. Study on the health-related quality of Life in patients after surgery for malignant bone tumors[J]. Asian Pac J Cancer Prev, 2012, 13(1): 127–130.
- [7] OTTAVIANI G, ROBERT RS, HUH WW, et al. Sociooccupational and physical outcomes more than 20 years after the diagnosis of osteosarcoma in children and adolescents: limb salvage versus amputation[J]. Cancer, 2013, 119(20): 3727–3736.
- [8] MALEK F, SOMERSON JS, MITCHEL S, et al. Does limb-salvage surgery offer patients better quality of Life and functional capacity than amputation? [J]. Clin Orthop Relat Res, 2012, 470(7): 2000–2006.
- [9] EISER C. Assessment of health-related quality of Life after bone cancer in young People: easier said than done[J]. Eur J Cancer, 2009, 45(10): 1744–1747.
- [10] BARR RD, WUNDER JS. Bone and soft tissue sarcomas are often curable—but at what cost?: a call to arms (and legs)[J]. Cancer, 2009, 115(18): 4046–4054.
- [11] ENNEKING WF, DUNHAM W, GEBHARDT MC, et al. A system for the functional evaluation of reconstructive proce-

- dures after surgical treatment of tumors of the musculoskeletal system[J]. Clin Orthop Relat Res, 1993, (286): 241 – 246.
- [12] DAVIS AM, WRIGHT JG, WILLIAMS JI, et al. Development of a measure of physical function for patients with bone and soft tissue sarcoma[J]. Quality of Life Res, 1996, 5(5): 508 – 516.
- [13] WELLS GA, SHEA B J, O'CONNELL D, et al. The Newcastle – Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta – analyses[EB/OL]. [2016 – 12 – 31] [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).
- [14] MAVROGENIS AF, ABATI CN, ROMAGNOLI C, et al. Similar survival but better function for patients after limb salvage versus amputation for distal tibia osteosarcoma[J]. Clin Orthop Relat Res, 2012, 470(6): 1735 – 1748.
- [15] BEKKERING WP, VLIET VLIELAND TP, KOOPMAN HM, et al. Quality of Life in young patients after bone tumor surgery around the knee joint and comparison with healthy controls[J]. Pediatr Blood Cancer, 2010, 54(5): 738 – 745.
- [16] ROBERT RS, OTTAVIANI G, HUH WW, et al. Psychosocial and functional outcomes in long – term survivors of osteosarcoma: a comparison of limb – salvage surgery and amputation[J]. Pediatr Blood Cancer, 2010, 54(7): 990 – 999.
- [17] YONEMOTO T, ISHII T, TAKEUCHI Y, et al. Education and employment in long – term survivors of high – grade osteosarcoma: a Japanese single – center experience[J]. Oncology, 2007, 72(5/6): 274 – 278.
- [18] RENARD AJ, VETH RP, SCHREUDER HW, et al. Function and complications after ablative and limb – salvage therapy in lower extremity sarcoma of bone[J]. J Surg Oncol, 2000, 73(4): 198 – 205.
- [19] DAVIS AM, DEVLIN M, GRIFFIN AM, et al. Functional outcome in amputation versus limb sparing of patients with lower extremity sarcoma: a matched case-control study[J]. Arch Phys Med Rehabil, 1999, 80(6): 615 – 618.
- [20] AKSNES LH, BAUER HC, JEBSEN NL, et al. Limb – sparing surgery preserves more function than amputation: a Scandinavian sarcoma group study of 118 patients[J]. J Bone Joint Surg Br, 2008, 90(6): 786 – 794.
- [21] JOHANSEN R, NIELSEN OS, KELLER J. Functional outcome in sarcomas treated with limb – salvage surgery or amputation[J]. Sarcoma, 1998, 2(1): 19 – 23.
- [22] MASON GE, AUNG L, GALL S, et al. Quality of Life following amputation or limb preservation in patients with lower extremity bone sarcoma[J]. Frontiers in Oncology, 2013, 3: 210.
- [23] AKAHANE T, SHIMIZU T, ISOBE K, et al. Evaluation of postoperative general quality of life for patients with osteosarcoma around the knee joint[J]. J Pediatr Orthop B, 2007, 16(4): 269 – 272.
- [24] EISER C, DARLINGTON AS, STRIDE CB, et al. Quality of Life implications as a consequence of surgery: limb salvage, primary and secondary amputation[J]. Sarcoma, 2001, 5(4): 189 – 195.

(2017-03-30 收稿 2017-06-22 修回)

(上接第 40 页)

- [12] 王琳珏, 马宝通, 李恩琪. 成人锁骨中段骨折手术治疗与非手术治疗的 Meta 分析[J]. 中华骨科杂志, 2011, 31(4): 308 – 315.
- [13] ANDERSEN K, JENSEN PO, LAURITZEN J. Treatment of clavicular fractures. Figure – of – eight bandage versus a simple sling[J]. Acta Orthop Scand, 1987, 58(1): 71 – 74.
- [14] ZLOWODZKI M, ZELLE BA, COLE PA, et al. Treatment of acute midshaft clavicle fractures: systematic review of 2144 fractures; on behalf of the Evidence – Based Orthopaedic Trauma Working Group[J]. J Orthop Trauma, 2005, 19(7): 504 – 507.
- [15] HILL JM, MCGUIRE MH, CROSBY LA. Closed treatment of displaced middle – third fractures of the clavicle gives poor results[J]. J Bone Joint Surg Br, 1997, 79(4): 537 – 539.
- [16] ESKOLA A, VAINIONPÄÄ S, MYLLYNNEN P, et al. Outcome of clavicular fracture in 89 patients[J]. Arch Orthop Trauma Surg, 1986, 105(6): 337 – 338.
- [17] CHAN Y, JUPITER B, LEFFERT D, et al. Clavicle malunion[J]. J Shoulder Elbow Surg, 1999, 8(4): 287 – 290.
- [18] NOWAK J, HOLGERSSEN M, LARSSON S. Can we predict long-term sequelae after fractures of the clavicle based on initial findings? A prospective study with nine to ten years of follow-up[J]. J Shoulder Elbow Surg, 2004, 13(5): 479 – 486.

(2017-03-01 收稿 2017-06-02 修回)

反映学术进展 引领学科发展