本文引用:胡光辉,刘亚峰. 唑来膦酸注射液对行髋关节置换术患者骨代谢的影响[J]. 新乡医学院学报,2023,40(10):960-964. DOI:10.7683/xxyxyxb.2023.10.010.

【临床研究】

唑来膦酸注射液对行髋关节置换术患者骨代谢的影响

胡光辉[1], 刘亚峰[2]

〔1. 开封市中心医院骨科,河南 开封 475000;2. 河南省洛阳正骨医院(河南省骨科医院)人工关节翻修科,河南 郑州 450000〕

摘要: **目的** 探讨唑来膦酸注射液对行髋关节置换术患者骨代谢的影响。**方法** 选择 2017 年 1 月至 2020 年 7 月于开封市中心医院骨科行髋关节置换术的 199 例患者为研究对象,根据治疗方式将患者分为对照组($n=93$)和观察组($n=106$)。2 组患者均行非骨水泥型全髋关节置换术,对照组患者于术后第 2 天口服碳酸钙 D3 咀嚼片,每次 600 mg,每日睡前 1 次,连续用药 2 a;观察组患者在对照组治疗基础上,分别于术后第 7 天及术后 1、2 a 各给予唑来膦酸注射液(100 mL)静脉滴注 1 次,滴注时间不少于 15 min。于术前及术后 2 a 分别采集 2 组患者静脉血,采用酶联免疫吸附法检测血清骨代谢指标水平,包括骨吸收标志物Ⅰ型胶原羧基端肽 β 特殊序列(β-CTX)、抗酒石酸酸性磷酸酶-5b(TRAP-5b)和骨形成标志物骨钙素(BGP)、骨特异性碱性磷酸酶(BALP)、Ⅰ型前胶原羧基末端肽(PICP)。分别于术前、术后 1 a 及术后 2 a,采用双能 X 射线吸收测定法及 Gruen 分区法检测 2 组患者假体周围骨密度值。采用 X 线片测量 2 组患者术后 2 a 股骨假体下沉距离。分别于术前及术后 2 a,采用 Harris 髋关节评分评估 2 组患者的髋关节功能。**结果** 术前,2 组患者的血清 β-CTX、TRAP-5b、BGP、BALP、PICP 水平比较差异无统计学意义($P>0.05$);术后 2 a,观察组患者的血清 β-CTX、TRAP-5b 水平显著低于对照组($P<0.05$),血清 BGP、BALP、PICP 水平显著高于对照组($P<0.05$);2 组患者术后 2 a 的血清 β-CTX、TRAP-5b 水平均显著低于术前($P<0.05$),血清 BGP、BALP、PICP 水平均显著高于术前($P<0.05$)。术前及术后 1 a,2 组患者的假体周围平均骨密度比较差异无统计学意义($P>0.05$);术后 2 a,观察组患者的假体周围平均骨密度显著高于对照组($P<0.05$);2 组患者术后 1 a 和术后 2 a 的假体周围平均骨密度均显著低于术前($P<0.05$);对照组患者术后 2 a 的假体周围平均骨密度显著低于术后 1 a($P<0.05$);观察组患者术后 1 a 与术后 2 a 的假体周围平均骨密度比较差异无统计学意义($P>0.05$)。术后 2 a,对照组和观察组患者的股骨假体下沉距离分别为(0.74 ± 0.20)、(0.57 ± 0.21) mm;观察组患者的股骨假体下沉距离显著小于对照组($t=5.844$,$P<0.05$)。术前,2 组患者的 Harris 髋关节各维度评分及总评分比较差异无统计学意义($P>0.05$);术后 2 a,观察组患者的 Harris 髋关节各维度评分及总评分均显著高于对照组($P<0.05$);2 组患者术后 2 a 的 Harris 髋关节各维度评分及总评分均显著高于术前($P<0.05$)。**结论** 唑来膦酸注射液可有效改善髋关节置换术后患者的骨转换指标,抑制骨吸收和减少假体周围骨量,增加假体周围骨密度,延缓术后假体下沉,改善患者髋关节功能,值得临床推广。

关键词: 唑来膦酸;髋关节置换术;骨代谢;骨密度

中图分类号: R687.4 **文献标志码**: A **文章编号**: 1004-7239(2023)10-0960-05

Effect of zoledronic acid injection on bone metabolism in patients undergoing hip replacement

HU Guanghui[1], LIU Yafeng[2]

〔1. *Department of Orthopedics, Kaifeng Central Hospital, Kaifeng* 475000, *Henan Province, China*; 2. *Department of Artificial Joint Revision, Luoyang Orthopedic-Traumatological Hospital of Henan Province (Henan Provincial Orthopedic Hospital), Zhengzhou* 450000, *Henan Province, China*〕

Abstract: **Objective** To investigate the influence of zoledronic acid injection on bone metabolism in patients undergoing hip replacement. **Methods** A total of 199 patients who underwent hip replacement in the Department of Orthopedics, Kaifeng Central Hospital from January 2017 to July 2020 were selected as the research subjects. According to the treatment methods, the patients were divided into the control group ($n=93$) and the observation group ($n=106$). The patients in the two groups underwent cementless total hip replacement. The patients in the control group took calcium carbonate D3 chewable tablets on the second postoperative day orally, 600 mg each time, once a day at bedtime for 2 years. On the basis of the treatment of the

DOI:10.7683/xxyxyxb.2023.10.010

收稿日期:2022-11-26

作者简介:胡光辉(1982-),男,河南开封人,学士,副主任医师,研究方向:骨关节外科相关疾病。

control group, the patients in the observation group were given intravenous infusion of 100 mL zoledronic acid injection on the 7th day and 1, 2 years after surgery, respectively, the infusion time was not less than 15 min. Venous blood samples were collected before and 2 weeks after surgery, and the levels of serum bone metabolism indexes such as type Ⅰ collagen carboxy-terminal peptide β specific sequence (β-CTX), tartrate resistant acid phosphatase (TRAP-5b), and bone formation markes such as bone glaprotein (BGP), bone-specific alkaline phosphatase (BALP) and type I procollagen carboxy-terminal peptide (PICP) were detected by enzyme-linked immunosorbent assay. Before surgery, 1 year and 2 years after surgery, the bone mineral density around the prosthesis of patients in the two groups was measured by dual-energy X-ray absorptiometry and Gruen partition method. The subsidence distance of the femoral prosthesis was measured by X-ray film at 2 years after surgery. Before surgery and 2 years after surgery, the hip function of patients in the two groups was evaluated by Harris hip score. **Results** There was no significant differences in serum β-CTX, TRAP-5b, BGP, BALP and PICP levels between the two groups before surgery ($P > 0.05$); at 2 years after surgery, the levels of serum β-CTX and TRAP-5b of patiens in the observation group were significantly lower than those in the control group ($P < 0.05$), and the levels of serum BGP, BALP and PICP were significantly higher than those in the control group ($P < 0.05$); the levels of serum β-CTX and TRAP-5b of patients in the two groups at 2 years after surgery were significantly lower than those before surgery ($P < 0.05$), and the levels of serum BGP, BALP and PICP were significantly higher than those before surgery ($P < 0.05$). There was no significant difference in the average bone mineral density around the prosthesis of patients between the two groups before surgery and 1 year after surgery ($P > 0.05$); at 2 years after surgery, the average bone mineral density around the prosthesis of patients in the observation group was significantly higher than that in the control group ($P < 0.05$); the average bone mineral density around the prosthesis of patients in the two groups at 1 and 2 years after surgery was significantly lower than that before surgery ($P < 0.05$); the average bone mineral density around the prosthesis of patients in the control group at 2 years after surgery was significantly lower than that at 1 year after surgery ($P < 0.05$); there was no significant difference in the average bone mineral density around the prosthesis of patients in the observation group between 1 year after surgery and 2 years after surgery ($P > 0.05$). At 2 years after surgery, the subsidence distance of femoral prosthesis of patients in the control group and the observation group was (0.74 ± 0.20) and (0.57 ± 0.21) mm, respectively; the subsidence distance of femoral prosthesis of patients in the observation group was significantly smaller than that in the control group ($P < 0.05$). Before operation, there was no significant difference in the Harris hip scores of each dimension and total score of patients between the two groups ($P > 0.05$); at 2 years after surgery, the Harris hip scores of each dimension and total score of patients in the observation group were significantly higher than those in the control group ($P < 0.05$); the Harris hip scores of each dimension and total score of patients in the two groups at 2 years after surgery were significantly higher than those before surgery ($P < 0.05$). **Conclusion** Zoledronic acid injection can effectively improve the bone turnover index of patients after hip replacement, inhibit the bone absorption and decrease the bone mass around the prosthesis, increase the bone density around the prosthesis, delay the sinking of the prosthesis, and improve the hip joint function of patients, which deserves to be promoted in clinical practices.

Key words: zoledronic acid; hip replacement; bone metabolism; bone density

近些年,随着我国人口老龄化的加剧,因骨质疏松而导致的髋部骨折如股骨颈骨折、股骨粗隆间骨折等发生率呈增高趋势[1]。目前,髋关节置换术是治疗上述髋部骨折的主要方式,在临床中取得不错疗效[2]。但由于多数中老年患者伴有不同程度的骨质疏松,髋关节置换术后可能出现假体周围骨折及内植物松动下沉等严重并发症。有研究发现,骨质疏松性髋部骨折患者在接受髋关节置换术的同时联合抗骨质疏松药物治疗,可显著降低其假体周围骨折及内植物松动下沉等并发症发生风险,提高手术治疗效果[3]。双膦酸盐是抗骨质疏松的一线用药,唑来膦酸是其代表药物,其可抑制破骨细胞形成和骨吸收,诱导破骨细胞凋亡,进而增加骨密度[4]。然而,目前唑来膦酸对行髋关节置换术患者术后 2 a 内骨代谢的影响及其机制尚不明确。基于此,本研究旨在探讨唑来膦酸注射液对行髋关节置换术患者骨代谢的影响,以期为临床应用提供参考。

1　资料与方法

1.1　一般资料

选择 2017 年 1 月至 2020 年 7 月于开封市中心医院骨科行髋关节置换术的 199 例患者为研究对象。病例纳入标准:(1)符合《中国老年骨质疏松症诊疗指南(2018)》[5]中骨质疏松诊断标准者;(2)经影像学检查证实为髋部骨折并接受全髋关节置换术者;(3)年龄 55 ~ 70 岁;(4)术前 1 a 内无双膦酸盐治疗史者;(5)患者临床病历资料及相关实验室检查资料完整者。排除标准:(1)伴有血液系统疾病

或凝血功能障碍等不宜手术治疗者;(2)合并有内分泌系统疾病者;(3)药物代谢和排泄器官存在严重功能性病变者;(4)恶性肿瘤者;(5)低钙血症者;(6)过敏体质或对本研究药物过敏者等。根据治疗方法将患者分为对照组(n=93)和观察组(n=106)。对照组:男 14 例,女 79 例;年龄 55 ~ 69(61.80 ± 6.66)岁;骨折类型:股骨颈骨折 75 例,股骨粗隆间骨折 18 例。观察组:男 18 例,女 88 例;年龄56 ~ 70(62.46 ± 6.44)岁;骨折类型:股骨颈骨折 86 例,股骨粗隆间骨折 20 例。2 组患者的性别、年龄、骨折类型比较差异无统计学意义(P>0.05),具有可比性。本研究通过医院医学伦理委员会审核批准。

1.2 治疗方法

2 组患者均行非骨水泥型全髋关节置换术。对照组患者于术后第 2 天开始给予碳酸钙 D3 咀嚼片(苏州惠氏制药有限公司,国药准字 H10950030)600 mg,每日睡前口服,连续用药 2 a。观察组患者在对照组治疗基础上,分别于术后第 7 天及术后 1、2 a 各给予唑来膦酸注射液(连云港正大天晴药业集团股份有限公司,国药准字 H20113138)100 mL 静脉滴注 1 次,滴注时间不少于 15 min。

1.3 观察指标

(1)骨代谢标志物:分别于术前及术后 2 a 采集 2 组患者静脉血约 5 mL,3 000 r · min^{-1} 离心 10 min,分离血清,采用酶联免疫吸附法检测血清骨代谢指标水平,包括骨吸收标志物Ⅰ型胶原羧基端肽 β 特殊序列(type Ⅰ collagen carboxy-terminal peptide β specific sequence,β-CTX)、抗酒石酸酸性磷酸酶-5b(tartrate resistant acid phosphatase,TRAP-5b)和骨形成标志物骨钙素(bone glaprotein,BGP)、骨特异性碱性磷酸酶(bone-specific alkaline phosphatase,BALP)、Ⅰ型前胶原羧基末端肽(type Ⅰ procollagen carboxy-terminal peptide,PICP),酶联免疫吸附测定试剂盒购自上海酶联生物科技有限公司,严格按照试剂盒说明书进行操作。(2)假体周围骨密度值:分别于术前、术后 1 a 及术后 2 a,依据 Gruen 分区法将股骨近端分为 7 个测量兴趣区[6],并采用双能 X 射线吸收测定法检测各个分区骨密度值,取均值。(3)股骨假体下沉距离:术后 2 a,采用 X 线片测量 2 组患者股骨假体下沉距离,股骨假体下沉距离 = $D_{术后2\ a}$ − $D_{术后即刻}$,其中 D =(假体柄实际长度/假体柄长)× 大转子顶点到假体柄肩边缘垂直距离。(4)髋关节功能:分别于术前及术后 2 a,采用 Harris 髋关节评分[7]法评估 2 组患者的髋关节功能,包括疼痛、功能、畸形和关节活动度 4 个维度,各维度分值分别为 44、47、4、5 分,总分值越高表示患者髋关节功能越好。

1.4 统计学处理

应用 SPSS 20.0 软件进行数据统计与分析。计量资料以均数 ± 标准差($\bar{x} \pm s$)表示,组内治疗前后比较采用配对 t 检验,2 组间比较采用独立样本 t 检验;计数资料以例数和百分率表示,组间比较采用 χ^2 检验;P<0.05 为差异有统计学意义。

2 结果

2.1 2 组患者手术前后骨代谢标志物水平比较

术前,2 组患者的血清 β-CTX、TRAP-5b、BGP、BALP、PICP 水平比较差异无统计学意义(P>0.05)。术后 2 a,观察组患者的血清 β-CTX、TRAP-5b 水平显著低于对照组,血清 BGP、BALP、PICP 水平显著高于对照组,差异有统计学意义(P<0.05)。2 组患者术后 2 a 的血清 β-CTX、TRAP-5b 水平显著低于术前,血清 BGP、BALP、PICP 水平显著高于术前,差异有统计学意义(P<0.05)。结果见表 1。

表 1 2 组患者手术前后骨代谢标志物水平比较

Tab.1 Comparison of bone metabolism marker levels of patients between the two groups before and after surgery

($\bar{x} \pm s$)

组别	n	β-CTX/(μg · L^{-1})	TRAP-5b/(U · L^{-1})	BGP/(U · L^{-1})	BALP/(U · L^{-1})	PICP/(mg · L^{-1})
对照组	93					
术前		1.08 ± 0.28	5.98 ± 1.84	114.48 ± 18.38	170.08 ± 16.22	460.50 ± 47.69
术后 2 a		0.88 ± 0.22[a]	3.88 ± 1.24[a]	157.77 ± 20.02[a]	188.38 ± 19.73[a]	511.19 ± 50.02[a]
观察组	106					
术前		1.10 ± 0.31	6.02 ± 1.77	113.89 ± 16.70	171.95 ± 15.14	462.27 ± 40.94
术后 2 a		0.62 ± 0.19[ab]	2.86 ± 1.06[ab]	185.55 ± 18.84[ab]	198.69 ± 20.05[ab]	587.89 ± 53.48[ab]

注:与术前比较[a]P<0.05;与对照组比较[b]P<0.05。

2.2 2 组患者手术前后假体周围骨密度比较

术前及术后 1 a,2 组患者的假体周围平均骨密度比较差异无统计学意义(P>0.05)。术后 2 a,观察组患者的假体周围平均骨密度显著高于对照组,差异有统计学意义(P<0.05)。2 组患者术后 1、2 a 的假体周围平均骨密度均显著低于术前,差异有统计学意义(P<0.05)。对照组患者术后 2 a 的假体周围平均骨密度显著低于术后 1 a,差异有统计学意

义($P<0.05$)。观察组患者术后 1 a 与术后 2 a 的假体周围平均骨密度比较差异无统计学意义($P>0.05$)。结果见表 2。

表 2　2 组患者手术前后假体周围平均骨密度比较

Tab.2　Comparison of average bone mineral density of patients between the two groups before and after surgery

($\bar{x}\pm s$)

组别	n	假体周围平均骨密度/($g\cdot cm^{-3}$)		
		术前	术后 1 a	术后 2 a
对照组	93	0.75 ± 0.20	0.64 ± 0.18[a]	0.54 ± 0.19[ab]
观察组	106	0.77 ± 0.19	0.68 ± 0.21[a]	0.70 ± 0.21[a]
t		0.720	1.447	5.642
P		>0.05	>0.05	<0.05

注:与术前比较[a]$P<0.05$;与术后 1 a 比较[b]$P<0.05$。

2.3　2 组患者的股骨假体下沉距离比较

术后 2 a,对照组和观察组患者的股骨假体下沉距离分别为(0.74 ± 0.20)、(0.57 ± 0.21)mm;观察组患者的股骨假体下沉距离显著小于对照组,差异有统计学意义($t=5.844$,$P<0.05$)。

2.4　2 组患者的髋关节功能比较

术前,2 组患者的各维度 Harris 髋关节评分及总评分比较差异无统计学意义($P>0.05$)。术后 2 a,观察组患者的各维度 Harris 髋关节评分及总评分均显著高于对照组,差异有统计学意义($P<0.05$)。2 组患者术后 2 a 的各维度 Harris 髋关节评分及总评分均显著高于术前,差异有统计学意义($P<0.05$)。结果见表 3。

表 3　2 组患者手术前后 Harris 髋关节评分比较

Tab.3　Comparison of Harris hip score of patients between the two groups before and after surgery　($\bar{x}\pm s$)

组别	n	Harris 髋关节评分				
		疼痛	功能	畸形	关节活动度	总分
对照组	93					
术前		25.50 ± 5.39	20.84 ± 4.88	1.98 ± 1.01	2.20 ± 1.10	50.52 ± 8.70
术后 2 a		32.30 ± 6.55[a]	34.49 ± 6.49[a]	2.77 ± 0.96[a]	3.47 ± 1.25[a]	73.03 ± 10.09[a]
观察组	106					
术前		26.72 ± 4.87	20.19 ± 5.37	1.90 ± 0.97	2.31 ± 1.16	51.12 ± 9.95
术后 2 a		37.87 ± 5.94[ab]	38.88 ± 6.77[ab]	3.20 ± 0.70[ab]	4.11 ± 0.82[ab]	84.06 ± 11.26[ab]

注:与术前比较[a]$P<0.05$;与对照组比较[b]$P<0.05$。

3　讨论

髋部骨折是常见的骨折类型,髋关节置换术是目前临床常用的治疗方法;然而由于髋关节置换打破了机体原有的破骨细胞和成骨细胞平衡,破骨细胞占主导优势,骨量丢失严重,患者容易出现髋关节部位疼痛甚至活动受限等功能障碍,严重者还可能出现假体周围骨折等并发症,因此,术后应该注意抗骨质疏松的治疗,以改善患者骨代谢状态。

唑来膦酸是第 3 代双膦酸类药物,唑来膦酸静脉滴注后生物利用度高,药物缓慢释放入血,可较长时间地维持有效的血药浓度,其主要药理作用是抑制骨的重吸收;唑来膦酸抑制骨的重吸收的机制目前尚未完全阐明,但目前公认的是其通过抑制破骨细胞活性、诱导破骨细胞凋亡、激活成骨细胞来抑制骨的重吸收[8]。黄晓林等[9]的一项体外研究显示,唑来膦酸在体外可能是通过调节核因子 κB 信号通路来抑制破骨细胞的形成。CHENG 等[10]研究也指出,唑来膦酸是通过激活去卵巢大鼠的核因子 κB 信号通路进而促进破骨细胞凋亡。骨代谢标志物是骨组织本身的代谢产物,临床常通过检测其浓度评估骨的吸收及形成情况。β-CTX 是目前国际上公认的代表骨吸收的特异性标志物,多见于成熟的骨胶原中,若破骨细胞活性增强,骨胶原可溶解并促进Ⅰ型胶原蛋白释放并分解为 C 末端肽和 N 末端肽,因此,β-CTX 水平可反映骨细胞的骨吸收活性。TRAP-5b 是近些年发现的反映骨吸收和破骨细胞活性的良好生物标志物,通过测定其血清水平,有助于了解机体在病理条件下的骨代谢状况。BGP 由成骨细胞和软骨细胞分泌,可以反映成骨细胞的活性,是临床常用的骨形成生物化学标志物;BALP 主要由骨细胞分泌,是骨形成的特异性标志物;PINP 是特异度和敏感度均较高的骨形成标志物,在双膦酸盐抗骨质疏松治疗过程中,检测血清 PINP 水平可有效评估其治疗效果[11-13]。本研究结果显示,术前 2 组患者的血清 β-CTX、TRAP-5b、BGP、BALP、PICP 水平比较差异无统计学意义;术后 2 a,观察组患者的血清 β-CTX、TRAP-5b 水平显著低于对照组,血清 BGP、BALP、PICP 水平显著高于对照组;这说明,唑来膦酸可有效改善髋关节置换术后患者骨代谢标志物指标,抑制骨吸收,与相关研究[14]结果一致。

全髋关节置换术植入的假体摩擦界面产生的磨损颗粒可刺激破骨细胞活化,促进溶骨性细胞因子分泌增加,促进假体周围骨吸收,其介导的骨溶解可加剧假体周围骨量的丢失,导致假体下沉,这也是全髋关节置换术失败的主要因素之一[15]。本研究结果显示,术前及术后 1 a,2 组患者的假体周围平均骨密度比较差异无统计学意义;术后 2 a,观察组患者的假体周围平均骨密度显著高于对照组;2 组患者术后 1 a 和术后 2 a 的假体周围平均骨密度均显著低于术前;对照组患者术后 2 a 的假体周围平均骨密度显著低于术后 1 a;观察组患者术后 1 a 的假

体周围平均骨密度与术后 2 a 比较差异无统计学意义;此外,术后 2 a,观察组患者股骨假体下沉距离小于对照组。以上结果说明,髋关节置换术后静脉注射唑来膦酸可有效抑制假体周围骨量减少,增加假体周围骨密度,延缓术后假体下沉,这与陈拥等[16]研究结果一致。原因可能为:唑来膦酸进入机体后可沉积在骨吸收部位的破骨细胞内,与羟磷灰石结合,抑制骨细胞活性,减少骨细胞释放 H^+,进而减少骨吸收;此外,其进入机体后还可抑制破骨细胞产生活化因子,降低骨转换,抑制骨质溶解,所以有助于骨密度的提高。但值得注意的是,唑来膦酸对骨密度的改善是一个缓慢的过程。

同时,本研究结果显示,术前 2 组患者的 Harris 髋关节各维度评分及总评分比较差异无统计学意义,观察组患者术后 2 a 的 Harris 髋关节各维度评分及总评分均显著高于对照组,说明髋关节置换术后唑来膦酸的使用有助于改善患者髋关节功能,这与叶征等[17]研究结果一致。

4 结论

唑来膦酸可有效改善髋关节置换术后患者骨转换指标水平,抑制骨吸收和减少假体周围骨量,增加假体周围骨密度,延缓术后假体下沉,改善患者髋关节功能,值得临床推广。但本研究样本量有限,随访时间仅 2 a,唑来膦酸对髋关节置换患者术后长期骨代谢的影响仍需进行更大样本量、更深入的研究进行论证。

参考文献:

[1] KUTSAL F Y, ERGIN ERGANI G O. Vertebral compression fractures: still an unpredictable aspect of osteoporosis[J]. *Turk J Med Sci*, 2021, 51(2): 393-399.

[2] 柏小金,韩小松,向柄彦,等. 后外侧微创入路行全髋关节置换术治疗老年股骨颈骨折的早期疗效[J]. 实用医学杂志, 2022, 38(12): 1456-1460.
BAI X J, HAN X S, XIANG B Y, *et al*. Analysis of early efficacy of total hip arthroplasty through posterolateral minimally invasive approach for elderly femoral neck fractures[J]. *J Pract Med*, 2022, 38(12): 1456-1460.

[3] BLACK D M, REID I R, NAPOLI N, *et al*. The interaction of acute-phase reaction and efficacy for osteoporosis after zoledronic acid: HORIZON pivotal fracture trial[J]. *J Bone Miner Res*, 2022, 37(1): 21-28.

[4] ZHOU W, LIU Y, GUO X, *et al*. Effects of zoledronic acid on bone mineral density around prostheses and bone metabolism markers after primary total hip arthroplasty in females with postmenopausal osteoporosis[J]. *Osteoporos Int*, 2019, 30(8): 1581-1589.

[5] 《中国老年骨质疏松症诊疗指南》工作组,中国老年学和老年医学学会骨质疏松分会,马远征,等. 中国老年骨质疏松症诊疗指南(2018)[J]. 中国骨质疏松杂志, 2018, 24(12): 1541-1567.
GUIDELINES FOR DIAGNOSIS AND TREATMENT OF OSTEOPOROSIS IN THE ELDERLY IN CHINA WORKING GROUP, OSTEOPOROSIS BRANCH OF CHINESE GERONTOLOGY AND GERONTOLOGY SOCIETY, MA Y Z, *et al*. 2018 China guideline for diagnosis and treatment of senile osteoporosis[J]. *Chin J Osteopor*, 2018, 24(12): 1541-1567.

[6] TEN BROEKE R H, HENDRICKX R P, LEFFERS P, *et al*. Randomised trial comparing bone remodelling around two uncemented stems using modified Gruen zones[J]. *Hip Int*, 2012, 22(1): 41-49.

[7] KUMAR P, SEN R, AGGARWAL S, *et al*. Reliability of modified Harris Hip score as a tool for outcome evaluation of total hip replacements in Indian population[J]. *J Clin Orthop Trauma*, 2019, 10(1): 128-130.

[8] ALSAMRI M T, AL-HAMMADI S, ISLAM B, *et al*. Zoledronic acid and bone cellular respiration[J]. *J Bone Miner Metab*, 2018, 36(4): 392-398.

[9] 黄晓林,廖健,洪伟,等. 破骨细胞形成过程中唑来膦酸的作用途径及机制[J]. 中国组织工程研究, 2019, 23(17): 2716-2721.
HUANG X L, LIAO J, HONG W, *et al*. Zoledronic acid in osteoclastogenesis: roles and mechanisms[J]. *J Clin Rehabil Tis Eng Res*, 2019, 23(17): 2716-2721.

[10] CHENG Y T, LIAO J, ZHOU Q, *et al*. Zoledronic acid modulates osteoclast apoptosis through activation of the NF-κB signaling pathway in ovariectomized rats[J]. *Exp Biol Med (Maywood)*, 2021, 246(15): 1727-1739.

[11] CLÉZARDIN P, COLEMAN R, PUPPO M, *et al*. Bone metastasis: mechanisms, therapies, and biomarkers[J]. *Physiol Rev*, 2021, 101(3): 797-855.

[12] XIONG Y, HE T, WANG Y, *et al*. CKD stages, bone metabolism markers, and cortical porosity index: associations and mediation effects analysis[J]. *Front Endocrinol (Lausanne)*, 2021, 12: 775066.

[13] DI MEDIO L, BRANDI M L. Advances in bone turnover markers[J]. *Adv Clin Chem*, 2021, 105: 101-140.

[14] 邱伟,连星烨. 唑来膦酸干预老年骨质疏松性股骨转子间骨折髋关节置换后患者骨密度,骨代谢标志物的 2 年随访[J]. 中国组织工程研究, 2021, 25(33): 5265-5272.
QIU W, LIAN X Y. Effect of zoledronic acid on bone mineral density and bone metabolism markers in elderly patients with osteoporotic intertrochanteric fracture after hip arthroplasty: 2-year follow-up[J]. *J Clin Rehabil Tis Eng Res*, 2021, 25(33): 5265-5272.

[15] YUAN M, SHI X, SU Q, *et al*. A prospective randomized controlled trial on the short-term effectiveness of domestic robot-assisted total knee arthroplasty[J]. *Chin J Repair Reconstruc Surg*, 2021, 35(10): 1251-1258.

[16] 陈拥,孙阳. 唑来膦酸对髋关节置换后股骨侧假体下沉的影响[J]. 中国组织工程研究, 2022, 26(12): 1812-1815.
CHEN Y, SUN Y. Effect of zoledronic acid on femoral implant subsidence after hip arthroplasty[J]. *J Clin Rehabil Tis Eng Res*, 2022, 26(12): 1812-1815.

[17] 叶征,陈舰,缪佳庆. 绝经期女性髋关节置换术后应用唑来膦酸对股骨假体周围骨密度及 PICP、β-CTX、ALP、BALP 水平的影响[J]. 临床和实验医学杂志, 2021, 20(19): 2085-2089.
YE Z, CHEN J, MIAO J Q. Effect of zoledronic acid on periprosthetic bone mineral density and levels of PICP, β-CTX, ALP and BALP in postmenopausal women after hip replacement[J]. *J Clin Exp Med*, 2021, 20(19): 2085-2089.

(本文编辑:郭 潇)