



Original Article

Comparison of Puddu osteotomy with or without autologous bone grafting: a prospective clinical trial[☆]



Marcus Ceregatti Passarelli, José Roberto Tonelli Filho, Felipe Augusto Mendes Brizzi, Gustavo Constantino de Campos, Alessandro Rozim Zorzi*, João Batista de Miranda

Universidade Estadual de Campinas (Unicamp), Departamento de Ortopedia e Traumatologia, Campinas, SP, Brazil

ARTICLE INFO

Article history:

Received 4 August 2016

Accepted 7 September 2016

Available online 14 September 2017

Keywords:

Knee

Osteoarthritis

Bone graft

Osteotomy

ABSTRACT

Objectives: To test the hypothesis that autologous iliac bone grafts do not enhance clinical results and do not decrease complication rates in patients undergoing medial opening-wedge high tibial osteotomy.

Methods: Forty patients allocated in a randomized, two-armed, double-blinded clinical trial were evaluated between 2007 and 2010. One group received bone graft, and the other group was left without filling the osteotomy defect. The primary outcome was the Knee Society Score. Radiographic measurement of the frontal anatomical femoral-tibial angle and the progression of osteoarthritis according to the modified Ahlback classification were used as secondary outcomes.

Results: There was no difference in KSS scale between the graft group (64.4 ± 21.8) and the graftless group (61.6 ± 17.3 ; $p = 0.309$). There was no difference of angle between the femur and tibia in the frontal plane between the groups (graft = 184 ± 4.6 degrees, graftless = 183.4 ± 5.1 degrees; $p = 1.0$), indicating that there is no loss of correction due to the lack of the graft. There was significant aggravation of osteoarthritis in a greater number of patients in a graft group ($p = 0.005$).

Conclusion: Autologous iliac bone graft does not improve clinical outcomes in medium and long-term follow-up of medial opening-wedge high tibial osteotomy fixed with a first generation Puddu plate in the conditions of this study.

© 2016 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

[☆] Paper developed at Universidade Estadual de Campinas (UNICAMP), Departamento de Ortopedia e Traumatologia (DOT), Campinas, SP, Brazil.

* Corresponding author.

E-mail: alessandrozorzi@uol.com.br (A.R. Zorzi).

<http://dx.doi.org/10.1016/j.rboe.2017.09.001>

2255-4971/© 2016 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Comparação de osteotomias de Puddu com ou sem enxerto ósseo autólogo: estudo clínico prospectivo

R E S U M O

Palavras-chave:

Joelho
Osteoartrite
Enxerto ósseo
Osteotomia

Objetivos: Avaliar a hipótese de que o enxerto ósseo autólogo da crista ilíaca não melhora o resultado clínico e não diminui a incidência de complicações em pacientes submetidos à osteotomia de Puddu.

Métodos: Foram avaliados 40 pacientes alocados de forma aleatória em dois grupos em um estudo clínico duplo cego entre 2007 e 2010. Um grupo recebeu enxerto ósseo e o outro grupo foi deixado sem preenchimento da osteotomia. O desfecho primário foi a escala clínica da Knee Society (KSS). A medida radiográfica do ângulo anatômico entre o fêmur e a tibia no plano frontal e a progressão da osteoartrite de acordo com a classificação modificada de Ahlback foram usadas como desfechos secundários.

Resultados: Não houve diferença da escala KSS no grupo com enxerto ($64,4 \pm 21,8$) e no grupo sem enxerto ($61,6 \pm 17,3$; $p = 0,309$). Não houve diferença do ângulo entre o fêmur e a tibia no plano frontal entre os grupos (com enxerto = $184 \pm 4,6$ graus; sem enxerto = $183,4 \pm 5,1$ graus; $p = 1,0$), indica que não há uma perda de correção pela falta do enxerto. Houve piora da osteoartrite em um número maior de pacientes no grupo com enxerto ($p = 0,005$).

Conclusão: O enxerto ósseo autólogo da crista ilíaca não melhorou o resultado clínico e não diminuiu a incidência de complicações em pacientes submetidos à osteotomia de Puddu, fixadas com placa-calço de primeira geração, nas condições deste estudo.

© 2016 Sociedade Brasileira de Ortopedia e Traumatologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The proximal tibial osteotomy with medial opening wedge, also known as Puddu osteotomy, is a classical surgical procedure for the treatment of knee osteoarthritis, which has been overshadowed by the development of arthroplasty, but that has resurged due to the increasing number of cases of osteoarthritis in young patients and new surgeries, such as meniscal transplantation and cartilage fillings, which require adequate mechanical alignment of the lower limb.¹ Compared to the other osteotomy techniques, the medial opening of the tibia have as advantages the less morbid access route, the possibility of easy intraoperative adjustment of wedge size, preservation of bone stock, correction closer to the apex of the deformity, and ease of association with other procedures in a single surgical time, such as reconstruction of the anterior cruciate ligament.^{1,2}

The main criticism of the technique of medial opening is the creation of a cleft in the metaphyseal cancellous bone, which can progress with complications of bone consolidation and the loss of correction due to cleft collapse. The use of autologous bone grafting of the iliac crest has been advocated since the beginning of this surgery to prevent these complications.^{3,4} Due to it being a painful procedure, associated with several complications, bone substitutes have been developed to fill the cleft. However, autologous bone grafting, due to its osteogenesis, osteoinduction and osteoconduction properties, remains the gold standard.⁵

The empirical experience suggests that, in openings of up to 10 mm, it is possible to leave the cleft unfilled. To confirm this observation, this team made a short-term evaluation of

the results of osteotomies with and without the addition of a bone graft, which showed no difference in the time of consolidation after six months of follow-up.⁶ Now, the objective of this paper is the late evaluation, after a minimum follow-up of four years, of the clinical and radiographic results obtained with or without the addition of the graft.

Method

Subjects

The study sample consisted of 46 patients undergoing Puddu osteotomy between 2007 and 2010, who were referred to surgical treatment in a university hospital after failure of non-surgical treatment.

Inclusion criteria:

- Individual osteoarthritis of the medial knee compartment associated with varus deformity;
- Failure of nonsurgical treatment;
- Double varus secondary to chronic instability of ligament structures of the posterolateral corner;
- Ability to read and understand the Free Informed Consent Form (FIC), and agreement with the participation in the research.

Exclusion criteria:

- Systemic inflammatory diseases;
- Age over 60 years or below 20 years;
- Alcoholism;

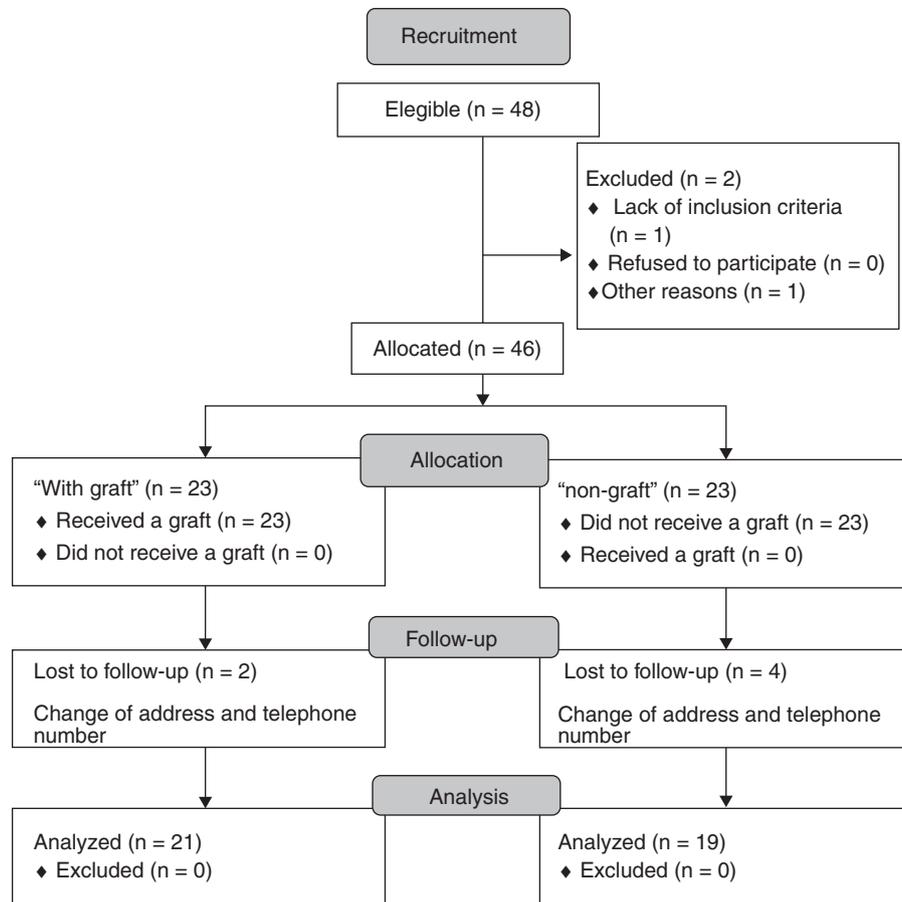


Fig. 1 – Study consort flowchart.

- Planned corrections with wedges larger than 12.5 mm;
- Previous surgeries in the affected knee;
- Previous infections in the affected limb;
- Pain in the lateral or anterior compartments of the affected knee;
- Lateral meniscus injury;
- Severe knee osteoarthritis (grades 4 and 5 of Ahlback classification).

The study was approved by the Research Ethics Committee (CEP 679/2006) and registered in the platform ClinicalTrials.gov (NCT00786942).

Allocation

Forty-six patients were randomly divided, with the use of a software (www.random.org), in two groups of 23 individuals. All of them underwent the same surgical procedure, except for the placement or not of a bone graft. After a minimum follow-up of four years, 40 patients were evaluated (Fig. 1).

Masking

The allocation was kept secret with the use of a sealed envelope, opened only after anesthetic induction by a nurse that was not involved with the study. In addition, in order to ensure

confidentiality between patients and evaluators (double-blind study) a iliac crest graft was harvested from all patients. In the “without graft” group, the bone was sealed under sterile conditions and stored in a freezer, with the approval of CEP.

Intervention

The valgus osteotomy of the proximal tibia, with medial opening wedge, known in our setting as Puddu osteotomy, is a classical and well-established technique.^{2,3,7} In this study, we used first-generation wedge-plate fixation.^{8,9} As previously stated, two groups were randomly created. To keep masking, and to avoid the clinical aggravation bias due to iliac crest pain, the graft was harvested in both groups. The intervention of this study was the placement of the graft. The control group was left without it.

Surgical technique

All cases were operated by the same surgeon. The detailed description of the technique has already been made in a previous publication.¹⁰

In all cases, knee arthroscopy was performed in the traditional portals to confirm the integrity of lateral compartment structures and debridement of free bodies, fragments of meniscus and excess synovial tissue of the medial

compartment (arthroscopic toilet). At that time, a nurse that was not involved in the research team opened the envelope with the indication of the patient's allocation. In the cases of the "no-graft" group, the bone was vacuum packed in triple polyamide packaging and frozen in a research laboratory. At the end of the procedure, a suction drain was placed in all cases.

Postoperative period

The drain was always removed on the first day after surgery. No type of immobilization was used and the limb active movement was stimulated on the first day after surgery. Therefore, no pharmacological prophylaxis for venous thromboembolism was used. To standardize loading, we chose to leave all patients with zero load until the eighth week (pair of crutches); gradual weight-bearing was started after this period. All patients had the same physical therapy protocol at the same medical facility where they were operated.

After hospital discharge, the subjects were evaluated weekly in an outpatient clinic, by two researchers blinded to the allocation. The radiographic evaluation was performed every fifteen days until consolidation, which was defined by Solomon and Apley criteria.¹¹ Following bone healing, they were evaluated every six months for the first two years, and then annually.

Outcomes

This study's main outcome was the clinical and functional result of the Puddu osteotomy after at least four years of follow-up, measured by KSS (Knee Society Score) scale.¹² This scale is divided in two parts: an objective one, which can vary from zero to one hundred; and a functional one, that can vary from zero to one hundred.

Other outcomes used were:

- Correction obtained in the frontal plane, measured in frontal knee X-ray, with monopodal weight-bearing, through the angle formed by the anatomical axis of the femur and tibia^{13,14};
- Radiographic progression of knee osteoarthritis through modified Ahlback method¹⁵;
- Conversion of arthroplasty or osteotomy review.

Statistics

To calculate the sample size, we considered a significant clinical difference between the means of the two groups of 20 points, with 80% power and significance with alpha less than 5%.

Data were presented as mean and standard deviation (SD) for continuous variables, or as absolute frequency for categorical variables. All *p* values reported are two-tailed. The level of significance was set at 0.05. The Kolmogorov-Smirnov test was applied to determine if the data followed normal distribution. The comparison among the continuous variables was made with Student's *t*-test for independent samples, when the parametric assumptions could be obtained; in other cases, Mann-Whitney test was used. Among the categorical

Table 1 – Demographic data of the research subjects.

	With graft n = 21	Without graft n = 19	<i>p</i>
Age (years)	49.7 ± 9.5	49.1 ± 9.2	0.801
BMI	29.0 ± 4.9	28.2 ± 6.6	0.204
Follow-up (months)	74.3 ± 14.4	70.6 ± 11.8	0.688
Wedge plate (mm)	10.3 ± 2.5	9.8 ± 2.0	0.607
Ligament lesion	12	10	0.328
Smokers	5	11	0.028 ^a

BMI, body mass index.

^a Significant.

Table 2 – Result of clinical evaluation through objective and functional KS scales.

	With graft n = 21	Without graft n = 19	<i>p</i>
Pre objective KS	48.9 ± 11.2	49.5 ± 11.6	0.830
Post objective KS	64.4 ± 21.8	61.6 ± 17.3	0.309
Pre functional KS	57.1 ± 16.5	59 ± 24.47	0.376
Post functional KS	74.8 ± 20.8	76.8 ± 29.4	0.374

KS, Knee score.

variables, Pearson's chi-square test or Fisher's test were applied.

All analyses were performed with the software IBM SPSS Statistics, (version 22.0 Armonk, NY, IBM Corp.).

Results

Forty-six patients were divided into two groups of 23, at the beginning of the study, for surgery; 40 were now available for this late assessment; 21 from the bone graft group and 19 from the non-graft group. Six patients were not found. No patient was converted into total knee arthroplasty at this time. Demographic data did not show differences between groups regarding the majority of possible variables, such as age, body mass index (BMI), wedge size of the wedge plate used to make the correction, presence of associated ligament lesions. There was a greater number of smokers in the "non-graft" group (Table 1).

The primary outcome, objective KS scale, did not show any difference between the groups (Table 2). KS functional scale did not show any differences between the groups either.

Limb alignment in the frontal plane was measured by the femorotibial (FT) angle, in supporting X-rays. The results are illustrated in Fig. 2. There was no difference in the incidence of correction loss in the non-graft group, as shown by the values obtained in the final segment (*p* = 1.0).

Table 3 shows the radiographic evolution of osteoarthritis, according to the modified Ahlback classification. The group "with graft" showed significant aggravation after surgery (*p* = 0.005).

No case underwent arthroplasty or review osteotomy.

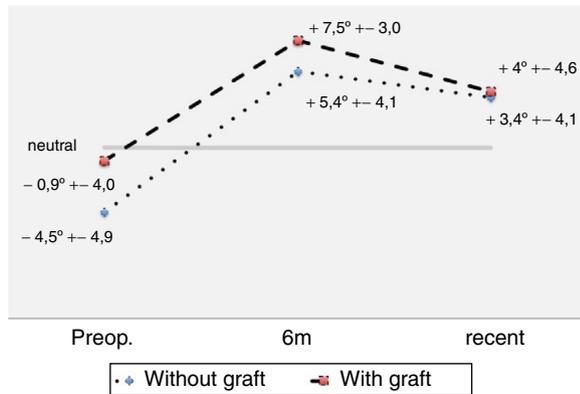


Fig. 2 – Progression of the angle formed by the anatomical axes of femur and tibia in radiographs with frontal plane support.

Table 3 – Radiographic progression of osteoarthritis according to the modified Ahlback classification.

Grade	With graft n = 21	Without graft n = 19	p
<i>Pre Ahlback</i>			
1	1	3	0.504
2	7	6	
3	13	10	
<i>Post Ahlback</i>			
1	1	0	0.005 ^a
2	0	5	
3	9	13	
4	9	1	
5	2	0	

^a Significant.

Discussion

The result of this study showed that the addition of autologous bone graft of the iliac crest did not improve the late clinical outcome of Puddu osteotomies and did not increase the risk of complications, such as loss of correction and radiographic deterioration of osteoarthritis of the knee when corrections of up to 12.5 mm are performed. In a previous paper,⁶ this team had already demonstrated the lack of benefits in adding this type of graft for the healing of the osteotomy, but there was doubt about the possibility of complications or poor outcome in a long-term follow-up.

This finding is consistent with biological reasoning, because the metaphyseal bone, contrary to common notion, does not need full contact if there is rigid stability.¹⁶ This is achieved by maintaining the integrity of the lateral tibial cortex, which functions as a fulcrum, from which formation of endosteal callus takes place, which progresses to the medial side of the osteotomy.^{6,9,17}

A recent systematic review with a meta-analysis that included 25 studies corroborates this finding.¹⁸ However, the authors warn about the fact that only one of these studies⁶ has a grade 1 level of evidence. All the other 24 are case series or

non-controlled comparative studies. Therefore, there is a need for more good quality clinical studies to clarify the subject.

Regarding the KSS scale, the post hoc analysis of statistical power showed that the sample size is sufficient to detect differences of 20 points among the means. There is some controversy over the value of the Minimal Clinically Important Difference (MCID) for this scale. Although some small differences such as 5.9 for objective KS, and 6.4 for functional KS have already been calculated,¹⁹ another study indicates that the MCID for KS-FS should be 34.5.²⁰ We subjectively adopted MCID as 20 in this study because we considered that the justification for a painful procedure, such as the removal of autologous graft from the iliac crest, would require a greater effect (effect size). In this sample we find a low Cohen coefficient ($d=0.14$). Thus, we thought that a larger sample might have some scientific value but no clinical applicability.

Regarding the loss of correction, we observed that both groups had progressive loss of the correction obtained with six months of surgery in this follow-up of more than four years of duration, but the loss was equal in both groups. As the evaluations were all done on monopodal weight-bearing radiographs, we did not take the measurements on the radiographs made immediately after the surgery, which had to be done without weight-bearing, due to the pain and inability of the patients to bear their weight at that stage. Thus, it is not possible to say if there was a loss in the period between surgery and consolidation. The correction angle in the frontal plane, in the long-term final evaluation of our study, is similar to that reported by other authors and is within the recommended target (three to six degrees of valgus between the anatomical axes of the femur and the tibia).²¹

Regarding osteoarthritis, it is difficult to find a biological explanation for the more marked progression in the “graft” group. Because the modified Ahlback classification considers the size of the posterior tibial osteophyte in the profile radiography, it can be argued that the graft may somehow stimulate osteophyte growth, but there are no data in the literature to prove this theory. Another possible explanation is that some hidden uncontrolled variable in this study has caused this phenomenon.

The main limitations of this study were the inclusion of patients with chronic ligament lesions associated with knee varus deformity, along with patients with primary osteoarthritis with a stable knee, which may interfere with the result of clinical scales and sample size, which was calculated for the outcome of osteotomy consolidation. However, since the requirements for the indication of Puddu osteotomy are many, it is difficult to obtain a sufficient sample if the inclusion criteria in the study are further restricted.

This study supports the idea that, in Puddu osteotomies with an opening of less than or equal to 12.5 mm, neither autologous bone graft nor costly bone substitutes ought to be used.

Conclusion

The use of autologous bone graft of the iliac crest in patients with varus deformity of the knee does not improve the mid- and long-term clinical results of the medial open wedge tibial

osteotomy, fixed with first-generation wedge plates, in corrections of up to 12.5 mm. Therefore, in these conditions, we avoid its use because it is a procedure that increases the patient's pain and morbidity.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Amendola A, Panarella L. High tibial osteotomy for the treatment of unicompartmental arthritis of the knee. *Orthop Clin North Am.* 2005;36(4):497-504.
2. Brinkman J-M, Lobenhoffer P, Agneskirchner JD, Staubli AE, Wymenga AB, van Heerwaarden RJ. Osteotomies around the knee: patient selection, stability of fixation and bone healing in high tibial osteotomies. *J Bone Joint Surg Br.* 2008;90(12):1548-57.
3. Hernigou P, Medevielle D, Debeyre J, Goutallier D. Proximal tibial osteotomy for osteoarthritis with varus deformity. A ten to thirteen-year follow-up study. *J Bone Joint Surg Am.* 1987;69(3):332-54.
4. Noyes FR, Mayfield W, Barber-Westin SD, Albright JC, Heckmann TP. Opening wedge high tibial osteotomy: an operative technique and rehabilitation program to decrease complications and promote early union and function. *Am J Sports Med.* 2006;34(8):1262-73.
5. De Long WC, Einhorn TA, Koval K, McKee M, Smith W, Sanders R, et al. Bone grafts and bone graft substitutes in orthopaedic trauma surgery. A critical analysis. *J Bone Joint Surg Am.* 2007;89(3):649-58.
6. Zorzi AR, da Silva HGPV, Muszkat C, Marques LC, Cliquet A, de Miranda JB. Opening-wedge high tibial osteotomy with and without bone graft. *Artif Org.* 2011;35(3):301-7.
7. Dugdale TW, Noyes FR, Styer D. Preoperative planning for high tibial osteotomy: the effect of lateral tibiofemoral separation and tibiofemoral length. *Clin Orthop Relat Res.* 1992;274(3):248-384.
8. Golovakha ML, Orljanski W, Benedetto KP, Panchenko S, Büchler P, Henle P, et al. Comparison of theoretical fixation stability of three devices employed in medial opening wedge high tibial osteotomy: a finite element analysis. *BMC Musculoskelet Disord.* 2014;15(1):230.
9. Staubli AE, Jacob HA. Evolution of open-wedge high-tibial osteotomy: experience with a special angular stable device for internal fixation without interposition material. *Int Orthop.* 2010;34(2):167-72.
10. Zorzi AR, Imamura TF, Piedade SR, Miranda JB. Osteotomia valgizante da tibia proximal com cunha aberta medial. *Ortopedia e Traumatologia Ilustrada.* 2011;2(3):79-86.
11. Wade R, Richardson J. Outcome in fracture healing: a review. *Injury.* 2001;32(2):109-14.
12. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res.* 1989;(248):13-4.
13. Specogna AV, Birmingham TB, Hunt MA, Jones IC, Jenkyn TR, Fowler PJ, et al. Radiographic measures of knee alignment in patients with varus gonarthrosis: effect of weightbearing status and associations with dynamic joint load. *Am J Sports Med.* 2007;35(1):65-70.
14. Specogna AV, Birmingham TB, DaSilva JJ, Milner JS, Kerr J, Hunt MA, et al. Reliability of lower limb frontal plane alignment measurements using plain radiographs and digitized images. *J Knee Surg.* 2004;17(4):203-10.
15. Keyes GW, Carr AJ, Miller RK, Goodfellow JW. The radiographic classification of medial gonarthrosis. Correlation with operation methods in 200 knees. *Acta Orthop Scand.* 1992;63(5):497-501.
16. Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: the diamond concept. *Injury.* 2007;38 Suppl 4:S3-6.
17. Staubli AE, De Simoni C, Babst R, Lobenhoffer P. TomoFix: a new LCP-concept for open wedge osteotomy of the medial proximal tibia - early results in 92 cases. *Injury.* 2003;34 Suppl. 2:B55-62.
18. Han JH, Kim HJ, Song JG, Yang JH, Bhandare NN, Fernandez AR, et al. Is bone grafting necessary in opening wedge high tibial osteotomy? A meta-analysis of radiological outcomes. *Knee Surg Relat Res.* 2015;27(4):207-20.
19. Lee WC, Kwan YH, Chong HC, Yeo SJ. The minimal clinically important difference for Knee Society Clinical Rating System after total knee arthroplasty for primary osteoarthritis. *Knee Surg Sports Traumatol Arthrosc.* 2016. Epub ahead of print.
20. Jacobs CA, Christensen CP. Correlations between knee society function scores and functional force measures. *Clin Orthop Relat Res.* 2009;467(9):2414-9.
21. Pipino G, Indelli PF, Tigani D, Maffei G, Vaccarisi D. Opening-wedge high tibial osteotomy: a seven- to twelve-year study. *Joints.* 2016;4(1):6-11.