

IMPACTO DA SAÍDA PRECOCE DO LEITO NA ARTROPLASTIA TOTAL DE JOELHO

IMPACT OF EARLY WITHDRAWAL FROM BED IN TOTAL KNEE ARTHROPLASTY

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RESUMO | Introdução: A osteoartrite é uma doença inflamatória, degenerativa e progressiva que causa dor, incapacidade funcional e imobilidade. Havendo insucesso do tratamento conservador, é indicada a Artroplastia Total de Joelho (ATJ). **Objetivos:** Analisar o impacto da saída precoce do leito no pós-operatório (PO) e identificar quais motivos retardam esse processo. **Método:** Estudo prospectivo e experimental com pacientes submetidos a um protocolo de mobilização precoce pós ATJ, de julho/2014 a março/2015. A estatística utilizou testes de Fischer e T de student não pareado. O nível de significância foi de 5% e os dados apresentados como média e desvio padrão. **Resultados:** Amostra de 30 pacientes, idade $67,5 \pm 7,4$ anos, 80% sexo feminino, osteoartrite como etiologia para ATJ. O grupo NS (não saíram do leito no 1ºDPO) teve mais dor (PO imediato $6,4 \pm 4,1$ contra $3,3 \pm 3,5$, $p=0,03$; 1ºDPO $7,1 \pm 3,2$ contra $3,8 \pm 3,5$, $p=0,01$; 2ºDPO $5,7 \pm 3,2$ contra $2,1 \pm 2,4$, $p=0,00$; 3ºDPO $4,6 \pm 2,8$ contra $1,7 \pm 2,4$, do grupo SS, $p=0,003$) que o grupo SS (saíram do leito no 1ºDPO). SS seguiu o protocolo com maior frequência ($p=0,003$), a média de permanência hospitalar foi maior no grupo NS ($5 \pm 2,5$ contra $2,8 \pm 0,8$, $p=0,00$) e a quantidade de atendimentos de Fisioterapia foi maior no grupo NS ($9,5 \pm 5,7$ contra $4,7 \pm 1,7$, $p=0,00$). O motivo mais frequente de impedimento para a saída do leito no 1ºDPO foi a não liberação médica (62%), seguido por indisposição, falta de prescrição de fisioterapia e dor. **Conclusão:** O protocolo foi benéfico em relação à dor, capacidade funcional e tempo de internação, podendo reduzir custos hospitalares.

Palavras-chave: Artroplastia; Prótese do joelho; Fisioterapia; Reabilitação; Deambulação Precoce.

ABSTRACT | Introduction: Osteoarthritis is a progressive inflammatory and degenerative disease that causes pain, functional disability and immobility. In case of failure of conservative therapy, Knee Arthroplasty (TKA) is indicated. **Objectives:** Impact Analysis of patient's early withdrawal from postoperative bed (PO) and to identify which motives delay this process. **Method:** Prospective and experimental study with patients submitted to a protocol of early mobilization post TKA, from July 2014 to March 2015. For the statistical analysis were used the tests of Fischer and T of unpaired student. The significance level was 5% ($p < 0.05$) and the data were presented as average and standard deviation. **Results:** Sample of 30 patients, age of 67.5 ± 7.4 years, 80% female, osteoarthritis as etiology for TKA. The NS group (did not leave the bed in 1st PO) presented more pain (PO immediate 6.4 ± 4.1 vs 3.3 ± 3.5 , $p=0.03$; 1st PO 7.1 ± 3.2 vs 3.8 ± 3.5 , $p=0.01$; 2nd PO 5.7 ± 3.2 vs 2.1 ± 2.4 , $p=0.00$; 3rd PO 4.6 ± 2.8 vs 1.7 ± 2.4 of SS group, $p=0.003$) than SS group (left the bed in 1st PO). SS group followed the protocol more frequently ($p=0.003$). The average hospital stay was higher in the NS group (5.0 ± 2.5 vs 2.8 ± 0.8 , $p=0.00$) and the amount of Physiotherapy appointments was higher in the NS group (9.5 ± 5.7 vs 4.7 ± 1.7 , $p=0.00$). The most frequent cause of impediment for leaving the bed in the 1st P.O. was non medical release (62%), followed by indisposition, lack of prescription of physiotherapy and pain. **Conclusion:** The protocol was beneficial regarding to pain, functional capacity and period of Hospital stay, which could reduce hospital costs.

Key words: Arthroplasty; Knee prosthesis; Physiotherapy; Rehabilitation; Early Deambulation.

INTRODUCTION

Osteoarthritis (OA) is a degenerative rheumatic disease that affects the synovial joints and is characterized by changes in the articular cartilage giving rise to areas of atrial fibrillation and cracking. Microfractures are also observed, as well as cysts and sclerosis in the subchondral bone and formation of osteophytes in articular edges¹. Such pathology is associated to pain, stiffness, deformity and progressive loss of function affecting the individual in multiple dimensions, from organic to social level². Its incidence is very high in our midst, being responsible for incapacity for work in approximately 15% of the adult population of the world. In Brazil, it ranks in third place in the list of Social Security insured parties who get a sick pay, involving 65% of the causes of disability, being only after cardiovascular diseases and mental disorders. It occurs predominantly in females during adulthood between the fourth and fifth decades, at the time of menopause³.

Total knee arthroplasty (TKA) has been stirring up the treatment of OA, changing the patient's functional status, quality of life and disabilities such as pain, stiffness and deformities caused by those articular disorders^{4,5,6,7}. Although the greatest concern is the relief of pain followed by the gain of articular amplitude and alignment of lower limbs, studies are increasingly focusing the deficit of muscle performance in these patients⁸.

Early post-operative rehabilitation is an important factor for the success of treatment in TKA, expected to commence in the immediate post-operative period with follow-up until functional independence of the patient. The absence of a rehabilitation treatment contributes negatively to the degree of knee function, leading to failure in rehabilitation^{9,10}. Likewise, functional rehabilitation of the knee in the post-operative period, mainly through kinesiotherapy exercises and early withdrawal of the patient from the bed are indispensable for better adaptation of the prosthesis⁹.

The rehabilitation program after total joint replacement maximizes the functional status of the patient in relation to mobility and daily life activities, and minimizes post-operative complications. There are few studies that standardize the rehabilitation

process regarding early withdrawal of the patient from bed and precocity of exercises, therefore making the comparison of methodology and results difficult.

Zuglianie et al. mention that TKA involves extensive tissue trauma, making analgesia of fundamental importance during this stage, but it should be considered that therapy with early joint mobilization is an important aspect to achieve good results¹.

Oliveira et al. studied the effectiveness of TKA associated to an early and intensive program of physiotherapy and concluded that the treatment proved to be effective in relation to pain, stiffness, function and, consequently, better quality of life for patients³. The objective of this study was analyzing the impact of early withdrawal of the patient from the bed on the first post-operative day in its rehabilitation and identifying the main reasons that slow down such process.

MATERIALS AND METHODS

This is a prospective and experimental study of 30 patients undergoing TKA, of both sexes, hospitalized in the ICU and nursing wards of Unimed Santa Helena Hospital. The individuals were oriented in time and space, with neurological evaluation compatible with 15 points on the Glasgow Coma Scale. After approval from the Research Ethics Committee of Santa Helena Hospital / Unimed Paulistana (an integral part of Plataforma Brasil), enrolled with the number 985,270 (CAAE 34854414.2.0000.5459), following the inclusion and exclusion criteria, each patient being previously informed by the Free and Informed Consent Form was included in the TKA physiotherapeutic protocol.

Non-collaborative patients or patients with cognitive disability, revisions of prosthesis, suspected prosthesis dislocation, neoplasms, association with other recent surgery on the same limb or contralateral limb, and hemodynamically unstable patients were excluded. After selection, patients were approached in their hospital beds by the physiotherapist in the immediate post-operative day, starting the institution's rehabilitation protocol in TKA, Chart 1.

<p>Preoperative Planning</p> <ul style="list-style-type: none"> -Guidance about the surgery and rehabilitation - Delivery of Guidelines Manual- Teach and instruct about breathing and metabolic exercises -Stretching exercises for lower limbs (harmstring, quadriceps, triceps surae) -Strengthening exercises for lower limbs (harmstring, gluteal muscles, quadriceps, abductor and adductor, triceps surae) -Gain of amplitude of movement, if necessary and possible -Instructions and beginning of gait training with walker -Electrothermal therapy and cryotherapy, if there is pain 	<p>Immediate PO</p> <ul style="list-style-type: none"> -Instructions to the patient / positioning -Electrotherapy, if there is pain -Cryotherapy -Breathing exercises -Metabolic exercises -Resisted exercises of the ankle, 3 series/10 repetitions. -Beginning of quadriceps isometry, 1 series/10 repetitions of 15 seconds -Active exercises of the non-operated limb -Discharge instructions
<p>POD 1</p> <ul style="list-style-type: none"> -Conduct maintained -Gain of amplitude of movement (passive/active assisted/active) of operated knee (90°) -Resisted exercises of non-operated limb, 3 series/10 repetitions. -Check if there is medical release to orthostatism and gait training in this phase and evaluate clinical conditions 	<p>POD 2</p> <ul style="list-style-type: none"> -Conduct maintained -Active gain of amplitude of movement in the operated limb -Sit on an armchair -Orthostatism with walker and weight bearing according to medical prescription -Gait training with walker and weight bearing according to medical prescription
<p>POD 3</p> <ul style="list-style-type: none"> -Conduct maintained -Reinforce discharge instructions 	

The outcomes studied were: pain, hospital stay average period, accession to the physiotherapeutic protocol, index of Physiotherapy referral by a doctor, amount of in-hospital physiotherapy sessions and factors that prevented leaving the bed on the first post-operative day.

In the comparison between groups using the criterion “left the bed or not”, the unpaired Student’s t-test was used. In the comparison between groups using the criterion “presence of pain”, the unpaired Student’s t-test was used. In the comparison between groups using the criterion “prescription of physiotherapy or not”, the Fisher’s exact test was used. In the comparison between the groups using the criterion “followed the physiotherapy protocol or not”, the Fisher’s exact test was used, assuming significant p values < 0.05. Data were presented as mean and standard deviation.

RESULTS

The average age of the sample comprised of 30 participants was 67.5 ± 7.4 years old, ranging from 52 to 82 years old. Regarding the gender, 24 (80%) were women. The mean weight was 75 ± 10.5 kilograms (kg). Mean BMI was 30.0 ± 3.9 kg/m², being that the group that left the bed on post-operative day 1 (SS) was heavier than patients in the other group (NS), but without any difference in mean BMI, where 47% of patients had some degree of obesity. In 100% of the cases studied, etiology for knee arthroplasty was OA. Data presented in Table 1.

Table 01. Characterization of groups that left the bed or not on post-operative day 1 after knee arthroplasty. São Paulo/SP, July/2014 to March/2015.

Left the bed	Age (years)	Female gender	Weight (kg)	BMI (kg/m ²)	Obesity
Yes	66.5±7.2	71% (12)	78.8±9.9	30.2±4.1	47% (8)
No	68.8±7.7	92% (12)	71±10	29.0±3.8	46% (6)
p	0.42	0.15	0.04	0.45	0.96

Key: BMI - body mass index, OA - osteoarthritis.

Regarding pain, the NS group presented more pain in all days of hospitalization when compared to SS group, with statistically significant difference. Data presented in Table 2.

Table 02. Pain assessment, comparing those groups that left the bed or not on post-operative day 1 after knee arthroplasty . São Paulo/SP, July/2014 to March/2015.

Variable	IPOD	POD 1	POD 2	POD 3
Left the bed	3.3±3.5	3.8±3.5	2.1±2.4	1.7±2.4
Did not leave the bed	6.4±4.1	7.1±3.2	5.7±3.2	4.6±2.8
p	0.03	0.01	0.00	0.03

Legend: VAS - visual analogue scale; IPO - immediate post-operative day; POD – post-operative day.

Regarding adherence to the physiotherapeutic protocol, SS group followed the protocol with more frequency than NS group, with statistically significant difference. The index of prescription of physiotherapy had no statistical difference between the groups. The mean hospital stay was 5.0 ± 2.5 days in group S, while 2.8±0.8 days in group SS. The number of Physiotherapy consultations performed was also higher in group S, with an average of 9.5 against 4.7 consultations on average in SS group. Data presented in Table 3 .

Table 03. Comparison of groups that left the bed or not on post-operative day 1 after knee arthroplasty . São Paulo/SP, July/2014 to March/2015.

Left the bed	Adherence to the protocol	Physiotherapy Prescription	Hospital Stay	In Physiotherapy Consultation
Yes	89% (51)	93% (56)	2.8±0.8	4.7±1.7
No	69% (36)	90% (47)	5±2.5	9.5±55.7
p	0.003	0.212	0.000	0.000

Legend: In Physiotherapy Consultation - number of Physiotherapy consultation performed.

The factors that prevented leaving the bed on post-operative day 1 were: lack of medical release in 8 (62%) cases, most often influenced by surgical complexity (bone loss, muscle anchoring, bleeding). Moreover, there were two (15%) cases of malaise (hemodynamic changes, nausea or dizziness); two (15%) cases where we observed lack of physiotherapy referral; and, one (8%) case in which pain was responsible for increased morbidity and hospitalization time. Data presented in Table 4.

Table 04. Factors that prevented patients from leaving the bed on post-operative day 1 after knee arthroplasty . São Paulo/SP, July/2014 to March/2015.

No medical release	Malaise	Lack of Physiotherapy referral	Pain
62% (8)	15% (2)	15% (2)	8% (1)

DISCUSSION

Indication of TKA to patients older than 60 years old is evident in this work (average 67.5 years old), given that this meets the findings in recent literature^{11, 12}. Data described by Meyer and Thober¹³ provide for the female gender as prevalent in knee arthroplasty surgeries with 77.7% of the cases, as well as Fuchs, Mattuella and Rabello¹¹, which showed 84.3%, and Carvalho Jr. et al. with 87.5%^{14,15}. In the present study, women were also prevalent, with 80% of the cases. When considering gender and age, we may observe hormonal changes resulting from menopause as a factor that predisposes this population to development of osteoarthritis of the knee.

In all cases, we analyzed osteoarthrosis as etiology for KTA. Some authors report osteoarthrosis of the knee as a major cause for surgery, but not in its entirety, varying in approximately 80% of the cases^{11,12}.

Obesity was present in our study in 47% of the cases. Population studies have consistently shown that obese individuals have increased risk for osteoarthritis of the knee in relation to those that are not obese. Data from the first epidemiological study conducted by the National Health and Nutrition Examination Survey (NHANES-I) show that obese women with body mass index over 30 and under 35 are nearly four times more prone to osteoarthritis of the knee than those with a BMI under 25¹⁴. In our study, the group that left the bed earlier had greater body weight, but with no statistical difference in the comparison of BMI. Dias A.S. et al.²⁴ suggests that this may be explained by the presence of other institutional protocols, which indicate that patients with a BMI >

25 are considered high-risk group for developing other complications associated with the restriction to bed for a period greater than 48 hours. That way, there is a careful treatment of the team to prevent complications in this group of patients.

In a study performed by Schneider et al.¹⁵, which evaluated the relation of overweight and obesity with musculoskeletal discomfort of postmenopausal women, those sites of musculoskeletal discomfort were observed. The greatest spot of pain was the lumbar spine (43.7%), followed by complaints related to the knee (40.6%), ankle/foot pain (28.1%), shoulder pain (28.1%), and hip pain (21.8%).

The factors most frequently observed for preventing patients from leaving the bed on post-operative day 1 were: lack of medical release, mostly influenced by surgical complexity (bone loss, muscle anchoring, bleeding), malaise (hemodynamic changes, nausea or dizziness), lack of physiotherapy referral and pain, responsible for increased morbidity and hospitalization time.

Patients with persistent pain since the immediate post-operative day without history of improvement must be subjected to an investigation for acute infection, instability of the prosthesis, misalignment and non-articular causes. Patients with substantial improvement of pain on the post-operative period that evolves to late pain may have such pain attributed to the loosening of components, late posterior instability or a late infection via hematogenic dissemination¹⁶.

In our study, there was a significant difference in pain throughout the days of hospitalization. NS group reported higher level of pain than SS

group, contributing to stay in bed. Pain is one of the main factors that limit ambulation and cause increased risk of thromboembolism by immobility, in addition to metabolic changes that affect several other systems^{17,18}. Because of that, individualized management of pain is fundamental, with the use of suitable analgesic techniques such as cryotherapy, used in our institutional protocol^{19,20}. In addition, early rehabilitation with a focus on accelerating post-operative recovery may reduce the time of hospitalization and return to activities of daily living^{21,22}. As for lack of physiotherapy referral between the groups, there was no significant difference.

Regarding the weaknesses of this study, failure in randomizing and controlling the sample may be taken into account. Furthermore, the fact that the number of professionals involved is high and that they knew they were taking part in the study may question control over the application of the physiotherapeutic protocol and data collection.

CONCLUSION

The protocol applied was beneficial in relation to pain, functional capacity and hospitalization time, which can reduce hospital costs.

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COMPETING INTERESTS

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

BIBLIOGRAPHICAL REFERENCES

1. Zugliani AH, Verçosa N, do Amaral JLG, Barrucand L, Salgado C, Karam MBH. Controle da Dor Pós-Operatória da

Artroplastia Total do Joelho: É Necessário Associar o Bloqueio do Nervo Isquiático ao Bloqueio do Nervo Femoral? Rev Bras Anesthesiol. 2007;57(5):514-524. doi: [10.1590/S0034-70942007000500006](https://doi.org/10.1590/S0034-70942007000500006)

2. Felice JC, Costa LFC, Duarte DG, Chahade WH. Elementos básicos do diagnóstico de Osteoartrose (OA). Temas de Reumatologia Clínica. 2002;3(3):68-81.

3. Oliveira TVC, Carvalho RRJ, Candido EAF, Lima PAL, Santana LS. Avaliação da efetividade da cirurgia de artroplastia total de joelho associada à fisioterapia sob o ponto de vista da funcionalidade. Scire Salutis. 2013;3(2):61-72. doi: [10.6008/ESS2236-9600.2013.002.0006](https://doi.org/10.6008/ESS2236-9600.2013.002.0006)

4. de Campos CC, Manzano GM, de Andrade LB, Filho AC, Nóbrega JAM. Translation and validation of an instrument for evaluation of severity of symptoms and the functional status in carpal tunnel syndrome. Arq Neuropsiquiatr. 2003;61(5):51-55. doi: [10.1590/S0004-282X2003000100009](https://doi.org/10.1590/S0004-282X2003000100009)

5. Fernandes MI. Tradução e validação do questionário de qualidade de vida específico para osteoartrose WOMAC para a língua portuguesa [dissertação]. São Paulo: Universidade Federal de São Paulo; 2003.

6. Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA. Patient outcomes after knee replacement. Clin Orthop Relat Res. 1998;356(7):93-110. doi: [10.1016/S0883-5403\(98\)90125-5](https://doi.org/10.1016/S0883-5403(98)90125-5)

7. Fortin PR, Clarke AE, Joseph L, Liang MH, Tanzer M, Ferland D et al. Outcomes of total hip and knee replacement: preoperative functional status predicts outcomes at six months after surgery. Arthritis Rheum. 1999;42(8):1722-1728. doi: [10.1002/1529-0131\(199908\)42:8<1722::AID-ANR22>3.0.CO;2-R](https://doi.org/10.1002/1529-0131(199908)42:8<1722::AID-ANR22>3.0.CO;2-R)

8. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. Clin Orthop Relat Res. 1989; (248):13-14. doi: [10.1097/00003086-198911000-00004](https://doi.org/10.1097/00003086-198911000-00004)

9. Firestone TP, Eberle RW. Surgical management of symptomatic instability following failed primary total knee replacement. J Bone Joint Surg Am. 2006;88(4):80-84. doi: [10.2106/JBJS.F.00825](https://doi.org/10.2106/JBJS.F.00825)

10. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. J Clin Epidemiol. 1993;46(12):1417-1432.

11. Fucks R, Matuella F, Rabello LT. Artroplastia total do joelho avaliação a médio prazo: dois a dez anos. Rev Bras Ortop. 2000;35(3):94-101.

12. Júnior LHC, Castro CAC, Gonçalves MBJ, Rodrigues LCM, Lopes FL, Cunha FVP. Complicações de curto prazo da artroplastia total de joelho: avaliação de 120 casos. Rev Bras Ortop. 2006;41(5):162-166.

13. Meyer M, Meyer BF, Thober E. Artroplastia total de joelho em pacientes obesos. *Rev Bras Ortop.* 2000;35(3):77-79.
14. Radominski SC. Obesidade e doenças músculo-esqueléticas. *Rev Bras Reumatol.* 1998;38(5):275-278.
15. Schneider RH, Rasia J, Berlezi EM, Bigolin SE. A relação do sobrepeso e obesidade com desconfortos musculoesqueléticos de mulheres pós-menopausa. *RBCEH.* 2007;4(1):28-38. doi: [10.5335/rbceh.2012.114](https://doi.org/10.5335/rbceh.2012.114)
16. Mandalia V, Eyres K, Schranz P, Toms AD. Evaluation of patients with a painful total knee replacement. *J Bone Joint Surg Br.* 2008;90(3):265-71. doi: [10.1302/0301-620X.90B3.20140](https://doi.org/10.1302/0301-620X.90B3.20140)
17. de Barros GAM, Lemonica L. Considerações sobre analgesia controlada pelo paciente em hospital universitário. *Rev Bras Anesthesiol.* 2003;53(1):69-82. doi: [10.1590/S0034-70942003000100010](https://doi.org/10.1590/S0034-70942003000100010)
18. Nett MP. Postoperative pain management. *Orthopedics.* 2010;33(9):23-26. doi: [10.3928/01477447-20100722-60](https://doi.org/10.3928/01477447-20100722-60)
19. Taylor JM, Gropper MA. Critical care challenges in orthopedic surgery patients. *Crit Care Med.* 2006;34(9):191-199. doi: [10.1097/01.CCM.0000231880.18476.D8](https://doi.org/10.1097/01.CCM.0000231880.18476.D8)
20. Dias AS, Rinaldi T, Barbosa LG. O impacto da analgesia controlada pelos pacientes submetidos a cirurgias ortopédicas. *Rev Bras Anesthesiol.* 2016;66(3):265-271. doi: [10.1016/j.bjan.2013.06.025](https://doi.org/10.1016/j.bjan.2013.06.025)
21. Lee HK, Lee JH, Chon SS, Ahn EK, Kim JH, Jang YH. The effect of transdermal scopolamine plus intravenous dexamethasone for the prevention of postoperative nausea and vomiting in patients with epidural PCA after major orthopedic surgery. *Korean J Anesthesiol.* 2010;58(1):50-55. doi: [10.4097/kjae.2010.58.1.50](https://doi.org/10.4097/kjae.2010.58.1.50)
22. Kauppila AM, Sintonen H, Aronen P, Ohtonen P, Kyllönen E, Arokoski JP. Economic evaluation of multidisciplinary rehabilitation after primary total knee arthroplasty based on a randomized controlled trial. *Arthritis Care Res.* 2011;63(3):335-341. doi: [10.1002/acr.20398](https://doi.org/10.1002/acr.20398)