



Syddansk Universitet

A Randomized, Controlled Trial of Total Knee Replacement

Skou, Søren Thorgaard; Roos, Ewa M.; Laursen, Mogens B

Published in:

The New England Journal of Medicine

DOI:

[10.1056/NEJMc1514794](https://doi.org/10.1056/NEJMc1514794)

Publication date:

2016

Document version

Publisher's PDF, also known as Version of record

Document license

Unspecified

Citation for pulished version (APA):

Skou, S. T., Roos, E. M., & Laursen, M. B. (2016). A Randomized, Controlled Trial of Total Knee Replacement. *The New England Journal of Medicine*, 374(7), 691-692. DOI: 10.1056/NEJMc1514794

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

contradict the results of the intention-to-treat analysis.

Martin R. Cowie, M.D.

Imperial College London
London, United Kingdom
m.cowie@imperial.ac.uk

Karl Wegscheider, Ph.D.

University Medical Center Eppendorf
Hamburg, Germany

Helmut Teschler, M.D.

University Hospital Essen
Essen, Germany

Since publication of their article, the authors report no further potential conflict of interest.

1. Momomura S, Seino Y, Kihara Y, et al. Adaptive servo-ventilation therapy for patients with chronic heart failure in a confirmatory, multicenter, randomized, controlled study. *Circ J* 2015; 79:981-90.
2. Nava S, Larovere MT, Fanfulla F, Navalesi P, Delmastro M, Mortara A. Orthopnea and inspiratory effort in chronic heart failure patients. *Respir Med* 2003;97:647-53.
3. Teschler H, Döhning J, Wang YM, Berthon-Jones M. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure. *Am J Respir Crit Care Med* 2001;164:614-9.

DOI: 10.1056/NEJMc1515007

THE EDITORIALISTS REPLY: With respect to the comments by Schäfer and colleagues: we think that further investigation in this area is required, albeit with appropriate informed consent. There are at least two major unanswered questions. First, we do not know whether the results of the

SERVE-HF trial were influenced by the specific adaptive servo-ventilation algorithm for adjustment of positive pressure. An ongoing trial (Effect of Adaptive Servo Ventilation on Survival and Hospital Admissions in Heart Failure [ADVENT-HF]; ClinicalTrials.gov number, NCT01128816) has different inclusion and exclusion criteria (it includes patients with both obstructive and central apneas) and uses a different adaptive servo-ventilation device with a less aggressive adjustment of positive pressure. The data and safety monitoring board for the ADVENT-HF trial has performed two interim analyses subsequent to the initial notification of the results of the SERVE-HF trial, and it has concluded that there are no safety concerns (Bradley TD: personal communication).

Second, we do not know whether the risks and benefits of adaptive servo-ventilation are different in specific subgroups of patients with sleep-disordered breathing and congestive heart failure. Thus, we continue to think that further investigation of this topic is required.

Ulysses J. Magalang, M.D.

Ohio State University Wexner Medical Center
Columbus, OH

Allan I. Pack, M.B., Ch.B., Ph.D.

University of Pennsylvania Perelman School of Medicine
Philadelphia, PA

Since publication of their article, the authors report no further potential conflict of interest.

DOI: 10.1056/NEJMc1515007

A Randomized, Controlled Trial of Total Knee Replacement

TO THE EDITOR: In the study reported by Skou and colleagues (Oct. 22 issue),¹ patients were excluded if they had symptomatic knee osteoarthritis with pain scores higher than 60 mm on a visual-analogue scale (on which scores range from 0 to 100, with higher scores indicating worse pain). We are unclear as to the rationale for excluding patients with this level of pain, who are commonly seen in orthopedic practice. We agree with the conclusion that total knee replacement is superior to the nonsurgical regimen investigated. However, we are concerned that the exclusion of 117 of 244 otherwise eligible patients (48%) because of severity of symptoms may have

led to substantial underestimation of the effect sizes of treatments in both groups, especially in the surgical group because of potentially increased crossover rates among the more severely symptomatic patients.

Reported serious adverse events (stiffness requiring manipulation of the knee while the patient was under anesthesia and deep venous thrombosis requiring anticoagulation) both occurred among 6% of patients in the total-knee-replacement group. These rates were higher than the respective rates (1.3%² and 1.5%³) reported elsewhere for much larger cohorts. The authors did not report the time-to-event end points, care

protocols (such as prophylaxis against deep venous thrombosis), and criteria for manipulation of the knee while the patient was under anesthesia. Collectively, these factors may lead to misinterpretation of the complications associated with total knee replacement.

David D. Teuscher, M.D.

American Academy of Orthopaedic Surgeons
Rosemont, IL

Jay R. Lieberman, M.D.

American Association of Hip and Knee Surgeons
Rosemont, IL
jay.lieberman@med.usc.edu

Dr. Lieberman reports receiving consulting fees and intellectual-property royalties from DePuy Synthes, holding stock options in Hip Innovation Technology, and receiving royalties and financial and material support from Elsevier. No other potential conflict of interest relevant to this letter was reported.

1. Skou ST, Roos EM, Laursen MB, et al. A randomized, controlled trial of total knee replacement. *N Engl J Med* 2015;373:1597-606.
2. Kim J, Nelson CL, Lotke PA. Stiffness after total knee arthroplasty: prevalence of the complication and outcomes of revision. *J Bone Joint Surg Am* 2004;86-A:1479-84.
3. Lewis CG, Inneh IA, Schutzer SF, Grady-Benson J. Evaluation of the first-generation AAOS clinical guidelines on the prophylaxis of venous thromboembolic events in patients undergoing total joint arthroplasty: experience with 3289 patients from a single institution. *J Bone Joint Surg Am* 2014;96:1327-32.

DOI: 10.1056/NEJMc1514794

THE AUTHORS REPLY: We agree with Teuscher and Lieberman that our results cannot be generalized to patients with a pain-intensity rating higher than 60 mm on a 100-mm visual-analogue scale during the previous week. However, at baseline, 42% of the patients reported pain higher than 60 mm when asked about worst pain during the previous 24 hours, and 22% reported, on average, at least severe pain during activities of daily living in the previous week. As stated in our article, the mean baseline Knee Injury and Osteoarthritis Outcome Score pain subscale score

of 49 (on a scale ranging from 0 to 100, with lower scores indicating more severe pain) was similar to previously reported scores in studies involving cohorts of patients who underwent total knee replacement.

In our study, patients who had severe knee stiffness during the rehabilitation period received manipulation of the knee while they were under anesthesia. A recent Danish multicenter study that included investigators from our department showed that among patients who underwent total knee replacement, 2.2% required manipulation of the knee while they were under anesthesia.¹

At admission to the hospital, all patients in our study received prophylaxis against deep venous thrombosis with 10 mg of rivaroxaban orally once daily for 1 to 3 days. Cases of deep venous thromboses were diagnosed on day 2, day 3, and day 184 after total knee replacement (the third case of deep venous thrombosis occurred in a patient after surgery for femoral-neck fracture during the follow-up period). Our trial was too small to provide reliable rates of adverse events associated with total knee replacement.

Søren T. Skou, P.T., Ph.D.

Aalborg University Hospital
Aalborg, Denmark
stskou@health.sdu.dk

Ewa M. Roos, P.T., Ph.D.

University of Southern Denmark
Odense, Denmark

Mogens B. Laursen, M.D., Ph.D.

Aalborg University Hospital
Aalborg, Denmark

Since publication of their article, the authors report no further potential conflict of interest.

1. Husted H, Jørgensen CC, Gromov K, Troelsen A. Low manipulation prevalence following fast-track total knee arthroplasty. *Acta Orthop* 2015;86:86-91.

DOI: 10.1056/NEJMc1514794

Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy

TO THE EDITOR: Amant et al. (Nov. 5 issue)¹ report on a study of outcomes in children exposed in utero to maternal cancer. Despite the impor-

tance of this study, we are concerned about some basic methodologic flaws.²

Although this study is presented as a “pro-