Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective
A randomized clinical trial involving 87 patients with 3 months of follow-up

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Background Approximately 12,000 hip and knee replacements were performed in Denmark in 2005. Accelerated perioperative interventions are currently implemented, but there is conflicting evidence regarding the effect. We therefore performed an efficacy study of an accelerated perioperative care and rehabilitation intervention in patients receiving primary total hip replacement, and both total and unicompartmental knee replacement.

Methods A randomized clinical trial was undertaken in which 87 patients were randomized to either a control group receiving the current perioperative procedure, or an intervention group receiving a new accelerated perioperative care and rehabilitation procedure. Outcome measures were length of stay (LOS) in hospital, and gain in quality of life (QOL) using EQ-5D from baseline to 3-month follow-up.

Results Mean LOS was reduced (p < 0.001) from 8 days (95% CI: 7.1–8.4) in the control group to 5 days (95% CI: 4.2–5.6) in the intervention group. This was accompanied by a greater gain in QOL of 0.08 (95% CI: 0.004–0.16) in the intervention group (p = 0.03).

Interpretation An accelerated perioperative care and rehabilitation intervention in patients undergoing primary total hip replacement, and total or unicompartmental knee replacement is indeed effective—and of advantage to both the hospital and the patient.

In Denmark in 2004, the incidence of total hip replacement (THA) was 142 per 100,000 inhabitants, and the incidence of total knee replacement (TKA) was 88 per 100,000 inhabitants (Danish National Board of Health 2006). The incidences of both are increasing (Pedersen et al. 2005, Danish National Board of Health 2006). In 2005, approximately 12,000 hip and knee replacements were performed in Denmark (Danish National Board of Health 2006). Hip and knee replacements are major surgical procedures that require postoperative interventions in order to minimize the perioperative stress response (Kehlet and Dahl 2003). New procedures to optimize perioperative intervention, defined as the period from hospitalization to discharge, have been given several names—such as multimodal intervention, joint care, accelerated intervention, and clinical pathway. There is conflicting evidence for the efficacy of accelerated interventions. Dowsey et al. (1999) concluded from their randomized clinical trial (RCT) that a clinical pathway in patients receiving total hip and knee replacement gives a better outcome and reduces the average length of stay (LOS). An RCT by Reilly et al. (2005) showed an average reduction in LOS of 3 days in patients who underwent an accelerated recovery protocol for unicompartmental knee arthroplasty (UKA). In contrast to these two studies, an RCT

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by Petersen et al. (2006) did not reveal any effect of a multimodal approach in patients undergoing hip replacement. A review of clinical pathways in hip and knee replacement, not including the two latest RCTs, concluded that clinical pathways for total hip and knee replacement reduce costs and LOS (Kim et al. 2003). A significant reduction in LOS has also been reported in several Danish non-RCT studies (Rasmussen et al. 2001, Husted et al. 2004, 2006).

In summary, the potential of accelerated perioperative interventions for patients undergoing total hip and knee replacement is great, but the overall level of evidence is low. We therefore investigated the efficacy of an accelerated perioperative care and rehabilitation intervention in patients undergoing primary total hip replacement, and total or unicompartmental knee replacement.

**Patients and methods**

This randomized clinical intervention trial followed the recommendations of the CONSORT Statement (Moher et al. 2001). The study took place in the Orthopedic Clinic of Holstebro Regional Hospital, Denmark, from June, 2004 to May, 2006. The procedures followed in the study were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study protocol was approved by the Medical Ethical Committee of Ringkjobing and Southern Jutland Counties (Ref.: 2627-04). The study was also registered with the Danish Data Protection Agency (J. no. 2004-41-4753).

**Study subjects**

All patients who were planned to undergo elective primary THA, TKA, or UKA were consecutively invited to participate in the study. All patients who met the inclusion criteria were given written and oral information of the study at the initial visit, and those who were interested gave their written consent. The exclusion criteria were (1) mental disability or (2) severe neurological disease. The patients were randomized to either the current procedure group (control group) or the new accelerated procedure group (intervention group). After randomization, the patients filled in a baseline questionnaire.

**Sample size**

The estimated sample size at follow-up was calculated using actual data on LOS from Holstebro Regional Hospital in 2004 together with the results of a pilot study in the first half of 2005. The risk of performing a type-1 error was set at 5% using a two-sided analysis, and the power of detecting a true difference was set at 80%. LOS was expected to be 8 days (SD 4.0) in the control group, and 6 days (SD 2.0) in the intervention group. Using a two-sample comparison of means, we needed at least 40 patients in each group, at follow-up. To account for possible loss of patients, 90 patients were included.

**Randomization**

A secretary not otherwise involved in the study performed a stratified randomization by drawing an opaque envelope with a number from one of three boxes. The identities of 58 hip patients were drawn from a box with 60 envelopes. The identities of 28 total knee patients were drawn from a box with 30 envelopes, and finally the identities of 4 patients destined to undergo unicompartmental knee replacement were drawn from a box with 4 envelopes. The sizes of the hip and knee groups were obtained from the ratios for THA, TKA, and UKA seen in 2004 and 2005.

**Pre-intervention period**

The current procedure (for control patients) was observed and analyzed during the 12-month period from June, 2004 to June, 2005, and a detailed description was made. We developed a new accelerated intervention from the results of analysis of the current procedure and from a description of the regimes from the Unit of Perioperative Nursing Care, Rigshospitalet, Denmark (Unit of Perioperative Nursing 2006). A new special care and rehabilitation unit with 4 male and 4 female beds was established, whereby the patients were treated in groups and the healthcare staff concentrated on controlling the postoperative pathophysiology and rehabilitation. All staff allocated to the new perioperative unit received education and participated in a pre-study trial period from January 2005 to
May 2005. After evaluation of this pilot study in 23 patients during May and June, 2005, the final accelerated intervention was defined in detail.

**Intervention**

**Control group.** Patients were hospitalized on the day before surgery, and placed in a general orthopedic ward. They were given hospital clothes to be worn during the whole stay, and were informed of the procedure and prepared for surgery. During the day before surgery the patients were individually informed of the path by the surgeon, anesthetist, and nurse. Final blood tests, heart EKG, and radiographs were taken. Immediately after surgery, the patient’s pain was evaluated and analgesics were given accordingly. On the day after surgery the patients started training in bed before lunch, and were mobilized out of bed after lunch by a physiotherapist. During the following days mobilization was increased, in order to reach the discharge criteria. During the stay, care was given in response to the patient’s actual needs and rehabilitation was adjusted according to the patient’s immediate state.

**Intervention group.** All patients—with one relative each—were invited to an information day on the Friday before their week of surgery. The purpose of the information day was to inform the patients (in groups) of the accelerated path, and also to prepare the patients for surgery through individual consultations with the surgeon, anesthetist, and nurse. Final blood tests, heart EKG, and radiographs were taken. All patients were hospitalized in the new accelerated unit on the day of surgery. The patients used their own clothes during the whole stay. Healthcare staff worked to achieve written preset daily goals regarding: (1) information, (2) pain relief, (3) nausea control, (4) nutrition, (5) mobilization, and (6) elimination. These goals are discussed individually below.

1. Information about the information day focused on partial goals during the hospital stay, the discharge planned for the fourth postoperative day, how to relieve pain, mobilization strategies, and how to get help.
2. Pain relief consisted of Oxycontin/Oxynorm and Paracetamol.
3. Zofran was used for control of nausea.
4. A nutrition screening was performed on the information day, and the patient ate according to this result in combination with a daily intake of two protein beverages, with a total fluid consumption of at least 2 liters.
5. Mobilization started on the day of surgery. On the first postoperative day, the goal was 4 h out of bed including training with a physiotherapist and an occupational therapist. Our aim was more than 8 h of mobilization per day for the rest of the hospital stay.
6. For elimination, we used Magnesia. Patients also followed a scheme with the above-mentioned preset goals for nutrition, fluid consumption, and mobilization.

For further detailed information regarding the accelerated intervention, please see “The Unit of Perioperative Nursing Care” at http://www.rigshospitalet.dk/rh.nsf/Content/unitofperioperativenursing-ortopedicsurgery.

**Discharge criteria.** There were equal discharge criteria in both groups: (1) acceptance of discharge, (2) sufficient pain control, (3) awareness of procedures for ending medication, (4) knowing the restrictions, (5) ability to walk safely with or without walking aids, (6) ability to walk on stairs, (7) ability to perform home exercises, (8) knowing how to increase home exercises, (9) ability to perform one’s personal needs, (10) helping aids having been delivered and installed, (11) operation wound showing no sign of infection, and (12) in knee patients, at least 90º of knee flexion.

**Attempts to reduce bias.** The two patient groups and their healthcare staff were kept separated during the study period, and the healthcare staff was not allowed to discuss the intervention. Two newly employed therapists who were not familiar with the usual procedures were mostly responsible for rehabilitation of patients in the intervention group. Healthcare personnel dealing with the control group were not aware of the procedures in the intervention group.

Because LOS was related to both the intervention and the outcome, we used doctors who were not otherwise involved in the study to decide when discharge criteria had been fulfilled. We used questionnaires for all data collection.

We investigated a possible time-change effect by collecting data from a historical control group (2004 data from Holsterbro Regional Hospital). We expected a yearly reduction in LOS of 0.8 days on average between the historical control group and the randomized control group, because of an
observed trend in reduced LOS seen from 2001 to 2005 in Denmark (Danish National Board of Health 2006).

Two nurses who were not otherwise involved in the study examined the extent of a possible contamination effect. They performed a structured observation, which focused on changes between two visits in 5 areas: information, pain control, nutrition, mobilization, and other care and rehabilitation procedures. Finally, we also investigated a possible contamination effect by collecting data from a concurrent control group (2005 data from Herning Regional Hospital). The hospitals of Herning and Holstebro share common ideals, but—geographically—cover different parts of the Central Denmark Region. We considered the two hospitals to be similar regarding the current intervention procedures during the study period. No significant differences between the two hospitals could be identified regarding sex, age, diagnoses, or operational procedures in 2004 and 2005.

Follow-up

LOS was recorded using register information from the hospital registration system. At 3 months after discharge, all patients were seen on an outpatient basis at Holsterbro Regional Hospital where they filled in a follow-up questionnaire.

Outcome measures

The primary outcome measure was LOS at discharge, and the secondary outcome measure was the patient’s gain in health-related quality of life (QOL) at 3-month follow-up. Side effects were collected from register data on mortality, readmissions, and complications that occurred within 3 months postoperatively.

Statistics

All data were entered twice using EpiData 3.1 (Lauritsen and Bruus 2003-2005). The data were analyzed using intention-to-treat analysis according to the recommendations in evidence-based medicine (Sackett et al. 2000). We calculated unadjusted crude and stratified mean LOS for THA, TKA, and UKA (with standard deviation) for the intervention group, the control group, and the groups of excluded patients: patients who refused to participate, the concurrent control patients, and the historical control patients. Because of a non-normal distribution of LOS, we calculated the unadjusted crude and unadjusted stratified median differences for THA, TKA, and UKA between the accelerated intervention and the current intervention using nonparametric equality-of-median test, combined with Hodges-Lehman median differences with 95% confidence interval. The adjusted effect of the accelerated intervention on LOS was estimated in a multivariate linear regression analysis, after controlling for assumptions (independence of random deviations, same distribution of random deviations, and normality of random deviations). The analysis included: randomization group, sex, age as a continuous variable, diagnosis of arthrosis or not, cemented implant or not, with the randomization stratification as a covariate. Results are reported for LOS from admission to discharge and also for LOS from day of surgery to discharge. Results for LOS are also presented as the proportion discharged at or before the fifth day, in order to estimate the Number Needed to Treat (Sackett et al. 2000).

QOL scores/values were obtained using a standardized instrument for measurement of health outcome: “EQ-5D” (Szende and Williams 2004). QOL score were calculated using the Official Danish Time Trade Off-scores (Pedersen et al. 2003). We calculated unadjusted crude and stratified mean QOL for THA, TKA, and UKA (with SD) for the two randomization groups. The unadjusted crude and unadjusted stratified mean difference in gain in QOL, from baseline to follow-up, between groups was analyzed using two-sample t-test. Because of non-normal distributions of QOL, unadjusted crude and stratified differences between groups at follow-up were calculated using nonparametric equality-of-median test, combined with Hodges-Lehman median differences with 95% confidence interval. The adjusted gain in QOL from baseline to follow-up was analyzed in a multivariate linear regression analysis, with nonparametric confidence intervals based on 1,000 bias-corrected and accelerated bootstrap replicates, according to Manca et al. (2005), after controlling for assumptions. The analysis included: randomization group, QOL at baseline, gender, age as a continuous variable, diagnosis of arthrosis or not, cemented implant or not, and the randomization stratification as a covariate. Results for QOL are presented as the proportion
described as being “well” at the 3-month follow-up. “Well” was defined as achievement of a QOL at or above the observed age-adjusted QOL for the Danish population (Pedersen et al. 2003). All analyses were performed using STATA 9.1 (StataCorp, College Station, TX). The significance level was set at $p < 0.05$.

Results

117 patients were eligible for the study. Of these, 27 were not included: 23 refused to participate, 2 were excluded due to mental disability, 1 patient was excluded because of physical disability from a neurological disease, and 1 patient was excluded because she did not submit any written consent before surgery. This left 90 patients for randomization. 45 patients were allocated to each group, with 30 THA patients to the control group and 28 THA patients to the intervention group. 13 TKA patients were allocated to the control group and 15 TKA patients were allocated to the intervention group. Finally, 2 UKA patients were allocated to each group (Figure). 3 patients in the control group were excluded after randomization (2 THA and 1 TKA). 1 was excluded because surgery was cancelled due to infection preoperatively, and 2 because they wanted surgery past the inclusion period. This left 87 patients to receive the allocated intervention: 42 in the control group (28 THA, 12 TKA, and 2 UKA), and 45 in the intervention group (28 THA, 15 TKA, and 2 UKA). Patients in the 2 groups were comparable at baseline (Table 1). For an overview of all patients, see Table 2. 1 patient died perioperatively, and LOS for this patient from admission to death was included in the intention-to-treat analysis. Complete data from baseline to 3-month follow-up were obtained from all other patients.

Average length of stay from admission to discharge (primary outcome)

Mean LOS was 4.9 (SD 2.4) in the intervention group and 7.8 (SD 2.1) in the control group. Overall, there was an unadjusted median reduction in LOS of 3.0 (95% CI: 3–4) days in the intervention group relative to the control group ($p < 0.001$). The adjusted mean difference yielded a reduction in LOS of 3.1 (95% CI: 2.3–4.0) days ($p < 0.001$). For further information of unadjusted crude LOS, unadjusted stratified LOS, and adjusted LOS in the two groups, see Table 3. The adjusted mean difference between the control and intervention groups from day of surgery to discharge yielded a reduction in LOS of 1.5 (95% CI: 0.7–2.3) days favoring the accelerated intervention ($p < 0.001$).
More patients in the intervention group were discharged at or before the fifth day (p < 0.001): 35 of 45 in the intervention group compared to 3 of 42 in the control group (THA 24 vs. 2, TKA 9 vs. 0, and UKA 2 vs. 1). This led to a Number Needed to Treat of 1 patient (95% CI: 1–2).

### Average quality of life (secondary outcome)

Both groups reported a substantial gain in QOL from baseline to 3-month follow-up. The gain in QOL was 0.42 (SD 0.31) in the intervention group and 0.26 (SD 0.31) in the control group. We observed a significant unadjusted crude difference in gain in QOL of 0.16 (95% CI: 0.02–0.29) favoring the intervention group. The adjusted mean difference likewise yielded a significant difference in gain in QOL of 0.08 (95% CI: 0.004–0.16) in favor of the intervention group (Table 4).

### Proportion of patients who were well at the 3-month follow-up

28 of 45 patients were classified as being well (at or above the observed age-adjusted QOL for the Danish population) in the intervention group, and 15 of 42 patients were classified as being well in the control group at the 3-month follow-up (THA 19/28 vs. 9/28, TKA 8/15 vs. 6/12, UKA 1/2 vs. 0/2). This led to a Number Needed to Treat of 3 (95% CI: 2–11) for the accelerated intervention.

### Profile of patients who refused to participate

The patients who refused to participate consisted of at least two groups. One group was characterized by younger age, with a higher proportion of males and of hip replacements with an uncemented prosthesis. The other group was characterized by older age, with a higher proportion of females and of knee replacements.

### Potential bias observed in concurrent and historical control groups

No obvious contamination was identified in the current intervention group under the structured observation. The observed average LOS of 7.8 days in the randomized control group was lower than the expected average of 8.5 days, after adjusting for time change. The observed average LOS

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**Table 1. Baseline data for 87 patients in the current intervention and accelerated intervention groups, Denmark 2005–2006**

| Group     | Accelerated intervention | Current intervention |
|-----------|--------------------------|----------------------|
| All (n)   | 45                       | 42                   |
| Female/male ratio | 25/20                   | 19/23                |
| Age, mean (SD)  | 64 (10.8)               | 66 (9.2)             |
| Mean QOL * (SD) | 0.46 (0.28)          | 0.53 (0.22)          |
| THA (n)   | 28                       | 28                   |
| Female/male ratio | 15/13                   | 11/17                |
| Age, mean (SD)  | 62 (11.3)               | 65 (9.5)             |
| Arthritis coxae / other | 27/1                    | 28/0                 |
| Implant cemented / uncemented ratio | 8/20                  | 12/16                |
| Mobility, level 1 / 2 / 3 b | 2/25/1               | 1/27/0               |
| Self-care, level 1 / 2 / 3 | 13/14/1              | 16/12/0              |
| Usual Activities, level 1 / 2 / 3 | 3/20/5              | 1/23/4               |
| Pain/Discomfort, level 1 / 2 / 3 | 0/13/15            | 0/14/14              |
| Anxiety/Depression, level 1 / 2 / 3 | 20/7/1              | 22/6/0               |
| Mean QOL (SD) | 0.45 (0.30)           | 0.49 (0.22)          |
| TKA (n)   | 15                       | 12                   |
| Female/male ratio | 9/6                    | 7/5                  |
| Age, mean (SD)  | 68 (9.1)               | 67 (10.2)            |
| Arthritis genus / other | 15/0                | 11/1                 |
| Mobility, level 1 / 2 / 3 | 1/14/0               | 0/12/0               |
| Self-care, level 1 / 2 / 3 | 10/5/0               | 11/1/0               |
| Usual Activities, level 1 / 2 / 3 | 2/8/5               | 2/7/3                |
| Pain/Discomfort, level 1 / 2 / 3 | 0/6/9               | 0/8/4                |
| Anxiety/Depression, level 1 / 2 / 3 | 8/7/0               | 11/1/0               |
| Mean QOL (SD) | 0.44 (0.24)           | 0.60 (0.22)          |
| UKA (n)   | 2                        | 2                    |
| Female/male ratio | 1/1                    | 1/1                  |
| Age, mean (SD)  | 60 (13.4)              | 61 (6.4)             |
| Arthritis genus / other | 2/0                 | 2/0                  |
| Mobility, level 1 / 2 / 3 | 0/2/0                | 1/1/0                |
| Self-care, level 1 / 2 / 3 | 1/1/0                | 1/1/0                |
| Usual Activities, level 1 / 2 / 3 | 0/2/0               | 0/1/1                |
| Pain/Discomfort, level 1 / 2 / 3 | 0/2/0               | 0/2/0                |
| Anxiety/Depression, level 1 / 2 / 3 | 0/2/0               | 1/1/0                |
| Mean QOL (SD) | 0.67 (0.05)           | 0.66 (0.22)          |

*a Quality of life from EQ-SD.

*b Statement from EQ-SD:

Level 1: no problems;
Level 2: some/moderate problems;
Level 3: unable to perform task/extreme problems.
in the concurrent control group was 8.7 days, as expected (Table 3).

**Adverse effects**

**Death.** 1 THA patient in the control group died perioperatively on the day after surgery because of a pulmonary embolism.

**Re-admission.** 3 patients were re-admitted to hospital within 3 months of discharge. The additional LOS after discharge was not included in the estimation of perioperative LOS for these 3 patients. In the control group, 1 TKA patient was re-admitted because of wound infection. This patient finally had to undergo revision surgery, which resulted in an additional LOS of 15 days. In the intervention group 2 patients were re-admitted: 1 TKA patient had an additional LOS of 11 days because of swelling and pain in the knee, and 1 THA patient had an additional LOS of 1 day because of dislocation of the hip. This led to a total additional LOS of 12 days in the intervention group.

**Discussion**

Our study is the first Scandinavian RCT to show a statistically significant and large, clinically relevant, reduction in length of stay using an accelerated perioperative approach in patients undergoing total hip, total knee, and unicompartmental knee replacement. It is also the first RCT to show that these patients also benefit from an accelerated intervention.

We believe that our attempts to minimize selection bias were successful. This was reached using consecutive inclusion, broad inclusion criteria, and only excluding patients who were mentally and severely physically disabled. Fewer than 5% of the eligible patients were excluded. Those patients who refused participation fell into two groups. One group, young male patients destined to have a uncemented hip implant, could easily be accelerated. The other group, elderly women destined to have knee replacement, would probably be more difficult to accelerate. We expect, however, that these two groups would perform as well on average as those who were included. Furthermore, our
sample was similar regarding sex, age, diagnosis, and implant type to that of concurrent and historical control groups.

We believe our attempts to mask the identity of the patients and the healthcare personnel were successful. Any potential placebo effect and Hawthorne effect (positive effect of being under study) were considered to be equal in the two groups, and these will be dealt with in a later study examining the effectiveness and the cost-effectiveness of the intervention. We believe that we successfully minimized any possible observer bias, using questionnaires. Moreover, we believe that the discharge procedures were identical in both groups, and we can certainly refute the idea that the discharge was more restrictive in the current intervention group.

Discharge was actually performed at an earlier time point in the randomized control group than in the historical control group and in the concurrent control groups. We also believe that our attempts to minimize contamination were successful. However, we cannot rule out a contamination effect of 0.5–1.0 day disfavoring the accelerated intervention, in comparing the randomized control group to the concurrent control group and the historical control group.

Using LOS as an outcome measure is rather problematic, as it is also part of the intervention. Thus, we stress the fact that LOS cannot be regarded as a single primary outcome but must be seen in relation to other outcome measures—such as we have done using QOL and adverse effects. We believe

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**Table 3. Unadjusted, crude and stratified mean length of stay (LOS) with standard deviation, in the accelerated intervention group, the current intervention group, and four other groups receiving the current procedure (499 patients). Median and median difference with 95% confidence limits between the accelerated and the current intervention group. Adjusted mean difference in length of stay, Denmark 2004–2006**

| Group | Eligible for randomized study | Non-randomized patients |
|-------|-------------------------------|-------------------------|
|       | Accelerated intervention | Current intervention | Excluded from study | Refused | Concurrent | Historical |
| Unadjusted | Crude (n) | 45 | 42 | 4 | 23 | 96 | 289 |
|          | Mean (SD) | 4.9 (2.4) | 7.8 (2.1) | 8.3 (1.7) | 7.2 (1.8) | 8.7 (2.8) | 9.3 (3.9) |
|          | Median | 4 | 7 | 3 (3–4) b | < 0.001 c |
|          | P-value |  |  | < 0.001 c |
| Stratified | THA, (n) | 28 | 28 | 3 | 10 | 53 | 179 |
|          | Mean (SD) | 4.4 (1.3) | 7.3 (1.5) | 9.0 (1.0) | 7.6 (1.4) | 7.8 (2.8) | 9.2 (4.3) |
|          | Median | 4 | 7 | 3 (2–4) | < 0.001 |
|          | P-value |  |  | < 0.001 |
|          | TKR, (n) | 15 | 12 | 1 | 12 | 43 | 110 |
|          | Mean (SD) | 6.1 (3.5) | 9.3 (2.5) | 8.5 | 7.2 (1.8) | 9.9 (2.5) | 9.6 (3.3) |
|          | Median | 4 | 8.5 | 4 (2–5) | 0.04 |
|          | P-value |  |  | 0.04 |
|          | UKA, (n) | 2 | 2 | 1 | 3.0 |
|          | Mean (SD) | 3.0 (0) | 6.0 (1.4) | 6.0 (1.4) | 3.0 |
|          | Median | 3 | 6 | 3 (2–4) | 0.3 |
|          | P-value |  |  | 0.3 |
| Adjusted | Difference, CI | 3.1 (2.3–4.0) d | 3.1 (2.3–4.0) d |
|          | P-value | < 0.001 |

a Difference: Median LOS current intervention – median LOS accelerated intervention.
b Hodges-Lehman median differences with 95% confidence interval.
c Difference between groups tested with nonparametric equality-of-medians test.
d Mean difference with 95% confidence interval from multivariate linear regression including randomization group, QOL at baseline, gender, age, diagnosis, implant type, and randomization stratification.
that the best way to handle LOS is to calculate costs for both perioperative LOS and re-admission LOS, and to include this in a cost-efficiency analysis. This will be dealt with in a future study.

Our analysis of LOS and QOL included adjustment for the most common confounders, as well as randomization stratification in order to obtain the most precise estimate of the effect of an accelerated intervention. We observed a marked difference between the results of the unadjusted and the adjusted analysis of QOL gain, indicating that future studies of QOL or quality-adjusted life year (QALY) must take baseline differences in group characteristics into account.

Regarding the effect of an accelerated intervention on LOS, the results of our study are in accordance with the study by Reilly et al. (2005). They used a true accelerated intervention in patients receiving unicompartitional knee replacement. True accelerated intervention was defined as an intervention aimed at discharge before the fifth postoperative day (Danish National Board of Health 2006). Our result is also in accordance with the work of Dowsey et al. (1999) who showed a significant, but minor average reduction in LOS of 1.5 days in hip and knee patients, when using a semi-accelerated intervention. Our result does, however, conflict with the study by Petersen et al. (2006), which did not show a reduction in LOS in hip patients when using a semi-accelerated intervention. The reason why only a minor reduction in LOS was reached in the study by Dowsey et al. and no reduction was achieved in the study by Petersen et al. can be explained by a contamination effect in the control group, as both studies reported a general reduction in LOS during the study period.

We believe, however, that we could have achieved an even shorter LOS for the knee patients if we had not included the criterion for the patients to be able to reach 90° of knee flexion before discharge.

Table 4. Unadjusted, crude, and stratified mean quality of life (QOL) with standard deviation. Mean and median difference with 95% confidence interval between the accelerated and the current intervention group at 3-month follow-up, and gain from baseline to follow-up. Adjusted mean difference in quality of life at 3-month follow-up, for 87 hip and knee patients, Denmark 2005–2006

| Group            | Accelerated intervention | Current intervention | Difference a | P-value  |
|------------------|--------------------------|----------------------|--------------|----------|
| Unadjusted       |                          |                      |              |          |
| Crude (n)        | 45                       | 42                   | 0.08 (0–0.16) | 0.003    |
| Follow-up        | 0.87 (0.15) b            | 0.79 (0.20)          | 0.08 (0–0.16) | 0.003    |
| Gain             | 0.42 (0.31)              | 0.26 (0.31)          | 0.16 (0.02–0.29) | 0.02    |
| Stratified       |                          |                      |              |          |
| THA (n)          | 28                       | 28                   | 0.13 (0–0.19) | 0.001    |
| Follow-up        | 0.88 (0.17)              | 0.76 (0.23)          | 0.13 (0–0.19) | 0.001    |
| Gain             | 0.44 (0.33)              | 0.27 (0.34)          | 0.16 (0.2–0.35) | 0.07    |
| TKA (n)          | 15                       | 12                   |              |          |
| Follow-up        | 0.86 (0.11)              | 0.86 (0.09)          | 0 (-0.07–0.08) | 0.1     |
| Gain             | 0.42 (0.28)              | 0.26 (0.25)          | 0.16 (-0.06–0.37) | 0.1     |
| UKA (n)          | 2                        | 2                    |              |          |
| Follow-up        | 0.85 (0.21)              | 0.80 (0.06)          | 0.05 (-0.13–0.25) | 0.3     |
| Gain             | 0.18 (0.17)              | 0.13 (0.16)          | 0.05 (-0.76–0.65) | 0.8     |
| Adjusted         |                          |                      | 0.08 (0.01–0.16) | 0.03    |

a Difference: QOL accelerated group – QOL current group.
b Mean ( Standard deviation).
c Hodges-Lehman median differences with 95% confidence interval.
d Difference between groups tested with nonparametric equality-of-medians test.
e Mean difference with 95% confidence interval.
f Difference between groups tested with two-sample t-test.
g Mean difference with 95% nonparametric confidence interval based on 1,000 bias-corrected and accelerated bootstrap replicates.
h Multivariate linear regression including randomization group, QOL at baseline, gender, age, diagnosis, implant type, and randomization stratification.
Omission of this criterion is in accordance with the Danish Health Technology Assessment (Danish National Board of Health 2006). Our result regarding LOS was robust enough to show a significant effect of a “true interventional part” of the study, excluding the observed LOS before surgery.

We have not found any RCT using EQ-5D as an outcome measure for patients undergoing hip or knee replacement. Our results are, however, in accordance with the non-RCT by Brunenberg et al. (2005). These authors used a similar intervention, but a before-after design. They demonstrated a reduction in LOS of 4 days. Their results regarding QOL difference from baseline to 3-month follow-up were of the same magnitude as ours. They showed a clinically relevant but non-significant difference in QOL at follow-up in favor of the accelerated intervention. Our results are, however, 0.1 QOL higher on average than theirs—both at baseline and at follow-up. We do not know why this difference arose. It could be a true difference, if surgery in the Netherlands is performed on the basis of other indications than in Denmark. Alternatively, there may have been a difference in the interpretation and understanding of the questions in the EQ-5D, or in the way EQ-5D is scored in the two countries.

Altogether, we observed adverse effects in 4 patients: 1 death and 3 re-admissions. This is in accordance with reporting from other Danish hospitals (Danish National Board of Health, 2006). There is a risk of accelerating the pathway too much; a very high re-admission rate of 13% within 30 days was reported from the hospital that achieved the shortest LOS, and an overall higher re-admission rate was observed for the knee patients undergoing the accelerated procedures (Danish National Board of Health 2006). We consider the reporting of any re-admission to be the best measure for comparison of adverse effects of premature discharge, as it is not affected by misclassifications in coding of complications. We therefore recommend focusing as much on adverse effects, such as perioperative infections, implant dislocation, and any re-admissions, as on LOS when implementing accelerated procedures.

We believe that the results seen regarding LOS and QOL were achieved mainly because of the new nurse-led organization, with an information day and early and more aggressive mobilization. There were only minor differences between the two procedures regarding pain relief, nausea reduction, nutrition, and elimination. One of the strengths of our study is that it was performed in a local hospital where the average patient is treated, and not in a university hospital, where highly selected and more special cases are treated. We therefore believe that our interventions can be widely implemented and that similar results can be achieved in other hospitals. Summing up what we know of accelerated interventions, we can say that there is great potential in the use of accelerated procedures and we believe that the evidence strongly favors the use of accelerated interventions in both hip and knee replacement.

Contributions of authors

All authors have contributed to the planning, interpretation and revision of the manuscript. KL collected the data, KL and OGS analyzed the data.

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