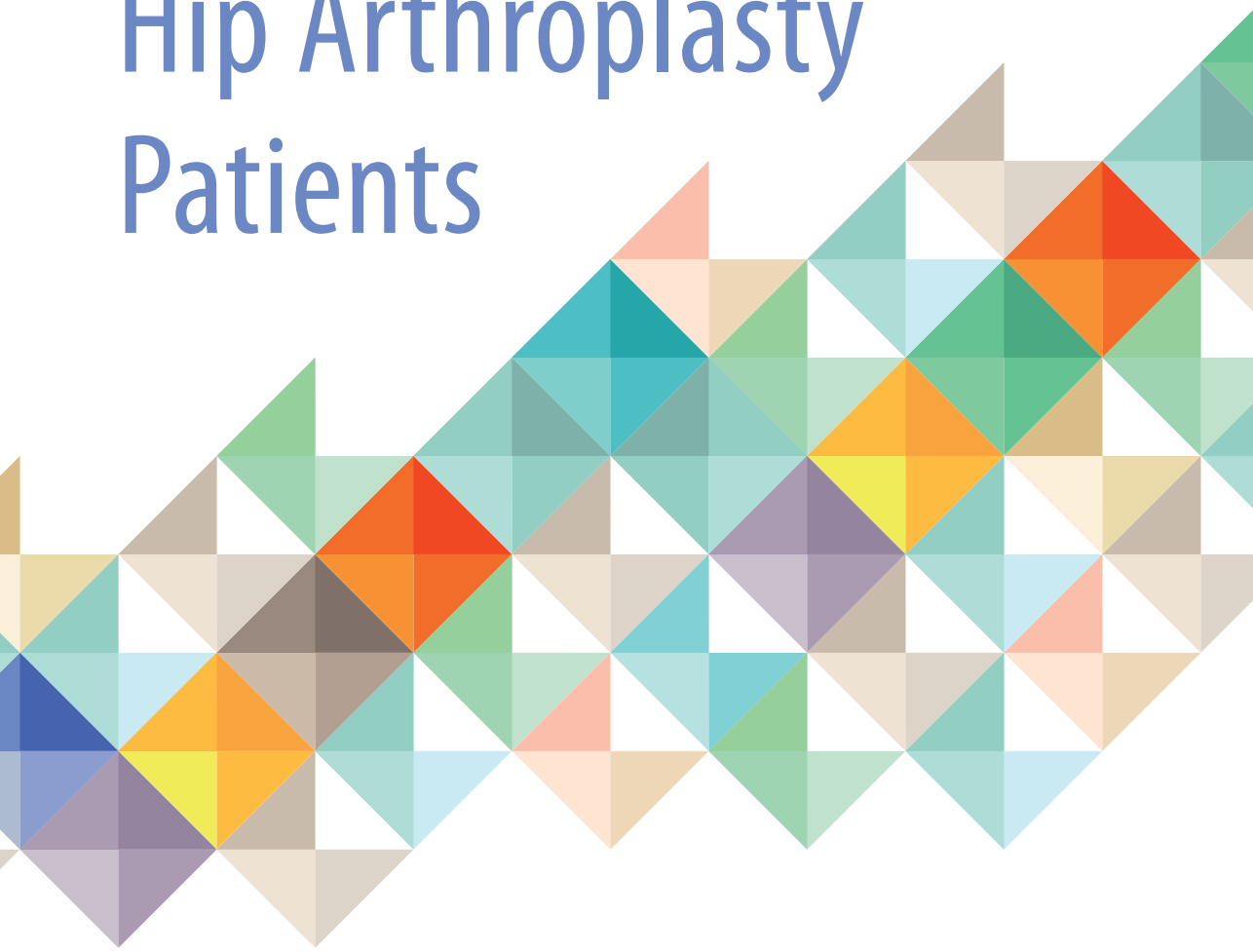
Optimizing Perioperative Care for Primary Total Hip Arthroplasty Patients



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Yvon Mariëlle den Hartog

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Optimizing Perioperative Care for Primary Total Hip Arthroplasty Patients

Optimalisatie van perioperatieve zorg voor primaire THP patiënten

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Chapter 1

General introduction

GENERAL INTRODUCTION

In orthopedic surgery, primary total hip arthroplasty (THA) is a very commonly performed surgery worldwide. It is one of the most cost-effective interventions available in modern surgery, which has been performed since the end of the 19th century with satisfying clinical results.[1,2] Nowadays THA is a good option for patients with end-stage osteoarthritis of the hip if conservative treatment fails to alleviate pain and limitations.[3,4] There is general agreement about the effectiveness of the surgical procedure and surgical techniques. Prostheses have also improved in recent years. However, the challenge remains to optimize perioperative care for patients undergoing primary THA.

In the past few years the number of registered THAs in the Netherlands increased from 22.943 in 2010 to 25.642 in 2013.[5] Due to the aging population and the related increase in the prevalence of osteoarthritis of the hip, a further increase in the number of primary THAs is to be expected.[6,7] This underscores the importance of optimized perioperative care for patients undergoing this procedure.

Efforts to achieve optimized perioperative care should focus on reducing the burden for the patient, by reducing length of hospital stay (LOS), rehabilitation time, postoperative pain, and complications after primary THA. Several aspects of the perioperative procedure for primary THA may contribute to reducing this patient burden. Three of these aspects are discussed below.

LENGTH OF HOSPITAL STAY

Postoperative care has evolved from various medical traditions. One of those traditions is bed rest after surgery.[8] Historically, LOS after primary THA amounted to several weeks,[9] including a long period of bed rest. However, bed rest increases muscle loss and weakness, impairs pulmonary function and tissue oxygenation, and predisposes to thrombo-embolic and pulmonary complications and orthostatic intolerance.[10]

In the past few years, there has been a continued interest in improving results after primary THA. Several studies have focused on the successful implementation of fast-track protocols for primary THA in both selected and unselected groups of patients.[8,9,11-19] These fast-track protocols are based on analysis of core care principles and effective pain management and efficient organization, allowing for optimized and safe perioperative care.[8,12,13,18] As a result, these protocols led to safe and rapid early rehabilitation, reduction of complications, reduction of bed rest, and hence reduction of LOS and a decrease of the use of hospital resources.[8]

However, previous studies have shown that LOS after primary THA is not only determined by organizational factors and medical traditions, but also by patient characteristics.[14,19,20-32] The proper identification of patients who need more rehabilitation time and extensive care after THA might provide further optimization of discharge and rehabilitation planning, even in a fast-track setting.

SURGICAL PROCEDURE

Although there is general agreement about the effectiveness of the surgical procedure itself, various surgical approaches for primary THA have been described.[33] In the Netherlands 61.3 % of the primary THAs in 2013 were placed using a posterolateral approach and 21.9 % with a straight lateral approach, while only 9.9 % used the anterior approach.[5] Each of these approaches has its own advantages and disadvantages.

Von Langenbeck initially described the posterolateral approach, which uses a split of the gluteus maximus muscle and remains posterior to the medial and minimal gluteal muscles.[34] The posterior hip capsule is incised, followed by a detachment of the pirifomis, superior and inferior gemelli and obturator internus muscle.[35] This approach provides good exposure of both the acetabulum and the proximal femur. Furthermore it preserves the abductor function.[36] However, higher dislocation rates have been reported for this approach when compared to other approaches to the hip joint.[37-40]

The straight lateral approach is also one of the principal methods for THA.[41] It provides complete and continuous observation of the entire hip and surrounding structures, which allows adequate access for orientation of the implant.[33,35,42] Disadvantages of this approach are moderate muscle and tendon trauma, and a tendency to develop a Trendelenburg gait and trochanteric bursitis after postoperative recovery.[33,35,43]

The anterior approach was already described by Carl Hueter in 1870,[44] and was first used for a primary hip replacement by Robert Judet in 1947.[45] In this approach, both intermuscular and internervous planes are used. Due to this anatomical approach, several advantages have been described in literature.[33,45-58] Preservation of muscle attachments might improve stability and reduce the risk of dislocation after surgery.

Furthermore, studies on this approach reported shorter rehabilitation time, shorter LOS, less surgical trauma and hence less blood loss and less pain. However this approach has its own unique set of complications and is sometimes criticized because of its technical difficulty.[33,43,46,47,56,59-63]

Since all approaches have their own advantages and disadvantages, there is still no consensus in literature which approach is most suitable for primary THA. In the past few years, the anterior approach is gaining popularity in the Netherlands, with an increase from 4.2% in 2010 to 9.9% in 2013 of all primary THAs.[5] However, there is an ongoing debate whether this still less frequently used approach is preferable to other approaches to the hip joint and whether the possible benefits of this approach outweigh the possible disadvantages.

PAIN MANAGEMENT

THA is associated with considerable postoperative pain.[1] Almost all pain after surgery arises as a result of tissue damage at the surgical site.[64] Formation of hematoma is also suggested to contribute to postoperative pain after THA.[65] This postoperative pain hinders early mobilization and rehabilitation, which has negative consequences on mobility, LOS and duration of overall recovery.[66] Analgesics are used to provide pain relief. However, most analgesics are known for their side effects, such as nausea, vomiting, dizziness or numbness of the limb, which could hinder postoperative mobilization and rehabilitation. Therefore, the challenge of analgesic regimes for THA is to obtain adequate pain relief in combination with maximum muscle control and without troublesome side effects. This will enable the patient to mobilize and rehabilitate early and safely, without pain.[67]

As part of perioperative pain treatment, local infiltration analgesia (LIA) has been described in literature.[64] LIA is a technique in which the surgical field is infiltrated with analgesics in order to provide better pain relief postoperatively. An analgesic used for this technique is ropivacaine.[64] LIA has been reported to be effective in total knee arthroplasty (TKA).[66,68,69] However, for THA only limited and inconclusive data are available from placebo-controlled and randomized trials.[1,67,70-74] None of these studies report on the use of LIA for primary THA by anterior approach. Moreover, although several studies describe pharmacokinetics of ropivacaine after epidural and intravenous administration,[75-78] pharmacokinetic parameters of ropivacaine for the application route of LIA for THA have not been investigated yet. The analgesic effect of LIA could possibly be improved by determining the concentration-time correlation of ropivacaine in serum after LIA in THA. Moreover, a statement can be made about toxicity of the determined ropivacaine serum levels after LIA for THA.

Furthermore, previous studies have shown that postoperative pain after primary THA is influenced by patient characteristics. The proper identification of patients who experience more postoperative pain might provide further insight into how pain is experienced by patients. Also, it may help to further optimize the postoperative pain management and the preoperative education of these THA patients.

OUTLINE OF THIS THESIS

The aim of this thesis is to investigate how perioperative care for primary THA patients could be optimized. Three main aspects of the perioperative procedure are therefore studied, all with several objectives:

- Length of hospital stay: Reducing LOS after primary THA without an increase in complications, re-admissions and reoperations. Also, identifying patient characteristics influencing LOS after primary THA.
- Surgical procedure: Investigating the anterior approach in comparison to other approaches for THA. Furthermore, summarizing possible advantages and disadvantages of this approach together with possibilities for solving these disadvantages.
- Pain management: Investigating if LIA has added value in a multimodal pain treatment protocol for primary THA by anterior approach. Furthermore, elucidating pharmacokinetic parameters of ropivacaine administered by LIA in THA patients. Also, identifying which patient-specific and surgical characteristics influence postoperative pain after primary THA in a fast-track setting.

Chapter 2 demonstrates the results of the introduction of a fast-track protocol for primary THA in Reinier de Graaf Hospital (RdGG) in the Netherlands. Differences in LOS before, during and after the introduction of a fast-track protocol for primary THA procedures for a group of unselected patients are analyzed. Furthermore, the number of complications, re-admissions and reoperations for this group are analyzed. It was hypothesized that LOS would decrease, without an increase in complications, re-admissions and reoperations. *Chapter 3* reports experiences with THA in an outpatient setting for a group of selected patients at RdGG. Furthermore this chapter investigates if postoperative results for this group of patients are satisfying for both the patient and the orthopedic surgeon. *Chapter 4* demonstrates which specific patient characteristics influenced prolonged LOS after the successful implementation of a fast-track protocol. Despite the reduction in mean LOS after the implementation of a fast-track protocol, there was still a large range in LOS with several outliers. The proper identification of patients who need more rehabilitation time and extensive care might allow for further optimization of discharge and rehabilitation planning.

Regarding the anterior approach for primary THA, *chapter 5* summarizes literature regarding advantages as well as disadvantages for this approach. The anterior approach is compared to other approaches to the hip with respect to several perioperative and postoperative aspects. This systematic review hypothesized that patients operated through the anterior approach recover faster and experience less postoperative pain than those operated by means of other approaches, since muscle attachments are preserved. Secondly, it was hypothesized that there were no other differences in outcome parameters between the anterior approach and other approaches. Furthermore, this chapter investigates if there is a clear description of a learning curve for surgeons using the anterior approach. *Chapter 6* describes specific complications noticed during the first unselected cases operated by means of the anterior approach (anterior supine intermuscular (ASI) approach), for primary THA at RdGG. Furthermore, this chapter describes specific adjustments that were applied to this procedure to prevent these complications.

Considering the optimization of pain treatment for primary THA, *chapter 7* focuses on perioperative pain management. It was hypothesized that LIA implemented in a multimodal pain protocol for THA through the anterior approach reduces pain scores postoperatively. Also, a reversed-infiltration method is introduced in this chapter, in which LIA is administered before the incisions have been made. It was hypothesized that this infiltration method would reduce postoperative pain scores even further, since LIA can be infiltrated more accurately in tissues that have not been damaged. Therefore, this chapter investigates the effect of both standard and reversed LIA in combination with the anterior approach for primary THA. *Chapter 8* focuses on the elucidation of pharmacokinetic parameters of ropivacaine administered by LIA in THA patients, by determining the concentration-time correlation of ropivacaine in serum. With clarified pharmacokinetic parameters of ropivacaine after THA, the analgesic effect of LIA could possibly be improved. Furthermore, recommendations about the dose of ropivacaine in LIA for THA can be given. Moreover, a statement can be made about toxicity of the determined ropivacaine serum levels after LIA for THA. Finally, *Chapter 9* investigates which patient-specific and surgical characteristics influence postoperative pain after primary THA by means of the anterior approach in a fast-track setting. The proper identification of patients who experience more postoperative pain after primary THA might allow for further optimization of postoperative pain management and preoperative education of these patients.

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Chapter 2

Reduced length of hospital stay after the introduction of a rapid recovery protocol for primary THA procedures

A retrospective cohort study with 1,180 unselected patients

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S.B.W. Vehmeijer

Acta Orthop. 2013;84(5):444-7.

ABSTRACT

Rapid recovery protocols after total hip arthroplasty (THA) haven been introduced worldwide in the last few years and they have reduced the length of hospital stay. We show the results of the introduction of a rapid recovery protocol for primary THA for unselected patients in our large teaching hospital.

In a retrospective cohort study, we included all 1,180 patients who underwent a primary THA between July 1, 2008 and June 30, 2012. These patients were divided into 3 groups: patients operated before, during, and after the introduction of the rapid recovery protocol. There were no exclusion criteria. All complications, re-admissions, and reoperations were registered and analysed.

The mean length of hospital stay decreased from 4.6 to 2.9 nights after the introduction of the rapid recovery protocol. There were no statistically significant differences in the rate of complications, re-admissions, or reoperations between the 3 groups.

In conclusion, in a large teaching hospital, the length of hospital stay decreased after introduction of our protocol for rapid recovery after THA in unselected patients, without any increase in complications, re-admissions, or reoperation rate.

INTRODUCTION

Historically, the length of hospital stay after primary THA has exceeded several weeks,[1] with a subsequent period of bed rest. In the last few years, rapid recovery protocols haven been introduced worldwide for elective primary THA. Various studies have shown that these protocols have reduced the length of hospital stay and the length of rehabilitation after primary THA.[1-9] Also a decrease in complication rate[2] and in re-admission rate[3] has been described. These rapid recovery protocols are based on analysis of clinical care principles and pain management in combination with revision of organizational factors, giving an optimized perioperative period that is safe for the patient.[8,10]

Reinier de Graaf Hospital (RdGG) is a large teaching hospital in the Netherlands. Introduction of the rapid recovery protocol for primary THA started in 2009, was done in several stages, and was complete in February 2011. In the present study, we analysed the differences in length of hospital stay before, during and after introduction of the rapid recovery protocol for primary THA procedures in a group of unselected patients at RdGG. We also examined the amount of complications, re-admissions, and reoperations for this group after introduction of the rapid recovery protocol.

PATIENTS AND METHODS

In this retrospective cohort study, we included all the patients who underwent a primary THA procedure between July 1, 2008 and June 30, 2012. There were no exclusion criteria; every patient who received a primary THA was included. The patients were divided into 3 groups, based on the period in which the surgery was performed. Group 1 had patients who were operated in the period before the rapid recovery protocol was introduced. Group 2 had patients who were operated between January 1, 2009 and January 31, 2011, during the period in which the rapid recovery protocol was introduced in several stages. Group 3 had patients who were operated after all the stages of the rapid recovery protocol had been introduced (Table 1).

All the patients had the same regimen. The discharge criteria were functional: patient able to walk 30 metres with crutches, to climb stairs, to dress independently, and to go to the toilet independently. In addition, sufficient pain treatment had to be achieved by oral medication before discharge, with VAS below 3 at rest and below 5 during mobilization.

Various surgical approaches were used - the straight lateral (SL) approach, the anterior supine intermuscular (ASI) approach, and the posterolateral (PL) approach - according to the preference of the surgeon. 15 orthopedic surgeons performed the THA proce-

Table 1: Rapid Recovery Protocol.

- Preoperative education
- Local infiltration anesthesia
- Standardized protocol for pain medication
- Opioid medication only on request (rescue medication)
- No compression bandages
- No drains
- No standard urine catheters
- Start rehabilitation and mobilization at day of surgery
- Checking the fulfillment of discharge criteria twice a day
- Optimization of the aftercare

All the several phases of the rapid recovery protocol.

dures during this period, either by themselves or by supervising a resident in orthopedic surgery.

The fulfilment of discharge criteria was analysed twice a day. Length of hospital stay was measured by number of nights. All patients were admitted on the day of surgery. Outliers in length of hospital stay were defined as being equal to or more than the ninety-fifth percentile. All complications, re-admissions, and reoperations were registered and analysed.

Statistics

Since the data were not normally distributed according to the Kolmogorov-Smirnoff test, they were analysed using the Kruskal-Wallis test and the Mann-Whitney test with Bonferroni correction. Values of $p < 0.05$ were considered significant. Data analysis was done with IBM SPSS Statistics for Mac, version 20.

RESULTS

For the total group of 1,180 patients, the mean age was 71 (22-94) years. More women than men were operated (815 as opposed to 265). The main indication for operation was primary osteoarthritis (89%). Other indications were posttraumatic arthritis, fracture of the femoral neck, avascular necrosis, and development disorders. Mean BMI was 27 (17-58). The most common ASA classification was ASA II (66%). Spinal anesthesia was given in 88% of the cases. Almost all operations were performed in an elective setting (98%). Most patients were discharged postoperatively to their own home (81%); others went to a temporary nursing home for further rehabilitation (18%) or were discharged to another department of our hospital for treatment for non-orthopedic pathology (0.4%).

Table 2: Demographics.

		Group 1	Group 2	Group 3	*p-value*
Age (years)		71 (SD 10)	71 (SD 9)	71 (SD 10)	0.2
Gender (% female)		68.2	69.3	69.0	1.0
BMI (kg/m^2)		26.7 (SD 4.3)	27.1 (SD 4.3)	26.9 (SD 4.2)	0.3
ASA classification	I	22	20	20	0.9
	II	66	66	66	
	III	13	14	14	
	IV	-	-	0.3	
Anesthesia (% spinal)		91	87	90	0.06
Priority (% elective)		99	99	98	0.3
Diagnosis (% primary)		93	88	88	0.2
Direction of discharge (%)	home	82	82	80	0.7
	TNH*	19	18	19	
	AD†	-	0.2	0.8	
Approach (%)	ASI	27	45	52	< 0.001
	SL	73	49	45	
	PL	-	6	4	
Side (% right)		56	55	55	1.0

Group 1 represents the patients who were operated in the period before the rapid recovery was introduced. Group 2 represents the patients who were operated in the period in which the rapid recovery protocol was introduced in several phases. Group 3 represents the patients who were operated after all the several phases of rapid recovery were introduced.

** TNH = Temporary nursing home for further rehabilitation.*

† AD = Another department of our hospital for treatment for non-orthopedic pathology.

The SL approach was mostly used, followed by the ASI approach and the PL approach. The demographic characteristics were equal for the 3 groups; only the surgical approach used was significantly different in groups 1 and 2 (Table 2).

1,180 patients received an unilateral primary THA between July 1, 2008 and June 30, 2012. In group 1, 157 patients were operated with a mean length of hospital stay of 4.6 (SD 1.2) nights. Group 2 consisted of 639 patients with a mean hospital stay of 3.7 (SD 1.3) nights, and group 3 consisted of 384 patients with a mean hospital stay of 2.9 (SD 1.4) nights. The differences in length of hospital stay were statistically significant between all 3 groups ($p < 0.001$). Median length of hospital stay decreased from 4 nights to 3 nights after the introduction of the rapid recovery protocol ($p < 0.001$) (Table 3 and Figure 1).

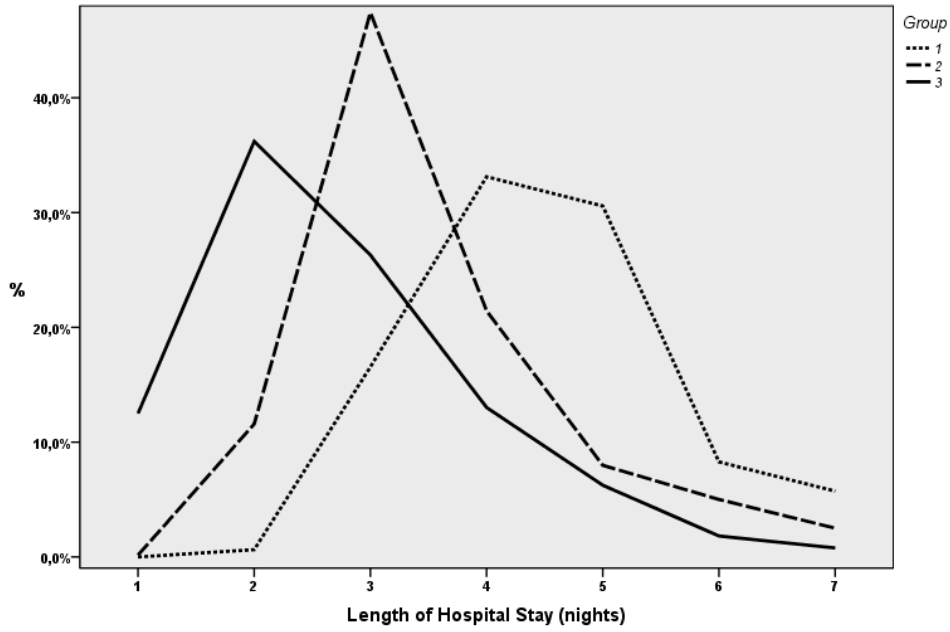
For the total group of 1,180 patients, 3.9% were re-admitted and 2.7% of them underwent a reoperation within the first 3 months after primary THA. The total reoperation rate was 4.6%. There was a decrease in re-admission rate and reoperation rate within the first 3 months after surgery and also a decrease in reoperation rate in total, after the

Table 3: Length of hospital stay, complications, readmissions, and reoperations after primary THA.

		Group 1	Group 2	Group 3	*p-value*
Length of hospital stay	Mean	4.6 (SD 1.2)	3.7 (SD 1.3)	2.9 (SD 1.4)	< 0.001
	Median	4	3	3	< 0.001
Complications (%)		7.6	7.0	7.8	0.9
Readmissions < 3 months (%)		4.5	3.4	4.4	0.7
Reoperations (%)		7.0	4.4	3.9	0.3
Reoperations < 3 months		3.8	2.3	2.9	0.5

Group 1 represents the patients who were operated in the period before the rapid recovery was introduced. Group 2 represents the patients who were operated in the period in which the rapid recovery protocol was introduced in several phases. Group 3 represents the patients who were operated after all the several phases of rapid recovery were introduced.

Figure 1: Percentage nights in hospital after primary THA for the 3 groups.



Group 1 represents the patients who were operated in the period before the rapid recovery was introduced. Group 2 represents the patients who were operated in the period in which the rapid recovery protocol was introduced in several phases. Group 3 represents the patients who were operated after all the several phases of rapid recovery were introduced.

Table 4: Reasons for readmission within the first 3 months after primary THA.

	Group 1	Group 2	Group 3
	n=157	n=639	n=384
Infection	5 (3.2%)	6 (0.9%)	7 (1.8%)
Dislocation	2 (1.3%)	9 (1.4%)	3 (0.8%)
Fracture	-	2 (0.3%)	-
Wound problems	-	5 (0.8%)	2 (0.5%)
Malposition prosthesis	-	-	1 (0.3%)
Anemia	-	-	3 (0.8%)
Pain, unknown cause	-	-	1 (0.3%)
Total	7 (4.5%)	22 (3.4%)	17 (4.4%)

Group 1 represents the patients who were operated in the period before the rapid recovery was introduced. Group 2 represents the patients who were operated in the period in which the rapid recovery protocol was introduced in several phases. Group 3 represents the patients who were operated after all the several phases of rapid recovery were introduced.

introduction of the rapid recovery protocol, but these decreases were not statistically significant (Table 3).

Complication after primary THA occurred u 7.4% of the 1,180 patients, with no statistically significant differences between the 3 groups. The most common reason for both re-admission and reoperation within the first 3 months was infection, followed by dislocation, wound problems, and fracture of the femur (Table 4).

In group 1 there were 17 outliers in length of hospital stay (11%), in group 2 there were 41 outliers (6%), and in group 3 there were 15 outliers (4%). Most outliers in group 1 had a prolonged hospital stay without any reason given in the patient charts.

DISCUSSION

Our findings of reduced length of hospital stay for primary THA after introduction of a rapid recovery protocol are in accordance with the results of various other studies.[2,4-8]

We found a decrease in re-admission rate and reoperation rate within the first 3 months after surgery, and also a decrease in reoperation rate in total, but these decreases were not statistically significant. This contrasts with previous studies showing a significant reduction in complication rate[2] and re-admission rate[3] within the first 3 months after THA after the introduction of a rapid recovery protocol. However, our re-admission rates were less than described in other studies even though the reasons for re-admission were the same.[4-6,11,12] Our reoperation rate is in accordance with the only other study that published the reoperation rate for primary THA after the introduction of a rapid recovery protocol.[5]

The proportion of patients discharged tot heir own home or discharged to a temporary nursing home for further rehabilitation did not change after the introduction of the rapid recovery protocol. This is in accordance with the results of a meta-analysis,[2] although another study showed a decrease in patients discharged to their own home after the length of hospital stay decreased.[9]

For group 1, there were 17 outliers in length of hospital stay (10.8), for group 2 there were 41 outliers (6.4%), and for group 3 there were 15 outliers (3.9%). These outliers were mainly for medical reasons. The introduction of pre-emptive delirium therapy for patients at risk reduced the prevalence of delirium and therefore reduced the length of prolonged hospital stay. This could explain the decline in outliers after the introduction of the rapid recovery protocol, although lack of postoperative delirium has been described in fast-track THA and total knee arthroplasty as well.[13] A possible reason for this occurrence could be the use of tramadol and piritramide in our standardized protocol for pain medication, both of which are opioids.

In conclusion, in our large teaching hospital implementation of the rapid recovery protocol led to a decrease in length of hospital stay for unselected THA patients, without any change in complication rate, re-admission rate, or reoperation rate. The re-admission rate was less than reported in other studies, but the reoperation rate was similar to that in other studies.

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Chapter 3

Total hip arthroplasty in an outpatient setting in 27 selected patients

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ABSTRACT

As a result of introduction of a fast- track program, length of hospital stay after total hip arthroplasty (THA) decreased in our hospital. We therefore wondered whether THA in an outpatient setting would be feasible. We report our experience with THA in an outpatient setting.

In this prospective cohort study, we included 27 patients who were selected to receive primary THA in an outpatient setting between April and July 2014. Different patient-reported outcome measures (PROMs) were recorded preoperatively and at 6 weeks and 3 months postoperatively. Furthermore, anchor questions on how patients functioned in daily living were scored at 6 weeks and 3 months postoperatively.

3 of the 27 patients did not go home on the day of surgery because of nausea and/or dizziness. The remaining 24 patients all went home on the day of surgery. PROMs improved substantially in these patients. Moreover, anchor questions on how patients functioned in their daily living indicated that the patients were satisfied with the postoperative results. 1 re-admission occurred at 11 days after surgery because of seroma formation. There were no other complications or reoperations.

In conclusion, at our hospital, with a fast-track protocol, outpatient THA was found to be feasible in selected patients with satisfying results up to 3 months postoperatively, without any outpatient procedure-specific complications or re-admissions.

INTRODUCTION

Traditionally, the length of hospital stay (LOS) after primary joint replacement has been more than several weeks.[1] In the past few years, fast-track protocols have been introduced worldwide. These protocols are based on principles of optimal clinical care and pain management in combination with a revision of organizational factors. This permits an optimized perioperative period in which patients can safely recover in a shorter period of time.[2,3] As a result of these improved factors, LOS has gradually been reduced.[2-6]

Reinier de Graaf Hospital (RdGG) is a large teaching hospital in the Netherlands. The introduction of a fast-track protocol for primary total hip arthroplasty (THA) started in 2009 and was completed in 2011. After the implementation of this protocol for unselected patients, mean LOS decreased from 4.6 to 2.9 nights[4] with a range of 1–7 nights. Since the LOS had been reduced, we wondered whether outpatient THA would be feasible at our hospital.

We therefore studied a selected group of patients who were treated for primary THA in an outpatient setting. We also investigated whether the postoperative results for this group of patients were satisfactory.

PATIENTS AND METHODS

In this prospective cohort study, we included all the patients who were considered for primary THA in an outpatient setting between April and July, 2014. Patients had to have met the following criteria: ASA I or II; wanting to go home on the day of surgery; and sufficient support from a carer at home during the first postoperative day. Exclusion criteria were cardiovascular impairment and insulin-dependent diabetes mellitus.

All operations were performed by the same orthopedic surgeon (SV) through an anterior supine intermuscular approach. All the patients received uncemented prostheses (Taperloc femoral prosthesis and a Universal cup; both Biomet, Warsaw, IN). They were admitted on the day of surgery. The postoperative follow-up period was at least 3 months.

Spinal anesthesia was by a low dose of bupivacaine (6–8 mg), to allow early mobilization directly after surgery. The multimodal protocol for perioperative pain medication was standardized (Table).

Wounds were closed subcutaneously with Monocryl 3-0 (Ethicon, Somerville, NJ), after which 2 layers of Dermabond (Ethicon) were applied. The wound was then covered with a transparent dressing (Tegaderm; 3M, St. Paul, MN) to allow visual inspection of the wound. This dressing remained on the wound for 14 days, and allowed patients to take a shower immediately after surgery.

Table: The standardized multimodal protocol for perioperative pain medication.

2 hours before surgery on the ward:

- Paracetamol (acetaminophen), 1000 mg per os.
- Celecoxib (Celebrex)A, 400 mg per os.
- Gabapentin, 600 mg per os.

Just before surgery:

- Dexamethasone, 0.15 mg/kg iv.B
- Esketamine, 15 mg iv.

4 hours after surgery:

- Paracetamol (acetaminophen), 1000 mg per os.

8 hours after surgery:

- Paracetamol (acetaminophen), 1000 mg per os.
- Gabapentin, 300 mg per os.

Before the night:

- Oxicodone (OxyContin), 10 mg per os.

Day 1:

- Paracetamol (acetaminophen), 1000 mg per os 4 times a day.
- Celecoxib (Celebrex)A, 200 mg per os in the morning.
- Gabapentin, 300 mg per os in the morning.

After day 1:

- Paracetamol (acetaminophen), 1000 mg per os 4 times a day (with a maximum of 2 weeks).
- Celecoxib (Celebrex)A, 200 mg per os in the morning (until 2 weeks after surgery).

Rescue medication:

- Celecoxib (Celebrex)A, 200 mg per os extra after the first night.
- Piritramide (Dipidolor), 10 mg im, which could be repeated every 4 hours.

[A] *In combination with celecoxib (Celebrex) all patients receive omeprazole, 20 mg per os once a day as prophylaxis. When the patient is already using a proton pomp inhibitor before admission, no omeprazole is administered.*
[B] *Dexamethasone solution in 50 mL saline is administered slowly to avoid adverse side affects such as severe perianal pain.*

Mean duration of surgery was 66 (47–81) min. Mean blood loss was 308 (0–650) mL and mean decrease in hemoglobin was 1.0 (0.5–2.1) g/dL.

The discharge criteria were functional: the patient had to be able to walk 30 m with crutches, to climb stairs, to dress independently, and to go to the toilet without help. In addition, sufficient pain treatment had to be achieved with oral medication before discharge, with VAS below 3 at rest and below 5 during mobilization. In addition, the wound had to be dry, patients could not be dizzy or nauseous, and hemoglobin levels should be higher than 9.7 g/dL. When a patient met all the discharge criteria, he/she had to make the final decision to go home or to spend a night in hospital.

EQ-5D increased from 0.71 (−0.04 to 0.96) preoperatively to 0.93 (0.68 to 1.00) at 6 weeks postoperatively and to 0.92 (0.44 to 1.00) at 3 months postoperatively. NRS for pain at

rest decreased from 3.6 (1–8) preoperatively to 0.6 (0–3) at 6 weeks postoperatively and to 1.0 (0–10) at 3 months postoperatively. NRS for pain during activity decreased from 6.6 (3–9) preoperatively to 1.4 (0–3) at 6 weeks postoperatively and to 1.9 (0–9) at 3 months postoperatively. All these changes were statistically significant ($p < 0.001$).

To score postoperative results, the patient-reported outcome measures (PROMs) EQ-5D (mobility, self-care, usual activities, pain/discomfort, anxiety/depression)[7,8] and the Numeric Rating Score (NRS) for pain at rest and during activity were recorded preoperatively and at 6 weeks and 3 months postoperatively.

Furthermore, anchor questions on how patients functioned in their daily living were scored at 6 weeks and 3 months postoperatively. The scoring of these questions varied from 1 (deteriorated very much since surgery) to 7 (improved very much since surgery). Anchor-based methods compare changes in scores on the instrument with an anchor, where the patients indicate whether they believe they are better than at baseline.[9]

Decrease in hemoglobin was defined as the hemoglobin level (g/dL) preoperatively minus the hemoglobin level just after surgery. All complications, re-admissions, and reoperations were registered and analyzed.

Statistics

If data were normally distributed according to the Kolmogorov-Smirnoff test, they were analyzed using an independent Student t-test; otherwise, a Mann-Whitney test with a Bonferroni adjustment was performed. Any p-values less than 0.05 were considered to be significant. Data analysis was done with IBM SPSS Statistics for Mac, version 20.

RESULTS

3 of the 27 patients stayed in hospital because of nausea and/or dizziness. The other 24 patients went home on the day of surgery. In these 24 patients, mean age was 63 (48–71) years, 15 were women, mean BMI was 26 (20–33), and 15 patients were ASA I.

Mean duration of surgery was 66 (47–81) min. Mean blood loss was 308 (0–650) mL and mean decrease in hemoglobin was 1.0 (0.5–2.1) g/dL.

EQ-5D increased from 0.71 (−0.04 to 0.96) preoperatively to 0.93 (0.68 to 1.00) at 6 weeks postoperatively and to 0.92 (0.44 to 1.00) at 3 months postoperatively. NRS for pain at rest decreased from 3.6 (1–8) preoperatively to 0.6 (0–3) at 6 weeks postoperatively and to 1.0 (0–10) at 3 months postoperatively. NRS for pain during activity decreased from 6.6 (3–9) preoperatively to 1.4 (0–3) at 6 weeks postoperatively and to 1.9 (0–9) at 3 months postoperatively. All these changes were statistically significant ($p < 0.001$).

Mean score for the anchor question on how patients functioned in their daily living was 6.2 at 6 weeks and 6.4 at 3 months (with 6 corresponding to much improvement

and 7 corresponding to very much improvement). There was 1 re-admission, 11 days after surgery, because of seroma formation. In addition, no complications or reoperations occurred until 3 months postoperatively.

DISCUSSION

To our knowledge, our hospital is the first in Europe to report on primary THA in an outpatient setting for a selected cohort of patients. In the USA, THA in an outpatient setting for selected patients has already been described.[1,10] Moreover, US centers have also reported on hemi- and total knee replacement in an outpatient setting.[11,12] Although this trend in the USA could well be patient costdriven, as some patients have to pay extra for each night that they stay in hospital, there does appear to be a general trend towards outpatient joint replacement. These reports show that outpatient joint replacement is feasible in selected patients.

In the present study, 24 of the 27 selected patients who were scheduled to receive THA in an outpatient setting went home on the day of surgery. The PROMs improved significantly for these 24 patients. Moreover, the anchor question on how the patients functioned in their daily living indicated that they were satisfied with the postoperative results. Only 1 re-admission occurred at 11 days after surgery because of wound leakage, which was the result of seroma formation. This complication could occur in other settings for THA, and it is therefore not likely to have been due to the outpatient setting. No surgery was performed in this particular case, and the wound healed otherwise without any further complication.

Why would one strive to perform joint replacement in an outpatient setting? An important reason might be hospital-acquired infection and the occurrence of multi-resistant micro-organisms in hospital.[13,14] An additional reason would be the lower costs associated with a shorter hospital stay.[10]

There might be concern about early loading of the implant during outpatient THA, especially with uncemented prostheses. However, no adverse effects of early full weight bearing of uncemented THAs have been described.[15-17] Moreover, early loading of the THA is not unique to outpatient THA. It is an important part of fast-track surgery. In the fast-track protocol in our hospital, all patients are mobilized with immediate full weight bearing on the day of surgery.

In the current fast-track setting that we use in our hospital, patients are not selected. All patients are treated with the same protocol. As a part of the introduction protocol for new treatments at our hospital, we performed a prospective risk analysis. Several critical risk factors were identified. Based on these, patient selection criteria for the outpatient setting were established. We did not, however, want to introduce new traditions in or-

thopedic practice that were not evidence-based,[18] so we kept these criteria to the absolute minimum, which we felt was necessary for the safe introduction of this protocol. The primary concerns after THA surgery were risk of cardiovascular incidents.[19] Historically, this risk has been approximately 0.5%.[20] This percentage has, however, been shown to decrease in a fast-track setting.[5] Despite this reduced risk, we excluded patients with a history of cardiovascular disease from outpatient THA. In addition, we excluded patients with insulin-dependent diabetes mellitus.

Only patients with ASA I and II were scheduled for this outpatient setting, because higher ASA score is associated with increased risk of postoperative complications.[21] Furthermore, increased ASA score has been described as a predictor of prolonged hospital stay,[22-25] which could be explained by the association of ASA score with comorbidities. In our fast-track setting, however, there was no effect of ASA score on LOS in a multivariate logistic regression model, confirming the results of den Hartog et al.[26]

The final selection criterion in this study was practical. Patients had to have sufficient support from a carer at home during the first postoperative night. Younger patients are more likely to have sufficient support at home (from cohabitants) than older people. Possibly as a result of this, the mean age of the patients in the present study was 63 years, which is less than the mean age of patients whom many surgeons see. Both younger age and living together with cohabitants have been found to be associated with shortened LOS.[26]

In addition to the selection criteria, as a result of the prospective risk analysis 3 discharge criteria were added to the standard fast-track discharge list. The most important of these was that patients wanted to go home on the day of surgery. After the orthopedic surgeon approved the discharge, the patient made the final decision to leave the hospital. If patients were not feeling comfortable with the idea of going home, they stayed in hospital. This was the case with one patient. She had been dizzy and nauseous during the day, but was fit to go home at the end of the afternoon. She preferred to spend a night in the hospital, however, and left the following morning after an uneventful night.

Dizziness, nausea, and vomiting, which continued during the afternoon of the day of surgery were also introduced as a discharge criterion. 2 patients were not allowed to leave the hospital because of this, one of whom (a patient aged 77) ended up spending 2 nights in hospital. Orthostatic intolerance and nausea and vomiting are likely to be caused by either the pain management or the surgery.[2] The challenge remains to optimize perioperative care even further to prevent the occurrence of these side effects.

Persistent wound leakage was also a reason not to discharge patients. With our wound-care protocol, all the patients had a (nearly) dry wound at discharge and no additional leakage occurred during the first night at home.

The final selection criterion in this study was practical. Patients had to have sufficient support from a carer at home during the first postoperative night. Younger patients are

more likely to have sufficient support at home (from cohabitants) than older people. Possibly as a result of this, the mean age of the patients in the present study was 63 years, which is less than the mean age of patients whom many surgeons see. Both younger age and living together with cohabitants have been found to be associated with shortened LOS.[26]

Finally, a hemoglobin level of higher than 9.7 g/dL was introduced as a discharge criterion. In patients without a history of cardiovascular disease, this is a relatively high level, which leaves room for a further drop in the days after surgery. The lowest postoperative hemoglobin level measured was 10.5 g/dL.

Since we studied a selected cohort of THA patients, we could not compare the results of our study population to the results of our total THA patient population. The set-up of a prospective randomized clinical trial would provide more information when comparing postoperative results between outpatient THA and inpatient THA in a fast-track setting.

In conclusion, at our hospital, with a fast-track protocol and using the anterior supine intermuscular approach, outpatient THA is feasible in selected patients and can give satisfactory results up to 3 months postoperatively without outpatient procedure-specific complications or re-admissions.

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Chapter 4

Which patient characteristics influence length of hospital stay after primary total hip arthroplasty in a 'fast-track' setting?

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ABSTRACT

After implementation of a 'fast-track' rehabilitation protocol in our hospital, mean length of hospital stay for primary total hip arthroplasty decreased from 4.6 to 2.9 nights for unselected patients. However, despite this reduction there is still a wide range across the patients' hospital duration. The purpose of this study was to identify which specific patient characteristics influence length of stay after successful implementation of a 'fast-track' rehabilitation protocol. A total of 477 patients (317 female and 160 male, mean age 71.0 years; 39.3 to 92.6, mean BMI 27.0 kg/m^2; 18.8 to 45.2) who underwent primary total hip arthroplasty procedure 1 February 2011 and 31 January 2013, were included in this retrospective cohort study. A length of stay greater than the median was considered as an increased duration. Logistic regression analyses were performed to identify potential factors associated with increased durations. Median length of stay was two nights (interquartile range 1), and the mean length of stay 2.9 nights (1 to 75). In all, 266 patients had a length of stay ≤ two nights. Age (odds ratio (OR) 2.46; 95% confidence intervals (CI) 1.72 to 3.51; $p < 0.001$), living situation (alone *vs* living together with cohabitants, OR 2.09; 95% CI 1.33 to 3.30; $p = 0.002$) and approach (anterior approach *vs* lateral, OR 0.29; 95% CI 0.19 to 0.46; $p < 0.001$) (posterolateral approach *vs* lateral, OR 0.24; 95% CI 0.10 to 0.55; $p < 0.001$) were factors that were significantly associated with increased length of stay in the multivariable logistic regression model.

INTRODUCTION

Length of stay (LOS) after total hip arthroplasty (THA) has reduced in recent years following the introduction of 'fast-track' rehabilitation protocols in both selected and unselected patients.[1-5] These studies have demonstrated reduction of LOS and rapid early rehabilitation can be undertaken safely without affecting outcomes. These protocols are based on analysis of core care principles and effective pain management and efficient organisation, allowing an optimised and safe peri-operative care.[1-5]

The Reinier de Graaf Hospital (RdGG) in the Netherlands is a large teaching hospital which introduced 'fast-track' rehabilitation for primary THA progressively from 2009. Introduction was incremental and was complete by February 2011. After the implementation of this 'fast-track' rehabilitation protocol, the mean LOS for primary THA had decreased from 4.6 to 2.9 nights for unselected patients in our hospital.[5] However, despite the mean reduction in LOS, there was still a wide range. Previous studies have shown that patient and provider characteristics could affect LOS after primary THA.[6-10] However, most of these studies were not performed in a 'fast-track' setting.[8-10] Early preoperative identification of patients who need extended rehabilitation time and enhanced care might provide further optimisation of discharge and rehabilitation planning. Therefore, the goal of this study was to identify specific patient characteristics which influence LOS using 'fast-track' rehabilitation principles in our institution.

PATIENTS AND METHODS

We conducted a retrospective cohort study of all 477 patients undergoing primary THA at RdGG between 1 February 2011 and 31 January 2013. All procedures were performed in a 'fast-track' setting. There were no exclusion criteria.

The surgery was undertaken by ten experienced surgeons, each with a minimum of 50 previous THAs prior to the start of the study. Surgical approach was according to the surgeon's preference. Patients were not assigned to a particular approach. Various surgical approaches were used: the anterior supine intermuscular (ASI) approach[11,12] the straight lateral (SL) approach[13,14] and the posterolateral (PL) approach.[15,16]

The discharge criteria were functionally based. Patients were required to be able to walk 30 metres with crutches, climb stairs, get dressed independently and to be able to go to the lavatory independently. In addition, adequate pain relief had to be achieved with oral medication before discharge, with a visual analogue score (VAS, 0 to 10,best to worst) < 3 at rest and < 5 during mobilisation.

The primary outcome measure was LOS, which was defined as the number of nights spent in hospital. LOS was divided into two groups, determined by the median value; a LOS greater than the median was considered to be an increased LOS.

Potential factors associated with an increased hospital stay were obtained from case note analysis. Factors include age, living situation, anaesthesia, approach, gender, body mass index (BMI), American Society of Anaesthesiologists (ASA) classification[17] and mobility-limiting comorbidities.

BMI was categorised into three groups according to the criteria of the World Health Organization:[18] normal weight (18.5 kg/m^2 to 25 kg/m^2), overweight (25 kg/m^2 to 30 kg/m^2) and obese (≥30 kg/m^2). ASA classification was categorised into: ASA I, ASA II and ASA III/IV.

To investigate the effect of mobility-limiting co-morbidities on LOS, two reviewers (YH, SV) independently assessed if specific co-morbidities reported in the case notes could potentially influence patient mobility. Rheumatoid arthritis; neurologic disorders (e.g. lumbar disc prolapse, multiple sclerosis, Parkinson's disease and paralysis after cerebral vascular accident); as well as osteoarthritis of the contralateral leg and/or adjacent joint were scored to be mobility-limiting. Disagreements in assessments were solved by consensus, and a final decision of a third reviewer (NM) was not required.

Statistical analysis

The associations between each variable and LOS were examined with univariate logistic regression analyses. Predictors that were associated with the outcome in univariate analyses (p-values < 0.15) were included in multivariable logistic regression analyses. In multivariable logistic regression analyses p-values < 0.05 were considered significant. Data analyses were conducted using R version 3.0.2 with package 'rms'.[19,20]

RESULTS

The mean LOS for the group as a whole (n = 477) was 2.9 nights (1 to 75) with a median of two nights (interquartile range (IQR 1). From the total of 477 patients, 266 patients had a LOS ≤ two nights and 211 a LOS > two nights. The large range in LOS was influenced by two patients. One of them had a LOS of 24 nights due to a prolonged state of confusion, the other had a LOS of 75 nights due to deep infection of their THA. Excluding these two outliers, LOS of the other 475 patients ranged between one and ten nights.

The mean age was 71.0 years (39.3 to 92.6) and mean BMI was 27.0 kg/m^2 (18.8 to 45.2). Most patients (31; 66.5%) were female. The most common surgical approach was the ASI approach, used in 265 patients (55.6%). The SL approach was used in 176 patients (36.9%)

Table 1: Demographic data for 477 patients undergoing total hip arthroplasty (THA), for the group with a length of hospital stay ≤ two nights, and for the group with a length of hospital stay of > two nights.

		Total n (%) n = 477	≤ 2 nights n (%) n = 266	> 2 nights n (%) n = 211
Age (years)		71.0 (9.9)*	67.7 (9.2)*	75.2 (9.1)*
Anaesthesia	Spinal	447 (93.7)	246 (92.5)	201 (95.3)
Approach	ASI	265 (55.6)	183 (68.8)	82 (38.9)
	Straight Lateral	176 (36.9)	58 (21.8)	118 (55.9)
	Posterolateral	36 (7.5)	25 (9.4)	11 (5.2)
Gender	Female	317 (66.5)	159 (59.8)	158 (74.9)
BMI (kg/m^2)	18.5 to 25	167 (35.0)	85 (32.0)	82 (38.9)
	25 to 30	213 (44.7)	134 (50.4)	79 (37.4)
	≥ 30	97 (20.3)	47 (17.6)	50 (23.7)
ASA score	I	100 (21)	72 (27.1)	28 (13.3)
	II	318 (66.7)	174 (65.4)	144 (68.2)
	III/IV	59 (12.3)	20 (7.5)	39 (18.5)
Living situation	Alone	169 (35.4)	62 (23.3)	107 (50.7)
Mobility-limiting comorbidity	Yes	93 (19.5)	54 (20.2)	39 (18.5)

**mean (standard deviation (SD))*

Table 2: Results of univariate and multivariate logistic regression for potential factors associated with a prolonged hospital stay.

Characteristic		Univariate Analyses		Multivariate Analyses	
		OR (95% CI)	p-value	OR (95% CI)	p-value
Age (yrs)		3.55 (2.58 - 4.88)*	<0.001	2.46 (1.72 - 3.51)*	<0.001
Living situation	Alone	3.39 (2.29 – 5.01)	<0.001	2.09 (1.33-3.30)	0.002
Anaesthesia	General	0.61 (0.28-1.34)	0.2	-	-
Approach		-	<0.001	-	<0.001
vs. SL	ASI	0.22 (0.15 – 0.33)	<0.001	0.29 (0.19 – 0.46)	<0.001
	PL	0.22 (0.10 – 0.47)	<0.001	0.24 (0.10 – 0.55)	<0.001
Gender	Male	0.5 (0.34 - 0.74)	<0.001	0.72 (0.45 - 1.15)	0.2
BMI (kg/m^2)		-	0.02	-	0.4
vs. 18.5-25	25 to 30	0.61 (0.40 – 0.92)	0.02	0.75 (0.47 - 1.21)	0.2
	≥ 30	1.10 (0.67 - 1.82)	0.7	1.02 (0.56 - 1.85)	0.9
ASA		-	<0.001	-	0.4
vs. I	II	2.13 (1.30 – 3.47)	0.004	1.26 (0.71 -2.23)	0.4
	III/IV	5.01 (2.51 – 10.03)	<0.001	1.72 (0.76 – 3.91)	0.2
Mobility-limiting comorbidity	Yes	0.89 (0.56 – 1.41)	0.6	-	-

Overall multivariate model fit: LR χ^2(9 representing df)=131.89, p <0.001)
LR, likelihood ratio; χ^2, chi squared; df, degrees of freedom
**inter-quartile odds ratio (OR) (78.3 vs 64.4).*

and the PL approach was used in 36 patients (7.5%). Most patients (447;93.7%) received spinal anaesthesia (Table 1).

Results of univariate and multivariable logistic regression analyses are presented in Table 2. Age (odds ration (OR) 2.46; 95% confidence intervals (CI) 1.72 to 3.51; $p < 0.001$), living situation (alone *vs* living together with cohabitants, OR 2.09; 95% CI 1.33 to 3.30; $p = 0.002$) and approach (ASI approach *vs* SL, OR 0.29; 95% CI 0.19 to 0.46; $p < 0.001$; PL approach *vs* SL, OR 0.24; 95%CI 0.10 to 0.55); $p < 0.001$) were factors that were significantly associated with increased LOS in a multivariable logistic regression model (Table 2). No difference in LOS was found comparing the ASI with the PL approach (ASI approach *vs* PL, OR 1.25; 95% CI 0.54 to 2.85; $p = 0.604$).

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DISCUSSION

The aim of this study was to identify any patient-specific characteristics influencing the LOS after the successful implementation of a 'fast-track' rehabilitation protocol. Age, living situation and surgical approach were associated with a significantly increased LOS over the median after primary THA in 477 unselected patients in our institution.

There is a growing interest in introducing 'fast-track' rehabilitation protocols with the aim of reducing LOS.[1-5] For the purposes of our study, more than two nights in hospital was considered an increased LOS. Many other studies investigating prolonged LOS have not used 'fast-track' rehabilitation and LOS greater than ten days was considered to be 'prolonged'.[8-10,21-23]

Living alone was associated with an increased LOS in our study, which is in accordance with other studies.[6,7] Although not investigated specifically in our study, marital status has been said elsewhere to have no influence on LOS.[9] However, this does necessarily correlate with the amount of assistance a patient can obtain after discharge as family or relatives might be able to provide assistance after discharge.

Other studies have identified older age as a predictor for increased hospital stay.[6-9,22] This can be explained by the association of increased age and co-morbidities with greater care needs after discharge. Our results confirm this association.

The influence of surgical approach on recovery and LOS after primary THA is open to debate. Our study demonstrated a significant difference on LOS, in favour of both the ASI and PL approaches compared with the SL approach. No difference in LOS was found comparing the ASI with the PL approach. Previously published studies have demonstrated that patients operated on using the anterior approach have a shorter LOS compared with that of a lateral approach.[24-26] Authors have suggested that using the muscle-splitting interval used for the anterior approach facilitates early recovery due to less muscle damage.[11,14,27-29] Other studies have also not demonstrated a difference

in LOS comparing the anterior or the posterior surgical approaches, as in our study.[30-31] Contrary to our results, other investigations have not shown differences LOS between the anterior and lateral approaches.[23] The nature and characteristics of these different studies are very variable, regarding the number of patients studied, randomisation and pro- or retrospective studied cohort. Furthermore, the experience of the surgeon with the studied surgical approaches and the potential presence of a 'learning curve' might explain some of the differences of the effect of surgical approach on LOS.[23,30-34] The definition of a 'learning curve' for THA procedures has been suggested to be 20 cases but this is contentious.[35] In our study all procedures were performed by experienced hip surgeons who performed more than 50 procedures before the start of this study, in order to overcome potential effects of limited surgical experience or the 'learning curve'.

In a systematic review, no difference between regional and systemic analgesia on LOS after THA has been found.[36] This is supported by our study, though the data was skewed with 477 of our patients (94%) having regional anaesthesia. Fast-track protocols favour spinal anaesthesia above general anaesthesia because of the potential side effects of the latter. These side effects might cause prolonged rehabilitation and therefore an increased LOS.[1-4,37]

Female gender has been reported to be associated with an increased hospital stay.[6,8,22,38,39] None of these studies give a clear explanation for their findings, except for the possibility of lower limb strength in women.[22] Our study demonstrated no effect of gender on LOS.

Obesity has been shown to be associated with a slower postoperative recovery[10] and an increased LOS.[21-40] Furthermore, patients with a greater body weight might be expected to have more problems mobilising after surgery[22] and therefore be expected to have an increased LOS after surgery, since the discharge criteria are mostly functional. However, our study demonstrated no effect of BMI on LOS. Other studies have similarly not shown an adverse effect of increased BMI on LOS.[6,10,23,38,41] Moreover, two other studies investigating the effect of BMI on LOS and perioperative complications after both THA and total knee arthroplasty also demonstrated no adverse effect of BMI.[9,42]

Increased ASA score has been described as a predictor for increased hospital stay.[6,10,23,38] This has been explained by the association of ASA score with co-morbidities. However, our study demonstrated no effect of ASA score on LOS after adjusting for other variables in the model. The lack of measurable effect of ASA on LOS might be influenced by our definition of increased LOS (> two nights) used in our study.

Furthermore, ASA score provides limited information regarding specific co-morbidities, in particular 'mobility limiting' co-morbidities. These co-morbidities might be associated with increased LOS. Therefore, we added 'mobility limiting' co-morbidities as potential factors associated with an increased hospital stay to our model. Our study demonstrated no effect of 'mobility limiting' co-morbidities on LOS.

The effect of type of fixation of the prosthesis has previously been investigated as a potential predictor for LOS,[10,23] but did not include this variable in our study as the type of fixation was guided by age of the patient in our hospital. Operating time,[23,38] smoking status,[6] peri-operative blood loss,[23,38] and the effect of different co-morbidities[9,21] have also been studied and appeared to have no influence on LOS.

Our study has some potential limitations. First, we divided our study group into two as defined by the median LOS of two nights. In the absence of a pre-determined cut off point, the most common approach is to take the sample median.[43] Using the sample median implies that various cut off points will be used in different studies so that results might be difficult to compare. In addition, much information is lost (e.g. every value above the median is considered equal), so the statistical power to detect a relation might be reduced.[43] However, we do not believe this to be a problem in the present study.

Second, a prospective study might have provided us with additional information to predict the LOS better, e.g. preoperative patient-reported outcome measures (PROMs), compared with the retrospective nature in the present study. We could not include PROMs in our analysis, as the PROMs data were recorded inconsistently within the case notes of the patients. However, this retrospective cohort study included all 477 patients who underwent primary THA after the successful implementation of fast-track rehabilitation in our hospital without any pre-determined selection criteria or bias.

Third, according to the International Classification of adult underweight (<18.5 kg/m^2), normal weight (18.5 kg/m^2 to 25 kg/m^2), overweight (25 kg/m^2 to 30 kg/m^2) and obese (>30 kg/m^2) according to BMI as used by the World Health Organization, patients included in our study were either of normal weight (35.0%), overweight (44.7%) or obese (20.3%). Although we think that the patients in our study are a good representation of the BMI range within the Dutch population, the case mix of the orthopaedic surgeons in other countries might differ.

Finally, it should be noted that few surgeons currently routinely use the ASI approach. In our study a majority of patients (55.6%) underwent operation using the ASI approach. The remainder of the patients underwent operation using the more commonly used SL and PL approach, allowing for our findings to inform most hip surgeons' practice.

In conclusion, older age, living alone and the lateral surgical approach were associated with a prolonged LOS after primary THA in a 'fast-track' setting for 477 unselected patients. This knowledge allows further optimisation of discharge and rehabilitation planning for patients with these characteristics.

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Chapter 5

The less invasive anterior approach for total hip arthroplasty: a comparison to other approaches and an evaluation of the learning curve

a systematic review

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ABSTRACT

There is still discussion about possible advantages and disadvantages of the less invasive anterior approach for total hip arthroplasty (THA). The purpose of our systematic review was to evaluate literature regarding the anterior approach in comparison to other approaches. Furthermore, we investigated if there is a description of a learning curve for the anterior approach.

Data were obtained from EMBASE, Cochrane, PsychINFO, CINAHL, Web-of-Science, Scopus, Google scholar, and PubMed since their inception up to June 2015. 2 reviewers independently selected the studies and independently conducted the quality assessment. Because studies were considered heterogeneous regarding outcome measures, determinants studied, and methodological quality, we decided to perform a "best evidence synthesis". A total of 64 studies met the inclusion criteria.

Strong evidence for no difference in component placement between the anterior approach and other approaches was found. Also, strong evidence for faster postoperative recovery and less need for assistive devices after the anterior approach were found. All other studied parameters only demonstrated conflicting evidence. Although the learning curve for the anterior approach is not yet clear, this learning curve should not be neglected.

In conclusion, the less invasive anterior approach provides benefits in the early postoperative period only, when compared to other approaches.

INTRODUCTION

The less invasive anterior approach for total hip arthroplasty (THA) was first performed by Robert Judet in 1947.[1] Both intermuscular and internervous planes are used for this approach and several advantages have been described in literature.[1-15] However this approach has its own unique set of complications and is sometimes criticized because of its technical difficulty.[6,11-13,16-21] Many publications demonstrated that extensive training is necessary, even for experienced surgeons to perform this technique and surgeons considering this approach should expect a substantial learning period.[1,6,8,19]

Recently Moskal *et al*.[22] wrote a review about the anterior muscle sparing approach with a fracture table for THA, considering complication rate, component placement and the learning curve. However, their article is not a systematic review, it is limited to the use of a fracture table and therefore it does not reflect all available literature on this subject. Hence, a clear overview about the anterior approach with a quality assessment and a best evidence synthesis is missing in literature.

The purpose of our systematic review was to evaluate the literature regarding advantages as well as disadvantages for the less invasive anterior approach for primary THA in comparison to other approaches for perioperative as well as postoperative aspects. First, we hypothesized that patients operated through the anterior approach recover faster and experience less postoperative pain in comparison to other approaches, since muscle attachments are preserved. Second, we hypothesized that there are no other differences in outcome parameters between the anterior approach and other approaches. Third, we wanted to investigate if there is a clear description of the learning curve for the anterior approach.

METHODS

Data sources and searches

We performed a search for relevant studies in EMBASE, Cochrane, PsychINFO, CINAHL, Web-of-Science, Scopus, Google scholar, and PubMed since their inception up to June 30, 2015. Search terms included the anterior approach, THA, complication rate, recovery time, component placement and learning curve. The full electronic search strategy for the EMBASE database is presented in Table 1.

Additionally, citation tracking was performed by manually screening the reference lists of eligible studies by 1 reviewer (YH).

Table 1: Full electronic search strategy for the EMBASE database.

('total hip prosthesis'/exp OR 'hip prosthesis'/de OR 'hip arthroplasty'/de OR (((hip) NEAR/3 (arthroplast* OR prosthe* OR replace* OR endoprosthes*)) OR THA OR THR OR THAs OR THRs):ab,ti) AND ('surgical approach'/de OR (((surgical* OR anterior OR hueter*) NEAR/6 (approach* OR route*))):ab,ti)

Study selection

2 reviewers (YH, NM) assessed the studies on whether they met the following inclusion criteria:

- Patients in the study underwent primary THA for osteoarthritis;
- The anterior approach was used;
- The study described an adequate follow up period;
- Both prospective and retrospective studies were included;
- The study described perioperative and/or postoperative parameters in comparison to another approach and/or described the learning curve for the anterior approach;
- Original data were available (no (systematic) review or meta-analaysis);
- The article was written in English.

Disagreement on inclusion was resolved by discussion, and a final decision of a third reviewer (SV) was not necessary.

Quality assessment

The methodological quality of observational studies can vary, which might influence the results and conclusions of these studies, and subsequently, the results and conclusions of a systematic review.

We scored the internal validity of the selected studies using eight questions from existing quality assessment tools.[23-25]

The following questions were used:

1. Inclusion of consecutive patients?
2. Description of in- and exclusion criteria?
3. Did the authors report the participation rate and did patients give informed consent?
4. Unbiased assessment of outcome and determinant?
5. Was the follow-up period appropriate?
6. Did they report a loss to follow-up less than 20%?
7. Is there any information about the sample size calculation?
8. Were statistical tests appropriate and did they adjust for cofounders?

2 reviewers (YH, NM) assessed the quality independently. Disagreements were solved by discussion, and a final decision of a third reviewer (SV) was not necessary.

Studies were classified as high quality when they scored ≥ 5 points and when minimally question 1, 4 and 8 were scored as "yes".[23-25]

Data extraction

1 reviewer (YH) extracted study characteristics and outcome determinants. The different aspects of primary THA that were analyzed were both perioperative and postoperative: surgery time, incision length, blood loss, complication rate, length of hospital stay (LOS), postoperative pain and pain medication consumption, questionnaire scores, accuracy of component placement checked by postoperative x-rays, and functional recovery.

Best evidence synthesis

Because the studies were considered heterogeneous with regard to outcome measures, determinants studied, and methodological quality, we decided not to pool data and to perform a "best evidence synthesis".[26,27]

The following ranking of levels of evidence was formulated[26,27]:

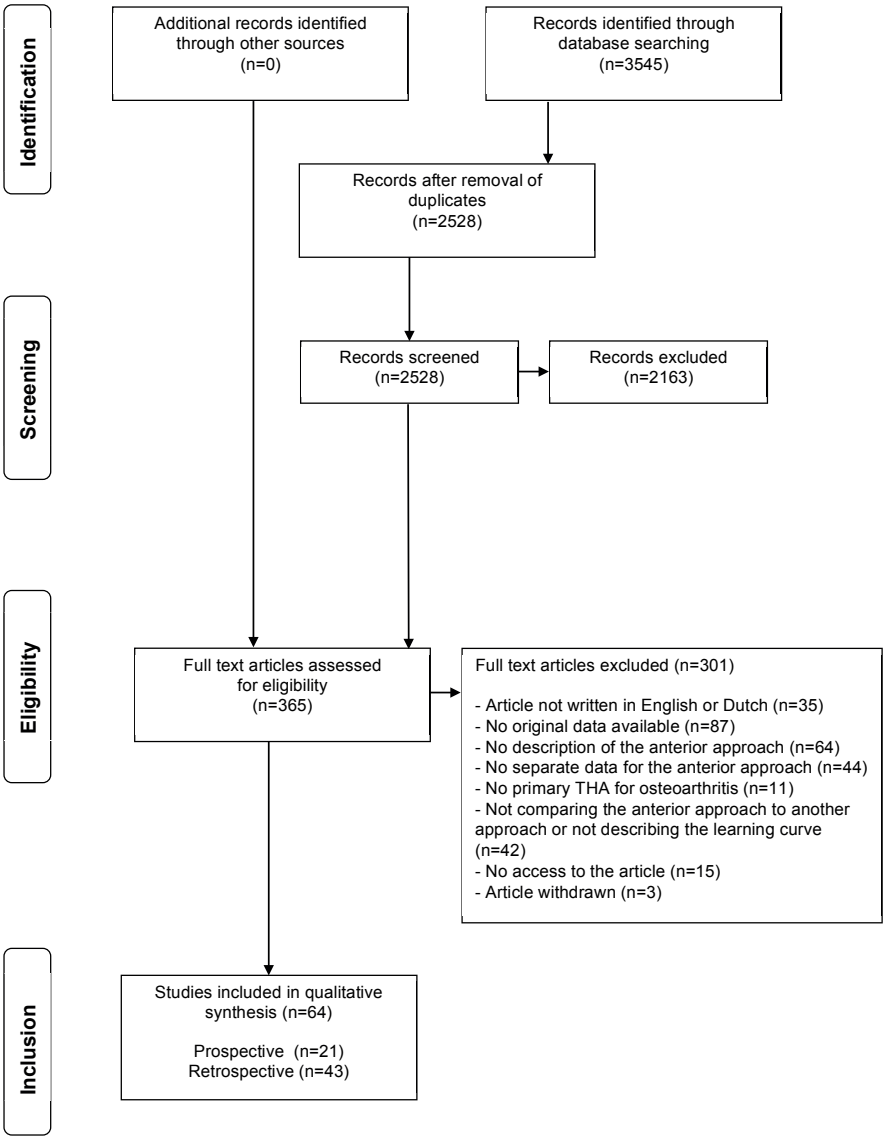
- Strong evidence is provided by 2 or more studies with high quality and by generally consistent findings in all studies (≥75% of the studies reported consistent findings);
- Moderate evidence is provided by 1 high quality study and 2 or more low-quality studies and by generally consistent findings in all studies (≥75%);
- Limited evidence is provided by low-quality studies or 1 high-quality study an by generally consistent findings (≥75%);
- Conflicting evidence is provided by conflicting findings (<75% of the studies reported consistent findings);
- No evidence is provided when no studies could be found.

RESULTS

Identification and selection of literature

The search resulted in 2,528 articles of which the abstracts were reviewed. Screening of the titles and abstracts resulted in 365 possibly relevant studies. Of these studies the full text articles were reviewed and 64 studies were included. Reasons for exclusion are presented in the flow chart of the study selection (Figure 1). Citation tracking was performed by manually screening the reference lists of eligible studies and additionally no other study was identified as possibly relevant.

Figure 1: Flow chart of the study selection according to PRISMA-statement.



Description of included studies

Table 2 presents the characteristics of the included studies. 21 prospective and 43 retrospective studies were included. A total of 50 studies compared the anterior to another approach. Of these 50 studies, only 9 studies were randomized (18%), the remaining 41 studies were nonrandomized (82%). All together these 50 comparative studies involve 5,691 patients operated by anterior approach. The randomized group numbers 346

Table 2: Characteristics of the included studies. Number of patients as well as demonstrated age, gender and BMI represents the patients operated by anterior approach. Control group represents healthy people who did not underwent surgery.

Study	Prospective / Retrospective	Follow up	N	Versus	Randomization	Age (years)	Gender (% male)	BMI (kg/m^2)	Experience surgeon	Table used
Abe et al. 2015 (69)	Retrospective	NR	129	80 P	Non-randomized	60 (24-85)	7.2%	22.8 (15.6-35.5)	NR	NR
Alecci et al. 2011 (15)	Retrospective	NR	221	198 L	Non-randomized	70.7±8.2	45.2%	NR	First 221 cases	S
Alexandrov et al. 2014 (70)	Retrospective	16.8 months	43	-	-	62 (38-83)	32.6%	26 (18-37)	First 43 cases	NR
Baba et al. 2014 (29)	Retrospective	1 year	36	40 P	Non-randomized	64.2±12.5	0%	NR	NR	S
Barrett et al. 2013 (38)	Prospective	12 months	43	44 P	Randomized	61.4±9.2	67.4%	30.7±5.4	Experienced	F
Berend et al. 2009 (8)	Retrospective	6 weeks	258	25 L, 372 ML	Non-randomized	NR	44%	NR	First 258 cases	S
Bergin et al. 2011 (39)	Prospective	4 weeks	29	28 P	Non-randomized	68.8±9.1	34%	26.3±5	NR	S
Bhandari et al. 2009 (1)	Retrospective	NR	1152	-	-	65.26±12.196	47.5%	28±5	Multicenter	F
Bhargava et al. 2010 (17)	Retrospective	2 years	81	-	-	57.8 (27-83)	51.3%	27.5 (16.4-42.8)	First 81 cases	F
Bremer et al. 2011 (60)	Retrospective	1 year	25	25 L	Non-randomized	70 (49-92)	40%	26 (18-35)	NR	F
Christensen 2014 (71)	Retrospective	NR	505	1288 P	Non-randomized	63.5±9.9	49.7%	27.6±9.1	First 505 cases	F
Christensen et al. 2015 (72)	Prospective	6 weeks	28	23 P	Randomized	64.3±9.1	46.4%	31.1±5.1	After 500 cases	NR
D'Arrigo et al. 2009 (28)	Prospective	6 weeks	20	20 ML, 20 MAL, 149 L	Randomized	64 (47-72)	60%	22.7 (26.5-21.7)	First 20 cases	F
De Geest et al. 2013 (49)	Retrospective	1 year	300	-	-	69.8 (34-95)	45%	NR	First 300 cases	F
Goebel et al. 2012 (45)	Retrospective	Hospital stay	100	100 L	Non-randomized	64.5±9.1	47%	26.7±3.2	NR	S
Goytia et al. 2012 (48)	Prospective	2 years	81	-	-	58 (27-83)	52.1%	27.5 (16.4-42.8)	First 81 cases	F
Hallert et al. 2012 (19)	Retrospective	1 year	200	-	-	67.4 (29-88)	39.5%	26.7 (17-43)	First 200 cases	S
Hamilton et al. 2015 (74)	Retrospective	NR	100	100 P	Non-randomized	62.5 (32-90)	36%	28.8 (19.2-46.3)	First 100 cases	F

Table 2: Characteristics of the included studies. Number of patients as well as demonstrated age, gender and BMI represents the patients operated by anterior approach. Control group represents healthy people who did not underwent surgery. (continued)

Study	Prospective / Retrospective	Follow up	N	Versus	Randomization	Age (years)	Gender (% male)	BMI (kg/m^2)	Experience surgeon	Table used
Hananouchi et al. 2009 (40)	Prospective	3 weeks	20	20 P	Non-randomized	55.1 (42-68)	10%	22.2 (15-27)	NR	S
den Hartog et al. 2015 (73)	Retrospective	NR	265	36 P, 176 L	Non-randomized	71 (39.3-92.6)	33.5%	27 (18.8-45.2)	After 50 cases	NR
Hozack et al. 2008 (31)	Prospective	6 months	43	36 L	Randomized	NR	NR	25 (18-30)	NR	S
Ilchmann et al. 2013 (42)	Prospective	2 years	113	142 L	Non-randomized	NR	NR	NR	First 113 cases	F
Jewett et al. 2011 (18)	Retrospective	1,8 years	800	-	-	62.5 (23-91)	46.8%	28 (19-43)	First 800 cases	F
Ji et al. 2015 (75)	Retrospective	NR	30	30 P	Non-Randomized	58.0±6.33	NR	32.92±5.14	First 30 cases	F
Klausmeier et al. 2010 (59)	Prospective	16 weeks	12	11 AL, 10 C	Non-randomized	56.9±3.3	66.7%	32.0±5.1	After 300 cases	F
Lamontagne et al. 2011 (61)	Retrospective	10 months	20	20 L, 20 C	Non-randomized	60.5±6.0	30%	28.5±4.9	NR	NR
Lugade et al. 2010 (64)	Prospective	16 weeks	12	11 AL, 10 C	Non-randomized	56.9±3.4	58.3%	32±5.1	After 300 cases	F
Maeda et al. 2015 (76)	Retrospective	NR	34	35 P	Non-randomized	61.7 (42-80)	10%	22.7±3.3	NR	S
Maffiuletti et al. 2009 (41)	Retrospective	6 months	17	17 P, 17 C	Non-randomized	68±6	58.8%	25.6±3.3	After 250 cases	S
Mantovani et al. 2012 (63)	Retrospective	300 days	20	20 L, 20 C	Non-randomized	60.5±6.0	30%	28.5±4.9	NR	NR
Martin et al. 2013 (36)	Retrospective	6 months	41	47 P	Non-randomized	63±10.6	35%	28.5±5.6	NR	F
Masonis et al. 2008 (50)	Retrospective	13.8 months	300	-	-	58.9 (15.6-90.2)	36%	29.0 (16.8-58.9)	First 300 cases	F
Mayr et al. 2009 (43)	Prospective	12 weeks	16	17 AL	Randomized	65 (55-84)	35.3%	27 (20.8-36.1)	NR	S
Melman et al. 2015 (83)	Retrospective	1 year	182	-	-	69±7.5	25%	28±4.6	First 182	S
Mjaaland et al. 2015 (77)	Prospective	4 days	84	80 L	Randomized	67.2±8.6	29.8%	27.7±3.6	Experienced	S

Table 2: Characteristics of the included studies. Number of patients as well as demonstrated age, gender and BMI represents the patients operated by anterior approach. Control group represents healthy people who did not underwent surgery. (continued)

Study	Prospective / Retrospective	Follow up	N	Versus	Randomization	Age (years)	Gender (% male)	BMI (kg/m^2)	Experience surgeon	Table used
Morris et al. 2013 (62)	Prospective	6 weeks	100	-	-	61.3±12.2	48%	30.3±6.6	NR	NR
Muller et al. 2014 (84)	Retrospective	5 years	150	-	-	64±12.36	48%	27.4±4.8	First 150 cases	F
Nakata et al. 2009 (9)	Retrospective	6 months	99	86 P	Non-randomized	62.9±1.2	16.2%	22.9±0.4	First 99 cases	S
Nam et al. 2013 (44)	Retrospective	6 weeks	90	90 P, 90 PN	Non-randomized	67.5±10.7	41.1%	28.7±5.4	Experienced	NR
Oinuma et al. 2007 (47)	Retrospective	3 months	99	-	-	62.5 (46-84)	13.7%	23.1 (18.1-37.7)	First 99 cases	S
Parvizi et al. 2013 (65)	Retrospective	NR	75	244 L	Non-randomized	54.75±9.77	64%	26.20±3.46	NR	S
Pilot et al. 2006 (56)	Prospective	72 h	10	10 P	Non-randomized	67.9	40%	29.1	First 10 cases	S
Poehling et al. 2014 (78)	Retrospective	8 weeks	126	96 MP	Non-randomized	64.8±12.4	46.8%	30.0±5.5	After 300 cases	S
Pogliacomi et al. 2012 (32)	Retrospective	1 year	30	30 L	Non-randomized	67.7	50%	27	First 30 cases	F
Pogliacomi et al. 2012 (33)	Retrospective	1 year	35	35 L	Non-randomized	64.57 (46-79)	54.3%	26.6±1.76	After 30 cases	F
Rathod et al. 2014 (66)	Prospective	1 year	11	11 P	Non-randomized	58±6.7	54.5%	25.9±2.23	After 100	NR
Rathod et al. 2014 (79)	Retrospective	16 months	286	293 P	Non-randomized	61.8±12	45.5%	26.4±5	First 286 cases	S
Reichert et al. 2015 (80)	Retrospective	3.7 years	85	86 L	Non-randomized	68.1	43.5%	27.5	Experienced	NR
Reininga et al. 2013 (57)	Prospective	6 months	35	40 P, 30 C	Randomized	60.3±7.7	31.4%	27.3±3.5	Experienced	F
Restrepo et al. 2010 (67)	Prospective	2 years	50	50 L	Randomized	62.02 (35.0-84.5)	34%	25.18 (18.8-29.9)	After 72 cases	S
Rodriquez et al. 2014 (34)	Prospective	1 year	60	60 P	Non-randomized	60±10	46.7%	27±4	After 150 cases	S
Sebečić et al. 2012 (35)	Retrospective	4 months	35	35 L	Non-randomized	66 (40-84)	54.3%	NR	First 35 cases	S
Sendtner et al. 2010 (30)	Prospective	1 year	74	60 L	Non-randomized	68.1±8.1	67.6%	28.8±4.9	First 74 cases	S

Table 2: Characteristics of the included studies. Number of patients as well as demonstrated age, gender and BMI represents the patients operated by anterior approach. Control group represents healthy people who did not underwent surgery. (continued)

Study	Prospective / Retrospective	Follow up	N	Versus	Randomization	Age (years)	Gender (% male)	BMI (kg/m^2)	Experience surgeon	Table used
Seng et al. 2009 (10)	Retrospective	6 weeks	182	22 L, 77 ML	Non-randomized	NR	NR	NR	First 182 cases	S
Sheth et al. 2015 (81)	Retrospective	3 years	1851	4226 AL, 667 L, 31747 P	Non-randomized	65±11	40%	28±5	NR	NR
Spaans et al. 2012 (20)	Retrospective	1 year	46	46 P	Non-randomized	69±9.8	52.2%	25±3	First 46 cases	F
Sugano et al. 2009 (37)	Retrospective	2 years	33	39 P	Non-randomized	56±13	12.1%	23±4	NR	S
Taunton et al. (82)	Prospective	12 months	27	27 MP	Randomized	62.05	44.4%	27.7	NR	S
Varin et al. 2013 (68)	Retrospective	291 days	20	20 L, 20 C	Non-randomized	60.5±6.0	30%	28.5±4.9	NR	F
Ward et al. 2008 (58)	Prospective	3 months	10	18 P, 11 AL, 30 MP	Non-randomized	64±2	NR	27.8±1.1	Experienced	F
Wayne et al. 2009 (11)	Retrospective	NR	100	100 L	Non-randomized	68 (35-90)	29%	26.6 (16-38)	First 100 cases	S
Woolson et al. 2009 (12)	Retrospective	2 years	247	-	-	67.7 (36-90)	39.0%	NR	First 247 cases*	F
Yi et al. 2013 (21)	Retrospective	12 months	61	-	-	55.6 (33-73)	53.7%	28.3 (18-44)	First 61 cases	F
Zawadsky et al. 2014 (46)	Retrospective	6 weeks	100	50 P	Non-randomized	59.8±11.1†	48%†	29.6± 5.9†	First 100 cases	S
						60.8±11.8‡	44%‡	28.6± 6.2‡		

**Divided over 5 surgeons, without training. † First 50 cases. ‡ Second 50 cases.*

NR = not reported.

L= lateral, ML = mini lateral, AL = anterolateral, MAL = mini anterolateral, P = posterior, MP = mini posterior, PN = posterior navigated, C = control group.

F = Fracture table, S = Standard surgery table.

Addendum table 2

Study	Included arthritis type	Excluded arthritis type	Fluoroscopy / Navigation
Abe et al. 2015 (69)	OA/AVN/RA	Perthes/Fracture	-
Alecci et al. 2011 (15)	-	-	-
Alexandrov et al. 2014 (70)	OA/AVN/RA	-	Fluoroscopy
Baba et al. 2014 (29)	OA/AVN/RA	-	-
Barrett et al. 2013 (38)	Non-inflammatory	Inflammatory	Fluoroscopy
Berend et al. 2009 (8)	OA	-	Fluoroscopy
Bergin et al. 2011 (39)	-	Infection/Fracture	-
Bhandari et al. 2009 (1)	OA/AVN/RA/Post-trauma	-	Fluoroscopy
Bhargava et al. 2010 (17)	OA/AVN	Dysplasia/Post-trauma	-
Bremer et al. 2011 (60)	-	Perthes/Dislocation	-
Christensen 2014 (71)	OA/AVN/Inflammatory/Post-trauma/Dysplasia	-	-
Christensen et al. 2015 (72)	-	Deformity/Poor bone quality	Fluoroscopy
D'Arrigo et al. 2009 (28)	-	RA/Fracture/Deformities	-
De Geest et al. 2013 (49)	OA/AVN/RA/Dysplasia	-	-
Goebel et al. 2012 (45)	-	-	-
Goytia et al. 2012 (48)	OA/AVN/RA/Dysplasia	"Complex" primary OA	Fluoroscopy
Hallert et al. 2012 (19)	-	Deformities	-
Hamilton et al. 2015 (74)	-	-	Fluoroscopy
Hananouchi et al. 2009 (40)	OA/AVN	-	Navigation
den Hartog et al. 2015 (73)	-	-	Fluoroscopy
Hozack et al. 2008 (31)	-	-	-
Ilchmann et al. 2013 (42)	-	Fracture	Fluoroscopy
Jewett et al. 2011 (18)	-	Bone loss	Fluoroscopy

Addendum table 2 (continued)

Study	Included arthritis type	Excluded arthritis type	Fluoroscopy / Navigation
Ji et al. 2015 (75)	-	-	Fluoroscopy
Klausmeier et al. 2010 (59)	-	Fracture	-
Lamontagne et al. 2011 (61)	-	Infection/Fracture	-
Lugade et al. 2010 (64)	-	-	-
Maeda et al. 2015 (76)	-	-	Navigation
Maffiuletti et al. 2009 (41)	-	-	-
Mantovani et al. 2012 (63)	-	Infection/Fracture	-
Martin et al. 2013 (36)	OA/AVN/Fracture/Dysplasia/FAI/SCFE	-	Fluoroscopy
Masonis et al. 2008 (50)	Unselected	-	Fluoroscopy
Mayr et al. 2009 (43)	-	-	-
Melman et al. 2015 (83)	OA	Fracture/Previous surgery	-
Mjaaland et al. 2015 (77)	OA/RA	Previous surgery	-
Morris et al. 2013 (62)	-	-	-
Muller et al. 2014 (84)	OA/AVN/Post-trauma/Dysplasia/Fracture	Hardware removal	-
Nakata et al. 2009 (9)	AVN/Dysplasia	Shortening osteotomy	-
Nam et al. 2013 (44)	OA/AVN/RA/Fracture/Dysplasia Crowe1&2	Dysplasia Crowe 3&4	Fluoroscopy
Oinuma et al. 2007 (47)	OA/AVN/Dysplasia Crowe1&2	Fracture/Dysplasia Crowe 3&4	-
Parvizi et al. 2013 (65)	-	-	-
Pilot et al. 2006 (56)	-	-	-
Poehling et al. 2014 (78)	-	Fracture/Prior surgery	Fluoroscopy
Pogliacomi et al. 2012 (32)	OA/AVN	Fracture/Deformities/Post-trauma	-
Pogliacomi et al. 2012 (33)	OA/AVN	Fracture/Femur deformities	-
Rathod et al. 2014 (66)	Degenerative OA	Dysplasia Crowe 3&4	Fluoroscopy
Rathod et al. 2014 (79)	OA/AVN/Post-trauma	Crowe 3&4/Previous surgery	Fluoroscopy

Addendum table 2 (continued)

Study	Included arthritis type	Excluded arthritis type	Fluoroscopy / Navigation
Reichert et al. 2015 (80)	-	-	-
Reininga et al. 2013 (57)	OA	-	Navigation
Restrepo et al. 2010 (67)	OA	-	-
Rodriquez et al. 2014 (34)	OA	Secondary OA/Fracture	Fluoroscopy
Sebečić et al. 2012 (35)	OA/Fracture	-	-
Sendtner et al. 2010 (30)	-	Tumor	-
Seng et al. 2009 (10)	First cases "selected"	-	Fluoroscopy
Sheth et al. 2015 (81)	Unselected	-	-
Spaans et al. 2012 (20)	OA	Secondary OA/Deformities	-
Sugano et al. 2009 (37)	OA/AVN	-	Navigation
Taunton et al. (82)	OA	Crowe 3&4/Infection/Deformities/Previous THA	Fluoroscopy
Varin et al. 2013 (68)	-	Infection/Fracture	-
Ward et al. 2008 (58)	-	-	-
Wayne et al. 2009 (11)	OA/AVN/RA/Dysplasia	-	-
Woolson et al. 2009 (12)	OA/AVN/RA/fracture/Dislocation	-	Fluoroscopy
Yi et al. 2013 (21)	OA/AVN/Fracture/dysplasia Crowe1&2	Acetabular protrusio/Deformities/Dysplasia Crowe3&4	Fluoroscopy
Zawadsky et al. 2014 (46)	OA/AVN	-	-

OA = osteoarthritis; AVN = avascular necrosis; RA = rheumatoid arthritis; FAI = femoral acetabular impingment; SCFE = slipped capital femoral epiphysis

patients (6.1%) and the nonrandomized group 5,345 patients (93.9%). The remaining 14 studies described solely the results of the anterior approach. These 14 studies involve 3,796 patients.

21 studies described or investigated the effect of a learning curve. Furthermore 30 studies described the results of the first THAs performed through the anterior approach. 18 studies did not mention the experience of the surgeon performing surgery with the anterior approach. Another 16 studies described the number of THAs performed through the anterior approach by the surgeon before the start of the study, or simply mentioned that the surgeon was experienced with the anterior approach. Follow up time in selected studies differed from several days up to 5 years. Regarding type of surgery table, a standard surgery table was used in 28 studies and 25 studies mentioned to use a fracture table. 11 studies did not mention the used kind of surgery table in their study. A total of 22 studies mentioned to use perioperative fluoroscopy for the anterior approach and 4 studies used perioperative navigation for component placement.

A total of 14 studies did not report information regarding the types of osteoarthritis, 37 studies provided information about the included types of osteoarthritis and 31 provided information about the excluded types of osteoarthritis in their study. Of these studies, 18 reported on both included and excluded types of osteoarthritis.

Quality assessment

The results of the quality assessment are presented in Table 3. A total of 23 studies were qualified as "high quality" and 41 studies were qualified as "low quality". In only 7 studies, a sample size calculation was presented.

Postoperative component placement

Postoperative component placement was measured regarding cup anteversion, cup inclination, femoral component alignment, and/or leg length discrepancy (LLD).

A total of 23 studies compared these results of the anterior approach to the anterolateral, lateral, or posterior approach, with strong evidence that there was no difference in postoperative component placement between the anterior approach and the different approaches[9,11,20,30,32-34,36,37,39-44,69,74-76,78-80,82] (Table 4). Of these studies only 9 reported on perioperative use of fluoroscopy[34,36,42,44,74,75,78,79,82] and 3 on perioperative use of navigation for component placement.[37,40,76] The only study demonstrating results against the anterior approach, was a study describing the first THAs performed through the anterior approach.[11]

Table 3: Quality assessment.

Study		1	2	3	4	5	6	7	8	Total	Quality
Christensen et al. 2015 (72)	Prospective	1	1	1	1	0	1	1	1	7	High quality
Goytia et al. 2012 (48)	Prospective	1	1	0	1	1	1	0	1	6	High quality
Mjaaland et al. 2015 (77)	Prospective	1	1	1	1	0	0	0	1	5	High quality
Morris et al. 2013 (62)	Prospective	1	1	1	1	1	0	0	1	6	High quality
Rathod et al. 2014 (66)	Prospective	1	1	1	1	1	0	0	1	6	High quality
Restrepo et al. 2010 (67)	Prospective	1	1	1	1	1	0	1	1	7	High quality
Rodriquez et al. 2014 (34)	Prospective	1	1	1	1	0	0	1	1	6	High quality
Sendtner et al. 2010 (30)	Prospective	1	1	0	1	1	1	0	1	6	High quality
Taunton et al. (82)	Prospective	1	1	1	1	1	1	0	1	7	High quality
Bhargava et al. 2010 (17)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
Bremer et al. 2011 (60)	Retrospective	1	1	1	1	1	0	0	1	6	High quality
De Geest et al. 2013 (49)	Retrospective	1	0	1	1	1	1	0	1	6	High quality
Hallert et al. 2012 (19)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
den Hartog et al. 2015 (73)	Retrospective	1	1	0	1	0	1	0	1	5	High quality
Martin et al. 2013 (36)	Retrospective	1	1	0	1	0	1	0	1	5	High quality
Melman et al. 2015 (83)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
Muller et al. 2014 (84)	Retrospective	1	1	1	1	1	1	0	1	7	High quality
Poehling et al. 2014 (78)	Retrospective	1	1	0	1	0	1	0	1	5	High quality
Rathod et al. 2014 (79)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
Reichert et al. 2015 (80)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
Sheth et al. 2015 (81)	Retrospective	1	1	0	1	1	1	1	1	7	High quality
Spaans et al. 2012 (20)	Retrospective	1	1	0	1	1	0	0	1	5	High quality
Sugano et al. 2009 (37)	Retrospective	1	0	0	1	1	1	0	1	5	High quality
Barrett et al. 2013 (38)	Prospective	0	1	1	1	1	0	1	1	6	Low quality
Bergin et al. 2011 (39)	Prospective	0	1	0	1	0	0	1	1	4	Low quality
D'Arrigo et al. 2009 (28)	Prospective	0	1	1	1	0	0	0	1	4	Low quality
Hananouchi et al. 2009 (40)	Prospective	1	0	1	1	0	0	0	1	4	Low quality
Hozack et al. 2008 (31)	Prospective	0	0	0	1	0	0	0	0	1	Low quality
Ilchmann et al. 2013 (42)	Prospective	1	1	1	0	1	1	0	1	6	Low quality
Klausmeier et al. 2010 (59)	Prospective	0	1	1	1	0	0	0	1	4	Low quality
Lugade et al. 2010 (64)	Prospective	0	0	1	1	0	0	0	1	3	Low quality
Mayr et al. 2009 (43)	Prospective	0	1	1	1	0	0	0	1	4	Low quality
Pilot et al. 2006 (56)	Prospective	0	0	1	1	0	0	0	1	3	Low quality
Reininga et al. 2013 (57)	Prospective	0	1	1	1	0	0	0	1	4	Low quality
Ward et al. 2008 (58)	Prospective	0	0	1	1	0	0	0	1	3	Low quality
Abe et al. 2015 (69)	Retrospective	0	1	0	1	0	0	0	1	4	Low quality

Table 3: Quality assessment. (continued)

Study		1	2	3	4	5	6	7	8	Total	Quality
Alecci et al. 2011 (15)	Retrospective	1	0	1	1	0	0	0	1	4	Low quality
Alexandrov et al. 2014 (70)	Retrospective	1	1	0	1	1	0	0	0	4	Low quality
Baba et al. 2014 (29)	Retrospective	0	0	0	1	1	0	0	1	3	Low quality
Berend et al. 2009 (8)	Retrospective	1	0	0	1	0	0	0	0	2	Low quality
Bhandari et al. 2009 (1)	Retrospective	0	1	0	1	0	0	1	1	4	Low quality
Christensen 2014 (71)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Goebel et al. 2012 (45)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Hamilton et al. 2015 (74)	Retrospective	1	0	0	1	0	0	0	0	2	Low quality
Jewett et al. 2011 (18)	Retrospective	1	0	0	1	1	1	0	0	4	Low quality
Ji et al. 2015 (75)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Lamontagne et al. 2011 (61)	Retrospective	0	1	1	1	0	0	0	1	4	Low quality
Maeda et al. 2015 (76)	Retrospective	0	0	0	1	0	0	0	1	2	Low quality
Maffiuletti et al. 2009 (41)	Retrospective	0	1	1	1	0	0	0	1	4	Low quality
Mantovani et al. 2012 (63)	Retrospective	0	0	1	1	0	0	0	1	3	Low quality
Masonis et al. 2008 (50)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Nakata et al. 2009 (9)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Nam et al. 2013 (44)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Oinuma et al. 2007 (47)	Retrospective	1	1	0	1	0	0	0	0	3	Low quality
Parvizi et al. 2013 (65)	Retrospective	1	1	0	1	0	0	0	1	3	Low quality
Pogliacomi et al. 2012 (32)	Retrospective	0	1	0	1	1	0	0	1	4	Low quality
Pogliacomi et al. 2012 (33)	Retrospective	0	1	0	1	1	0	0	1	4	Low quality
Sebečić et al. 2012 (35)	Retrospective	0	0	0	1	0	0	0	0	1	Low quality
Seng et al. 2009 (10)	Retrospective	1	0	0	1	0	0	0	0	2	Low quality
Varin et al. 2013 (68)	Retrospective	0	1	1	1	0	0	0	1	4	Low quality
Wayne et al. 2009 (11)	Retrospective	1	1	0	1	0	0	0	1	4	Low quality
Woolson et al. 2009 (12)	Retrospective	1	0	0	1	0	0	0	0	2	Low quality
Yi et al. 2013 (21)	Retrospective	1	0	0	1	0	0	0	0	2	Low quality
Zawadsky et al. 2014 (46)	Retrospective	1	0	0	1	0	1	0	1	4	Low quality

1. *Inclusion of consecutive patients?*
2. *Description of in- and exclusion criteria?*
3. *Did the authors report the participation rate and did patients give informed consent?*
4. *Unbiased assessment of outcome and determinant?*
5. *Was the follow-up period appropriate?*
6. *Did they report a loss to follow-up of less than 20%?*
7. *Is there any information about the sample size calculation?*
8. *Were statistical test appropriate and did they adjust for confounders?*

Table 4: Results of the studies for the different parameters that were analyzed, which demonstrated strong evidence.

Parameter	No difference		In favor of the anterior approach		Against the anterior approach	
	Low Quality	High Quality	Low Quality	High Quality	Low Quality	High Quality
Strong evidence						
Accuracy of component placement	Bergin et al. 2011 (39) Hananouchi et al. 2009 (40) Ilchmann et al. 2013 (42) Maffiuletti et al. 2009 (41) Mayr et al. 2009 (43) Nam et al. 2013 (44) Pogliacomi et al. 2012 (32) Pogliacomi et al. 2012 (33) Abe et al. 2015 (69) Maeda et al. 2015 (76)	Martin et al. 2013 (36) Rodriquez et al. 2014 (34) Sendtner et al. 2010 (30) Spaans et al. 2012 (20) Sugano et al. 2009 (37) Poehling et al. 2014 (78) Reichert et al. 2015 (80) Taunton et al. (82)	Nakata et al. 2009 (9) Hamilton et al. 2015 (74) Ji et al. 2015 (75)	Rathod et al. 2014 (79)	Wayne et al. 2009 (11)	-
Functional recovery	-	-	Barrett et al. 2013 (38) Goebel et al. 2012 (45) Nakata et al. 2009 (9) Seng et al. 2009 (10)	Martin et al. 2013 (36) Rodriquez et al. 2014 (34)	-	-
Need for assistive device	-	Rodriquez et al. 2014 (34)	Hozack et al. 2008 (31) Nakata et al. 2009 (9) Zawadsky et al. 2014 (46)	Sugano et al. 2009 (37) Christensen et al. 2015 (72) Taunton et al. (82)	-	Poehling et al. 2014 (78)

Functional recovery and need for assistive devices

9 studies compared functional recovery after the anterior approach to the lateral or posterior approach[9,10,34,36,38,45,72,78,82] (Table 4). There is strong evidence for significantly faster return to function and daily activity, significantly achieving functional milestones earlier, and significantly less time to postoperative recovery, for patients operated through the anterior approach in comparison to other approaches (Table 4). Furthermore, a total of 8 studies compared postoperative need for assistive devices after the anterior approach to the lateral or posterior approach[9,31,34,37,46,72,78,82] (Table 4). There is strong evidence that patients operated through the anterior approach need less assistive devices, like a cane, crutches or a walker, for mobilizing postoperatively, in comparison to other approaches (Table 4).

Other outcome parameters

Regarding all other studied outcome parameters, only conflicting evidence was found with mainly low quality studies (Table 5). For these parameters, there were no differences regarding better or worse results for the 2 different surgery tables, or for the use of a specific approach when compared to the anterior approach.

Learning curve

The effect of a learning curve for the anterior approach was described in 21 studies, of which 8 were high quality studies.[1,10-12,15,17-21,28,32,46-50,70,79,83,84] Parameters for describing this learning curve were surgery time, blood loss, hospital stay, (major) complications, component placement, questionnaire scores, and perioperative fluoroscopy time.

All studies investigating surgery time described a clear reduction throughout time, after gaining more experience.[10,19,20,28,32,46-48,50,70,79,83] This reduction was approximately 30 minutes. A significant drop in blood loss after gaining more experience is also described.[10,48,70] Regarding complication rate, the effect of a learning curve was clearly demonstrated. However the number of cases when the learning curve was mentioned to be ended, varied greatly from 10-200.[1,12,15,18,19,21,46,84] Others only studied the first 20-46 cases and did not observe an ending of the learning curve regarding blood loss, LOS and complication rate.[20,28] Another study describes that no learning effect regarding surgery time is achieved within the first 100 THAs performed through the anterior approach.[11]

2 studies described improvement of component placement regarding LLD and/or positioning of the acetabular component after 100 cases.[50,79] Another study describing the results of the first 300 cases operated through the anterior approach, demonstrated that most outliers regarding median acetabular cup abduction angle occurred during the first 100 cases. These first 100 cases had significantly steeper cup positions when compared to the second and third 100 cases.[49]

Table 5: Results of the studies for the different parameters that were analyzed, which only demonstrated conflicting evidence.

Parameter	No difference		In favor of the anterior approach		Against the anterior approach	
	Low Quality	High Quality	Low Quality	High Quality	Low Quality	High Quality
Conflicting evidence						
Complication rate	Alecci et al. 2011 (15) Barrett et al. 2013 (38) Hozack et al. 2008 (31) Pogliacomi et al. 2012 (32) Pogliacomi et al. 2012 (33) Sebečić et al. 2012 (35) Seng et al. 2009 (10) Wayne et al. 2009 (11)	Martin et al. 2013 (36) Rodriquez et al. 2014 (34) Sendtner et al. 2010 (30) Sugano et al. 2009 (37)	Baba et al. 2014 (29)	Poehling et al. 2014 (78) Sheth et al. 2015 (81)	D'Arrigo et al. 2009 (28) Christensen 2014 (71)	Spaans et al. 2012 (20)
Destination of discharge	Bergin et al. 2011 (39)	Martin et al. 2013 (36) Restrepo et al. 2010 (67) Rodriquez et al. 2014 (34) Poehling et al. 2014 (78)	Berend et al. 2009 (8) Zawadsky et al. 2014 (46)	-	-	-
Muscle damage/limp	Pilot et al. 2006 (56)	Sendtner et al. 2010 (30)	Bergin et al. 2011 (39) Ilchmann et al. 2013 (42) Nakata et al. 2009 (9)	Bremer et al. 2011 (60)	-	Mjaaland et al. 2015 (77)
Gait analysis and hip function	Maffiuletti et al. 2009 (41) Mantovani et al. 2012 (63) Reininga et al. 2013 (57) Varin et al. 2013 (68) Ward et al. 2008 (58)	Sugano et al. 2009 (37)	Klausmeier et al. 2010 (59) Lamontagne et al. 2011 (61) Lugade et al. 2010 (64) Mayr et al. 2009 (43)	Rathod et al. 2014 (66) Rodriquez et al. 2014 (34)	-	-

Table 5: Results of the studies for the different parameters that were analyzed, which only demonstrated conflicting evidence. (continued)

Parameter	No difference		In favor of the anterior approach		Against the anterior approach	
	Low Quality	High Quality	Low Quality	High Quality	Low Quality	High Quality
Surgery time	Berend et al. 2009 (8) Hananouchi et al. 2009 (40) Hozack et al. 2008 (31) Mayr et al. 2009 (43) Nakata et al. 2009 (9) Pogliacomi et al. 2012 (33) Sebečić et al. 2012 (35)	Restrepo et al. 2010 (67) Rodriquez et al. 2014 (34)	Bergin et al. 2011 (39) Parvizi et al. 2013 (65)	-	Alecci et al. 2011 (15) Barrett et al. 2013 (38) D'Arrigo et al. 2009 (28) Ilchmann et al. 2013 (42) Pilot et al. 2006 (56) Pogliacomi et al. 2012 (32) Seng et al. 2009 (10) Wayne et al. 2009 (11) Zawadsky et al. 2014 (46)	Martin et al. 2013 (36) Sendtner et al. 2010 (30) Spaans et al. 2012 (20) Mjaaland et al. 2015 (77) Poehling et al. 2014 (78)
Incision length	Hananouchi et al. 2009 (40) Lamontagne et al. 2011 (61)	Sugano et al. 2009 (37)	Bergin et al. 2011 (39) Pilot et al. 2006 (56) Sebečić et al. 2012 (35)	Martin et al. 2013 (36) Sendtner et al. 2010 (30) Mjaaland et al. 2015 (77)	Barrett et al. 2013 (38)	-
Blood loss	Bergin et al. 2011 (39) Hananouchi et al. 2009 (40) Hozack et al. 2008 (31) Ilchmann et al. 2013 (42) Pilot et al. 2006 (56) Pogliacomi et al. 2012 (33) Seng et al. 2009 (10)	Martin et al. 2013 (36) Restrepo et al. 2010 (67)	Alecci et al. 2011 (15) D'Arrigo et al. 2009 (28) Mayr et al. 2009 (43) Parvizi et al. 2013 (65) Pogliacomi et al. 2012 (32) Sebečić et al. 2012 (35)	-	Barrett et al. 2013 (38) Berend et al. 2009 (8) Nakata et al. 2009 (9)	Spaans et al. 2012 (20)

Table 5: Results of the studies for the different parameters that were analyzed, which only demonstrated conflicting evidence. (continued)

Parameter	No difference		In favor of the anterior approach		Against the anterior approach	
	Low Quality	High Quality	Low Quality	High Quality	Low Quality	High Quality
Blood replacement	Berend et al. 2009 (8) Bergin et al. 2011 (39) Hozack et al. 2008 (31) Ilchmann et al. 2013 (42) Pogliacomi et al. 2012 (33) Wayne et al. 2009 (11)	Martin et al. 2013 (36) Restrepo et al. 2010 (67) Sendtner et al. 2010 (30)	Alecci et al. 2011 (15) Parvizi et al. 2013 (65) Pogliacomi et al. 2012 (32)	-	Seng et al. 2009 (10)	-
Hb decrease	Parvizi et al. 2013 (65) Pilot et al. 2006 (56)	Martin et al. 2013 (36) Restrepo et al. 2010 (67)	Alecci et al. 2011 (15)	Sendtner et al. 2010 (30)	Wayne et al. 2009 (11)	Mjaaland et al. 2015 (77)
Length of hospital stay	Berend et al. 2009 (8) Bergin et al. 2011 (39) D'Arrigo et al. 2009 (28) Hozack et al. 2008 (31) Pogliacomi et al. 2012 (33) Sebečić et al. 2012 (35) Seng et al. 2009 (10)	Spaans et al. 2012 (20) Rodriquez et al. 2014 (34) Restrepo et al. 2010 (67) Poehling et al. 2014 (78)	Alecci et al. 2011 (15) Barrett et al. 2013 (38) Goebel et al. 2012 (45) Ilchmann et al. 2013 (42) Pogliacomi et al. 2012 (32) Wayne et al. 2009 (11) Zawadsky et al. 2014 (46)	Martin et al. 2013 (36) Christensen et al. 2015 (72) den Hartog et al. 2015 (73)	-	-
Pain/pain medication consumption	Hozack et al. 2008 (31) Pogliacomi et al. 2012 (33)	Restrepo et al. 2010 (67) Rodriquez et al. 2014 (34) Reichert et al. 2015 (80)	Alecci et al. 2011 (15) Barrett et al. 2013 (38) Goebel et al. 2012 (45) Ilchmann et al. 2013 (42) Pogliacomi et al. 2012 (32) Zawadsky et al. 2014 (46)	Christensen et al. 2015 (72) Mjaaland et al. 2015 (77)	-	Poehling et al. 2014 (78)

Table 5: Results of the studies for the different parameters that were analyzed, which only demonstrated conflicting evidence. (continued)

Parameter	No difference		In favor of the anterior approach		Against the anterior approach	
	Low Quality	High Quality	Low Quality	High Quality	Low Quality	High Quality
Questionnaire scores	Mayr et al. 2009 (43) Pogliacomi et al. 2012 (33)	Martin et al. 2013 (36) Rathod et al. 2014 (66) Spaans et al. 2012 (20) Sugano et al. 2009 (37) Reichert et al. 2015 (80)	Berend et al. 2009 (8) Barrett et al. 2013 (38) D'Arrigo et al. 2009 (28) Hozack et al. 2008 (31) Ilchmann et al. 2013 (42) Maffiuletti et al. 2009 (41) Pogliacomi et al. 2012 (32) Sebečić et al. 2012 (35) Seng et al. 2009 (10)	Restrepo et al. 2010 (67) Rodriquez et al. 2014 (34) Poehling et al. 2014 (78)		Taunton et al. (82)

Perioperative fluoroscopy time was mentioned twice as parameter for describing the learning curve. These studies demonstrated a decrease in time within the first 81 cases,[48] and a significant decrease in time after 100 cases within a total of 300 cases.[50]

Another 7 studies described reduction in surgery time, blood loss, and/or complications within the first 30-99 cases, without a clear description of the number of surgeries defining the learning curve.[17,32,46-48,70,83]

A definition of the learning curve is mentioned to be 100 cases, regarding surgery time and component placement.[50] However, the number of cases in a high volume hip arthroplasty center is mentioned to be around 40 cases or 6 months.[10] Furthermore, a multicenter study among 1,152 patients described surgeons who performed less than 100 cases through the anterior approach were twofold more likely to have complications (20.2 % versus 9.8 %, p = 0.049).[1]

DISCUSSION

The purpose of this systematic review was to evaluate the available literature for the anterior approach for primary THA in comparison to other approaches. The different perioperative and postoperative parameters that were analyzed were surgery time, incision length, blood loss, complication rate, LOS, postoperative pain and pain medication consumption, questionnaire scores, accuracy of component placement, and functional recovery. We hypothesized that since muscle attachments are preserved, patients recover faster and experience less pain, in comparison to other approaches. Moreover, we hypothesized that there are no differences in other outcome parameters in comparison to other approaches. Last, we wanted to investigate if there is a clear description of the learning curve for the anterior approach.

This systematic review demonstrates strong evidence that there is no difference in component placement between the anterior approach and the different other approaches. Strong evidence was found for a faster postoperative recovery after primary THA through the anterior approach when compared to primary THA through other approaches. Moreover, strong evidence was found for less need for assistive devices during postoperative mobilizing after THA through the anterior approach when compared to primary THA through other approaches. All the other parameters studied in this systematic review only demonstrated conflicting evidence regarding differences in outcome. For these parameters, there were no differences regarding better or worse results for the 2 different surgery tables, or for the use of a specific approach when compared to the anterior approach.

The anterior approach uses a muscle splitting interval and therefore we hypothesized that using the anterior approach results in less postoperative pain. However, this sys-

tematic review demonstrates only conflicting evidence regarding differences in postoperative pain and pain medication consumption between the anterior approach and the other approaches, although only 1 of the 14 studies demonstrated results against the anterior approach.

Although the anterior approach is sometimes criticized due to its technical difficulty, this systematic review demonstrates no higher risk for malposition of component placement when the anterior approach is used. Regarding postoperative complication rate, only conflicting evidence was demonstrated. Moreover, no influence of approach was seen on surgical site infection in a multivariate regression model in 30,491 THA patients operated by the anterior approach.[51] Although LFCN neuropraxia is a complication that is known for the anterior approach, no differences were observed between patients who reported LFCN neuropraxia versus those without symptoms, regarding UCLA, WOMAC, SF-12.[13] However, although there is conflicting evidence regarding complication rates between the anterior approach and the different approaches, the only 3 studies demonstrating results against the anterior approach, were studies describing the first THAs performed through the anterior approach.[20,28,71] Suggesting that the learning curve for this approach should not to be neglected.

The effect of this learning curve for the anterior approach was described in 21 studies, of which only 8 were high quality studies.[1,10-12,15,17-21,28,32,46-50,70,79,83,84] Ending of this learning curve varied greatly between these studies and has been mentioned to be 10 to 200 cases. This high range may be influenced by the experience of surgeons, since a multicenter study among 1,152 patients described surgeons who performed less than 100 cases through the anterior approach were twofold more likely to have complications.[1] Moreover, another study suggests the learning curve might be less in a high volume hip center.[10] Since these results vary greatly, we conclude the amount of cases during the learning curve for the anterior approach is still not clear. However, a learning curve for the anterior approach is not unique and is also observed for other approaches for THA.[28,52] Moreover amounts for learning curves for other approaches to the hip joint are still not clear either.

Considering component placement, cup inclination range between 35° to 55° was considered accurate.[53] Femoral component angulation between 3° varus and 3° valgus was considered as accurate aligned.[30,54,55] The difference in leg length between the contralateral hip and the operated hip was defined as the postoperative LLD and a maximum of 10 mm was considered acceptable.[53] This systematic review demonstrates strong evidence that there was no difference in postoperative component placement between the anterior approach and the other different studied approaches.

Some potential limitations of our systematic review need to be discussed. Firstly, since the amount of cases for the learning curve is still not clear, not all included studies of this systematic review used the same number of cases for the learning curve, and

some authors mentioned to be experienced and beyond the learning curve, while other authors with the same experience mentioned to be within the learning curve for the anterior approach. Although combining all data may give worse results for the anterior approach because of the effect of this learning curve, the inclusion of all these studies in this systematic review gives a clear overview of all available literature regarding the anterior approach.

Second, only 23 "high quality" studies were included in our systematic review. For scoring the internal validity of the selected studies we used 8 questions from existing quality assessment tools.[23-25] From the total of 64 included studies the majority were qualified as "low quality" studies. However, this systematic review is an overview of all available literature regarding the anterior approach and it seems there are no more "high quality" studies on this topic available. To provide better evidence, more high quality research on the differences between the anterior approach and the other approaches needs to be done by randomized controlled trials.

In conclusion, this systematic review demonstrates strong evidence that there is no difference in approach regarding component placement. Strong evidence was found for faster postoperative recovery and less need for assistive devices during postoperative mobilizing in favor of the anterior approach when compared to other approaches. All the other parameters studied in this systematic review only demonstrated conflicting evidence. The learning curve for the anterior approach is still not clear. Although it seems surgeon's experience with this surgical approach influences the outcome. Since this systematic review demonstrates that there are few "high quality" studies on this subject, more high quality research on the anterior approach needs to be done to provide better evidence for both differences in outcome between the anterior approach and other approaches as well as a clear description of the learning curve.

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Chapter 6

The anterior supine intermuscular approach for total hip arthroplasty: reducing the complication rate by improving the procedure

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ABSTRACT

This study describes specific complications noticed during the first unselected cases operated by anterior approach for THA in our hospital and specific adjustments that were applied on the procedure to prevent these complications. We retrospectively analyzed the differences between 202 patients who were operated by a standardized approach and 248 patients who were operated after adjustments were implemented on the procedure. Injury to the lateral femoral cutaneous nerve (LFCN), fractures of the greater trochanter and dislocation were specific complications that were noticed with the initial technique.

Prevalence of injury to the LFCN decreased from 7.9 % to 0.8 % ($p < 0.001$), fractures of the greater trochanter decreased from 5.4 % to 0.8 % ($p = 0.004$) and the incidence of dislocation decreased from 4.5 % to 1.6 % ($p = 0.074$).

INTRODUCTION

The direct anterior intermuscular approach for THA was first performed by Robert Judet in 1947.[1] The literature makes numerous positive claims relating to this approach given that it uses both an intermuscular and internervous plane.[1-9] Preservation of muscle attachments to bone improves stability and decreases the risk of dislocation.[1,10] Furthermore, a shorter rehabilitation period with less surgical trauma is attributed to the muscle splitting interval.[7,9,11,12,22] Less pain, shorter hospital stay and less operative time are also described for the direct anterior approach.[3,5-9,12-14] However this approach is also technically demanding and it has its own unique set of specific complications.[2,4,11,15,16]

In our hospital the anterior supine intermuscular (ASI) approach for THA was introduced in September 2007. We noticed some specific complications with this approach after its initial introduction. Firstly, LFCN lesions occurred more often than expected, as did greater trochanteric fractures and dislocations. In 2010 we altered the technique in order to reduce the specific complications related to the anterior approach.[1-5,9,7,10-15,17-19] We describe the results of the implementation of these alterations with respect to the prevalence of general and specific complications.

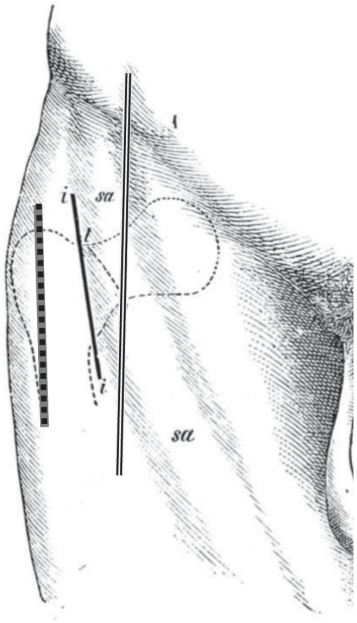
MATERIALS AND METHODS

In this retrospective cohort study we analyzed the differences between two cohorts of unselected THA patients operated by ASI approach by one orthopedic surgeon. The first cohort of 202 patients was operated between December 2008 and April 2010. The surgical approach for this first cohort was standardized as described by Bender *et al*.[6] A radiolucent operative table with fluoroscopy was used in all cases. Patients were positioned supine and both legs were draped free. Femoral exposure was gained through a figure-of-four position in which the foot was placed under the contralateral leg. Traction devices were not used.

From May 2010 to October 2010 no ASI procedures were performed. In this period the technique was adapted in three ways.

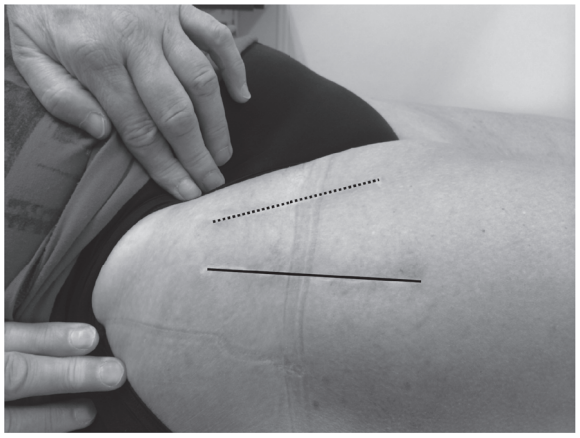
- The incision was placed more laterally than described originally by Hueter and others[1,2,6] to prevent injury to the LFCN. In the first cohort the starting point of the incision was placed approximately two centimeters lateral to the anterior superior iliac spine (ASIS) and pointed towards the patella. In the second cohort the skin incision was placed five centimeters lateral to the ASIS and pointed towards the head of the fibula. (Figure 1 and 2)
- In the first cohort, the release of the lateral capsule was performed with the leg in the figure-of-four position. A Hohmann bone retractor was placed at the tip of the

Figure 1: The altered position of the skin incision.



The black line represents the position of the initial skin incision as described by Hueter (1,2,6). The double line represents the position of the LFCN. The broken line represents the position of the skin incision in cohort 2.

Figure 2: The altered position of the skin incision.

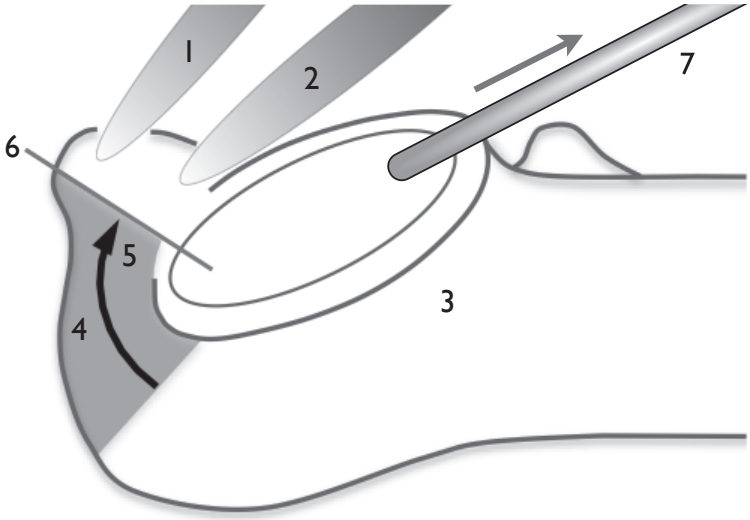


The broken line marks the position of the initial skin incision. The black line marks the position of the altered skin incision.

greater trochanter, which was levered over the tensor fascia lata. The tension that was put on the retractor often led to damage to the tensor muscle but also to fractures of the tip of the greater trochanter. In the second cohort, the capsular release was performed with the leg in neutral position. This reduced tension on the tensor fascia lata. The Hohmann retractor was placed more anterior, to avoid fractures of the vulnerable posterolateral tip of the greater trochanter. Also a blunt bone-hook was placed in the femoral osteotomy. With this hook the femur was pulled out of the wound instead of pushed out by the retractor.

- A thorough release of the posterolateral and posterior capsule and the external obturator tendon will lead to an excellent visualization of the femoral osteotomy after which the femoral component is easily placed. The early dislocations of THAs in the first cohort were, however, presumed to be due to this extensive dissection. In the second cohort, this capsular release was performed in a more controlled manner. Prior to the release, the femur was elevated out of the wound with a blunt bone-hook which was placed in the proximal femur osteotomy. No force was put on the Hohmann retractor at the anterolateral point of the greater trochanter (Figure 3). The release was limited to the anterolateral capsule. The posterolareral capsule was left intact in order to preserve the piriformis, gemelli and the external obturator ten-

Figure 3: The altered release of the proximal femur.



Schematic view of the pirifomis tendon (1) together with the obturator externus tendon (2) and the proximal femur (3). The grey zone (4) represents the capsular attachment that has to be released, the arrow (5) indicates the direction of the release. The grey line (6) represents the border of the release of the joint capsule, which should not be crossed on the medial side. The blunt bone hook (7) is pulled in the direction of the green arrow, in order to elevate the femur out of the wound.

don attachment.[26] The grey line indicated in Figure 3 was never crossed. Only after a sufficient release was obtained the leg was placed in a figure-of-four position under the other leg with a slight extension in the hip. This was done to obtain better access for broaching and femoral component placement. Because of the possible injury to the femoral nerve, this extension of the hip never exceeded 30 degrees.

The second cohort of 248 patients was operated between November 2010 and December 2012.

Both cohorts were compared regarding length of hospital stay, surgery time, the specific complications mentioned before, and rates of total complications, re-admissions ad reoperations.

Length of hospital stay was measured by number of nights. A standardized hospitalization and rehabilitation protocol was used for all cases. Patients were mobilized at the day of surgery when possible. Surgery time was measured by number of minutes. In case of cementation, the surgery time was corrected by 12 minutes per cemented component.

All femoral components were placed press-fit except for the cases in which insufficient stability was obtained during surgery. In those cases the femoral component was cemented. Age above 70 and insufficient stability were both reasons for cementation of the cup, otherwise the cup was placed press-fit. No screws were used to improve uncemented cup stability. The used fixation types for both cohorts are mentioned in Table 1. There were no significant differences in fixation types between both cohorts ($p = 0.166$).

Femoral head size depended on the type of cup used and differed between both cohorts ($p < 0.001$). For cohort 1 the most frequent used head size was 28 mm, for cohort 2 this was 36 mm. Head sizes and prostheses for both cohorts are shown in Table 1.

Injury of the LFCN was defined as numbness and/or burning sensation on the anterolateral thigh. At outpatient visits patients were specifically asked and investigated for these symptoms. Fractures of the greater trochanter were analyzed by examination of the surgery reports and by retrospective examination of all the available postoperative radiographs of the involved hip in comparison to the preoperative radiographs of the involved hip by two investigators (YH, SV). Both displaced and non-displaced fractures were reported as fractured, even in the absence of symptoms. The rate of dislocations was documented via appropriately collected hospital data.

To avoid 'learning curve issues" the first 50 patients operate on by ASA approach in our hospital were excluded. In both cohorts all patients who were operated by ASI approach in the mentioned period were included, there were no further exclusion criteria. Follow-up period was minimally one year.

Table 1: Femoral head size diameter, fixation types, and prosthesis component types used for the 2 cohorts.

	Cohort 1 N = 202	Cohort 2 N = 248	Total N = 450
Femoral head size diameter			
28 mm	76.5	5.2	37.1
32 mm	1.5	26.2	15.1
36 mm	6.4	68.5	40.7
>36 mm	15.6	0	7.1
Fixation types			
Un-cemented	56.9	63.7	60.7
Reversed hybrid	43.1	35.5	38.9
Cemented	0.0	0.8	0.4
Femoral component			
Taperloc® (Biomet, Warsaw, In, USA)	100	100	100
Acetabular component			
Apollo® (Zimmer, Warsaw, In, USA)	43.1	19.0	29.8
Magnum® (Biomet, Warsaw, In, USA)	15.4	0	6.9
Mallory-Head® (Biomet, Warsaw, In, USA)	33.7	15.7	23.8
Exceed® (Biomet, Warsaw, In, USA)	7.9	58.5	35.8
Regenerex® (Biomet, Warsaw, In, USA)	0	6.9	3.8

Cohort 1 represents the patients who were operated before the adjustments were applied on the ASI procedure. Cohort 2 represents the patients who were operated after the adjustments were applied on the ASI procedure.

Statistical Analysis

Data analyses were conducted with IBM SPSS Statistics for Mac, version 20. For all statistics p-values less than 0.05 were considered significant. If data were not normally distributed, data were analyzed using the Mann-Whitney Test, otherwise an independent student T-test was done.

RESULTS

All 450 unselected patients operated by ASI approach were included. There were no patients lost to follow up. All patient characteristics are summarized in Table 2. After the adjustments were applied on the ASI technique, the prevalence of injury to LFCN decreased from 7.9 % to 0.8 % ($p < 0.001$), fractures of the greater trochanter decreased from 5.4 % to 0.8 % ($p = 0.004$), and the prevalence of dislocation decreased from 4.5 % to 1.6 % ($p = 0.074$) (Table 3).

Table 2: Demographics for both cohorts.

		Cohort 1 N = 202	Cohort 2 N = 248	Total N = 450	p-value
Age (years)		70.9 (SD 9.2)	68.3 (SD 10.3)	69.5 (SD 9.9)	0.005
Gender (% female)		69.3	63.7	66.2	0.212
BMI (kg/m^2)		26.7 (SD 3.7)	26.5 (SD 3.9)	26.6 (SD 3.8)	0.695
ASA classification (%)	I	26.2	27.8	27.1	0.700
	II	64.4	63.3	63.8	
	III	9.4	8.5	8.9	
	IV	-	0.4	0.2	
Anesthesia (% spinal)		88.1	92.7	90.7	0.051
Priority (% elective)		100	99.2	99.6	0.201
Diagnosis (% primary)		95.0	94.8	94.9	0.889
Discharge destination (% to home)		84.7	86.7	85.8	0.563
Side (% right)		63.4	46.8	54.2	< 0.001

Cohort 1 represents the patients who were operated before the adjustments were applied on the ASI procedure. Cohort 2 represents the patients who were operated after the adjustments were applied on the ASI procedure.

Table 3: Length of hospital stay, surgery time, and rate of complications, readmissions and reoperations for the 2 cohorts.

	Cohort 1 N = 202	Cohort 2 N = 248	Total N = 450	p-value
Length of hospital stay (nights)	3.5 (SD 1.4)	2.4 (SD 1.8)	2.9 (SD 1.7)	< 0.001
Surgery time (minutes)	77.8 (SD 22.7)	85.9 (SD 22.2)	82.3 (SD 22.8)	< 0.001
LFCN neuropraxia (%)	7.9	0.8	4.0	< 0.001
Fracture greater trochanter (%)	5.4	0.8	2.9	0.004
Dislocation (%)	4.5	1.6	2.9	0.074
Infection (%)	2.0	1.6	1.8	0.770
Fracture femoral shaft (%)	1.0	1.6	1.3	0.567
DVT (%)	0.5	0.4	0.4	0.884
Pulmonary embolism (%)	0.0	0.0	0.0	1.000
Total complications (%)	19.3	6.9	12.4	< 0.001
Readmission (%)	7.4	4.8	6.0	0.251
Reoperation (%)	6.4	3.2	4.7	0.109

Cohort 1 represents the patients who were operated before the adjustments were applied on the ASI procedure. Cohort 2 represents the patients who were operated after the adjustments were applied on the ASI procedure.

Fractures of the greater trochanter were all chip-fractures and only one patient required secondary fixation. In cohort one, a total of eight dislocations occurred for femoral head size diameter of 28 mm and one dislocation occurred for a femoral head size diameter of 36 mm. In cohort two, two dislocations occurred for femoral head size diameter of 28 mm and two dislocations occurred for femoral head size diameter of 32 mm. All dislocations occurred within 10 weeks of surgery. In cohort one, three hips dislocated twice. Two of these required a cup revision. In cohort two, no recurrent dislocations occurred. Two dislocations occurred after trauma. Furthermore, one revision in the second cohort was needed because of femoral subsidence. Mean length of hospital stay, mean surgery time, and the rate of other complications, re-admissions and reoperations for both cohorts are listed in Table 3. Total rate of complications decreased significantly from 19.3 % to 6.9 % ($p < 0.001$) after the adjustments had been applied on the procedure.

DISCUSSION

The ASI procedure is known to be technically demanding. This study demonstrates the specific complications that can be expected using this approach, which could be potential pitfalls for other surgeons who perform this approach. We also describe the specific adjustments that we made to the procedure to avoid these pitfalls. Furthermore we demonstrate the results of the implementation of these adjustments on the prevalence of these specific complications. There was a significant decrease in complication rate after specific adjustments were applied to the ASI procedure in our hospital. Prevalence of injury to LFCN decreased from 7.9 % to 0.8 % ($p < 0.001$), fractures of the greater trochanter decreased from 5.4 % to 0.8 % ($p = 0.004$), and the prevalence of dislocation of THA decreased from 4.5 % to 1.6 % ($p = 0.074$). This decrease in the various complications could be partly due to the effect of a learning curve. Many publications demonstrated that extensive training is necessary for surgeons performing the ASI technique.[9,11,15] There is a decline in complication rate, operating time and blood loss after the surgeon has gained more experience.[1] In our hospital the ASI approach was introduced in September 2007. Because the known effect of a learning curve and a patient selection for the first 50 patients who were operated by ASI approach in our hospital, these first 50 cases were excluded for this study.

Although patients were not selected, age differed significantly between both cohorts ($p = 0.005$). Because older age is associated with co-morbidities this could be a reason for decrease in the different complication rates. However, there was no significant difference in ASA classification between both cohorts.

Mean length of hospital stay decreased significantly between the two cohorts and was most likely due to the effect of the learning curve and due to the introduction of the rapid recovery protocol in our hospital, which was implemented between January 2009 and January 2011.[22] This introduction of rapid recovery could also explain the difference in type of anesthesia between both cohorts, because less general anesthesia is given for this protocol. However, this difference in type of anesthesia was not significant between both cohorts.

Mean surgery time for the first cohort was significantly less when compared to the mean surgery time for the second cohort. However this mean surgery time for both cohorts is less than described in literature.[3] We could not well explain this difference in surgery time. A possible reason for this could be the awareness of the surgeon of the importance of the release of the posterior capsule for the procedure in the second cohort. This awareness could result in a longer procedure.

The LFCN and its branches are within the field of dissection between the sartorius muscle and the tensor fascia lata muscle and thus at risk of injury.[11] This risk is not only due to sharp dissection but also to traction lesions. An anatomical study in which the LFCN was dissected bilaterally in 17 formalin-preserved cadavers demonstrated that numerous anatomical variations of the LFCN should be considered and that the skin incision should be placed as lateral and distal to the anterior superior iliac spine as possible.[17] In previous studies the rate of injury of the LFCN was described between 0.5 % and 14.8 %.[1,4,5,9,12,15,18] Another study reported 67 % sensory deficits in the anterolateral thigh area after primary THA in 132 patients and the authors suggest that LFCN injury is underreported in general literature.[2] However, in this report the incision was placed one to two centimeters lateral to the ASIS, which could explain their high rate of LFCN injury also.

Although some studies have described an excellent anatomic vision of both the femur and the acetabulum for the ASI approach,[7,8,13] femoral exposure and preparation are very different from more conventional approaches. Therefore it is difficult to obtain straight and direct access to the femoral canal,[11,18] and a release of the capsule has to be performed. Furthermore, release of one or more of the short external rotator tendons depending on the requirement for femoral mobility has been described as well.[1] Insufficient release of the capsule can lead to fractures of the greater trochanter.[14] Equipment related fractures are also described in literature for this approach.[5] However fractures of the greater trochanter had no consequences for the most of our patients. In fact only two patients suffered with clinical consequences, one patient got instructions for non-weight bearing mobilization during six weeks, another patient underwent a reoperation for re-fixation of the greater trochanter, which did not alter the complaints she had before the second procedure. In previous studies the rate of these fractures has been described as 6.5 %.[3] Fewer incidences of 0.7-1.0 % have also been described.[1,13,14]

However, this could be an underreporting due to the absence of clinical consequences in most of the patients.

Although excessive release of the soft tissue of the proximal femur could result in instability,[15] incorrect positioning of the prosthetic components due to minimally releases can cause dislocations as well.[10,19] Previous studies describe rate of dislocation for the ASI approach between 0 % and 2.5 %.[1,3,5,7,10,12,13,15,19] These rates of dislocation are significantly lower than the dislocation rates generally quoted for other approaches.[5,11]

The femoral head size utilized differed significantly between both cohorts. For cohort 1 the most frequent used head size was 28 mm, for cohort 2 this was 36 mm. This could be a reason for the decrease in dislocation rate between both cohorts, because large diameter heads are associated with fewer dislocation rates. Moreover, the size of the femoral head has been mentioned as a weak influential factor for dislocation.[20,21] For cohort one, a total of eight dislocations occurred for femoral head size diameter of 28 mm and one dislocation occurred for a femoral head size diameter of 36 mm. For cohort two, a total of two dislocations occurred for femoral head size diameter of 28 mm and two dislocations occurred for femoral head size diameter of 32 mm.

Total rate of complications decreased significantly from 19.3 % to 6.9 % ($p < 0.001$) after the adjustments had been applied on the procedure. This rate of complications included injury to the LFCN, dislocations of THA, fractures of the greater trochanter, infection, fractures of the femoral shaft, DVT and pulmonary embolism. This rate of complications is in accordance to previous studies, which describe a complication rate between 5.4 % and 13 %.[3,5,13] The re-admission rate decreased from 7.4 % to 4.8 % and the reoperation rate decreased from 6.4 % to 3.2 % after the adjustments had been applied on the procedure, however these decreases were not significant. The re-admission rate after THA varies from 4-11 % in literature although some studies only describe the re-admission rate within the first three months after surgery.[23-25] Our reoperation rate is slightly higher than described in literature, however most of these studies again only describe the reoperation rate reported within the first three months after surgery.[1,5,9]

A weakness of this study is that we included both cemented and uncemented prostheses. There was no significantly difference between both cohorts for percentage of cementation with the same criteria for cementation being used for both cohorts. The strength of this study is that it describes all the first 450 unselected cases operated by ASI approach by one orthopedic surgeon in our hospital. Follow-up period was a minimum of one year and no patients were lost to follow-up.

In conclusion, the ASI procedure is a technically demanding procedure and has its own unique set of complications. We describe the specific adjustments that we made to this procedure to avoid these specific complications. After we applied these adjustments the complication rate of injury to the LFCN, dislocation of THA and fracture of the greater trochanter all decreased.

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Chapter 7

No effect of the infiltration of local anaesthetic for total hip arthroplasty using an anterior approach
a randomised placebo-controlled trial

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ABSTRACT

Only limited data are available regarding the infiltration of local anaesthetic for total hip arthroplasty (THA), and no studies were performed for THA using the anterior approach. In this prospective, randomised placebo-controlled study we investigated the effect of both standard and reverse infiltration of local anaesthetic in combination with the anterior approach for THA. The primary endpoint was the mean numeric rating score for pain four hours postoperatively. In addition, we recorded the length of hospital stay, the operating time, the destination of the patient at discharge, the use of pain medication, the occurrence of side effects and pain scores at various times postoperatively.

Between November 2012 and January 2014, 75 patients were included in the study. They were randomised into three groups: standard infiltration of local anaesthetic, reversed infiltration of local anaesthetic, and placebo. There was no difference in mean numeric rating score for pain four hours postoperatively ($p = 0.87$). There were significantly more side effects at one and eight hours postoperatively in the placebo group ($p = 0.02$; $p = 0.03$), but this did not influence the mobilisation of the patients. There were no differences in all other outcomes between the groups.

We found no clinically relevant effect when the infiltration of local anaesthetic with ropivacaine and epinephrine was used in a multimodal pain protocol for THA using the anterior approach.

INTRODUCTION

Total hip arthroplasty (THA) is associated with considerable postoperative pain,[1] most of which results from tissue damage at the surgical site.[2] Another cause is haematoma formation.[3] Postoperative pain hinders mobilisation and rehabilitation as well as overall recovery.[4] The challenge of analgesic regimens for THA is to obtain adequate pain relief and maximum muscle control to enable the patient to mobilise and rehabilitate early, without causing side effects.[5]

Local anaesthetic may be infiltrated into the tissues around the surgical field to achieve control of pain while avoiding physiological disturbance,[2] and this is nowadays widely used as part of a multimodal pain management strategy, owing to its simplicity and apparent safety. Local infiltration has been reported to be effective in total knee arthroplasty (TKA);[4,6,7] however, for THA only limited and inconclusive data are available from placebo-controlled and randomised trials.[1,5,8-12] None of these studies reported on the use of local infiltration when the anterior approach is used for THA. This approach is used for THA in our hospital. Lower postoperative pain scores and lower consumption of analgesics has been described when this approach is used.[13-18] We hypothesised that the infiltration of local anaesthetic as part of a multimodal pain protocol in THA undertaken using the anterior approach would reduce pain postoperatively. We also introduced a reverse infiltration method, in which local anaesthetic is administered before the incisions are made. We hypothesised that this would reduce postoperative pain even further, as the anaesthetic can be injected more accurately in tissues that have not yet been damaged. We therefore investigated the effect of both standard and pre-incision local anaesthetic infiltration in combination with the anterior approach for primary THA.

PATIENTS AND METHODS

In this prospective, randomised placebo-controlled trial we included patients with osteoarthritis (OA) of the hip, for whom primary THA had been recommended with surgery being performed through the anterior approach. The operations were performed by a single surgeon (SV). The patients were all American Society of Anesthesiologists (ASA)[19] grades I and II. Exclusion criteria included mental illness, a medical contraindication for spinal anaesthesia, neurological conditions that might influence the perception of pain, cardiovascular impairment in the present or past, allergy to any element of the medication in the protocol, alcohol or drug abuse, rheumatoid arthritis (RA) and a body mass index (BMI) > 40 kg/m^2. The study had ethical approval (NL39970.098.12, METC 12-029) and was registered in EudraCT (2012-000989-37). All patients were admitted on the day of surgery.

A nurse randomised patients in the operating theatre, just prior to surgery. Opaque sealed envelopes were used to randomise them into three different groups. Group 1 patients received local anaesthetic by standard infiltration; group 2 patients received local anaesthetic by reversed infiltration; and group 3 patients received placebo by infiltration of saline at 0.9 %.

Local anaesthetic was infiltrated in a clockwise peri-acetabular fashion after reaming the acetabulum, and then into the capsule and the gluteus minimus and medius muscles. The vastus lateralis muscle and the tensor fascia lata were infiltrated after introducing the femoral component, and infiltration of the subcutaneous tissue was undertaken just before closure of the wound. Reverse infiltration started with infiltration of the subcutaneous tissue followed by incision of the skin and subcutaneous tissue; infiltration of the capsule, the gluteus minimus and medius muscle and the vastus lateralis and tensor fascia lata muscle was followed by incision of the joint capsule; and a clockwise peri-acetabular infiltration was undertaken just before reaming the acetabulum. A total of 100 mL of local anaesthetic was used for peri-acetabular infiltration and for infiltration of the capsule, the gluteus minimus and medius muscle and the lateral vastus muscle; and 20 mL were used for infiltration of the subcutaneous tissue. The infiltration consisted of ropivacaine 2 mg/ml and adrenalin 1 mg/ml in a ratio of 99:1.

No drains were used postoperatively. All patients received spinal anaesthesia with a low dose of bupivacaine (6 mg to 8 mg). Propofol is given by Target Controlled Infusion (TCI), which is often used in anaesthesia to control the concentration of selected drugs in the plasma or at the site of its effect. In our protocol patients received propofol 1-2 mcg/ml set as target concentration administered through a TCI diprifusorpump[20,21] using the Marsh model.[22]

A standardised protocol of oral postoperative medication consisted of 1 g paracetamol four times a day, celecoxib 200 mg, gabapentin 300 mg and tramadol 100 mg (one dose of each, only for the first night after operation). Rescue medication consisted of the opioid piritramide 10 mg (maximum six times a day) and extra celecoxib 200 mg (maximum once a day). Postoperative physiotherapy was undertaken twice a day, starting four to six hours after surgery and focusing on regaining function, movement and gait.

All patients received the same regimen. The discharge criteria were functional: the ability of the patient to walk 30 metres with crutches, to climb stairs and to dress and go to the bathroom independently. In addition, adequate pain relieve had to be achieved before discharge. The numeric rating score (NRS; zero to ten, best to worst.) for pain had to be < 3 at rest and < 5 during mobilisation. All patients were reviewed six weeks postoperatively.

The primary endpoint of this study was the mean NRS for pain, four hours after surgery. We expected the influence of local anaesthetic infiltration to be greatest at this time.[5-7] The clinically relevant difference in NRS was defined as a mean reduction

of 3 points,[23] which represents a decrease in the severity of pain that corresponds to a patients' perception of adequate pain control. Secondary endpoints were the length of stay in hospital (LOS; nights); operating time (minutes); the destination of the patient at discharge; the extent of postoperative use of (rescue) pain medication and the amount and duration of side effects of pain medication and anaesthesia. The postoperative NRS for pain was also measured at many other times: at one hour and eight hours after surgery; before and after mobilisation; and at the time of the least and most severe pain reported on that day; at days 1 and 2 after surgery in the morning and afternoon; before and after mobilisation twice a day; and the time of the least and most severe pain experienced that day.

Nurses and physiotherapists, who were blinded to the group in which the patient was randomised, scored the NRS for pain, the amount pain medication which was used and the extent and duration of side effects including urinary retention, cardiac arrhythmia, dizziness, hypotension, convulsions, headache and nausea and vomiting at the different times. The investigator (YH) who analysed the data was blinded, as were the patients. The surgeon (SV) also was blinded for both standard infiltration groups. Data were analysed after all included patients were discharged. At that moment the researcher was unblinded.

Statistical analysis

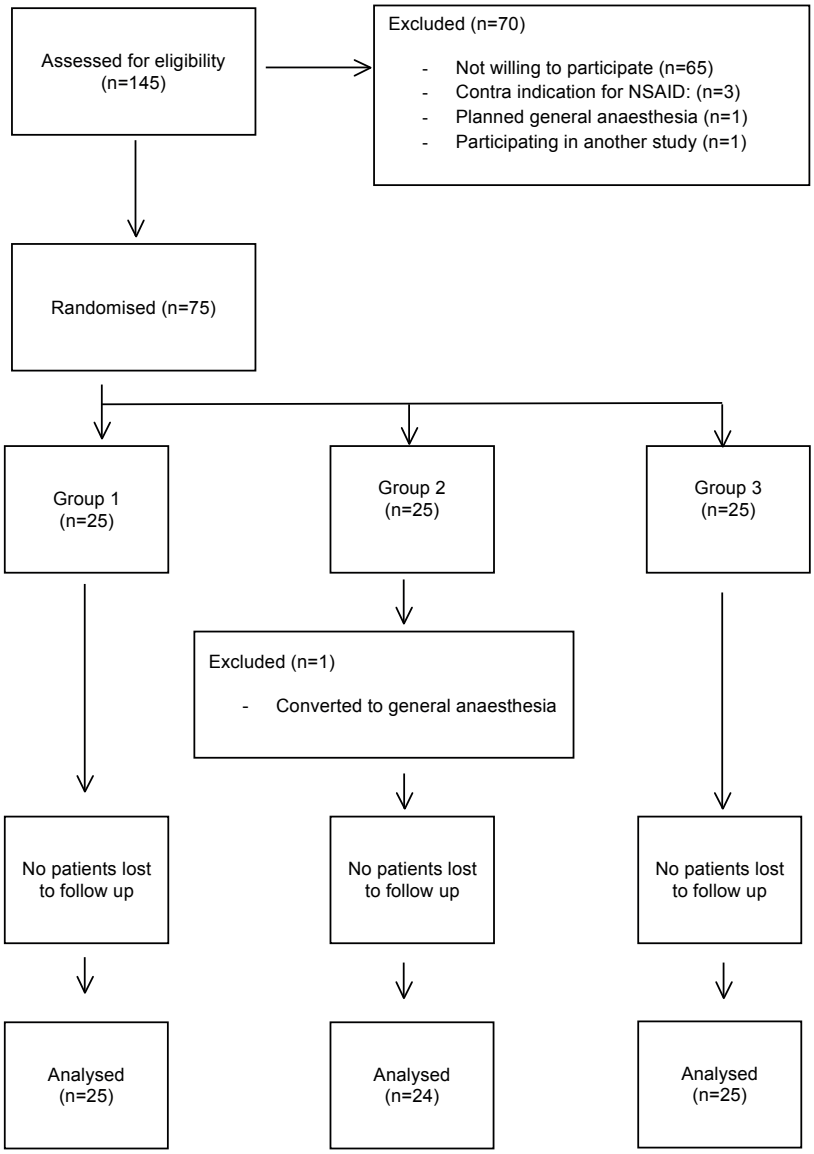
No relevant literature describing the effect of reversed local anaesthetic infiltration with primary THA was found, nor on the effect of local infiltration used during THA using the anterior approach. Therefore, the sample size calculation was based on analysis of variance (ANOVA) for the three groups and a clinically relevant difference in NRS of 3.[23] Based on a resulting effect size of 0.7, a sample size of 25 per group was needed. This resulted in 75 patients in total, divided into the three groups.

Data were not normally distributed. Therefore, the Kruskall–Wallis test was used to analyse differences between the three groups, four hours after surgery (ordinal data). If needed, a *post hoc* Mann–Whitney *U* test was performed with a Bonferroni adjustment. Nominal data were analysed with a chi-squared test. Results within the groups were analysed with a Friedman test and a *post hoc* Wilcoxon's signed ranks test, if needed, and $p < 0.05$ was considered significant. Data are presented as means and ranges. Data analysis was conducted with IBM-SPSS Statistics version 20 (IBM-SPSS, Armonk, New York).

RESULTS

Between 1 November 2012 and 9 January 2014 a total of 75 patients were included in the study, randomised into three groups of 25. One patient in group 2 was excluded

Figure 1: Flowchart of patients.



because general anaesthesia was given during surgery. No patients were lost to follow-up (Figure 1).

The mean age of the patients was 67.1 years (42.7 to 84.6) and the mean BMI was 27.1 kg/m^2 (20.1 to 38.9). Most patients were women and lived with a partner. The demographics of the patients are shown in Table 1. One patient had a previous arthroscopy of the ipsilateral hip and 16 patients had undergone contralateral THA.

An uncemented THA (a Universal acetabular component and a Taperloc femoral component; Biomet, Warsaw, Indiana) was used in 74 patients; one patient received a cemented THA (Exceed Muller acetabular component and a Taperloc femoral prosthesis, Biomet) because of severe osteoporosis. The mean LOS was 1.8 nights (one to seven) and mean operating time was 79.2 minutes (49 to 116). Most patients were discharged to their own home (Table 2).

Table 1: Patient demographics. Data are presented as mean and range, unless otherwise described.

		Group 1 n = 25	Group 2 n = 24	Group 3 n = 25	Total n = 74
Age (yrs)		64.3 (42.7 – 83.9)	69.0 (48.7 – 84.6)	68.0 (55.0 – 83.7)	67.1
BMI (kg/m^2)		27.0 (22.4 – 37.6)	27.6 (21.0 – 38.9)	26.7 (20.1 – 38.1)	27.1
Gender (n)	male	10	13	13	36
ASA classification (n)	I	12	6	9	27
Living situation (n)	alone	6	6	4	16

Table 2: Mean numeric rating score (NRS) at four hours postoperatively, length of stay (LOS), surgery duration and destination of discharge for the three different groups. Data are presented as mean and range, unless otherwise described. Data analyses were performed with a Kruskall-Wallis test (NRS decrease, LOS, surgery time), and a chi-squared test (destination of discharge).

	Group 1 n = 25	Group 2 n = 24	Group 3 n = 25	Total n = 74	p-value
NRS at 4 hrs postoperatively	3.1 (0.0 – 9.0)	2.9 (0.0 – 7.0)	2.9 (0.0 – 6.0)	3.0	0.87
LOS (nights)	1.8 (1 - 7)	1.8 (1 - 4)	1.8 (1 - 3)	1.8	1.00
Surgery duration (mins)	76.3 (49 – 113)	81.4 (57 – 116)	80.1 (50 – 111)	79.2	0.53
Destination discharge (n to home)	25	22	25	72	0.66

There was no significant difference in the mean NRS for pain four hours after surgery between the groups (Table 2). Furthermore, the LOS, operating time, the destination of the patient at discharge (Table 2), use of (rescue) pain medication (Table 3) and mean NRS for pain at the other times (Table 4) did not differ significantly between the groups.

There were significantly more side effects at one and eight hours postoperatively in group 3 when compared with group 2 (Table 5). Side effects that occurred after one

Table 3: Number of patients using (rescue) pain medication for the three different groups. Data analyses were performed with a chi-squared test.

Pain medication		Group 1 n = 25	Group 2 n = 24	Group 3 n = 25	p-value
Day 0	1 hr postoperative	4	5	4	0.88
	4 hrs postoperative	23	22	23	0.99
	8 hrs postoperative	23	21	22	0.53
Day 1	Morning	25	22	23	0.34
	Afternoon	17	18	17	0.30
Day 2	Morning	11	14	15	0.34
	Afternoon	2	3	7	0.12
Rescue medication					
Day 0	1 hr postoperative	6	2	3	0.27
	4 hrs postoperative	3	1	2	0.56
	8 hrs postoperative	4	3	3	0.69
Day 1	Morning	1	0	0	0.40
	Afternoon	0	1	1	0.29
Day 2	Morning	0	0	0	1.00
	Afternoon	1	0	1	0.11

Table 4: Mean numeric rating scores (NRS) at multiple moments for the three different groups. Data are presented as mean and range. Data analyses were performed with a Kruskall-Wallis test.

NRS		Group 1 n = 25	Group 2 n = 24	Group 3 n = 25	Total	p-value
Day 0	1 hr postoperative	1.3 (0.0 – 7.0)	1.4 (0.0 – 8.0)	1.9 (0.0 - 6.0)	1.5	0.20
	Before mobilisation	2.7 (0.0 – 6.0)	2.8 (0.0 – 6.0)	2.4 (0.0 – 6.0)	2.6	4.88
	After mobilisation	3.2 (0.0 – 10.0)	2.7 (0.0 – 6.0)	2.9 (0.0 – 6.0)	2.9	0.88
	8 hrs postoperative	2.9 (0.0 – 8.0)	2.3 (0.0 – 6.0)	2.1 (0.0 – 7.0)	2.4	0.56
	Less pain that day	0.8 (0.0 – 3.0)	0.8 (0.0 – 3.0)	0.9 (0.0 – 3.0)	0.8	0.77
	Most pain that day	4.1 (0.0 – 10.0)	3.7 (0.0 – 6.0)	3.7 (0.0 – 8.0)	3.8	0.80
Day 1	Morning	2.4 (0.0 – 5.0)	1.4 (0.0 – 5.0)	1.1 (0.0 – 3.0)	1.6	0.39
	Before mobilisation morning	2.5 (0.0 – 7.0)	1.6 (0.0 – 4.0)	1.0 (0.0 – 3.0)	1.7	0.09
	After mobilisation morning	3.0 (0.0 – 9.0)	2.2 (0.0 – 5.0)	1.5 (0.0 – 4.0)	2.3	0.09
	Afternoon	1.9 (0.0 – 6.0)	1.5 (0.0 – 5.0)	1.3 (0.0 – 3.0)	1.6	0.87
	Before mobilisation afternoon	1.6 (0.0 – 4.0)	1.3 (0.0 – 4.0)	1.1 (0.0 – 3.0)	1.3	0.66
	After mobilisation afternoon	1.7 (0.0 – 4.0)	2.0 (0.0 – 5.0)	1.5 (0.0 – 6.0)	1.7	0.30
	Less pain that day	1.2 (0.0 – 3.0)	0.9 (0.0 – 3.0)	0.7 (0.0 – 5.0)	0.9	0.34
	Most pain that day	4.0 (2.0 – 8.0)	3.5 (0.0 – 10.0)	3.1 (1.0 – 7.0)	3.5	0.33
Day 2	Morning	2.6 (1.0 – 6.0)	1.9 (0.0 – 4.0)	1.6 (0.0 – 7.0)	2.0	0.17
	Before mobilisation morning	2.7 (0.0 – 6.0)	1.3 (0.0 – 3.0)	0.9 (0.0 – 3.0)	1.5	0.42
	After mobilisation morning	2.2 (0.0 – 4.5)	1.9 (0.0 – 3.5)	1.5 (0.0 – 4.0)	1.8	0.35
	Afternoon	1.3 (0.0 – 2.0)	2.5 (2.0 – 3.0)	1.6 (0.0 – 3.0)	1.8	0.15
	Before mobilisation afternoon	1.8 (1.0 – 2.0)	1.5 (0.0 – 3.0)	0.9 (0.0 – 2.0)	1.3	0.38
	After mobilisation afternoon	2.5 (2.0 – 4.0)	2.3 (0.0 – 3.0)	1.4 (0.0 – 3.0)	1.9	0.24
	Less pain that day	1.3 (0.0 – 2.0)	1.5 (0.0 – 3.0)	0.6 (0.0 – 2.0)	1.1	0.25
	Most pain that day	3.7 (2.0 – 6.0)	3.5 (3.0 – 4.0)	3.4 (1.0 – 7.0)	3.5	0.62

Table 5: Number of patients in whom side effects occurred for the three different groups. Data analyses were performed with a chi-squared test.

Nausea		Group 1 n = 25	Group 2 n = 24	Group 3 n = 25	p-value
Day 0	1 hr postoperative	0	0	2	0.13
	4 hrs postoperative	1	1	0	0.59
	8 hrs postoperative	1	1	0	0.55
Day 1	Morning	1	2	3	0.60
	Afternoon	1	0	1	0.40
Day 2	Morning	1	2	0	0.36
	Afternoon	1	0	0	0.05
Vomiting					
Day 0	1 hr postoperative	0	0	2	0.13
	4 hrs postoperative	0	0	0	1.00
	8 hrs postoperative	1	0	1	0.56
Day 1	Morning	1	0	2	0.40
	Afternoon	0	0	1	0.32
Day 2	Morning	0	1	0	0.27
	Afternoon	0	0	0	1.00
Other side effects					
Day 0	1 hr postoperative	3	1	7	0.05
	4 hrs postoperative	3	4	3	0.86
	8 hrs postoperative	1	0	6	0.02
Day 1	Morning	3	3	6	0.52
	Afternoon	2	4	3	0.67
Day 2	Morning	2	2	6	0.16
	Afternoon	0	0	3	0.04
All side effects					
Day 0	1 hr postoperative	3	1	11	0.02*
	4 hrs postoperative	4	5	3	0.86
	8 hrs postoperative	3	1	7	0.03†
Day 1	Morning	5	5	11	0.82
	Afternoon	3	4	5	0.87
Day 2	Morning	3	5	6	0.29
	Afternoon	1	0	3	0.17

** p-values for differences within the groups: p = 0.32 (group 1-2); p = 0.01 (group 2-3); p = 0.09 (group 1-3)*

† p-values for differences within the groups: p = 0.64 (group 1-2); p = 0.02 (group 2-3); p = 0.07 (group 1-3)

hour were dizziness, hypotension and retention of urine. Side effects that occurred after eight hours were dizziness, headache and retention of urine, and this included two of the patients who developed retention one hour postoperatively. However, these side effects did not influence mobilisation. No differences between the three groups were seen at the other times.

Adequate pain relief was achieved in all patients before discharge. Two had a LOS of > three nights. One patient had a LOS of seven nights due to a fracture of the femur on the same side after a fall; this was not, however, a consequence of cardiac arrhythmia, dizziness, convulsions or hypotension. The prolonged LOS for the other patient (four nights) was due to waiting for sufficient aftercare.

DISCUSSION

This was a randomised, placebo-controlled trial in which we investigated the effect of both standard and reverse local anaesthetic infiltration in combination with the anterior approach for primary THA. No differences in NRS for pain four hours after surgery were detected between the three groups. Furthermore, there was no difference in LOS, operating time, destination of the patient at discharge, use of (rescue) pain medication, and mean NRS for pain at the other times between the three groups. Thus, it seems that a multimodal pain medication regimen provides adequate postoperative pain relief for patients undergoing THA using the anterior approach, and the addition of local anaesthetic to this protocol has no clinically relevant effect.

There were statistically significantly more side effects at one and eight hours postoperatively in the placebo group than in the reverse local infiltration group, although these side effects did not have an influence on postoperative mobilisation and numerically were still infrequent. The side effects that we studied were urinary retention, cardiac arrhythmia, dizziness, hypotension, convulsions, headache and nausea and vomiting. It seems unlikely that these were influenced by the lack of local anaesthetic in the control group.

In our study, all patients received spinal anaesthesia with a low dose of bupivacaine and at this dose no prolonged analgesic side effects are expected. The postoperative pain could therefore be measured under comparable conditions. The NRS after surgery ranged from 0 to 10 at various times, but no differences were found in mean pain scores or decrease in scores between the three groups. All groups included patients with high pain scores. Therefore, it seems that the high pain scores of the non-responders are due to factors other than those which were investigated, such as psychosocial, behavioural and psychophysiological factors.[24,25] Further research on patients with persistent pain

despite pain management is therefore required. Two patients had a LOS of > three nights, but these were not due to inadequate pain relief or its side effects.

Only limited and inconclusive data are available regarding the effect of the infiltration of local anaesthetic for THA. Kerr and Kohan[2] reported satisfactory results, but without the use of a control group. Two studies recorded a good response to local infiltration in comparison with a placebo. However, no multimodal pain protocol was used, and in one study[5] there was a predominance of men in the local infiltration group. The other study combined the results of patients undergoing TKA and THA.[8] Compared with epidural infusion[9] or patient-controlled analgesia (PCA),[1,10] positive effects of local infiltration were also described. However, the study comparing local infiltration with epidural infusion was not blinded and did not use a multimodal pain protocol. Moreover, one study comparing local infiltration to PCA was underpowered.[1] No effect of local infiltration compared with placebo was seen in two other studies.[11,12] None of these studies, however, reported on the use of local infiltration with the anterior approach to the hip.

In the literature, there seems to be a consensus on the use of local infiltration during TKA.[4,6,7] Although postoperative pain scores are higher after TKA than after THA,[26] one would expect some effect of local infiltration in THA. The minimal or absent effect in other studies could be the result of the difficulty of administering local infiltration at the sites where damage to the tissues is caused both during and at the end of the procedure. It seems easier to detect damaged or affected tissues after TKA. We therefore hypothesised that the reversed infiltration would be more effective, but this method of administration did not seem to influence the effect.

Not all postoperative pain arises as a result of tissue damage at the surgical site. A local haematoma causes pain.[3] The anteromedial part of the hip joint is innervated by the obturator nerve, the anterior hip capsule by the femoral nerve, the posteromedial part of the capsule by the sciatic nerve and the posterolateral part by the superior gluteal nerve.[27] In the event of haematoma formation, all these areas might be affected. Apparently, it is not possible with the current technique of local infiltration to give an effective blockade to all these nerves in all patients.

We hypothesised that local infiltration combined with a multimodal pain protocol in THA using the anterior approach would reduce pain scores postoperatively. The advantages of the anterior approach regarding early function rehabilitation, lower postoperative pain scores and less pain medication consumption have been described elsewhere.[13-18,28] This could account for the absence of a clinically relevant effect of local infiltration when using this surgical approach.

In conclusion, this prospective, randomised placebo-controlled trial showed no clinically relevant effect when local anaesthetic infiltration is used with ropivacaine and adrenaline in a multimodal pain protocol for THA using the anterior approach.

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Chapter 8

Clinical pharmacokinetics of ropivacaine using local infiltration analgesia technique in total hip arthroplasty: a pilot study

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ABSTRACT

Total hip arthroplasty (THA) is associated with considerable postoperative pain as a result of tissue damage at the surgical site. Single-shot local infiltration analgesia (LIA) is based on a systematic infiltration of local analgesics into the tissues around the surgical field to achieve satisfactory pain control with little physiological disturbance. However, for THA no clinical relevant effect of LIA is detected. The reason for lack of effect of LIA for THA is not yet clear. The purpose of this study was to elucidate pharmacokinetic parameters of ropivacaine administered by LIA in THA patients.

LIA for THA in our hospital consists of ropivacaine and epinephrine given in three syringes. For determining ropivacaine serum concentrations, blood samples were collected at multiple moments from just before infiltration, until 48 hours after infiltration of the first LIA mixture.

Pharmacokinetic analysis of serum concentrations of ropivacaine was performed.

A total of 12 patients was included in this prospective-cohort pilot-study. C_{max} was 0.52 mg/l (SD 0.19) and T_{max} was 6.0 h (SD 2.0). The mean Weibull rate constant was 0.039 h^{-1} (SD 0.011) and the mean shape factor was 1.03 (SD 0.18).

This pilot-study demonstrates a pharmacokinetic model for absorption and diffusion of ropivacaine after LIA for THA. These parameters do not differ from those for total knee arthroplasty. It seems not likely that a higher dose of ropivacaine can optimise the effect of LIA after THA. Serum levels of ropivacaine in our study never exceeded toxicity levels.

INTRODUCTION

Total hip arthroplasty (THA) is associated with considerable postoperative pain as a result of tissue damage at the surgical site.[1,2] This postoperative pain hinders mobilisation and rehabilitation with consequences on mobility, duration and overall recovery.[3] The challenge of analgesic regimes for THA is to obtain adequate pain relief and maximum muscle control to enable the patient to mobilise and rehabilitate early without troublesome side effects.[4] Single-shot local infiltration analgesia (LIA) is based on a systematic infiltration of local analgesics into the tissues around the surgical field to achieve satisfactory pain control with little physiological disturbance[2] and is nowadays widely applied as part of a multimodal pain management strategy due to its simplicity and apparent safety.[5,6] The analgesic ropivacaine is frequently used for this technique.[2]

LIA has been reported to be effective in total knee arthroplasty (TKA).[7-9] However, for THA mostly limited and inconclusive data are available from placebo-controlled and randomised trials.[1,4,10] Most studies describe protocols based on best practices with only limited publication on the doses used. Our own recent randomised controlled trial on LIA for THA demonstrated no clinical relevant effect when LIA with ropivacaine and epinephrine is applied in a multimodal pain protocol for THA with the anterior approach.[11]

The reason for lack of effect of LIA for THA is not yet clear; differences in ropivacaine pharmacokinetics of the locally applied analgesics between TKA and THA might be responsible for this.

Although several studies describe pharmacokinetics of ropivacaine after epidural and intravenous administration,[12-15] and even after continuous perfusion in the surgical wound after major joint replacement surgery,[10] pharmacokinetic parameters of ropivacaine for the application route of one-shot LIA for THA have not been investigated yet. The purpose of this study was to elucidate pharmacokinetic parameters of ropivacaine administered by one-shot LIA in THA patients, by determining the concentration-time correlation of ropivacaine in serum. With clarified pharmacokinetic parameters of ropivacaine after THA, we could investigate possible causes for lack of effect of LIA after THA. Furthermore, recommendations about the dose of ropivacaine in LIA for THA can be done, to possible improve the analgesic effect of LIA. Moreover, a statement about toxicity of the determined ropivacaine serum levels after LIA for THA can be made.

METHODS

In this prospective-cohort pilot-study we included patients with osteoarthritis of the hip who were diagnosed for primary THA, who were aged 18 years and older, and were willing to participate. Exclusion criteria are listed in Table 1.

Table 1: Exclusion criteria.

- Unwilling to participate
- Known allergy for amide-type local anaesthetics
- Morbid obesity (BMI ≥ 40 kg/m^2)
- Liver failure (total bilirubin > 34 µmol/l, serum albumin < 35 g/l)
- Using CYP1A2 inhibitors or CYP3A4 inhibitors

The local Medical Ethics Committee decided that the study did not fall under the scope of the Medical Research Involving Human Subjects Act because of the minimally invasive burden for patients. However, written informed consent was obtained from all patients.

One-shot LIA for THA in our hospital consists of ropivacaine (2 mg/ml) and epinephrine (1 mg/ml) in a ratio of 99:1, given in three syringes of 50 ml each infiltrated into tissues around the surgical field. One syringe is infiltrated in a clockwise infiltration periacetabular, after reaming the acetabulum. The second syringe is infiltrated into the gluteus minimus muscle, the gluteus medius muscle, and the vastus lateralis muscle, after placing the femoral component. The third syringe is infiltrated in the subcuteal tissue, just before closure of the wound.

Standard blood samples were taken at one till three days before surgery and 24 hours after surgery to assess bilirubin and serum albumin for determining patients' liver function.

For determining ropivacaine serum concentrations, extra peripheral venous blood samples were collected through an internally mounted venous cannula just before infiltration and at 30 minutes, at 1, 2, 4, 8, 12, 24, 36, and 48 hours after infiltration of the first LIA mixture. In case the patient was discharged from the hospital within 48 hours after infiltration of the first LIA mixture, serum concentrations were determined just before discharge as well.

Blood samples were stored at 2 to 8 ºC for a maximum period of 24 hours. The samples were centrifuged and serum was stored in the freezer at -18 ºC until determination. Ropivacaine in these serum samples was analysed according to a standard validated analytical procedure in the laboratory for pharmacy of Reinier de Graaf Hospital. Total serum ropivacaine concentration was measured with a reversed-phase high-performance liquid chromatography method with Diode Array Detection.

Pharmacokinetic (PK) analysis of the serum concentrations of ropivacaine was performed by using the computer program MwPharm (version 3.83; MediWare, Zuidhorn, The Netherlands).[16,17] Since a full pharmacokinetic analysis was not possible due to the lack of data after intravenous administration, we choose for the following procedure. The pharmacokinetic model was taken from Simon et al.,[12] who described a 3-compartment model after intravenous administration of deuterium-labelled ropivacaine in

Table 2: Demographics of the included patients and patients' liver function. All data are presented as mean, standard deviation and range.

		Mean	Range
Age	years	68 (SD 11)	47 – 85
BMI	kg/m^2	26.9 (SD 2.1)	22.1 – 30.3
eGFR*	ml/min	94 (SD 34)	50-154
Total Bilirubin	µmol/l	6.8 (SD 1.7)	5 -10
Albumin	g/l	37 (SD 4)	30 - 42
ALAT	U/l	30 (SD 22)	15 -88

* eGFR (ml/min/1.73m^2) calculated with the Cockcroft and Gault formula

patients participating in their study on the effect of age on the systemic absorption and systemic disposition of ropivacaine after epidural administration. For our study, we used the PK parameters of patients over 60 years (group 3 of Simon et al.[12]). For clearance (CL), fast distribution clearance (CLd(r), denoted CL12 in MwPharm), slow distribution clearance (CLd(s), denoted CL13 in MwPharm), and volume of the central compartment (Vc, denoted V1 in MwPharm) values were taken from table 2 of Simon et al.,[12] after conversion to the appropriate units. The volumes of the shallow peripheral compartment (V2) and deep peripheral compartment (V3) were derived from the values for the volume of distribution at steady state and elimination half-life. The resulting parameter values, normalised to body weight, were: CL 18 l/h/70 kg, CL12 58 l/h/70 kg, CL13 24 l/h/70 kg, V1 0.10 l/kg, V2 0.18 l/kg, V3 0.41 l/kg. The standard deviation of the inter-individual variability was not reported for each parameter in the paper of Simon et al.[12] Therefore we assumed that the coefficient of variation for the clearance parameters (CL, CL12, CL13) was 40%, i.e., close to that of CL in table 2 of Simon et al, and for the volume parameters (V1, V2, V3) was 30%, i.e., close to that of V1. The population parameters of the intravenous model were fixed during the analysis, but individual values were estimated for each patient.

Several models describing the absorption kinetics from the site of administration to the central compartment were tested: first-order with lag-time, zero-order with lag-time, Gamma function, Weibull function and Inverse Gaussian function. Bioavailability was estimated during the analysis, or fixed to 1. The model parameters of the absorption function were estimated using the Iterative Two-Stage Bayesian analysis implemented in MwPharm.

The residual standard deviation was estimated during the population analysis, using additional, proportional and combined additional and proportional error models. The Akaike Information Criterion (AIC) of each model was calculated to select the best fitting model.

Mean total serum maximum ropivacaine concentration (C_{max}) and mean time for reaching maximum ropivacaine concentration (T_{max}) were determined from the observed serum concentration data.

We could not perform a clear sample size calculation, since no relevant literature on concentration-time correlation of ropivacaine in serum could be found. Therefore we decided to perform a pilot study on 12 patients.

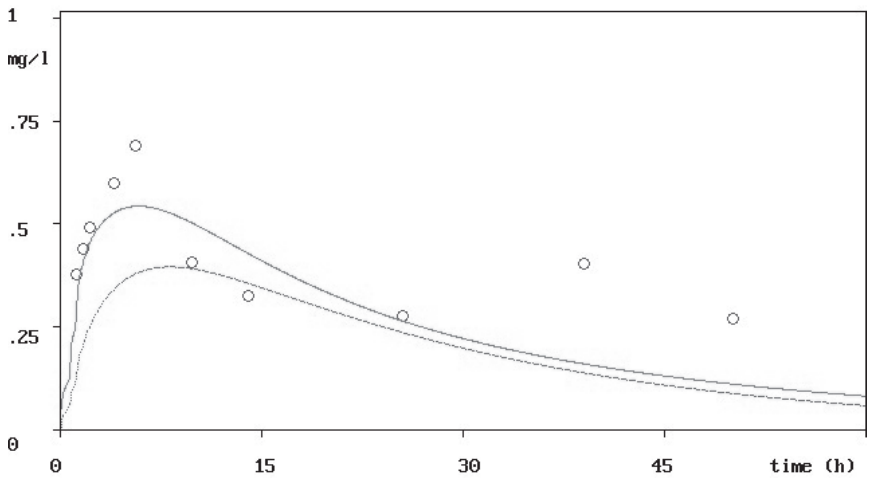
RESULTS

A total of 12 patients was included in this study, consisting of seven men and five women. Mean age was 68.2 years (SD 10.9) and mean BMI was 26.9 kg/m^2 (SD 2.1). Demographics of the included patients are listed in Table 2.

C_{max} was 0.52 mg/l (SD 0.19; range 0.27 - 0.87) and T_{max} was 6.0 h (SD 2.0; range 2.8 - 9.3). In most patients a second peak in the curve after administration of the first LIA injection was detected as well (Figure 1).

Comparing the absorption models tested, the Weibull model was found to fit best to the data, resulting in the lowest AIC value (-73), compared to the first-order with lag-time (-11), zero-order with lag-time (+30), Gamma function (-19) and Inverse Gaussian function (-6). The model with bioavailability fixed to 1 and a proportional error resulted in the lowest AIC value, with a proportional error of 29%.

Figure 1: Graphical presentation of the Weibull function of patient 2.



The upper line represents the individual model predicted ropivacaine serum concentration, the lower line represents the population predicted ropivacaine serum concentration, and the dots represent observed ropivacaine serum concentrations.

Table 3: Results with the Weibull model including rate constant (kd), and shape factor (n) together with standard errors (SE) for all 12 patients. Furthermore mean kd and n for the population are presented, together with the standard deviation.

Patient	kd unit/h	SE	n	SE
1	0.0369	0.0085	0.82	0.08
2	0.0499	0.0119	0.75	0.07
3	0.0316	0.0060	1.02	0.07
4	0.0406	0.0053	1.16	0.07
5	0.0416	0.0085	1.04	0.09
6	0.0298	0.0065	1.04	0.08
7	0.0387	0.0086	1.10	0.10
8	0.0482	0.0045	1.17	0.08
9	0.0412	0.0086	1.19	0.10
10	0.0540	0.0045	1.17	0.08
11	0.0347	0.0085	0.89	0.08
12	0.0337	0.0076	1.16	0.09
Population	0.0394 (SD 0.0109)		1.03 (SD 0.18)	

The results with the Weibull model for all patients are listed in Table 3. The mean Weibull rate constant was 0.039 h^{-1} (SD 0.011) and the mean shape factor was 1.03 (SD 0.18). A graphical presentation of the serum concentration with the Weibull absorption function for a typical patient is shown in Figure 1.

DISCUSSION

The purpose of this study was to elucidate pharmacokinetic parameters of wound-infiltrated ropivacaine in THA administered by one-shot LIA. Regarding LIA for THA, mostly limited and inconclusive data are available from placebo-controlled and randomised trials.[1,4,10] With clarified pharmacokinetic parameters of ropivacaine after THA, we could investigate possible causes for lack of effect of LIA after THA.

Regarding pharmacokinetic parameters of ropivacaine after continuous perfusion in the surgical wound after major joint replacement surgery, mean C_{max} is described to be 0.71 µg/ml (range 0.30 – 1.28) and T_{max} was reached 24 h after initiation of the infusion.[10] Our C_{max} was 0.52 mg/l (range 0.27 - 0.87) and T_{max} was 6.0 h (range 2.8 - 9.3). The difference in T_{max} can be explained by the continuous perfusion in the surgical wound after surgery in the study of Bianconi *et al*.[10]

Our study demonstrates no differences between pharmacokinetic parameters of ropivacaine after LIA in THA and after one-shot LIA in TKA with similar doses of ropivacaine (referred to unpublished data from our departments). Moreover, since these pharmacokinetic parameters do not differ from those of one-shot TKA and since doses of ropivacaine are the same for THA and TKA, lack of effect of LIA seems not to be due to the dose of ropivacaine used in THA either. Therefore, we conclude that other causes than pharmacokinetic parameters of ropivacaine are responsible for lack of effect of LIA after THA and it seems unlikely that a higher dose of ropivacaine can optimise the effect of LIA after THA.

Ropivacaine blocks nociceptors around the joint. Apparently it is not possible with the current one-shot LIA technique to give an effective blockage of all these nociceptors around the hip joint.

Systemic toxicity is a major concern of high dose local anaesthetics. Our model demonstrates total ropivacaine serum maximum concentrations range between 0.27 and 0.87 mg/l. Since central nervous system – and cardiovascular toxicity threshold of ropivacaine in venous blood serum has been described to be 2.2 mg/l,[18] serum levels of ropivacaine in our study never exceed these toxicity levels.

Therefore we can conclude that LIA with ropivacaine in the doses described in our study is safe for patients.

As for other local anaesthetics, our profile describes flip-flop kinetics, with a rapid initial phase (T_{max} = 6.0 h; range 2.8 - 9.3) followed by a second peak in the curve after admission of the first LIA injection. This flip-flop kinetics is also described for ropivacaine during continuous epidural infusion.[14] At the time of the second peak, patients in our study are being mobilised by a physiotherapist. This rehabilitation therapy can contribute to increased perfusion of the hip joint and therefore can cause an increased transport of ropivacaine to the perfusing blood. This could be a possible cause for this second peak in ropivacaine after LIA for THA. Because of this flip-flop kinetics, absorption and disposition kinetics could not directly be derived from the concentration-time curve. Therefore, the computer program MwPharm was used in our study to describe pharmacokinetic models. According to AIC, the most appropriate model was chosen.

Some potential limitations of our study need to be addressed. First, our statement about toxicity of the determined ropivacaine serum levels is based on ropivacaine levels in venous blood serum. In bolus injections, arterial blood serum concentrations could be at much higher level compared to venous blood serum concentrations. Hence venous blood serum might not be representative for systemic toxicity effects on various parts of the body after this bolus injection. However, since T_{max} in our study is 6 hours, venous blood serum concentrations are not likely to be detectable lower than those of arterial blood serum. Moreover, no toxic adverse effects (e.g. cardiovascular or central nervous system effects) were reported in our study.

Second, only 12 patients were included in this study. We could not perform a clear sample size calculation, since no relevant literature on concentration-time correlation of ropivacaine in serum could be found. Therefore we decided to perform a pilot study with 12 patients.

Third, although all patients in our study received same amounts of ropivacaine, C_{max} ranged from 0.27 to 0.87 mg/l. The amount and function of hepatic enzymes CYP3A4 and CYP1A2 are different for each patient, which causes differences in metabolism rates and drug concentrations. Furthermore, despite standardised injection sites for LIA in THA, it is assumed that ropivacaine is not precisely equally injected in the surgical field for all patients in our study. This can lead to a different diffusion profile from the joint capsule into the blood, which may contribute to these inter-patient differences as well. Until now, specific patient characteristics were never taken into account, and further research including more patients is required to investigate these inter-patient differences more precisely.

In conclusion, this pilot-study demonstrates a pharmacokinetic model for absorption and diffusion of ropivacaine after LIA for THA. Pharmacokinetic parameters after LIA in THA are clarified, and these parameters do not differ from those of TKA. Therefore, other causes than pharmacokinetic parameters of ropivacaine are responsible for lack of effect of LIA after THA. It seems not likely that a higher dose of ropivacaine can optimise the effect of LIA after THA. Serum levels of ropivacaine in our study never exceeded toxicity levels. Further research is required to investigate inter-patient differences in serum maximum ropivacaine concentrations more precisely.

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Chapter 9

Which patient-specific and surgical characteristics influence postoperative pain after THA in a fast-track setting?

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ABSTRACT

In our hospital a fast-track setting including a multimodal pain protocol is used for total hip arthroplasty (THA). Despite this multimodal pain protocol there is still a large range in reported postoperative pain between patients, which hinders mobilization and rehabilitation postoperatively. The goal of this study was to identify which patient-specific and surgical characteristics influence postoperative pain after THA in a fast-track setting.
All 74 patients with osteoarthritis of the hip who underwent primary THA procedure by anterior supine intermuscular approach between November 2012 and January 2014 were included in this prospective cohort study. The protocol for pain medication was standardized.
Postoperative pain determined with the Numeric Rating Score was collected at 17 standardized moments. Linear mixed models were used to examine potential patient-specific and surgical factors associated with increased postoperative pain.
Pain patterns differed substantially across individuals. Adjusted for other variables in the model, preoperative use of pain medication (regression coefficient 0.78 (95%CI 0.28 – 1.26); p = 0.005) and preoperative neuropathic pain scored by DN4 (regression coefficient 0.68 (95%CI 0.15 – 1.20); p = 0.02) were the only factors significantly associated with higher postoperative pain scores.
The knowledge of which factors are associated with higher postoperative pain scores after THA in a fast-track setting may help optimizing perioperative postoperative pain management and preoperative education of these patients.

INTRODUCTION

Total hip arthroplasty (THA) is associated with considerable postoperative pain.[1] Almost all pain after surgery arises as a result of tissue damage at the surgical site.[2] This postoperative pain hinders early mobilization and rehabilitation with subsequent consequences on mobility and overall recovery.[3] In the last few years fast-track protocols have been introduced worldwide for elective primary THA. These are partly based on pain management protocols and include a rigorous perioperative pain management program, which allow for an optimized perioperative period.[4,5] In 2009, a fast-track protocol including a multimodal pain protocol was successfully introduced in our teaching hospital.[6] The multimodal pain protocol, developed to reduce acute postoperative pain to enable quick mobilization and rehabilitation included paracetamol, celecoxib, gabapentine, dexamethasone and esketamine.[7-12] Furthermore, we use the anterior supine intermuscular (ASI) approach for THA procedures in our hospital. Since this approach uses both an intermuscular and internervous plane and causes less surgical trauma, lower postoperative pain scores and less pain medication consumption have been described for this approach.[13-18] Despite the introduction of a multimodal pain protocol and use of the ASI approach, there is still a large range in reported postoperative pain between patients.

Previous studies have shown that specific patient- and provider characteristics could influence postoperative pain.[19-27] Only one of these studies reported solely on postoperative pain after primary THA.[21] None of these studies were performed in a fast-track setting and no multimodal pain protocols developed to reduce acute postoperative pain were included in these studies.

The proper identification of patients who are at risk to experience more postoperative pain directly after primary THA might provide details for further optimization of postoperative pain management and preoperative education of these patients. Therefore, the goal of this study was to identify which patient-specific and surgical characteristics influence postoperative pain after primary THA by ASI approach in a fast-track setting including a multimodal pain protocol.

PATIENTS AND METHODS

All 74 patients with osteoarthritis of the hip who underwent primary THA procedure by ASI approach between November 2012 and January 2014 were included in this prospective cohort study. All procedures were performed in a fast-track setting, by one experienced orthopedic hip surgeon (SV). Patients with neurological conditions which potentially influence pain perception; American Society of Anaesthesiologists

Table 1: The standardized multimodal protocol for perioperative pain medication.

Timing	Medication
2 hours before surgery	Paracetamol (acetaminophen) 1000 mg per os. Celecoxib (Celebrex®)* 400 mg per os. Gabapentin 600 mg per os.
Just before surgery	Dexamethasone 0.15 mg/kg iv.† Esketamine 15 mg iv.
4 hours after surgery	Paracetamol (acetaminophen) 1000 mg per os.
8 hours after surgery	Paracetamol (acetaminophen) 1000 mg per os. Gabapentin 300 mg per os.
Before the night	Tramadol 100 mg supp.
Day 1	Paracetamol (acetaminophen) 1000 mg per os 4 times a day. Celecoxib (Celebrex®)* 200 mg per os in the morning. Gabapentin 300 mg per os in the morning.
After day 1	Paracetamol (acetaminophen) 1000 mg per os 4 times a day (with a maximum of 2 weeks). Celecoxib (Celebrex®)* 200 mg per os in the morning (until 2 weeks after surgery).
Rescue medication	Celecoxib (Celebrex®)* 200 mg per os extra after the first night Dipidolor 10 mg im, which could be repeated every 4 hours.

**In combination with celecoxib (Celebrex®) all patients will receive omeprazol 20 mg per os once a day as prophylaxis. When the patient was already using a proton pomp inhibitor before admittance no omeprazol was administered. † Dexamethasone solution in 50cc saline is administered slowly to avoid adverse side affects like severe perianal pain.*

(ASA) classification III/IV; medical contra-indication for spinal anesthesia; cardiovascular impairment in the present or past; known allergy against any element of the medication that is given for the multimodal pain protocol; abuse of alcohol or drugs; rheumatoid arthritis; BMI > 40 kg/m^2; and patients with cognitive impairment were excluded.

All patients received spinal anesthesia with a low dose of bupivacaine (6-8 mg intrathecally). Propofol was administered for sedation and to allow a single shot of esketamine. The multimodal protocol for perioperative pain medication was standardized (Table 1). Before discharge, adequate pain relief had to be achieved by oral pain medication: the Numeric Rating Score (NRS) for pain had to be below 3 in rest and below 5 during mobilization (NRS; 0 to 10, best to worst).

Postoperative pain determined with the NRS was collected at 17 standardized moments, from 1 hour after surgery until the afternoon of the second day after surgery (Table 2).

Potential factors associated with increased postoperative pain (gender; ASA classification; age; BMI; diabetes mellitus (DM); surgery time; incision length; living situation; preoperative pain determined with the NRS, preoperative use of pain medication; use of antidepressants; as well as preoperative scores of the neuropathic pain diagnostic questionnaire (DN4), and Amsterdam Preoperative Anxiety and Information Scale (APAIS) for anxiety and information requirements) were examined with univariable linear mixed models for repeated measures. Decision to include these variables was based

Table 2: Postoperative pain determined with the NRS was collected at 17 standardised moments, from 1 hour after surgery until the afternoon of the second day after surgery.

Baseline	Baseline (n=74)
Day 0	1 hour postoperative (n=69) 4 hours postoperative (n=74) Before (n=65) & after mobilization (n=72) 8 hours postoperative (n= 69)
Day 1	Morning (n=67) Before (n=72) & after mobilization (n=71) Afternoon (n=60) Before (n=54) & after mobilization (n=54)
Day 2	Morning (n=39) Before (n=41) & after mobilization (n=41) Afternoon (n=14) Before (n=15) & after mobilization (n=15)

on guidance from directed acyclic graphs.[28] Based on the criteria in the original article about the APAIS by Moerman and others,[29] the APAIS anxiety scale was dichotomized (4-10: no, 11-20: yes), and the APAIS need-for-information scale was divided into three categories (2-4: no or little, 5-7: average, and 8-10: high). The DN4 questionnaire score was dichotomized (1-3 unlikely; 4-7 likely).[30,31] Factors that were associated with the outcome in univariable analyses (p-values < 0.20) were included in multivariable analyses. In the multivariable analyses p-values less than 0.05 were considered significant. Missing data were assumed to be missing at random. Regression coefficients are presented with their 95% confidence intervals. The statistical analyses were performed using R version 3.1.2 with package 'nlme'.[32,33]

RESULTS

Mean age of all patients was 67.1 year (range 42.7 – 84.6) and mean BMI was 27.1 kg/m^2 (range 20.1 – 38.9). Mean LOS was 1.8 nights (range 1 - 7). Most patients lived together with cohabitants (n = 58; 78.4 %) and were discharged to their own home (n = 72; 97.3 %). Patient characteristics are listed in Table 3.

73 patients received an uncemented prostheses (Taperloc® femoral prosthesis and an Universal® cup, both Biomet, Warsaw, In, USA), one patient received a cemented prosthesis because of inferior bone quality due to severe osteoporosis. (Exceed Muller® cup and a Taperloc® femoral prosthesis, both Biomet, Warsaw, In, USA).

Pain patterns differed substantially across individuals. Moreover, pain varied across the standardized moments (Table 4). Adjusted for the other factors in the model, preoperative use of pain medication (regression coefficient 0.78 (95%CI 0.28 – 1.26); p = 0.005) and preoperative neuropathic pain scored by DN4 (regression coefficient 0.68

(95%CI 0.15 – 1.20); p = 0.02) were the only factors that were significantly associated with higher postoperative pain scores (Table 5). All other factors demonstrated no effect on postoperative pain.

Table 3: Patient characteristics for the total group of 74 patients undergoing primary total hip arthroplasty.

		Total n (%) n = 74
Age (year)		67.1 (42.7 – 84.6)*
BMI (kg/m^2)		27.1 (20.1 – 38.9)*
Gender	male	36 (48.6 %)
ASA classification	ASA2	47 (63.5 %)
Surgery time (minutes)		79.2 (49 - 116)*
Diabetes Mellitus		7 (9.5 %)
Incision length (cm)		9.97 (7.5 – 12.0)*
Living situation	with cohabitants	58 (78.4 %)
Preoperative antidepressants use		4 (5.4 %)
Preoperative pain medication use		50 (67.6 %)
Preoperative pain (NRS)†		5.26 (0 - 9)*
DN4	likely	16 (21.6 %)
APAIS anxiety	yes	15 (23.1 %)
APAIS information	no/little	24 (37.5 %)
	average	24 (37.5 %)
	high	16 (25.0 %)

** mean (range) , † n = 72 patients*

Table 4: Pain scores determined with the NRS at the standardized moments.

NRS		N	mean (range)
Preoperative		72	5.26 (0.0 – 9.0)
Day of surgery	1 h	69	1.51 (0.0 – 8.0)
	4 h	74	2.97 (0.0 – 9.0)
	Before mobilization	69	2.62 (0.0 – 6.0)
	After mobilization	65	2.93 (0.0 – 10.0)
	8 h	72	2.40 (0.0 – 8.0)
Day 1	Morning	67	1.63 (0.0 – 5.0)
	Before mobilization	72	1.71 (0.0 – 7.0)
	After mobilization	71	2.25 (0.0 – 9.0)
	Afternoon	60	1.57 (0.0 – 6.0)
	Before mobilization	54	1.26 (0.0 – 4.0)
	After mobilization	54	1.73 (0.0 – 6.0)
Day 2	Morning	39	2.00 (0.0 – 7.0)
	Before mobilization	41	1.54 (0.0 – 6.0)
	After mobilization	41	1.84 (0.0 – 4.5)
	Afternoon	14	1.82 (0.0 – 3.0)
	Before mobilization	15	1.27 (0.0 – 3.0)
	After mobilization	15	1.93 (0.0 – 4.0)

Table 5: Regression coefficients with 95% CIs for potential factors associated with increased postoperative pain after THA in a fast-track setting.

		Univariable analyses		Multivariable analysis	
		coefficient (95% CI)	p-value	coefficient (95% CI)	p-value
Age		0.006 (-0.02 – 0.03)	0.66	-	-
BMI		0.03 (-0.03 – 0.09)	0.28	-	-
Gender	male vs. female	-0.31 (-0.79 – 0.18)	0.22	-	-
ASA classification	ASA2 vs. ASA1	0.30 (-0.21 – 0.80)	0.25	-	-
Surgery time		-0.01 (-0.03 – 0.0005)	0.06	0.0004 (-0.01 – 0.01)	0.96
Diabetes Mellitus		-0.05 (-0.88 – 0.78)	0.92	-	-
Incision length		0.02 (-0.26 – 0.31)	0.89	-	-
Living situation	with cohabitants vs. alone	0.53 (-0.05 – 1.10)	0.08	0.50 (-0.08 – 1.07)	0.11
Preoperative antidepressants use	yes vs. no	0.66 (-0.39 – 1.71)	0.22	-	-
Preoperative pain medication use	yes vs. no	0.68 (0.18 – 1.18)	0.009	0.78 (0.28 – 1.26)	0.005
Preoperative pain		0.10 (-0.01 – 0.21)	0.08	-0.02 (-0.13 – 0.09)	0.73
DN4	likely vs. unlikely	0.70 (0.13 – 1.28)	0.02	0.68 (0.15 – 1.20)	0.02
APAIS anxiety	yes vs. no	-0.06 (-0.67 – 0.54)	0.84	-	-
APAIS information	average vs. no/little	-0.02 (-0.61 – 0.56)	0.93	-0.21 (-0.74 – 0.31)	0.45
	high vs. no/little	0.50 (-0.16 – 1.15)	0.15	0.45 (-0.12 – 1.02)	0.15

Factors that were associated with the outcome in univariable analyses (p-values < 0.20) were included in a multivariable linear mixed model for repeated measures. In the multivariable analyses p-values less than 0.05 were considered significant.

DISCUSSION

The aim of this study was to identify which patient-specific and surgical characteristics influence postoperative pain after primary THA by ASI approach in a fast-track setting, using a multimodal pain protocol which was developed to reduce acute postoperative pain to enable quick mobilization and rehabilitation. The only two factors associated with increased postoperative pain adjusted for the other factors in the model, were preoperative use of pain medication (regression coefficient 0.78 (95%CI 0.28 – 1.26); p = 0.005) and preoperative neuropathic pain scored by DN4 (regression coefficient 0.68 (95%CI 0.15 – 1.20); p = 0.02).

In our study, we used a multimodal pain protocol, including paracetamol, celecoxib, gabapentin, dexamethasone and esketamine.[7-12] This pain protocol is part of a fast-track setting and is developed to reduce acute postoperative pain to enable patients to quickly mobilize and rehabilitate in an optimized and safe perioperative period.[4,5] Mean postoperative pain score determined with the NRS collected at 17 standardized moments, varied from 1.51 (range 0.0 – 8.0) to 2.97 (range 0.0 – 9.0). These results demonstrate that the use of our multimodal pain protocol enables adequate postoperative pain relief in which patients are able to mobilize and rehabilitate quickly. However, despite this

pain protocol, a large range in reported postoperative pain between patients still exists, including some outliers with high postoperative pain scores.

Pain has been described to be a sensory and emotional experience that is influenced by multiple factors.[34,35] Although several other studies reported on effects of specific patient- and provider characteristics on postoperative pain,[19-27] none of these studies were performed in a fast-track setting with a multimodal pain protocols developed to reduce acute postoperative pain (and hence enable early mobilization), were included in these studies. Since no literature reports on the effect of potential factors associated with increased postoperative pain in a fast-track setting, our model included various potential factors that have been described to be associated with postoperative pain based on a non-fast-track setting.[19-27,36] The use of a multimodal pain protocol in our study might have influenced the effects of these characteristics on postoperative pain and could be a reason for discrepancy between our results and results of these other studies.

Preoperative use of pain medication provides information on the preoperative pain levels of patients and has been shown to be associated with more severe postoperative pain.[26,27] Our study supports these findings. In contrast, another study on postoperative pain 12 to 24h after elective abdominal surgery, demonstrated no effect of preoperative use of pain medication on postoperative pain.[23]

Our multimodal protocol for postoperative pain medication was standardized for all patients. The effect of this pain protocol might therefore not be sufficient for single patients who are used to pain medication. On the other hand, in a study on postoperative pain after thoracic surgery a decrease in postoperative pain medication use for patients who used pain medication preoperatively was found.[37]

DN4 is a validated questionnaire for neuropathic pain,[30,31] which was preoperatively scored for all patients in our study. The differences between neuropathic pain and non-neuropathic (nociceptive) pain have been described in literature.[30] Osteoarthritis, the main indication for THA in our study, causes non-neuropathic pain.[30] Patients who experience non-neuropathic pain from osteoarthritis preoperatively, are more likely to benefit from THA and will experience less pain postoperatively. Since preoperative neuropathic pain is not caused by osteoarthritis of the hip,[30] THA will probably not resolve this neuropathic pain. As a consequence, these patients will be more likely to experience more postoperative pain after primary THA.

In the present study, none of the other factors were significantly associated with postoperative pain. All of these potential factors have been described to be associated with postoperative pain in non-fast-track setting studies.[19-27,36] Contrasting results on the effect of age on postoperative pain have been reported in literature, including an association between younger age and a higher level of postoperative pain[20,23,24,27] as well as a lack of effect of age on the level of postoperative pain.[26,38]

BMI has been shown to be associated with an increased inflammatory response,[38] which is related to higher levels of postoperative pain,[39] whereas others demonstrated no effect of BMI on postoperative pain scores.[24,39,40] In our study we excluded patients with BMI > 40 kg/m^2, which might be a reason for lack of effect of BMI on postoperative pain.

Regarding gender, contrasting results on the effect on postoperative pain have been reported in literature as well. These results include both higher postoperative pain for female patients[24,27,38] and no effect of gender on postoperative pain.[22,23,25,26]

Higher ASA classification has also been shown to be associated with increased postoperative pain.[23] However, in our study we only included patients with ASA classification I or II, which might be a reason for lack of effect of ASA classification on postoperative pain.

An increased incision length results in increased tissue damage, and might subsequently result in increased postoperative pain. This relation has been described in literature.[24] In our study the ASI approach was used. Since this approach uses both an intermuscular and internervous plane, less surgical trauma and hence lower postoperative pain scores and less pain medication consumption have been described.[13-18]

Use of antidepressants provides information on patients' mental state, which could be predictive for the patients' response on pain medication and pain experience.[25] Moreover, in literature depression symptoms have been mentioned to be related to higher level of postoperative pain.[23,38,41]

Furthermore, we used different validated questionnaires preoperatively for all patients to define preoperative pain and pain characteristics, including the APAIS.[29] Anxious patients respond differently to anesthesia and pain than non-anxious patients and therefore require larger doses of anaesthetics.[19,20,25,42,43] It has been reported that the anxiety/'worry' component of the APAIS is positively associated with the occurrence of early postoperative pain, whereas a strong information seeking behavior reduces the incidence of severe postoperative pain.[24] This is in contrast to others who report that patients who require more information about impending discomforts preoperatively may sensitize the individual to the experience.[19]

Some potential limitations of our study should be discussed. First, only 74 patients were included. However, simulation studies showed that with mixed models with relatively small samples sizes, appropriate inferences regarding the point and interval estimates for fixed effects can be made.[44,45] A strength of the present study is that linear mixed models, not only model the correlation between repeated measures of the same patient, they also assess fluctuations in postoperative pain over time. Second, although others investigated effects of occupation and/or level of education,[19,23,40,41] SF-36,[24] and heart rate and blood pressure[36] on postoperative pain, we were not able to include

these variables in our model, because these variables were not reported in a consistent way in the patient files.

A qualitative systematic review of Ip and others[36] identified factors associated with postoperative pain and analgesic consumption. Type of surgery was an important predictive factor for postoperative pain. This suggests that results of our study are applicable for primary THA. Furthermore, this could be another reason for the discrepancy between different studies describing postoperative pain after different types of surgery, besides differences in the pain protocol used.

In conclusion, only preoperative use of pain medication and preoperative neuropathic pain were associated with increased postoperative pain after primary THA in a fast-track setting, including a multimodal pain protocol which was developed to reduce acute postoperative pain to enable quick mobilization and rehabilitation. This knowledge provides further details for optimization of postoperative pain management and preoperative patient education.

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Chapter 10

General conclusion and perspective

GENERAL CONCLUSION AND PERSPECTIVE

The aim of this thesis was to investigate how perioperative care for primary THA patients could be optimized. Three main aspects of the perioperative procedure were therefore studied: length of hospital stay (LOS), surgical procedure, and pain management.

LENGTH OF HOSPITAL STAY

Fast-track protocols combine efficient organization with analyses of core care principles which will ensure effective pain management, early mobilization and reduction of surgical stress and allow for optimized and safe perioperative care which will finally result in a reduction of LOS.[1-4] However, although a reduced LOS is often thought to be the main goal of fast-track protocols, it is actually the result of fast-track and should merely be seen as a good indicator for the successful implementation of a fast-track protocol.

A prolonged hospital stay in combination with a period of perioperative bed rest will have various undesirable effects and, consequently, a negative impact on perioperative care. Distorted sleep as a result of high noise levels at the hospital ward, as well as the use of certain drugs and the postoperative inflammatory response are related to early postoperative fatigue.[5,6] A long period of postoperative bed rest results in loss of weight and muscle mass and associated weakness, and is therefore related to late postoperative fatigue.[5,7] Furthermore, patients are exposed to multi-resistant microorganisms in the hospital as well as hospital-acquired infections.[8,9] The successful implementation of a fast-track protocol results in a reduction of LOS and consequently in the reduction of the undesirable effects and negative impacts of prolonged hospital stay on perioperative care.

Chapter 2 describes the implementation of a fast-track protocol in a large Dutch teaching hospital, which led to a significant decrease in LOS for unselected THA patients without a change in complication rate, re-admission rate or reoperation rate. As LOS

decreased, we wondered whether we could achieve a further reduction in LOS and perform THA in an outpatient setting. *Chapter 3* confirms that outpatient THA through the anterior approach can be performed successfully in a cohort of selected patients, with satisfying results up to 3 months postoperatively, and without troublesome side effects.

Since it proved possible to perform outpatient THA in selected patients, the challenge is to reduce the number of selection criteria to enable all patients to be treated in an ambulatory setting. Proper identification of patient characteristics influencing patient recovery might be used to improve perioperative care as well as discharge and rehabilitation planning. These improvements might enlarge selection criteria for outpatient THA in the future. Hence, proper patient identification seems the key to optimizing perioperative care for THA patients even further.

However, since it might not be feasible to perform outpatient THA for all patients in the near future, probably specific patient categories need to be identified. Examples of these categories are the outpatient THA category, patients with a LOS of 1 night and patients who need more time to recover postoperatively such as fragile elderly. For this last patient category, cooperation with geriatric care for postoperative hospitalization is recommended to establish safe and optimized perioperative care.

Regarding proper identification of patients who need more rehabilitation time and extensive care, we identified outliers in LOS after the introduction of a fast-track procedure. *Chapter 4* describes our study among 477 unselected patients who received primary THA in a fast-track setting, which demonstrated that older age, living alone and the straight lateral approach were associated with a prolonged LOS. Since two of these three patient characteristics, age and living situation, cannot be changed, the information about these two characteristics can only be used for optimizing the organization of care regarding preoperative patient information and rehabilitation planning.

SURGICAL PROCEDURE

By contrast, the surgical approach is a factor in the surgical process that can be changed by the orthopedic surgeon in order to provide better patient care by reducing LOS, even though changing a surgical approach can cause learning curve issues. In the past few years, the anterior approach is gaining popularity in the Netherlands, with an increase from 4.2 % in 2010 to 9.9 % of all primary THAs in 2013.[10] However, there is an ongoing debate whether this still less frequently used approach is preferable to other approaches to the hip joint and whether the possible benefits of this approach outweigh the possible disadvantages.

Although some may consider the anterior approach just another hype in orthopedic surgery, beneficial results of the anterior approach have been described. In *Chapter 4*,

our own study on the effects of patient characteristics on LOS in our hospital demonstrated an association of the anterior approach with a decrease in LOS in a fast-track setting, when compared to the straight lateral approach. In *Chapter 5*, our systematic review of all available literature regarding the anterior approach demonstrated benefits of the anterior approach in the early postoperative period as well. The purpose of this systematic review was to evaluate all available literature about the anterior approach compared to other approaches for primary THA. Long-term effects seem not to be influenced by approach, whereas short-term effects are influenced positively by the anterior approach. However, in a fast-track setting these positively influenced short-term effects might provide additional benefits.

A possible drawback of the anterior approach is the learning curve for surgeons using this approach. This learning curve is not yet clear. Although there is a learning curve for the anterior approach and this approach is sometimes criticized for its technical difficulty, our systematic review demonstrated that there was no higher risk for postoperative complications or malposition of component placement when the anterior approach is used. Moreover, a learning curve is not unique for the anterior approach. It also exists for other approaches of the hip joint.

Specific complications following the anterior approach can be prevented if a surgeon is more experienced or if the pitfalls for this procedure are known. When we introduced the anterior approach (ASI) in our hospital, we noticed some specific complications for this approach, which could be potential pitfalls for other surgeons who perform this approach. *Chapter 6* describes that LFCN lesions occurred more often than expected, and fractures of the greater trochanter and dislocations were seen as well. As a result of these observations, the technique was altered in order to avoid these complications in our hospital.

Since the anterior approach has several early postoperative benefits, this approach might be a good option for orthopedic surgeons at the start of their career. If standard education is enlarged with this approach, and residents in orthopedic surgery are not only educated in the kind op approach used in their hospital, these residents can learn to use the anterior approach during their residency in a similar way as they learn to use other approaches to the hip. In view of the benefits for the anterior approach, experienced orthopedic surgeons should also consider converting to this approach, although the question remains if a surgeon who is familiar with an approach other than the anterior approach should convert this approach for the short-term benefits only, knowing that there is a learning curve.

PAIN MANAGEMENT

Postoperative pain also contributes to postoperative patient burden and reduces patient satisfaction after primary THA. Furthermore, postoperative pain could hinder rapid postoperative mobilization.[11] Perioperative analgesia of the surgical tissue theoretically provides less postoperative pain and therefore could result in an optimized postoperative rehabilitation and faster recovery. However, *chapter 7* demonstrates no effect of local infiltration analgesia (LIA) on postoperative pain in our randomized placebo-controlled trial. This trial investigated the effect of both standard and reversed LIA in combination with the ASI technique for primary THA. Our study only investigated patients operated through the ASI approach. Since the anterior approach is associated with lower postoperative pain scores and less pain medication consumption than other approaches, the effect of LIA on postoperative pain might not have been detectable in our study population.

Chapter 8 presents a pharmacokinetic model for the absorption and diffusion of ropivacaine after LIA for THA, which are similar to those after TKA. Since LIA has been reported to be effective in total knee arthroplasty (TKA),[37,73,74] it seems unlikely that a higher dose of ropivacaine can optimize the effect of LIA after THA. Apparently it is not possible with the current LIA technique to achieve an effective blockage of all nerves innervating the hip joint. Therefore a possible explanation for the lack of effect of LIA in THA must be sought in the innervation of the hip joint. More research on local blocking of the nerves that innervate the hip joint is needed. Blocking these nerves might reduce postoperative pain even further.

Although THA patients operated by means of the anterior approach experienced lower pain scores compared to patients operated by means of another approach, we observed patients with high pain scores postoperatively, up to an NRS of 10 for the anterior approach (*chapter 7)*. All patients received as much pain medication as required. However, some patients, the so-called non-responders, seemed to experience more pain than others. Furthermore, pain patterns differed substantially across individuals. Therefore the question arises if other factors than postoperative pain management are also responsible for the amount of postoperative pain. In *chapter 9* we tried to identify which specific patient characteristics influence postoperative pain after primary THA by ASI. Adjusted for other predictors in the model, preoperative use of pain medication and preoperative neuropathic pain scored by neuropathic pain diagnostic questionnaire (DN4) were the only factors that were significantly associated with higher postoperative pain scores after primary THA by ASI in a fast-track setting. This knowledge may help to further optimize the postoperative pain management and aftercare. Furthermore making expectations after primary THA regarding postoperative pain more reliable can optimize the preoperative education of these patients.

PERSPECTIVE

In conclusion, it seems to be preferable to introduce fast-track protocols for THA, because these protocols have proven to be effective in improving postoperative outcome on multiple levels, and consequently in reducing LOS without troublesome side effects. Patient selection is not needed for these fast-track protocols. Also, it is possible to perform outpatient THA for selected patients. The challenge remains to reduce the number of selection criteria for outpatient THA.

While some may consider the anterior approach just another hype in orthopedic surgery, our systematic review demonstrated early postoperative benefits for the anterior approach when compared to other approaches. Therefore, this approach might be a good option for orthopedic surgeons at the start of their career. However, in view of the benefits, experienced orthopedic surgeon should also consider converting to this approach, even though the learning curve should not be underestimated. A multimodal pain protocol may help to achieve adequate pain treatment after primary THA by means of the anterior approach, with satisfactory results for most patients. The addition of LIA to this protocol does not seem to have any effect and can therefore be omitted.

All factors mentioned above will contribute to better perioperative care for primary THA patients and should therefore be considered in clinical practice. However, no doubt the challenge remains to optimize care around primary THA even further.

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Chapter 11

Summary

In orthopedic surgery, primary total hip arthroplasty (THA) is a very commonly performed surgery worldwide. It is a good option for patients with end-stage osteoarthritis of the hip if conservative treatment fails to alleviate pain and limitations. There is general agreement about this effectiveness of the surgical procedure. Prostheses have also improved in recent years. However, the challenge remains to optimize perioperative care for patients undergoing primary THA.

The aim of this thesis was to investigate how perioperative care for primary THA patients could be optimized. Three main aspects of the perioperative procedure were therefore studied: length of hospital stay (LOS), surgical procedure, and pain management.

LENGTH OF HOSPITAL STAY (LOS)

Historically, LOS after primary THA amounted to several weeks, including a long period of bed rest. A prolonged hospital stay in combination with a period of perioperative bed rest will have various undesirable effects and, consequently, a negative impact on perioperative care.

In the past few years, there has been a continued interest in introducing fast-track protocols after THA. These fast-track protocols are based on analysis of core care principles and effective pain management and efficient organization, allowing for optimized and safe perioperative care and hence in a reduction of LOS.

Chapter 2 describes the implementation of a fast-track protocol in a large Dutch teaching hospital.

In a retrospective cohort study we included all 1180 patients who underwent a primary THA between 1 July 2008 and 30 June 2012. These patients were divided into three groups: patients operated before, during and after the introduction of the rapid recovery protocol. There were no exclusion criteria. All complications, re-admissions and reoperations were registered and analyzed.

The implementation of a fast-track protocol led to a significant decrease in LOS for unselected THA patients without a change in complication rate, re-admission rate or reoperation rate.

As LOS decreased, we wondered whether we could achieve a further reduction in LOS and perform THA in an outpatient setting. In *chapter 3* we report our experience with THA in an outpatient setting. In this prospective cohort study, we included 27 patients who were selected to receive primary THA by anterior approach in an outpatient setting between April and July 2014. Different patient-reported outcome measures (PROMs) were recorded preoperatively and at six weeks and three months postoperatively. Furthermore, anchor questions on how patients functioned in daily living were scored at six weeks and three months postoperatively. Three of the 27 patients did not go home on the day of surgery because of nausea and/or dizziness. The remaining 24 patients all went home on the day of surgery. PROMs improved substantially in these patients. Moreover, anchor questions on how patients functioned in their daily living indicated that the patients were satisfied with the postoperative results. One re-admission occurred because of seroma formation. There were no other complications or reoperations. This confirms that outpatient THA through the anterior approach can be performed successfully in a cohort of selected patients, with satisfying results up to three months postoperatively, and without troublesome side effects.

Despite the reduction in LOS after the implementation of a fast-track protocol, there is still a wide range across the patients' hospital duration. The purpose of *chapter 4* was to identify which specific patient characteristics influence LOS after successful implementation of a 'fast-track' rehabilitation protocol. A total of 477 patients who underwent primary THA procedure between 1 February 2011 and 31 January 2013, were included in this retrospective cohort study. A LOS greater than the median was considered as an increased duration. Logistic regression analyses were performed to identify potential factors associated with increased durations. Median LOS was two nights, and the mean LOS 2.9 nights. In all, 266 patients had a length of stay of more then two nights. This study demonstrated that older age, living alone and the straight lateral approach were factors that were significantly associated with increased LOS in the multivariable logistic regression model.

SURGICAL PROCEDURE

Although there is general agreement about the effectiveness of the surgical procedure itself, various surgical approaches for primary THA have been described. Each of these approaches has its own advantages and disadvantages. In the past few years, the anterior approach is gaining popularity. However, there is an ongoing debate whether this

still less frequently used approach is preferable to other approaches to the hip joint and whether the possible benefits of this approach outweigh the possible disadvantages.

Chapter 5 describes our systematic review with the purpose to evaluate literature regarding the anterior approach in comparison to other approaches. Furthermore, we investigated if there is a description of a learning curve for the anterior approach.

Data were obtained from EMBASE, Cochrane, PsycINFO, CINAHL, Web-of-Science, Scopus, Google scholar, and PubMed since their inception up to June 2015. Two reviewers independently selected the studies and independently conducted the quality assessment. Because studies were considered heterogeneous regarding outcome measures, determinants studied, and methodological quality, we decided to perform a "best evidence synthesis". A total of 64 studies met the inclusion criteria.

Strong evidence for no difference in component placement between the anterior approach and other approaches was found. Also, strong evidence for faster postoperative recovery and less need for assistive devices after the anterior approach were found. All other studied parameters only demonstrated conflicting evidence. This demonstrates long-term effects seem not to be influenced by approach, whereas short-term effects are influenced positively by the anterior approach. Although the learning curve for the anterior approach is not yet clear, this learning curve should not to be neglected.

When we introduced the anterior approach (anterior supine intermuscular (ASI) approach) in our hospital, we noticed some specific complications for this approach, which could be potential pitfalls for other surgeons who perform this approach. *Chapter 6* describes these specific complications. Injury to the lateral femoral cutaneous nerve (LFCN), fractures of the greater trochanter and dislocation were specific complications that were noticed with the initial technique. We applied specific adjustments on the procedure to prevent these complications. We retrospectively analyzed the differences between 202 patients who were operated by a standardized anterior approach and 248 patients who were operated after adjustments were implemented on the procedure. Prevalence of injury to the LFCN decreased from 7.9 % to 0.8 % ($p < 0.001$), fractures of the greater trochanter decreased from 5.4 % to 0.8 % ($p = 0.004$) and the incidence of dislocation decreased from 4.5 % to 1.6 % ($p = 0.074$).

PAIN MANAGEMENT

THA is associated with considerable postoperative pain. This postoperative pain hinders early mobilization and rehabilitation, which has negative consequences on mobility, LOS and duration of overall recovery. Analgesics are used to provide pain relief. However, most analgesics are known for their side effects. Therefore, the challenge of analgesic regimes for THA is to obtain adequate pain relief without troublesome side effects.

Local infiltration analgesia (LIA) is a technique in which the surgical field is infiltrated with analgesics (ropivacaine) in order to provide better pain relief postoperatively. Only limited data are available regarding the infiltration of local anaesthetic for THA and no studies were performed for THA using the anterior approach.

Chapter 7 describes a prospective, randomized placebo-controlled study in which we investigated the effect of both standard and reverse infiltration of local anaesthetic in combination with the anterior approach for THA. The primary endpoint was the mean numeric rating score (NRS) for pain four hours postoperatively. In addition, we recorded the length of hospital stay, the operating time, the destination of the patient at discharge, the use of pain medication, the occurrence of side effects and pain scores at various times postoperatively.

Between November 2012 and January 2014, 75 patients were included in the study. They were randomized into three groups: standard infiltration of local anaesthetic, reversed infiltration of local anaesthetic, and placebo. We found no clinically relevant effect when the infiltration of local anaesthetic with ropivacaine and epinephrine was used in a multimodal pain protocol for THA using the anterior approach.

The reason for lack of effect of LIA for THA is not yet clear. The purpose of *chapter 8* was to elucidate pharmacokinetic parameters of ropivacaine administered by LIA in THA patients. For determining ropivacaine serum concentrations, blood samples were collected at multiple moments from just before infiltration, until 48 hours after infiltration of the first LIA mixture. This pilot-study demonstrates a pharmacokinetic model for absorption and diffusion of ropivacaine after LIA for THA. These parameters do not differ from those for total knee arthroplasty. It seems not likely that a higher dose of ropivacaine can optimise the effect of LIA after THA. Serum levels of ropivacaine in our study never exceeded toxicity levels.

The fast-track protocol for THA in our hospital includes a multimodal pain protocol. Despite this pain protocol there is still a large range in reported postoperative pain between patients, which hinders mobilization and rehabilitation postoperatively. The goal of *chapter 9* was to identify which patient-specific and surgical characteristics influence postoperative pain after THA in a fast-track setting. All 74 patients with osteoarthritis of the hip who underwent primary THA procedure by ASI approach between November 2012 and January 2014 were included in this prospective cohort study. The protocol for pain medication was standardized. Postoperative pain determined with the NRS was collected at 17 standardized moments. Linear mixed models were used to examine potential patient-specific and surgical factors associated with increased postoperative pain. Pain patterns differed substantially across individuals. Adjusted for other variables in the model, preoperative use of pain medication and preoperative neuropathic pain scored by DN4 were the only factors significantly associated with higher postoperative pain scores. The knowledge of which factors are associated with higher postoperative

pain scores after THA in a fast-track setting may help optimizing perioperative postoperative pain management and preoperative education of these patients.

Chapter 12

Nederlandse samenvatting

Wereldwijd is de primaire totale heup prothese (THP) een frequent uitgevoerde orthopedische operatie. Het is een goede optie voor behandeling van pijn en beperkingen bij patiënten met vergevorderde artrose van de heup, indien conservatieve behandeling faalt. Er bestaat algemene consensus over de effectiviteit van deze operatieve ingreep. Ook zijn de heupprotheses zelf de laatste jaren verbeterd. Er blijft echter een uitdaging bestaan om de perioperatieve zorg voor patiënten die een THP operatie ondergaan verder te optimaliseren.

Het doel van dit proefschrift is te onderzoeken hoe deze perioperatieve zorg voor primaire THP patiënten geoptimaliseerd kan worden. Drie hoofdaspecten van de perioperatieve procedure werden daarvoor bestudeerd: opnameduur in het ziekenhuis, de chirurgische procedure zelf en pijn behandeling.

OPNAMEDUUR IN HET ZIEKENHUIS

Historisch bedroeg de opnameduur na het plaatsen van een THP enkele weken, dit was inclusief een lange periode van bedrust. Verlengde opnameduur in combinatie met een periode van bedrust heeft verscheidene ongewenste effecten met als consequentie een negatieve invloed op perioperatieve kwaliteit van zorg. In de afgelopen jaren is er een toenemende interesse ontstaan voor de introductie van fast-track protocollen, ook na THP. Deze fast-track protocollen zijn gebaseerd op de analyse van basis zorg principes, effectieve pijn behandeling en efficiënte organisatie. Dit zorgt voor een geoptimaliseerde en veilige perioperatieve zorg met als gevolg een afname van opnameduur.

Hoofdstuk 2 beschrijft de introductie van een fast-track protocol in een groot Nederlands opleidingsziekenhuis. In een retrospectieve cohort studie includeerden we alle 1180 patiënten die primaire THP ondergingen tussen 1 juli 2008 en 30 juni 2012. Deze patiënten werden verdeeld in drie groepen: patiënten geopereerd voor, tijdens en na de introductie van het fast-track protocol. Er waren geen exclusie criteria. Alle complicaties, heropnames en heroperaties werden geregistreerd en geanalyseerd. De invoer van een

fast-track protocol leidde tot een significante afname van opnameduur voor een groep ongeselecteerde THP patiënten, zonder een verandering in aantallen complicaties, heropnames of heroperaties.

Aangezien de opnameduur significant afnam na de introductie van een fast-track protocol, ontstond de vraag of nog een verdere afname van opnameduur te bereiken zou zijn en of het mogelijk zou zijn om THP in dagbehandeling uit te voeren. In *hoofdstuk 3* rapporteren we onze ervaring met THP in dagbehandeling. In deze prospectieve cohort studie includeerden we 27 patiënten die waren geselecteerd voor primaire THP via voorste benadering in dagbehandeling, tussen april en juli 2014. Verschillende patient-reported outcome measures (PROMs) werden zowel preoperatief als zes weken en drie maanden postoperatief bijgehouden. Tevens werden anchor questions over hoe patiënten functioneerden in het dagelijks leven gescoord, zes weken en drie maanden postoperatief. Drie van de 27 patiënten gingen niet met ontslag op de dag van de operatie als gevolg van misselijkheid en/of duizeligheid. De overige 24 patiënten gingen allen naar huis op de dag van de operatie. PROMs verbeterden substantieel voor deze patiënten. Verder gaven de anchor questions aan dat patiënten tevreden waren met de postoperatieve resultaten. Eén heropname vond plaats als gevolg van seroomvorming. Er waren geen overige complicaties of heroperaties. Dit bevestigt dat THP middels de voorste benadering in dagbehandeling succesvol kan worden uitgevoerd, met goede resultaten tot aan drie maanden postoperatief en zonder dat ernstige complicaties optreden.

Ondanks de afname van opnameduur na de introductie van een fast-track protocol, bestaat er nog steeds een forse spreiding in opnameduur tussen de verschillende patiënten. Het doel van *hoofdstuk 4* is om te identificeren welke specifieke patiënten karakteristieken deze opnameduur beïnvloedden, na de succesvolle invoer van een fast-track protocol. Een totaal van 477 patiënten ondergingen een primaire THP tussen 1 februari 2011 en 31 januari 2013. Zij werden geïncludeerd in deze retrospectieve cohort studie. Een opnameduur van meer dan de mediaan werd beschouwd als een verlengde opnameduur. Multivariabele logistische regressie analyses werden uitgevoerd om potentiele factoren te identificeren welke geassocieerd zijn met een verlengde opnameduur. De mediaan van opnameduur was twee nachten en de gemiddelde opnameduur was 2.9 nachten. Van alle patiënten hadden 266 een opnameduur van meer dan twee nachten. Deze studie toonde aan dat oudere leeftijd, alleen wonen en de straight lateral benadering factoren waren welke geassocieerd zijn met een toegenomen opnameduur.

CHIRURGISCHE PROCEDURE

Ondanks dat er algemene consensus bestaat over het effect van de chirurgische procedure zelf, worden er verschillende chirurgische benaderingen voor primaire THP beschreven. Elk van deze benaderingen heeft zijn eigen voor- en nadelen. In de afgelopen jaren is de voorste benadering fors in populariteit toegenomen. Er bestaat echter een voortdurende discussie of deze minder frequent gebruikte benadering naar het heupgewricht te prefereren is boven andere benaderingen en of de mogelijke voordelen van deze benadering opwegen tegen eventuele nadelen er van.

Hoofdstuk 5 beschrijft ons sytematic review waarin de literatuur geëvalueerd wordt aangaande de voorste benadering. Deze benadering wordt vergeleken met de andere benaderingen. Verder onderzochten we of er een duidelijke definitie bestaat voor de learning curve voor de voorste benadering.

Data werden verkregen uit EMBASE, Cochrane, PsycINFO, CINAHL, Web-of-Science, Scopus, Google scholar, en PubMed sinds het ontstaan tot en met juni 2015. Twee reviewers selecteerden onafhankelijk van elkaar de studies en voerden onafhankelijk van elkaar quality assessments uit. Omdat de studies heterogeen werden beschouwd met betrekking tot de uitkomstmaten, bestudeerde determinanten en methodologische kwaliteit, werd er besloten om een "best evidence synthesis" uit te voeren. Een totaal van 64 studies voldeed aan de inclusie criteria.

Er werd sterk bewijs gevonden dat er geen verschil bestaat in postoperatieve component positie tussen de voorste benadering en andere benaderingen. Verder werd er sterk bewijs gevonden voor sneller postoperatief herstel en minder gebruik van hulpmiddelen indien de voorste benadering wordt gebruikt voor THP. Alle overige bestudeerde parameters lieten slechts tegenstrijdig bewijs zien. Dit laat zien dat lange termijn effecten niet beïnvloed lijken door de gekozen benadering, terwijl korte termijn effecten positief beïnvloed worden door het gebruik van de voorste benadering. Ondanks dat de learning curve voor de voorste benadering niet geheel duidelijk is, moet deze learning curve niet genegeerd worden.

Tijdens de introductie van de voorste benadering (anterior supine intermuscular (ASI) approach) in ons ziekenhuis, bemerkten we een aantal specifieke complicaties voor deze benadering, welke potentiële valkuilen kunnen zijn voor andere chirurgen die deze benadering gaan gebruiken. *Hoofdstuk 6* beschrijft deze specifieke opgemerkte complicaties. Letsel aan de n.cutaneus femoralis lateralis, fracturen van het trochanter major en luxaties van de heup waren specifieke complicaties welke opvielen bij de initiële techniek. Er werden specifieke aanpassingen gedaan aan de chirurgische procedure om deze complicaties te voorkomen. Wij analyseerden retrospectief de verschillen tussen 202 patiënten welke waren geopereerd via de standaard voorste benadering en 248 patiënten welke waren geopereerd nadat de aanpassingen aan de procedure waren

gedaan. Het voorkomen van letsel aan de n.cutaneus femoralis lateralis nam af van 7.9 % naar 0.8 % ($p < 0.001$), fracturen van het trochanter major namen af van 5.4 % naar 0.8 % ($p = 0.004$) en luxaties van de heup namen af van 4.5 % naar 1.6 % ($p = 0.074$).

PIJN BEHANDELING

De THP operatie is geassocieerd met aanzienlijke postoperatieve pijn. Deze pijn hindert vroege mobilisatie en revalidatie, wat negatieve consequenties heeft op mobiliteit, opnameduur en duur van het totale herstel. Analgetica worden gebruikt als pijnstilling. Echter de meeste analgetica staan bekend om hun bijwerkingen. Er bestaat daardoor een uitdaging om adequate pijnstilling rondom de THP operatie te bereiken zonder dat daarbij vervelende bijwerkingen optreden.

Local infiltration analgesia (LIA) is een techniek waarbij het operatiegebied geïnfiltreerd wordt met een lokaal analgeticum (ropivacaine), met als doel om postoperatief betere pijnstilling te verkrijgen. Er zijn slechts beperkte data beschikbaar met betrekking tot het gebruik van LIA bij THA en in geen van deze studies werd de voorste benadering voor THP uitgevoerd. *Hoofdstuk 7* beschrijft een prospectieve gerandomiseerde placebo-gecontroleerde studie waarin we het effect van zowel standaard als omgekeerde LIA onderzoeken in combinatie met de voorste benadering voor THP. Primair eindpunt van deze studie was de gemiddelde numeric rating score (NRS) vier uur postoperatief. Daarnaast werden opnameduur, operatieduur, ontslagbestemming van de patient, gebruik van pijnmedicatie, het voorkomen van bijwerkingen, en pijnscores op verschillende postoperatieve tijdstippen bijgehouden. Tussen november 2012 en januari 2014 werden 75 patiënten geïncludeerd in deze studie. Ze werden gerandomiseerd in drie groepen: standaard LIA, omgekeerde LIA en standaard placebo. We vonden geen klinisch relevant verschil tussen deze drie groepen met betrekking tot de verschillende uitkomstmaten.

De reden voor gebrek aan effect van LIA voor THP is niet geheel duidelijk. Het doel van *hoofdstuk 8* was derhalve om de farmacokinetische parameters van ropivacaine te onderzoeken wanneer dit wordt toegediend middels LIA in THP patiënten. Om de ropivacainie serum concentraties te bepalen werden bloedmonsters verzameld op verschillende momenten, van net voor de infiltratie tot en met 48 uur na de infiltratie van het eerste LIA mengsel. Deze pilotstudie toont een farmacokinetisch model voor absorptie en diffusie van ropivacaine van LIA na THP. Deze parameters verschillen niet van die van LIA na totale knieprothese. Het lijkt dan ook niet waarschijnlijk dat een hogere dosis ropivacaine het effect van LIA na THP kan optimaliseren. Serum levels van ropivacaine in onze studie overschreden nooit de toxiciteits-grens.

Het fast-track protocol voor THP in ons ziekenhuis bevat een multimodaal pijn protocol. Ondanks het gebruik van dit pijn protocol bestaat er een grote spreiding in

gerapporteerde postoperatieve pijn scores tussen patiënten. Het doel van *hoofdstuk 9* was om te identificeren welke patient specifieke en chirurgische karakteristieken invloed hebben op postoperatieve na THP in een fast-track setting. Alle 74 patiënten die een primaire THP middels voorste benadering ondergingen voor artrose van de heup, tussen november 2012 en januari 2014 werden geïncludeerd in deze prospectieve cohort studie. Het protocol voor pijn medicatie was gestandaardiseerd. Postoperatieve pijn bepaald middels NRS werd bijgehouden op 17 gestandaardiseerde momenten. Lineair mixed models werden gebruikt om potentiele patient specifieke en chirurgische factoren te onderzoeken welke geassocieerd waren met toegenomen postoperatieve pijn. Pijn patronen verschilden substantieel tussen de verschillende individuen. Gecorrigeerd voor de overige variabelen in het model waren preoperatief gebruik van pijn medicatie en preoperatieve neuropatische pijn, gescoord met de DN4, de enige factoren welke significant geassocieerd waren met hogere postoperatieve pijn scores. Deze kennis kan helpen om perioperatieve pijn behandeling en preoperatieve educatie van deze patiënten te optimaliseren.

CURRICULUM VITAE

Yvon den Hartog werd op 6 oktober 1980 geboren in Assen. Na het behalen van haar VWO diploma op het Dr. Nassaucollege te Assen ging zij in 1999 geneeskunde studeren aan de Erasmus Universiteit te Rotterdam. Tijdens haar studie roeide zij in de eerstejaars dames acht van ARSR Skadi en nam zij deel aan het bestuur van deze vereniging.
Na het afronden van haar coschappen startte zij in 2007 met de opleiding tot orthopedisch chirurg. Haar vooropleiding volgde zij in het MCRZ (thans Maasstadziekenhuis) te Rotterdam (opleider dr. E. Van der Harst).
Haar opleiding vervolgde zij in het Erasmus MC te Rotterdam (opleider prof. dr. J.A.N. Verhaar), het Elisabethziekenhuis te Tilburg (opleider dr. J. De Waal Malefijt) en het Reinier de Graaf Gasthuis te Delft (opleider dr. R.M. Bloem).
Tijdens het vijfde jaar van haar opleiding startte zij in het Reinier de Graaf Gasthuis met wetenschappelijk onderzoek, wat uiteindelijk heeft geresulteerd in dit proefschrift.
Eind 2013 rondde zij haar opleiding tot orthopedisch chirurg af. Hierna volgde zij een fellowship heupchirurgie in het Reinier de Graaf Gasthuis te Delft. Aansluitend werkte zij anderhalf jaar als chef de clinique in het Ikaziaziekenhuis te Rotterdam. Sinds 1 januari 2016 is zij werkzaam als fellow kinderorthopedie in het Máxima Medisch Centrum te Veldhoven.

LIST OF PUBLICATIONS

den Hartog YM, Vehmeijer SBW. Letter to the editor, comments on "High complication rate in the early experience of minimally invasive total hip arthroplasty by the direct anterior approach." Acta Orthop. 2013;84(1):116-7.

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den Hartog YM, Verburg H, Niesten DD. Extra-corporeal migration of the patellar component after total knee arthroplasty by lateral approach – a case report. Nederlands Tijdschrift voor Orthopaedie. 2013;20(4):117-9.

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den Hartog YM, Mathijssen NMC, Vehmeijer SBW. Total hip arthroplasty in an outpatient setting in 27 selected patients. Acta Orthop. 2015;2:1-4.

den Hartog YM, Mathijssen NMC, Vehmeijer SBW. The less invasive anterior approach for total hip arthroplasty: a comparison to other approaches and an evaluation of the learning curve. Hip Int. 2016;6(2):105-20.

PHD PORTFOLIO

Courses	Year	ECTS
- Scientific writing in English	2012	2.0
- Statistical courses		
- Basis statistics SPSS	2012	2.0
- Advanced statistics SPSS	2012	2.0
Oral Presentations		
- *Introducing Rapid Recovery for THA; a Retrospective Cohort Study* - European Hip Society, Milan, Italy	2012	1.0
- *Introduction of rapid recovery for primary THA – a retrospective cohort study* - Rapid recovery congress, The Hague, the Netherlands	2013	0.5
- *Points of discussion in rapid recovery* - Rapid recovery congress, The Hague, the Netherlands	2013	0.5
- *Which patient characteristics influence length of hospital stay after primary total hip arthroplasty in a 'fast-track' setting?* - EFORT, London, United Kingdom	2014	1.0
- *The effect of LIA in a multimodal pain protocol for THA by direct anterior approach – outcome of a prospective, randomised, placebo-controlled trial in 75 patients* - Rapid recovery congress, Delft, the Netherlands	2014	1.0
- *The anterior supine intermuscular approach for total hip arthroplasty: reducing the complication rate by improving the procedure* - European Hip Society, Stockholm, Sweden	2014	1.0
- *No effect of local infiltration analgesia for total hip arthroplasty through a direct anterior supine intermuscular approach, a randomised placebo controlled trial* - European Hip Society, Stockholm, Sweden	2014	1.0
- *Total Hip Arthroplasty In An Outpatient Setting For A Cohort Of Consecutive Patients* - EFORT, Prague, Czech Republic	2015	1.0
- *Which Patient-Specific And Surgical Characteristics Influence Postoperative Pain Patterns After Primary THA By DAA In A Fast-Track Setting?* - EFORT, Prague, Czech Republic	2015	1.0
Poster presentations		
- *Comparison the straight lateral approach with the anterior supine intermuscular approach for primary total hip arthroplasty in 337 patients* - European Hip Society, Stockholm, Sweden	2014	1.0
- *Using Video Analysis On The Operating Room For Total Hip Arthroplasty To Improve Efficiency And Reduce Surgery Time* - EFORT, Prague, Czech Republic	2015	1.0
(Inter)national Conferences		
- NOV annual meeting, The Hague, the Netherlands	2012	0.5
- European Hip Society, Milan, Italy	2012	1.0
- NOV autumn meeting, Veldhoven, the Netherlands	2012	0.5
- NOV annual meeting, Amsterdam, the Netherlands	2013	0.5
- Rapid recovery congress, The Hague, the Netherlands	2013	0.3
- EFORT, Istanbul, Turkey	2013	1.0

- NOV autumn meeting, Veldhoven, the Netherlands	2013	0.5
- NOV annual meeting, Rotterdam, the Netherlands	2014	0.5
- Rapid recovery congress, Delft, the Netherlands	2014	0.3
- EFORT, London, United Kingdom	2014	1.0
- NOV autumn meeting, Veldhoven, the Netherlands	2014	0.5
- European Hip Society, Stockholm, Sweden	2014	1.0
- NOV annual meeting, Maastricht, the Netherlands	2015	0.5
- EFORT, Prague, Czech Republic	2015	1.0
- NOV autumn meeting, Veldhoven, the Netherlands	2015	0.5

Lecturing

- Rapid Recovery for primary THA - ROGO dag, Rotterdam, the Netherlands	2012	0.6
- The anterior supine intermuscular approach for total hip arthroplasty: reducing the complication rate by improving the procedure - ROGO dag, Tilburg, the Netherlands	2013	0.6

Other

- Reviewer international orthopedic journals	2015	2.0

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