Diplomarbeit

A Comparison between Spinal Anesthesia versus General Anesthesia with and without the Use of Peripheral Nerve Blocks in Total Knee Arthroplasty

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Graz, am 13.11.2020 *Lucas Kaltenegger eh*

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List of Abbreviations

A.	artery
ACB	adductor canal block
ACL	anterior cruciate ligament
ASA	American Society of Anesthesiologists
AORI	Anderson Orthopedic Research Institute
Art.	articulation
BCIS	bone cement implant syndrome
BMI	body mass index
CO	carbon monoxide
CPM	Continuous Passive Motion
CSE	combined spinal and epidural anesthesia
CSF	cerebrospinal fluid
Fig.	figure
GA	general anesthesia
Hb	hemoglobin
ICU	intensive care unit
IPACK	Interspace between poplitea artery and posterior capsule of knee
IV	intravenous
KSS	Knee Society Score
LA	local anesthetic
LAST	local anesthetic systemic toxicity
M.	muscle
max.	maximum
ME	morphine equivalent
MET	metabolic equivalent threshold
N.	nerve
NRS	Numerical Rating Scale
NSAIDs	nonsteroidal anti-inflammatory drugs
OA	osteoarthritis
OR	operating room
p.a.	posterior anterior
PACU	post anesthesia care unit
PAI	periarticular injection
PE	pulmonary embolism

PCA	patient-controlled anesthesia
PCL	posterior cruciate ligament
PNB	peripheral nerve block
PTT	partial thromboplastin time
PFC	Press Fit Condylar
SA	spinal anesthesia
SGA	supraglottic airway
RA	rheumatoid arthritis
RBC	red blood cells
ROM	range of motion
Tab.	table
TKA	total knee arthroplasty
TXA	tranexamic acid
VAS	Visual Analog Scale
VTE	venous thromboembolism
WHO	World Health Organization
WOMAC	Western Ontario & McMaster Universities Osteoarthritis Index

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Zusammenfassung (German)

Hintergrund

Die Knieendoprothetik (K-TEP) ist eine der am häufigsten durchgeführten Operationen, bei der immer wieder über das optimale Anästhesieverfahren debattiert wird: Allgemeinanästhesie oder Spinalanästhesie, mit oder ohne peripherer Nervenblockade. Ziel dieser Studie ist es, die verschiedenen Anästhesiemethoden für die K-TEP und ihre Auswirkungen auf den postoperativ klinischen Verlauf zu vergleichen.

Methodik

Im Zeitraum von Januar 2018 bis Februar 2019 wurden 656 Patienten und Patientinnen am Universitätsklinikum LKH Graz einer primären K-TEP unterzogen. Die Patienten und Patientinnen wurden entsprechend ihrer erhaltenen Anästhesieart in vier Gruppen eingeteilt. Es wurden ein bis 24 Monate nach der Operation, retrospektiv die Auswirkungen dieser verschiedenen Anästhesietechniken auf das postoperative klinische Ergebnis untersucht. Primär wurde dabei auf den Effekt auf den Opioidkonsum und auf das Schmerzempfinden eingegangen. Sekundär wurde auf Mortalitäts- und Komplikationsraten, Blutmanagement, Einleitungszeiten, Hospitalisationszeit und andere Parameter des postoperativen Verlaufs Wert gelegt.

Ergebnisse

Von 656 Patienten und Patientinnen erhielten 425 (64.8%) eine Allgemeinanästhesie und 231 (35.2%) eine Spinalanästhesie. Eine multivariable Analyse ergab einen signifikant niedrigeren Gesamtopioidverbrauch bei der Anwendung einer Spinalanästhesie um 2.08 mg (95% CI 0.1-4.1, $P<0.04$) Morphinäquivalent und eine Zeitersparnis von 6.95 Minuten (95% CI 5.17–8.72, $P<0.001$) bei der Narkoseneinleitung. Im Gegenzug wurde ein höherer perioperativer Blutverlust von 90.1 ml (CI 95% 17.91–162.23, $P=0.015$) beobachtet. Die Anwendung einer peripherer Nervenblockaden erreichte eine Verringerung des frühen postoperativen Morphinkonsums von 3.59 mg (95% CI 1.5-5.7, $P=0.00$), verlängerte jedoch die Zeit bis zur Inzision um 8.48 Minuten (95% CI 6.63–10.36, $P<0.001$). Es wurden keine signifikanten Unterschiede hinsichtlich der Komplikations- und Mortalitätsrate, des Bedarfs an Bluttransfusionen, der Hospitalisationszeit, der Zeit bis zum Beginn des Gangtrainings und der postoperativen Flexibilität festgestellt ($P>0.05$).

Schlussfolgerung

In dieser Studie wurde für Patienten und Patientinnen bei Knietotalendoprothetische-Operationen mit Spinalanästhesie kürzere Anästhesie-Einleitungszeiten sowie geringere postoperative Opioiddosierungen beobachtet. Die zusätzliche Durchführung von peripheren Nervenblockaden führte zu geringerem Opioidbedarf sowie zu niedrigerem Schmerzniveau in der frühen postoperativen Phase.

Abstract

Background

Total knee arthroplasty (TKA) is one of the most performed surgeries and there have been a lot of debates to determine the best anesthetic approach, including general anesthesia, spinal anesthesia, with or without peripheral nerve blocks. The aim of this study was to analyze and compare the different anesthetic methods for TKA and their effects on the postoperative clinical outcome.

Patients and Methods

In the period from January 2018 until February 2019, 656 patients underwent primary TKA in University Hospital of Graz. The patients were divided into four groups according their received anesthesia: general anesthesia and spinal anesthesia, with and without peripheral nerve block. One to 24 months after operation, the effects of those anesthetic techniques on the postoperative clinical outcome were retrospectively examined. The main focus was on the effect on the opioid consume and on the perception of pain. Secondary emphasis was placed on mortality and complication rates, blood management, anesthetic induction time, hospitalization time and other parameters of the postoperative course.

Results

Of 656 patients, 425 (64.8%) received general anesthesia and 231 (35.2%) spinal anesthesia when undergoing TKA. Multivariable analysis revealed significantly lower total opioid intake when applying spinal anesthesia by 2.08 mg (95% CI 0.1-4.1, $P<0.04$) of morphine-equivalent and a reduction of 6.95 minutes (95% CI 5.17–8.72, $P<0.001$) till skin incision. In return, a higher perioperative blood loss of 90.1 ml (CI 95% 17.91–162.23, $P=0.015$) was observed. The application of a peripheral nerve block achieved a reduction of early-postoperative piritramide intake of 3.59 mg (95% CI 1.5-5.7, $P=0.001$), but lengthened induction time by 8.48 minutes (95% CI 6.63–10.36, $P<0.001$). No statistically significant differences were found regarding the complication and mortality rate, need of blood transfusions, length of stay, time until gait training started, and postoperative flexibility ($P>0.05$).

Conclusion

In this study, shorter anesthetic induction times and lower postoperative opioid dosages were observed for patients undergoing total knee arthroplasty with spinal anesthesia. The additional implementation of peripheral nerve blocks led to a lower need for opioids and to lower pain levels in the early postoperative phase.

1 Introduction

The topic of this thesis "A Comparison between Spinal Anesthesia versus General Anesthesia and the Use of Peripheral Nerve Blocks in Total Knee Arthroplasty" deals with the knee, total knee arthroplasty (TKA) and in addition with different anesthetic methods specific for TKA. It presents an interdisciplinary collaboration of the orthopedic/traumatological and anesthetic departments. Finally, a retrospective study is presented and the results were compared with the latest and most important research about this topic.

1.1 The Knee and the Total Knee Arthroplasty

The first part of this thesis focuses on the knee in general and TKA. Indications and contraindications for performing TKA are presented and as well as diagnosis und preoperative management. The topic of the surgical process is explained in detail, including implantation techniques, prosthesis designs and surgical alternatives. The methods of postoperative care and rehabilitation are discussed separately. This chapter of the thesis also deals with common peri- and postoperative complications after TKA and finally shows the early and long-term clinical outcome.

1.1.1 The Knee Joint

1.1.1.1 Anatomy of the Knee Joint

In the following section, the anatomy of the knee joint is briefly explained and visually shown to get a general overview of the knee, its components and function.

1.1.1.1.1 General Aspects

The knee, in technical terminology the Articulatio (Art.) genus, is the biggest joint of the human body, formed by three bones: the femur, the tibia and the patella. More specifically, the knee is a composite joint, consisting of the Art. femoropatellaris and the Art. femorotibialis. It presents a special form of hinge joint, called trochoginglymus. It allows bending of the knee through sliding and rolling movements and furthermore, rotating movements exclusively in bended position. The complex movements of the knee are possible through the interaction of different muscles, ligaments, menisci and bursas [1, 2].

1.1.1.1.2 Bone Structures

As already mentioned, the knee consists of three bones, which form two joints. The femoropatellar articulation, consisting, as the name already says, of the femur and the patella and secondly the femorotibial articulation, with the femur and the tibia [2].

The biggest bone of the knee joint is the femur. Distally the femur widens and forms the Condylus medialis and lateralis (Fig. 1). The condyles are connected on the ventral surface through the Facies patellaris, which connects with the patella. The condyles are separated by the Fossa intercondylaris at the dorsal surface. Proximal of the condyles are the Epicondylus medialis and in accordance on the other side, the epicondylus lateralis, serving as insertion points for muscles and ligaments [2].

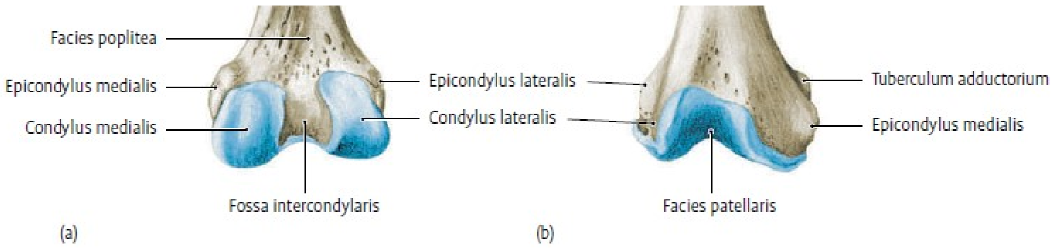

Figure 1: Distal part of the femur from dorsal (a) and ventral (b) [1].

The knee joint facing parts of the tibia are the medial and the lateral tibial condyles of the tibia head as seen in Fig. 2. They are separated by an elevation in between, called the intercondylar eminence. It consists of the medial and lateral intercondylar tuberculum, which form the attachment point for the cruciate ligaments. The surface on the top of the tibia, on the tibia plateau, presents the articular surface [1, 2].

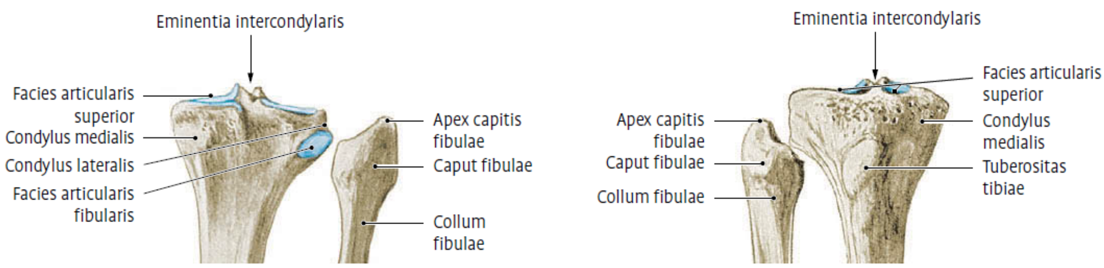

Figure 2: Proximal part of the tibia and fibula from dorsal (left) and ventral (right) [1].

The third bone structure of the knee joint is the patella, shown in Fig. 3. The patella, colloquially the kneecap, is the biggest sesamoid bone with a triangular shape, in which the basis is aligned proximal and the tip is pointing distal. The basis serves as muscular insertion for the tendon of the M. quadriceps femoris. The apex provides the connection to the tibial tuberosities through the Lig. patellae. On the outer side, the patella has a rough surface, while the inner side forms a smooth articular surface [1, 2].

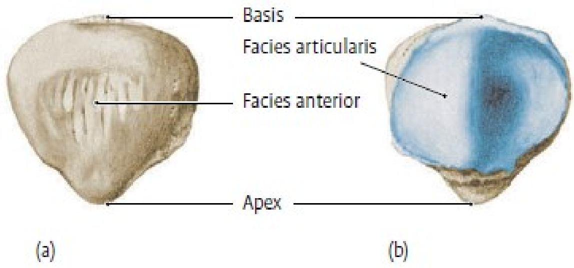

Figure 3: Patella from ventral (a) and dorsal (b) [1].

1.1.1.1.3 Ligaments

In general, ligaments can be divided according to their function into three different types: reinforcing ligaments for protecting articular capsules, leading ligaments for guiding movements and inhibiting ligaments for movement limitations. Furthermore, ligaments can be either extracapsular, capsular or intracapsular [2]. The most important ligaments of the knee joint can be seen in Fig. 4 and Fig. 5.

Ventral of the knee joint is the Lig. patella, serving as continuation of the M. quadriceps and reaching from the tip of the patella to the tibial tuberosity [2]. Lateral as well as medial of the patellar ligament aligns the Retinaculum patellae, reinforcing the capsule on the sides and working as a reserve flexing apparat [1].

There are two collateral ligaments on the knee joint. Firstly, the Lig. collaterale tibiale, which connects the Epicondylus medialis femoris with the Fac. medialis tibiae. The posterior fibers are bond with the medial meniscus. Secondly, the Lig. collateral fibular, located on the lateral side of the knee joint. It has its origin at the Epicondylus lateralis femoris and goes to the Caput fibulae [1].

The popliteal oblique ligament strengthens the dorsal part of the knee. It is part of the insertion tendon of the M. semimembranosus and reaches from distal medial to proximal lateral [1]. The Lig. Popliteum arcuatum arises from the Apex capitis fibulae and runs into the capsule and intracapsular to the lateral femoral epicondyle. Its function is to support the dorsal lateral part of the capsule [1, 2].

The cruciate ligaments, Ligg. cruciate, are located between the synovial stratum and stratum fibrosa of the articular capsule, which indicates that they are extraarticular but intracapsular. The anterior cruciate ligament (ACL) arises from the Area intercondylar anterior of the shinbone to the inner surface of the lateral condyle femoris. Contrary is the posterior cruciate ligament (PCL), the stronger ligament of both. It has its origin on the Area intercondylar posterior and connects to the lateral surface of the medial femoral condyle [1, 2]. The cruciate ligaments secure the movements of the knee joint in the sagittal, frontal and furthermore in the horizontal plane and prevents a shifting of the femur from the tibia [1].

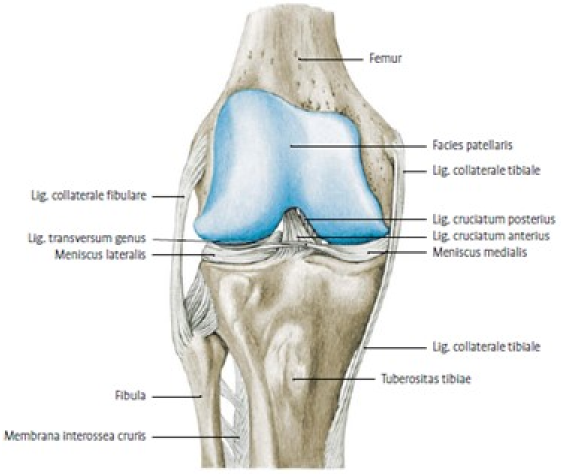

Figure 4: Ligaments of the knee from ventral with removed capsule [1].

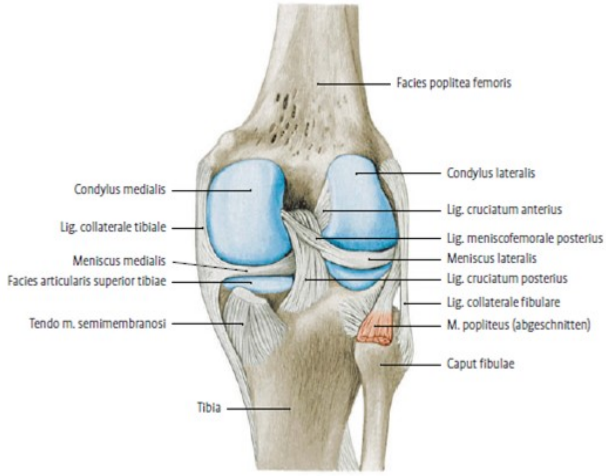

Figure 5: Ligaments of the knee from dorsal with removed capsule [1].

1.1.1.1.4 Menisci

The menisci are essential parts of the Art. femorotibial. The condyles of the femur and the plateau of the tibia head cannot lie directly flat to each other because of their incongruities. For this reason, the menisci lie in between, to improve their contact. Furthermore, they decrease the pressure on the articular surface, and they help to guide movements. When the knee is bending the menisci are pushed dorsal by the femoral condyles [1].

Fig. 6 shows the two menisci of the knee joint, the medial half-moon shaped medial one and the nearly circular lateral one. They are wedged shaped articular discs, made of fibrous cartilage, and are located between the femoral and tibial joint surfaces. The blood supply for the menisci is provided by the A. media genus, but only reaches the borders. The central parts are free of vessels and are supplied by the synovia. The menisci are both attached with tight ligaments from their anterior and posterior horn to the Area intercondylar anterior or rather posterior. In addition, they are linked together with the Lig. transversum genus (Fig. 6) at both front horns [1, 2].

The medial meniscus has the form of a half-moon and is tightly fixed with the Lig. collateral tibial. Through this attachment, it is less moveable than the lateral meniscus. The front horn, the Crus anterius, is thinner than the Crus posterius. About 95% of all damages of the menisci fall back to the medial meniscus, which is especially fragile during the outer rotation of the tibia due its limited mobility [1, 2]. On the contrary, the lateral meniscus is circular shaped. Because of no fixed attachment with a collateral ligament it is much more flexible and therefore less vulnerable [2].

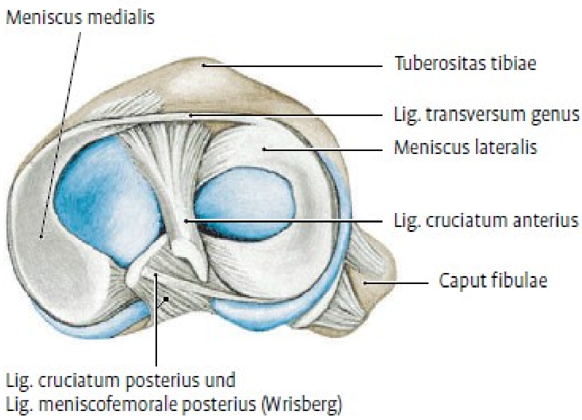

Figure 6: Proximal surface of the tibia with the menisci and cruciate ligaments [1].

1.1.1.1.5 Muscles

The skeletal muscles are the locomotive system of the human body. Generally, each skeletal muscle has at least two attachment points, one origin and one insertion or more. Tendons mostly form the attachments. The tendons merge into the muscular fibres and form the muscle [1].

Precise movements of joints are possible through the interaction of different muscles and ligaments. Another purpose of the muscles is stabilization and protection of joints and bones. They can be classified equal their function into flexors, extensors, internal rotators, and external rotators, but also into adductors and abductors. However, the knee has neither adductors nor abductors. For a general overview, Tab. 1 shows all muscles of the knee joint as well as their function, nerval innervation, origin, and insertion bone.

Table 1: Muscles of the knee joint and their function, origin, insertion and neural innervation [1, 3].

Muscle	Origin	Insertion	Neural Innervation
Extensors			
M. quadriceps femoris	Hip (ileum) and femur	Patella and tibial tuberosity via the Patellar ligament	N. femoralis (L2-L4)
M. rectus femoris	*Hip (ilium)*	*Patella*	*N. femoralis*
M. vastus medialis	*Femur*	*Patella*	*N. femoralis*
M. vastus lateralis	*Femur*	*Patella*	*N. femoralis*
M. vastus intermedius	*Femur*	*Patella*	*N. femoralis*
Flexors			
M. gastrocnemius	Femur	Tendo-calcanei	N. tibialis (S1-S2)
Caput medial	*Femur*	*Tendo calcanei*	*N. tibialis (S1-S2)*
Caput lateral	*Femur*	*Tendo calcanei*	*N. tibialis (S1-S2)*
M. plantaris	Femur	Tendo calcanei	N. tibialis (S1-S2)
Flexors and internal rotator			
M. semimembranosus	Hip (ischium)	Tibia, Pes anserinus	N. tibialis (L5-S2)
M. semitendinosus	Hip (ischium)	Tibia, Pes anserinus	N. tibialis (L5-S2)
M. gracilis	Hip (Pubis)	Tibia (Pes anserinus)	N. obturatorius (L1-L2)
M. sartorius	Hip (ilium)	Tibia (Pes anserinus)	N. femoralis (L2-L3)
Flexors and external rotator			
M. biceps femori	Hip (ischium) and femur	Fibula	N. tibialis (L5-S2)
Caput longum	*Ischium*	*Fibula*	*N. tibialis (L5-S2)*
Caput breve	*Femur*	*Fibula*	*N. tibialis (L5-S2)*
Others			
M. popliteus	Femur	Tibia	N. tibialis (L5-S2)

1.1.1.1.6 Joint Capsule, Joint Cavity and Bursas

In general, the bone parts creating the joint, are covered with hyaline cartilage and form an articulation surface. The joint is enclosed by the capsule, creating the joint cavity filled with the synovial fluid. The joint capsule is fixed on the border of transition from bone to cartilage. Structures in joints can be in different sections, intraarticular or intracapsular but extraarticular. Intraarticular are all structures with contact to the synovial fluid. Intracapsular but extraarticular are structures between the fibrous and synovial membrane. The synovial fluid nourishes intraarticular parts, which do not have any direct blood supply by vessels [1].

The joint cavity is widely ramified through its prominent ligaments, joint communicating bursas, the two menisci and several folds formed by fatty deposits and the synovial membrane. The purpose of those folds is to increase the movability of the components in the joint. The biggest fatty deposit is the infrapatellar fat pad, the so-called Hoffa's fat pad. It is located at the basis of the patella and its lateral parts are called the plicae alares. The several bursa sacs are supporting the function of the knee joint by protecting bones and surrounding tissues from mechanical pressure produced by grinding tendons. A bursa is defined as a synovial membrane filled with a synovial liquid. Bursas can be classified into communicating and non-communicating bursas, depending on their connection to the joint cavity [1]. The most important bursas of the knee joint, as well as their location are shown in Tab. 2.

Table 2: Most important communicating and not communicating bursas of the knee and their location [1].

Bursa (B.)	**Location**
<u>Communicating Bursas</u>	
B. suprapatellaris	Ventral of the knee joint, above the patella, covered with the M. quadriceps
B. m. semimembranosus	Dorsal of the knee joint, under the origin of the M. semimembranosus
B. subtendinea m. gastrocnemii lateralis	Dorsal at the origin of the M. gastrocnemius
B. subtendinea m. gastrocnemii medialis	Dorsal at the origin of the M. gastrocnemius
Recessus subpoplitues	Between the articular capsule and the origin of the M. popliteus
<u>Not-communicating Bursas</u>	
B. subcutanea praepatellaris	ventral of the patella
B. infrapatellaris profunda	Between Lig. patellae and the fibrous membrane

1.1.1.2 Functional Biomechanics of the Knee Joint

The knee joint is able to perform flexion and extension and when bended also internal and external rotation. Abduction or adduction in the knee is not possible. The movements are restricted through ligaments and muscles. Especially the cruciate and the collateral ligaments are limiting and leading the motions. An overview of the possible movements and theirs limits are shown in Tab. 3 [1].

Table 3: Movements and their extent and as well as the status of the ligaments [1].

Movement	**Active**	**Passive**	**cruciate ligg.**	**collateral ligg.**
Flexion	120°	160°	tight	loose
Extension	0°	5-10°	loose	tight
<u>Extended knee</u>				
Internal rotation	5-10°		loose	tight
<u>Flexed Knee</u>				
Internal rotation	10°	10°	loose	tight
External rotation	40°	40°	tight	loose

The characteristics of the different ligaments at different position of the knee are shown in Fig 7. As seen the collateral ligaments are tight stretched at maximal extension and by doing so avoiding rotation movements. When the knee is in flexed position the lateral collateral ligament is completely loose and the medial collateral ligament mostly, while the cruciate ligaments are stretched [1, 2].

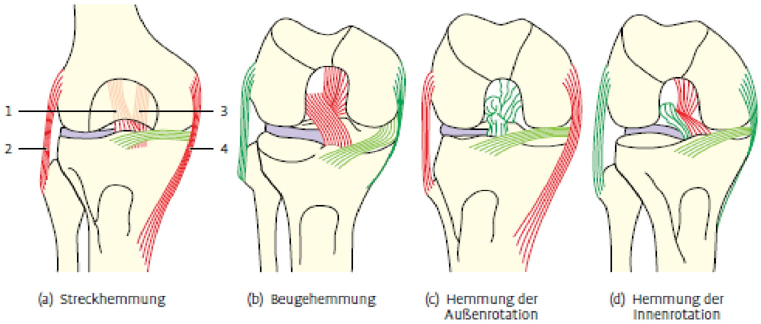

Figure 7: Collateral and cruciate ligaments during maximal movement of the knee. Tight ligaments are red, loose ones green. 1= ACL, 2= Lig. collaterale fibulare, 3= PCL, 4= Lig. collaterale tibiale [1].

As already mentioned, rotation movements of the knee are only possible in flexed position. Doing so, the internal rotation reaches not more than 10°. The extent of the external rotation is larger with a maximum of 40°. During internal rotation, the cruciate ligaments are twisted together and tightened and, in that way, stopping further rotation. The external rotation on the other hand, twists apart the cruciate ligaments and looses them. In reverse behave function the collateral ligaments: in internal rotation loose, in external rotation tight (Fig. 7). Furthermore the capsule itself restricts movements when the knee rotates [1].

1.1.2 Knee Arthroplasty

1.1.2.1 General Aspects and Statistics

Operations on the knee joint are procedures with high relevance in hospitals. Actually, they are by far the most performed operations of the musculoskeletal system in Austria. The Austrian National database analysis counted in total 79 231 operations of the knee joint in the year 2017. Only operations on the eye had been ranked higher regarding quantity of performed surgeries [4].

A substantial proportion of this amount is contributed by the TKAs. In Austria 20 153 primary TKAs were performed in the year 2017, in 95.7% of the cases with diagnosed osteoarthritis or chronic arthritis [5]. In other words, these were about 230 primary TKAs per 100 000 inhabitants. In comparison, there were only 202 primary knee replacements per 100 000 inhabitants performed in the year 2015 in Austria. These statistics are showing that the number of primary TKA are constantly growing each year as seen as well as in Fig. 8 [6].

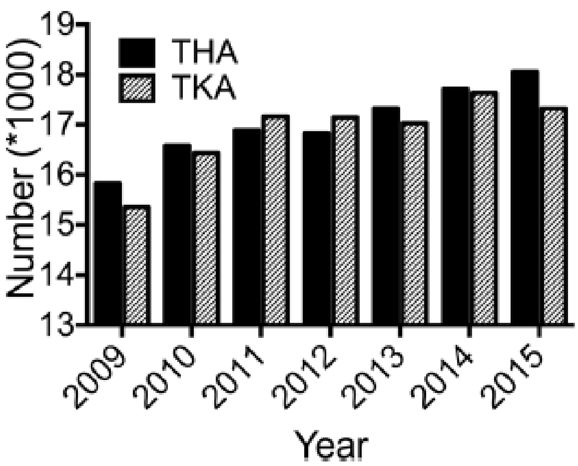

Figure 8: Primary THA and TKA performances per year in Austria from 2009 to 2015 [6].

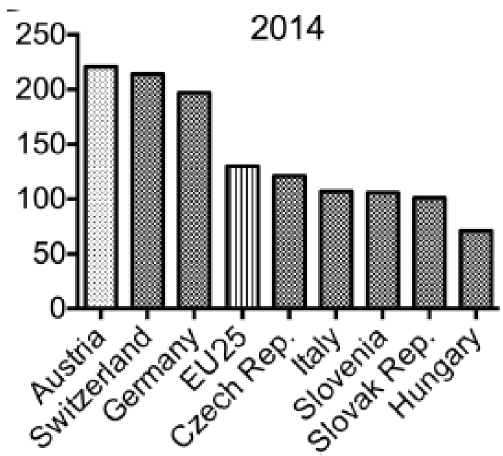

Figure 9: Knee replacement surgeries performed in 2014 per 100.000 inhabitants in Austria and neighboring countries [6].

Internationally compared, Austria had the highest rate of TKA per inhabitant of all OECD countries in 2014 (Fig. 9) [6]. Worldwide there is a large variation of primary TKA performances per 100 000 inhabitants, ranging from 30 to over 200 TKAs [7]. Statistics have also shown big regional differences in aspect of implant techniques, use of bone cement and patellar resurfacing. Factors, that could explain such international variety, are patient demographics, national conditions such as healthcare system, numbers or availability of medical facilities and surgeons, and as well as the ability of the national surgeons [7].

1.1.2.2 Indications for TKA

No generally valid indication criteria for TKA have yet been established. Some studies already have presented different international guidelines and indication criteria, but based on limited and low-quality evidence [8]. About 10-20% of patients are unsatisfied with the outcome of a TKA [9], which may occur due a rushed decision. To reduce such a dissatisfaction, standardized guidelines should be established which surely can give the indication for conducting the surgery. However, the fact that evaluated parameters often do no correlate, for example clinical symptoms and radiographical changes, complicates to find evidence-based indications [8].

One of the most recent guidelines is presented by the "Deutsche Gesellschaft für Orthopädie und Unfallchirurgie (DGOU)" by Luetzner et al. This guideline aims to simplify the decision for TKA by demonstrating minimal requirements (main criteria), additional important aspects (minor criteria), and as well as relative and absolute contraindications for TKA [9].

The main criteria present the minimal requirements and must be fulfilled. They consist of knee pain, inadequate response to conservative treatment, radiological confirmation of osteoarthritis or osteonecrosis, adverse impact of knee disease on the quality of life of the patient and the burden of suffering due to the knee disease. These main criteria should exist at least for 3-6 month before considering surgical intervention [10].

On the other hand, the minor criteria, which are not necessary for indication but can strengthen the recommendation of undergoing a TKA. These involve limitations of everyday movements and restrictions in physical activities and occupation. Other parts of the minor criteria are malalignment of the knee joint, instability of the knee and reduction of the range of motion [9, 10].

1.1.2.2.1 Osteoarthritis

The severe knee pain because of osteoarthritis knee joint is the most common cause for undergoing TKA with an incidence of 95% of all TKAs [11].

1.1.2.2.1.1 Definition and Classification

Osteoarthritis is defined as an abrasion of the cartilaginous articular surface of a joint. Firstly, the osteoarthritis can be divided into a primary or a secondary osteoarthritis of which the primary occurs idiopathically. Additionally it could also be separated into a located and generalized form, whereby generalized means the affection of three or more joint groups [12]. On the other hand, there is the less common secondary osteoarthritis with a known etiology [13, 14].

The osteoarthritis can affect various parts of the knee joint. It can be unicompartmental patellofemoral, unicompartmental femorotibial or bicompartmental femorotibial. If the arthrosis involves all three joints of the knee, it is termed as tricompartmental patellofemorotibial gonarthrosis, also known as pangonarthrosis. The osteoarthritis preferably destroys the lateral or medial compartment of the femorotibial joint and is therefore divided into a varusgonarthrosis or valgusgonarthrosis [15].

The most used classification is done by the evaluation of the x-ray presented by Kellgren and Lawrence , which divides the OA into five grades as seen in Tab. 4 [16].

Table 4: Classification of OA by the Kellgren-Lawrence method.

Grade	Changes of the joint seen on x-ray
0	No signs of arthrosis
I	Initial osteophytes
II	Definitive osteophytes, moderate joint space narrowing, moderate subchondral sclerosis
III	Loss of half of the joint space, extensive osteophytes, extensive subchondral sclerosis
IV	Joint destruction, most to complete loss of joint space height, cystic change, subluxation

1.1.2.2.1.2 Symptoms

Patients suffer mostly from pain in the knee, which is often accompanied by swelling and partly with joint effusion. Initially the pain is load-dependent, later in more advanced progression, the pain also occurs during nighttime and while resting. Typically the symptoms improve after moving for a while [16].

Usually, the progression of the primary osteoarthritis proceeds slowly while the secondary osteoarthritis can worsen rapidly [16]. At first, the mobility of the knee is more limited in flexion movements than in extension, due a periarthropathy of the neighboring structures. With further degradation comes along a flexion restriction up to 90°, which is usually more tolerable than the extension deficit of 10-20°. These limitations stimulate the development of the osteoarthritis, which results in axis misalignments and pain associated physical inactivity. Consequently it comes to an atrophy of the M. quadriceps and a worsening of the nutritive supply of the cartilage [17].

1.1.2.2.1.3 Risk Factors

According a study of O’Neill et al. risk factors for knee OA can be separated into two categories. Firstly, into systemic factors, including gender, genetics, ethnicity, BMI, bone mineral density and age. Secondly into mechanical or local factors, including joint structure and alignment, trauma, physical activity, muscle strength and occupation [18].

An unavoidable risk is the age. The estimate lifetime risk for developing symptomatic knee OA is about 40% for men and 47% for women. Incidence rates are rising sharply after the age of 50, and leveling off after age 70 [19].

After age, obesity is the second most common risk factor for developing osteoarthritis. Overweight (BMI 25-30 kg/m2) and obese (BMI>30 kg/m2) people have a 2.66 times higher risk to develop knee OA than people with normal BMI. On the other hand, weight loss is associated with a high reduction of the risk of developing knee OA. Other significant risk factors are ethnic differences, genetic components and decreased bone mineral density [18].

1.1.2.2.2 Inflammatory Arthritides

The risk that inflammatory arthritides can lead to advanced knee joint destruction and consequently to the necessity of a TKA, has decreased dramatically. The reason is mainly the utilization of disease-modifying antirheumatic drugs. The most common inflammatory disease of the knee is the rheumatoid arthritis. Others are the gout, the psoriatic arthritis and the spondyloarthritis [20].

1.1.2.2.3 Other Causes

There is a wide variety of other diseases, abnormalities and disorders that may destroy the cartilage of the knee and require the need of a TKA. However, the risk to progress that far is highly unlikely. TKA might be indicated for posttraumatic arthritis after sports-related injuries or accidents. Furthermore the risk also exists for tumor diseases, sequelae of infections, avascular necrosis and congenital joint abnormalities [21].

1.1.2.3 Contraindications for TKA

The contraindications for TKA can be divided into two groups. The absolute contraindications, which prohibit the execution of a TKA completely and the relative ones, which discourage the performance of a TKA, but do not exclude it [9].

Undergoing TKA is absolutely forbidden with existing florid systemic or local infections as well as dysfunction of soft tissues and skin. Included are also general contraindications for surgeries, acute cardiovascular events, severe illness or vascular dysfunction [9, 22].

Relative contraindications are a clearly reduced lifespan because of comorbidities and a BMI >40kg/m². Obesity is associated with peri- and postoperative risks, more difficult condition for an operation, higher risk of mispositioning of the prosthesis and general worse postoperative outcome. An operation may be also contraindicated by an insufficient extension of the knee of neurological etiology [9, 10].

1.1.2.4 Conservative Therapy

Regarding Luetzner et al. [9] conservative therapy should be carried out primary for at least 3 months before considering invasive methods. The general goal is reduction of pain, improvement of functionality of the knee, and delaying operative interventions. The first step of conservative therapy consists of change of lifestyle including weight reduction and avoiding overload on the knee. Another approach of conservative therapy is pharmacological. Thereby pharmaceuticals can be applied locally, perorally or intraarticularly. Oral medication includes especially NSARs, but also other nonopioids like paracetamol or metamizole are possible. For treatment of severe and chronic pain, opioids are often the last pain reducing choice. Alternatively, infiltration of the knee joint with cortisone could be considered. A principal element of conservative therapy is as well physiotherapy for strengthening the involved muscles and for maintaining flexibility. Some patients also benefit from cryotherapy, ultrasound therapy and applying of heat for treating chronicle complaints. Orthopedic aids and shoe inlays are also recommended to reduce the pressure on the joint by improvement of the force distribution [10, 13].

1.1.2.5 Surgical Treatment

If conservative treatment fails, surgical intervention should be considered. There are several different surgical approaches for the treatment of chronicle knee pain and osteoarthritis. The most common operation and gold standard for treating chronicle severe knee pain is the TKA with a frequency of 83%, followed by unicondylar knee replacements with 14%. The remaining surgical possibilities for treating severe knee pain are the knee arthroscopy and the correction of the axis by osteotomy [23].

1.1.2.5.1 Prosthesis Designs

Surgeons have many different possibilities to choose from when it comes to performing a TKA. There are several prosthesis designs and manufactures, for different requirements and individual preferences. A knee prosthesis basically consists of at least two components anchored in the bones and one interposed slide or rotary module. Most available systems are modular with a metal tibia tray containing polyethylene spacers. The designs of the prosthesis mostly differ in their mechanical constraint. Therefore, there are three general designs: unconstrained, semi-constrained and constrained. Apart from this, they can also vary through the existence of hinges and bearings. Furthermore, the implants can be attached to the bone with different fixation techniques. Either fixation with bone cements or relying on the bone growth into the prosthesis surface are possible Another decision to make is about the handling of the patella if it is going to be resurfaced or kept as it is. Lastly, there are different approaches of the implantation technique of the prosthesis [13, 21].

1.1.2.5.1.1 Unconstrained Implants

Unconstrained implants replace the cartilage surface of two or three compartments with a femoral component, a tibial component and if necessary, with a patellar component. These implants enable nearly normal knee joint function with similar roll and slide movements, but limited rotation options. The congruence between the two components is given by the inlay, which adjust the contact surface and the distribution of the pressure. For unconstrained implants it is essential that the joint is sufficient stabilized through the collateral ligaments and muscles, while constrained implants are stabilized through the implant itself and its coupling mechanism [24, 25].

Another important aspect is the handling of the cruciate ligaments. The ACL is mostly unnecessary when putting in an unconstrained prosthesis and is usually removed. Regarding the PCL, there exist two different approaches. Implant designs can either retain the posterior cruciate ligament, which is called cruciate-retaining, or on the other hand remove the PCL, known as cruciate-substituting/posterior stabilized. The advantages of the cruciate-retaining method are a smaller intracondylar bone removal and the maintaining of stabilizing and proprioceptive qualities of the PCL. However, the PCL is often already damaged due the arthrosis and must be removed and replaced by a special inlay. This inlay stabilizes the knee sagittal with a pin fitting into a notch [21, 25].

Depending on the congruence between the components, two different bearings are used, the mobile and the fixed bearing. At the fixed-bearing variation, the polyethylene inlay is fixed on the tibial component. In contrast stands the mobile bearing, in which the inlay can rotate and slide on the tibial component. It can furthermore be divided into floating models, with anterior posterior translation and with rotating movements, and into rotating models, with inner and outer rotation [13, 24, 25].

1.1.2.5.1.2 Semi-Constrained Implants

When the collateral ligaments cannot provide sufficient knee stability semi-constrained or even constrained implants are considered. Semi-constrained implants partially compensate the instability in frontal and sagittal plane. This is provided by an extended pin in the polyethylene inlay, which connects to an intercondylar box on the femoral component for supporting movements. Semi-constrained implants are usually indicated for mediolateral instability as well as for distinct varus or valgus position [24, 25].

1.1.2.5.1.3 Constrained Implants

Nowadays constrained implants present a treatment mainly for revision surgery. However, they are rarely also used primarily for severe cases, including severe deformity and instability. Less than 1% of the primary implanted prosthesis are constrained. These implants are divided regarding their coupling mechanism into rotating-hinge and fixed-hinge models. The disadvantage of these systems is the lack of mobility and therefore more force is shifted on the components of the prosthesis and on the fixation in the bone. For this reason, the shaft of the prosthesis is prolonged femoral and as well as tibial to guarantee more stability. Consequently, there is more loss of bone substance and higher shear forces affect the interface of cement and bone [13, 21, 24].

1.1.2.5.2 Fixation Techniques

As already mentioned, the implants are fixed with the use of cement or without to the bone. The trend shows that the variation with cement got the upper hand over the years because of improvements of the cementing technique. Studies have even shown that nowadays cement is used in up to 90% of the cases of TKAs. The main reason is that the rate of loosening prosthesis occurs 1,5 more often when using cement-free fixation [7].

1.1.2.5.3 The Implantation of the Prosthesis

The TKA is basically performed by resecting the destructed articular surfaces of the tibia and femur, followed by resurfacing with metal and polyethylene prosthetic components. In this chapter a condensed version of a standard TKA is explained with the most common approaches and methods.

The implantation of a knee prosthesis usually begins with a vertical skin incision at the anterior midline area of the knee for a deep medial parapatellar approach. The patella is then everted with a lateral flap which exposes the distal femur and allows easy access into the joint. Disturbing soft tissues and osteophytes on the edges of the bone are then removed. Then the menisci and the ACL then carefully excised [25, 26].

The knee is set up upright in flexed position to determine the appropriate prosthesis sizes and the correct alignment with the use of manual instruments and navigation systems. Subsequently the surgeon begins with the bone resections suitable for the surface of the prosthetic fixations. There are two different initial preparation approaches: the tibia first and the femur first technique, second being the traditional, more common one. Special instrumentation systems allow precise bone cuts and help to reproduce anatomic alignment of the knee joint [25, 26].

After the cuts of the bone and before definitive fixation of the prosthesis, the position, the stability, and the range of motion are checked appropriately. Soft tissues balancing is a crucial step to achieve a joint with functional ligaments and with a symmetric flexion and extension gap [25, 26].

In the next step a jet lavage is performed to prepare the bones for the implantation of the implants. After a final lavage and removing of fragments of bone and excess cement, the surgeon can go ahead with the closure. Closuring is done in layers starting with the retinaculum, then fat, subcutaneous tissue and lastly the skin. Before closure a drain system with a vacuum mechanism is usually installed to collect blood postoperatively. [25, 26].

1.1.2.5.4 Perioperative Care

Information about anesthesia and anesthetic techniques in general and specific for TKA, are explained in detail on the second part of this thesis.

1.1.2.5.4.1 Minimizing Perioperative Blood Loss

The perioperative blood loss ranges approximately from 650 to 1400 ml when performing TKA [27]. By using blood saving techniques this amount can minimized. Common techniques for TKA are the use of a tourniquet and the administration of tranexamic acid. The lost blood can also be retransfused with intraoperative autotransfusion.

1.1.2.5.4.2 Antimicrobial Prophylaxis

Infections of the prosthesis and of the wound can drastically be minimized to under 1% using systemic prophylactic antibiotics prior surgery. Recommended are in particular cephalosporine of the second generation. A preoperative single shot or/and an administration for three days intravenously have proven satisfactory results. The first dose of antibiotic is usually applied 30 to 60 minutes before the operative intervention [25].

1.1.2.5.4.3 Thrombosis Prophylaxis

There exists a substantial risk for patients undergoing TKA for venous thromboembolic events when no preventive measures are introduced. The development of a deep vein thrombosis (DVT) or pulmonary embolism (PE) are potentially lethal complications of knee surgery. There is a chance to suffer a DVT following TKA of 40 to 88%. Furthermore, the risk for an asymptomatic PE ranges from 10% to 20%, for symptomatic PE from 0,5% to 3% and has a mortality rate up to 2% [21].

Fortunately, the incidence of venous thromboembolic events can be dramatically decreased by the use of prophylactic anticoagulation to approximately 1% [21]. The most relevant method to prevent a thrombosis or an embolism is a therapy with low dosage heparin, the use of fondaparinux or other anticoagulants. The anticoagulant or heparin are given about six hours postoperative, to prevent high blood loss during the operation and should last about six weeks [24, 25].

1.1.2.5.5 Postoperative Care and Rehabilitation

An adequate postoperative management after TKA is essential to achieve the best possible outcome, fast return to full function and increasement in the quality of life. Postoperative treatment includes minimization of postoperative morbidity, adequate pain management and appropriate physical therapy. The rehabilitation depends on different factors, like type of implant, operative approach and as well as the individual condition of the patient [21, 24].

After surgery, the patient is referred to the PACU and when stable to the orthopedic ward. During the ward rounds patients are examined by checking the peripheral circulation, sensitivity, and motor function of the operated extremity. Furthermore, the drains, with the collected postoperative blood loss, and the bandages are controlled [13].

A postoperative knee radiography takes place standardly one to three days after implantation in two plains. Complete blood test and electrolytes are measured on the first postoperatively day and then on every second day. Especially the hemoglobin values form an important indicator for postoperative blood loss and the need of blood cell transfusions. Existing drainages should be removed 12-24 hours postoperative, depending on the postoperative bleeding [21, 24]. Patient usually stay hospitalized five to 15 days, depending on comorbidities and local practice [24]. The typical follow-up schedule starts with wound review and suture removal within two weeks. Clinically improvement should be noticeable between the sixth and twelfth postoperative week. Fully recovery should be expected between one and two years after the operation [21].

1.1.2.5.6 Mobilization and Physical Therapy

The mobilization of the patient usually can be started on the first postoperative day with the help of a physiotherapist. Starting with active and passive exercises early on to achieve maximal flexion has shown reliable results. If possible, patients can try walking attempts using assistive devises. An extensive physical therapy includes range of motion exercises, gait training and training in activities of daily life. Also, the treatment with a CPM (Continuous Passive Motion) machine along with quadriceps muscle strengthening has shown positive results in the postoperative rehabilitation. Rehabilitation goals should always be set realistically according the preoperative flexion range [21, 25].An average maximal flexion of total knee prosthesis is an angle around 115 degrees [28].

Additionally, several physical possibilities can influence the rehabilitation process positively including lymph drainages, compression, and cryotherapy. Such measures attribute to a reduced inflammatory reaction and help to reduce secretion and bleeding [24]. Even computer-controlled cooling therapy devices are used and have shown a better outcome in early remobilization concerning ROM and pain [29].

1.1.2.5.7 Surgical Alternatives to TKA

Other surgical approaches than TKA are knee arthroscopy, osteotomy, joint resurfacing only and unicompartmental arthroplasty [30].

Knee arthroscopy only have little value in the treatment of chronicle knee pain. Several different techniques are used, including simple lavage, debridement, abrasion, attempted repair of cartilage defects, and arthroscopic cartilage transplantation to reduce pain and increase the range of motion [10, 31].

Another alternative is the unicompartmental knee arthroplasty, which is limited to either to the medial or the lateral compartment. It is indicated when the knee is affected unicompartmental, with intact stability and physiological axes without large deformities and sufficient mobility. The advantages over the TKA include a quicker recovery, improved range of motion and a less invasive operation. Studies have shown that especially older patient benefit from this approach. However, unicompartmental knee prosthesis have exposed a higher revision rate than total knee replacements [10, 31].

One of the best options for younger and more active patients with unicompartmental arthrosis is the knee osteotomy. It is especially considered for patients under 55 years [32]. For the treatment of a varus knee a high tibia osteotomy is indicated, for a valgus knee a distal femoral osteotomy. The basic goal of an osteotomy above the knee is to unload the damaged compartment by realigning the mechanical axis of the lower extremity. With this method it is possible to delay the time until TKA for about 10-15 years [10, 33].

1.1.2.6 Complications in TKA

Fortunately, complications are infrequent with TKA. They can be divided into general and special complications, but also according their occurrence into intraoperative, perioperative and postoperative [31].

General complications include development of a thrombosis and embolism, postoperative hematoma, injuries of vessels and nerves, secondary bleeding, and wound healing disturbances. Special complications involve any problems regarding the knee joint, its ligaments, bones, muscles and of course with the prosthesis [25].

Intraoperative injuries of nerves are exceedingly rare. Affected is mostly the N. peroneus with an incidence of 0 - 9,5%. However, the prognosis seems to be particularly good and lasting damages are an exception. Even rarer are injuries of the vessels. The frequency of damaging the A. poplitea during a TKA has an incidence rate of 0,03-0,05% [26, 31].

Fractures during the operation may happen because of wrong technical execution, like too much bone resection or wrong fixation of the components. Perioperative fractures are mostly located in the femoral condyles or supracondylar [26, 31].

Sealing disturbances of the skin can be categorized into protracted wound secretion, skin necrosis and superficial infect. It is important to differentiate from deep infections of the prosthesis. The priority is the prevention of infection spreading into the deep tissues to the prosthesis [24].

The ligaments can be easily damaged during surgery. The reason is mainly inadequate tissue protection due wrong positioning or not carefully performed meniscal resection. An irreversible damaged ligament mostly leads to the necessity of implanting a constrained prosthesis. Another ligament saving possibility is an operative reconstruction by transossary refixation or interligamental suture [24, 25, 31].

The complex geometry of knee implants favors abrasion of the polyethylene components. The abrasion can provoke aseptic loosening and instability of the prosthesis with a 1-2% possibility within 10 years. The abrasion-related loss of substance is associated with patients' activity, the quality of the polyethylene and the implant design [25].

Anterior knee pain, or also known as patellofemoral pain, is most of the time associated with errors of rotational alignment. About 15% of patients suffer from this pain after endoprosthetic interventions on the knee [25].

Infections can either appear locally with redness, swelling and overheating or effect the entire body with symptom like fever and chills. There is a classification into an early infection, which appears until four weeks postoperative, and into a late infection. The average rate of an infection of the prosthesis for a primary implantation is about 1-2% [25].

1.1.2.7 General Outcome

The general outcome is defined as the mortality rate, the improvement in quality of life, patient satisfaction and the durability of the prosthesis. The outcome depends on multiple factors such as prosthesis design, age, level of physical activity, causative disease, obesity and more [34].It is important to mention, that about one of five patients are unsatisfied with the outcome after TKA. According Bourne et al. only 81% patients were satisfied after one year. One of the factors most strongly associated with postoperative dissatisfaction are that patients' unfilled grand expectations. Further important factors are pain, stiffness and complications requiring hospital readmission [35, 36].

Long term results of TKA prostheses are generally excellent and a durability of at least ten years is desirable. It has been shown that knee prostheses withstand for 15 years in 90–95% of the cases. Furthermore, the mortality rate is relatively low, with a range from 0.5 to 1% per year. Importantly to say, that postoperative mortality in TKA is mostly related to preexisting medical comorbidities [26, 37]. Other designs, as posterior stabilized knee replacement and constrained prostheses, have shown similar long-term outcomes and postoperative good functionality. Regarding the fixation method, cemented prostheses have constantly achieved better results than the uncemented fixation. Primary patella resurfacing and not resurfacing have a similar outcome [26].

Reoperation may be needed for a variety of problems, whereby loosening of the prosthesis presents the main raison with 23-40%. Other causes are infections and instability. A study showed a revision rate of 8% in 16 years for patients with primary osteoarthritis [24, 26].

Regarding implant infections, patient with prolonged hospitalization are more often afflicted. As a result, it is necessary to remove the implant, apply an extended course of antibiotics dosage and proceed with a re-implantation. In the first postoperative year, up to 1% of the patients undergoing TKA, may get an infection of the prosthesis [21].

The longevity of the implant largely reflects the total load that the implant takes over time. As excepted, younger TKA recipients are more active than older patients. Therefore, their implants are much more likely to fail in their time implanted, with a 35% risk for men between 50 and 54 years [38, 39].

A worse outcome was observed for obese patients, with a BMI more than 30 kg/m. They have an increased rate of getting an infection and they are up to 1.67 times more likely to undergo a revision operation compared to not obese patients [40].

1.2 Anesthesia for Total Knee Arthroplasty

1.2.1 Introduction

The second part of this thesis deals with the anesthetic management especially for TKA, with a precise view on the perioperative anesthesiologic methods and postoperative pain management. Particular attention is placed on general and spinal anesthesia and as well as on peripheral nerve blocks including their effect on the clinical outcomes after TKA.

In general, anesthesia allows the performance of surgical and other painful interventions by safely producing analgesia, absence of anxiety and adequate muscle relaxation. At the same time, intraoperative maintenance of physiologic homeostasis is achieved [41].

After preoperative evaluation, anesthesiologists may choose between general or spinal anesthesia or even combine. This decision is made according the patients' preferences and existing comorbidities. Anesthesia services include postoperative observation and stabilization in the post-anesthesia care unit (PACU) or intensive care unit (ICU) and as well as management of acute and chronic perioperative pain [41].

1.2.2 Anesthetic Preoperative Evaluation

At least one day before performing a TKA, the patient should be evaluated by an anesthesiologist. According the most recent guidelines of the "Österreichische Gesellschaft für Anästhesiologie, Reanimation und Intensivmedizin (ÖGARI)" the anesthetic preoperative evaluation should at a minimum contain an anamnesis and a clinical examination including following [42]

- Adequate anamnesis and review of the medical history, pertinent medical records, the current medication intake, and questions about bleeding tendency.
- Assessment of weight, height, and calculation of the BMI.
- Measurement of blood pressure and pulse with evaluation of frequency and rhythm.
- A physical examination, including auscultation of lungs and heart and an overall clinical inspection of the patient.
- Evaluation and comparison of pupils with a swinging flashlight test.
- In case of suspected neurological diseases an orientating neurological examination.

In addition, an assessment of the airways is done. To assess the conditions for intubation and mask ventilation the anesthetist interprets the Mallampati-score, the thyromental distance and performs the protrusion test of the lower jaw. Furthermore, an orientating examination of the teeth is appropriate. Finally, the anatomical regions for a planned regional anesthesia and for the insertion of the iv lines are inspected [42].

A crucial step is the cardiovascular evaluation for determining the perioperative risk. This is initially done by evaluating the physical status during the anamnesis by determining the metabolic equivalent threshold (MET) or using the NYHA classification. The overall perioperative risk for morbidity and mortality is often internationally estimated with the physical status classification system of the American Society of Anesthiologists (ASA). Further diagnostics are depending on the results of the anamnesis and clinical examination and are not primarily done. Other tests for risk evaluation include 12-lead resting ECG for pathological cardiac anamnesis, chest x-ray (p-a. and lateral) for reduced exercise capacity (MET <4), spiroergometric and stress ECG for MET <4, and echocardiography in cases of suspected cardiac insufficiency. Pathological findings during the cardiopulmonary examination should interdisciplinary be optimized and if required consulted by a specialist [42].

The required parameters of the blood count are adjusted to the initial findings of the preoperative evaluation. As standard for big operations, like TKA, anesthetists preoperatively request hemoglobin values, leucocyte and platelets count, serum electrolytes, liver and kidney function parameters, and finally blood type. Additionally, thyroid hormones, blood glucose and HbA1c can be measured for selected patients [42]

Inconspicuous anamnesis of blood tendency and ASA 1-2 do not require further analysis of the blood coagulation. Otherwise an examination includes aPTT, PTZ, fibrinogen, platelet count and von Willebrand factor [42].

1.2.3 Anesthetic Management for TKA

1.2.3.1 Monitoring, Venous Access, Positioning

For TKA a standard configuration for intraoperative monitoring is set up according the ASA. It includes pulse oximetry for oxygen saturation, ECG, and a noninvasive blood pressure device. Additionally, body temperature should be measured. Advanced monitoring is added only as indicated by patients comorbidities and alarms are set for parameters deviating from the norm [43]. For general anesthesia measurement of ventilation parameters are necessary e.g. end-tidal inhalation when volatiles are administered, end tidal carbon dioxide, volume of expired gas and inspired oxygen concentrations [16, 41].

Regarding venous access for unicompartmental primary TKA one peripheral IV catheters gauge size 16 to 20 should be enough. For more complex interventions like bilateral TKA or patients with ASA higher than two a second IV catheter may be placed [44]. It is a frequent practice to apply an indwelling urinary catheter for TKA, if necessary, with measurement of the fluid intake to determine fluid balance. The indwelling urinary catheter also deals with postoperative urinary retention which occurs relatively often with an incidence of up to 46.3% [45].

When performing TKA patients are positioned supine, which allows easy access to a patient supplied by a laryngeal mask airway or an endotracheal tube for anesthetic management [44].

1.2.3.2 Choice of Anesthetic Technique

For performing TKA are generally two choices of anesthetic techniques: general or regional anesthesia. Regarding the regional anesthesia, spinal anesthesia is exclusively used when doing a TKA and peridural anesthesia is typically excluded. The choice of anesthesia should be based on a range of factors, like the patients' comorbidities and condition, patients' preferences, and the extent of the operation. The use of peripheral nerve blocks should also be considered, mainly for treatment of postoperative pain. It is important to mention that for patients with many comorbidities the application of general or spinal anesthesia may be skipped and only peripheral nerve block can be used. The advantages and disadvantages of the different approaches are contrasted below [44].

1.2.3.2.1 General Anesthesia

General anesthesia (GA) is the more often used anesthetic method for TKA compared to spinal anesthesia [46]. It accomplishes to put the patient in a state with a temporary, reversible functional inhibition of the central nervous system with hypnosis and unconsciousness, amnesia, analgesia, and blockade of autonomic and sensory responses due surgery. Muscle relaxation can be achieved, if necessary for intubation, although usually it is not indicated with regard to operations on the knee [16, 41].

The advantages of GA include high efficiency, the uncomplicated use for coagulation disorders and the lack of risk of nerve damages due administration of SA. On the other hand, the physiological effects of GA may be more serious and may present a bigger burden for the circulatory system. Aspiration, postoperative hoarseness, an increased incidence of postoperative nausea and vomiting are some of the disadvantageous risks that come along with GA [16].

The course of GA can be divided into three distinct phases which are induction, maintenance and emergence [41].

1.2.3.2.1.1 Induction

The induction of GA can either be done with intravenous and/or inhalation agents, although the induction per inhalation is very unusual. In general, the induction is performed by the administration of a sedative-hypnotic combined with an iv opioid. After the patient is unresponsive and stop breathing neuromuscular blocking agent for endotracheal intubation are administered. This procedure is followed by addition of an inhalation agent or continuous iv application of a hypnotic medication once the airway has been secured. Propofol or thiopental are well-established induction hypnotics [16, 41].

1.2.3.2.1.2 Airway Management

A crucial task of anesthetists is providing adequate airway management for ventilation, oxygenation and for anesthetic gas delivery. To achieve this purpose are several devices for airway management available, including facemasks, supraglottic airways devices and endotracheal tubes [41, 44].

The use of airway devices is often associated with a sore throat, dysphonia, and/or dysphagia. The incidence range for those undesirable side effects reaches from 13% to 49% for SGA [47, 48], for endotracheal intubation from 21% to 72% [49-51].

1.2.3.2.1.3 Maintenance

The maintenance of GA is started right after the induction usually by employing inhalation agents continuously. The repertoire of inhalation agents includes isoflurane, sevoflurane and, desflurane. Alternatively, only sedative hypnotic IV agents, like propofol can be administered per syringe driver. This method is the so called total intravenous anesthesia (TIVA) [16, 41].

1.2.3.2.1.4 Emergence

Emergence is defined as the return of consciousness and movement after the operation is completed. Emergence from GA starts after the administration of anesthetic agents is stopped and their effects wear off. A close communication between surgeon and anesthetist is thereby decisive, for appropriate duration of anesthesia. The endotracheal tube or SGA is removed when the patient fulfils the extubation criteria [41, 52]. In general, they include sufficient spontaneous breathing (breathing volume > 500ml or 8ml/kg, breathing rate 10-15/min, FIO2 <0.5), restored pharyngeal and laryngeal defensive reflexes, contact ability, body temperature >35°C and stable condition of the patient [53]. The stable patient can then be transported to the post-anesthesia care unit (PACU), where the patient is going for postoperative observation [53].

1.2.3.2.2 Neuraxial Anesthesia

There are three different techniques for the anesthetists for selection when it comes to neuraxial anesthesia and analgesia. Those include the spinal, the epidural and the combined spinal-epidural (CSE) method [41].

The mechanism of spinal anesthetic methods is in principle the same. For the intervention a needle or/and a catheter are placed between vertebrae followed by the injection of a local anesthetic into the subarachnoid space for spinal anesthesia or into the epidural space for epidural anesthesia [41]. For both techniques, the needle can be inserted using a midline or a paramedian approach. Thereby the positioning of the patient into sitting or into lateral decubitus position are common [54].

Additionally, the administration can be differentiated between single shot injection and continuous injection. Single shot injection is usually performed for spinal anesthesia while continuous infusion with a catheter is preferred for epidural anesthesia. CSE is the combination of these two techniques [55, 56].

In contrast to GA, spinal anesthesia provides maintenance of consciousness, spontaneous breathing, and defensive reflexes. It also has postoperative analgesic effects, especially right after operation and consequently lowers the need of opioids. Nevertheless, spinal anesthesia comes with risks of epidural bleeding, infections and nerve lesions with motoric and sensory impairments [16].

Although spinal anesthesia is considered a safe method with a rare occurrence of serious and permanent complications, up to 4.2 patients per 100.000 patients may experience permanent complaints according the 'pessimistically' results of Cook et al. [57]. A serious complication is the high spinal anesthesia which comes with blockade of the respiratory muscles. Other complications are unintentional subdural injection, direct trauma to nerve tissue, postdural puncture headache, postoperative urinary retention, transient neurologic symptoms (TNS), local anesthetic systemic toxicity (LAST), spinal epidural hematoma, back pain and infections [16, 58].

1.2.3.2.2.1 Local Anesthetics

Local anesthetics are used in spinal anesthesia and peripheral nerve blockade. They act by blockade of voltage gated sodium channels and in higher concentrations as well as of potassium channels. The mechanism inhibits the formation of action potentials and consequently the forwarding of information about temperature, pressure, pain, sensory and motoric impulses partially or completely [16].

The duration of spinal anesthesia is determined by the local anesthetic used and the total dose. Local anesthetics are classified in three groups. Short acting (30-60min), medium long acting (60-120min) and long acting (till 400 min) agents. The use of long acting agents has been a proven method when performing TKA especially with bupivacaine or ropivacaine. Also medium acting agents e.g. prilocaine are used [16]. There is the possibility to combine local anesthetics with adjuvant medication like dexamethasone or dexmedetomidine. This addition prolongs the duration of anesthesia, shortens latency and increases the density of sensory and motor blockade [54].

1.2.3.2.2.2 Spinal Anesthesia

When performing spinal anesthesia, a local anesthetic is injected subarachnoid in a mid- to low-lumbar intervertebral space, below the end of the conus medullaris. The relevant anatomic structures and the penetrated layers are seen in Fig. 10. The needle is mostly inserted between L3/4 for blockade of the spinal nerve roots. The needle puncture is usually followed by a single shot injection of anesthetic solution into cerebrospinal fluid (CSF) which provides a reliable duration of the blockade for primary unilateral TKA. Alternatively, an attachment of a catheter in the subarachnoid space for continuous spinal anesthesia is an option but rarely used for knee replacement. All in all spinal anesthesia has a lower failure rate than the epidural method, a better motoric blockade and it has a rapid response of 5 to 10 min [44, 53].

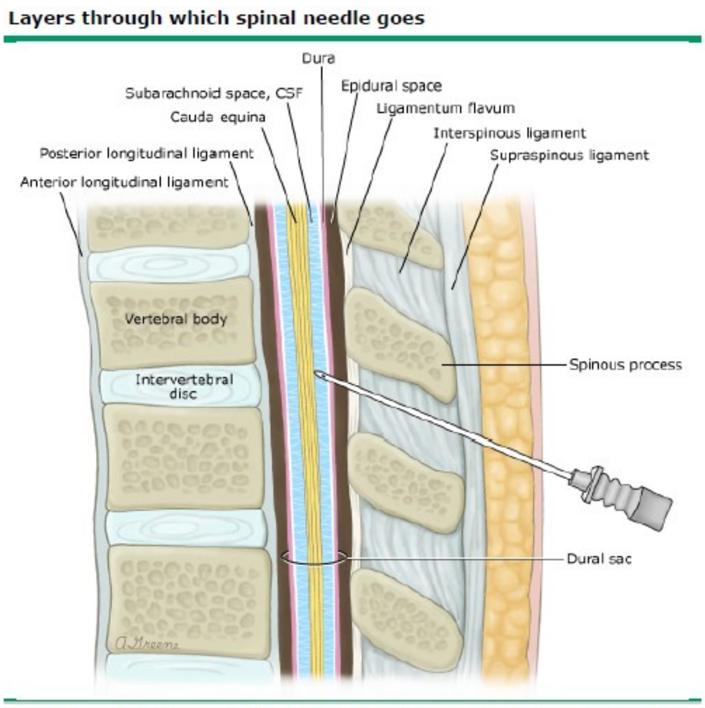

Figure 10: Layers through which spinal needle goes [59].

1.2.3.2.3 Peripheral Nerve Blocks

Peripheral nerve blocks are an important and widely used technique in anesthetic management. They are used for execution of surgical procedures but in TKA mostly used for peri- and postoperative pain management. For TKA they are usually combined with general or spinal anesthesia. With the effect of peripheral nerve block, pain and opioid consumption can be significantly reduced [13, 60, 61].

The principle of the peripheral nerve block is the injection of a local anesthetic into the perineural space of nerve cords. It is possible to apply an anesthetic solution as single shot application or a percutaneously catheter insertion for continuously administration or for bolus injections is for prolonged analgesia. Thereby the blockade and its effect is determined by the local anesthetic, the dose and the concentration [13].

For an adequate peripheral nerve block, the nerve cord should be located beforehand, to avoid intraneural injection and minimize nerve damage. There are several techniques for this purpose, including electro stimulation of the nerve, use of ultrasound guidance and the nowadays obsoleted method of intentional induction of paresthesia. The use of ultrasound guidance is state of the art and can be combined with electro stimulation [53].

Peripheral nerve blocks of the lower extremities often come along with motoric weakness. Consequently, higher risk of falling postoperatively when walking might be expected, but has been disproved [62]. Further risks are the same as for spinal injection like infection, hematoma, allergic reaction and damaging of the nerve [13].

1.2.3.2.3.1 Relevant Nerve Innervation of the Knee

For performing peripheral nerve blockade for TKA, it is essential to have basic knowledge about the pathway of the nerves and as well as their motoric and sensible innervation and separating branches.

In general, there are four nerves responsible for the innervation of the knee joint including the femoral nerve, the sciatic nerve, the lateral femoral cutaneous and posterior obturator nerve, seen in Fig. 11. The femoral nerve contains most of the innervations, including the nerves to the vastus medialis, intermedius, lateralis, the medial and intermediate femoral cutaneous and saphenous nerves. Secondly, with less innervations, the sciatic nerve, separating into the peroneal and tibial nerve. The smallest contribution arises from the lateral femoral cutaneous and posterior obturator nerves [63].

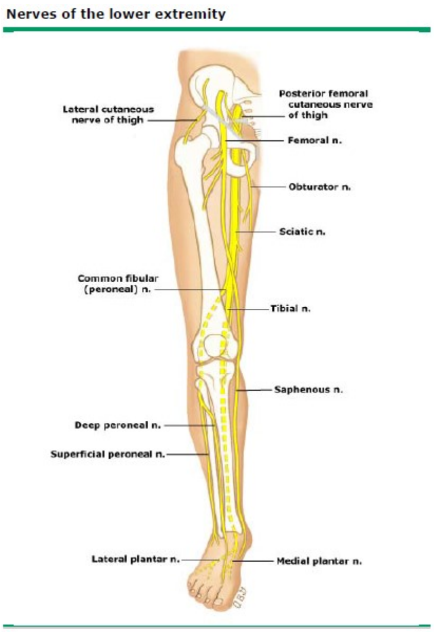

Figure 11: Nerves of the lower extremity [44].

1.2.3.2.3.2 Choice of Peripheral Nerve Block

For TKA anesthetists and surgeons have a wide variety of different peripheral nerve blocks to choose from. It is possible to apply local anesthetics on each nerve separately or combine the block of two or more nerves. The most used blocks are the femoral, the adductor canal block (ACB) and the sciatic nerve block. Also, the fascia iliac compartment block is common. Rarely performed for TKA are the lumbar plexus block, the obturator nerve block and the IPACK block [44].

The femoral nerve block has been the standard procedure for postoperative pain management after unilateral primary TKA for a long time. It is often preferred because of the easy execution and large innervation area. However, the ACB is been gaining in importance over the last few years. The preference of this method is based on the same efficacy as the femoral nerve block but associated with less motoric block [64-69]. Especially the lesser quadriceps weakness by the ACB is emphasized that facilitates ambulating and rehabilitation after knee surgery. The reason is the absence of innervations of rectus femoris vastus and intermedius muscles [44]. Despite this weakness no higher risk for postoperative falls have been evidenced [64]. More precisely it seems that patients with nerve block seem to have no increase in the rate of falls compared to patients with no block [62].

It is important to know that neither the femoral nerve block nor the ACB affect the innervation of the whole knee. Missing is the contribution from the sciatic nerve. For this reason patients planned for complex revision or with high opioid tolerance or chronic pain are recommended to receive a femoral plus sciatic nerve block [44].

1.2.1 Surgical Issues that affect Anesthesia

In the following part surgical issues are explained that can occur during anesthesia for TKA and may influence its effectiveness. Consequently, further anesthetic interventions may be required. Those surgical issues include nerve injuries, blood loss, thromboprophylaxis, antifibrinolytics, cementing and prosthesis, and the use of a tourniquet.

1.2.1.1 Blood Loss and Blood Transfusion

Studies have shown an average perioperative blood loss from approximately 650 to 1400 ml when performing TKA [27] and an average of 18,3% of the patients after primary TKA have to get a red blood transfusion [70]. Nonetheless, it has been proven, that with perioperative protocols and transfusion guidelines, the transfusion rate can be minimalized to almost zero. This is primarily possible by an adequate use of local infiltration analgesia and tranexamic acid [71, 72].

The indication of a red blood transfusion does not only depend on hemoglobin values. The decision is made with the aid of transfusion triggers, which includes parameters of the O2-transport and of the tissues oxygenation, and of course the hemoglobin [73]. Nevertheless, the use of hemoglobin concentration is widely used as guide values for the indication of red blood transfusion. According different medical societies a transfusion should be considered for young, healthy patients with a perioperative Hb- concentration under 6-7 g/dl, for patients with comorbidities under 8-10 g/dl [74-77].

It is important to mention that the transfusion of red blood contains certain serious risks like febrile reaction (1:60), circulatory overload (1:100), allergic reactions (1:250), transfusion-related acute lung injury (1:12 000), and virus transmission, especially of hepatitis B (<1:208 000 to 1:843 000), hepatitis C (1:1.15 Mio.) and HIV (<1:1.467 Mio.) [78]. To avoid the use of donated blood and to prevent such complications the use of autologous transfusion is getting increasingly attractive for surgeons. Methods of autologous blood transfusion are autotransfusion, preoperative autologous blood donation and preoperative isovolumic hemodilution. For autotransfusion therapy, blood lost by the patient during an operation is collected, heparinized, reprocessed by centrifugation and cleaning procedures and then retransfused. With this method about 50% of the perioperative lost red blood can be given back to the patient within six hours [53]. Although, autologous reinfusion drain systems are a safer alternative than homologous blood transfusion, their influence on postoperative hemoglobin may be questionable and postoperative homologous blood transfusion eventually may be needed [79-81].

1.2.1.2 Thromboprophylaxis

When performing spinal anesthesia, it is important to firstly look out for antithrombic and/or antiplatelet medication. Not considered, spinal or epidural hematoma and other bleedings may occur [82]. The incidence for hematoma doing epidural anesthesia lies at 1:150 000, for spinal anesthesia it reaches 1:220 000. To minimalize those risks, it is necessary to keep the coagulation parameters in safe values with Quick >50%, aPTT <40s and platelet count >80.000 – 100.000. Already existing anticoagulation medication should be strictly paused for a certain time interval before and after intervention [16].

1.2.1.3 Antifibrinolytics

The administration of antifibrinolytic agents is an often-used method to reduce blood loss when performing TKA. Notably tranexamic acid (TXA), which is preferred because of its excellent serum-to-joint space diffusion pharmacokinetics [83]. Alternatively, epsilon-aminocaproic acid (EACA) is reasonable, despite less supporting data. According to the guidelines TXA should mostly be used for patients without a baseline high risk for thromboembolic events, like prior venous thromboembolism or prior arterial thromboembolic events [84-86]. However, TXA might not increase thromboembolic events or mortality after all [87-89], even not for patients with higher risk [72, 90-93].

With administration of TXA, total blood loss and the number of transfusions can significantly be reduced [87, 90, 94-101]. The amount of total blood loss is in average about 591 mL lower associated to the effect of antifibrinolytics [96] and TXA can lower the transfusion rate of at least one unit of red blood cells by 50% [88].

1.2.1.4 Cementing of the Prosthesis

As explained above cementing is nowadays considered as standard procedure when it comes to fix the TKA prosthesis to the bone. The process of cementing itself can rarely cause a cardiovascular reaction, the so-called bone cement implantation syndrome (BCIS). This syndrome consists of hypoxia, hypotension, unexplained loss of consciousness and consequently can lead to cardiac arrest. Its pathophysiology mechanism is not exactly known but probably results from pulmonary embolism of cement or fat, which increases the pulmonary vascular resistance and leads to right heart compromise or even failure. It might also occur due increased intramedullary pressure [102-104].

1.2.1.5 Tourniquet

To keep perioperative blood loss during TKA within limit and to create a bloodless surgical field a thigh tourniquet is typically attached. Beside less intraoperative blood loss, this method enables a clean operative field, reduces operative time and improves fixation with cement [105].

The applied cuff pressure is set according the systolic blood pressure and as well as the diameter of the extremity. For the lower extremity it is recommended to take at least twice the preoperative systolic blood pressure up to max. 450 mmHg. Thereby it is essential to watch the time the tourniquet is applied and keep it as low as possible to prevent complications. The tourniquet is usually inflated after prepping the patient for surgery and deflated just prior or after closing the wound [105, 106].

A tourniquet time beyond two hours provokes pressure damage of the soft tissues beneath the cuff and can develop a metabolic acidosis in the extremity. Another complication is the detachment of a DVT with a subsequently pulmonary embolism. Prolonged tourniquet increases the occurrence of nerve lesions, arterial spasm, and development of a DVT. Intraoperative increase of blood pressure and heart rate, as well as pain reactions can be associated to the use of a tourniquet [13, 16].

However, the use of a tourniquet has been surrounded by controversy of its efficiency and because of its complications. Tourniquets may increase peri- and postoperative pain and therefore, opioid consumption in comparison to tourniquetless TKA. Also reduced early range of motion and potentially a delay in early rehabilitation were reported [107-110].

1.2.2 Perioperative and Postoperative Multimodal Pain Control

Pain management is an important and decisive subject of the anesthetic and surgical department. It has high significance for the outcome after TKA because the postoperative phase of TKA is associated with high pain levels. Adequate pain control should provide sufficient analgesia for early mobilization and rehabilitation and on the other hand keep the use of opioids low [111]. Early well-treated acute pain may prevent persistent of postoperative pain after TKA later on [112], and therefore, reduce opioids intake [113].

It is recommended to use a multimodal approach for managing pain by combining different techniques. As a consequence, lower doses of each technique are necessary, which reduces theirs side effects [114, 115]. Pain controlling possibilities are one or more peripheral nerve block, continuous spinal anesthesia, periarticular infiltration of local anesthetics and multiple system analgesics, including patient-controlled anesthesia (PCA).

An adequate pain management should already begin before surgery by evaluating existing pain and used pain medication, especially history of opioid intake. Current individual pain should be documented by objectifying the pain level. For documentation visual (VAS) or numerical (NRS) scales are used perioperatively. Patient with a numerical pain scale of 3 or more should obtain pain reducing medication [25].

The figure below (Fig. 12) gives an overview of the intra- and postoperative techniques of pain management in distinct phases.

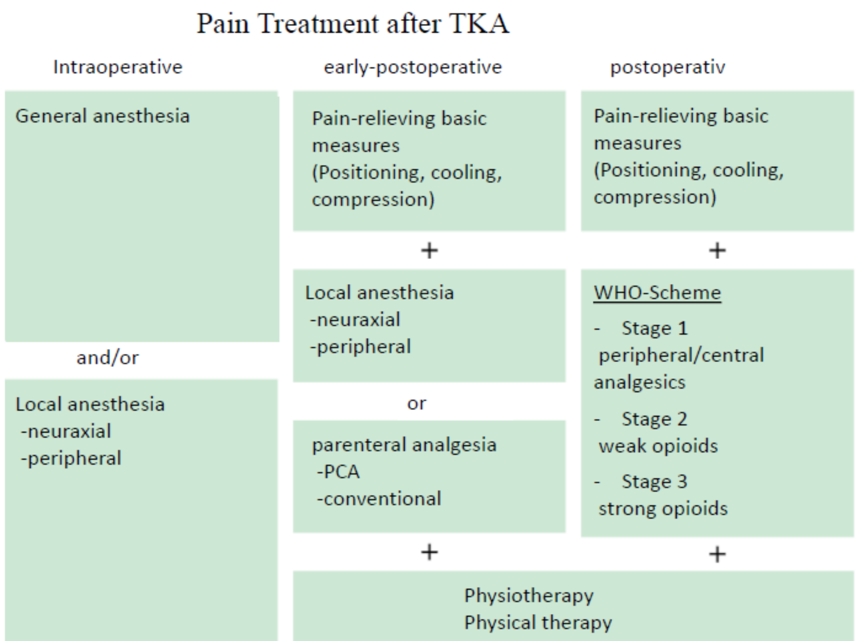

Figure 12: Peri- and postoperative pain management, and pain reducing techniques [25].

1.2.2.1 Systemic Analgesics

In general, the pharmacological pain management should be adjusted according the pain relief ladder with three steps presented by the WHO as seen in Fig. 13.

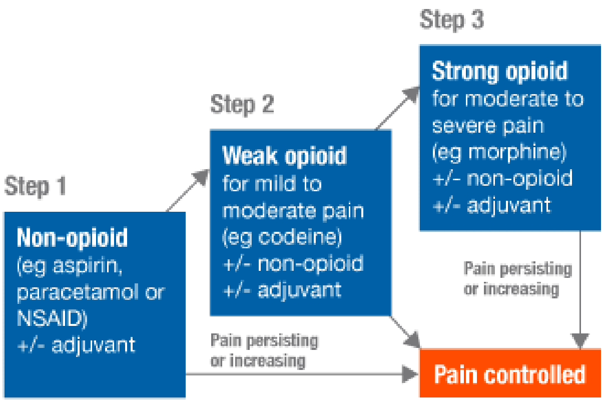

Figure 13: Pain management with the WHO pain relief ladder [117].

Preoperatively administration of preemptive oral pain medication may be beneficial for pain management. Often used are cyclooxygenase-2 (COX-2) inhibitors, nonsteroidal anti-inflammatory drugs (NSAR), gabapentinoids or oral opioids. Those can be continued throughout the hospitalization and after discharge [44].

According the WHO scheme the use of nonopioid analgesic should be applied first. However, with exclusively nonopioid use about 30% of patients are still experiencing pain after TKA. The most used nonopioids pain killer are paracetamol, metamizole, NSARs and coxibs. Before administration it is important to check their side effects and contraindication, especially when used on frail patients. Paracetamol mostly seems to be less effective after TKA. NSARs and coxibs have gastrointestinal, cardiovascular, and renal side effects that must be considered. Long use of NSARs should be accompanied by proton pump inhibitors as prophylaxes [16].

Opioids are typically used for severe and chronic pain and are indispensable for pain treatment after TKA. Nevertheless they are always combined with nonopioids which may spare opioid use up to 30% [116]. Most common agents are tramadol, codeine, oxymorphone, hydrocodone, fentanyl, morphine and especially piritramide for TKA. Opioids should only be used for patients with severe and chronic pain after exploiting other pain-relieving methods. By reducing the use of opioids it is possible to reduce related side effects like nausea, pruritus, sedation and most importantly respiratory depression [44].

In the postoperative phase, the patient-controlled anesthesia (PCA) has shown significant pain reduction and patients' satisfaction. With the use of programmed pumping system, the patient can admit pain medication intravenously by him-/herself according to his/her pain level. Doing so, dose intervals and limits are set to prevent overdosage. The PCA is often used with opioids, especially piritramide and rarer tramadol or morphine. For the use of PCA a good compliance of the patient is required and as well as an introduction for the patient on how to use the device [25].

1.2.3 Post-Anesthesia Care

After emergence and extubation, if intubated, the patient is usually transferred to the post anesthesia care unit (PACU) for recovery and observation. The PACU is typically supervised by anesthesiology department to manage monitoring, to treat postoperative occurring complications and to plan the transfer to the ward. Critically ill and unstable patients and those who are still intubated might be admitted directly to an intensive care unit (ICU).

In general, the patient is monitored the same way as in operating theatre. Further monitoring devices can be applied according patients' condition, age, and comorbidities. Especially right after surgery the patients' status is crucial and vulnerable and therefore, needs permanent observation [53, 116].

Anesthetists must deal with a wide variety of complication in the PACU. Postoperative nausea and vomiting are a common postanesthetic effect, especially after GA as aforementioned. The operation might cause respiratory or cardiovascular complications as well as neurological problems. Furthermore delayed emergence or delirium, hypothermia or hyperthermia and distress due to awareness during anesthesia may occur [41].

After fulfilling the hospital-specific criteria for discharge the patient can be transferred from the PACU to the ward of the treating department for further postoperative treatment.

1.3 Study

Total knee arthroplasty is one of the most frequent performed surgeries. While the techniques of this operation have been advancing over the years, the anesthetic methods have also been evolving. Regarding the anesthetic process, there are two possibilities to choose from: either general anesthesia (GA) or spinal anesthesia (SA). In addition, peripheral nerve block (PNB) can be applied to both variations, for better perioperative pain management. GA has been mostly used the last decade, but in the last few years, a growing interest has been given to SA. Although the evidence is limited, several publications have appeared in recent years documenting a low superiority of SA over GA. However, there are many controversies about determining the ideal anesthetic procedure for TKA.

The main objective of this thesis was to compare the anesthetic possibilities for TKA and to determine the advantages and disadvantages of each. For this purpose, an own study was implemented in the orthopedic and traumatological department of the Medical University of Graz. Thereby, a data collection was done, followed by a statistical analysis to look for significant differences regarding the clinical postoperative outcome. Furthermore, the effect of peripheral nerve blocks in TKA was evaluated. The current study includes an introduction, the methods used, the obtained results, a discussion and comparison with other recent studies, and a brief conclusion. The hypothesis of this retrospective study declared that there are no differences between GA and SA regarding the postoperative clinical outcome and that the use of a PNB has no effects.

2 Material und Methods

Study

In the period from 02.01.2017 until 12.02.2018, all patients undergoing primary TKA in the Department of Orthopedics and Traumatology at Graz University Hospital were evaluated. In total, 656 patients were analyzed, whereby patients receiving a primary constrained or semi-constrained prosthesis or undergoing revision surgery were excluded. The etiology for undergoing a TKA did not matter. It is important to mention that this study was performed after approval by the ethics committee of the Medical University of Graz (EK 30-253 ex 17/18, Chairperson Prof. J. Haas).

Methods

Relevant information for this study were extracted from the 08.01.2019 until the 20.02.2019 from the patient data management system. To ensure data privacy, access to that network was only given by the department of orthopedics and by anonymizing each patient. For data collection, different medical records were looked up, including preoperative evaluation and examination reports, perioperative operation reports from surgeons and anesthesiologists as well as the reports from the PACU. Regarding the postoperative course, ward round reports from nurses and doctors, medical charts, process reports from the physiotherapists, laboratory reports, discharge reports and follow-up evaluations from each patient were checked. All collected data and values were listed in a Microsoft Excel file for documentation and further analysis.

Basic information of each patient included age at surgery, gender, date of surgery, height, weight, and BMI. Specific for TKA, the used model and the affected side were noted. Concerning the anesthetic management, following parameters were investigated: the ASA-classification, the anesthetic technique, the agent used for spinal anesthesia (e.g. bupivacaine), use of a PNB and its type (femoral/ sciatic/ ACB/ Fascia iliac compartment/ obturatorius/ saphenous/ combinations), duration till skin incision [min], use of dexamethasone and its type of application (IV. /perineural) and finally the use of an adjuvant like clonidine.

For the evaluation of pain management, the amount of administrated piritramide [mg] (intraoperative/PACU/postoperative two days) and intraoperative fentanyl [µg] were listed. In addition, the use of PCA and its period of attachment [days], time until first postoperative piritramide application, pain levels using the NRS (preoperative, postoperative for three days, three times daily) and previous existing chronic opioid therapy were evaluated.

Relevant information about blood management, including the need for red blood cell transfusion (RBC), the applied bags of RBC [units], total amount of blood retransfused [ml], the total collected blood in the drain [ml] and its time of service [days]. The preoperative Hb [g/dl], the Hb on the first postoperative day and then the Hb value on every second day after surgery were investigated for each case.

In order to have a look at the patients' postoperative course, the protocol contained data about duration until removal of the urinary catheter [days], time till gait training was started [days], length of stays [days], complications during the stays according to Gosling and Gouma [117] and onset of postoperative delirium and behavioral changes. Furthermore, the incidence rate of inpatient falls, thromboembolic events, occurring paresthesia and infections were documented. Finally, the measurements of the ROM of the knee before surgery and during the follow-up examination, preferably six-weeks postoperative, were noted.

Basically, patients were separated into four groups according to the received anesthetic procedure and divided into the use of a PNB. The division of the groups was as follows:

Group GA:	General anesthesia without peripheral nerve block.
Group GA&B:	General anesthesia with peripheral nerve block.
Group SA:	Spinal anesthesia without peripheral nerve block.
Group SA&B:	Spinal anesthesia with peripheral nerve block.

After comparing these four groups to each other, a comparison of GA vs SA and of PNB-used vs no PNB-used were conducted separately to look for significant differences. For parameters in which the use of a PNB had no relevance, a general comparison only of GA and SA was performed.

Analysis and Statistics

The gathered values of each group were analyzed and compared to each other using Microsoft Office Excel and IBM SPSS 26.0. Descriptive statistics were used to show baseline information about frequencies, means, standard deviations, counts and percentages as appropriate. Cross tables, including the chi-square test and the odds ratio, were conducted to display multivariate frequency distributions of different variables. The identification of differences between groups was mostly done by using the Mann-Whitney-U-test for non-parametric parameters and the t-test-for-independent-samples for parametric values. The ANOVA-test with two-factor analysis of variance was used, including post-hoc comparison, to identify whether there were significant differences between the four groups regarding specific parameters. The Kruskal-Wallis-test was applied for differentiation between a nominal variable and ranked variable. Normal distribution, which is required for certain tests, was confirmed visually by checking diagrams and the Q-Q plot and furthermore by using the Komogorov-Sminov-test as well as the Shapiro-Wilk-test.

The Levene-test checked the equality of the variances. In all instances, two-sided P-values <0.05 were considered significant.

3 Results

Overall Demographic Data

In total, 656 patients underwent a TKA in the investigated period. Regarding sex, 425 (64.8%) were female and 231 (35.2%) were male, as displayed in Tab. 5. The average age of patients undergoing TKA was 70.58 (±8.42) years, more specifically 69.5 (±9.17) years for men and 71.17 (±7,95) years for women. The youngest patient was only 24 years old, being the only patient below 40, and the oldest patient was 91 years old. As regards the BMI most of the patients were overweight (41%) or obese (39%). Only 19.8% had a normal BMI and one patient was underweight. The distribution of the prosthesis model was the following: Attune was used for 475 (72.4%) patients, ACS for 95 (14.5%), LCS for 21 (3.2%) and finally PFC for 65 (9.9%) patients. The results showed that 55.3% of the prostheses were implanted on the right extremity and 44.7% on the left side.

Table 5: Demographic data of the four groups.

		GA		GA&B		SA		SA&B		Total	
		Mean	Frequency	Mean	Frequency	Mean	Frequency	Mean	Frequency	Mean	Frequency
Age (years)		69,28 ±7,74		70,79 ±8,30		70,93 ±8,40		70,14 ±9,23		70,58 ±8,43	
BMI (kg/m²)		31,4 ±6,6		29,0 ±4,6		29,9 ±6,1		31,0 ±7,1		29,8 ±5,7	
Gender	male		17 (29,3%)		120 (35,3%)		60 (40,0%)		34 (31,5%)		231 (35,2%)
	female		41 (70,7%)		220 (64,7%)		90 (60,0%)		74 (68,5%)		425 (64,8%)
ASA	1,00		1 (1,7%)		17 (5,0%)		9 (6,0%)		2 (1,9%)		29 (4,4%)
	2,00		24 (41,4%)		153 (45,0%)		63 (42,3%		54 (50,0%)		294 (44,9%)
	3,00		29 (50,0%)		151 (44,4%)		68 (45,6%)		44 (40,7%)		292 (44,6%)
	4,00		4 (6,9%)		19 (5,6%)		9 (6,0%)		8 (7,4%)		40 (6,1%)
	Total		58 (100%)		340 (100%)		149 (100%)		108 (100%)		655 (100%)

The Kruskal-Wallis test confirmed distribution equality among the four groups for age (p=0.489), BMI (p=0.056), gender (p=0.348) and ASA (p=0.73).

Anesthetic Methods

Regarding the anesthetic methods used, it was calculated that 60.4% (396) of the time GA and 39.5% (258) SA were performed. When a spinal anesthesia was done, bucaine was the most frequent agent, namely in 78.7% of the cases. A PNB was applied for 448 patients (68.6%) whereby the femoral nerve block combined with the sciatic block was mostly performed with 58.4%, secondly the femoral nerve block only with 33.3%. Of all the patients, 18.2% received dexamethasone, typically via the IV. route. Adjuvants were applied on 12% of the patients. The distribution of the anesthetic procedures in the four groups is listed as followed, in Tab 6.

Table 6: Frequency of the anesthetic methods: GA and SA, with or without a PNB.

Type of anesthesia	Frequency (n)	Frequency (%)
GA without PNB	58	8,8
GA with PNB	340	51,8
SA without PNB	150	22,9
SA with PNB	108	16,5

The overall percentage distribution of ASA-classifications was ASA1 4.4%, ASA2, 44.9%, ASA3, 44.6%, and ASA4 6.1% as seen in Tab5. Among the four groups with the different anesthetic approaches, there were no relevant significant differences regarding age, BMI, gender, and ASA physical status.

Complications and Delirium

The results showed that 630 (96.2%) patients did not suffer from any surgery related complications postoperatively. Unfortunately, one patient from the SA&B group died after a middle cerebral artery infarction. Two patients suffered from permanent damage, whereby one from a prothesis infection with a following amputation and one patient from persistent long-term complaints and pain. Five patients consequently needed a reoperation, including three revisions after implant infection, one inlay luxation and one avulsion of the tibial tuberosity. All in all, there were 17 temporary complications without the necessity of a reoperation: Four DVTs, six peripheral nerve-related problems (five with PNB (OR 2.302, 95% CI 0.267 - 19.834, *P=0.435*), one wound healing disturbance, two postoperative soft-tissues hematomas, one patient seeing double images and one patient with cardial complaints. In total, 20 falls were documented, whereby 16 included patients with a PNB, which resulted to an OR 1.86 (95% CI 0.61 - 5.64, *P=0.265*). Concerning the anesthetic method, 13 of patients that fell had received GA. Accordingly, an OR 0.822 (95% CI 0.32 - 2.09, *P=0.676*) was calculated for the use of SA regarding the occurrence of falls. Delirium and behavioral changes were noticeable in ten cases, whereby six patients were from GA&B group and four from the SA group with an odds ratio for GA of 1.028 (95% CI 0.29 - 3.68, *P=0.967*) and for the use of a PNB of 0.684 (95% CI 0.19 - 2.45, *P=0.557*).

Pain Medication and Pain Intensity

Firstly, the piritramide values had to put into equivalence to morphine for standardization and better comparison with other studies. According the systemic review of Hinrichs et al. [118] the analgesic potency of piritramide in morphine is 0.7-0.75:1 for iv application. However, it is important to mention that the onset of action, onset of strongest effect and duration of action are not the same within those two agents. In the current study piritramide values were converted to morphine equivalent (ME) by multiplying the values of piritramide by 0.7 and keeping the same unit (mg). For the statistical calculation of pain medication with opioids and of pain intensity in the postoperative course all patients receiving PCA and patients with chronic preoperative opioid therapy had to be excluded. Consequently, only 508 patients out of 656 patients were analyzed for those parameters. The reason is firstly because the amount of opioids administered by postoperative PCA were not documented and secondly, because patients with chronic opioid therapy need higher doses of morphine due to their higher tolerance against the effects of opioids [119]. It is important to mention that before applying strong opioids WHO level three, standard medication of WHO level one and level two against pain were exploited.

Table 7: Average total opioid consumption according the anesthetic method and the use of a PNB.

	GA group (n=41)	GA&B group (n=274)	SA group (n=106)	SA&B group (n=87)
ME IntraOP	7,97 ±4,7	2,00 ±2,6	0,12 ±0,9	0,07 ±0,5
ME PACU	8,17 ±6,1	5,21 ±4,4	6,32 ±5,5	3,1 ±3,6
ME D0 Total	9,45 ±6,6	5,90 ±5,2	9,54 ±5,5	5,17 ±4,9
ME D1	6,02 ±7,2	5,40 ±5,3	4,66 ±4,9	5,52 ±6,5
ME D2	2,18 ±4,4	2,47 ±3,7	1,98 ±3,5	2,59 ±4
Me PostOp	17,65 ±15,1	13,78 ±9,8	16,19 ±10,1	13,28 ±11
Me Total	**25,62 ±14,1**	15,78 ±10,3	16,30 ±10	13,36 ±11

The total opioid consumption was defined as the intraoperative opioid administration and the postoperative opioid intake until the second postoperative day. The highest total opioid consumption was significantly observed in the GA group (*P<0.001)* as seen in Tab.7. Values were lower in the other three groups, although no significant differences were seen among them (*P>0.05*). However, the SA&B group got along with the fewest number of opioids**.** The comparison between the groups is shown in Fig. 14.

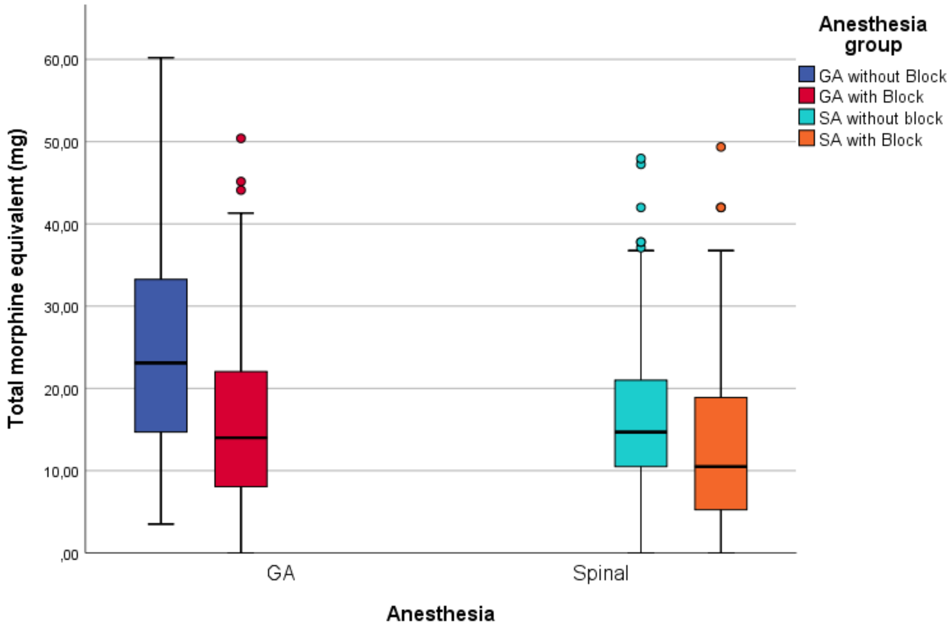

Figure 14: Total opioid consumption in the four groups.

When comparing just the differences between general and spinal anesthesia regardless of the administration of PNB, the total opioid consumption was reduced with SA, with a mean difference of 2.08 mg ME (95% CI 0.1 – 4.1, *P=0.04*). The use of a PNB reached a reduction of total opioid intake of averagely 3.59 mg ME (95% CI 1.5 – 5.7, *P=0.001*). The comparison between GA and SA, and between with and without PNB is listed in Tab.8.

Table 8: Total opioid consumption in GA and SA, with and without PNB.

		Numbers (n)	Mean Value (mg)
Anesthesia	GA	315	17,1 ±11,3
	SA	193	15 ±10,6
PNB	No	146	18,8 ±11,9
	Yes	361	15,2 ±10,5

Intraoperatively, the opioid administration was significantly the highest in the GA group (*P<0.001*) with averagely 8 mg (±4.7) ME, followed by the GA&B (*P<0.001*) group with 2 mg (±2.6) ME and then both spinal anesthesia groups. The spinal anesthesia groups showed no significant differences compared to each other. During surgery, a mean of 2.68 mg (95% CI 2.16 – 3.2, *P<0.001*) ME was applied more when using GA in contrast to SA.

Regarding the postoperative course, the total postoperative use of opioids in the four groups had the same pattern as the total opioid intake, however, without any significance (*P>0.05*). On postoperative day0, both groups with PNB, GA&B and SA&B, showed significant lower need of opioids than the groups without PNB (*P<0.001*). Later, on postoperative day1 and day2, no significantly differences were observed among the four groups. The values for these parameters are shown in Tab. 7 and visualized in Fig 15.

When just comparing the administration of a PNB vs no PNB the use of a PNB saved a mean of 3.78 mg ME (95% CI 2.76 - 4.81, *P<0.001*) on day0. No significant differences were observed on the postoperative days, d1 and d2, with the application of a PNB. There were no significant differences comparing general anesthesia with spinal anesthesia in the postoperative course observed.

Concerning pain management, a PCA was applied for 14.4 % of all patients, whereby it was mostly stopped on the second (26.1 %) or third (38.6 %) postoperative day.

For analyzing the postoperative pain levels during the inpatient course, the maximal pain values were explored for each day separately. Furthermore, pain peaks were defined as NRS≤5 and then compared within the four groups. The average max pain per day per group is shown in Tab. 9. The SA group without PNB showed significantly higher pain levels (*P<0.001*) compared to the other three groups on d0. On the following days, day1 and day2, no significantly differences were observed. The pain course is juxtaposed with the course of pain consumption in Fig. 15.

Table 9: Average max pain score (NRS) in the postoperative course in the four groups.

	GA	GA&B	SA	SA&B
NRS D0	1,00 ±1,24	0,51 ±0,87	**1,61 ±1,68**	0,86 ±1,32
NRS D1	2,41 ±1,64	2,41 ±2,51	2,57 ±1,56	2,51 ±1,6
NRS D2	1,51 ±1,38	1,57 ±1,48	1,43 ±1,62	1,48 ±1,46
NRS D3	o,98 ±1,21	0,92 ±0,78	1,01 ±1,21	0,78 ±1,06

The following table (Tab. 10) shows the occurrence of pain peaks in the four groups during the postoperative course. The highest pain peaks were noted in the first postoperative day in all groups. Thereby, the GA&B group had the highest relative frequency for pain peaks with 10.4%, followed by the GA group with 9,8%, the SA group with 6,9% and the SA&B group with 4,6%.

Table 10: Relative frequency of pain peaks (NRS≤5) in the four groups during the postoperative course.

		GA	GA&B	SA	SA&B
NRS D0 ≤5	No	41 (100%)	104 (98,1%)	272 (99,3%)	87 (100%)
	Yes	0 (0%)	2 (1,9%)	2 (0,7%)	0 (0%)
NRS D1 ≤5	No	37 (90,2%)	95 (89,6%)	255 (93,1%)	83 (95,4%)
	Yes	**4 (9,8%)**	**11 (10,4%)**	19 (6,9%)	4 (4,6%)
NRS D2 ≤5	No	40 (97,6%)	101 (95,3%)	268 (97,8%)	86 (98,9%)
	Yes	1 (2,4%)	5 (4,7%)	6 (2,2%)	1 (1,1%)
NRS D3 ≤5	No	40 (97,6%)	105 (99,1%)	273 (99,6%)	87 (100 %)
	Yes	1 (2,4%)	1 (0,9%)	1 (0,4%)	0 (0%)

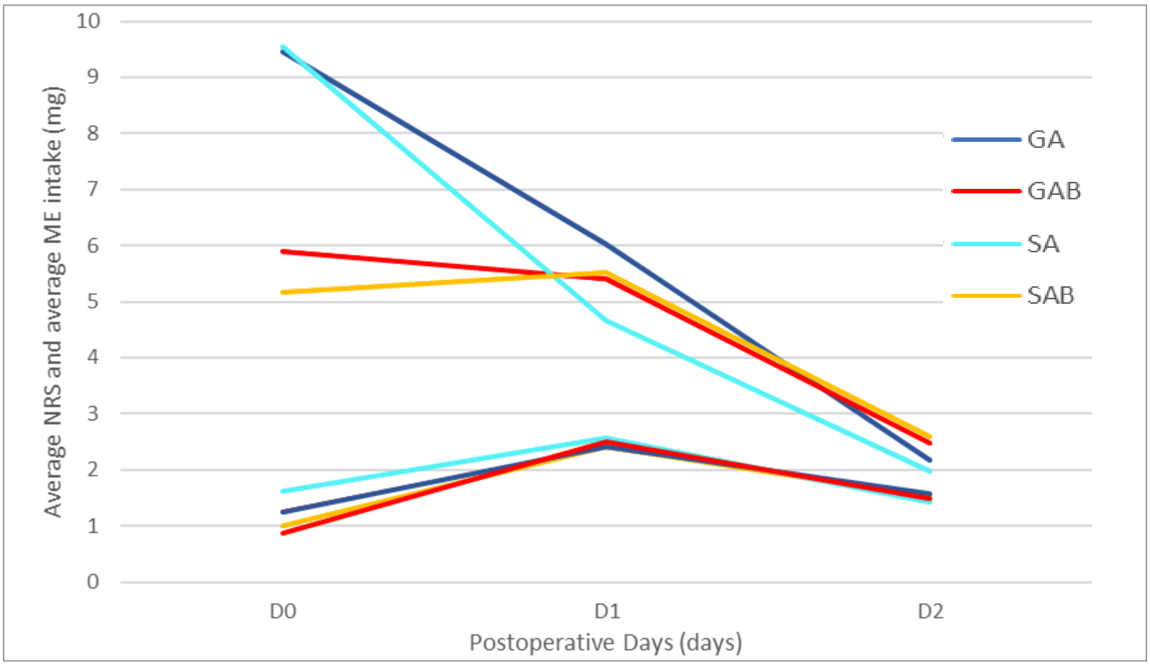

Figure 15: Comparison of average NRS (below) and average ME intake (above) of the four groups in the postoperative course.

Comparing the effect of the different PNB types on postoperative pain levels and total opioid consumptions, no significant superiority of a block variation could be found (*P>0.05*).

Time to Incision

The overall mean duration until incision by the surgeon was 52.34 min (±11.72, 95% CI 51.4 - 53.2). Time to incision with GA was in average 55.09 min (±11.93, 95% CI 53.9 - 56.3) and with SA 48.12 min (±10.05, 95% CI 46.9 - 49.4) regardless of the use of a PNB. That difference between GA and SA is significant with a middle difference of 6.95 min (95% CI 5.17 – 8.72, *P<0.001*).

Comparing just the effect of a PNB a mean difference of 8.48 min (95% CI 6.63 – 10.36, *P<0.001*) was observed when using a PNB compared to no PNB used. In this case, average time to incision with a PNB was 54.98 min (±11.78, 95% CI 53.9 - 56.1), and without PNB 46.5 min (±9.24, 95% CI 45.2 - 47.8).

The mean values and standard mean deviations of all four groups are separately demonstrated in Tab. 11. As seen, the longest time to incision was required in the GA&B group, followed by the SA&B group. The faster groups excluded a PNB, the SA group being the most timesaving variation, secondly the GA group. All groups had a significant advantage over the GA&B group (*P<0.001*). The SA group had slightly but non-significantly decreased time to incision compared to the GA group (*P>0.05*). In overall, the SA groups were superior to the GA groups regarding the time to incision and the use of a PNB was significantly more time consuming.

Table 11: Time to incision [min] with spinal or general anesthesia with or without a PNB.

	Mean Value [min]	95% CI [min]
GA without PNB	48,98 ±9,76	46,3 – 51,7
GA with PNB	56,05 ±11,97	54,8 – 57,3
SA with PNB	51,63 ±10,54	49,6 – 53,6
SA without PNB	45,6 ±8,88	44,2 – 47,1
Total	52,34 ±11,72	51,4 – 53,2

Blood Loss, Drain and Transfusions

The postoperative blood loss collected by the drain was in average 797 ml when using GA and 887.1 ml when using SA independently of the use of a PNB. A middle difference of 90.1 ml (CI 95% 17.91 – 162.23) was calculated with a significant *P= 0.015* and with variance equality (*P= 0.687*). The blood loss of each group separately is shown in Fig. 16. The drain was usually removed on the second postoperative day for all patients (2.1 days ±0.52).

No significant differences in amount of retransfusion, need of bags of RBC and total volume transfusion in the four groups could be identified. Total volume transfusion included retransfusion volume and volume of the RBC bags (300 ml). The retransfusion rate and the total transfusion volume were slightly higher in the SA&B group compared to the others. The odds ratio for the need of a bag of RBC was insignificantly higher for SA with OR 1.146 (95% CI 0.72 – 1.82, *P=0.557*).

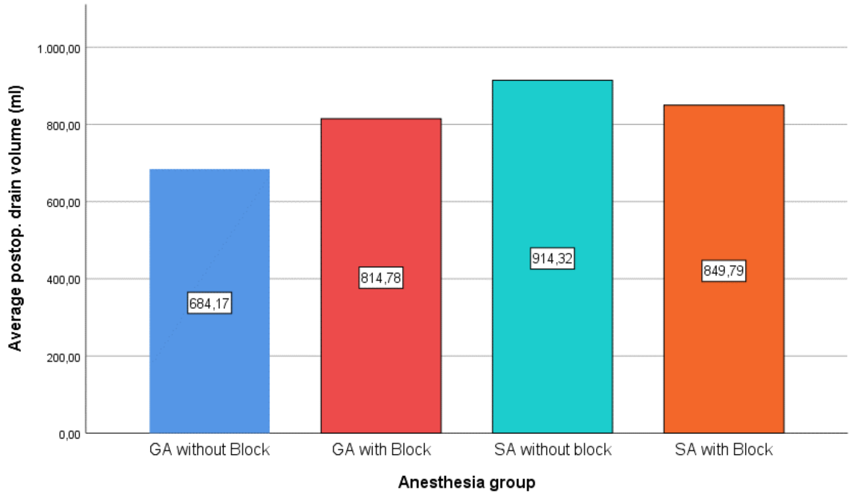

Figure 16: Total postoperative drain volume [ml] with the following mean values: GA 684.2 ml, GA&B 814.8 ml, SA&B 3 849.8 ml, SA 914.3ml.

Postoperative Parameters: Length of stay, urinary catheter, gait training, ROM

In average, patients stayed in the hospital for 9.1 days (±1.8) before being discharged, whereby five days was the shortest length of stay and 18 days the longest. There were no significant differences among the four groups. Fig. 15 demonstrates the distribution of the length of stay in the four groups.

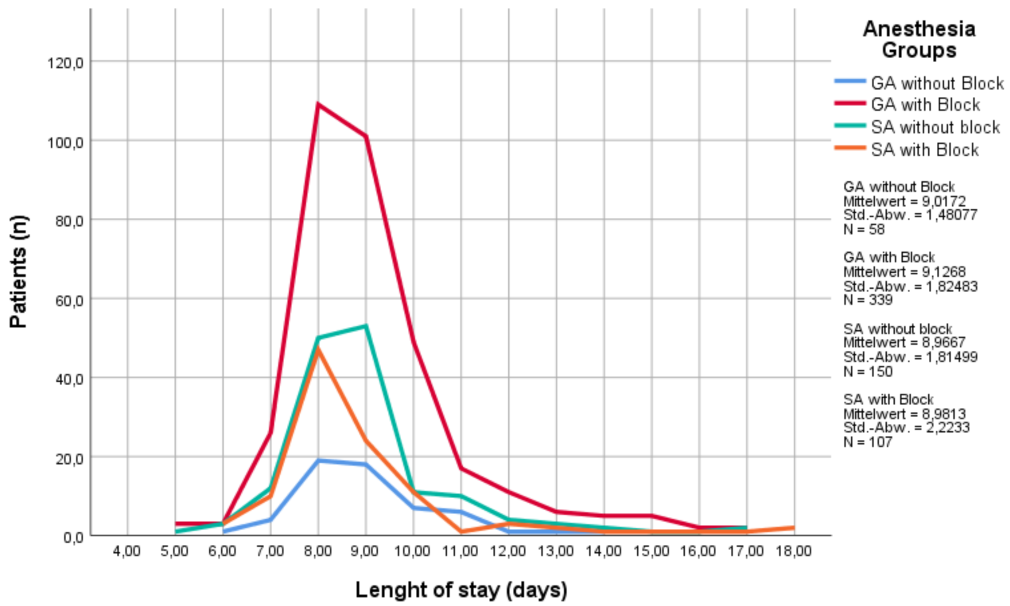

Figure 17: Distribution of the length of stay in days in the four groups.

Usually, patients were able to stand up and start gait training on the second postoperative day (± 1.01 days). Whereby 33.4% commenced gait training on the first postoperative day, 47.9% on the second, and 10.2% on the third.

In total 469 patients had a urinary catheter inserted, which was normally removed on the second postoperative day (± 1.17 days) with an incidence rate of 45.2%.

In addition, the preoperative and six-week postoperative ROM of the knee were measured, whereby 250 cases were available with both measurements. Among them, 120 had reduced ROM, 44 patients without change, and 86 with increased ROM in the evaluation six week after surgery.

There were no significant differences between GA and SA and the use of a PNB observed, regarding the preoperative and postoperative flexion range, the duration of catheter attachment, and duration till gait training commenced ($P>0.05$).

4 Discussion

The most important finding of this thesis was a lower total opioid consumption with the use of SA as anesthetic method. Furthermore, the time to incision was shortened with SA and by skipping a PNB. The administration of a PNB was able to achieve a reduction of early-postoperative piritramide-equivalent intake.

Numerous studies have shown significant differences in patients' outcome regarding the choice of anesthetic method [120, 121]. The obtained results were analyzed and compared with current and important studies related to differences in GA and SA for TKA. In overall, this study confirmed that SA was either equivalent or even superior to GA in some aspects. In addition, the variations with the use of a PNB may be favored over the methods without a PNB for selected patients. Particularly useful for the comparison were the systemic review study from Johnson et al. [121] including studies with large data records and the systemic review from Turnbull et al. [120].

<u>Comparison of demographic data</u>

First of all, the collected demographic data of this study were compared with trends and findings from the Austrian National Database by the study from Leitner et al. [6]. In Austria, the mean age of people receiving TKA has remained relatively constant over the last few years with an average age of 69.4 to 69.7 years [6]. On the other hand, Austrians mean age has been constantly increasing [122]. The rise of TKA performed per year is therefore explained by the increasing proportion of elderly people. The main age range of TKA-patients lies between 60 and 79 years. About two-thirds of all patients for knee replacement are usually placed in that range [123]. In the current study the mean age of the patients was slightly higher with an average of 70.58 (± 8.42) years which may be connected to the increasing life expectancy and evolving techniques which are leading to reduced surgical risk when operating elderly people. Another possibility may be a decreased execution of TKA on younger patients. A slight trend towards TKA on younger patients was observed during the study period of Leitner et al. [6].

Another important statistic is the gender distribution of the patients undergoing TKA. According to the study of Culliford et al. [125] with 23 843 TKA patients, women were in average 45% more likely to go into operation theater for knee replacement. The female to male ratio in that study varied between 1.18:1 and 1.42:1 [125]. In the current study the patients undergoing TKA presented a higher female to male ratio of 1.84:1.

Culliford et al. compared the age of the genders and found out that women were about 1.5 years older than men when receiving TKA [125]. In the presented study the average age of women was 69.5 years and of men 71.2 years, which reflects a similar difference in mean age between the genders.

Mortality and complications

Several studies have shown a lower incidence rate of complications when performing TKA in favor of SA instead of GA.

The occurrence of postoperative cardiovascular, respiratory, and renal complications is reduced with neuraxial anesthesia according Baldawi et al. [124]. In addition, thromboembolic incidents, like DVT and embolisms, seem to be lower [125]. Several studies have proven a decreased overall mortality when using SA [125-129]. Memtsoudis et al. [130] observed a significantly higher 30-days mortality for GA with an odd ratio of 1.83 (95% CI 1.08 – 3.1, *P=0.02*). The study of Chen et al. evaluated 7 977 patients and showed a higher overall mortality rate for GA beginning at 5 years after surgery, but no differences in the short-term mortality rate. However, many studies did not find any significant differences in the mortality rate between GA and SA [124, 128, 129, 131].

Liu et al. [131] showed in their study with 16 555 knee arthroplasty patients differences concerning the occurrence of infectious events. They figured out that anesthetic management with spinal or epidural anesthesia was 49% less likely to cause pneumonia and 23% to cause composite systemic infections within 30-days postoperatively. On the other side, no significant differences regarding mortality, surgical wound infection, and sepsis were found. Contrary, Chang et al. [132] showed higher odds for surgical site infections under GA (OR 2.21, 95% CI 1.25 - 3.90, *P= 0.007*). In the presented study, the number of infections (three) was too low to make any valid statements about the occurrence of local or systemic infections.

An aspect speaking against SA is the higher incidence of block failures and of rare but more devastating nerve injuries, epidural abscesses and spinal hematomas [133]. These problems were fortunately absent in the current investigation.

It is well known that GA has a higher rate of postoperative nausea, vomiting and delirium, which also applies to TKA [133]. Minimal nonsignificant increased odds for postoperative delirium with GA were observed in this thesis. In the study of Memtsoudis et al. [134], a large national cohort with 1 694 195 patients, lower odds for postoperative delirium occurrence were seen for SA compared to GA (OR 0.83, 95% CI 0.76 to 0.92). However, regarding early postoperative delirium, other factors may be more decisive, like opioid-sparing analgesic techniques, depth of periprocedural sedation, and sedative selection [134, 135]. Postoperative nausea and vomiting were not determined in the current study, especially because the difficulty to obtain such information retrospectively.

In total, 20 inpatient falls were documented in this study, whereby 80% included a PNB with an OR 1.86 (95% CI 0.61 - 5.64, *P=0.265*) for inpatient falls with PNB. Contrary to common concerns and the current study, another study of Memtsoudis et al. [62] with 3042 patients identified significantly that PNB does not have any association to the risk of inpatient falls (OR 0.85, CI 0.71-1.03) but rather advanced age and increasing comorbidity burden.

Macfarlane et al. [136] showed in their systemic review with 28 studies involving 1538 patients no correlation between mortality or any complications and the chosen anesthetic technique. This statement was verified in the presented study by showing no significant differences regarding the mortality and complications. This study demonstrated a higher risk for nerve related problems, like muscle weakness of the lower extremity and paresthesia when using a PNB. For PNB and as well as for GA the occurrence of early postoperative falls and delirium was higher. Nevertheless, these differences showed no significance. The overall low incidence rate of complications and mortality traces back to the safety of modern anesthetic techniques. This low rate makes it difficult to determine any superiority of an anesthetic method regarding the complications and mortality. Therefore, studies with higher numbers of patients are required to obtain significant results.

It is important to mention that the anesthetic method is often adjusted to the preexisting comorbidities and the physical status of the patients. Therefore, complications often result from those comorbidities and may not be assigned to the use of the anesthetic procedure itself. However, some studies included those comorbidities in their calculations and showed that the differences between GA and SA were even larger in patients with more comorbidities and suggesting SA for sicker patients [129, 131]. Pugely et al. showed that beside the anesthetic choice, other parameters have significant influence on the complication rate like high age, black race, female gender, elevated serum creatinine, high ASA class, long operative time [129]. This study could not significantly approve that higher ASA scores are related to the higher incidence rate of complications, which were defined by Gosling et al. (*P>0.05*). However, patients with higher ASA were significantly more often affected by inpatient falls and the need of blood transfusions (*P<0.001*).

Blood loss and blood transfusion

The current study demonstrated a similar rate of blood transfusion for SA and GA both with and without a PNB. Contrary, some studies [126-129] found a decreased rate of transfusion requirement for SA.

There were no significant differences concerning the need of blood transfusion with RBC evaluated in this study. The risk of needing an RBC transfusion in the four groups was as follows: GA 15.5%, GA&B 11.8%, SA 14%, and SA&B 13.8%. Comparing just SA and GA, SA showed a higher insignificant risk for the need of RBCs (OR 1.146, 95% CI 0.72 - 1.82, *P=0.557*). On the contrary, a significant result was published by Memtsoudis et al. [130] favoring SA (GA 18.5% vs. SA 15.15%). A similar effect of SA on the transfusion rate of RBC was seen in the study of Hu et al. [128] with lower odds for SA (OR 0.45, 95% CI 0.22 - 0.94, *P=0.06*).

Regarding the perioperative blood loss, Hu et al. [128] and Macfarlane et al. [136] could not identify any influence of the anesthetic method. However, a significant middle difference of 90.1 ml was calculated in the current study when comparing SA (887.1 ml) with GA (797 ml) in favor of GA.

Length of stay

Several studies evaluated the length of stay after TKA, with findings of a significant advantage for SA. Baldawi et al. [124] showed in their study a postoperative hospital stay of 4.9 days (±4.2) for SA and 5.2 days (±4.25) for GA and they also presented a prolonged hospitalization for GA. Johnson et al. [121] analyzed 12 studies and exhibited a reduced length of stay of averagely 0.4 days when performing SA (95% CI 0.03 - 0.76, *P=0.03*). Similar results with significance were observed as well in other studies [129, 130, 137]. However, it can be argued whether these slight differences have clinical value on the general outcome. In contrary to the other studies, the meta analysis Hu et al. [128] did not find any differences in the length of stay between GA and SA. In addition, this study was not able to detect any superiority of an anesthetic method.

Time to incision

Only a few other studies could be found considering that parameter, and none was investigating it especially for TKA. Sasano et al. [138] showed an average duration of 49 min (±11.8) from entrance to incision for 172 orthopedic surgeries. In the current study 52.34 min (±11.72) time to incision were averagely measured. However, Sasano et al. included all orthopedic interventions and did not differentiate from the anesthetic methods. The use of SA was able to undercut the time to incision of GA by 6.95 minutes. Two other studies also showed such superiority of SA, but specifically for surgeries on the spine. Pierce et al. [139] presented a significant shorter time period till incision for SA with 39.3 min compared to GA with 46.6 min. In the study of Singeisen et al. [140] a profit of 19 min was achieved when using SA instead of GA. However, these two studies also included measurements of the post-operative anesthetic management. They evaluated the total anesthesia time with exclusion of the surgery time, which involved the postoperative time of emergence and transfer to the PACU. This information was absent in the current study but should be included for an overall view of the effect of each anesthetic method.

Another crucial difference was observed when using a PNB. In the analysis of this study, a reduction of the time to incision of 8.48 min was found with significance when skipping the administration of a PNB. No other studies were found analyzing the effect of the application of a PNB on the anesthetic time management.

Pain and opioid consumption

It was an important purpose of this study to draw attention to the early postoperative pain levels and total opioid consumption after TKA.

The total opioid consumption was significantly higher with GA by 2.08 mg ME compared to SA. Beside that, a block of a peripheral nerve was able to reduce the total intake of ME by 3.59 mg with significance. Thereby, the use of a PNB significantly saved 3.78 mg ME on day0 but did not show significant differences on postoperative day1 and day2. However, it is questionable if such low differences on the opioid consumption are even relevant for clinical practice.

Donauer et al. [141] analyzed 2 346 cases of knee arthroplasty and associated regional anesthesia with lower opioid consumption (OR 0.20 [95% CI 0.13 - 0.30], $P < 0.001$) and pain levels (OR 0.53 [95% CI 0.36 - 0.78], $P = 0.001$) on the first postoperative day. Although, in their study regional anesthesia included neuraxial and as well as peripheral nerve blockade and did not differentiate among them for their analysis. Furthermore, Donauer et al. used different opioids, including sufentanil, morphine and fentanyl and converted them into ME, whereby in our study only piritramide was administered.

In the systemic review of Chan et al. [142] 29 randomized-controlled studies were analyzed and they observed that PNB comes along with less pain at rest and on movement in the first 72 hours after surgery. In contrary to the current study, they observed a significant lower total opioid consumption with a PNB, although it is not clear if the intraoperative opioid administration was considered.

Another study about the effects of PNB in TKA was demonstrated by Jenstrup et al. [143]. Like in the current study, they measured reduced opioid consumption in the early postoperative phase. Furthermore, patients reported lower pain during movement but not when resting.

Liu et al. [144] showed significant lower opioid requirements and reduced pain with PNB in the first 72 postoperative hours for patients ≤65 years. However, they always used a combination of a lumbar plexus block and a sciatic nerve block, which was never used in this study.

A comparison of different PNB types was done by Dong et al. [145]. In their systemic review, they proved equal effectiveness of the adductor canal block and the femoral nerve block concerning pain reduction. Both variations showed significant lower pain levels after TKA. Similarly, there was no superiority of any PNB observed in the presented study.

Significantly higher maximum pain levels ($P<0.001$) were observed on the day of surgery postoperatively in the ward with patients receiving SA an no PNB for the surgery. Both groups with PNB showed lower pain levels. The following days, d1 and d2, did not show any differences regarding pain in the four groups. Pain peaks were mostly observed on the first postoperative day d1, in all groups. However, the two groups receiving general anesthesia, GA and GA&B, showed higher relative frequency of pain peaks on that day.

The study of Harsten et al. [146], analyzing 120 patients, showed superiority of SA during the first two postoperative hours regarding the pain score compared to GA. However, after six hours the pain levels of the SA group had increased and significantly overpassed the values of the GA group. Harsten et al. also showed higher pain levels on the first and second day after surgery, whereby the current study showed equality in pain levels among the different anesthetic methods during those days.

The administration of PNB lowered the pain levels and as well as the opioid consumption on postoperative day0. The review of Dada et al. [147] with 28 articles explained the occurrence of rebound pain after PNB for orthopedic surgery. Thereby, hyperalgesia appears between eight and 24 hours after block administration when the PNB wears off. This effect was no observed in the current study.

Limitations of this study

This study had several limitations, the first of which was its retrospective nature. A key limitation of this research was also that the postoperative satisfaction of each patient was not evaluated. Another weakness of the current study was the relatively small number of cases, namely 656, and the short postoperative period between one and a maximum of two years. It is also important to mention, that the data was collected from various sources from different departments Those include anesthetic and surgical reports and as well as documentation from nursing staff. Therefore, a uniform data documentation might not be guaranteed.

4.1 Conclusion

In conclusion, patients treated with SA were showing a reduced total opioid intake by 2.08 mg of ME and a lower time until skin incision by 6.95 minutes in comparison to GA. However, SA was associated with a higher perioperative blood loss of 90.1 ml. The administration of a PNB was able to achieve a reduction of early-postoperative ME intake by 3.59 mg on postoperative day0, and achieve a reduction of total opioid consumption of 3.78 mg ME. In addition, lower pain levels were achieved with a PNB. Beside that, the administration of a PNB entailed an increase of 8.48 minutes to the time to incision compared to not using a PNB.

As recommendation, further studies about that topic should also include the doses of preoperative preemptive applied non-opioids in their data collection, because it seems that

NSARs, COX-2 inhibitors and others may have significant effects on the postoperative pain situation and perioperative inflammation processes [120]. In addition, an analysis of postoperative nausea and vomiting might present decisive information. As already mentioned, the postoperative time consumption of the anesthetic department should be included as well. To get precise results with higher significance, a larger database should be collected over a longer period. Future investigations should compare intermediate and long-term outcome differences and the presented patients should be observed over the following years, especially regarding the long-term complication and mortality rate. More clinical outcome studies are needed to determine a significant superior anesthesia technique and to establish pathways to improve the outcome after TKA.

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