VILNIUS UNIVERSITY

Eglė
TERTELIENĖ

Evaluation of early outcome after total knee arthroplasty in Lithuania and periprosthetic infection management solutions

SUMMARY OF DOCTORAL DISSERTATION

Medicine and health sciences,
Medicine (M 001)

VILNIUS 2020

This dissertation was written between 2015 and 2019 in Vilnius University, Faculty of Medicine, Institute of Clinical Medicine, Clinic of Rheumatology, Orthopaedics Traumatology and Reconstructive Surgery

Academic supervisor – Prof. Habil. Dr. Algirdas Venalis (Vilnius University, medicine and health sciences, medicine - M 001).

Academic consultant - Prof. Habil. Dr. Narūnas Porvaneckas (Vilnius University, medicine and health sciences, medicine - M 001).

This doctoral dissertation will be defended in a public meeting of the Dissertation Defence Panel:

Chairman – Prof. Dr. Valentinas Uvarovas (Vilnius University, medicine and health sciences, medicine - M 001).

Members:
Prof. Dr. Irena Butrimienė (Vilnius University, medicine and health sciences, medicine - M 001),
Prof. Dr. Alfredas Smailys (Lithuanian University of Health Sciences, medicine and health sciences, medicine - M 001),
Assoc. Prof. Dr. Sigita Stropuvienė (Vilnius University, medicine and health sciences, medicine - M 001),
Prof. Dr. Annette W-Dahl (Lund University, Sweden, medicine and health sciences, medicine - M 001).

The dissertation will be defended at a public meeting of the Dissertation Defence Panel at 1 p.m., on 6th of March 2020 in Room 203 of the Faculty of Medicine, Vilnius University.

Address: M.K. Čiurlionio g. 21/27, Vilnius LT- 03101, Lithuania tel. +37061208131; e-mail: egle.terteliene@gmail.com

The text of this dissertation can be accessed at Vilnius University library as well as on the website of Vilnius University: www.vu.lt/lt/naujienos/ivykiu-kalendorius

VILNIAUS UNIVERSITETAS

Eglė
TERTELIENĖ

Ankstyvieji kelio sąnario endoprotezavimo rezultatai Lietuvoje bei periprotezinės infekcijos gydymo algoritmų taikymo analizė

DAKTARO DISERTACIJOS SANTRAUKA

Medicinos ir sveikatos mokslai,
Medicina M 001

VILNIUS 2020

Disertacija rengta 2015– 2019 metais Vilniaus universiteto Medicinos fakulteto, Klinikinės medicinos instituto, Reumatologijos, ortopedijos traumatologijos ir rekonstrukcinės chirurgijos klinikoje.

Mokslinis vadovas – prof. habil. dr. Algirdas Venalis (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina - M 001).

Mokslinis konsultantas – prof. habil dr. Narūnas Porvaneckas (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina - M 001).

Gynimo taryba:

Pirmininkas – **prof. dr. Valentinas Uvarovas** (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina - M 001).

Nariai:

prof. dr. Irena Butrimienė (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina - M 001),

prof. dr. Alfredas Smailys (Lietuvos sveikatos mokslų universitetas, medicinos ir sveikatos mokslai, medicina - M 001),
doc. dr. Sigita Stropuvienė (Vilniaus universitetas, medicinos ir sveikatos mokslai, medicina - M 001),
prof. dr. Annette W-Dahl (Lundo universitetas, Švedija, medicinos ir sveikatos mokslai, medicina - M 001).

Disertacija ginama viešame Gynimo tarybos posėdyje 2020 m. kovo mėn. 6 d. 13 val. Vilniaus Universiteto, Medicinos fakulteto Didžiojoje 203 auditorijoje.

Adresas: M.K. Čiurlionio g. 21/27, Vilnius LT- 03101, tel. +37061208131; el. paštas egle.terteliene@gmail.com

Disertaciją galima Vilniaus Universiteto centrinėje bibliotekoje ir VU interneto svetainėje adresu: *https://www.vu.lt/naujienos/ivykiu-kalendorius*

ABBREVIATIONS

DAIR – Debridement, antibiotics and implant retention
EP – Endoprosthesis
EQ-5D – A questionnaire for measuring quality of life considering general health condition of the patient
TKA – Total knee arthroplasty
LAR – Lithuanian Arthroplasty Register
OA – Osteoarthritis
CI - Confidence interval
RA – Rheumatoid arthritis
RCT – Randomized controlled trial
SD – Standard deviation

SUMMARY

1. INTRODUCTION

Total knee arthroplasty (TKA) is a common and effective surgical procedure in orthopedic surgery today (1) and it is considered one of the most successful procedures, both medically and economically (8-10). For patients with advanced arthritis knee endoprosthesis (EP) helps relieve pain, restores joint function and significantly improves the quality of life (1).

There are more than 3 000 knee replacement surgeries performed in Lithuania annually (2). The number of TKA surgeries is growing in Lithuania and worldwide (3-5, 7). The numbers are rising due to the ageing population and increasing amount of patients suffering from degenerative joint disease (11-13). 90-97% of all interventions are performed due to osteoarthritis (OA) – the most common reason of knee replacement (2, 14). Less than 2% of TKA surgeries are performed due to rheumatoid arthritis (RA) damage to the joint (2, 14, 6).

The results of knee replacement surgeries are influenced by age and gender of the patient, diagnosis, type of the implant and surgical technique. In order to evaluate the results of treatment, clinical studies and studies of arthroplasty registries are conducted. Randomized controlled trials (RCT) are considered as a gold standard of research, however, such type of studies analysing TKA results are complicated because of strict patient inclusion criteria and ethical limitations (16). As an alternative, many countries have established national registries in order to assess early and late results of TKA surgeries (15). Lithuanian Arthroplasty Register (LAR) was established in 2011 in Lithuania and has been working successfully up to this date. Currently there are about 30 000 primary hip replacement surgeries and 3 000 revision hip replacement surgeries, 21 000 primary knee replacement surgeries and 1 300 revision knee

replacement surgeries registered. The main purpose of the registries is not only to evaluate patient-related factors that determine the success of operations, but also to evaluate implants and surgical techniques by identifying risky implants and informing the medical community as early as possible (17). Irresponsible data recording can lead to false conclusions, and, for this reason, in countries with existing EP registries data validation procedures are being performed (18, 19). This allows to assess the reliability and completeness of the data collected. LAR validation procedure has been performed in this study in order to assess the completeness of revision surgeries data registration.

Periprosthetic knee joint infection is one of the most difficult complications to treat and it is the most common reason for revision TKA, especially in the early postoperative period (22). Comparing postoperative TKA results of patients with osteoarthritis and rheumatoid arthritis it is estimated that postoperative infection is more common in patients with rheumatoid arthritis (20). This is thought to be due to intensifying immunosuppressive treatments for rheumatoid arthritis, endoprosthesis in elderly patients with longer disease duration, more comorbidities and inadequate response to immunosuppressive therapy (21). Evidence-based diagnostic and treatment algorithms for periprosthetic infection recommend that only surgical interventions (DAIR procedure, single or two-stage revision surgery) should be used in combination with antibiotic therapy to treat this challenging complication (23-28). Inadequate treatment makes the eradication of infection extremely difficult, requires significant financial resources, and degrades the quality of life of patients. In this study we evaluated treatment modalities for patients after knee replacement with suspected periprosthetic infection in comparison with the internationally recognized and evidence-based algorithms for the treatment of periprosthetic joint infection.

1.1 Aim and objectives of the study

To evaluate the early results of knee replacement surgeries in Lithuania and to assess the compliance of nationally applied periprosthetic infection treatment algorithms with international guidelines.

Objectives:

1. To determine the reliability of the Lithuanian Arthroplasty Register by assessing the completeness of the revision surgeries registration.
2. To determine patients' satisfaction with the result of knee replacement surgery.
3. To investigate the results of knee replacement surgery in patients with rheumatoid arthritis.
4. To determine the frequency of antibiotic administration in patients with suspected periprosthetic knee infection.
5. To determine the frequency of revision surgeries due to periprosthetic infection in patients with or without antibacterial therapy.

1.2 Relevance, novelty and practical significance of the study

In order to achieve the best results after joint replacement surgery, specific knowledge of the longest-lasting implants and surgical technique ensuring best possible patient function is required. One of the most accurate scientific instruments to investigate the results of joint EP surgeries are Registers. Since 2011, data on hip and knee replacement surgeries performed in Lithuanian health care institutions has been collected nationally. Revision surgeries and their causes are also recorded. All the data is collected, analysed and interpreted in order to identify risky implants and patient-related risk factors. While presenting the conclusions of the analysis of the register

data, it is necessary to keep in mind that the data has been collected correctly. Incomplete or inaccurate registration of data can lead to false conclusions which may mislead the medical community. So far, the LAR completeness and reliability have not been evaluated, however, it is an important part of every scientific register. This research will assess the completeness of the LAR so that better reliability of the future register-based treatment recommendations would be ensured.

Infection is one of the most common complications of TKA surgery. Inadequate treatment of periprosthetic infection often leads to antimicrobial resistance and, in most cases, to necessity of substantial surgical interventions. Analysing the literature we found no studies conducted investigating the modes of antimicrobial treatment of periprosthetic infection after endoprosthesis surgery. This study will provide an overview of situation about following worldwide accepted algorithms of periprosthetic infection treatment in Lithuania, as well as information on rational use of antibiotics. This will allow to introduce evidence-based recommendations and to manage the process of treating periprosthetic infection better.

2. PATIENTS AND METHODS OF THE STUDY

This research project was divided into two parts. In the first part early (up to 2 year after surgery) TKA results were analysed and LAR validation procedure was performed – the reliability of the register was evaluated by assessing accuracy of registering revisions. Evaluation of the results of patients suffering from rheumatoid arthritis, who underwent knee replacement surgery, was performed separately.

In the second part of the study the analysis of periprosthetic infection was conducted. The frequency of periprosthetic infection after primary TKA, modes of antibiotic use when periprosthetic infection is suspected, as well as revision rates were evaluated by comparing patients with and without antimicrobial treatment.

A study permission Nr. 158200-16-832-371 (2016 07 12) was obtained by Vilnius Regional Biomedical Research Ethics Committee.

2.1 Registration of arthroplasty surgeries

The Lithuanian Arthroplasty Register was established in 2011. All primary and revision joint arthroplasties are registered in this register. Data is collected via electronic database, which has been designed by the examples of European arthroplasty registers, i.e. using the data registration model recommended by the European Arthroplasty Register (85). Data registered: demographic characteristics of the patient, preoperative diagnosis, earlier surgeries of the affected joint, operated extremity, date of the operation. Operation technique, surgical approach, surgical drainage used, bone transplant, additional measures (pulse lavage systems of bone canals, bone cement mixing systems), bone cement, cementing technique, brand and type of the implant are also registered. Revisions are registered in a separate form – date of revision, causes, date of primary

operation, surgical approach, type of the revision, cementation and operation technique, implants used are registered. Every orthopedic surgeon who performs joint replacement surgeries is given a personal name and password for accessing LAR database. In some hospitals, registration is done by physicians themselves, in others – by physician assistants. An orthopedic surgeon (or his or her assistant) who performed a primary or revision joint replacement surgery, logs into the LAR database and completes an electronic endoprosthesis surgery registration form.

2.2 Unsuccessful primary total knee arthroplasty

Primary TKA is considered unsuccessful if repeated surgery (revision) is done in any period of time after primary surgery. LAR defines revision as reoperation of the joint with endoprosthesis that involves exchange, addition or removal of at least one endoprosthesis component. Replacement of all components of the implant is not necessary for a repeated surgery identification as revision. For example, a replacement of an insert when periprosthetic infection is suspected, or an implantation of patellar component when knee endoprosthesis is already implanted, is considered as revision TKA. Such surgeries as arthrodesis or amputation are also classified as revisions, because previous endoprostheses are removed. However, soft tissue surgical interventions such as wound revision for superficial soft tissue infection, or arthroscopic surgeries are not recorded as revisions (14, 52, 86, 87) because the components of endoprosthesis are not removed or replaced. Repeated (revision) TKA surgeries are recorded in a separate form by the operating surgeon (or his/her assistant). Revision surgery is attributed to the individual patient who underwent the primary intervention if it was performed after 2011 (the start of registering). The patient is identified by unique identification number and the side of the endoprosthetic knee joint.

2.3 Inclusion and exclusion criteria for participation in a study

The following patient inclusion and exclusion criteria for participation in a study were used to evaluate the early outcomes of knee replacement surgery, the accuracy of LAR revisions recordings, periprosthetic infection rates and antibiotic treatment patterns, as well as to analyse patients who underwent knee replacement surgery due to rheumatoid arthritis:

Inclusion criteria

1. Patients who underwent primary TKA September 1, 2013 - September 1, 2015.
2. Patients, who agreed to participate in the study.

Exclusion criteria

1. Patients who disagreed to participate in the study.

2.4 Early results of TKA

During the study period 4 269 TKA surgeries, performed on 4 069 patients, were registered in LAR database. The study included all cases of primary TKA registered in the LAR database from September 1, 2013, until September 1, 2015. Patients were followed up for two years after the primary surgery, with the longest follow-up period extending to September 1, 2017. Patient follow-up was discontinued if the patient underwent repeated operation of the primary endoprosthesis during the observation period or death of the patient was recorded during the observation period. Patients who had not undergone revision surgery during the mentioned period were considered successful, i.e. with functioning endoprosthetic joints.

Those patients who underwent repeated surgery (revision) were considered as unsuccessful cases.

Primary TKA surgeries were performed in twenty-two Lithuanian medical institutions. After surgery was performed, an orthopedic surgeon completed an electronic registration form. Every patient was given an identification number, which later helped to determine whether the patient had undergone repeated surgery on the same joint. To identify implants used in surgery, the reference number system was chosen in the created database. Such an implant identification instrument helped to identify accurately which specific parts of the EP were used for implantation and to classify them properly. Each part of the implant had a unique number, which subsequently helped to identify the part of the implant, both for the evaluation of the primary and revision surgery. It helped to avoid data recording errors and provided very accurate information about which specific parts of the EP were used for a particular patient.

To evaluate early outcomes after knee joint EP, overall endoprosthesis survival was calculated and implant survival by gender, preoperative diagnosis and age was compared. Additionally, analysis of risk factors that could affect implant survival was performed.

2.5 Lithuanian Arthroplasty Register validation procedure

Reliability of the register is one of the most important factors presenting and evaluating endoprosthesis results. The reliability of the register is determined by its accuracy and completeness, i.e. whether all revisions actually performed during the survey period are recorded in the database. A telephone survey of the patients enrolled in the study was carried out to evaluate this important parameter. Contact data of the patients (telephone numbers) were obtained from the medical institutions where the patients had been operated. The administrations of medical institutions were provided with scientific research

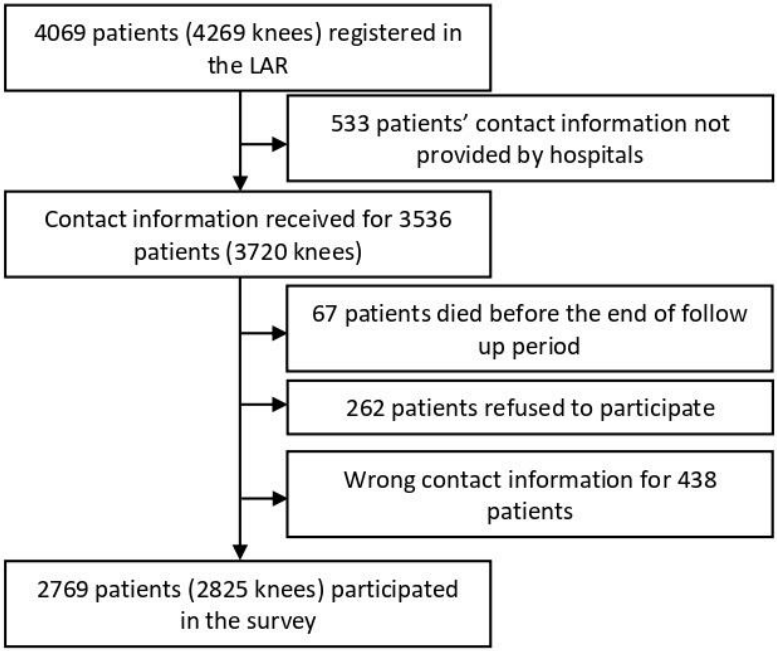
documents – description of a study and permission of the Biomedical Research Ethics Committee. With the consent of the medical institution administration, contact details (telephone numbers) were collected from patients' medical records. Two years after the primary TKA, one of the researchers called the patients and asked about the repeated surgeries of the same joint after the primary implantation. The purpose of the telephone survey was to compare data about revisions from patient surveys and revisions recorded in the database. Patients were asked if they had any additional surgeries on their affected joint after primary arthroplasty surgery. If the answer was positive, the patients were inquired of what kind of surgeries they had, what was operated, was the problem solved, which hospital the patient had surgery in. Patient survey data was compared with LAR data. If revision had not been registered in LAR, we contacted the medical institution where a surgery took place with a request of medical documentation of the patient. The medical documentation data was compared with the patient survey data to determine if the operation performed matched the LAR definition of revision.

In order to ensure the reliability of the data obtained, a separate analysis, of patients whose contacts were not received or who refused to participate in the study, was performed. The researchers formulated a hypothesis that perhaps people in not surveyed group of patients were older or had a significantly higher number of revisions. To confirm or reject this hypothesis, to assess whether the groups were statistically significantly different, interviewed and non-interviewed patients were compared for age and sex distribution.

Out of the twenty-two hospitals that performed TKA surgeries, nine small hospitals were unable to provide contact data of 533 patients (549 knees). Hospitals could not provide contact information of these patients because telephone numbers had not been registered in medical documentation during the study period. Before contacting the patients, the researchers contacted the Lithuanian Institute of Hygiene. In the State Register of Death Cases and Their

Causes, managed by this institution, it was verified that the patient was not dead. 67 patients (67 knees) were identified deceased before patient interviews were started. For 438 patients (565 knees) the participating medical institutions provided inaccurate phone numbers or contact data that changed during the 2-year follow-up period. After subtracting non-participating subjects, 3 031 patients were contacted (3 091 knees). When contacted by telephone, 262 patients (266 knees) refused to participate in the study. In total 2 769 patients (2 825 knees) were interviewed. The detailed characteristics of the subjects are presented in Figure 2.5.1.

Figure 2.5.1. Results of questionnaire regarding 4069 patients.



2.6 Comparison of rheumatoid arthritis and osteoarthritis patients

In order to evaluate the subjective status of the patients 2 years after the primary knee replacement surgery, the respondents were asked if they were satisfied with the joint endoprosthesis. To make the data suitable for statistical analysis, patients were able to choose between three possible responses – satisfied, moderately satisfied, or unsatisfied. The respondents were also asked to rate their condition on a scale of 0 to 10. According to the literature data, patients with rheumatoid arthritis (RA) feel more satisfied after joint replacement surgery, so the hypothesis was formulated that patients with RA will have a greater satisfaction after primary knee replacement surgery than patients with osteoarthritis (OA). In order to confirm or reject the hypothesis formulated, a comparison of the subjective status of RA and OA patients was performed 2 years after the primary TKA operation. In addition, a comparative analysis of implant survival in rheumatoid arthritis and osteoarthritis patients was performed.

2.7 Prevalence of periprosthetic infection and antibiotic prescribing modes

One of the aims of this research was to analyse the prevalence of periprosthetic infection, the most common complication of primary knee replacement surgery, and to evaluate its treatment methods. For this purpose, the respondents were interviewed by telephone 2 years after the primary TKA operation. Patients were asked these questions: "Did you take antibiotics after surgery?", "When did you take antibiotics?", "How long have you been taking antibiotics?", "For what reason did you take antibiotics during that period of time?", "Who prescribed the antibiotic?".

The respondents were divided into three groups:

- Group 1. Patients who received antibiotic treatment without surgical intervention for 1 week or more during the two-year period after primary knee replacement

surgery. Treatment was given for problems associated with knee endoprosthesis.

- Group 2. Patients who received antibiotic treatment for 1 week or more during the two-year period after primary knee replacement surgery for problems not related to knee endoprosthesis (pneumonia, bronchitis, urinary tract infection, tonsillitis).
- Group 3. Patients who have not been treated with antibiotics in two-year period after primary knee replacement surgery or who have been on antibiotic treatment for less than 1 week.

Frequency of revisions due to infection and implant survival 2 years after primary knee replacement surgery were compared between the groups of respondents, assessing revisions performed due to all causes.

At the end of the survey, all patients were asked whether surgical interventions in the joint with endoprosthesis had been performed in two years period after the primary knee replacement surgery. Analysis of medical documentation was performed to all respondents who claimed to have a revision due to a periprosthetic infection, or an infection was reported as a cause of revision in the database of the LAR. The researchers contacted the administrations of the medical institutions, provided a description of the research and permission from the Biomedical Ethics Committee. With the consent of the administration, medical documents of inpatient treatment were provided from the archive. Results of microbiological culture tests and surgery protocols were analysed in case histories to assess whether the periprosthetic infection was the real cause of the revision surgery.

According to the literature, prosthetic joint puncture and aspiration of synovial fluid are one of the most important steps in the diagnostic and treatment algorithm of periprosthetic infection. If

infection of the prosthetic joint is suspected, diagnostic puncture of the knee joint, synovial fluid culture tests should be performed prior to the administration of antibacterial medications to identify the causative agent and to determine the microorganism resistance to antibiotics. In order to evaluate periprosthetic infection treatment habits of Lithuanian orthopedic surgeons, patients who responded using antibiotics for problems related to the operated knee joint were asked if the prosthetic joint or its area had been punctured after the operation. This information allowed us to evaluate how world-recognized algorithms for diagnosis and treatment of periprosthetic infection are being followed in Lithuania and whether this affects the outcome of the treatment of prosthetic joint infection.

2.8 Statistical analysis

Averages, frequencies, medians and 95% confidence intervals (CI) were used for descriptive statistics of joint replacement surgery data. The *t-test* was used to compare quantitative data, whereas the Chi-square test was used to compare categorical data. The Kaplan-Meier method was used to evaluate EP survival curves. The log-rank test was used to compare survival curves. Cox regression was used to analyse the influence of additional factors on implant survival. The impact of different variables (age, sex, preoperative diagnosis) on the frequency of revisions was analysed. Patient age at the day of surgery was used as a quantitative variable, the increase of which reflects the increasing risk of revision. Meanwhile, preoperative diagnosis and gender were coded as qualitative variables in the Cox regression equation.

The difference was considered statistically significant when $p<0.05$. Data analysis was performed using STATA software package.

3. RESULTS

3.1 Early results of total knee arthroplasty

In the study period, 2 225 women and 600 men underwent primary TKA surgery. The mean patients age was 68.49 (SD±8.89). The average age at the time of TKA was 66.42 (SD±10.12) for men and 69.04 (SD±8.45) for women (p=0,000).

TKA surgery registration form provides a diagnosis classifier, which includes the following diagnoses: primary osteoarthritis, post-traumatic osteoarthritis, aseptic bone necrosis, rheumatoid arthritis, unicompartmental osteoarthritis and others. Assessing the distribution of diagnoses between years 2013 and 2015, primary osteoarthritis was identified as the main cause of knee replacement surgery for patients enrolled in the study (Table 3.1.1).

Table 3.1.1. *Causes of primary knee replacement surgeries*

Diagnosis	**Cases**	**Percent, %**
Primary osteoarthritis	2522	89.27
Post-traumatic osteoarthritis	129	4.57
Aseptic necrosis	57	2.02
Rheumatoid arthritis	75	2.65
Unicompartmental osteoarthritis	18	0.64
Others	24	0.85
Total	2825	100.0

Until September 1, 2017 there were 51 revision surgeries registered for patients who underwent primary TKA during year 2013 – 2015. That is 1.8% from 2013 – 2015 primary TKA surgeries. The

main cause of the revision was infection, which accounted for 44% of revisions. Revisions and their causes are presented in Table 3.1.2.

Table 3.1.2. *Causes of revision knee replacement surgeries*

Cause of revision	Cases (%)
Infection	23 (44.23)
Loosening of the tibial component	5 (9.62)
Dislocation of the patella	1 (1.92)
Patellofemoral pain	4 (7.69)
Pain of unspecified cause	3 (5.77)
Limited range of motion	3 (5.77)
Loosening of the femoral component	3 (5.77)
Instability of collateral ligaments	2 (3.85)
Technical error in surgery	3 (5.77)
Other	4 (9.62)
Total	51 (100.00)

The overall survival rate of the knee joint implants was 98.33% 24 months after the primary surgery (Figure 3.1.3). Comparing EP survival results between the sexes (Figure 3.1.4), we discovered that female patients have slightly better implant survival (98.5%) than males (97.71%), but the difference was not statistically significant (p=0.1597).

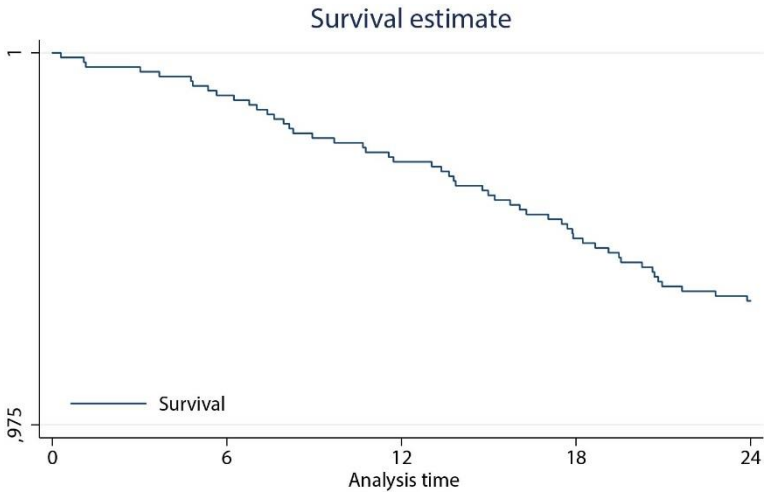


Figure 3.1.3. *Kaplan-Meier knee EP survival curve – 98.33% (95% CI 97.82/98.73)*

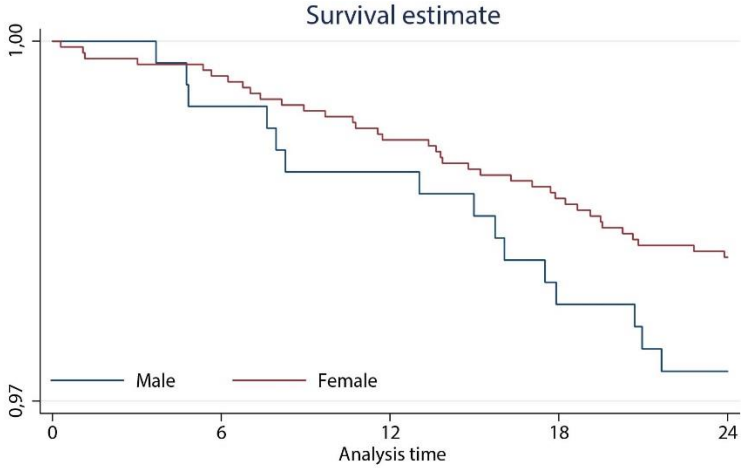


Figure 3.1.4. *Comparison of male 97.71% (95% CI 96.22/98.61) and female 98.5% (95% CI 97.93/98.91) knee joint EP survival results*

Comparison of implant survival results when arthroplasty was performed due to osteoarthritis and due to rheumatoid arthritis was made and implant survival was found to be 98.6% when EP was performed due to OA, while 98.77% when the surgery was performed due to RA (Figure 3.1.5). The difference between these groups of diagnosis was not statistically significant (p=0.9049). Comparing the survival of knee joint implants between the two age groups, i.e. over 65 and up to 65 years, no significant difference was observed – in patients under the age of 65 implant survival was 98.59% while in patients over 65 years it was 98.61% (Figure 3.1.6) (p=0.3640).

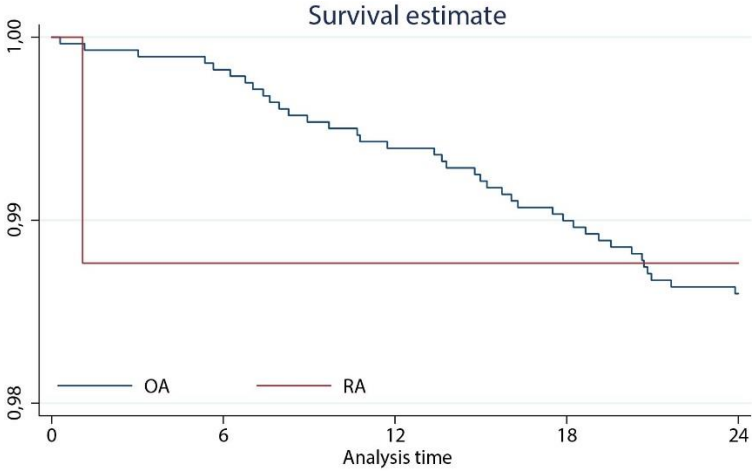


Figure 3.1.5. *Comparison of primary osteoarthritis 98.6% (95% CI 98.09/98.97) and rheumatoid arthritis 98.77% (95% CI 91.56/99.83) survival results*

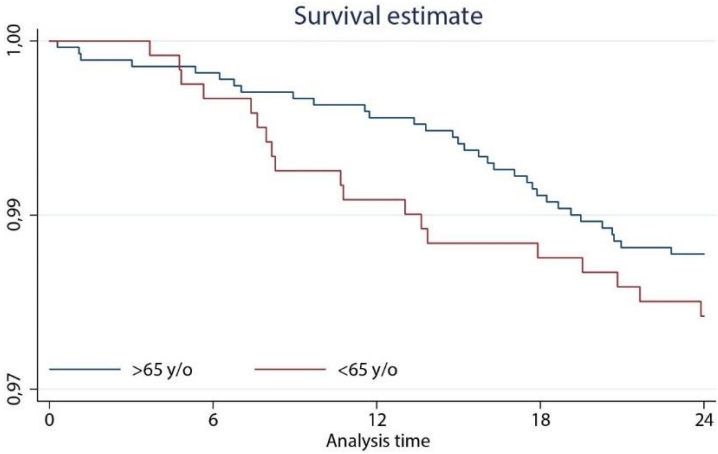


Figure 3.1.6. *Comparison of knee joint EP survival between two groups of patients by age: >65 years 98.61% (95% CI 97.99/99.04) and <65 years 98.59% (95% CI 97.53/99.20)*

Cox regression analysis based on age, sex and preoperative diagnosis of the patient showed that none of these factors had a significant effect on implant survival rate (Table 3.1.7).

Table 3.1.7*. Results of Cox regression analysis*

Variables	Relative risk	95% CI	p value
Age	0.99	0.96 – 1.02	0.36
Sex	1.47	0.80 – 2.70	0.21
Diagnosis OA	1.46	0.20 – 10.77	0.71

One of the aims of this research was to evaluate patient satisfaction with the result of knee replacement surgery and to compare the results between rheumatoid arthritis patients and patients who underwent TKA surgery for other reasons. 88% of patients in the RA group and 80% of patients in the other diagnoses group were found to be completely satisfied with the outcome of the operation 2 years after the primary knee replacement surgery. Detailed results of patient

satisfaction with the surgery are presented in Figures 3.1.8 and 3.1.9. No statistically significant difference was observed between these groups (p=0.2).

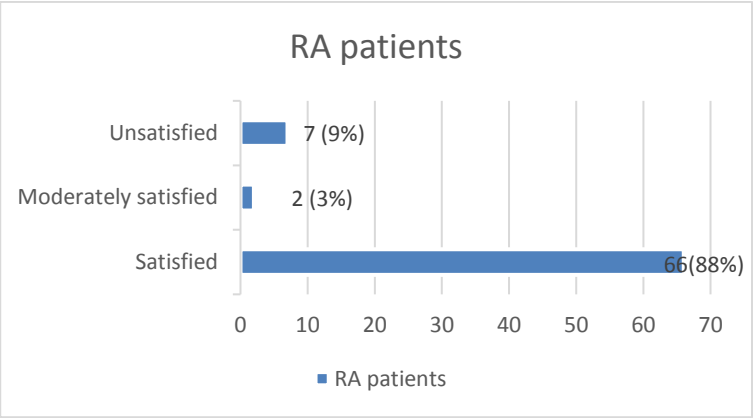


***Figure 3.1.8**. Results of rheumatoid arthritis patients satisfaction with the result of the surgery 2 years after primary operation*

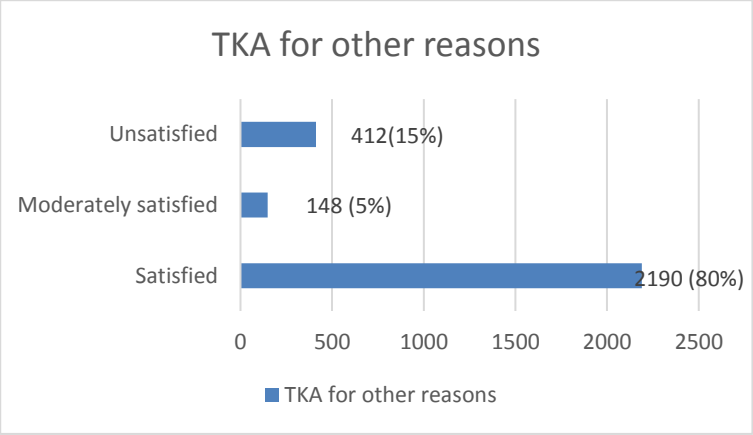


***Figure 3.1.9**. Results of patients' satisfaction with the result of the surgery 2 years after primary operation, when it was performed due to other reasons*

Interviewed patients were asked how they would rate their health that day, after joint replacement surgery, on a scale from 0 to 10. After summarizing the results, it was found that patients rated their health 7.91 (SD±1.42) on an average 2 years after primary knee replacement surgery. Comparison of health status between different sexes, age groups and diagnoses patients were also performed. The results of the analysis are presented in Tables 3.1.10, 3.1.11 and 3.1.12.

***Table 3.1.10**. Male and female patient health status evalution 2 years after primary knee replacement surgery*

Sex	Cases	Mean	95% CI	p value
Male	600	8.12	8.00 – 8.23	0.0001
Female	2225	7.85	7.79 – 7.91	

***Table 3.1.11**. Health status evaluation of different age groups patients' 2 years after primary knee replacement surgery*

Age group	Cases	Mean	95% CI	p value
>65 years	1921	7.74	7.68 – 7.81	0.000
<65 years	904	8.25	8.16 – 8.34	

***Table 3.1.12.** Osteoarthritis and rheumatoid arthritis patients health status evaluation 2 years after primary knee replacement surgery*

Diagnosis	Cases	Mean	95% CI	p value
Osteoarthritis	2522	7.90	7.84 – 7.95	0.2103
Rheumatoid artrhitis	75	8.11	7.84 – 8.38	

3.2 Reliability of Lithuanian Arthroplasty Register

Out of 2 769 patients surveyed, 61 responded to have the same joint reoperated within two-year period after primary knee replacement surgery. Analysis of the medical documentation of all patients who responded positively revealed that 51 surgeries were true revisions, meeting the LAR definition of revision. The other 10 operations included surgical interventions in the prosthetic joint but did not involve replacement, addition or removal of at least one component of the endoprosthesis. Analysing in more detail it was found that these surgical interventions consisted of two wound revisions, two operations on the periprosthetic fracture without removal of the endoprosthesis components, three surgeries were performed on the other side knee joint, two patients operated due to rupture of patella ligament, and one due to the rupture of quadriceps muscle. Detailed reasons of surgical interventions unrelated to endoprosthesis components are presented in Table 3.2.1.

Table 3.2.1. *Causes of surgical interventions*

Reason	**No.**
Wound revision	2
Periprosthetic fracture not affecting the implants	2
Revision on the contralateral side	3
Operation for patella ligament rupture	2
Quadriceps muscle rupture	1
Total	10

51 cases of revisions were identified by patient interviews and analysis of medical documentation. 46 revisions were identified by the analysis of study population in the database of the LAR. Comparison of data from patient surveys with LAR-recorded revisions revealed 5 revisions (9.8%) that were not recorded in LAR. The analysis of medical documentation revealed that it was 1 arthrodesis, 1 implant removal surgery, 1 replacement of the endoprosthesis and 2 replacement of the tibial component surgeries. Figure 3.2.2 shows the survival rate of implants comparing LAR-recorded and unrecorded revisions. Statistical analysis revealed no significant difference between the groups compared (p=0.6285).

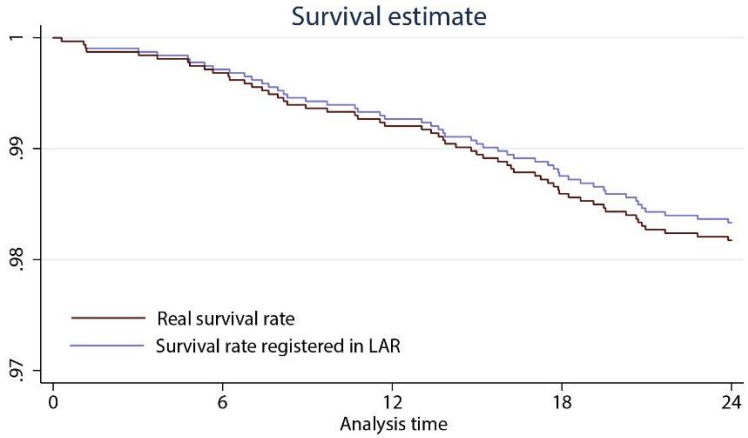


Figure 3.2.2. *The survival rate of implants comparing LAR-recorded and unrecorded revisions. 98.33% (95% CI 97.82/98.73) and 98.17% (95% CI 97.64/98.59)*

Analysing and comparing demographic data and number of revisions of patients whose contact data was not received or who

refused to participate in the study, no significant difference was observed (Table 3.2.3).

Table 3.2.3. *Comparison of patients who participated and who did not participate in the study*

Data	**Participants, n = 2825 TKA**	**Hospitals did not provided data to, n = 549 TKA**	**Refused to participate in the study, n = 266**	**p value**
Age (years), mean ± SD	68 ± 8	68 ± 8	71 ± 8	0.995
Gender: F/M	2225/600 (79%/21%)	446/103 (81%/19%)	223/43 (84%/16%)	0.08
No. revised	46 (1.6%)	9 (1.6%)	3 (0.9%)	0.397

3.3 The frequency of periprosthetic infection and habits of prescribing antibiotics

Out of the 2 769 patients interviewed, 188 (7%) answered that they were prescribed antibiotic treatment within the first two years after primary knee replacement surgery and prior to any surgical intervension. Analysing the reasons for prescribing antibiotics in detail, 132 of 188 (70%) patients reported that treatment was prescribed due to prosthetic knee problems (Group 1), while 56 (30%) patients (Group 2) reported antibiotic treatment due to other reasons (pneumonia, bronchitis, urinary tract infection, tonsillitis). The third group consisted of patients who had not received antibiotic therapy

within the 2-year follow-up period. Group 1 patients who received antibiotic therapy for prosthetic knee problems were additionally evaluated. Out of the 132 patients in the first group, 68 (52%) reported using antibiotics as a prophylaxis for prosthetic joint infection. The remaining 64 (49%) patients responded that antibiotic treatment was prescribed because of suspected periprosthetic infection (prosthetic joint swelling, pain, redness, wound secretion). Analysing these three groups of patients, a hypothesis was made that patients who had been treated with antibiotics for prosthetic knee problems were older and had more complicated preoperative diagnosis. These factors could influence the decision to prescribe antibiotic treatment. However, there was no statistically significant difference between patients who received antibiotic treatment for prosthetic knee problems and those who did not receive antibiotics comparing the groups of patients by age, gender and preoperative diagnosis (Table 3.3.1).

Table 3.3.1. *Comparison of demographic data and preoperative diagnosis of patients who received antibiotic treatment for prosthetic knee problems, who received antibiotics for prophylaxis and who did not receive antibiotic therapy*

	Antibiotic therapy	**Antibiotic prophylaxis**	**All TKA surgeries**	**p value**
Age (years), mean ± SD	67.95 ± 9.2	69.54 ± 8.6	68.49 ± 8.9	0.3
Sex				
Male	16	11	600	0.2
Female	48	57	2225	
Diagnosis				
Osteoarthritis	51	56	2522	0.7
Other	13	12	303	

Out of the 132 patients treated with antibiotics for prosthetic knee problems, 96 (73%) reported that treatment was prescribed by an orthopedic surgeon, 7 (5%) - by a family doctor, and 6 (5%) - by a physical medicine and rehabilitation doctor, 1 (1%) - by an internal medicine physician, and 22 patients (17%) did not remember which of the doctors was the first to prescribe antibiotic treatment (Table 3.2.2). Analysing the duration of treatment, it was found that 34 (26%) patients were treated with antibiotics for more than 1 month.

Table 3.3.2. *Doctors who prescribed antibiotics for problems with a prosthetic knee joint*

Doctor, who prescribed antibiotics	**Number of patients, (%)**
Orthopedic surgeon	96 (73%)
Family doctor	7 (5%)
Physical medicine and rehabilitation doctor	6 (4%)
Internal medicine physician	1 (1%)
Did not remember	22 (17%)
Total	132 (100%)

Only 32 first group patients indicated that puncture was performed on their prosthetic knee joint, 23 of them had revision surgeries, 21 of which due to periprosthetic infection. It was found in the study that for 100 out of the 132 patients treated with antibiotics for prosthetic knee problems knee joint puncture had not been performed (Table 3.3.3).

Table 3.3.3. *Analysis of patients, who received antibiotic treatment for problems, related with prosthetic knee*

Received antibiotics due to problems with the operated knee (Group 1)	**Patients (%)**
Number of TKA patients / out of all	132/2769 (4.8%)
-as prophylaxis	68/132 (52%)
-as treatment	64/132 (48%)
Antibiotics prescribed by orthopedic surgeon	96/132 (73%)
Antibiotics for more than 1 month	34/132 (26%)
Diagnostic knee aspiration performed	32/132 (24%)

According to the study, 32 of the 132 first group patients, who were treated with subsequently antibiotics, underwent revision surgery on the same joint in a two-year period after primary knee replacement surgery. No revisions were performed in the second group of patients, who received antibiotics due to other reasons. In a third group of patients, who received no antibiotic therapy, 23 revision surgeries were identified. Periprosthetic infection was identified to be the cause of revision surgery in 22 first group patients and 3 patients from the third group (Table 3.3.4).

Table 3.3.4. *Reasons of revisions in groups 1, 2 and 3*

Revision diagnosis	Patients prescribed antibiotics due to problems in operated knee (Group 1) n=132	Patients prescribed antibiotics for other reasons (Group 2) n=56	Non-antibiotic users (Group 3) n= 2581
Infection	22 (16.7%)	0	3 (0.1%)
Loosening of the tibial component	5 (3.8%)	0	0
Dislocation of the patella	0	0	1 (0.04%)
Patellofemoral pain	0	0	4 (0.2%)
Pain of unknown origin	1 (0.8%)	0	2 (0.08%)
Limited range of motion	0	0	3 (0.1%)
Loosening of the femoral component	1 (0.8%)	0	2 (0.08%)
Instability of collateral ligaments	1 (0.8%)	0	2 (0.08%)
Technical error in surgery	0	0	3 (0.1%)
Other reasons	2 (1.5%)	0	3 (0.1%)
Total	32 (24%)	0	23 (0.89%)

In the first group of patients, who received antibiotic therapy for prosthetic joint problems, implant survival 2 years after primary surgery was 76% (95% CI 68-83). Meanwhile, in the third group of patients who received no antibiotic therapy, the 2-year revision rate was 99.3% (95% CI 99-99.6) (Figure 3.3.5).

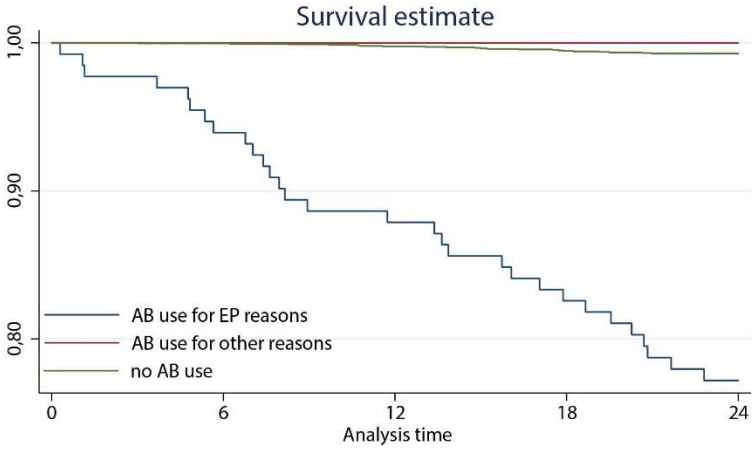


Figure 3.3.5. *Kaplan – Meier survival of knee joint endoprostheses, comparing group 1 (patients who received antibiotic treatment for prosthetic knee problems), group 2 (patients who received antibiotic treatment for problems unrelated with prosthetic knee joint) and group 3 (patients who did not receive antibiotics) of patients: 76.66% (95% CI 68.35/83.06), 100% and 99.20% (95% CI 98.78/99.48).*

4. CONCLUSIONS

1. The completeness of the registration of knee replacement operations at national level was 90.2%, which is sufficient to evaluate the results nationally.

2. Evaluating patient satisfaction with knee replacement surgery it was estimated that 88% of patients were satisfied with the result.

3. Comparing patients who had surgery due to rheumatoid arthritis with patients operated due to other reasons, no significant difference in endoprosthesis survival was found, but patients with rheumatoid arthritis had an 8% higher rate of satisfaction with the results of the surgery.

4. Evaluating antibiotic prescription when periprosthetic knee joint infection is suspected, it was found that 7% of all surveyed patients were prescribed antibiotics without surgical intervension, and it does not match international guidelines for the treatment of periprosthetic infection.

5. In patients, who were suspected to have periprosthetic infection and received antibiotic treatment without surgical intervention, the rate of revisions reached 24%, while in the group of patients who did not use antibiotics the rate of revisions was 0,8%.

5. PRACTICAL RECOMMENDATIONS

The Lithuanian Arthroplasty Register was established in 2011. In this project a great deal of research has been done and relevant results have been spread to Lithuanian and worldwide orthopedic traumatologists, state institutions and patient organizations. In this dissertation, the LAR validation procedure was performed in order to assess the completeness of registering revision surgeries and it revealed that, in accordance with the guidelines, issued by the International Association of Endoprosthetic Registers, the LAR data is reliable and capable of providing scientific advice. Periprosthetic infection is the most difficult and the most common complication of knee arthroplasty. According to international algorithms for the treatment of periprosthetic infection, only surgical intervention in combination with systemic antibiotics is the gold standard treatment for this complication. Despite the fact that this problem is widely discussed in international literature and at national and international conferences, in this dissertation it was found that in 73% of cases it was exactly the orthopedic surgeon who prescribed antibiotic treatment for suspected periprosthetic infection. It is worth mentioning that in most cases antibiotic treatment was prescribed without prosthetic joint puncture and a joint fluid culture test, so the treatment for suspected periprosthetic infection was given without complete patient examination. Antibiotic treatment without an accurate diagnosis not only complicates the choice of further surgical and antibiotic treatment, but also leads to unnecessary antibiotic use and increased antimicrobial resistance. Inadequate empirical treatment with broad-spectrum antibiotics can have a significant negative impact on society, despite the fact that several patients will avoid revision knee replacement. Therefore, rational antibiotic selection based on microbiological culture and antibiotic susceptibility testing results is one of the key aspects of successful treatment of periprosthetic

infection. In conclusion, this research identified existing problems and revealed the need to continue an extensive information campaign on contemporary guidelines for the diagnosis and treatment of periprosthetic infection actively.

Data of the study were presented in international conferences by poster presentations and oral presentations:

- June 14-19, 2016 poster presentation „Infection in total knee replacement: where we are, and where we are heading“ was presented in the international conference „Evolutionary medicine: pre-existing mechanisms and patterns of current health issues“
- June 5-10, 2018 poster presentation „Validation of the Lithuanian arthroplasty register“ was presented in the international conference „Evolutionary medicine: health and diseases in changing environment“
- April 15-16, 2019 oral presentation “Inadequate evaluation and management of suspected infections after TKA surgery in Lithuania. A retrospective study of 2,769 patients with 2-year follow-up” was presented in the 2nd Annual Conference on Orthopedics, Rheumatology and Osteoporosis, Milan, Italy
- May 31 – June 2, 2019 oral presentation “Inadequate evaluation and management of suspected infections after TKA surgery in Lithuania. A retrospective study of 2,769 patients with 2-year follow-up” was presented in the 8th International Congress of Arthroplasty Registries, Leiden, the Netherlands

LIST OF PUBLICATIONS

1.Tertelienė, Eglė; Grigaitis, Kazimieras; Robertsson, Otto; Porvaneckas, Narūnas; Dadonienė, Jolanta; Venalis, Algirdas. Validation of Lithuanian Arthroplasty Register telephone survey of 2769 patients operated for total knee replacement // Medicina. Kaunas ; Basel : LSMU ; MDPI AG. ISSN 1010-660X. eISSN 1648-9144. 2019, vol. 55, no. 6, p. 1-6. DOI: 10.3390/medicina55060310. [DB: Science Citation Index Expanded (Web of Science)] [M.kr.: M 001] [IF: 1,467; AIF: 4,541; Q3 (2018, InCites JCR SCIE)] [Aut. ind.: 0,170]

2.Tertelienė, Eglė; Grigaitis, Kazimieras; Robertsson, Otto; Stucinskas, Justinas; Tarasevicius, Sarunas; Porvaneckas, Narunas; Venalis, Algirdas. Inadequate evaluation and management of suspected -infections after TKA surgery in Lithuania: a retrospective study of 2,769 patients with 2-year follow-up // Acta Orthopaedica. Oxon : Taylor & Francis. ISSN 1745-3674. eISSN 1745-3682. 2019, vol. 90, no. 4, p. 373-376. DOI: 10.1080/17453674.2019.1614763. [DB: Scopus; MEDLINE; Science Citation Index Expanded (Web of Science)] [M.kr.: M 001] [IF: 3,217; AIF: 2,492; Q1 (2018, InCites JCR SCIE)] [Aut. ind.: 0,148]

CURRICULUM VITAE

Name, Surname: Egle Terteliene

Address: Santariškių 79-4, Vilnius, Lithuania.

Mobile phone: +370 612 08 131

E-mail: egle.terteliene@gmail.com

Education:

2015 – 2019 PhD student, Vilnius University, Faculty of Medicine

2007 - 2012 Doctor rheumatologist professional qualification, Vilnius University, Faculty of Medicine

2006 – 2007 Medical doctor, Vilnius University, Faculty of Medicine

2000 – 2006 Doctor professional qualification, Vilnius University, Faculty of Medicine

Current position:

from 2012 09 Doctor rheumatologist, Karoliniškių outpatient clinic, Vilnius

from 2015 02 Doctor rheumatologist, Private hospital „Kardiolitos klinikos“, Vilnius

Experience:

2000 – 2006 member of Vilnius University Students' Representative office at Faculty of Medicine

2007 – until now member of Lithuanian Rheumatologists Association

2012 – until now member of EMEUNET network

2012 June participant in EULAR Congress in Berlin, Germany

2016 June participant in EULAR Congress in London, UK

2016 September 1-3rd, participant in 35th Annual Meeting of the European Bone and Joint Infection Society in Oxford, UK

2017 June 30th-July 1st EULAR 2017 Epidemiology Course

2018 November 29th – December 01st , 5th International Musculoskeletal Ultrasound Course, Athens, Greece

2019 October 3-5th, 5th International Symposium Intra Articular Treatment Lisbon (Portugal)

Multiple national conferences and seminars in Lithuania.

Languages: Lithuanian (native), English, Russian

FOR NOTES

Vilniaus universiteto leidykla
Saulėtekio al. 9, LT-10222 Vilnius
El. p. info@leidykla.vu.lt,
www.leidykla.vu.lt
Tiražas 20 egz.