Aus der Klinik und Poliklinik für Orthopädie und Unfallchirurgie
der Universität zu Köln
Direktor: Universitätsprofessor Dr. med. P. Eysel

Pathologische Wundheilungsstörungen nach Wirbelsäulenoperationen – Zusammenhang zwischen Operationsdauer und isoliertem Keim

Inaugural-Dissertation zur Erlangung der Doktorwürde
der Medizinischen Fakultät
der Universität zu Köln

vorgelegt von
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promoviert am 21. Juni 2023

Gedruckt mit Genehmigung der Medizinischen Fakultät der Universität zu Köln
2023

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Danksagung

Diese Arbeit und die dahinter stehende Forschung wären nicht möglich gewesen, ohne die außergewöhnliche Unterstützung von PD Dr. med. Max J. Scheyerer, dessen Enthusiasmus, Wissen und Liebe zum Detail mich inspiriert und meine Arbeit von Beginn an auf Kurs gehalten haben.

Mein großer Dank gilt besonders dem Direktor der Klinik für Orthopädie und Unfallchirurgie der Uniklinik Köln, Univ.-Prof. Dr. Peer Eysel, der mir als wertvoller Berater zur Seite stand, bei jeder Schwierigkeit Rat wusste und mich bei allen Schritten dieses Vorhabens begleitete. Ich danke ihm von ganzem Herzen für seine uneingeschränkte Unterstützung. Ich möchte mich daher bei den verehrten Univ.-Prof. Dr. Peer Eysel, PD Dr. med. Max J. Scheyerer und bei allen Kolleginnen und Kollegen des Klinikums bedanken, die kein Mühen gescheut haben, mir behilflich zu sein.

Auch meinem ärztlichen Kollegen, Dr. med. Maximilian Lenz, der meine Beiträge supervidiert und geduldig viele Fragen beantwortet hat, danke ich ebenso ausdrücklich wie den übrigen Kollegen, die einen großen Beitrag zur Entwicklung dieser Studie geleistet haben. Ebenfalls möchte ich mich bei Akansha Perera für seine Unterstützung und Hilfsbereitschaft danken.

Ich danke der Universität zu Köln und allen ihren Mitarbeiterinnen und Mitarbeitern für die Aufnahme zum Promotionsstudium und für die uneingeschränkte Unterstützung zum Gelingen meines Vorhabens.

Diese große Reise hätte ich ebenso wenig ohne die Hilfestellung meines Verteidigungskomitee (PD Dr. med. Max J. Scheyerer, Direktor Prof. Dr. Jonathan Jantsch, &

Beisitzer: Dr. med. Maximilian Weber) bestreiten können, das mir großzügig Wissen und Erfahrung zur Verfügung gestellt hat. Darüber hinaus wäre dieses Unterfangen nicht möglich gewesen, ohne die großzügige Unterstützung der Regierung des Königreichs Saudi-Arabien, König Salman bin Abdulaziz und seines vertrauenswürdigen Kronprinzen der Prinz Muhammad bin Salman, des saudischen Gesundheitsministeriums und der saudischen Botschaft in Deutschland vom saudischen Kulturattaché in Berlin, der meine Recherche unterstützte.
Darüber hinaus möchte ich nicht vergessen, meiner geliebten Mutter (Mohriza) meinen aufrichtigen Dank auszusprechen, die mich mit ihrer Seele begleitet hat, auch wenn sie mich mit ihrem Körper verlassen hat. An meinen lieben Vater (Mohammad), der den Grundstein für mein Wissen gelegt und mich vor Abschluss meines Studiums verlassen hat. Meiner Frau (Fadwa), meiner Lebensgefährtin, die sich hingegeben und ihren Komfort geopfert hat und

allein die Verantwortung für das Haus und die Kinder getragen hat und meine Distanz zu ihr und meine langen Aufenthalte außerhalb des Hauses ertragen hat, um mein Forschungsprojekt abzuschließen. An meinen Bruder (Othman), der mir von Moment zu Moment gefolgt ist und mich moralisch und emotional unterstützt hat, bis ich diese Arbeit vollendet hatte. An den Rest meiner Schwestern, Brüder und Verwandten möchte ich meinen Dank richten. Ihnen Allen, meine lieben Freunde, widme ich diese Botschaft.

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Index of abbreviations

ASA	American Society of Anaesthesiologists
BMI	Body mass index
CCI	Charlson comorbidity index
CRP	C-reactive protein
CSF	Cerebrospinal fluid
IQR	Interquartile range
NPWT	Negative pressure wound therapy
PLIF	Posterior lumbar interbody fusion
SSI	Surgical site infections

1. Abstract

Introduction: Various factors have been known to influence the risk of developing postoperative surgical site infections (SSI). One of the most common risk factors for SSI is the duration of the surgery itself. The objective of this study is to examine if a relationship between the duration of surgery and the spectrum of pathogens causing postoperative surgical site infections exists.

Methods: Patients who had at least one revision surgery of the spine due to SSI, with at least one positive intraoperative culture were selected chronologically through the hospital patient management system. Patients who were operated primarily due to spondylodiscitis were excluded from this study. Age, gender, ethnicity, and nationality of patients were not deemed as exclusion criteria for this study. Patient data such as age, gender, body mass index, ASA classification, diagnoses, duration of primary surgery, pathogens discovered through postoperative blood cultures and intraoperative cultures, among others, were collected anonymously and stored electronically. The statistical analysis of the data was carried out through the Statistical Package for the Social Sciences software version 28 (SPSS, Chicago, Illinois, USA) with a significance level of 0,05.

Results: 75 patients were included in this study. There were 36 male and 39 female patients. The median age of the population was 64 years. Patients were primarily operated mainly due to spinal stenosis, spinal disc herniation, vertebral fracture, and metastasis. The mean duration of the primary surgery was 131,5 minutes. There were 19 positive postoperative blood cultures in the study population. The most common species were *Staphylococcus aureus*, *Staphylococcus haemolyticus* and *Staphylococcus hominis*. The difference of mean of the surgical duration between the groups of pathogen species discovered in postoperative blood cultures was tested and was found out to be statistically significant (ANOVA $p = 0,002$).

Discussion: The duration of surgery has been known to increase the risk of postoperative SSI through numerous studies. This study further analysed the relationship between surgical duration and SSI and found out that the surgical duration predisposes SSI to be caused by certain pathogenic species.

Conclusion: The knowledge of pathogen predisposition according to the duration of surgery must be further studied through clinical research and incorporated into guidelines for the selection of an appropriate antibiotic or antibiotic combination for the empiric treatment of post-surgical SSI.

Einleitung: Verschiedene Faktoren sind bekannt, einen Einfluss auf die Entwicklung von postoperativen Wundinfektionen auszuüben. Die Dauer des operativen Eingriffs ist durch viele Studien als einen Risikofaktor für postoperative Wundinfektionen identifiziert worden. Das Ziel dieser Studie ist es, die Beziehung zwischen der Dauer des operativen Eingriffs und dem Spektrum der Wundinfektionen verursachenden Pathogenen zu untersuchen.

Methoden: Patienten wurden retrospektiv und chronologisch über das interne Patientenmanagementsystem ausgewählt. Um in dieser Studie eingeschlossen zu werden, sollten die Patienten mindestens eine Revisionsoperation der Wirbelsäule wegen einer Wundinfektion gehabt haben, und sollten mindestens in einer dieser Revisionsoperationen eine positive intraoperative Kultur bezüglich Pathogenen haben. Patienten aller Altersgruppen, Geschlechte, Ethnien und Nationalitäten waren in dieser Studie eingeschlossen. Patienten, die primär wegen Spondylodiszitis operiert worden sind, sind von der Studie ausgeschlossen worden. Patientendaten wie, unter anderem, Alter, Geschlecht, Body-Mass-Index, ASA-Klassifikation, Diagnosen, Dauer des primären operativen Eingriffs und Pathogenspezies, die durch postoperativen Blutkulturen und intraoperativen Kulturen identifiziert worden sind, sind anonym gesammelt und elektronisch gespeichert worden. Die statistische Datenanalyse erfolgte mithilfe der Statistical Package for the Social Sciences software Version 28 (SPSS, Chicago, Illinois, USA) mit einem Signifikanzniveau von 0,05.

Ergebnisse: 75 Patienten sind in dieser Studie eingeschlossen worden, davon waren 36 männlich und 39 weiblich. Das mediane Alter der Studienpopulation war 64 Jahre. Patienten wurden vor allem wegen Spinalkanalstenose, Bandscheibenvorfall, Spinalfraktur und Metastasen primär operiert. Die mittlere Dauer des primären operativen Eingriffs war 131,5 Minuten. Es waren 19 positiven Blutkulturen nachweisbar. Die häufigsten Pathogenspezies, die nachgewiesen wurden, sind *Staphylococcus aureus*, *Staphylococcus haemolyticus* und *Staphylococcus hominis*. Es gab einen statistisch signifikanten Unterschied der Dauer des Eingriffs zwischen der nachgewiesenen Pathogenspezies (ANOVA $p = 0,002$).

Diskussion: Es ist bekannt durch zahlreiche Studien, dass die Dauer der Operation das Risiko für die Entwicklung von postoperativen Wundinfektionen erhöht. Diese Studie hat die Beziehung zwischen der Dauer der Operation und die Wundinfektionen verursachenden Pathogenspezies noch genauer untersucht und herausgefunden, dass die Dauer des Eingriffs das Vorkommen von unterschiedlichen Pathogenspezies prädisponiert.

Zusammenfassung: Die Beziehung zwischen der Prädisposition von chirurgischen Wundinfektionen verursachenden Pathogenspezies und der Dauer des operativen Eingriffs sollte noch weiter durch klinische Studien untersucht werden. Die Dauer des Eingriffs sollte in den Leitfaden für die Wahl eines passenden empirischen Antibiotikums für die Therapie von chirurgischen Wundinfektionen eingeschlossen werden.

2. Introduction

2.1. Anatomy and functions of the human vertebral column

The human vertebral column consists of vertebrae, intervertebral discs, and ligaments [2, 3, 1]. The vertebral column can be divided into five segments – cervical spine, thoracic spine, lumbar spine, sacrum, and coccyx (Figure 1). The vertebrae display considerable differences among the five spinal segments due to the functional variations. Despite these differences, the common structure of the vertebrae consists of the vertebral body located anteriorly and the vertebral arch located posteriorly (Figure 2). The vertebral body consists of a superior surface and an inferior surface. The thickness of the vertebral body increases from the cervical spine to the lumbar spine. The spaces between two vertebral bodies are occupied by intervertebral discs, which consist of an outer fibrous ring (Anulus fibrosus) and an inner gelatinous core (Nucleus pulposus). The vertebral arch is connected to the vertebral body at the pedicle. The vertebral arch consists of seven processes – four articular processes each with a facet joint, two each on the superior and inferior surfaces, two transverse processes and one spinous process. The purpose of the articular processes is to form the zygapophyseal joints between neighbouring vertebrae, while the function of the transverse and spinous processes is to serve as a point of attachment for muscles and ligaments. The vertebral body and the vertebral arch enclose the vertebral foramen, which houses the spinal cord. The vertebral foramen decreases in area from the cervical vertebrae to the lumbar vertebrae. The notches between the posterior section of the vertebral body and the articular processes of two adjacent vertebrae form the intervertebral foramen, which occupies the spinal nerves from each vertebral level (Figure 2).

The cervical spine consists of seven vertebrae (C1 – C7), with the first cervical vertebra being the Atlas and the second being the Axis. The thoracic spine consists of twelve vertebrae (T1 – T12) and possess a surface for the articulation with the ribs. The lumbar spine and sacrum each consists of five vertebrae (L1 – L5 and S1 – S5 respectively) and the coccyx consists of three to five vertebrae (Co1 – Co5). The sacrum and coccyx lack intervertebral discs. The shape of the vertebral column is characterised by four curvatures in the median plane – two lordotic curves in the cervical and lumbar spines and two kyphotic curves in the thoracic spine and sacrum.

The ligaments of the vertebral column serve an important role in stabilisation. The anterior and posterior surfaces of the vertebral bodies are supported by the anterior and posterior longitudinal ligaments respectively. Both the anterior and posterior longitudinal ligaments limit vertebral hyperextension and hyperflexion, respectively, while the posterior longitudinal ligament additionally serves in reducing disc herniations. Furthermore, the ligamentum flavum connects paired laminae of adjacent vertebrae, the supraspinous ligament connects the apices

of spinous processes and the interspinous ligament connects adjoining spinous processes (Figure 2).

The functions of the vertebral column are diverse in nature. The vertebral column houses the spinal cord, which is of utmost importance for the functionality of humans. Furthermore, the vertebral column acts as a support for the human body and transfers the weight of the upper body to the lower body, which is evident through the increasing thickness of the vertebral bodies from the cervical spine to the lumbar spine. The four curvatures of the spine and the intervertebral discs also serve in dampening the impact of axial shock acting on the human body through bipedal mobility. The thoracic spine also acts as a point of anchor for the rib cage, providing it with stability. The dynamic function of the spine is due to the intervertebral joints, which allow movement in three axes – ventral and dorsal flexion, lateral flexion, and rotation.

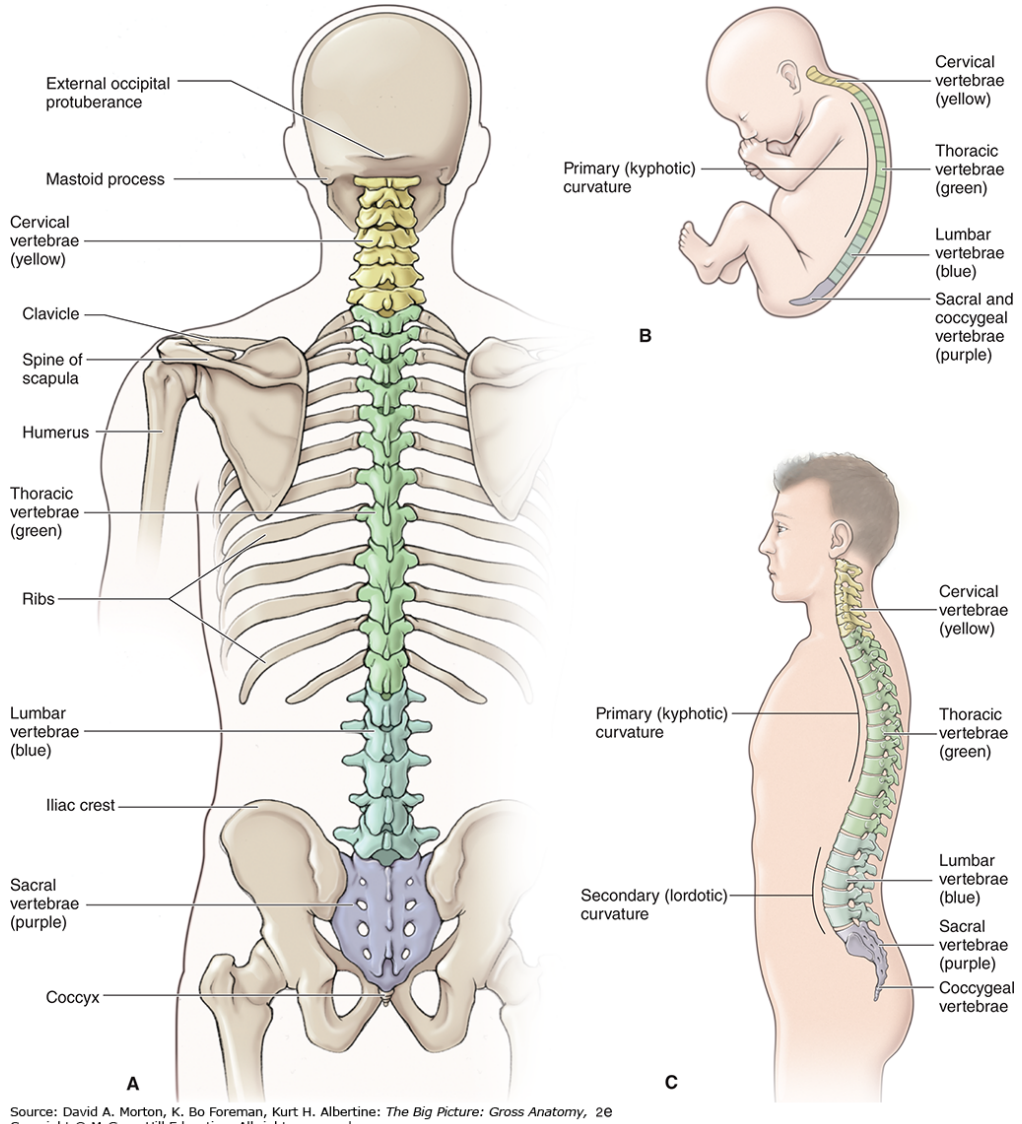

Figure 1: Human vertebral column. A. Posterior view of the vertebral column. B. Primary curvature of newborn. C. Normal curvatures of an adult. [1]

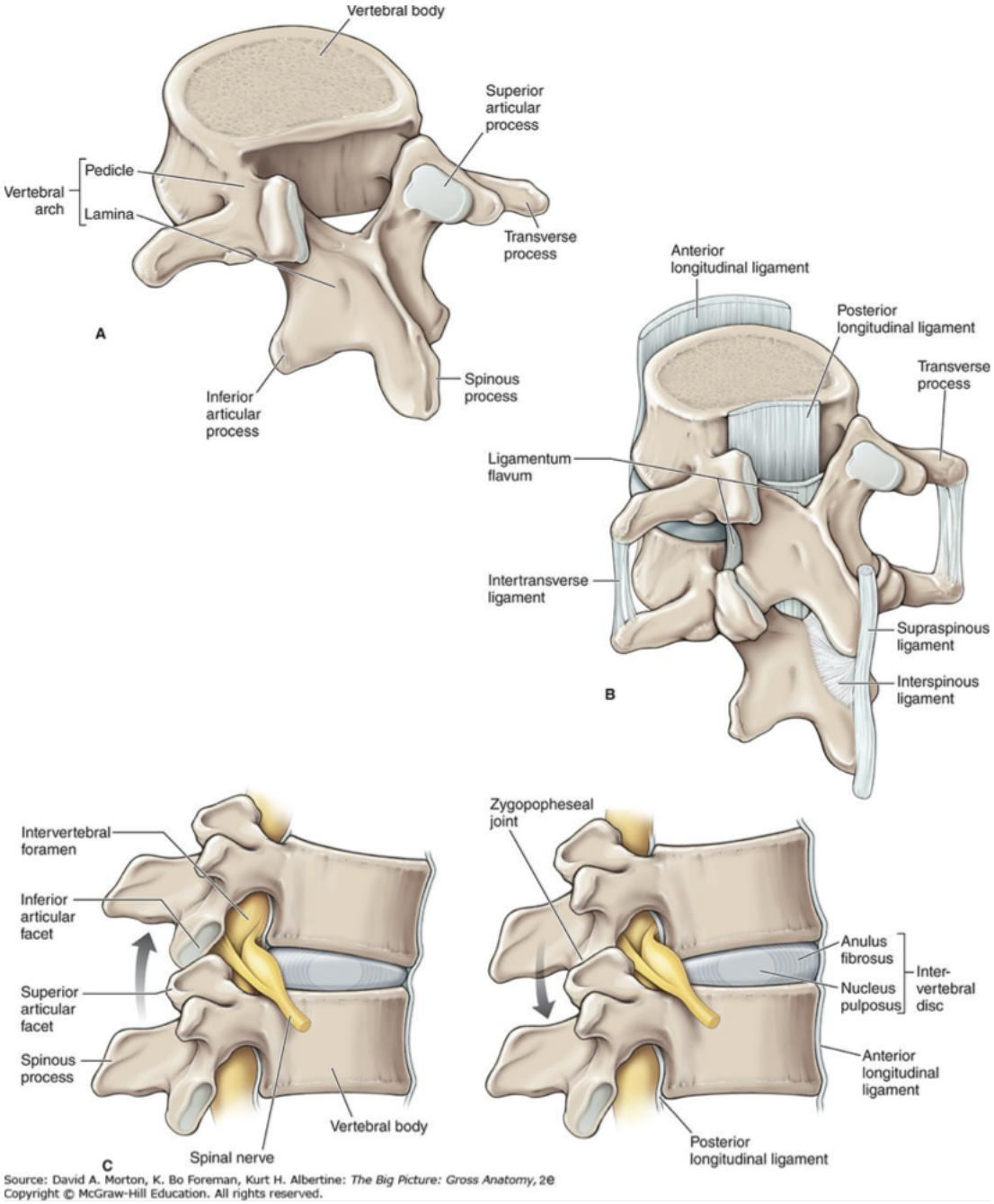

Figure 2: Vertebrae, ligaments and intervertebral discs. A. Posterolateral view of a typical vertebra. B. Vertebrae ligaments. C. Lateral view of two vertebrae and intervertebral (IV) discs; observe the IV discs and facet joints during vertebral flexion and extension. [1]

2.2. Common orthopaedic ailments of the spine

Orthopaedic ailments of the spine can be summarised into five categories: traumatic, infectious, degenerative, neoplastic and deformities [4].

2.2.1. Traumatic injuries to the spine

Traumatic injuries to the spine are commonly caused by fractures. Spinal fractures can occur in the vertebral bodies, such as burst fractures and compression fractures, and in the vertebral arch, such as the Jefferson fracture and the clay-shoveler's injury [2]. Furthermore, traumatic injuries to the spine can also be caused due to dislocation of vertebrae, such as spondylolisthesis. These conditions can be of enormous threat to the patient, as they can lead to instability of the vertebral column, which can in turn cause spinal injuries such as spinal stenosis, paralysis, radiculopathy, neurogenic claudication and cauda equina syndrome [2, 5]. Therefore, it is of vital importance in the clinical management of traumatic spinal injuries that the patient is sufficiently assessed for spinal stability using physical examination and radiographic imaging, and immobilised until the spine is cleared [2].

2.2.2. Infectious diseases of the spine

Infectious diseases of the spine can affect both the vertebrae and the intervertebral discs. Spondylitis (which is osteomyelitis of the vertebrae) is a condition where the vertebral bone is infected. In pyogenic vertebral osteomyelitis, the vertebrae are infected by pathogens such as *Staphylococcus aureus* and *Enterobacter spp.* which cause destruction to the vertebrae. Tuberculous vertebral osteomyelitis, also known as Pott's disease, occurs commonly among immunocompromised patients and in underdeveloped nations. Discitis is a condition when the intervertebral discs are infected. Primary discitis is rare and occurs more commonly among children. Secondary postoperative discitis occurs mostly due to *Staphylococcus aureus* and *Staphylococcus epidermidis* infections of the intervertebral disc [2].

2.2.3. Degenerative diseases of the spine

Intervertebral disc herniation is a common degenerative condition of the spine. It occurs when the Nucleosus pulposus herniates through the degenerative Anulus fibrosus. Disc herniations can occur in the central, posterolateral, foraminal and extraforaminal zones. Central herniations can compress the spinal cord, while more lateral herniations bear the risk of compressing the exiting spinal nerves, causing radiculopathy. It has been identified that disc herniations have a lifetime incidence of 13% to 40% and occur most commonly between the fourth and fifth lumbar vertebrae and between the fifth lumbar vertebra and the sacrum [5].

2.2.4. Neoplastic diseases of the spine

Spinal metastases and haemangiomas are examples of neoplastic diseases of the vertebral column. Metastatic tumours are the most common extradural tumours of the spine and occur most commonly in the thoracic and lumbar vertebral bodies due to the amount of red bone marrow. The most common primary source of spinal metastases are lymphoma, lung, breast and prostate. Spinal metastases can cause destruction to the vertebral bodies and cause spinal cord compression. Haemangiomas are primary tumours of the vertebral column and are mostly benign and asymptomatic, but large haemangiomas can cause loss of spinal stability and lead to fractures [2].

2.2.5. Deformities of the spine

The most common examples of spinal deformities are scoliosis and kyphosis. Scoliosis is defined as the deviation of the spine from the vertical axis greater than ten degrees. Scoliosis can be subdivided into idiopathic scoliosis, which is the most common form of scoliosis, and syndromic scoliosis. Idiopathic scoliosis can be classified into congenital scoliosis, infantile scoliosis, juvenile scoliosis, adolescent scoliosis, and adult scoliosis, depending on the age of the patient at diagnosis. Syndromic scoliosis occurs due to skeletal syndromes such as Marfan syndrome or neurofibromatosis, or due to neuromuscular conditions such as cerebral palsy [5].

Kyphosis is a condition that occurs when the physiological kyphosis of the spine is more pronounced and gives rise to pathologies. Congenital kyphosis and Scheuermann kyphosis are the most common forms of kyphosis. Even though kyphosis can be mild and asymptomatic, severe forms can cause pain, discomfort and disability such as paralysis [5].

2.3. Aspects of orthopaedic spine surgery

2.3.1. Surgical approaches to the spine [6, 7]

Surgical approaches to the spine can be divided into anterior and posterior approaches. The choice of a particular approach depends on the spinal pathology in question and the desired view of the spine.

The location of pathologies of the cervical spine can be divided into pathologies of the Atlas and Axis (C1 - C2 vertebrae) and of the subaxial cervical spine (C3 – C7). The posterior approach to the C1 – C2 vertebral space can be employed for spinal fusion, decompression laminectomy and for the treatment of tumours, most C1 – C2 ligamentous instabilities, traumatic fractures, congenital malformations, inflammatory diseases such as rheumatoid arthritis, degenerative diseases, and infections. Dangers of this approach to the first two vertebrae include the damage of large cutaneous nerves and vertebral artery, and dural and spinal cord injury. The posterior approach to the subaxial cervical spine is used for posterior cervical spine fusion, laminectomy, treatment of tumours, treatment of facet joint dislocations, nerve root exploration and discectomy. Complications of this approach include profuse bleeding of the venous plexus in the cervical canal and rarely the damage of posterior primary rami of the cervical nerve roots. Anterior approaches to the cervical spine can be used to expose the anterior vertebral bodies from C3 to C7 for discectomy, interbody fusion, excision of tumours, treatment of osteomyelitis and abscess drainage. Complications of this approach include acute airway obstruction from swelling or haematoma, CSF leak, injury to the vertebral artery, transient or permanent dysphagia and nerve root or spinal cord injury.

The most common approaches to the thoracic spine include the posterolateral approach and the anterior transthoracic approach. The posterolateral approach (also known as costotransversectomy) is used for abscess drainage, vertebral body biopsy, tumour treatment and for anterolateral spinal decompression. Complications of this procedure include dural damage resulting in CSF leaks and the damage of segmental intercostal arteries during rib resection. The anterior transthoracic approach is not often used due to the many complications it can cause, such as the damage of intercostal vessels during rib resection and during the surgical exposure to the vertebrae. Nonetheless, this approach can be used for the treatment of infections, fusion, correction of scoliosis, correction of kyphosis, osteotomy, anterior spinal cord decompression and biopsy.

Posterior approach to the lumbar spine is used most commonly for discectomy, exploration of nerve roots, spinal fusion and tumour excision and carries the risk of damaging the venous plexus, segmental blood vessels and nerve roots. The anterior approaches to the lumbar spine, such as the anterior transperitoneal and retroperitoneal approaches, can be used for L5/S1

fusion surgery. These approaches bear the risk of damaging the presacral nervous plexus, which is vital to uphold sexual function of the patient, and important vessels such as the aorta, inferior vena cava and the middle sacral artery, causing profuse bleeding. The anterolateral retroperitoneal approach to the lumbar spine allows access from L1 to S1 and allows, among others, access to levels above L4, which is difficult with the transperitoneal approach, and the drainage of an infection without risk of postoperative ileitis. Damage to nervous structures such as the sympathetic chain and genitofemoral nerve and blood vessels such as the vena cava and segmental lumbar arteries and veins are complications of this approach.

In order to minimise disruption to bone and soft tissue in spinal surgery, minimally invasive techniques have been introduced lately. Facet joint screw fixation, transsacral lumbar interbody screw fixation, lumbar interspinous spacers and lateral interbody approaches such as direct lateral interbody fusion are examples of the most common minimally invasive surgical techniques of the spine.

2.3.2. Instrumentation in spine surgery [8, 9]

Instrumentation is a common aspect of spine surgery. The most common metal substances used for spinal instrumentation are stainless steel, cobalt-chromium alloys, and titanium alloys. Even though these metals are commonly used, they are susceptible to implant failure through defects and exposure to repeated high stresses, corrosion and friction and wear, causing local inflammation, scarring and toxic or allergic reactions. Nonmetals used in spinal instrumentation include polymers, ceramics, and composites. Polymers such as polymethylmethacrylate are used in spinal surgery as they have found to be rigid and brittle. Ceramics most commonly used in spinal instrumentation due to their hardness and brittleness are alumina, zirconia, and hydroxyapatite. Composites consist of a matrix material and a filler. The most common composites used in spinal surgery are fibre-reinforced polymers such as carbon fibre composites.

2.3.3. Assessing the outcome of spinal surgeries

The outcome of spinal surgeries can be assessed by comparing the scores of various scales used prior to and after surgery. These scales include, among others, the Oswestry Disability Index, Neck Disability Index, 36-Item Short Form Health Survey and the Zurich Claudication Questionnaire [7].

2.4. Complications of spinal surgery

Perioperative complications of spinal surgery present in various levels of severity. The incidence of perioperative complications following spinal surgery depend on the surgical procedure performed and can be subdivided into medical complications, neurological complications, soft tissue complications, vascular complications, cerebrospinal fluid fistulas and pseudomeningoceles, pseudoarthrosis, and surgical site infections [10].

2.4.1. Medical complications

Medical complications due to spinal surgery can affect many organ systems [10]. Pulmonary complications such as pneumonia, acute pulmonary injury, pulmonary abnormalities (such atelectasis, infiltrates, lobar collapse, and effusions) and pulmonary embolism have been described as serious factors affecting the morbidity of patients [11]. Cardiac complications following spinal surgery include postoperative chest pain and arrythmia [12]. Renal and urinary tract complications include the probably the most common complication of spine surgery, urinary tract infections, and the less frequent renal failure [10]. Furthermore, gastrointestinal complications such as postoperative ileus and constipation (due to perioperative opiate intake) are common complications following spine surgery [13].

2.4.2. Neurological complications

Neurological complications of spine surgery can occur due to various reasons. Firstly, the positioning of the patient plays a central role in giving rise to neurological complications such as brachial plexus injury, peripheral nerve injury (ulnar nerve injury being the most common), ischemic damage or stretch injury to the spinal cord due to spinal hyperextension [10]. The surgical approach may cause various neurological complications such as dysphasia, dysphonia, Horner's syndrome, spinal cord ischemia, paraparesis and paralysis. [10].

2.4.3. Vascular complications

Due to the close proximity of vascular structures to the vertebral column, they are at risk of iatrogenic damage during surgery leading to complications such as bleeding and thrombosis. Such bleeding can range from benign bleeds to fatal bleeds causing death [10]. Vascular complications of surgical procedures concerning the cervical spine include direct injury to the carotid artery, thrombosis of the carotid artery, injury to the vertebral artery and bleeding from the epidural plexus. [14–16]. Procedures of the thoracic spine, although rare, can lead to injury of the aorta, vena cava, pulmonary arteries and veins, and segmental vessels [10]. During lumbar spine procedures, venous structures such as the iliac veins are more frequently injured

than arterial structures through surgery using the anterior approach, while injuries to arteries such as the iliac artery are more common among the posterior approach [10].

2.4.4. Cerebrospinal fluid fistulas and pseudomeningoceles

Cerebrospinal fluid leakage due to iatrogenic intraoperative dural tears can lead to cerebrospinal fluid fistulas and pseudomeningoceles [10, 17–20]. Cerebrospinal fluid fistulas and pseudomeningoceles can result in back pain, radicular pain, headache, meningismus, other signs of meningitis, and wound healing disorders [10, 21].

2.4.5. Pseudoarthrosis

Pseudoarthrosis can be defined as the non-union of the spine following spinal fusion surgeries with an incidence ranging from 5% to 35% [10]. This can result in pain, increasing deformity and neurological signs and symptoms. Advanced patient age, preoperative thoracolumbar kyphosis of >20 degrees, and the number of fused vertebral levels are some of the many factors that have been proven to significantly increase the risk of pseudoarthrosis [22–24].

2.4.6. Surgical site infections

As surgical site infection (SSI) has been identified as one of the most common complications following spinal surgery, and as it is the main focus of this dissertation, it will be discussed separately and in detail below.

2.5. Surgical site infections

2.5.1. Incidence of SSI

Surgical site infection is a common complication of orthopaedic spine surgery. Even though numerous studies have reported the incidence of SSI in their study populations to be as low as 0,65% and 0,99%, other studies have reported that SSI has a much higher incidence of up to 17,6% [25–29]. A meta-analysis performed by Zhang X, et al. in 2022 with a sum of 26 studies reported the overall incidence of SSI to be 2,9% [30].

2.5.2. Epidemiology of SSI

SSI have been known to have drastic effects on the patient's wellbeing and the healthcare system. The duration of hospital stay of patients have been reported to have increased by 9,7 days to 2 weeks [31, 32]. Furthermore, SSI has been found out to result in an increased number of rehospitalizations, total surgical procedures, and to adversely affect the quality of life of the patients [32, 33]. The number of patients with SSI requiring reoperation has been reported to range from as low as 4% to as high as 100% [26, 34–36]. A study performed by Lissovoy, et al. in 2009 states that SSI have caused 406.730 additional hospital days and hospital costs exceeding $900 million on a national level in the United States [31].

2.5.3. Risk factors

Various factors, both intrinsic and extrinsic with regard to the patient, can predispose a patient for SSI following orthopaedic spine surgery.

The demographic characteristics of patients have been discussed as unalterable risk factors for SSI. Two studies performed by Ogihara, et al. in 2018 and 2021 have mentioned that male patients are more commonly associated with SSI than female patients [25, 37]. This has been contradicted by Zhang, et al. through their meta-analysis in 2022, stating that the gender of patients was not associated with a statistically significant increase in the incidence of SSI [30]. Although it has been widely accepted that the advance age of patients increases the risk of SSI occurrence, some studies have found no such association [38, 39, 35, 40–42, 30]. Furthermore, the number of prior surgeries has been revealed to increase the risk of SSI [30, 39, 40, 43]. Tomov, et al. (2015) reported that 67% of patients with SSI had prior operations versus the 16% of patients without SSI [40].

The comorbidities of patients undergoing spine surgery have been considered as risk factors for SSI. Obese patients have been reported to have a predisposition for SSI. The body mass index (BMI) of patients has been found out to increase the risk of SSI following spine surgery, with a meta-analysis by Jiang J, et al. in 2014 reporting a 1,87 for BMI regarding SSI and a

meta-analysis by Abdallah, et al. in 2013 reporting a 21% increase in the risk of SSI with every 5-unit increase of the BMI [44–48]. Patients with diabetes mellitus have been found out to have a higher risk for SSI than patients without diabetes [30, 38, 43, 44, 49–53]. Ando, et al. (2014) and Jiang, et al. (2021) have found out that patients with diabetes make up 50% and 31,71% of the total number of patients with SSI respectively [49, 38]. A history of hypertension has also been mentioned as a risk factor for SSI by numerous studies including AlGamdi, et al. (2021) with 62,5% and Cizik, et al. (2012) with 47,62% of all patients with SSI suffering from hypertension [54, 36, 30, 43]. Patients with malignant tumours appear to possess a predisposition for SSI, as revealed by various studies [40, 49, 50]. Furthermore, patients with anaemia and patients with perioperative hypoalbuminemia have been shown to be at risk for SSI following spine surgery [40, 55].

The Charlson Comorbidity Index (CCI) was introduced by Charlson, et al. in 1987 to classify the prognostic comorbidity of patients [56]. The CCI was later modified by Deyo, et al. in 1992 [57]. The rate of SSI has been found to increase with the CCI score, as reported by Nota, et al. in 2015 and Andrés-Cano, et al. in 2018 [47, 58].

Patients with an anamnestic use of noxa have been identified to be at risk for postoperative SSI. A history of smoking has been found out to be present in 28% to 56,76% of patients with SSI when compared to 14% and 50% of patients without SSI respectively [40, 59]. Consumption of alcohol has also been discovered to be in a statistically highly significant association with the incidence of SSI [40].
It has been reported by Durkin, et al. (2015) and Spatenkova, et al. (2021) that SSI are significantly more common during the warmer months of the year when compared to the colder months [60, 61]. Spatenkova, et al. (2021) revealed that 14% of the patients operated during the warm months had SSI following surgery, while only 6,2% of the patients operated during the cold season had SSI [61].

Several intraoperative aspects have been found out to affect the risk of developing postoperative SSI. The location of surgery of the vertebral column can pose an increased risk of SSI [30, 39, 62]. The level of the spine posing the highest risk of SSI has been disputed among various studies. Even though numerous studies have reported that operations of the thoracic spine carry an increased likelihood of infection, some studies state that operations of the cervical spine poses a significant risk for SSI [37, 40, 44]. A study performed by Cizik, et al. (2012) identified that lumbosacral and thoracic procedures carried a 2,03 and 2,57 times higher risks for SSI, respectively [36]. The surgical technique also affects the rate of SSI in patients. Minimally invasive surgery has been lauded with a lower risk of SSI when compared to open surgery, while the use of an endoscope has been debated as a protective factor against postsurgical SSI [45, 25, 63]. The surgical approach of spinal interventions seems to

influence the risk of developing an SSI, as a posterior approach and a combined anterior and posterior approach have been recognised to be associated with a higher risk of SSI [39, 47, 64, 65]. Even though the volume of blood loss during surgery has been reported by numerous studies to be significantly higher among patients who later developed a SSI, a meta-analysis performed by Zhang, et al. (2022) states that an increased blood loss during surgery is not associated with a significant increase in SSI [42, 51, 54, 59, 66, 30]. However, the transfusion of blood products has been confirmed by numerous studies to be a risk factor for the occurrence of SSI, as the number of transfusions and the volume of transfusions have been observed to be higher among patients who developed SSI following surgery when compared with patients who did not develop SSI [30, 39, 50, 54, 66]. A retrospective study performed by Osterhoff, et al. (2015) reports an odds ratio of 3,1 for patients who were administered with blood transfusions 48 prior to surgery to present with SSI [41]. Several studies have identified an intraoperative iatrogenic dural tear as a risk factor for SSI [39, 67]. Takenaka, et al. (2019) presents that patients with a dural tear developed a significantly higher number of SSI at 1,8% when compared to patients without a dural tear, which was 0,7% [67]. Furthermore, Maragakis, et al. (2009) state that patients who were administered an FiO_2 of less than 50% are subjected to a higher risk of acquiring SSI following surgery [39]. Although some studies report that the local subcutaneous fat thickness is involved in increasing the risk for SSI, with Peng, et al. (2019) stating that a subcutaneous fat thickness of more than 4 cm possessing an odds ratio of 5,562 to present with SSI, Osterhoff, et al. (2015) analysed 244 patients and concluded that the subcutaneous fat thickness does not significantly increase the risk of SSI [59, 41]. The duration of surgery has been identified by numerous studies as a common risk factor for postoperative SSI, with a higher rate of SSI among surgeries with a longer duration [40, 51, 54, 58, 68–70]. Hosseini, et al. (2016) performed a study which proposes a probable cause for the relationship between the duration of surgery and the increasing rate of SSI. It was found out that the recolonisation of a surgeons hands become detectable at the fifth hour of surgery, which might be the reason for the association between longer surgery durations and increased risk of SSI [71]. Finally, the duration of hospital stay prior to and following surgery has been discussed as a possible cause for increased SSI [45, 54, 58, 64].

2.5.4. Common pathogens

The spectrum of pathogens causing SSI has been analysed by a multitude of studies. Most studies report gram-positive bacteria to be the most common pathogen to cause SSI, although several studies have mentioned gram-negative bacteria to cause the majority of SSI [62, 38, 72]. Among the gram-positive bacteria, methicillin sensitive Staphylococcus aureus, methicillin resistant Staphylococcus aureus and coagulase negative Staphylococcus have been reported to be the most common [73, 60, 45, 37]. Pseudomonas aeruginosa, Escherichia coli and

Klebsiella pneumoniae have been discussed as the most common gram-negative bacteria to cause SSI [38, 44, 72]. Overall, most studies have stated that Staphylococcus aureus was by far the most common pathogen to cause SSI, even though several studies have stated Pseudomonas aeruginosa and Escherichia coli to be the most common pathogenic cause of SSI [45, 74, 38, 72]. Monomicrobial SSI have been identified as more common than polymicrobial SSI, with the incidence of polymicrobial SSI ranging from 4,3% to 43,5% of all positive cultures [25, 37, 35, 62].

A retrospective hospital-registry study performed by Long, et al. (2021) was able to identify an anatomic gradient with regard to the pathogens causing SSI after spinal fusion surgery [62]. It was recognised that SSI of the cervical spine were predominantly caused by gram-positive bacteria of the skin flora, whereas SSI of the lumbosacral spine were mostly caused by gram-negative enteric bacteria. The point of inflection between the gram-positive and gram-negative bacteria was found to be significantly located at the thoracolumbar junction.
Although focusing on the most common pathogens is important when deciding which antibacterial therapy is most fitting, it is of utmost importance to consider rare bacterial strains to be the cause of SSI in cases of therapeutic resistance [75]. A case report published by Savini, et al. (2014) presents a patient with SSI after a discectomy caused by a mannitol-nonfermenting Staphylococcus aureus isolate [76]. SSI caused by such rare strains might be mistaken for contaminants and the rightful treatment might not be delivered.

Another hurdle in treating postoperative SSI is culture negativity. Several studies have reported patients with clinical SSI but with negative bacterial cultures, which have been known to range from 1,3% to 21,4% of the patients with clinical SSI [37, 62, 72].

2.5.5. Preventive measures

As SSI have been known to negatively impact the quality of life and prognosis of patients and to impose a massive burden on the healthcare system, it is of utmost importance to device methods to reduce the incidence of SSI in patients [31, 32].

The prevention of SSI can be started prior to surgery using prophylactic antibiotics [77, 78]. Several studies have highlighted the positive effect of prophylactic parenteral antibiotic administration prior to surgery [50, 51, 79]. Maciejczak, et al. (2019) revealed that patients who were administered 72 hour antibiotic prophylaxis had a lower risk of developing SSI at 3,6%, while patients who received a one-dose prophylaxis carried a 7,1% risk to develop SSI following surgery [50].
The use of intraoperative vancomycin powder in spine surgery has been disputed among professionals as to its ability to reduce the incidence of SSI [80]. A meta-analysis by Xie, et al. (2017) examined 20 studies and reported a favourable effect of intra-wound vancomycin

powder on reducing post-surgical SSI [81]. Furthermore, preliminary results of the ongoing "VANCO Trial" have confirmed the protective effects of intra-wound vancomycin application [82]. Despite these results, a retrospective cohort study performed by Tafish, et al. (2021) states that intra-wound vancomycin application was not significantly associated with a lower incidence of SSI in patients who underwent spinal surgeries [83]. Tomov, et al. (2015) analysed a protocol consisting of 0,3% Betadine wound irrigation and 1 g of intra-wound vancomycin powder application, and reported that this intervention significantly reduced the occurrence of SSI by 50%, with infections caused by methicillin resistant *Staphylococcus aureus* dropping from 30% to 7% and multi-bacterial infections dropping from 37% to 27% [40]. However intra-wound vancomycin powder might affect the rate of development of SSI, possible adverse effects of this practice have been reported. Zhang, et al. (2021) retrospectively analysed seven cases of severe hypotension and shock during wound closure or immediately following surgery which were all associated with local application of vancomycin powder [84]. The post-application effects of vancomycin powder were identified to be a result of anaphylaxis, which is presented with delayed occurrence, severe hypotension, and circulatory collapse [84].

Furthermore, the intraoperative use of various lavage techniques has also been known to alter the incidence of SSI. Fei, et al. (2017) studied the effects of traditional saline lavage, pulse lavage, closed drainage and iodine lavage on the rate of postsurgical infections following posterior lumbar interbody fusion (PLIF) surgeries and found out that pulse lavage, closed drainage and iodine lavage were significantly associated with much less rates of SSI following surgery [85].

Two techniques of surgical wound closure, the use of staples and 2-octyl-cyanoacrylate, was studied in a comparative study by Ando, et al. (2014) [49]. It was concluded that the use of 2-octyl-cyanoacrylate was associated with a significantly less rate of postoperative SSI than the use of staples. A study by Wachter, et al. (2010) also revealed that the use of 2-octyl-cyanoacrylate was associated with a lower incidence of postoperative SSI [86]. Furthermore, it was found out that the use of 2-octyl-cyanoacrylate was more time saving and cost effective than the use of staples [49].

The effects of negative pressure wound therapy (NPWT) has been a topic of discussion with regards to reducing the number of postoperative SSI [87, 88]. Naylor, et al. (2020) analysed the effects of NPWT on patients undergoing spinal surgeries [89]. It was concluded that patients who underwent spinal surgery through an anterior approach benefitted from NPWT and that NPWT prevents the increased rates of SSI.

The course of patient care following surgery can also be used as an opportunity to reduce the incidence of SSI. Gao, et al. (2018) compared the effects of total parenteral nutrition and enteral nutrition in patients after sacrectomy and found out that patients who received total

parenteral nutrition had a lower rate of postoperative SSI when compared to patients who received enteral nutrition [90].

2.5.6. Management

The management of postoperative SSI is of vital importance to prevent the drastic results of SSI on the patient's wellbeing and the healthcare system [31, 32]. A retrospective survey by Yin, et al. (2018) named a few possible methods to manage postoperative SSI [74]. These include a timely diagnosis of SSI, aggressive and meticulous debridement, and the use of antibacterial substances. The Robert Koch Institute (Berlin, Germany) published a series of recommendations to prevent an increase in SSI rates following surgery [91]. Preoperative decolonisation was recommended for patients with nasal colonisation of Staphylococcus aureus. The preoperative duration of hospital stay was suggested to be held at a minimum. It was also recommended to determine the need for preoperative systemic antibiotic prophylaxis. Furthermore, the importance of postoperative wound care was highlighted. It was suggested that the first change of dressing should take place around 48 hours after surgery and that the inspection of the surgical wound by a physician is crucial. Moreover, the Robert Koch Institute recommended wound drainages to be removed as early as possible.

2.6. Research question and objective

As numerous studies performed up to date have been able to identify, among others, the duration of surgery as a risk factor of utmost importance that increases the chance of developing a surgical site infection, the objective of this research is to further investigate the relationship between SSI and the duration of surgery.

The research question is formulated as follows: does the duration of surgery influence the spectrum of pathogens causing postoperative surgical site infections?

Patient data such as the duration of surgery and the species of pathogens discovered through postoperative blood culture reports are used for analysis to arrive at a conclusion to accept or reject the hypothesis that surgical duration influences the spectrum of pathogens causing postoperative SSI. Other patient data, for example the age, gender, diagnosis, and ASA classification, will be collected to further examine factors that affect the nature of SSI.

3. Material and Methods

3.1. Selection of the study population

This study was performed as a retrospective clinical analysis. Patients who underwent wound revision surgeries of the cervical, thoracic, and lumbar spinal levels in the department of orthopaedics and trauma surgery of the University Hospital of Cologne following a primary surgery of the spine were chronologically searched using the clinical software ORBIS (DH Healthcare GmbH, Bonn, Germany).

Patients of all genders, ages, ethnicities, and nationalities were included in this study. In order to be included in this study, patients had to have at least one wound revision surgery with a positive bacterial culture from a sample taken intraoperatively. If a patient has had more than one wound revision surgery of the spine with positive intraoperative bacterial cultures, data of the first wound revision surgery to have a positive intraoperative bacterial culture was chosen for the analysis. Furthermore, patients who underwent their primary surgery with the indication of spondylodiscitis were deemed unsuitable for this study. The reason for this exclusion was the primary objective of this study, which was to analyse postoperative surgical site infections caused independently from the primary surgical diagnosis. As the pathogens causing spondylodiscitis could serve as the primary origin of post-surgical wound healing disorders, it was deemed as a confounding factor and named as a reason for exclusion. Nonetheless, patients diagnosed with spondylodiscitis for their revision surgeries were included in this study, as the spondylodiscitis in these cases developed secondarily as a part of the surgical site infection.

Several data regarding patient characteristics such as the date of birth, gender, weight, and height were collected. Furthermore, the diagnosis of the primary surgery of the patients, the date of the primary surgery, the duration of the primary surgery, the date of the revision surgery of interest, and the American Society of Anaesthesiologists (ASA) score of the revision surgery were collected. The duration of stay of the patients in the intensive care unit, if applicable, was also recorded. In order to analyse the effects of antibacterial therapy on postoperative surgical site infections, the applied antibiotics and the duration of application were also collected. The bacterial species discovered in the intraoperative cultures and in the postoperative blood cultures were noted. Moreover, several laboratory parameters such as serum C-reactive protein (CRP), leukocytes, procalcitonin, creatinine, glomerular filtration rate (GFR), urea and

uric acid of the period from one day prior to the revision surgery to ten days following the revision surgery were collected.

3.2. Approval for data collection

Patient data was collected according to the data protection guidelines of the University Hospital of Cologne, Germany, and a signed declaration for a retrospective data collection was submitted accordingly.

3.3. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences software version 28 (SPSS, Chicago, Illinois, USA). The value for α was set to 0,05, according to convention, and statistical tests were deemed as statistically significant when the p-value was less than 0,05.

Data regarding patient characteristics were summarised using descriptive statistics and frequencies. The age of patients was calculated using the date of the revision surgery of interest and the date of birth. Furthermore, the BMI of the patients was also calculated.

Continuous data were analysed for normal distribution, as the presence or lack of normal distribution would decide the use of parametric or non-parametric statistical tests. Continuous data were considered to be normally distributed by analysing graphically using a histogram with a normality curve, and numerically using the Kolmogorov-Smirnov test, which is suitable for sample sizes of more than 50, with a p-value greater than or equal to 0,05 [92]. The mean value and the standard deviation were used to summarise normally distributed continuous variables, while the median and the interquartile range (IQR) were used to summarise variables lacking a normal distribution [93].

In order to test for any relationships between two categorical variables, contingency tables were generated along with the Pearson's chi-squared test. If the Pearson's chi-squared test results in a statistically significant association between the variables, the Cramér's V test or the Phi-coefficient were used to measure the association between the variables.

Tests for the difference of mean were used to analyse for associations between categorical variables and continuous variables. If the continuous variable follows a normal distribution, parametric tests such as the student's t-test (in the case of a binary categorical variable) and the analysis of variance (ANOVA; in the case of a non-binary categorical variable) were used. In the case of a statistically significant result from an ANOVA test, the Bonferroni post hoc test was used to analyse the relationship between the individual groups. If the continuous variable does not follow a normal distribution, non-parametric tests such as the Mann-Whitney test (in

the case of a binary categorical variable) and the Kruskal Wallis test (in the case of a non-binary categorical variable) were used.

When two continuous variables needed to be tested for any possible relationship, the Pearson's correlation (when both variables have a normal distribution) or the Spearman's rank correlation (if at least one of the variables was not normally distributed) was used. The degree of correlation was assessed using the Pearson's correlation coefficient or Spearman's rank correlation coefficient. Cut-off points were set to interpret the correlation coefficient, with 0,00 – 0,10 as negligible, 0,10 – 0,39 as weak, 0,40 – 0,69 as moderate, 0,70 – 0,89 as strong and 0,90 – 1,00 as a very strong correlation [94].

Graphical representation of data was done through bar charts, pie charts, histograms, and scatterplots, depending on the variables in question.

4. Results

4.1. Descriptive statistics and frequencies

4.1.1. Age and gender

Seventy-five patients were included in this retrospective study. Of the 75 patients, 36 were male (48%) and 39 were female (52%) (Figure 3).

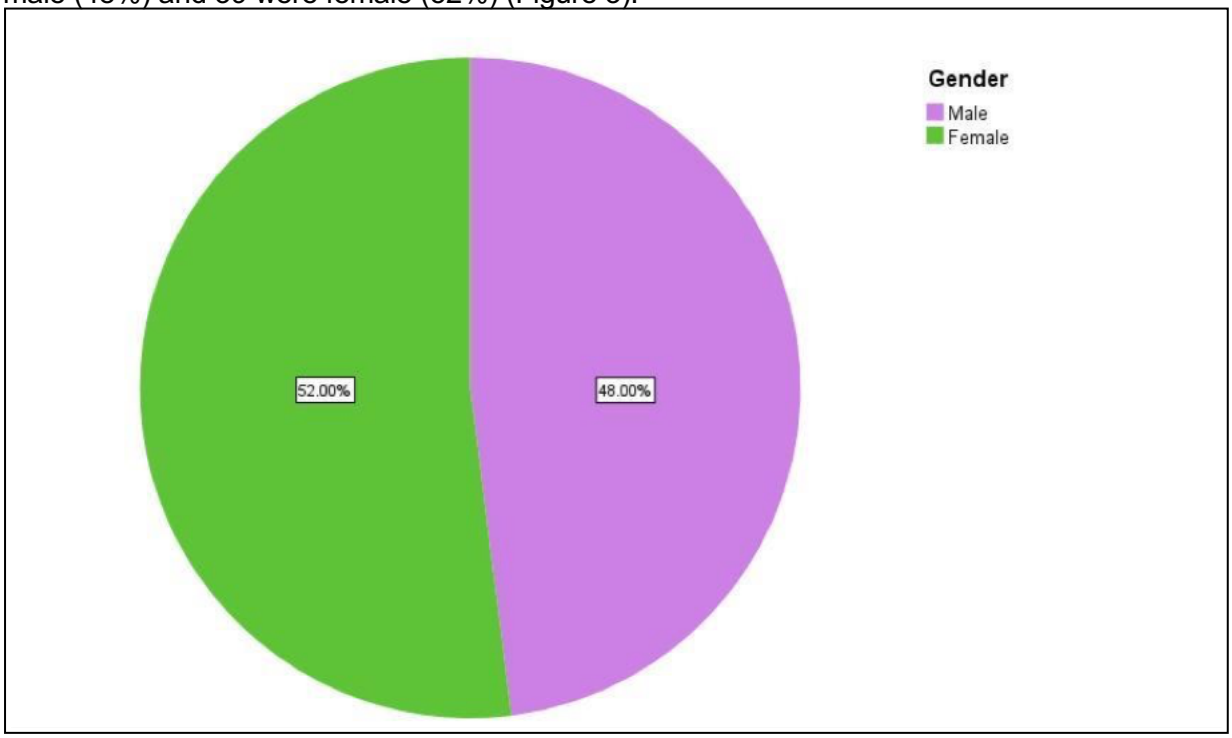

Figure 3: Gender distribution of the study population

The median age of the study population was 64 years (IQR 20, range 15 – 85). The median age of the male patients was 65,5 years (IQR 16, range 15 – 84) and the median age of the female patients was 63 years (IQR 33, range 21 – 85). Figures 4 and 5 represent the ages of the overall study population and of the male and female patients in three boxplots.

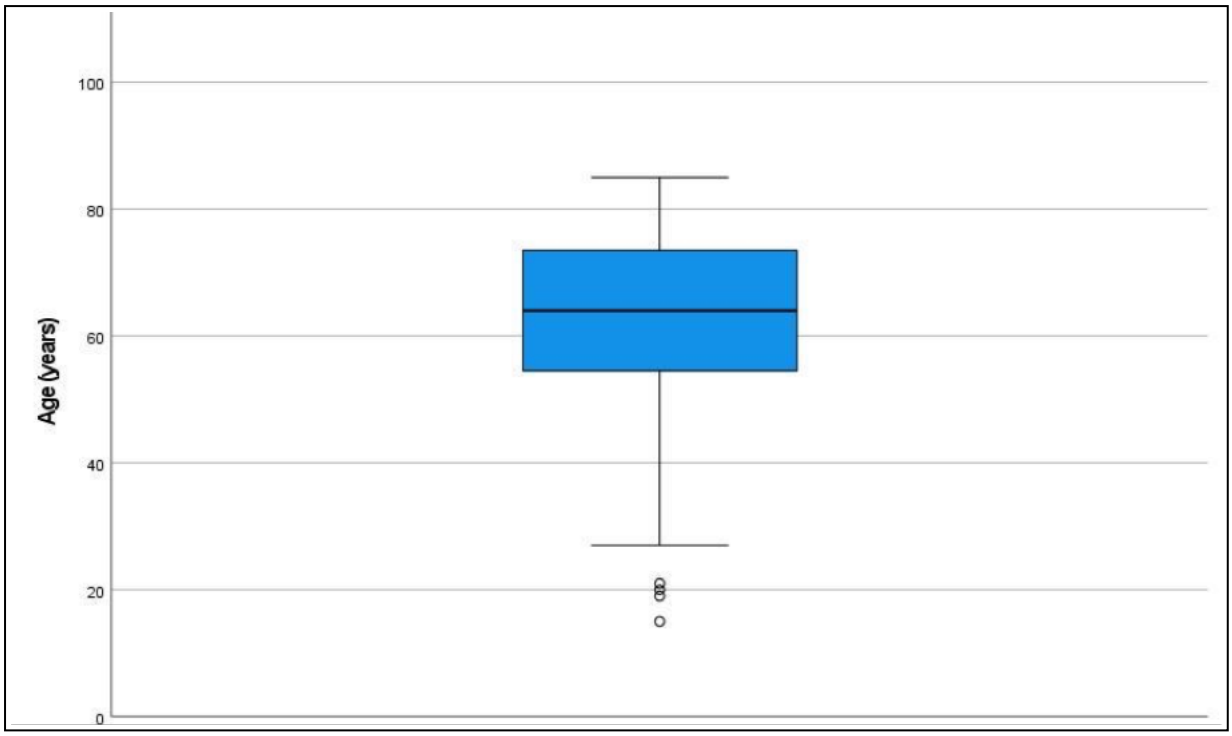

Figure 4: Boxplot of the age of the overall study population

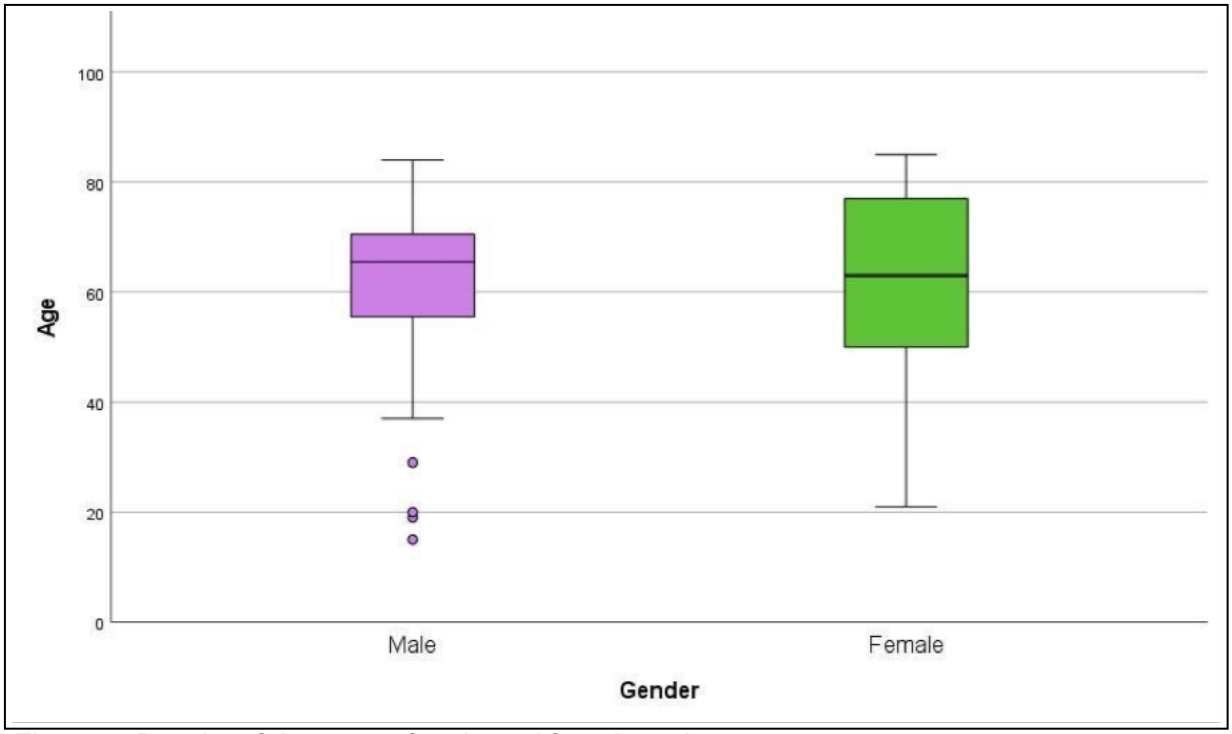

Figure 5: Boxplot of the ages of male and female patients

4.1.2. Height, weight, and BMI

The study population had a median height of 1,70 m (IQR 0,14, range 1,09 – 1,87) and a median weight of 82 kg (IQR 26, range 49 - 185). The male patients had a median height of 1,78 m (IQR 0,13, range 1,22 – 1,87) and a median weight of 87,5 kg (IQR 27, range 49 - 185), and the female patients had a median height of 1,65 m (IQR 0,1, range 1,09 – 1,84) and a median weight of 78 kg (IQR 29, range 54 - 145). The BMI of the patients was calculated, resulting in a median BMI of 29,00 kg/m^2 (IQR 9,17, range 15,70 – 124,29) of the overall study population. The median BMI of the male patients was 27,77 kg/m^2 (IQR 8,04, range 15,70 – 124,29) and the median BMI of the female patients was 29,38 kg/m^2 (IQR 11,26, range 20,28 – 58,92). The BMI of the patients was stratified according to the World Health Organisation's classification of obesity. 3 patients fell into the underweight category, while 19 were of normal weight, 23 were overweight (pre-obese) and 30 were obese. Among the male patients, 3 were underweight, 9 were of normal weight, 10 were pre-obese and 14 were obese, while among the female patients, none were underweight, 10 were of normal weight, 13 were pre-obese and 16 were obese. Figures 6 and 7 display the BMI categories in two bar charts for the overall population, male patients, and female patients.

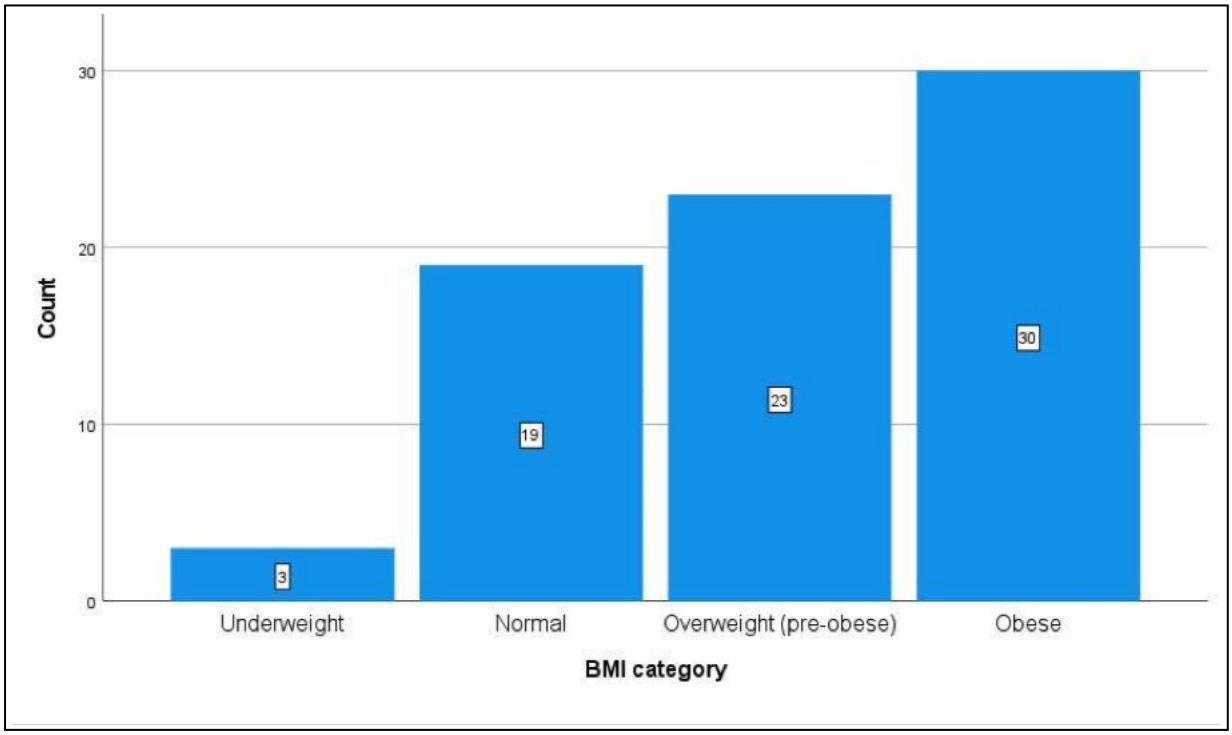

Figure 6: BMI categories of the study population

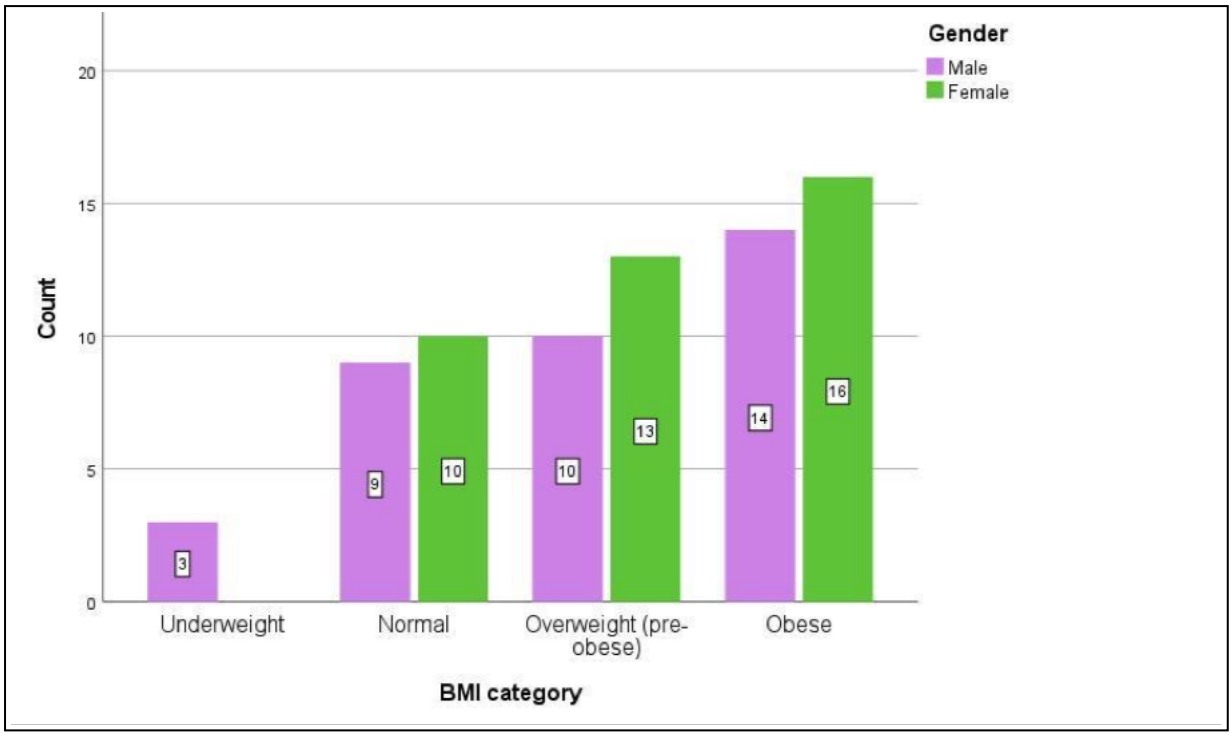

Figure 7: BMI categories of male and female patients

4.1.3. ASA classification

The ASA classification of the patients was noted as follows: 4 patients were classified as ASA 1, 27 as ASA 2, and 41 as ASA 3. None of the patients were classified as ASA 4, ASA 5, or ASA 6. 3 patients did not have a record of the ASA classification. Among the male patients, 2 were classified as ASA 1, 14 as ASA 2, and 18 as ASA 3. Among the female patients, 2 were classified as ASA 1, 13 as ASA 2, and 23 as ASA 3. Figure 8 presents the ASA classification of the study population.

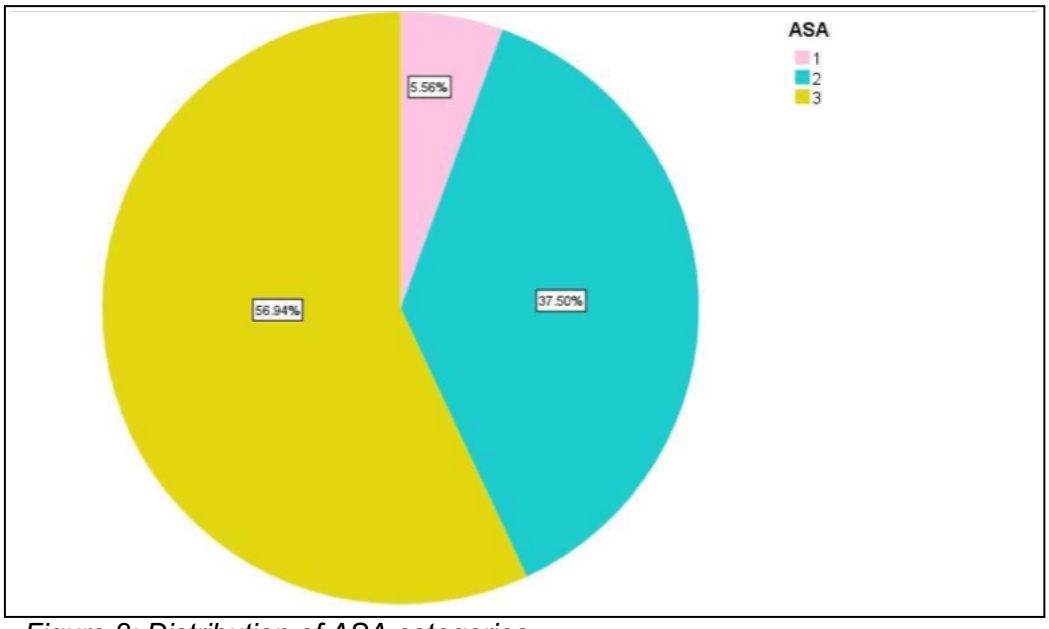

Figure 8: Distribution of ASA categories

4.1.4. Main diagnosis of the primary surgery

The main diagnosis of the primary spine surgery of the patients were analysed. The most common diagnoses were spinal stenosis (n = 15, 20%), spinal disc herniation (n = 11, 14,7%), vertebral fracture (n = 10, 13,3%), metastasis (n = 10, 13,3%), foraminal stenosis (n = 9, 12%), abscess (n = 3, 4%), adjacent segment degeneration (n = 2, 2,7%), scoliosis (n = 2, 2,7%) and others such as spondylolisthesis, intraspinal granuloma, chordoma, etc. (n = 13, 17,3%). The pie chart in Figure 9 displays the main diagnoses with their proportions.

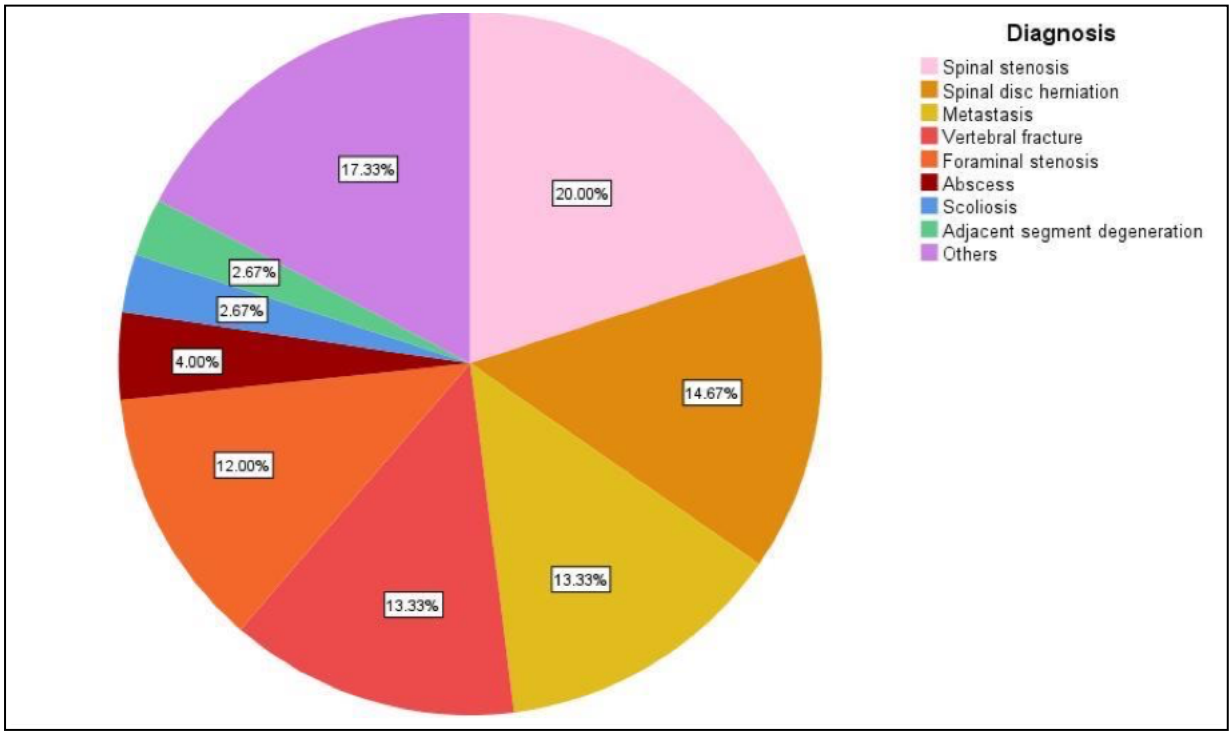

Figure 9: Diagnosis for primary surgery

4.1.5. Primary surgery

The earliest primary surgery of the study population took place on the 09.03.2007, while the latest primary surgery took place on the 23.09.2022. The mean duration of the primary surgery of the overall study population was 131,5 ± 70,9 minutes (range 23 - 285). The mean duration of the primary surgery of the male patients was 135,9 ± 71,9 mins (range 23 - 276), while the mean duration of the primary surgery of the female patients was 127,4 ± 70,7 mins (range 33 - 285).

4.1.6. Antibiotic treatment after primary surgery

58 patients (77,3%) received antibiotic treatment after the primary surgery for a median duration of one day (IQR 0, range 1 - 9). The most frequent duration of the application of antibiotic treatment was one day (n = 52), followed by 3 days (n = 3), 4 days (n = 1), 6 days (n

= 1), and 9 days (n = 1). The antibiotics applied were cefazolin (n = 52), clindamycin (n = 3), flucloxacillin (n = 2), nitrofurantoin (n = 1), and ceftriaxone (n = 1). 29 male patients (80,6%) were treated with antibiotics, with a median duration of one day (IQR 0, range 1 - 9). The most common antibiotic given to male patients was cefazolin (n = 27). 29 female patients (74,4%) were treated with antibiotics, with a median duration of one day (IQR 0, range 1 - 6). The most common antibiotic given to female patients was also cefazolin (n = 24).

4.1.7. Intensive care unit stay

Among the overall study population, 23 patients (30,7%) had a stay of a median duration of 2 days (IQR 2, range 1 - 34) in the intensive care unit. 13 male patients (36,1%) stayed a median duration of 2 days (IQR 1, range 1 - 7) in the intensive care unit, while 10 female patients (25,6%) stayed a median duration of also 2 days (IQR 8, range 1 - 34).

4.1.8. Postoperative blood cultures

Positive blood cultures were identified among 19 patients (25,3%) following the primary surgery. 12 male patients (33,3%) and 7 female patients (17,9%) had positive blood cultures. Among the positive blood cultures of the overall study population, the bacterial species identified were as follows:

Staphylococcus aureus	n = 7 (35%)
Staphylococcus haemolyticus	n = 2 (10%)
Staphylococcus hominis	n = 2 (10%)
Escherichia coli	n = 1 (5%)
Enterococcus faecalis	n = 1 (5%)
Staphylococcus capitis	n = 1 (5%)
Gram-positive Staphylococci	n = 1 (5%)
Serratia marcescens	n = 1 (5%)
Staphylococcus epidermidis + Gram-positive Staphylococci	n = 1 (5%)
Cutibacterium acnes + *Enterococcus faecalis* + *Staphylococcus warneri* + *Acinetobacter iwoffii*	n = 1 (5%)
Staphylococcus aureus + *Staphylococcus haemolyticus*	n = 1 (5%)

Table 1: Most common pathogenic species of postoperative blood cultures

The most common bacterial species among the male patients was *Staphylococcus aureus* (n = 6), followed by *Staphylococcus haemolyticus* (n = 2), whereas all bacterial species isolated among the female patients were found once each.

4.1.9. Revision surgery

The revision surgery of interest of the patients was defined as the first revision surgery with a positive intraoperative culture. The revision surgery of interest of the study population took place from 17.04.2020 to 30.09.2022.

4.1.10. Cultures of intraoperative samples

Samples from the surgical site were obtained intraoperatively during the revision surgery of interest under strictly sterile conditions and analysed for microbial growth. Among the multitude of positive cultures, the most common species were as follows:

Staphylococcus aureus	n = 17 (22,7%)
Staphylococcus epidermidis	n = 12 (16%)
Cutibacterium acnes	n = 10 (13,3%)
Staphylococcus aureus + *Staphylococcus epidermidis*	n = 3 (4%)
Staphylococcus epidermidis + *Cutibacterium acnes*	n = 3 (4%)
Corynebacterium tuberculostearicum	n = 2 (2,7%)
Enterococcus faecalis	n = 2 (2,7%)
Pseudomonas aeroginosa	n = 2 (2,7%)
Serratia marcescens	n = 2 (2,7%)
Staphylococcus aureus + *Escherichia coli*	n = 2 (2,7%)

Table 2: Most common pathogenic species of intraoperative cultures

Staphylococcus aureus (n = 11) followed by *Cutibacterium acnes* (n = 7) were the most common species identified among the male patients, while *Staphylococcus epidermidis* (n = 8) followed by *Staphylococcus aureus* (n = 6) were the most common species identified among the female patients.

4.1.11. Laboratory parameters

Several laboratory parameters were collected from the patients from prior to the revision surgery until 10 postoperative days.

The study population had a median CRP of 42,4 mg/L (IQR 105,5, range 0,6 – 313,4) preoperatively. Male patients had a median CRP of 37,65 mg/L (IQR 148,25, range 2,5 – 313,4), while female patients had a median CRP of 46,3 mg/L (IQR 104,9, range 0,6 – 276,1) preoperatively. There were no missing preoperative CRP levels among the study population. The median CRP levels are displayed in Figure 10.

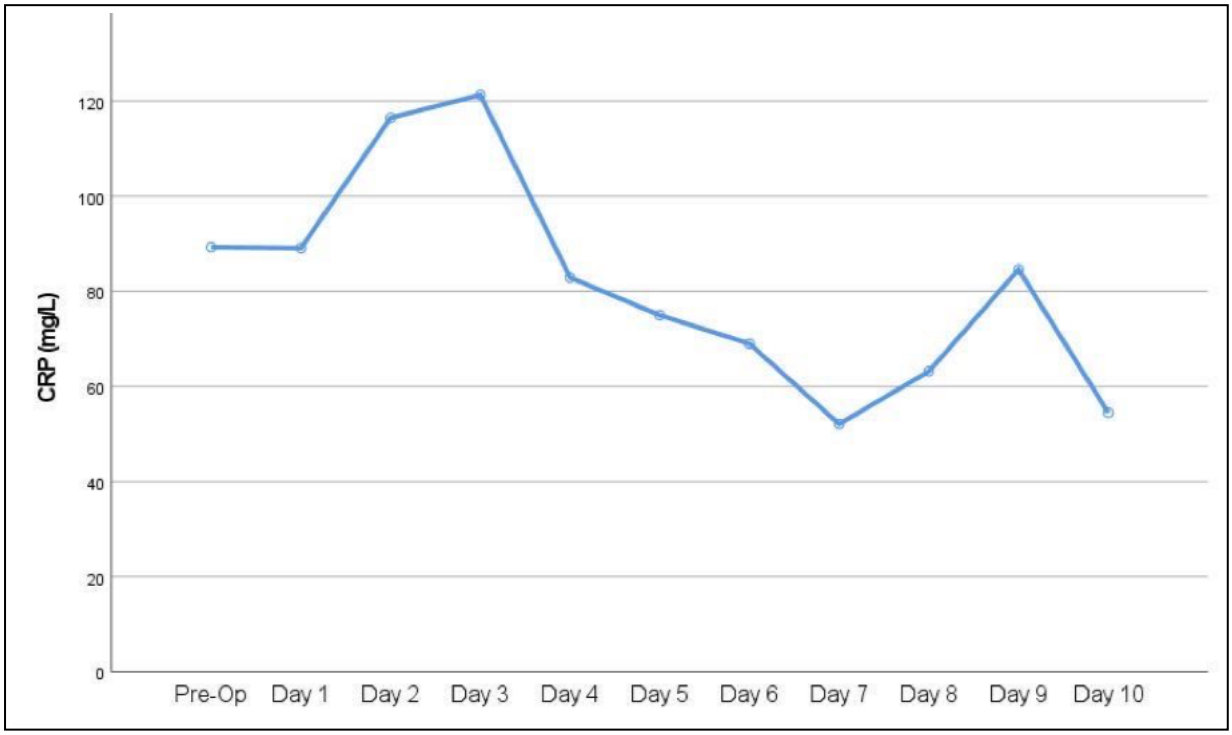

Figure 10: Median CRP from preoperative to postoperative day 10

The leukocyte count among the study population prior to surgery was at a median value of 9,01 10^9/L (IQR 4,59, range 2,09 – 22,34). Male patients had a median leukocyte count of 8,94 10^9/L (IQR 3,68, range 3,06 – 22,34) while female patients had a mean leukocyte count of 10,16 ± 4.23 10^9/L (range 2,09 – 20,26). None of the patients lacked a preoperative leukocyte count. Figure 11 displays the course of the leukocyte count until the 10th postoperative day.

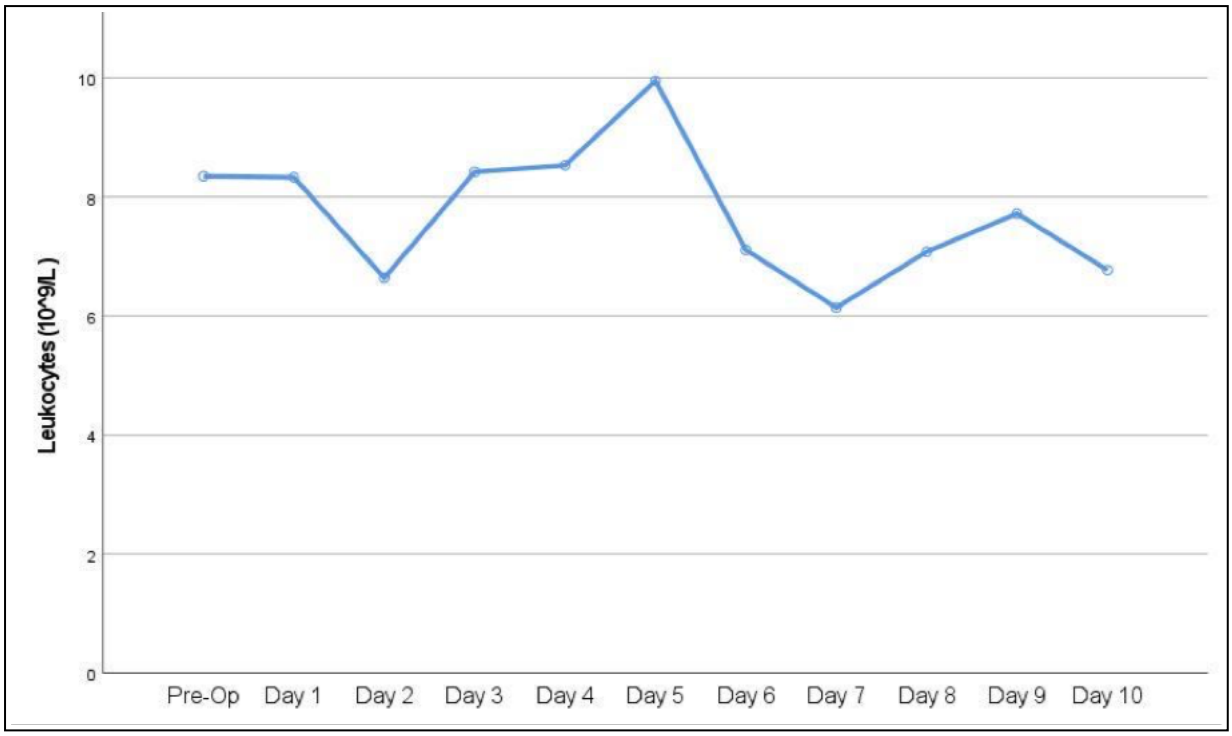

Figure 11: Median leukocyte count from preoperative to postoperative day 10

Only 7 patients (9,3%), 6 male (16,7%) and 1 female (2,6%), had valid preoperative procalcitonin measurements. Procalcitonin was measured preoperatively at a median value of 0,11 ng/mL (IQR 1,59, range 0,07 – 2,10). Male patients had a preoperative mean procalcitonin of 0,843 ± 0,897 ng/mL (range 0,07 – 2,10).

All patients had valid preoperative creatinine values. The median creatinine of the population lays at 0,83 mg/dL (IQR 0,43, range 0,25 – 3,16), with male patients having a median creatinine

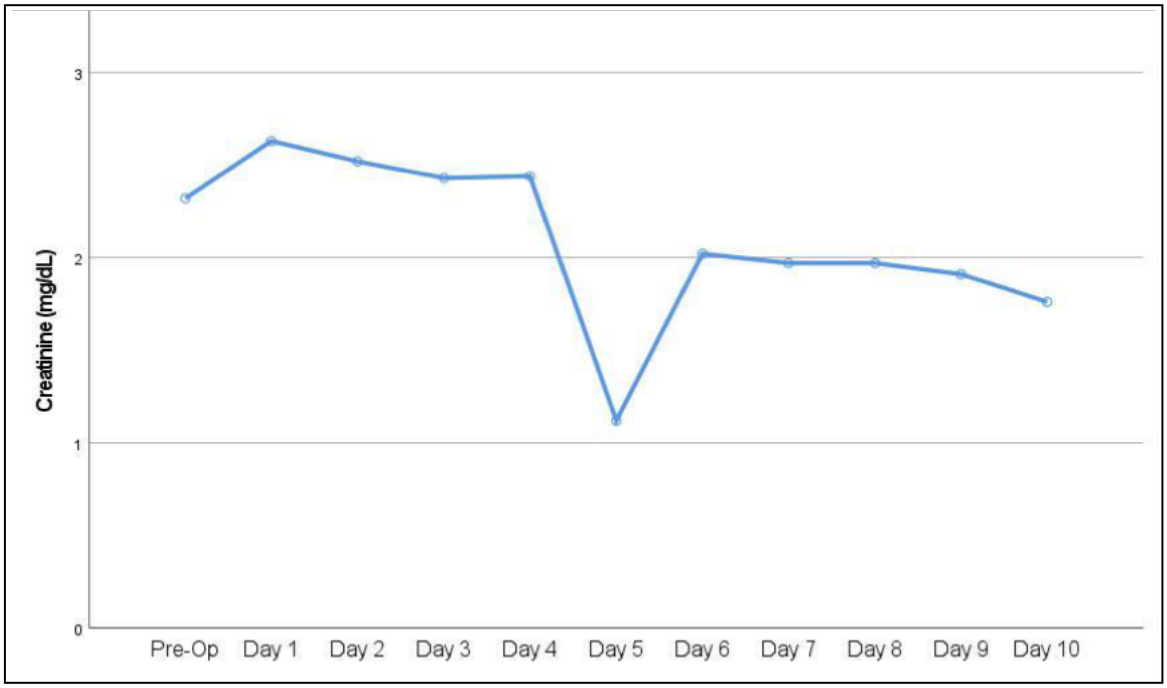

Figure 12: Median creatinine from preoperative to postoperative day 10

of 0,97 mg/dL (IQR 0,52, range 0,43 – 3,03) and female patients having a median creatinine of 0,76 mg/dL (IQR 0,24, range 0,25 – 3,16). Figure 12 displays the development of the creatinine levels.

Valid preoperative GFR levels were found among all patients. The overall median preoperative GFR level was 76 mL/min/1,73 m^2 (IQR 46, range 19 - 201). It was 76,5 mL/min/1,73 m^2 (IQR 48, range 24 - 201) among the male and 72 mL/min/1,73 m^2 (IQR 42, range 19 - 185) among the female patients. Figure 13 shows the GFR levels until the 10th postoperative day.

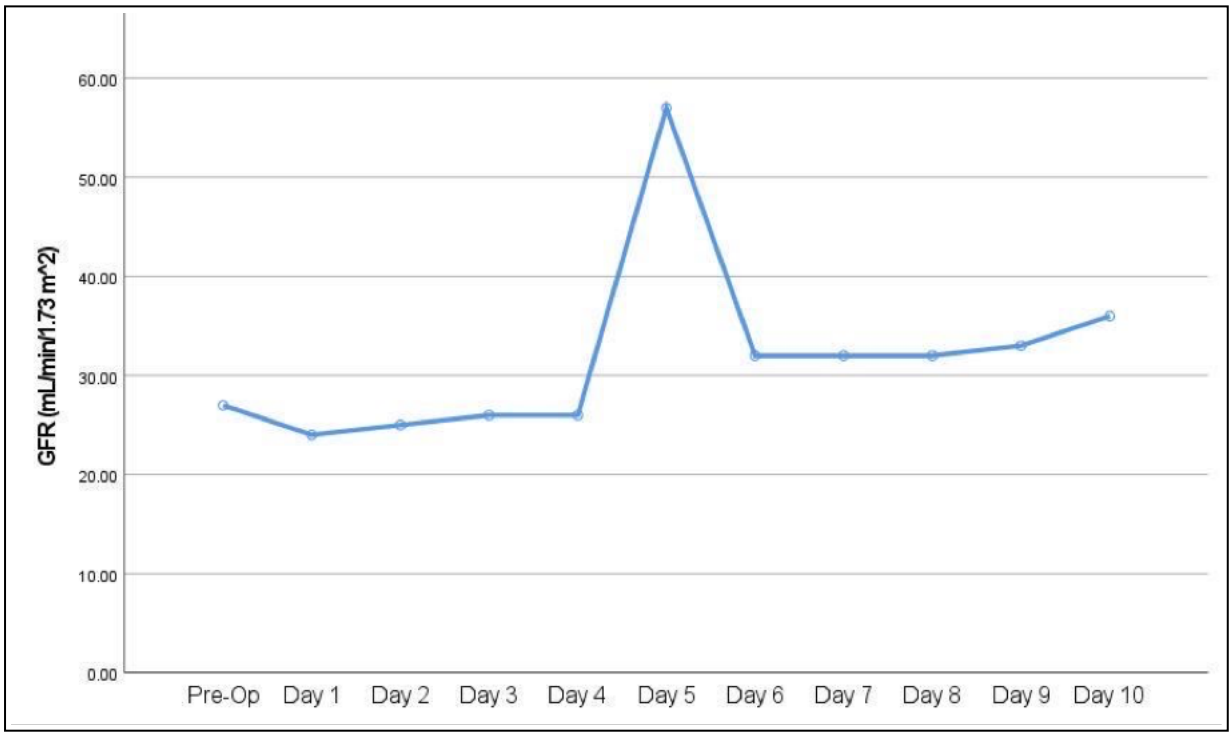

Figure 13: Median GFR from preoperative to postoperative day 10

The median preoperative blood urea level of the population was 32 mmol/L (IQR 22, range 6 - 163). The median preoperative urea level of the male patients was 33 mmol/L (IQR 21, range 6 - 163) and of the female patients was 27 mmol/L (IQR 20, range 10 - 78). 2 male and none of the female patients lacked valid preoperative urea levels. Figure 14 shows the blood urea levels from prior to surgery until the 10th postoperative day.

There were 72 valid values for preoperative uric acid levels (34 male and 38 female). The median lays at 4,65 mg/dL (IQR 2,28, range 2,2 – 14,2) among the overall population, while it was 4,95 mg/dL (IQR 2,98, range 2,2 – 14,2) and 4,45 mg/dL (IQR 2,45, range 2,2 – 9,3) among the male and female patients, respectively.

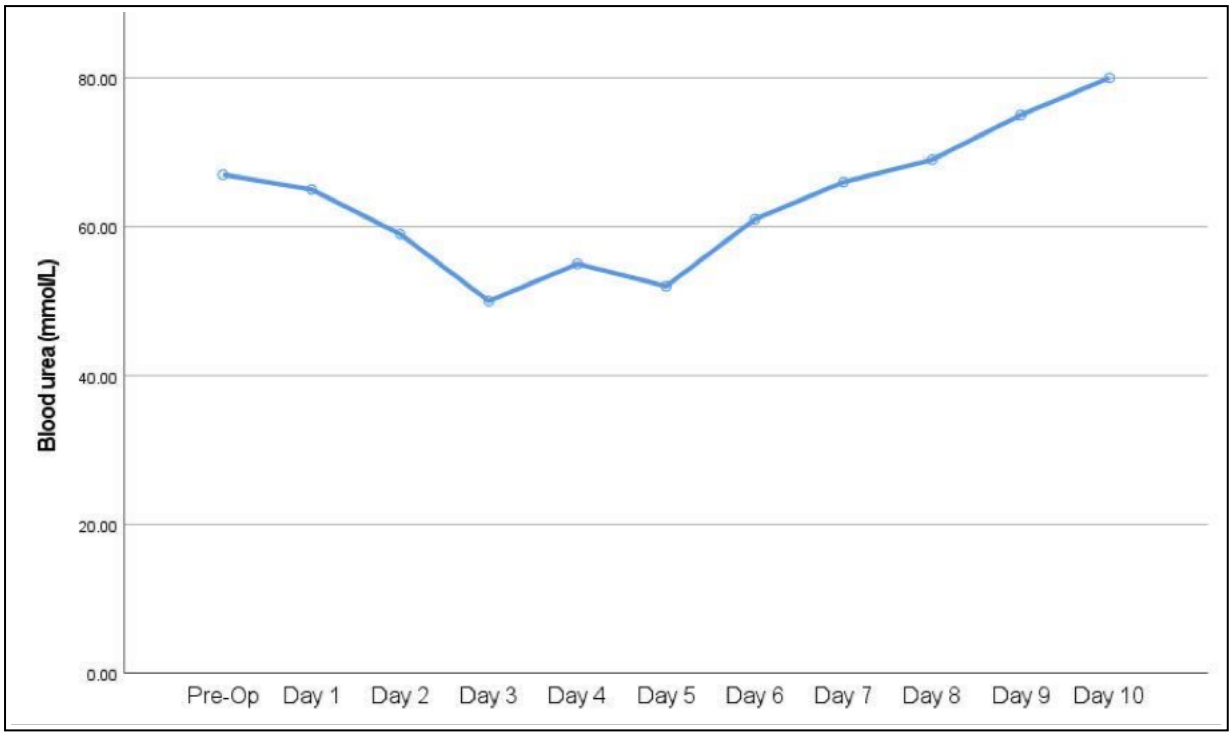

Figure 14: Median urea level from preoperative to postoperative day 10

4.2. Frequency distribution between categorical variables

4.2.1 Postoperative blood cultures versus intraoperative cultures

Contingency tables were created between postoperative blood cultures taken after the primary surgery and intraoperative cultures of the revision surgery. The association between the two variables was tested using the chi-squared test, which resulted in a highly significant association ($p < 0,001$). A Cramér's V value of 0,907 ($p < 0,001$) depicts a strong association between the two variables.

4.2.2. Postoperative blood cultures versus gender

In order to determine if a relationship exists between pathogens discovered postoperatively through blood cultures and gender, a chi-squared test was performed. The distribution of frequencies among the groups are displayed in Table 3. There was no statistically significant relationship between gender and postoperatively discovered pathogens ($p = 0,214$).

Pathogen	**Male**		**Female**	
	N	**%**	**N**	**%**
Staphylococcus aureus	6	85,7%	1	14,3%
Escherichia coli	0	0%	1	100%
Enterococcus faecalis	0	0%	1	100%
Staphylococcus haemolyticus	2	100%	0	0%
Staphylococcus hominis	1	50%	1	50%
Staphylococcus capitis	1	100%	0	0%
Gram-positive Staphylococci	0	0%	1	100%
Serratia marcescens	0	0%	1	100%
Staphylococcus epidermidis + gram-positive Staphylococci	1	100%	0	0%

Cutibacterium acnes + Enterococcus faecalis + Staphylococcus warneri + Acinetobacter iwoffii	1	100%	0	0%
Staphylococcus aureus+ Staphylococcus haemolyticus	0	0%	1	100%

Table 3: Pathogens of postoperative blood cultures vs. gender

4.2.3. Postoperative blood cultures versus BMI categories

BMI categories were tested for a relationship with pathogens of postoperative blood cultures. Of the 19 positive postoperative blood cultures, 6 cultures were positive among the normal weight patients, 5 among the overweight patients and 8 among the obese patients. The chi-squared test performed resulted in a statistically insignificant result (p = 0,204). Table 4 shows the distribution of frequencies of each group.

Pathogen	**Normal weight**		**Overweight**		**Obese**	
	N	**%**	**N**	**%**	**N**	**%**
Staphylococcus aureus	2	28,6%	4	57,1%	1	14,3%
Escherichia coli	1	100%	0	0%	0	0%
Enterococcus faecalis	0	0%	0	0%	1	100%
Staphylococcus haemolyticus	0	0%	0	0%	2	100%
Staphylococcus hominis	2	100%	0	0%	0	0%
Staphylococcus capitis	1	100%	0	0%	0	0%
Gram-positive Staphylococci	0	0%	0	0%	1	100%
Serratia marcescens	0	0%	0	0%	1	100%
Staphylococcus epidermidis + gram-positive Staphylococci	0	0%	0	0%	1	100%

Cutibacterium acnes + Enterococcus faecalis + Staphylococcus warneri + Acinetobacter iwoffii	0	0%	0	0%	1	100%
Staphylococcus aureus+ Staphylococcus haemolyticus	0	0%	1	100%	0	0%

Table 4: Pathogens of postoperative blood cultures vs. BMI

4.2.4. Postoperative blood cultures versus ASA classification

Patients who had a record of an ASA classification were tested for a relationship with postoperative blood culture reports. The number of positive cultures increased with the ASA category, with only one positive blood culture among ASA 1 patients, seven positive cultures among ASA 2 and 10 among ASA 3 patients. The chi-squared test did not result in a statistically significant result (p = 0,467). Table 5 is the contingency table between postoperative blood cultures and the ASA classification.

Pathogen	**ASA 1**		**ASA 2**		**ASA 3**	
	N	**%**	**N**	**%**	**N**	**%**
Staphylococcus aureus	0	0%	2	28,6%	5	71,4%
Escherichia coli	0	0%	1	100%	0	0%
Enterococcus faecalis	0	0%	0	0%	1	100%
Staphylococcus haemolyticus	0	0%	1	100%	0	0%
Staphylococcus hominis	1	50%	0	0%	1	50%
Staphylococcus capitis	0	0%	0	0%	1	100%
Gram-positive Staphylococci	0	0%	1	100%	0	0%
Serratia marcescens	0	0%	0	0%	1	100%
Staphylococcus epidermidis + gram-positive Staphylococci	0	0%	1	100%	0	0%

Cutibacterium acnes + *Enterococcus faecalis* + *Staphylococcus warneri* + *Acinetobacter iwoffii*	0	0%	1	100%	0	0%
Staphylococcus aureus+ *Staphylococcus haemolyticus*	0	0%	0	0%	1	100%

Table 5: Pathogens of postoperative blood cultures vs. ASA classification

4.2.5. Postoperative blood cultures versus diagnosis of primary surgery

As the primary diagnosis could influence the type of postoperative pathogens causing SSI, a chi-squared test was performed between postoperative blood culture results and the diagnosis for the primary surgery. Diagnoses with the most number of positive blood cultures were spinal stenosis (n = 4), and foraminal stenosis (n = 3). There was no statistically significant relationship between the two variables (p = 0,309).

4.2.6. Postoperative blood cultures versus antibiotic treatment

A chi-squared test was performed between the pathogens found in postoperative blood cultures and antibiotic treatment following the primary surgery. Only patients who received cefazolin and ceftriaxone had positive blood cultures. Patients who received cefazolin had 16 positive blood cultures, while patients who received ceftriaxone had only one positive blood culture. Table 6 shows the distribution of frequencies. The test was not statistically significant with a p value of 0,999.

Pathogen	**Cefazolin**		**Ceftriaxone**	
	N	**%**	**N**	**%**
Staphylococcus aureus	6	85,7%	1	14,3%
Escherichia coli	1	100%	0	0%
Enterococcus faecalis	1	100%	0	0%
Staphylococcus haemolyticus	1	100%	0	0%
Staphylococcus hominis	1	100%	0	0%
Staphylococcus capitis	1	100%	0	0%

Gram-positive Staphylococci	1	100%	0	0%
Serratia marcescens	1	100%	0	0%
Staphylococcus epidermidis + gram-positive Staphylococci	1	100%	0	0%
Cutibacterium acnes + Enterococcus faecalis + Staphylococcus warneri + Acinetobacter iwoffii	1	100%	0	0%
Staphylococcus aureus+ Staphylococcus haemolyticus	1	100%	0	0%

Table 6: Pathogens of postoperative blood cultures vs. antibiotic treatment

4.2.7. Other outcomes

Chi-squared tests were performed between several other variables.

The chi-squared test performed between the BMI categories and ASA classification resulted in a statistically insignificant result with a p value of 0,118. Nevertheless, out of the 72 patients who had valid values for this analysis, ASA 3 was mostly recorded among overweight and obese patients (n = 16 each). Table 7 and Figure 15 display the distribution of frequencies among the groups.

BMI category	**ASA 1**		**ASA 2**		**ASA 3**	
	N	**%**	**N**	**%**	**N**	**%**
Underweight	1	33,3%	2	66,7%	0	0%
Normal weight	2	11,1%	7	38,9%	9	50%
Overweight (pre-obese)	0	0%	7	30,4%	16	69,6%
Obese	1	3,6%	11	39,3%	16	57,1%

Table 7: BMI category vs. ASA classification

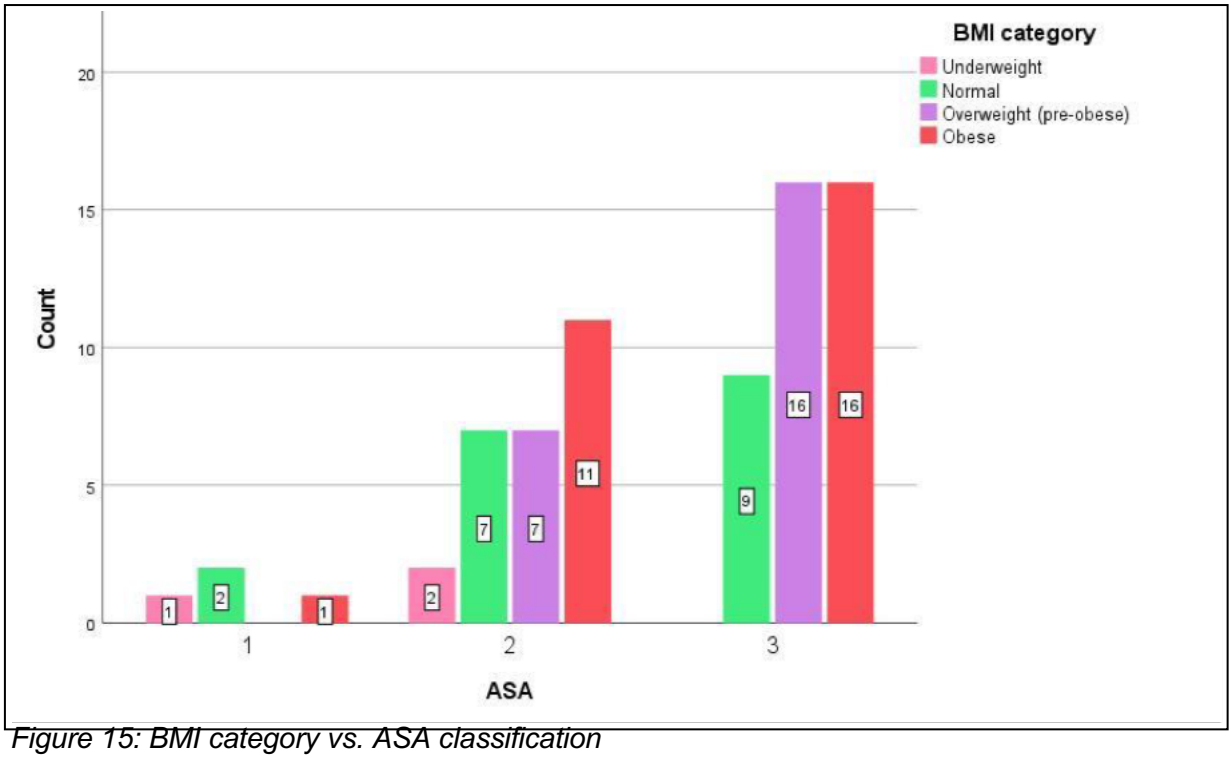

Figure 15: BMI category vs. ASA classification

Furthermore, there were more obese females than males, with a count of 16 and 14, respectively (Figure 7). The distribution of frequencies among BMI categories and gender was analysed using a chi-squared test. The result was not statistically significant (p = 0,326).

4.3. Differences of mean and median

4.3.1. Postoperative blood cultures versus duration of primary surgery

An ANOVA test was performed between postoperative blood culture results and the duration of the primary surgery. It was found out that the duration of primary surgery has a statistically significant relationship with the pathogens discovered postoperatively (p = 0,002). Pathogens such as *Staphylococcus epidermidis* + gram-positive Staphylococci, *Staphylococcus hominis* and *Staphylococcus aureus* were discovered after shorter surgical durations (40, 69 and 101 minutes, respectively) while pathogens such as *Enterococcus faecalis, Staphylococcus capitis, and Staphylococcus haemolyticus* were discovered after surgeries that lasted longer (285, 276 and 226 minutes, respectively). Figure 16 depicts the mean duration of surgery for each group of postoperatively discovered pathogens. It was not possible to further analyse the relationship between the duration of primary surgery and postoperatively discovered pathogens using the Bonferroni post hoc test, as at least one group had fewer than two cases.

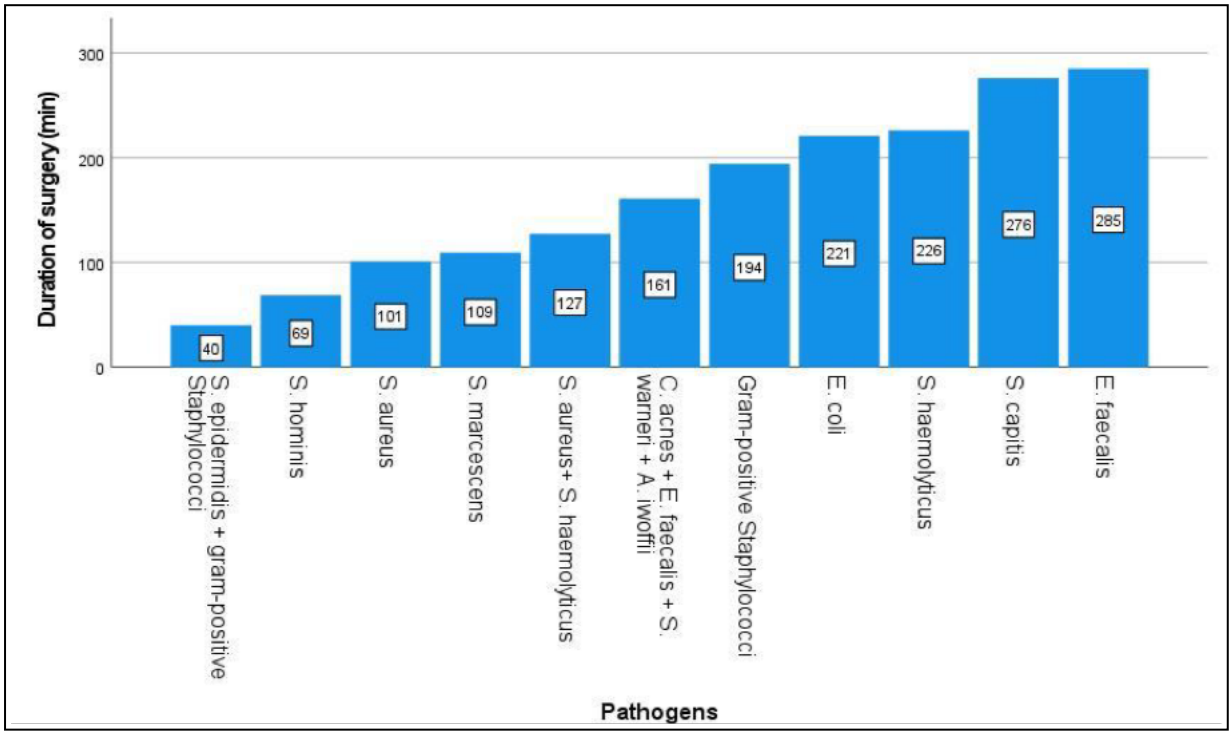

Figure 16: Pathogens of postoperative blood cultures vs. duration of surgery

4.3.2. Postoperative blood cultures versus age

The continuous variable age was tested for normality and was found out to lack a normal distribution. Therefore, the Kruskal Wallis test was used to test age against postoperatively discovered pathogens. The pathogens *Staphylococcus haemolyticus* and *Staphylococcus epidermidis* + gram-positive Staphylococci were most frequently found among younger patients, while *Escherichia coli, Staphylococcus aureus* and *Cutibacterium acnes* +

Enterococcus faecalis + *Staphylococcus warneri* + *Acinetobacter iwoffii* were most frequently found among older patients. The results of the test are displayed in Figure 17. The test was statistically insignificant with a p value of 0,287.

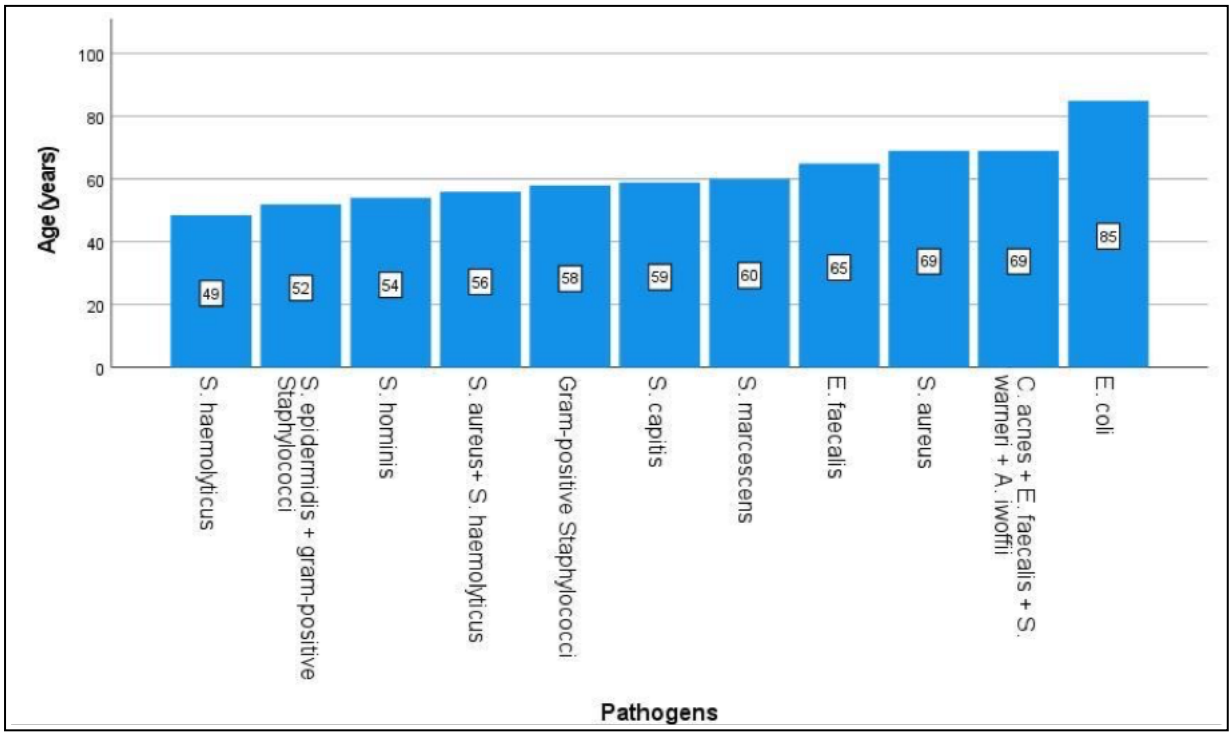

Figure 17: Pathogens of postoperative blood cultures vs. age

4.3.3. Postoperative blood cultures versus BMI

The Kruskal Wallis test performed between the BMI of patients and the postoperatively discovered pathogens showed that some pathogens such as *Staphylococcus capitis* and *Escherichia coli* are more common among patients with a lower BMI, while pathogens such as *Enterococcus faecalis* and gram-positive Staphylococci are more common among patients

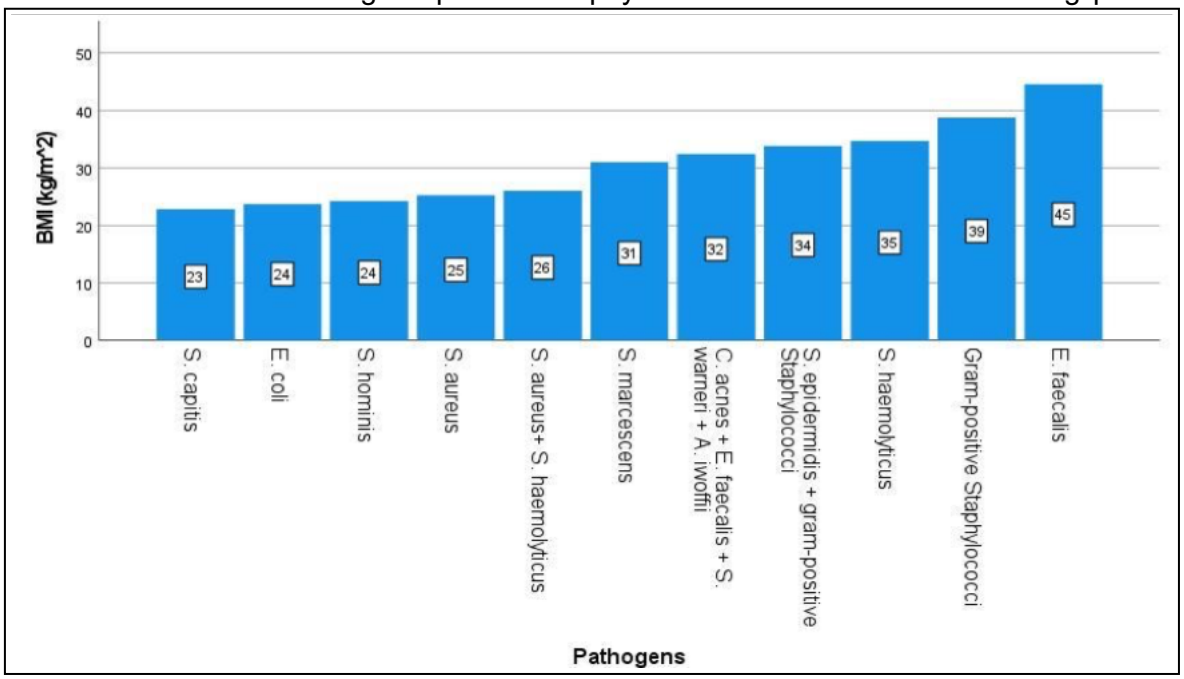

Figure 18: Pathogens of postoperative blood cultures vs. BMI

with a higher BMI. This result was statistically insignificant with a p value of 0,277. Figure 18 shows a chart displaying the average BMI of each postoperatively discovered pathogen.

4.3.4. Postoperative blood cultures versus duration of antibiotic treatment

The median duration of the administration of antibiotic treatment following the primary surgery did not significantly differ among the postoperatively discovered pathogen groups (p = 1,000), as all the patients included in the test were administered postoperative antibiotics for just a single day.

4.3.5. Postoperative blood cultures versus intensive care unit stay

The duration of postoperative intensive care unit stay was tested for an association with postoperatively discovered pathogens using the Kruskal Wallis test. *Staphylococcus aureus*, *Enterococcus faecalis* and *Staphylococcus haemolyticus* were associated with a shorter duration of intensive care unit stay, while gram-positive Staphylococci were associated with a longer duration of intensive care unit stay (Figure 19). This result was not statistically significant (p = 0,310).

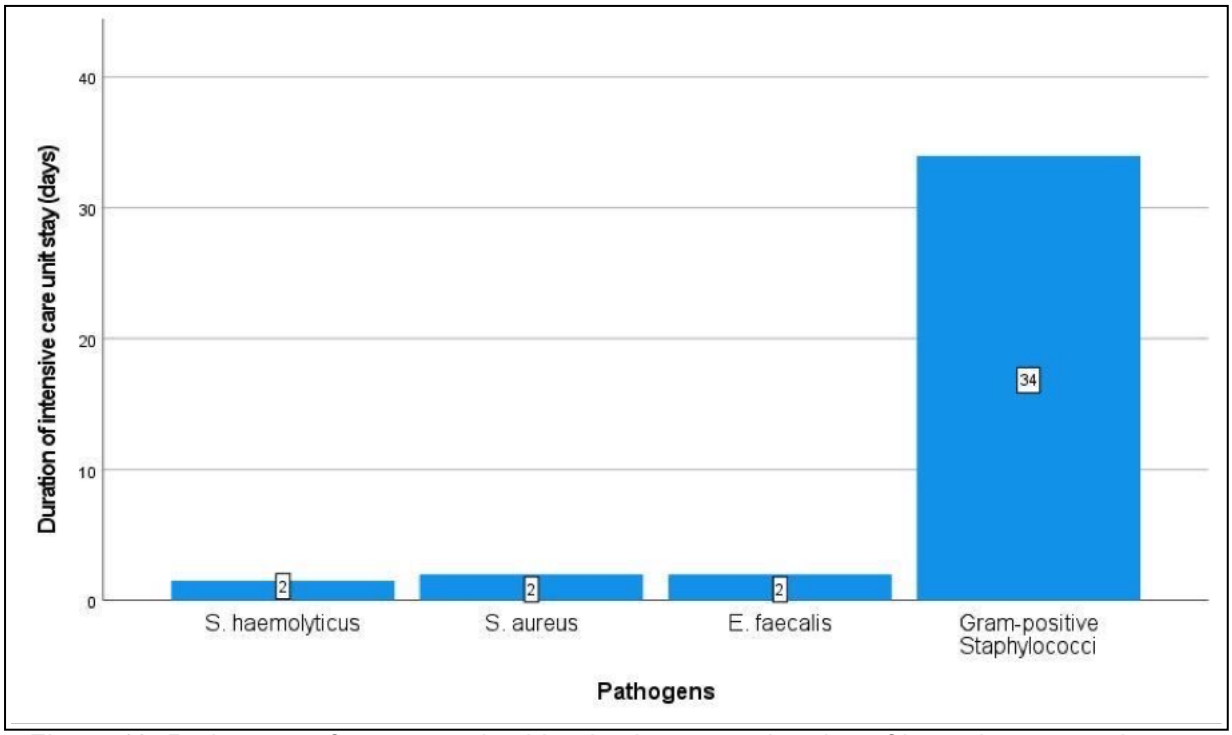

Figure 19: Pathogens of postoperative blood cultures vs. duration of intensive care unit stay

4.3.6. Intraoperative cultures versus laboratory parameters

Laboratory parameters such as CRP, leukocytes, procalcitonin, creatinine, GFR, blood urea and uric acid levels were analysed to determine if certain pathogens cause the levels of these parameters to increase significantly more than other pathogens.

A Kruskal Wallis test was performed between the preoperative CRP levels and the pathogens of the intraoperative cultures. Pathogens such as *Escherichia coli, E. coli* + *Streptococcus agalactiae* + *Streptococcus constellatus* + *Peptoniphilus spp.* were associated with a much lower CRP level than pathogens such as *S. aureus* + *E. coli* and *Staphylococcus epidermidis* + *Clostridium perfringens*, who had a much higher median CRP level (Figure 20). This result was not statistically significant (p = 0,341).

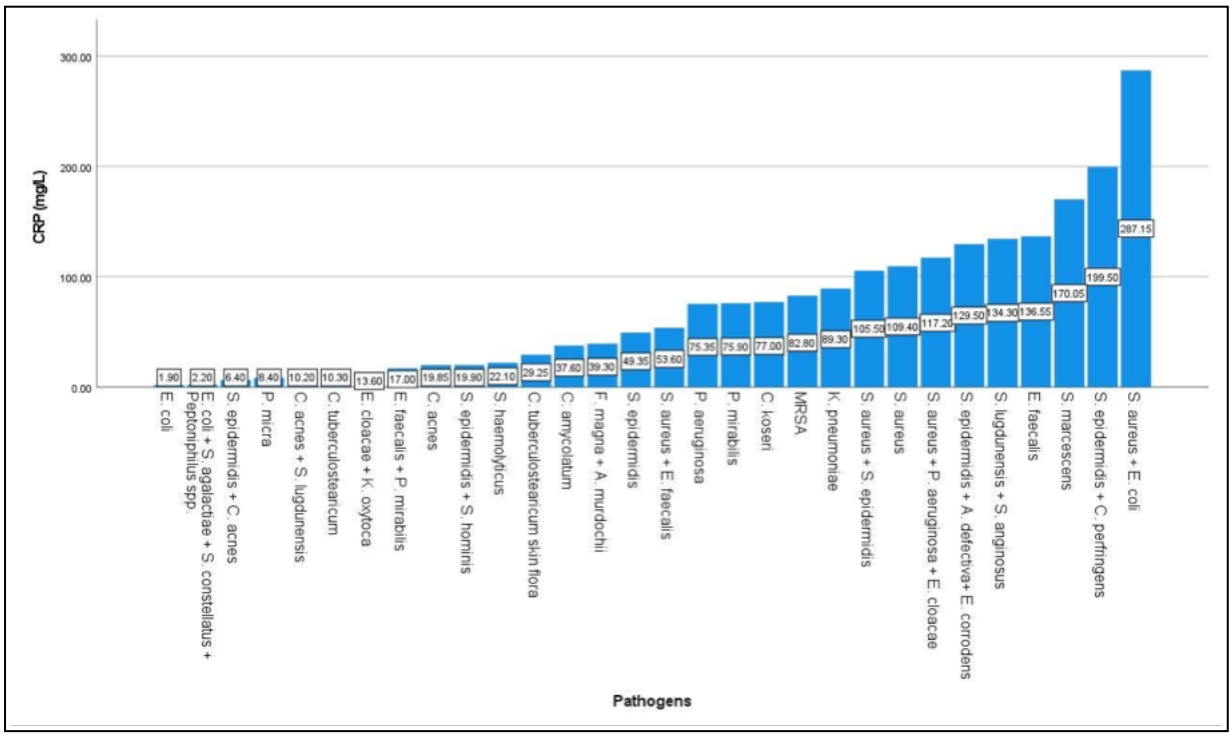

Figure 20: Pathogens of intraoperative cultures vs. CRP

The preoperative leukocyte count was analysed for a relationship with the intraoperative culture pathogen groups using the Kruskal Wallis test. Various pathogens displayed a lower leukocyte count than other pathogens (Figure 21). This result was not statistically significant (p = 0,584).

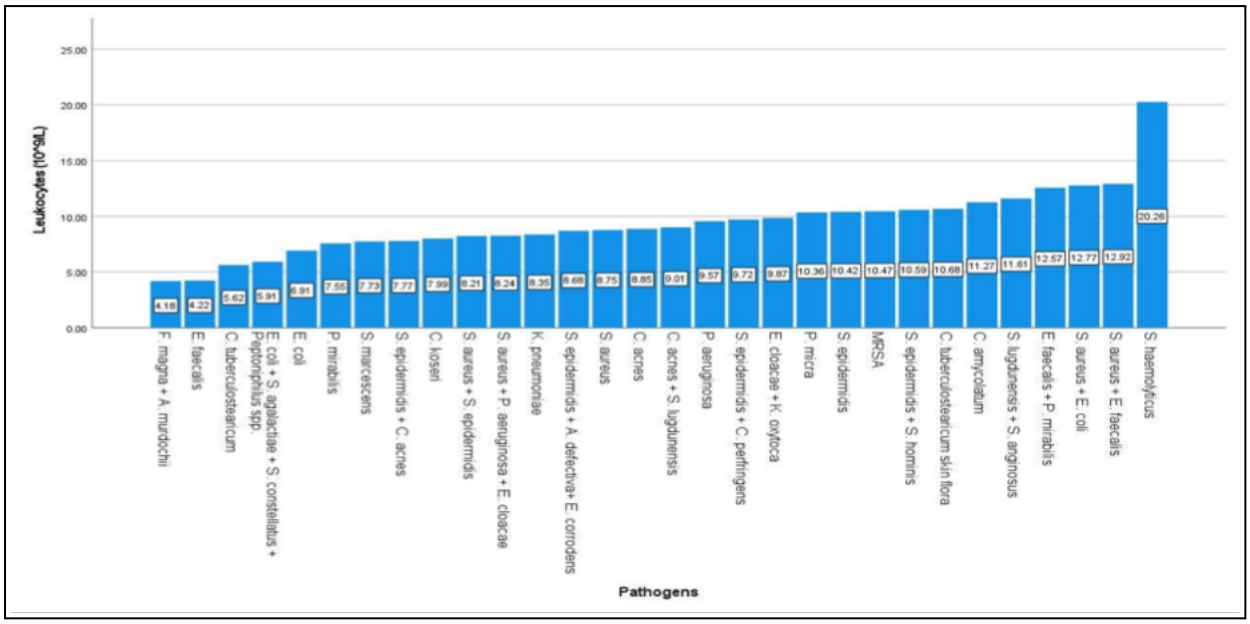

Figure 21: Pathogens of intraoperative cultures vs. leukocyte count

A Kruskal Wallis test analysed the association between preoperative procalcitonin levels and intraoperative culture results (Figure 22). *Staphylococcus aureus* positive cultures had a much higher median procalcitonin value when compared with the other cultures. The test resulted in a statistically insignificant p value of 0,219.

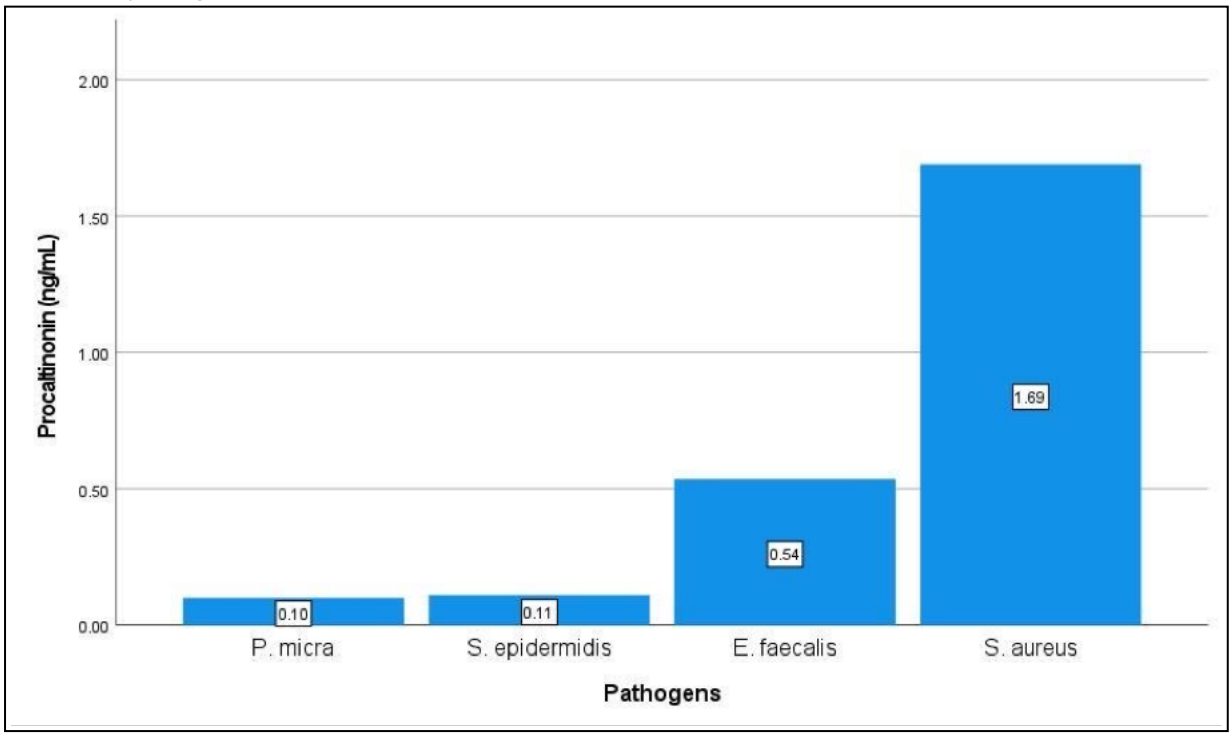

Figure 22: Pathogens of intraoperative cultures vs. procalcitonin

Several pathogens of intraoperative culture reports, such as *Klebsiella pneumoniae* and *S. aureus* + *E. coli*, had higher median preoperative creatinine levels, while other pathogens such as *Citrobacter koseri* and *Staphylococcus epidermidis* + *Clostridium perfringens* had a lower

median preoperative creatinine level (Figure 23). This association was tested through the Kruskal Wallis test. Even though the median values differed between pathogen groups, this result was not statistically significant (p = 0,453).

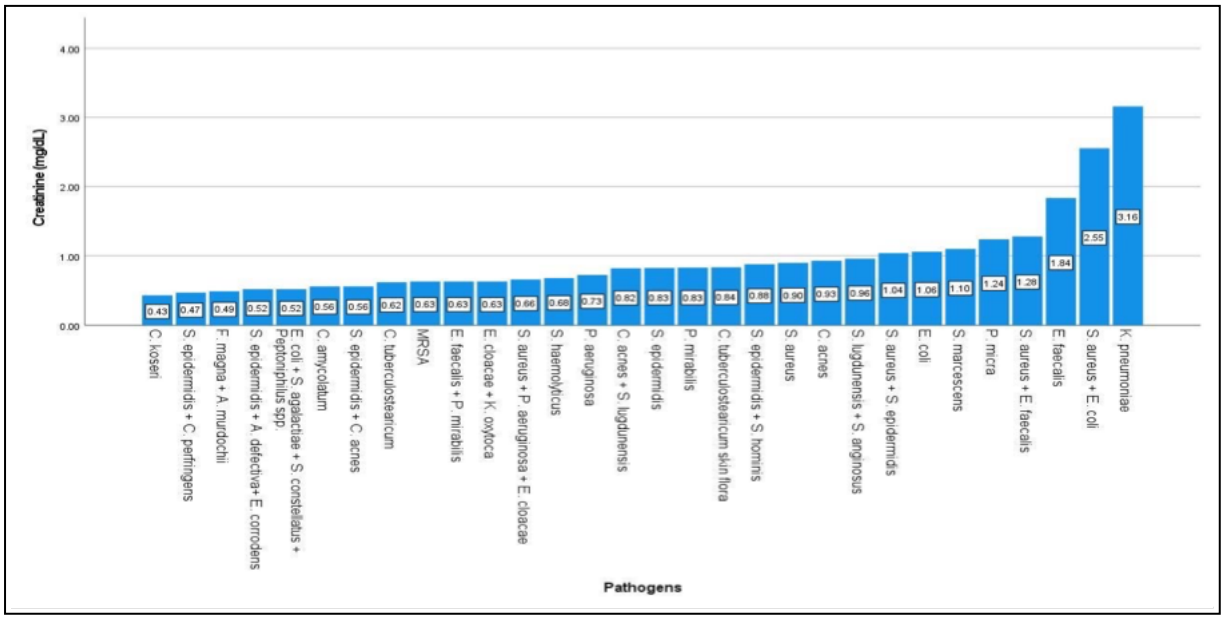

Figure 23: Pathogens of intraoperative cultures vs. creatinine

The GFR of the patients was tested for a relationship with intraoperatively detected pathogens using the Kruskal Wallis test (Figure 24). Even though pathogens such as *Klebsiella pneumoniae* and *S. aureus* + *E. coli* had lower median GFR levels and pathogens such as

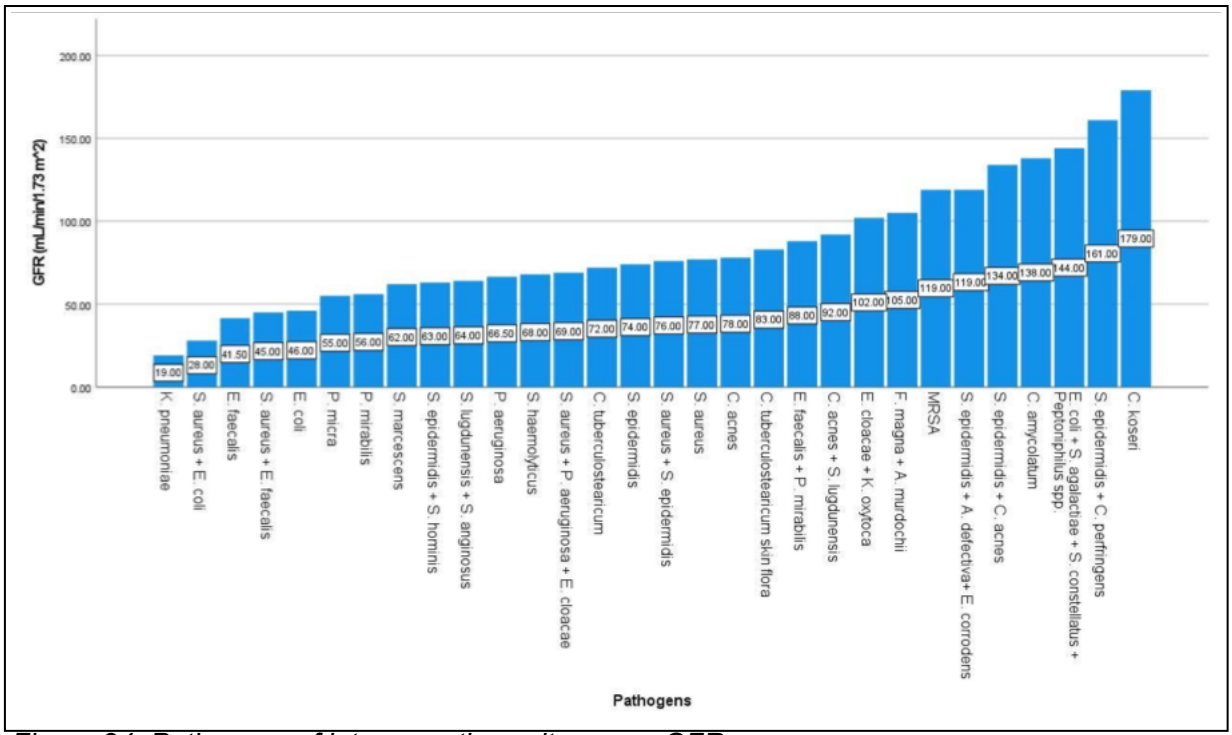

Figure 24: Pathogens of intraoperative cultures vs. GFR

Citrobacter koseri and *Staphylococcus epidermidis* + *Clostridium perfringens* had higher median GFR levels, this result, too, was not statistically significant (p = 0,558).

Preoperative blood urea and blood uric acid levels showed a difference of average between pathogen groups of intraoperative culture results (Figures 25 and 26). The Kruskal Wallis test performed to test these relationships did not result in statistically significant results (p = 0,295 for blood urea and p = 0,499 for blood uric acid).

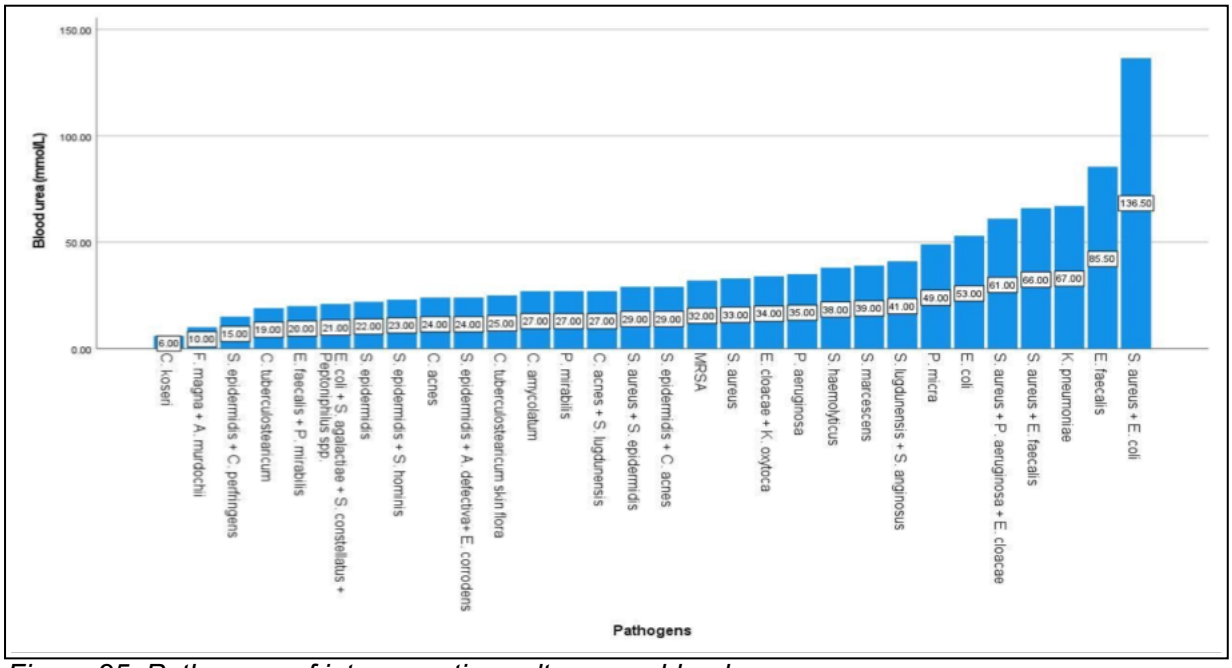

Figure 25: Pathogens of intraoperative cultures vs. blood urea

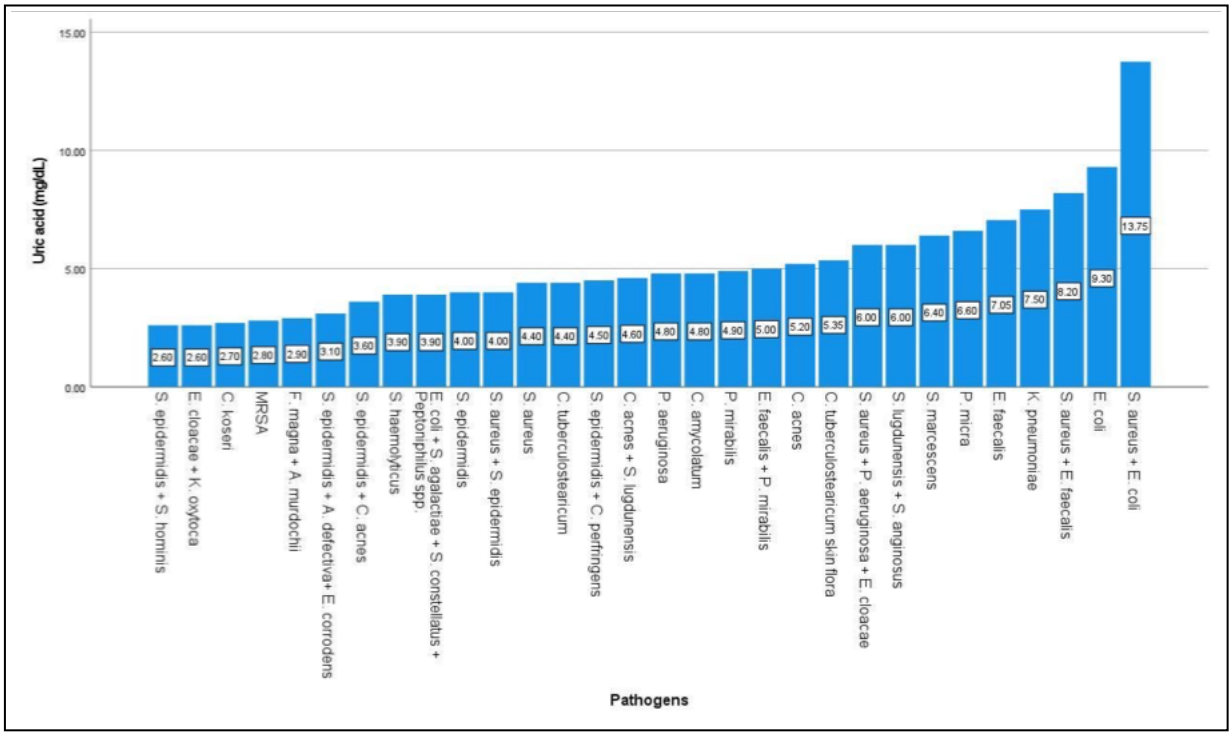

Figure 26: Pathogens of intraoperative cultures vs. uric acid

4.3.7. Other outcomes

The duration of surgery was tested for any association with gender, diagnosis of primary surgery, ASA classification and postoperatively administered antibiotics.

Male patients had a longer duration of surgery, while female patients had a shorter duration of surgery (Figure 27). This difference of mean was not statistically significant (student's t test, p = 0,616).

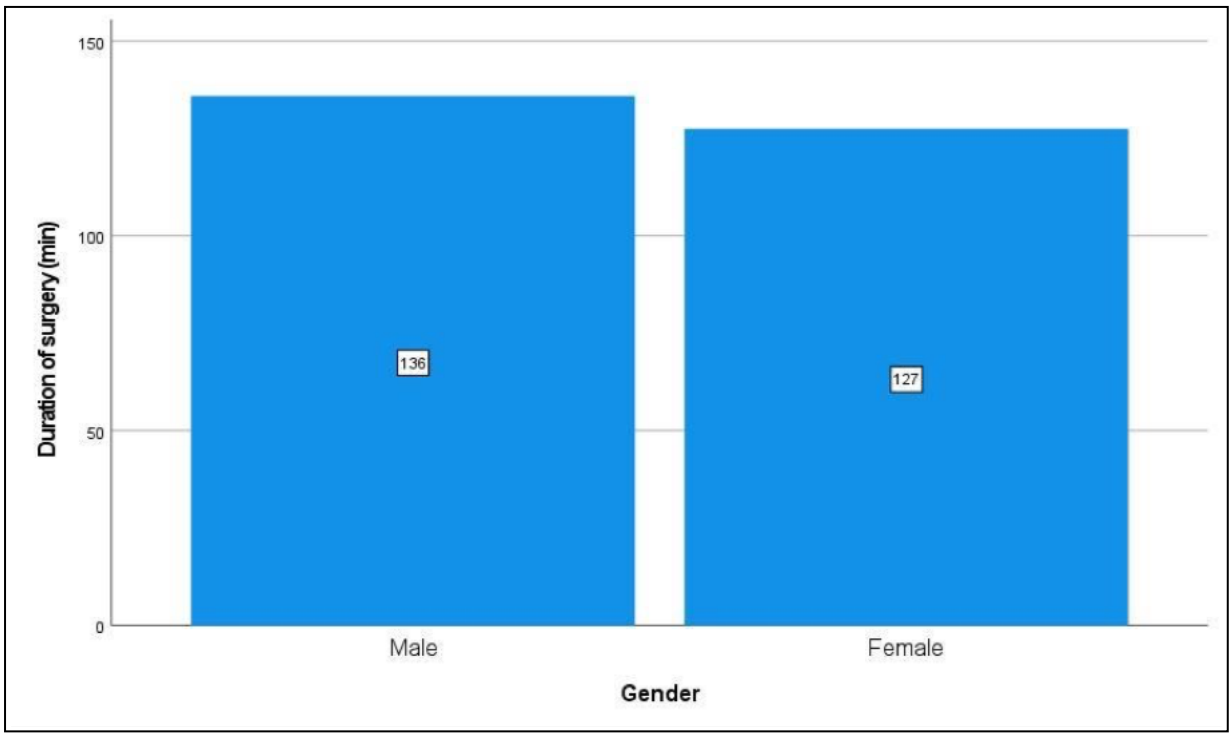

Figure 27: Mean duration of surgery vs. gender

The diagnosis of the primary surgery had different mean values of the surgical duration among its groups (Figure 28). This difference was not statistically significant (ANOVA test, p = 0,054).

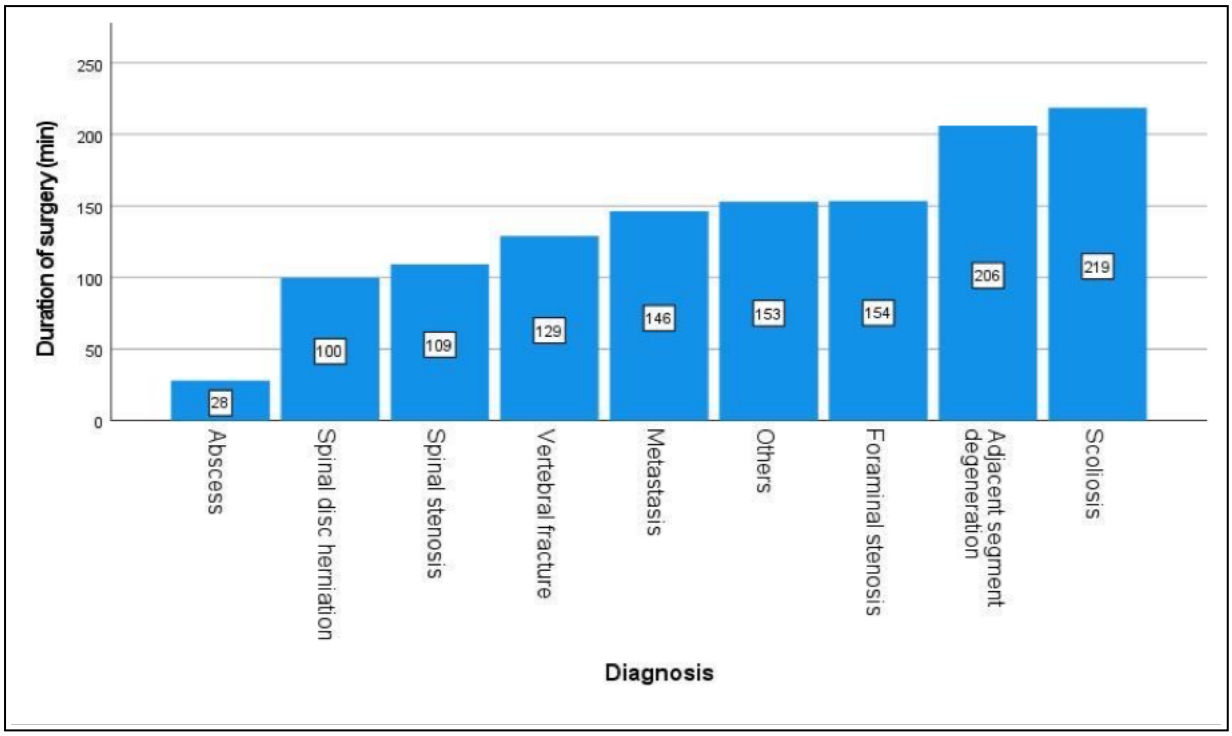

Figure 28: Mean duration of surgery vs. diagnosis of primary surgery

Patients with the ASA categories 1, 2 and 3 had mean surgical durations of 74,5 ± 60,1, 144,4 ± 68,7, and 126.25 ± 70,4 minutes respectively (Figure 29). The difference of mean of surgical duration among these groups were not statistically significant (ANOVA test, p = 0,158).

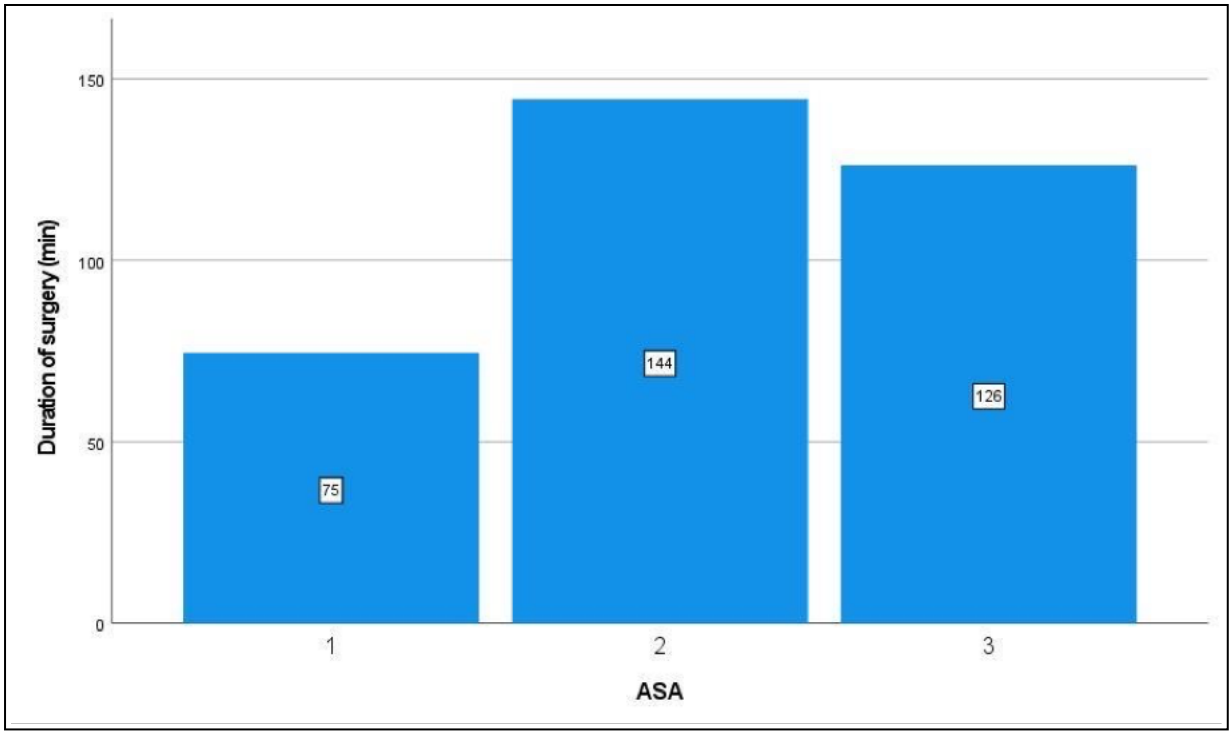

Figure 29: Mean duration of surgery vs. ASA classification

Furthermore, the duration of surgery differed among the antibiotics administered following surgery (Figure 30), although this result was not statistically significant (ANOVA test, p = 0,979).

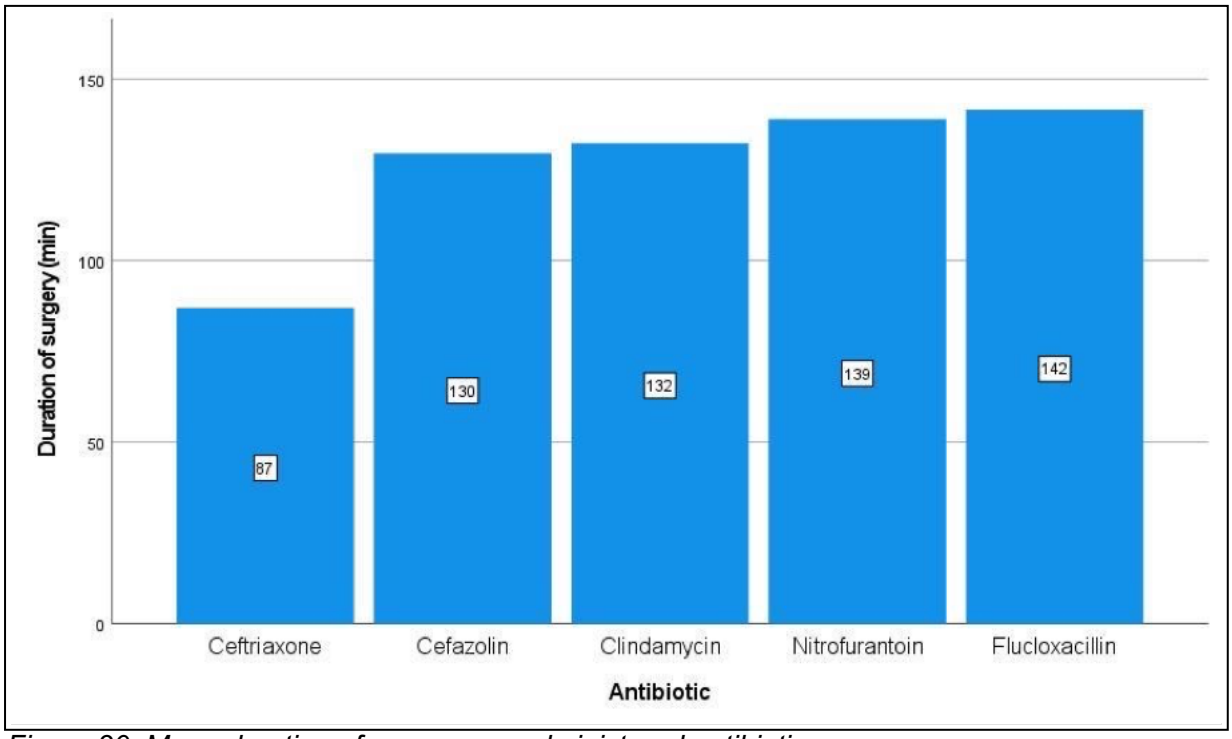

Figure 30: Mean duration of surgery vs. administered antibiotics

It was of interest to determine if the duration of intensive care unit stay is affected by the diagnosis of the primary surgery and the ASA classification. Diagnoses such as spinal stenosis, vertebral fracture and material removal were associated with a longer duration of

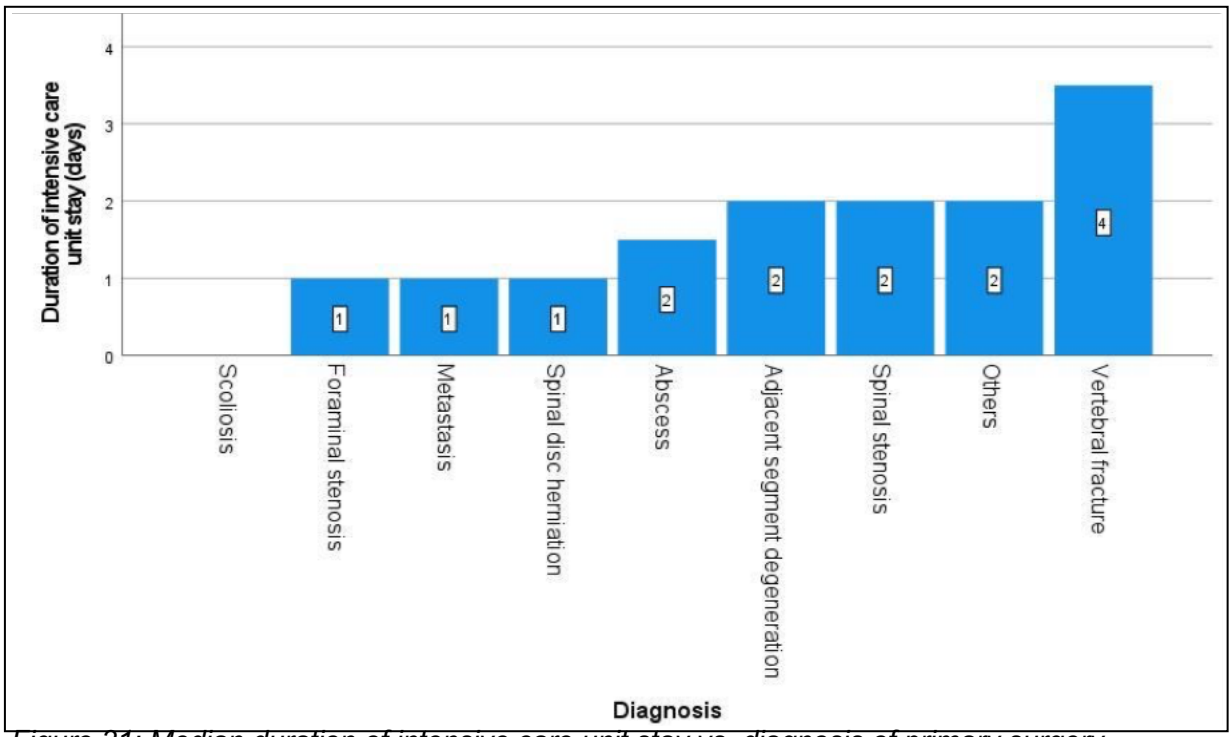

Figure 31: Median duration of intensive care unit stay vs. diagnosis of primary surgery

intensive care unit stay, while intraspinal granuloma, metastasis and dural leakage with CSF fistula were associated with a shorter duration of stay (Figure 31).

Moreover, the median duration of intensive care unit stays among ASA 2 and 3 were 2 days each. None of the patients with an ASA 1 classification had stayed in the intensive care unit.

A Kruskal Wallis test resulted in a statistically insignificant result for the association between intensive care unit stay and diagnosis of primary surgery (p = 0,255). The Kruskal Wallis test performed to identify a statistically significant relationship between intensive care unit stay and ASA categories was not able to reject the null hypothesis (p = 0,363).

Finally, age was tested against the diagnosis of the primary surgery and the ASA classification of the study population.

Among the subjects, repositioning spondylodesis, chordoma and spinal stenosis were more prevalent among older patients, while hyperkyphosis, infect related loosening of instrumentation and scoliosis were more common among younger patients (Figure 32). This relationship was tested through the Kruskal Wallis test, which resulted in a statistically significant relationship (p = 0,008).

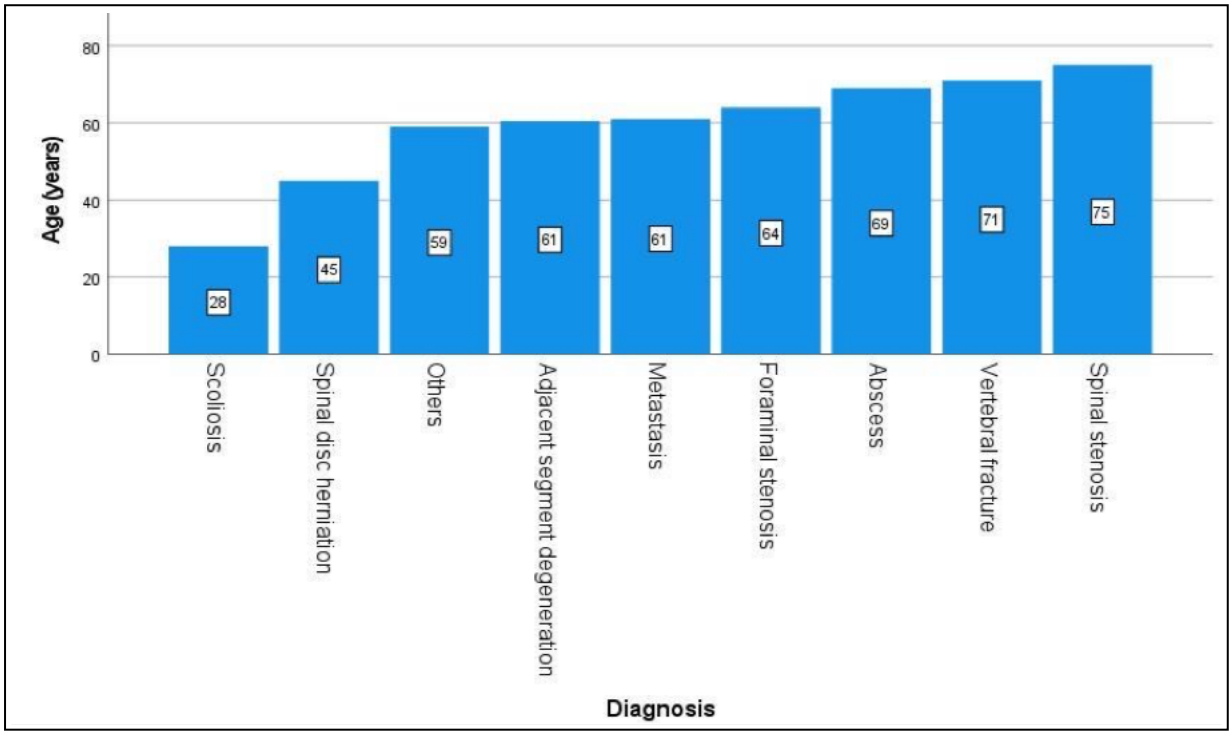

Figure 32: Age vs. diagnosis of primary surgery

The median age of patients in each of the ASA categories was also calculated. The median age of patients with ASA 1 was 68 years, ASA 2 was 58 years, and ASA 3 was 28 years (Figure 33). This difference was tested using the Kruskal Walls test for statistical significance. The difference of median among the ASA categories was statistically significant (p < 0,001). When the three ASA categories were tested against each other for difference of median of age, all

three pairs resulted in statistically significant differences (p = 0,025 for ASA 1 versus 2, p < 0,001 for ASA 1 versus 3 and p = 0,017 for ASA 2 versus 3).

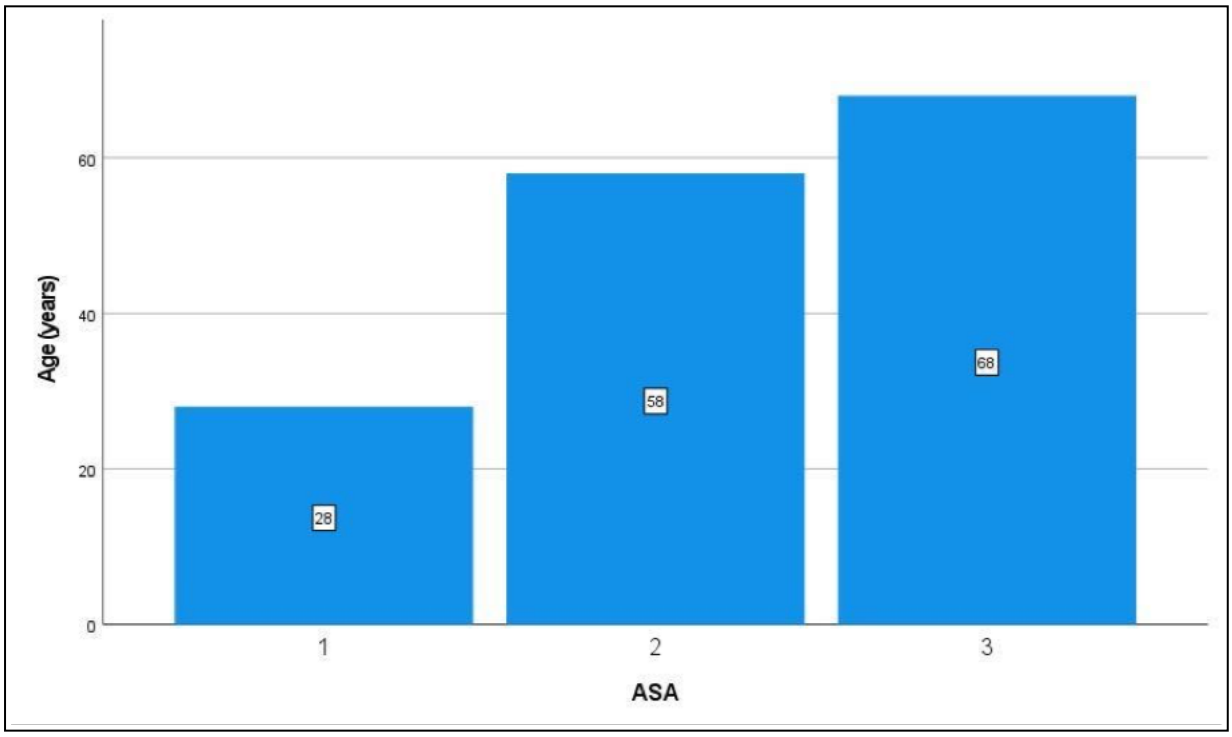

Figure 33: Age vs. ASA classification

4.4. Correlations

4.4.1. Duration of primary surgery versus age

The duration of primary surgery was plotted against patient age using a scatterplot (Figure 34), which shows a negative association. This association was tested using the Spearman's correlation. This test resulted in a correlation coefficient of -0,008, showing a negligible negative correlation. This correlation was not statistically significant (p = 0,95).

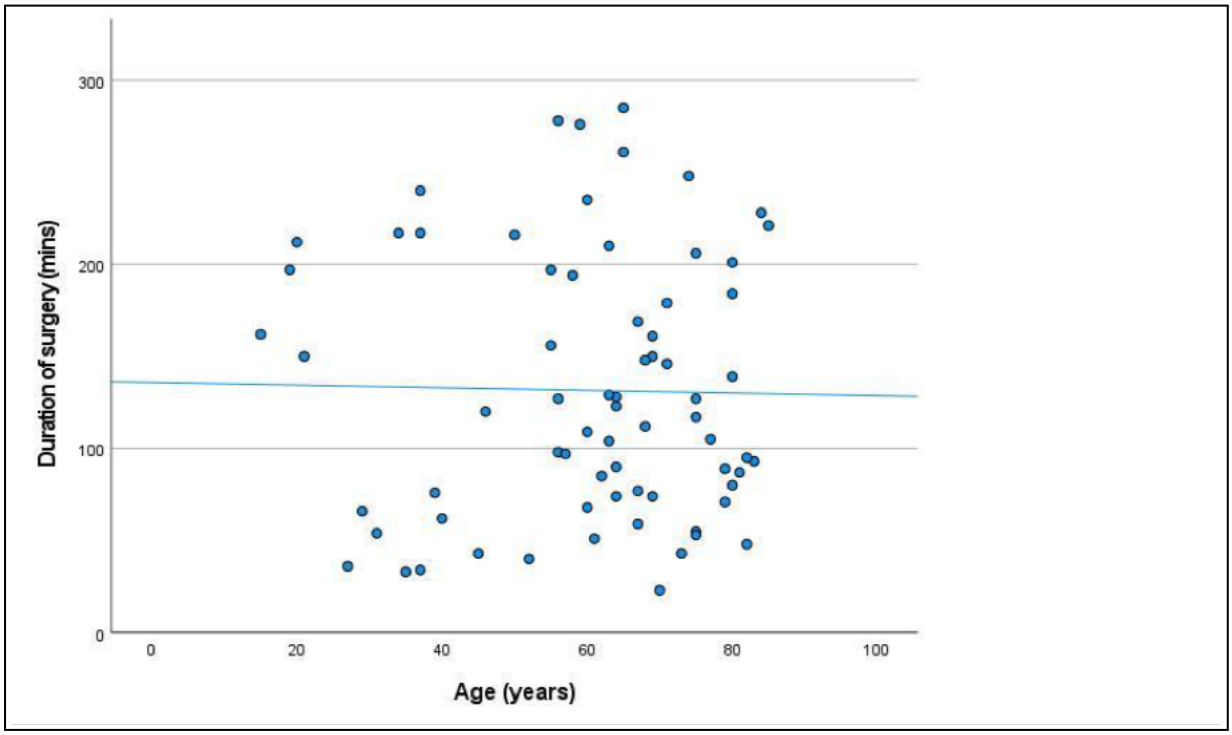

Figure 34: Duration of surgery vs. age

4.4.2. Duration of primary surgery versus BMI

When the BMI of patients was compared with the duration of the primary surgery, it was found out that the lower the BMI of the patients was, the longer the surgery lasted (Figure 35). Spearman's correlation test resulted in a correlation coefficient of -0,109, which was interpreted as a weak negative correlation between duration of surgery and BMI. This correlation was not statistically significant (p = 0,366).

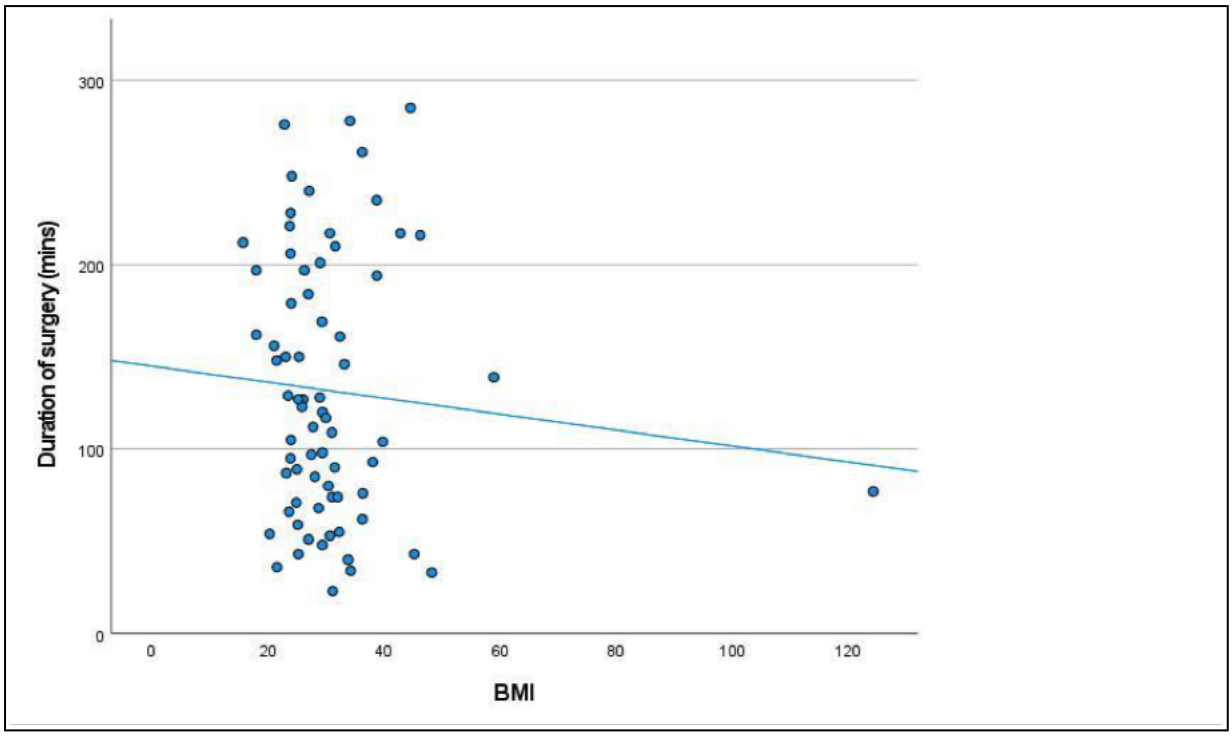

Figure 35: Duration of surgery vs. BMI

4.4.3. Duration of primary surgery versus duration of antibiotic treatment

Figure 36 depicts a scatterplot of the duration of surgery versus the duration of postoperative antibiotic treatment. It is evident through the scatterplot that the duration of surgery and the duration of postoperative antibiotic treatment have a positive association. The Spearman's correlation tested this association and calculated a correlation coefficient of +0,268. This weak positive correlation was statistically significant (p = 0,044).

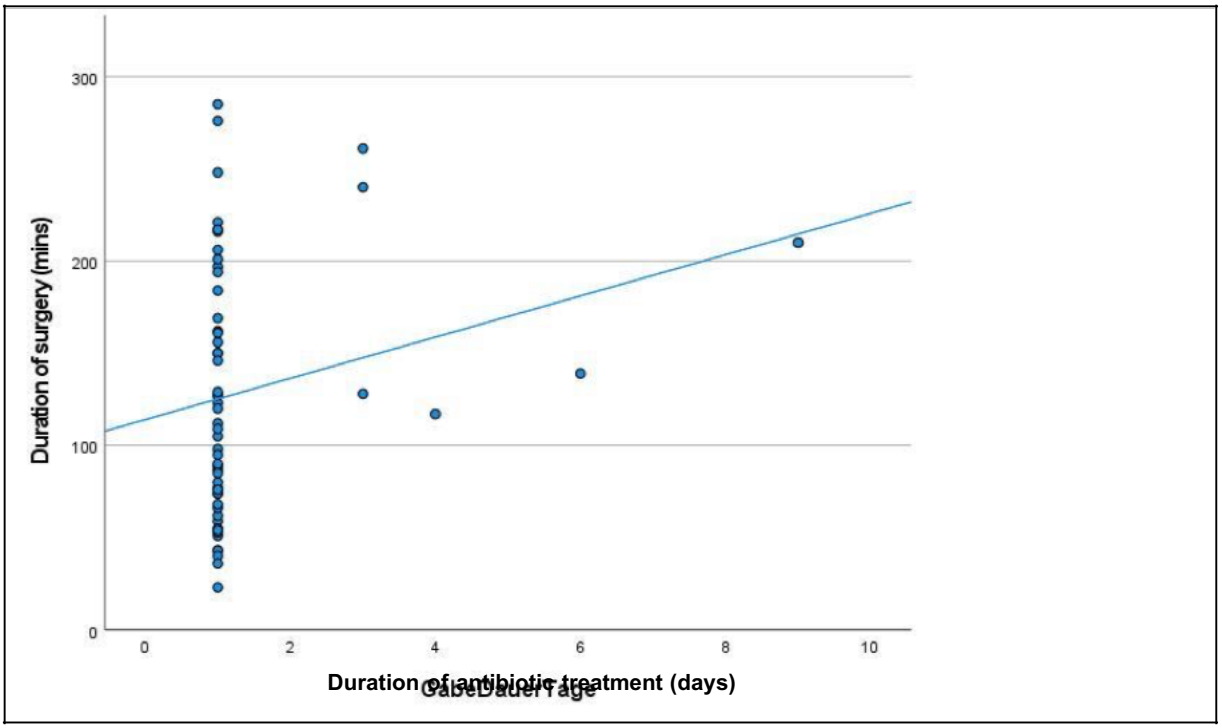

Figure 36: Duration of surgery vs. duration of antibiotic treatment

4.4.4. Duration of primary surgery versus duration of intensive care unit stay

The duration of primary surgery was compared with the duration of postoperative intensive care unit stay and tested for statistical significance (Figure 37). Although there was no statistical significance (p = 0,928), there was a negligible positive correlation between surgical duration and the duration of intensive care unit stay (correlation coefficient = +0,021).

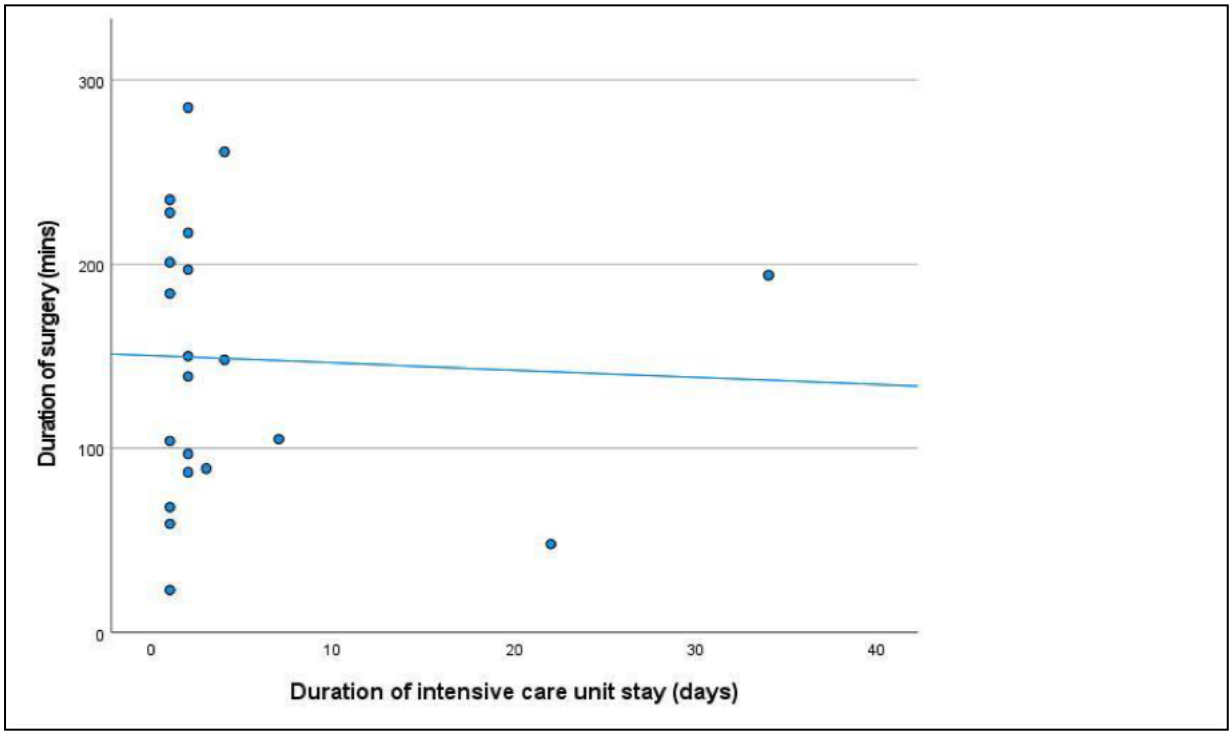

Figure 37: Duration of surgery vs. duration of intensive care unit stay

4.4.5. Duration of antibiotic treatment versus age

The duration of postoperative antibiotic treatment was tested for any possible association with patient age. The scatterplot in Figure 38 displays a positive correlation between the two variables. The Spearman's correlation coefficient of this association was +0,067, which can be interpreted as a negligible positive correlation. This correlation was not statistically significant (p = 0,619).

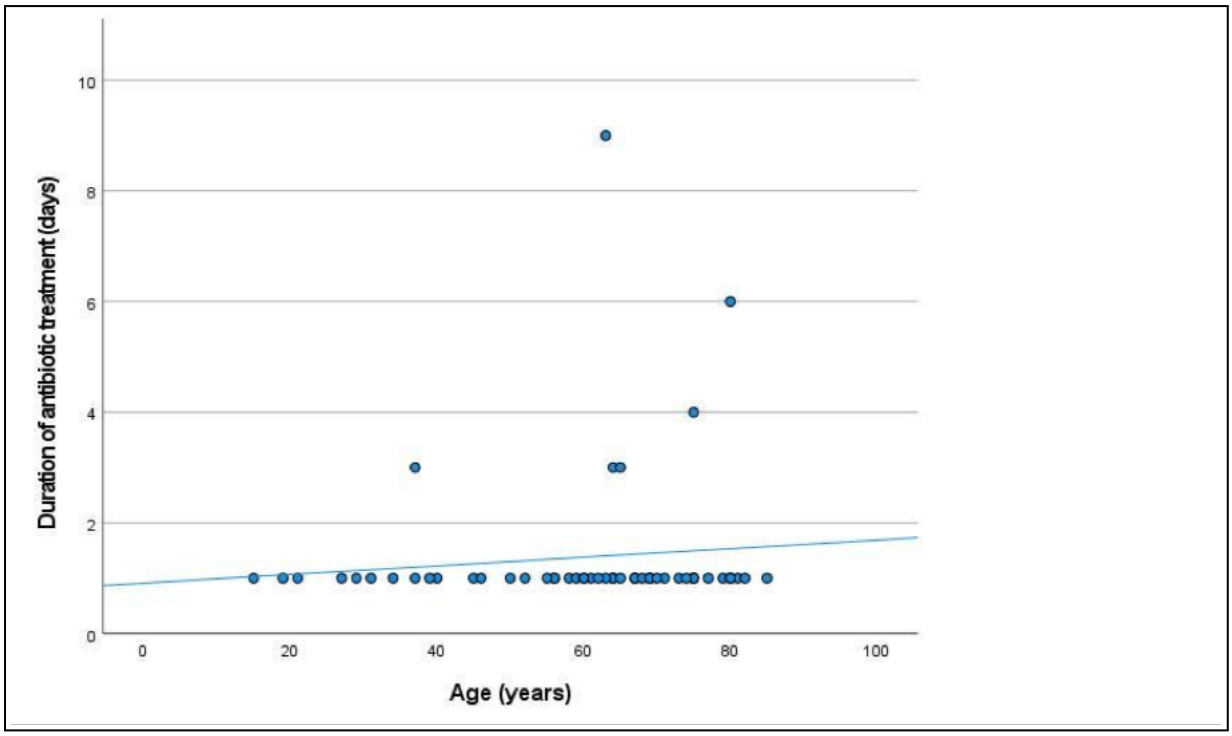

Figure 38: Duration of antibiotic treatment vs. age

4.4.6. Duration of antibiotic treatment versus intensive care unit stay

The relationship between the duration of postoperative antibiotic treatment and the duration of intensive care unit stay was analysed. There was a weak positive correlation between the two variables with a Spearman's correlation coefficient of +0,248. This relationship was found out to be not statistically significant (p = 0,373).

4.4.7. Age versus intensive care unit stay

The correlation of patient age and intensive care unit stay was examined using the Spearman's correlation test. The outcome was that age and the duration of intensive care unit stay was negatively associated (Figure 39), with a correlation coefficient of -0,043 suggesting a negligible correlation. Despite this outcome, the test result was not statistically significant, with a p value of 0,845.

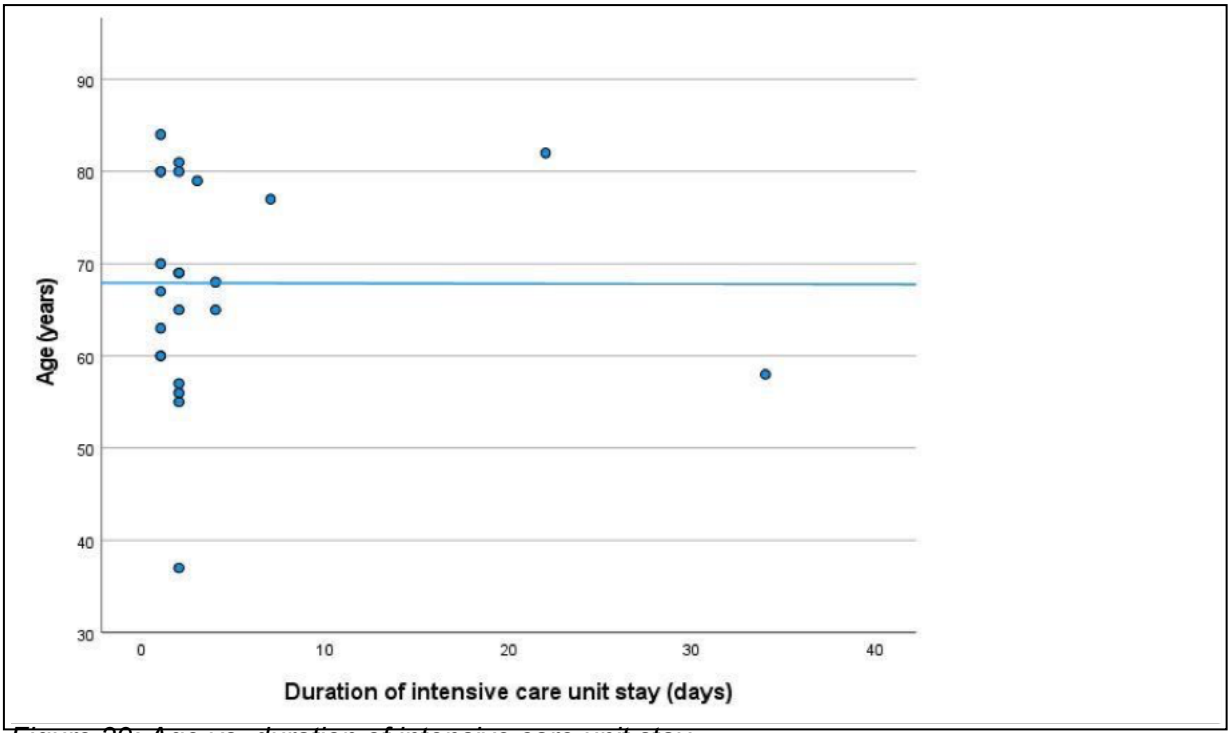

Figure 39: Age vs. duration of intensive care unit stay

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5. Discussion

This study focuses on how the duration of surgery can influence the nature of postoperative SSI. Postoperative blood cultures following the primary surgery were used to identify the pathogens causing postoperative SSI, as they were closer to the primary surgery in time than intraoperatively obtained cultures during the revision surgery. Positive blood cultures following surgery could also be due to infection sources other than the surgical site. Therefore, reports of the cultures which originate from samples obtained intraoperatively under strictly sterile conditions during the revision surgery were analysed. It was found out, as mentioned above under 4.2.1., that a highly significant and strong relationship exists between the groups of the two variables. This attests that the pathogens of the blood cultures taken after the primary surgery mostly, if not all, origin from the surgical site. Therefore, the use of postoperative blood culture reports for the analysis can be justified as appropriate.

5.1. SSI, its causes, and preventive strategies

SSI is a common manifestation in orthopaedic spine surgery, with an incidence ranging from 0,65% to 17,6% [25, 27]. SSI has been known to have extreme effects on the patient's postoperative wellbeing and on the healthcare system [31, 32]. Patients might possess certain predisposing factors for the development of an SSI, such as obesity, diabetes mellitus, and anaemia [46, 48, 30, 40]. Furthermore, intraoperative risk factors such as the location of surgery, surgical technique, and longer surgical durations can increase the chance of developing a postoperative SSI [30, 25, 40]. The reason for longer durations of spinal surgery to cause increased numbers of postoperative SSI could be the recolonisation of the surgeon's hands with the course of time, with significant recolonisation being detected at around five hours of surgery [71]. Therefore, if a surgery is suspected to last long, surgeons could be advised to pay extra attention to scrubbing in and could be asked to rescrub after around five hours [71].

SSI are mostly caused by gram-positive pathogens such as methicillin sensitive Staphylococcus aureus, methicillin resistant Staphylococcus aureus, and coagulase negative Staphylococci, while gram-negative bacteria such as Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumoniae are also known to cause SSI [73, 60, 38, 44]. An interesting division of SSI causing bacteria according to the spinal level to be operated was reported by Long et al. (2021), where gram-positive bacteria were mostly found in SSI of the cervical spine, while gram-negative bacteria were the principle causes of SSI of the lumbosacral spine [62].

Due to the massive influence of SSI on the wellbeing of patients and on the health-care system, several preventive strategies have been identified. Preoperative preventive measures such as prophylactic antibiotics have been reported to decrease the occurrence of postoperative SSI

[78]. Even though the use of iodine-based adhesive drapes in spinal surgery could be mentioned as a probable method of reducing postoperative infections of the surgical site, studies have showed no beneficial effect of iodine-based adhesive drapes [95]. In fact, the use

of adhesive drapes has been reported to increase the rate of infections of the surgical site [95]. The prevention of SSI can also be done intraoperatively through numerous methods. The local application of intraoperative vancomycin powder has been established among orthopaedic spine surgeons and has a favourable effect in reducing the occurrence of postoperative SSI [81, 82]. The use of pulse lavage, closed drainages, iodine lavage and 2-octyl-cyanoacrylate for wound closure can also decrease the chance of developing an SSI [85, 49].

5.2. The influence of surgical duration on SSI

There are numerous factors that can increase the risk of developing an SSI. Various studies performed on the risk factors for SSI report that the longer the surgical duration, the higher the chances are of developing an SSI [40, 51, 54, 58, 68, 70]. It has been hypothesised that the reason for this influence of surgical duration on the development of SSI is the recolonisation of the surgeon's hands after about five hours of surgery [71].

This study was able to identify an important role the surgical duration plays in the nature of postoperative SSI. The analysis of the collected data proved that a relationship exists between the duration of surgery and the spectrum of pathogens that cause postoperative SSI. As discussed under 4.3.1. and displayed in Figure 16, there exists a certain inclination for particular bacterial strains to cause an SSI depending on the surgical duration. Bacterial species such as *Staphylococcus epidermidis* + gram-positive Staphylococci, *Staphylococcus hominis* and *Staphylococcus aureus* cause postoperative SSI most commonly among shorter surgical durations. On the other hand, species such as *Enterococcus faecalis, Staphylococcus capitis, and Staphylococcus haemolyticus* cause SSI when the surgery lasts longer.

This relationship is an important factor that can influence the postoperative patient wellbeing. Even though the duration of surgery largely depends on the surgical procedure performed and local factors of the surgical site, it is of utmost importance to weigh the advantages and disadvantages of a longer surgical duration against the postoperative complications.

The discovery of this relationship between the surgical duration and the pathogen spectrum causing SSI is also important in the treatment of SSI following surgery. When patients show clinical signs of infection (such as fever, redness and swelling of the surgical wound, etc.), it is common clinical practice to first obtain blood cultures from the patients and then to administer patients with empiric antibiotics. The results of this research can serve in modifying the guidelines of the postsurgical empiric antibiotic treatment, after further study. Such a guideline, which includes surgical duration as a determining factor, can increase the chances of the

clinician using the proper and fitting antibiotic or antibiotic combination in combatting the pathogen causing the SSI and avoid increasing the chances of the development of resistant strains.

5.3. Effects of surgical duration on postoperative patient wellbeing

This study also analysed the effects of surgical duration on the course of patient care following surgery. It was found out that a weak, yet positive, correlation exists between the surgical duration and the duration of postoperative antibiotic use (4.4.3.). As surgical duration is known to increase the risk of SSI, it is comprehensible that the duration of postsurgical antibiotic use increases when the duration of surgery increases [54, 58, 70, 68]. Even though this study detected further factors that have a positive or negative correlation with the surgical duration, such as the duration of intensive care unit stay, these results were not statistically significant.

5.4. Influence of pathogens on laboratory parameters

Laboratory parameters obtained immediately before the revision surgery were analysed for any relationship with the species of pathogens discovered in the SSI through intraoperative cultures obtained during the revision surgery (4.3.6.). The laboratory parameters CRP, leukocyte count, procalcitonin, creatinine, GFR, blood urea and blood uric acid all showed a difference of median among the pathogens discovered immediately afterwards through intraoperative cultures (Figures 20 - 26). Even though such a link exists between the groups of pathogens causing SSI, Kruskal Wallis tests performed on each preoperative laboratory parameter and the intraoperative culture pathogens revealed that the differences of median were not statistically significant.

5.5. Other findings of this study

Even though the primary objective of this study was to identify a relationship between the spectrum of pathogens causing postoperative SSI, the statistical analysis of other variables was able to deliver secondary results of epidemiological interest.

The patient age was found out to differ significantly among the reasons for the primary surgery (4.3.7. and Figure 32). Patients who were older were most commonly operated due to reasons such as repositioning spondylodesis, chordoma and spinal stenosis, while patients who were younger were most commonly operated due to hyperkyphosis, infect related loosening of instrumentation and scoliosis.

Furthermore, it was found out that the patient age varies significantly among the categories of the ASA classification (4.3.7. and Figure 33). The ASA category that was assigned to the

patients increased from ASA 1 to ASA 3 (none of the patients of this study were assigned ASA 4, 5 and 6) with the increasing age of the patients.

6. Conclusion

This study was able to prove a relationship exists between the duration of surgery and the species of pathogens causing postoperative SSI. The predisposition of pathogenic species to cause SSI depending on the duration of surgery must be further examined through research. Furthermore, the duration of surgery can be included in clinical guidelines that may assist the clinician in choosing a suitable and appropriate empiric antibiotic for the treatment of a clinically apparent surgical site infection and to repeat perioperative prophylactic antibiotics. This might decrease the iatrogenic development of resistant pathogenic strains and decrease the duration of SSI considerably, which could possibly increase the patient wellbeing significantly, decrease the duration of postoperative hospital stay and decrease the burden on the healthcare system.

7. References

1. Morton DA (ed) (2019) The big picture. Gross anatomy, 2nd ed. McGraw-Hill's AccessMedicine. McGraw-Hill Education LLC, New York, N.Y.
2. Brunicardi FC, Andersen D, Billiar TR, Dunn DL, Kao LS, Hunter JG, Matthews JB, Pollock RE (eds) (2019) Schwartz's principles of surgery, 11th ed. McGraw-Hill's AccessMedicine. McGraw-Hill Education LLC, New York, N.Y.
3. Aumüller G, Aust G, Conrad A, Engele J, Kirsch J, Maio G (2020) Duale Reihe Anatomie, 5. aktualisierte Auflage. Duale Reihe. Thieme, Stuttgart
4. Canale ST, Beaty JH (2012) Campbell's Operative Orthopaedics E-Book, 12th. Mosby
5. McMahon PJ, Skinner HB (eds) (2021) Current diagnosis & treatment in orthopedics, 6th edition. A Lange medical book. McGraw-Hill Education LLC, New York, N.Y.
6. Hoppenfeld S (2012) Surgical Exposures in Orthopaedics. The Anatomic Approach, 4th ed. Wolters Kluwer Health, Philadelphia
7. Baaj AA, Mummaneni PV, Uribe JS, Vaccaro AR, Greenberg MS (2016) Handbook of spine surgery, Second edition. Thieme, New York, Stuttgart, Delhi, Rio de Janeiro
8. Warwick D (2022) Apley and Solomon's Concise System of Orthopaedics and Trauma, 5th ed. Taylor & Francis Group, Milton
9. Benzel EC (2015) Biomechanics of spine stabilization. CME credit available, 3. ed. Thieme, New York
10. Bridwell KH, DeWald RL (2011) The Textbook of Spinal Surgery (2 Volumes), 3E
11. Jules-Elysee K, Urban MK, Urquhart BL, Susman MH, Brown AC, Kelsey WT (2004) Pulmonary complications in anterior-posterior thoracic lumbar fusions. The spine journal : official journal of the North American Spine Society 4(3):312–316. doi: 10.1016/j.spinee.2003.11.008
12. Fujita T, Kostuik JP, Huckell CB, Sieber AN (1998) COMPLICATIONS OF SPINAL FUSION IN ADULT PATIENTS MORE THAN 60 YEARS OF AGE. Orthopedic Clinics of North America 29(4):669–678. doi: 10.1016/S0030-5898(05)70040-7
13. Faciszewski T, Winter RB, Lonstein JE, Denis F, Johnson L (1995) The surgical and medical perioperative complications of anterior spinal fusion surgery in the thoracic and lumbar spine in adults. A review of 1223 procedures. Spine 20(14):1592–1599. doi: 10.1097/00007632-199507150-00007
14. Chozick BS, Watson P, Greenblatt SH (1994) Internal carotid artery thrombosis after cervical corpectomy. Spine 19(19):2230–2232. doi: 10.1097/00007632-199410000-00020

15. Golfinos JG, Dickman CA, Zabramski JM, Sonntag VK, Spetzler RF (1994) Repair of vertebral artery injury during anterior cervical decompression. Spine 19(22):2552–2556. doi: 10.1097/00007632-199411001-00010
16. Smith MD, Emery SE, Dudley A, Murray KJ, Leventhal M (1993) Vertebral artery injury during anterior decompression of the cervical spine. A retrospective review of ten patients. The Journal of bone and joint surgery. British volume 75(3):410–415. doi: 10.1302/0301-620X.75B3.8496209
17. Jones AA, Stambough JL, Balderston RA, Rothman RH, Booth RE (1989) Long-term results of lumbar spine surgery complicated by unintended incidental durotomy. Spine 14(4):443–446. doi: 10.1097/00007632-198904000-00021
18. Lee KS, Hardy IM (1992) Postlaminectomy lumbar pseudomeningocele: report of four cases. Neurosurgery 30(1):111–114. doi: 10.1227/00006123-199201000-00020
19. Schumacher HW, Wassmann H, Podlinski C (1988) Pseudomeningocele of the lumbar spine. Surgical neurology 29(1):77–78. doi: 10.1016/0090-3019(88)90127-9
20. Jankowitz BT, Atteberry DS, Gerszten PC, Karausky P, Cheng BC, Faught R, Welch WC (2009) Effect of fibrin glue on the prevention of persistent cerebral spinal fluid leakage after incidental durotomy during lumbar spinal surgery. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 18(8):1169–1174. doi: 10.1007/s00586-009-0928-6
21. Jesse CM, Schermann H, Goldberg J, Gallus M, Häni L, Raabe A, Schär RT (2022) Risk Factors for Postoperative Cerebrospinal Fluid Leakage After Intradural Spine Surgery. World neurosurgery 164:e1190-e1199. doi: 10.1016/j.wneu.2022.05.129
22. Kim YJ, Bridwell KH, Lenke LG, Cho K-J, Edwards CC, Rinella AS (2006) Pseudarthrosis in adult spinal deformity following multisegmental instrumentation and arthrodesis. The Journal of bone and joint surgery. American volume 88(4):721–728. doi: 10.2106/JBJS.E.00550
23. Kim YJ, Bridwell KH, Lenke LG, Rhim S, Cheh G (2006) Pseudarthrosis in long adult spinal deformity instrumentation and fusion to the sacrum: prevalence and risk factor analysis of 144 cases. Spine 31(20):2329–2336. doi: 10.1097/01.brs.0000238968.82799.d9
24. Kim YJ, Bridwell KH, Lenke LG, Rinella AS, Edwards C, Edward C (2005) Pseudarthrosis in primary fusions for adult idiopathic scoliosis: incidence, risk factors, and outcome analysis. Spine 30(4):468–474. doi: 10.1097/01.brs.0000153392.74639.ea
25. Ogihara S, Yamazaki T, Inanami H, Oka H, Maruyama T, Miyoshi K, Takano Y, Chikuda H, Azuma S, Kawamura N, Yamakawa K, Hara N, Oshima Y, Morii J, Okazaki R, Takeshita Y, Tanaka S, Saita K (2018) Risk factors for surgical site infection after lumbar

laminectomy and/or discectomy for degenerative diseases in adults: A prospective multicenter surveillance study with registry of 4027 cases. PloS one 13(10):e0205539. doi: 10.1371/journal.pone.0205539

26. Molinari RW, Khera OA, Molinari WJ (2012) Prophylactic intraoperative powdered vancomycin and postoperative deep spinal wound infection: 1,512 consecutive surgical cases over a 6-year period. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 21 Suppl 4:S476-82. doi: 10.1007/s00586-011-2104-z
27. Lucasti CJ, Dworkin M, Radcliff KE, Nicholson K, Woods BI (2019) What Factors Predict Failure of Nonsurgical Management of a Lumbar Surgical Site Infection? International journal of spine surgery 13(3):239–244. doi: 10.14444/6032
28. Gamain R, Coulomb R, Houzir K, Molinari N, Kouyoumdjian P, Lonjon N (2019) Anterior cervical spine surgical site infection and pharyngoesophageal perforation. Ten-year incidence in 1475 patients. Orthopaedics & traumatology, surgery & research : OTSR 105(4):697–702. doi: 10.1016/j.otsr.2019.02.018
29. Taha MM, Abouhashem S, Abdel-Rahman AY (2014) Neurosurgical wound infection at a university hospital in Egypt; prospective study of 1,181 patients for 2 years. Turkish neurosurgery 24(1):8–12. doi: 10.5137/1019-5149.JTN.6464-12.1
30. Zhang X, Liu P, You J (2022) Risk factors for surgical site infection following spinal surgery: A meta-analysis. Medicine 101(8):e28836. doi: 10.1097/MD.0000000000028836
31. Lissovoy G de, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB (2009) Surgical site infection: incidence and impact on hospital utilization and treatment costs. American journal of infection control 37(5):387–397. doi: 10.1016/j.ajic.2008.12.010
32. Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ (2002) The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital: adverse quality of life, excess length of stay, and extra cost. Infection control and hospital epidemiology 23(4):183–189. doi: 10.1086/502033
33. Nacke E, Ramos N, Stein S, Hutzler L, Bosco JA (2013) When do readmissions for infection occur after spine and total joint procedures? Clinical orthopaedics and related research 471(2):569–573. doi: 10.1007/s11999-012-2597-8
34. Maslow J, Hutzler L, Slover J, Bosco J (2015) Etiology of Readmissions Following Orthopaedic Procedures and Medical Admissions. A Comparative Analysis. Bulletin of the Hospital for Joint Disease (2013) 73(4):269–275
35. Castellà L, Sopena N, Rodriguez-Montserrat D, Alonso-Fernández S, Cavanilles JM, Iborra M, Ciercoles A, Pulido A, Gimenez M, Hernandez Hermoso JA, Casas I (2020) Intervention to reduce the incidence of surgical site infection in spine surgery. American journal of infection control 48(5):550–554. doi: 10.1016/j.ajic.2019.09.007

36. Cizik AM, Lee MJ, Martin BI, Bransford RJ, Bellabarba C, Chapman JR, Mirza SK (2012) Using the spine surgical invasiveness index to identify risk of surgical site infection: a multivariate analysis. The Journal of bone and joint surgery. American volume 94(4):335–342. doi: 10.2106/JBJS.J.01084

37. Ogihara S, Yamazaki T, Shiibashi M, Chikuda H, Maruyama T, Miyoshi K, Inanami H, Oshima Y, Azuma S, Kawamura N, Yamakawa K, Hara N, Morii J, Okazaki R, Takeshita Y, Nishimoto J, Tanaka S, Saita K (2021) Risk factors for deep surgical site infection after posterior cervical spine surgery in adults: a multicentre observational cohort study. Scientific reports 11(1):7519. doi: 10.1038/s41598-021-87110-4

38. Jiang W, Shi H, Deng X, Hou W, Wan D (2021) The incidence of incision infections after lumbar fusion and the significance of dynamically monitoring serum albumin and C-reactive protein levels. Annals of palliative medicine 10(10):10870–10877. doi: 10.21037/apm-21-2512

39. Maragakis LL, Cosgrove SE, Martinez EA, Tucker MG, Cohen DB, Perl TM (2009) Intraoperative fraction of inspired oxygen is a modifiable risk factor for surgical site infection after spinal surgery. Anesthesiology 110(3):556–562. doi: 10.1097/ALN.0b013e3181974be7

40. Tomov M, Mitsunaga L, Durbin-Johnson B, Nallur D, Roberto R (2015) Reducing surgical site infection in spinal surgery with betadine irrigation and intrawound vancomycin powder. Spine 40(7):491–499. doi: 10.1097/BRS.0000000000000789

41. Osterhoff G, Burla L, Werner CML, Jentzsch T, Wanner GA, Simmen H-P, Sprengel K (2015) Role of Pre-Operative Blood Transfusion and Subcutaneous Fat Thickness as Risk Factors for Surgical Site Infection after Posterior Thoracic Spine Stabilization. Surgical infections 16(3):333–337. doi: 10.1089/sur.2014.081

42. Oktay K, Özsoy KM, Çetinalp NE, Erman T, Güzel A (2021) Efficacy of prophylactic application of vancomycin powder in preventing surgical site infections after instrumented spinal surgery: A retrospective analysis of patients with high-risk conditions. Acta orthopaedica et traumatologica turcica 55(1):48–52. doi: 10.5152/j.aott.2021.18372

43. Xing D, Ma J-X, Ma X-L, Song D-H, Wang J, Chen Y, Yang Y, Zhu S-W, Ma B-Y, Feng R (2013) A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 22(3):605–615. doi: 10.1007/s00586-012-2514-6

44. Ojo OA, Owolabi BS, Oseni AW, Kanu OO, Bankole OB (2016) Surgical site infection in posterior spine surgery. Nigerian journal of clinical practice 19(6):821–826. doi: 10.4103/1119-3077.183237

45. Ee WWG, Lau WLJ, Yeo W, Bing Y von, Yue WM (2014) Does minimally invasive surgery have a lower risk of surgical site infections compared with open spinal surgery? Clinical orthopaedics and related research 472(6):1718–1724. doi: 10.1007/s11999-013-3158-5
46. Abdallah DY, Jadaan MM, McCabe JP (2013) Body mass index and risk of surgical site infection following spine surgery: a meta-analysis. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 22(12):2800–2809. doi: 10.1007/s00586-013-2890-6
47. Nota SPFT, Braun Y, Ring D, Schwab JH (2015) Incidence of surgical site infection after spine surgery: what is the impact of the definition of infection? Clinical orthopaedics and related research 473(5):1612–1619. doi: 10.1007/s11999-014-3933-y
48. Jiang J, Teng Y, Fan Z, Khan S, Xia Y (2014) Does obesity affect the surgical outcome and complication rates of spinal surgery? A meta-analysis. Clinical orthopaedics and related research 472(3):968–975. doi: 10.1007/s11999-013-3346-3
49. Ando M, Tamaki T, Yoshida M, Sasaki S, Toge Y, Matsumoto T, Maio K, Sakata R, Fukui D, Kanno S, Nakagawa Y, Yamada H (2014) Surgical site infection in spinal surgery: a comparative study between 2-octyl-cyanoacrylate and staples for wound closure. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 23(4):854–862. doi: 10.1007/s00586-014-3202-5
50. Maciejczak A, Wolan-Nieroda A, Wałaszek M, Kołpa M, Wolak Z (2019) Antibiotic prophylaxis in spine surgery: a comparison of single-dose and 72-hour protocols. The Journal of hospital infection 103(3):303–310. doi: 10.1016/j.jhin.2019.04.017
51. Lai Q, Song Q, Guo R, Bi H, Liu X, Yu X, Zhu J, Dai M, Zhang B (2017) Risk factors for acute surgical site infections after lumbar surgery: a retrospective study. Journal of orthopaedic surgery and research 12(1):116. doi: 10.1186/s13018-017-0612-1
52. Satake K, Kanemura T, Matsumoto A, Yamaguchi H, Ishikawa Y (2013) Predisposing factors for surgical site infection of spinal instrumentation surgery for diabetes patients. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 22(8):1854–1858. doi: 10.1007/s00586-013-2783-8
53. Lazennec J-Y, Fourniols E, Lenoir T, Aubry A, Pissonnier M-L, Issartel B, Rousseau M-A (2011) Infections in the operated spine: update on risk management and therapeutic strategies. Orthopaedics & traumatology, surgery & research : OTSR 97(6 Suppl):S107-16. doi: 10.1016/j.otsr.2011.07.002

54. AlGamdi SS, Alawi M, Bokhari R, Bajunaid K, Mukhtar A, Baeesa SS (2021) Risk factors for surgical site infection following spinal surgery in Saudi Arabia: A retrospective case-control study. Medicine 100(17):e25567. doi: 10.1097/MD.0000000000025567
55. He Z, Zhou K, Tang K, Quan Z, Liu S, Su B (2020) Perioperative hypoalbuminemia is a risk factor for wound complications following posterior lumbar interbody fusion. Journal of orthopaedic surgery and research 15(1):538. doi: 10.1186/s13018-020-02051-4
56. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of chronic diseases 40(5):373–383. doi: 10.1016/0021-9681(87)90171-8
57. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. Journal of clinical epidemiology 45(6):613–619. doi: 10.1016/0895-4356(92)90133-8
58. Andrés-Cano P, Cerván A, Rodríguez-Solera M, Antonio Ortega J, Rebollo N, Guerado E (2018) Surgical Infection after Posterolateral Lumbar Spine Arthrodesis: CT Analysis of Spinal Fusion. Orthopaedic surgery 10(2):89–97. doi: 10.1111/os.12371
59. Peng W, Liang Y, Lu T, Li M, Li D-S, Du K-H, Wu J-H (2019) Multivariate analysis of incision infection after posterior lumbar surgery in diabetic patients: A single-center retrospective analysis. Medicine 98(23):e15935. doi: 10.1097/MD.0000000000015935
60. Durkin MJ, Dicks KV, Baker AW, Lewis SS, Moehring RW, Chen LF, Sexton DJ, Anderson DJ (2015) Seasonal Variation of Common Surgical Site Infections: Does Season Matter? Infection control and hospital epidemiology 36(9):1011–1016. doi: 10.1017/ice.2015.121
61. Spatenkova V, Bradac O, Jindrisek Z, Hradil J, Fackova D, Halacova M (2021) Risk factors associated with surgical site infections after thoracic or lumbar surgery: a 6-year single centre prospective cohort study. Journal of orthopaedic surgery and research 16(1):265. doi: 10.1186/s13018-021-02418-1
62. Long DR, Bryson-Cahn C, Pergamit R, Tavolaro C, Saigal R, Chan JD, Lynch JB (2021) 2021 Young Investigator Award Winner: Anatomic Gradients in the Microbiology of Spinal Fusion Surgical Site Infection and Resistance to Surgical Antimicrobial Prophylaxis. Spine 46(3):143–151. doi: 10.1097/BRS.0000000000003603
63. Basques BA, Golinvaux NS, Bohl DD, Yacob A, Toy JO, Varthi AG, Grauer JN (2014) Use of an operating microscope during spine surgery is associated with minor increases in operating room times and no increased risk of infection. Spine 39(22):1910–1916. doi: 10.1097/BRS.0000000000000558
64. Cooper K, Glenn CA, Martin M, Stoner J, Li J, Puckett T (2016) Risk factors for surgical site infection after instrumented fixation in spine trauma. Journal of clinical neuroscience

: official journal of the Neurosurgical Society of Australasia 23:123–127. doi: 10.1016/j.jocn.2015.08.023

65. Hayashi H, Murakami H, Demura S, Kato S, Yoshioka K, Shinmura K, Yokogawa N, Ishii T, Fang X, Shirai T, Tsuchiya H (2015) Surgical site infection after total en bloc spondylectomy: risk factors and the preventive new technology. The spine journal : official journal of the North American Spine Society 15(1):132–137. doi: 10.1016/j.spinee.2014.08.007
66. Woods BI, Rosario BL, Chen A, Waters JH, Donaldson W, Kang J, Lee J (2013) The association between perioperative allogeneic transfusion volume and postoperative infection in patients following lumbar spine surgery. The Journal of bone and joint surgery. American volume 95(23):2105–2110. doi: 10.2106/JBJS.L.00979
67. Takenaka S, Makino T, Sakai Y, Kashii M, Iwasaki M, Yoshikawa H, Kaito T (2019) Dural tear is associated with an increased rate of other perioperative complications in primary lumbar spine surgery for degenerative diseases. Medicine 98(1):e13970. doi: 10.1097/MD.0000000000013970
68. Li D, Guo W, Qu H, Yang R, Tang X, Yan T, Tang S, Yang Y, Ji T, Dong S (2013) Experience with wound complications after surgery for sacral tumors. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 22(9):2069–2076. doi: 10.1007/s00586-013-2765-x
69. Kim JH, Ahn DK, Kim JW, Kim GW (2015) Particular Features of Surgical Site Infection in Posterior Lumbar Interbody Fusion. Clinics in orthopedic surgery 7(3):337–343. doi: 10.4055/cios.2015.7.3.337
70. Boriani S, Bandiera S, Donthineni R, Amendola L, Cappuccio M, Iure F de, Gasbarrini A (2010) Morbidity of en bloc resections in the spine. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 19(2):231–241. doi: 10.1007/s00586-009-1137-z
71. Hosseini P, Mundis GM, Eastlack R, Nourian A, Pawelek J, Nguyen S, Akbarnia BA (2016) Do Longer Surgical Procedures Result in Greater Contamination of Surgeons' Hands? Clinical orthopaedics and related research 474(7):1707–1713. doi: 10.1007/s11999-016-4832-1
72. Shi H, Zhu L, Jiang Z-L, Huang Z-H, Wu X-T (2021) The use of incisional vacuum-assisted closure system following one-stage incision suture combined with continuous irrigation to treat early deep surgical site infection after posterior lumbar fusion with instrumentation. Journal of orthopaedic surgery and research 16(1):445. doi: 10.1186/s13018-021-02588-y

73. Liu J-T, Liao W-J, Chang C-S, Chen Y-H (2015) Management of Deep Infection after Instrumentation on Lumbar Spinal Surgery in a Single Institution. BioMed research international 2015:842010. doi: 10.1155/2015/842010
74. Yin D, Liu B, Chang Y, Gu H, Zheng X (2018) Management of late-onset deep surgical site infection after instrumented spinal surgery. BMC surgery 18(1):121. doi: 10.1186/s12893-018-0458-4
75. Boff L, Sousa Duarte H de, Kraychete GB, Castro Santos MG de, Vommaro RC, Lima COGX, Lima-Morales D, Wink PL, Oliveira Ferreira E de, Picao RC, da Rocha VM (2021) Characterization of an emergent high-risk KPC-producing Klebsiella pneumoniae lineage causing a fatal wound infection after spine surgery. Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases 96:105122. doi: 10.1016/j.meegid.2021.105122
76. Savini V, Nigro R, Marrollo R, Polilli E, Campitelli I, Buonaguidi R, Fazii P, Carretto E (2014) Surgical wound infection by mannitol-nonfermenting Staphylococcus aureus after lumbar microdiscectomy. International journal of clinical and experimental pathology 7(5):2670–2672
77. (2008) The Mont Reid surgical handbook, Sixth edition. Mobile medicine. Saunders/Elsevier, Philadelphia, PA
78. Vandenberg C, Niswander C, Carry P, Bloch N, Pan Z, Erickson M, Garg S (2018) Compliance With a Comprehensive Antibiotic Protocol Improves Infection Incidence in Pediatric Spine Surgery. Journal of pediatric orthopedics 38(5):287–292. doi: 10.1097/BPO.0000000000000812
79. Dimovska-Gavrilovska A, Chaparoski A, Gavrilovski A, Milenkovikj Z (2017) The Importance of Perioperative Prophylaxis with Cefuroxime or Ceftriaxone in the Surgical Site Infections Prevention after Cranial and Spinal Neurosurgical Procedures. Prilozi (Makedonska akademija na naukite i umetnostite. Oddelenie za medicinski nauki) 38(2):85–97. doi: 10.1515/prilozi-2017-0026
80. Joaquim AF, Milano JB, Daniel JW, Dantas FLR, Onishi FJ, Bertolini EdF, Mudo ML, Botelho RV (2018) Spine surgery - the use of vancomycin powder in surgical site for postoperative infection prevention. Revista da Associacao Medica Brasileira (1992) 64(8):663–669. doi: 10.1590/1806-9282.64.08.663
81. Xie L-L, Zhu J, Yang M-S, Yang C-Y, Luo S-H, Xie Y, Pu D (2017) Effect of Intra-wound Vancomycin for Spinal Surgery: A Systematic Review and Meta-analysis. Orthopaedic surgery 9(4):350–358. doi: 10.1111/os.12356
82. Schär RT, Zimmerli S (2022) VANCO Trial-Preliminary Results on the Safety Profile of Intrawound Vancomycin Powder in Complex Spine Surgery. World neurosurgery 162:7–8. doi: 10.1016/j.wneu.2022.03.041

83. Tafish RT, Alkhaldi AF, Bourghli A, Althunian TA (2021) Effectiveness of topical vancomycin in the prevention of spinal surgical site infections: a retrospective cohort study. Antimicrobial resistance and infection control 10(1):136. doi: 10.1186/s13756-021-01006-6
84. Zhang X, Zhai W, Li M, Guo X (2021) Circulatory collapse during wound closure in spine surgery with an unknown cause: a possible adverse effect of topical application of vancomycin? BMC anesthesiology 21(1):4. doi: 10.1186/s12871-020-01220-6
85. Fei J, Gu J (2017) Comparison of Lavage Techniques for Preventing Incision Infection Following Posterior Lumbar Interbody Fusion. Medical science monitor : international medical journal of experimental and clinical research 23:3010–3018. doi: 10.12659/msm.901868
86. Wachter D, Brückel A, Stein M, Oertel MF, Christophis P, Böker D-K (2010) 2-Octyl-cyanoacrylate for wound closure in cervical and lumbar spinal surgery. Neurosurgical review 33(4):483–489. doi: 10.1007/s10143-010-0258-5
87. Labler L, Keel M, Trentz O, Heinzelmann M (2006) Wound conditioning by vacuum assisted closure (V.A.C.) in postoperative infections after dorsal spine surgery. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 15(9):1388–1396. doi: 10.1007/s00586-006-0164-2
88. Zhang H, Li Q (2018) Improved vacuum sealing drainage for treatment of surgical site infection following posterior spinal internal fixation: A case report. Medicine 97(7):e9952. doi: 10.1097/MD.0000000000009952
89. Naylor RM, Gilder HE, Gupta N, Hydrick TC, Labott JR, Mauler DJ, Trentadue TP, Ghislain B, Elder BD, Fogelson JL (2020) Effects of Negative Pressure Wound Therapy on Wound Dehiscence and Surgical Site Infection Following Instrumented Spinal Fusion Surgery-A Single Surgeon's Experience. World neurosurgery 137:e257-e262. doi: 10.1016/j.wneu.2020.01.152
90. Gao S, Zheng Y, Liu X, Tian Z, Zhao Y (2018) Effect of early fasting and total parenteral nutrition support on the healing of incision and nutritional status in patients after sacrectomy. Orthopaedics & traumatology, surgery & research : OTSR 104(4):539–544. doi: 10.1016/j.otsr.2018.02.006
91. (2018) Prävention postoperativer Wundinfektionen : Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz 61(4):448–473. doi: 10.1007/s00103-018-2706-2

92. Mishra P, Pandey CM, Singh U, Gupta A, Sahu C, Keshri A (2019) Descriptive statistics and normality tests for statistical data. Annals of cardiac anaesthesia 22(1):67–72. doi: 10.4103/aca.ACA_157_18
93. Mishra P, Pandey CM, Singh U, Keshri A, Sabaretnam M (2019) Selection of appropriate statistical methods for data analysis. Annals of cardiac anaesthesia 22(3):297–301. doi: 10.4103/aca.ACA_248_18
94. Schober P, Boer C, Schwarte LA (2018) Correlation Coefficients: Appropriate Use and Interpretation. Anesthesia and analgesia 126(5):1763–1768. doi: 10.1213/ANE.0000000000002864
95. Webster J, Alghamdi A (2015) Use of plastic adhesive drapes during surgery for preventing surgical site infection. The Cochrane Database of Systematic Reviews 2015(4). doi: 10.1002/14651858.CD006353.pub4

8. Appendix

8.1. Legend of figures

8.2. Legend of tables

9. Publication of results

9.1. Congress presentation of partial results

Algarny S, Lenz M, Perera A, Eysel P, Scheyerer MJ (2022) Pathologische Wundheilungsstörungen nach Wirbelsäulenoperationen – Zusammenhang zwischen Operationsdauer und isoliertem Keim. 17. Jahrestagung der Deutschen Wirbelsäulengesellschaft. Posterpräsentation. Posternummer P 062, DOI: https://doi.org/10.1007/s00586-022-07413-6.

9.2. Paper publication of partial results

European Spine Journal volume 31, pages 3163–3249 (2022) -My Study in page 3226-
DOI: https://doi.org/10.1007/s00586-022-07413-6

9.3. Paper publication of end and last results

Algarny, S., Perera, A., Egenolf, P., Weber, M., Heck, V., Walter, S., Eysel, P., Scheyerer, M.J. & Lenz, M. (2023). Postoperative surgical site infections in orthopaedic spine surgery: can the duration of surgery predict the pathogen spectrum? In vivo, 37(4), approved for publication.