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# 2016

# Research articles in medicine & pharmacy

RĪGA STRADIŅŠ UNIVERSITY

# Collection of Scientific Papers 2016

Research articles in medicine & pharmacy

**Internal Medicine**
**Surgery**
**Medical Basic Sciences**
**Stomatology**

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# Contents

# Laboratory Parameters and Treatment Applied to Septic Patients

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## Abstract

Systemic illness caused by microbial invasion of normally sterile parts of the body is referred to as "sepsis", which is an increasingly common cause of morbidity and mortality, particularly in the elderly, immunocompromised, and critically ill patients (Dellinger, 2013). Sepsis develops in 750,000 people annually, and more than 210,000 of them die in US. A cohort study shows that mortality ranged between 28.3 % and 41.1 % on different continents.

The aim of this study was to clarify septic patients' clinical course, laboratory parameters and to assign a therapy.

The retrospective analysis of 72 patients' medical records was carried out. The research included patients of both sexes and all ages hospitalised at Riga Eastern Clinical University Hospital inpatient "Gaiļezers" between 2011 and 2014. All the patients involved in the study had severe sepsis and at least one organ dysfunction.

Majority of patients – 67 (93.05 %) – had immunocompromised background – tumours, intra-abdominal infections, complicated soft tissue infections, cardiovascular, endocrine, lung, liver, kidney diseases, HIV, viral hepatitis and alcohol addiction. All patients, at the time of hospitalisation, had elevated C reactive protein (CRP).

In-hospital patients sought medical attention too late, and at a prehospital stage, no patients received antibiotic therapy. In-hospital patients had received a broad-spectrum of antibiotic therapy.

*Keywords*: septic patients, intensive care units, sepsis treatment, antimicrobial therapy.

## Introduction

Derided from the Greek word *sipsi* (make rotten) sepsis is a syndrome associated with severe infection, typically pneumonia or gastrointestinal or urinary tract infection, and its successful treatment continues to represent a very important unmet clinical need. Causes thereof are heterogeneous, and its clinical features are diverse, making one of the most challenging syndromes both to recognise and to manage (Hall, 2011).

Sepsis is widespread among hospitalised patients worldwide. Severe sepsis and septic shock is a major cause of patient admission and mortality in intensive care units and the difficulty to diagnose the initial stage of the disease is a major obstacle to the reduction of mortality from sepsis. Patients

with sepsis spend longer in hospital, and longer in intensive care units than patients admitted for other reasons and a substantial proportion of these patients have long term functional, cognitive, and psychological deficits at one year (Iwashyna, 2010; Davydow, 2008).

In patients with severe sepsis, mortality remains higher than 25–30 %, and even 40–50 % when shock is present (Vincent, 2014).

Despite the advances in medicine, such as vaccination, antibacterial treatment options and acute patient care, mortality is high prom sepsis. No effective specific anti-sepsis treatments exist; therefore, management of patients with sepsis relies mainly on early recognition allowing appropriate therapeutic measures to be started rapidly, including administration of appropriate antibiotics, source control measures when necessary, and resuscitation with intravenous fluids and vasoactive drugs when needed.

## Aim

The aim of the research was to evaluate the disease course of severe sepsis patients, indicators of laboratory analyses and applied treatment at Riga Eastern University Hospital clinical centre "Gaiļezers".

## Material and Methods

The retrospective analysis of 72 patients' medical records was carried out, stratified by year of treatment outcome (dead/alive). The research included patients of both sexes and all ages hospitalised at Riga Eastern Clinical University Hospital inpatient "Gaiļezers" between 2011 and 2014. All the patients involved in the study had severe sepsis and at least one organ dysfunction. Blood test on sterility and identification of blood culture was performed for all patients.

The research was carried out with the approval of the ethics committee of Riga Eastern Clinical University Hospital "Gaiļezers".

Statistical methods. Data was described using means with standard deviations (SD) and median with interquartile range (IQR) for continuous variables and percentages for categorical variables. For the comparison of the study data, the non-parametric methods were used: Mann–Whitney U for continuous data and chi-square tests for categorical data. P value, less than $p < 0.05$, is accepted as statistically significant. Data statistical analysis was done in IBM SPSS Statistics.

## Results

Summarising the results, 40 (55.6 %) patients involved in the study were men, 32 (44.4 %) were women. The age of patients ranged between 22 and 90. The average age was 63.4 (SD 15.9) years. Most patients 65 (90.3 %) were taken to hospital with medical emergency.

The average duration of the patient's illness and hospitalisation time was 5.6 (SD 8.2) days. Median 3.0 (IQR 2.0 to 5.0) days.

The study included 40 (55.5 %) retired persons, 9 (12.5 %) second group disabled people, 15 (20.8 %) working age patients, but not daily employed and 8 (11.1 %) daily employed patients.

From all 72 (100 %) patients included in the study, 67 (93.05 %) had immunocompromised background – tumours, intra-abdominal infections, complicated soft tissue infections, cardiovascular, endocrine, lung, liver, kidney diseases, HIV, viral hepatitis and alcohol addiction. 5 (6.9 %) patients were not diagnosed with related diseases.

All patients at the time of hospitalisation had elevated C reactive protein (CRP), ranging from 46.35 mg/L to 926.65 mg/L. More than a half of patients' 56 (77.7 %) CRP was above 259 mg/L. 60 (83 %) patients at the time of hospitalisation had elevated IL-6. Leukocytosis was diagnosed with 59 (81.9 %) patients. Leukopenia was diagnosed with 6 (8.3 %) patients. 32 (44.4 %) patients had elevated liver indicators (ALAT, ASAT). 39 (54.1 %) patients had elevated kidney indicators. Nevertheless, the renal

replacement therapy during hospitalisation was received by 13 (18.1 %) patients. For dead patients (n = 36.50 %) the renal replacement therapy was received by 25 % (p = 0.12).

None of the patients before hospitalisation had visited family doctor to get the necessary treatment.

All patients included in the study had severe sepsis and at least one organ dysfunction.

Plating of blood was positive in 32 (44.4 %) patients. Blood agent in culture grows – *Streptococcus* beta-haemolytic group B was 1 (3.1 %), *Escherichia coli* – 3 (9.37 %), *Staphylococcus epidermidis* – 5 (15.6 %), *Staphylococcus hominis* – 1 (3.1 %), *Staphylococcus aureus* – 7 (21.9 %), *Staphylococcus haemolyticus* – 1 (3.1 %), *Prevatella oralis* – 1 (3.1 %), *Streptococcus pneumonia* – 10 (31.3 %), *Klebsiella pneumonia* – 1 (3.1 %), *Clostridium difficile* – 1 (3.1 %), *Streptococcus* beta-haemolytic group A – 1 (3.1 %).

Evaluating the antibiotic therapy received by severe sepsis patients, results indicate that intravenous injection was most frequently prescribed – ceftriaxone 1 gram, tazocin (piperacillin and tazobactam) 4.5 grams, tienam (imipenem and cilastatin) 500 milligrams, meronem (meropenemum) 1 gram, metronidazol 500 milligrams, ciprofloxacin 200 milligrams.

## Discussion

The sepsis is one of the most frequent reasons for hospitalisation in intensive care units worldwide. Early sepsis detection and timely treatment administration with appropriate antibiotics are the most important factors in improving the outcome of sepsis. However, initial sepsis clinical signs and symptoms are non-specific, creating the risk of late diagnosis. Our medical investigation also indicated that sepsis diagnosis was made too late, as long as patients were stationed after 5.6 days of sick days. None of the patients had turned to their family therapist with complaints before.

Surviving Sepsis Campaign (SSC) is an international programme that makes guidelines to improve the management of this serious clinical condition and to reduce the high mortality rates. The first SSC guideline which was published in 2004 classified the recommendations as resuscitation bundle including elements for first six hours resuscitation and management bundle including elements for first 24 hours management. The guideline was renewed in 2008. Many studies revealed that clinical implementation of these bundle elements improve the quality of sepsis care; reduce the hospital mortality. In 2012 the SSC 2008 guideline was updated and in 2015 updated again; recommendations classified as to be completed within three hours and to be completed within six hours (Tufan, 2015). Of note, the 6-hour bundle has been updated; the 3-hour SSC bundle is not affected.

To be completed within 3 hours of time of presentation[1]:

1) measure lactate level;
2) obtain blood cultures prior to administration of antibiotics;
3) administer broad spectrum antibiotics;
4) administer 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L. According to the guidelines, level of lactic acid was established within the first three hours for all the patients, samples of blood culture before the initiation of antibacterial therapy were also received and broad-spectrum of antibiotic therapy was ordered afterwards. Injection of 30 ml/kg crystalloid in case of hypotension was not investigated.

To be completed within 6 hours of time presentation:

1) apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mmHg;
2) in the event of persistent hypotension after initial fluid administration (MAP < 65 mmHg) or if initial lactate was ≥ 4 mmol/L, re-assess volume status and tissue perfusion and document reassessment of volume status and tissue perfusion with: repeat focused exam (after initial fluid

[1] "Time of presentation" is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.

resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings. Or two of the following: Measure CVP, Measure $ScvO_2$, Bedside cardiovascular ultrasound, Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge;

3) re-measure lactate if initial lactate elevated (Dellinger, 2013; The ARISE Investigators and the ANZICS Clinical Trials Group, 2014; Levy, 2014; Mouncey, 2015; Yealy, 2014).

Several studies show, and guidelines will, early initiation of antimicrobial therapy has reduced the duration of hospitalisation of patients and limiting the development of resistance to antibiotics (Angus, 2013; Van den Bosch, 2014).

Studies indicate that older patients, male gender, African Americans, patients with chronic health problems are particularly prone to the development of severe sepsis, so the prevention strategies should be targeted to these groups (Mayr, 2014). Our data indicated that most patients were in the age group between 60 and 79 (n = 32.44 %) and 20 (62.5 %) died. Severe sepsis occurs more often to patients with chronic obstructive pulmonary disease, tumours, chronic kidney, liver diseases and diabetes. Other risk factors that increase the possibility of developing sepsis are long-term care at care establishments, malnutrition, use of immunosuppressive medications, immunocompromised patients. Data of our investigation were similar to the worldwide data – 93.05 % of all patients involved in the investigation had immunocompromised immunological status and that is a significant risk factor. The significance on the relationship between socioeconomic status and blood stream infection has also been reported (Mendu, 2012). In our examination it was *Streptococcus pneumonia* that increased the most (31.3 %) to patients aged 60–79 years old. However, blood culture was mostly positive for less than a half of patients (44.4 %); it makes diagnosis and treatment of sepsis even harder.

Chronic obstructive pulmonary disease exemplifies a chronic health disorder that predisposes patients to increased risk of severe sepsis. The risk arises because of increased risk of lower respiratory tract infection and, if infection is present, an increased risk of organ dysfunction, such as acute respiratory failure, because of decreased physiological reserve. Many other chronic diseases, such as cancer, cirrhosis, AIDS, are associated with an increased risk of sepsis or organ dysfunction (Mrus, 2005). Social behaviours are also associated with sepsis, with an increased incidence and worse outcomes in people who misuse alcohol (O'Brien, 2009) and an increased risk of death from pneumococcal pneumonia in smokers, despite sparse data on the effects of smoking in sepsis.

Diagnostic considerations – unlike troponin for acute coronary syndrome or a radiograph for fracture, sepsis does not have only one diagnostic test and instead is a clinically defined syndrome subject to revision (Bone, 1992). The prodrome of sepsis can be non-specific or brief and the short term mortality high.

Diagnostic microbiology stands at the epicentre of the tests for sepsis in patients. Microbiological studies for the detection of bacteria or fungi in blood, blood fluids, or relevant tissues continue to rely for the most part on conventional culture-based systems, which remain the gold standard. Blood cultures are positive in 30–40 % of patients with severe sepsis and septic shock (Bochud, 2004). In our study we were similar, blood plating was positive in 32 (44.4 %) patients.

Recently, a quantity of publications have revealed that genetic variation especially single nucleotide polymorphism of cytokines in the innate immune system may influence the risk of sepsis. Among these cytokines, Interleukin-6 (IL-6) is one of the most important members which may be associated with sepsis risk and outcome. Some studies have indicated that IL-6 may play a key role in the inflammatory response to microbial invasion (Gao, 2015). Our data indicated a heightened level of IL-6 for a majority of patients – 83 %. Previous studies revealed that high IL-6 level was associated with increased severe sepsis mortality and risk.

Nowadays, clinicians have greatly improved care for septic shock. Urgent resuscitation using intravenous fluids and vasopressors as well as rapid administration of broad spectrum antibiotics are probably the most basic and universally accepted interventions. Various trials have compared different types of vasopressors, associations of vasopressors and inotropes, and pressure targets. End goal-directed therapy

algorithms are designed to optimise oxygen delivery by use of fluids, vasopressors, inotropes, and blood products. Patients who have a poor response to resuscitation and patients with known severe ventricular dysfunction might merit advanced hemodynamic monitoring (Gelinas, 2016).

Prompt initiation of appropriate antibiotics is crucial. The SSC guidelines (Angus, 2013) suggested that antibiotics should ideally be started within one hour of the diagnosis of severe sepsis or septic shock. But our study, it should be taken into account that in this case at the moment of hospitalisation, sepsis was not developed or proven yet to all the patients, because for diagnosing sepsis, by definition, a number of physiological indicators and the results of laboratory investigations, as well as the identification of focuses of infection that caused these modifications are required. And it was the possible reason for dilatory diagnosis of sepsis in other therapeutic departments (not emergency department), or at prehospital stage. Because early initiation of antimicrobial therapy reduces bacterial load and hence the mortality of septic patients.

The empiric antibiotic regimen should be broad enough to cover all likely pathogens and be guided by local epidemiological data and the medical history of the patient, including previous infections, susceptibility profiles of colonizing microorganisms, and recent exposure to antimicrobial drugs. Pharmacokinetic and pharmacodynamics considerations related to appropriate tissue penetration and the presence of hepatic or renal dysfunctions should also be taken into account. Drug clearance of mainly renally eliminated drugs, and thus the required dose can differ up to 10-fold due to the variability in renal function in patients with severe infections. Effect of antibacterial therapy was possibly affected also by the dysfunction of kidney, established by our investigation in 54.1 % of cases and hepatic damage, established in 44.4 % of cases.

The empirical antibiotic regimen could rely on either one antibiotic or on two or more antibiotics. Monotherapy consists typically of an extended-spectrum penicillin with or without a beta-lactamase inhibitor, a third or fourth generation cephalosporin, or a carbapenem, Combination therapy is usually an association of a beta-lactam with an aminoglycoside, a fluoroquinolone, an anti-Gram-positive drug, or an antibiotic active against multiresistant Gram-negative bacteria (Ferrer, 2014).

In the last decade much effort was put in the development of early risk scales, to recognize sepsis patients timely, but it is still necessary to improve patient recognition and response. Basically, there are necessary such scales that can be used outside intensive care units, directly in the emergency or hospital wards. But in daily routine such scales are not applied, because they are complicated and only provided for particular group of patients. There are applied many scales in the world, for example, APACHE (Acute Physiology and Chronic Health evaluation), SOFA (Sepsis-related Organ Failure Assessment), MODS (Multiple Organ Dysfunction Score), RAPs (Rapid Acute Physiology Score), which are used to divide patients into categories after severity of disease, indicating the level of organ dysfunction and predicating potential risk of death. Therefore, the aim is to recognise patients with systematic inflammation timely, before it transforms, endangering tissues and organs. The mortality of sepsis correlates with disease severity, it increases from systemic inflammatory response syndrome (SIRS) to septic shock; therefore, appropriate beginning of treatment is important. However, investigations of one ideal scale are being continued worldwide.

## Conclusions

After the results of laboratory analyses, we can conclude that patients enter hospital too late and consequently, therapy is not initiated on time. Blood culture was mostly positive for less than a half of patients (44.4 %); it makes diagnosis and treatment of sepsis even harder. But all patients received broad-spectrum of antibiotic therapy, as stated in the guidelines.

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# Childhood Intussusception: 10-year Experience at Children's Clinical University Hospital in Riga

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**Abstract**

Intussusception is the most common cause of intestinal obstruction in children between the age of 3 months and 3 years. Non-surgical methods are the main treatment, but still intussusception reduction techniques remain varied and controversial.

The aim of the study was to review the experience of Children's Clinical University Hospital in the management of intussusception over the last 10 years, with a focus on assessing the efficacy of non-operative reduction.

Retrospective descriptive study was conducted at Children's Clinical University Hospital, Riga. The study included data from medical records of patients with intussusception between January 2006 and December 2015 at the hospital. Patients' demographics, clinical presentation, treatment modalities, recurrence and length of hospital stay were studied. The method of non-operative reduction was pneumatic reduction. Data analysis was carried out using the Microsoft Excel and IBM SPSS Statistics. Results were considered statistically significant with CI > 95 %, $p < 0.05$.

The study included 148 patients (93 males, 55 females), ratio 1.7 : 1. Mean age 23.7 ± 27.4 months (range 2 to 161 month). Duration of presenting symptoms 18 ± 17 h, most common symptom – abdominal pain (83.1 %). Main diagnostic method – abdominal sonography, made in 81.1 %, with sensitivity of 95.8 %. Secondary intussusception found in 4.7 % with Meckel's diverticulum (n = 5) and polyp (n = 2) as lead point. Pneumatic reduction was performed in 85 patients, with success rate of 82.5 %. In surgical group (n = 61) predominantly laparotomy with manual reduction in 24.3 % was used. The overall recurrence rate was 6.8 %. Mean hospital stay was 4.6 days, in non-surgical group 2.5 days vs. surgical group 7.5 days ($p < 0.01$).

Pneumatic reduction is the main intussusception treatment method at Children's Clinical University Hospital. There is no statistically significant correlation between patient's age, length of symptoms and pneumatic reduction success rate. Pneumatic reduction is minimally invasive for patients, has high success rate (82.5 %) and low complication rate, decreases length of hospital stay.

*Keywords*: intussusception, pneumatic reduction, recurrence, lead point.

## Introduction

Intussusception is the most common cause of intestinal obstruction in infants and young children between the age of 3 months and 3 years, and the peak age of presentation is 4 to 10 months [7, *508*; 14, *518*]. It is acquired invagination of one portion of the intestine into the adjacent bowel and described by the proximal, inner segment of intestine first and the outer distal, receiving portion of intestine last [7, *508*]. Intussusception results in venous congestion and bowel wall oedema, and if left untreated, arterial obstruction, bowel necrosis and perforation may occur [14, *518*]. 80 % to 95 % of paediatric intussusceptions are ileocolic and idiopathic, mostly caused by lymphoid hyperplasia as the "lead point" in its pathogenesis [14, *519*]. Secondary intussusception is observed in 1.5 % to 12 % of cases, on average 6 % [5, *141*; 8, *509*; 14, *519*]. The most common causes are Meckel's diverticulum, polyps and duplications. Systemic conditions such as Henoch-Schönlein purpura, Peutz-Jeghers syndrome can also increase the risk of intussusception [14, *519*]. Secondary intussusception proportion increases with age, particularly after 2 years of age [7, *515*].

Techniques for intussusception reduction remain varied and controversial. Treatment may be non-surgical (pneumatic or hydrostatic pressure enemas under fluoroscopy or sonography) or surgical (laparoscopy, open surgery with manual reduction and/or resection or enterostomy) [3, *4*; 7, *511*; 12, *60*; 14, *522*].

Hydrostatic reduction was first described in 1876. Barium or water-soluble contrast enema are used for hydrostatic reduction under fluoroscopy, with no more than three attempts, no more than three minutes each. Hydrostatic reduction is complete when contrast medium freely flows through the ileocecal valve into terminal ileum. Success rate ranges between 42 % and 95 % [7, *519*].

Air reduction was first described in 1897. It is being advocated as faster, safer, much leaner method with less exposure time to radiation. The maximum safe air pressure is 80 mmHg for younger infants and 120 mmHg for older ones [7, *520*]. Pneumatic reduction is currently the most popular standard method with success rate of 84 % to 100 % [12, *60*; 14, *522*]. Disadvantages of fluoroscopic reduction methods are related to exposure to radiation, poor visualisation of lead points, relatively poor visualisation of reduction process, resulting in false-positive reduction. Complications as bowel perforation, barium peritonitis, tension pneumoperitoneum, fewer and septicaemia are described [7, *520*; 8, *1138*].

Sonographically guided hydrostatic intussusception reduction was first described in 1985 [12, *59*]. Reduction can be done without general anaesthesia. The enema bag is raised initially to three feet and subsequently elevated to a maximum of 5.5 feet if reduction is not achieved after two attempts. A successful reduction is confirmed when the entire caecum and thickened ileocaecal valve are visualised with free flow of fluid into the distal small bowel [12, *60*]. Advantages of such method are excluding the need of radiation, possibility for parents to take part in treatment process, significantly higher sensitivity in detecting pathologic lead points, and earlier evaluation for bowel perforation signs. The major disadvantage, however, is the need in sonographic experience in intussusception diagnostic and reduction evaluation [12, *63*].

Operative reduction is required when non-operative reduction is either contra-indicated (peritonitis, perforation) or unsuccessful [14, *519*]. At this moment, there are no approved guidelines for intussusception treatment.

## Aim

The goal of this study is to review the experience of Children's Clinical University Hospital in the management of paediatric intussusception over the last 10 years, with a focus on assessing the efficacy of non-operative reduction.

## Material and Methods

This is a retrospective descriptive study conducted at Children's Clinical University Hospital (CCUH) of Riga. Children who presented with intussusception between January 2006 and December 2015 at CCUH were included in the study. Data were extracted from medical records. Patients demographics, clinical presentation, duration of symptoms, treatment modalities, complication rate, and length of

hospital stay were studied. Indications for non-surgical treatment for patients with intussusception before 2009 were age till 12 months, length of symptoms till 24 hours, no signs of ileus on abdominal plain x-ray, no massive bleeding from gastrointestial tract, no signs of peritonitis. After 2009, indications were changed to length of symptoms till 36 hours and age till 24 months, other indications remained the same.

The method of non-operative reduction in our institution was pneumatic reduction under fluoroscopy. The procedure was performed by paediatric surgeon. During pneumatic reduction, air is insufflated via Foley catheter (size of 18-Fr to 22-Fr, depending on a patient's size, with balloon inflated with 10 ml of water) placed inside a patient's rectum under pressure monitoring with a maximum of 120 mmHg. Manipulation was made under general anaesthesia. Successful reduction was demonstrated by free flow of air into terminal ileum and disappearance of caecal soft tissue mass. In surgical reduction both methods, laparoscopy and laparotomy, were used.

Data analysis was carried out using the Microsoft Excel and IBM SPSS Statistics. Results were considered statistically significant when $p \leq 0.05$.

## Results

Between January 2006 and December 2015, 148 patients (94 male, 54 female) with intussusception were admitted to CCUH. Intussusception was diagnosed more often in males than in females, male to female ratio was 1.7 : 1. Number of cases increased in last years (Figure 1), that can be explained with the increasing number of cases transmitted from regional hospitals to Children's Clinical University Hospital of Riga.

Mean age at presentation was 23.7 ± 27.4 months (range 2 to 161 months). More than half of the patients (50.7 %) presented were at the age before one, 28.4 % in the age group 1 to 3 year-olds and 20.9 % older than 3 years (Figure 2). Duration of presenting symptoms was 18 ± 17 hours (range 1 to 72 hours). Distribution of the patients in relation to the duration of symptoms is presented in Table 1. The most common symptom reported was intermittent crampy abdominal pain, found in 123 (83.1 %) patients. Classic clinical triad (intermittent, crampy abdominal pain, "red currant jelly" stool, vomiting) was reported only in 26.4 % (39) patients. Presence of palpable abdominal mass was not described in medical literature. Common presenting symptoms are represented in Table 2.

Main diagnostic methods used at Children's Clinical University Hospital were abdominal sonography and plain abdominal X-ray. Computer tomography for intussusception confirmation was used only once in a 10-year period. Abdominal sonography was made in 81.1 % (120) patients with sensitivity of 95.8 % (Figure 3). Possible pathologic lead point was found in 41.7 % (50) of cases (Figure 4). In recent years sonography use in control for early recurrence has increased, made in 55 (37.2 %) patients, revealed 12 (8.1 %) recurrence cases. Plain abdominal X-ray was made in 66.9 % (99) patients, ileus signs were found in 58.6 % (58), irregular distribution of gases in 29.3 % (29) and normal – in 12.1 % (12) cases.

*Figure 1.* Distribution of patients with intussusception per year

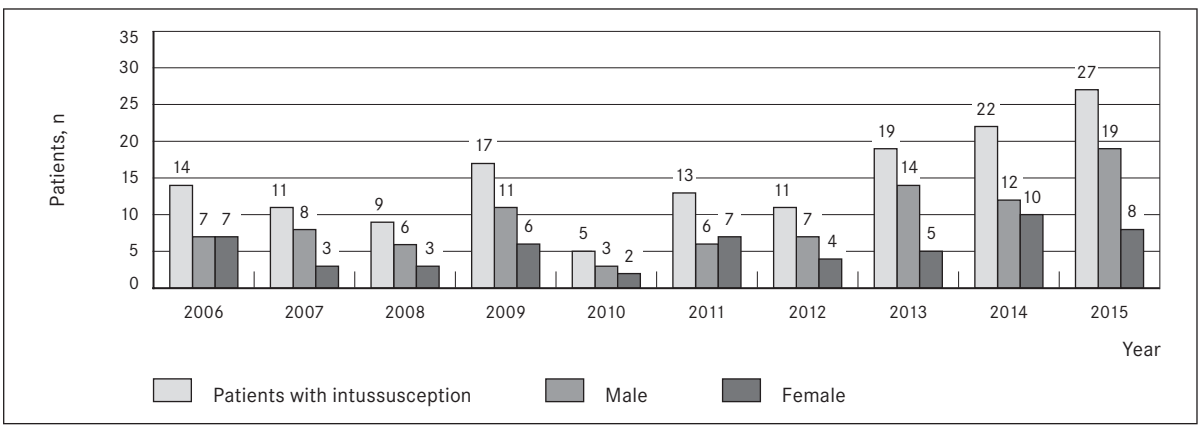


*Figure 2.* Frequency of intussusceptions in different age groups and sexes

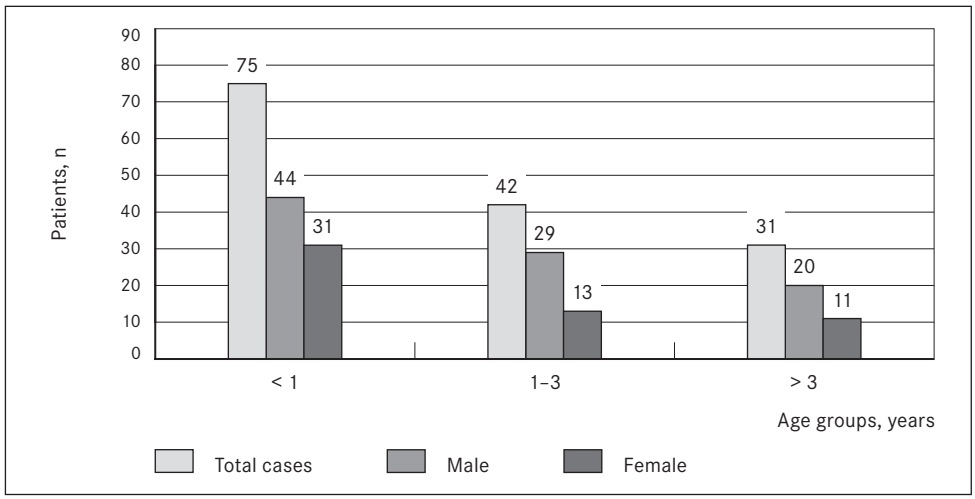



*Table 1.* Distribution of patients in relation to the duration of symptoms

| Duration of symptoms, h | Number of patients, n (%) | Successful non-operative reduction, % |
|---|---|---|
| < 24 | 111 (75) | 62.2 |
| 24–48 | 30 (20.3) | 46.7 |
| > 48 | 7 (4.7) | 28.6 |

*Table 2.* Distribution of intussusception symptoms

| Presenting symptom | Number of patients, n (%) |
|---|---|
| Abdominal pain | 123 (83.1) |
| Vomiting | 109 (73.6) |
| Red currant jelly stool | 64 (43.2) |
| Lethargy | 42 (28.4) |
| Irritability | 43 (29.1) |

*Figure 3.* Intussusception sonographic view – target sign (examination and image made by K. Soldatenkova)

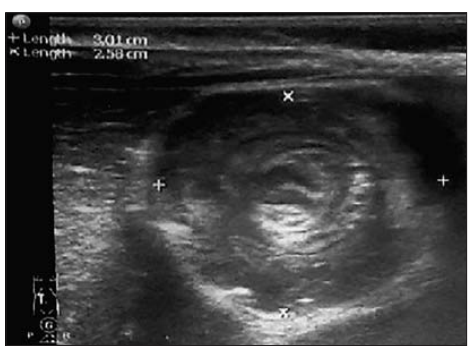
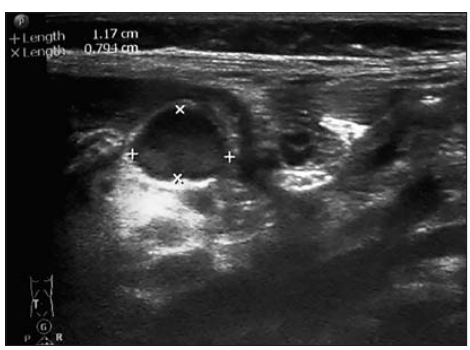


*Figure 4.* Mesenterial lymphadenitis sonographic view (examination and image made by K. Soldatenkova)



Pneumatic reduction was performed in 103 patients, among which 85 (82.5 %) cases were successful, no bowel perforation was observed after procedure. In total, 57.4 % of patients were treated with pneumatic reduction. No statistically significant correlation between pneumatic reduction success rate and patient's age, length of symptoms was found (Table 3).

*Table 3.* Pneumatic reduction success rate in correlation to age and symptoms length

| Criterion | Number of patient | | Pneumatic reduction attempt | | Successful pneumatic reduction | | Success rate, % | p value |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | | |
| All patients | 148 | 100.0 | 103 | 69.5 | 85 | 57.4 | 82.5 | |
| < 1 year | 75 | 51.0 | 55 | 73.3 | 43 | 57.3 | 78.2 | 0.997 |
| 1–3 years | 42 | 28.0 | 27 | 64.3 | 24 | 57.1 | 88.9 | |
| > 3 years | 31 | 21.0 | 21 | 67.7 | 18 | 58.1 | 85.7 | |
| Symptoms < 24 h | 111 | 76.7 | 86 | 77.5 | 69 | 62.2 | 80.2 | 0.090 |
| Symptoms 24–48 h | 30 | 20.3 | 15 | 50.0 | 14 | 46.7 | 93.3 | |
| Symptoms > 48 h | 7 | 4.7 | 2 | 28.6 | 2 | 28.6 | 100.0 | |

A total of 61 patients in the study required operative reduction (Figure 5). The most frequently performed was laparotomy with manual reduction in 36 (24.3 %) patients, laparotomy with bowel resection and primary bowel anastomosis in 5 (3.4 %), laparotomy with bowel resection and stoma in 2 (1.4 %) patients. Laparoscopic reduction was attempted in 25 patients, among whom 18 (12.2 %) were successful. Conversion to open reduction was required in five patients due to difficult reduction, and in one because of the need for bowel resection. In one case laparoscopy was made as diagnostic operation after spontaneous intussusception reduction and persistent clinical symptoms, but no intussusception was found during the operation. Together in two (1.4 %) patients with clinically and sonographically confirmed intussusception after observation period under sonogaphy control spontaneous reduction was diagnosed without a need for further non-surgical or surgical treatment. Comparison of pneumatic reduction group and surgical reduction group is shown in Table 4.

In our study 136 (91.9 %) patients were with intussusception at the hepatic flexure (ileocolic), 82 (60.3 %) of whom had successful non-operative reduction; other forms of intussusception were less common (Table 5).

*Figure 5.* Treatment methods for patients with intussusception

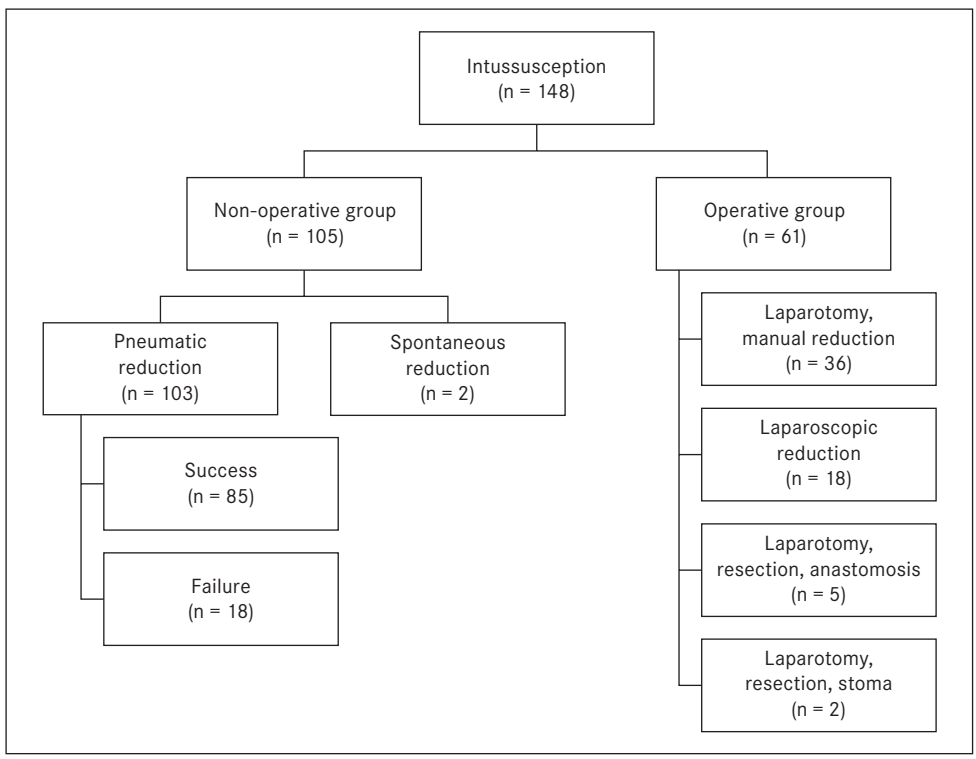


*Table 4.* Comparison of pneumatic reduction and operative reduction groups

| Criterion | Pneumatic reduction group (n = 85) | Operative reduction group (n = 61) | p value |
|---|---|---|---|
| Gender, n (%) | Male 48 (56.5) | Male 44 (72.1) | 0.053 |
| | Female 37 (43.5) | Female 17 (27.9) | |
| Age, month (mean) | 21.9 ± 22.6 | 24.0 ± 28.3 | 0.619 |
| Age groups, n (%) | | | |
| < 1 year | 43 (57.3) | 32 (42.7) | 0.968 |
| 1–3 years | 24 (58.5) | 17 (41.5) | |
| > 3 years | 18 (60.0) | 12 (40.0) | |
| Length of symptoms, h (mean) | 15.5 ± 15.3 | 22.6 ± 18.9 | 0.013 |
| Length of symptoms, n (%) | | | |
| < 24 h | 69 (63.3) | 40 (36.7) | 0.069 |
| 24–48 h | 14 (46.7) | 16 (53.3) | |
| > 48 h | 2 (28.6) | 5 (71.4) | |
| Symptoms, n (%) | | | |
| Intermittent pain | 68 (80.0) | 53 (86.9) | 0.276 |
| Vomiting | 58 (68.2) | 49 (80.3) | 0.103 |
| Red currant jelly stool | 30 (35.3) | 34 (55.7) | 0.014 |
| Plain abdominal X-ray, ileus | 30 (52.6) | 28 (66.7) | 0.324 |
| Intussusception type, n (%) | | | |
| Idiopathic | 84 (98.9) | 55 (90.2) | 0.051 |
| Secondary | 1 (1.1) | 6 (9.8) | |
| Length of hospital stay, days (mean) | 2.5 ± 1.9 | 7.5 ± 3.8 | < 0.001 |

*Table 5.* Distribution of intussusception forms in relation to the treatment method

| Intussusception form | Pneumatic reduction cases, n | Operative reduction cases, n | Spontaneous reduction, n | Total, n (%) |
|---|---|---|---|---|
| Ileocolic | 82 | 52 | 2 | 136 (91.9) |
| Ileoileocolic | 0 | 2 | 0 | 2 (1.4) |
| Ileoileal | 3 | 4 | 0 | 7 (4.7) |
| Colocolic | 0 | 2 | 0 | 2 (1.4) |
| Appendicocaecal | 0 | 1 | 0 | 1 (0.7) |

A pathological lead point was noted in 86 (58.1 %) patients, with prevalence of acute mesenterial lymphadenitis in 79 (91.9 %) patients as primary or idiopathic intussusception possible reason. The cause for secondary intussusception was found in 7 (4.7 %) patients. Five cases of Meckel's diverticulum and two cases of bowel polyps were found. One patient was admitted to Children's Clinical University Hospital with intussusception after Rota virus vaccine in close history. Distribution of patients with pathological lead point are presented in Table 6. Pathological cause was found in 10 of 18 unsuccessful pneumatic reduction cases: two cases of Meckel's diverticulum, eight cases of acute mesenteric lymphadenitis.

Recurrence was divided in two groups. Early recurrence during same hospitalisation in first 24–72 hours after non-surgical or surgical treatment. Together 12 (8.1 %) cases were included, seven cases after surgical and five cases after non-surgical treatment. Distribution of used treatment methods is shown in Table 7. Ten from 148 children had more than one episode between 2006 and 2015, overall recurrence rate was 6.8 % (10/148). Number of recurrence episodes ranged from one to four times. Higher number

occurred in males with Meckel's diverticulum. Only in two patients it was possible to identify pathological lead factor (Meckel's diverticulum and bowel polyp). The period of intussusception recurrence onset ranged from 1 month to 4.8 years.

Mean post reduction hospital stay was 4.6 days (range, 1–18 days). In pneumatic reduction group mean hospital stay was 2.5 days (range, 1–7 days) versus 7.5 days (range, 3–17 days) in surgical group: laparoscopy – 5.6 days, laparotomy with manual reduction – 7.6 days. There was a statistically significant difference in length of hospital stay between non-operative and operative groups ($p < 0.001$).

*Table 6.* Distribution of patients with pathological lead point in relation to age

| Age (years) | Number of patients, n (%) | Number of patients with pathological lead point, n (%) | Idiopathic intussusception, n | Secondary intussusception, n |
|---|---|---|---|---|
| < 1 | 75 (51) | 30 (40.0) | 24 | 6 |
| 1–3 | 42 (28) | 29 (69.0) | 29 | 0 |
| > 3 | 31 (21) | 27 (87.1) | 26 | 1 |
| Total | 148 (100) | 86 (58.1) | 79 | 7 |

*Table 7.* Patients with recurrent intussusception treatment methods

| Treatment method | Number of patients, n |
|---|---|
| Pneumatic reduction | 2 |
| Laparotomy, manual reduction | 3 |
| Laparoscopic reduction | 2 |
| Laparotomy, resection, stoma | 2 |
| Spontaneous reduction | 3 |
| Total | 12 |

## Discussion

Intussusception is the most common cause of intestine obstruction in infants and children between the age of 3 months and 3 years, and the peak age of presentation is 4 to 10 months [6, *23*; 7, *508*; 14, *518*]. If diagnosed early, intussusception may be easily treated by non-surgical methods. For a successful management of intussusception, it is important to recognise pattern, risk factors, diagnostic and treatment methods [3, *1*; 5, *139*]. This study is the first retrospective analysis of Children's Clinical University Hospital's 10-year experience.

The study included 148 patients, with mean age of 23.7 months (range, 2–161, median 13 months), more than a half (50.7 %) below the age of one. Statistically significant prevalence in males with ratio 1.7 : 1. Median age in our study is higher to the data from the analysed literature, with median age 7–19 months [3, *2*; 8, *1839*; 11, *217*], but agrees with male : female ratio 1.3–2 : 1 [3, *2*; 8, *1840*; 11, *218*].

Typical intussusception symptoms or "clinic triad" include crampy, intermittent pain, red currant jelly stool and vomiting [5, *140*] or abdominal mass [14, *519*] is seen in less than 25 % of patients. The leading symptom also varies according to publications, Wong et al. described vomiting as leading symptoms (76.3 % of patients) [14, *520*], but Guney et al. found abdominal pain in all patients [5, *140*]. Red currant jelly stool was observed in 12.4–71.5 % of patients [5, *140*; 8, *1839*]. Various studies [8, *1840*; 10, *843*; 14, *520*] have reported palpable abdominal mass as statistically significant risk factor for unsuccessful non-operative reduction, because this may signify relatively longer duration of intussusception, complete intestinal obstruction. In our study "classic triad" (pain, vomiting, red currant jelly stool) was found in 26.4 % of cases, with intermittent abdominal pain as the leading symptom in 83.1 % of cases, consistent with literature. Palpable abdominal mass was not evaluated due to lack of information in medical records.

Sonography has become the diagnostic standard for confirmation of suspected intussusception, with high sensitivity (98–100 %) and specificity (88–100 %), [5, *139*; 12, *59*; 14, *519*] especially in ileocolic intussusception form [2]. In our study abdominal sonography was performed in 81.1 % of patients, with sensitivity of 95.8 %. Abdominal radiography is the second diagnostic method used in the study – 99 cases (66.9 %), no cases of perforation detected. Tareen et al. analysed a 15-year experience in necessity of abdominal radiography (AR) in children with intussusception. They concluded that AR should always be performed when clinical peritonitis is present, but is not otherwise necessary in children with suspected or confirmed intussusception [13, *90*].

The vast majority of patients with intussusception does not have a pathologic lead point and is classified as primary or idiopathic intussusception [8, *508*]. In idiopathic intussusception, the most common cause is mesenterial lymphadenitis [1, *648*; 8, *509*; 14, *520*]. Secondary intussusception with identifiable cause range from 1.5 % to 12 %. Most common found pathologies are Meckel's diverticulum, polyps, duplications [5, *141*; 8, *509*; 14, *519*]. These anatomic causes tend to increase in proportion by age, especially after 2 years of age [8, *509*], in some studies after 4–5 years of age [1, *648*]. The current study showed secondary intussusception in 4.7 %. Various studies have reported anatomical lead point as statistically significant risk factor for unsuccessful non-operative treatment [5, *141*; 14, *520*], especially in correlation with age after 2 years of age, anamnesis over 48 hours [8, *1841*; 12, *60*] and palpable abdominal mass [3, *2*; 14, *520*].

Intussusception reducing techniques remain varied and controversial, there are no guidelines found in literature [12, *59*]. The two main directions are isolated: non-surgical and surgical. All analysed publications advocate non-surgical methods as main intussusception treatment methods, but no unified opinion can be found about such methods' subtypes, contraindications, attempts' number and specialist (surgeon vs. radiologist) who perform this manipulation [8, *1838*; 12, *60*]. At present, pneumatic reduction under fluoroscopy is the most popular method and is being advocated as a cleaner and faster technique, with high success rate 75–100 % [3, *2*; 12, *60*; 14, *520*]. Sanchez et al. in retrospective analysis reviewed 31 cases of intussusception and compared sonographically guided hydrostatic saline enema reduction with pneumo and hydroreduction under fluoroscopy. Analysis showed success rate for sonographically and fluoroscopically assisted reduction 100 % and 84 %, respectively. The advantage of sonography compared to fluoroscopy is no concern over excessive radiation exposure, evaluation of possible pathologic lead points, greater sensitivity in visualising small fluid collections for diagnosis of possible perforation [12, *61*]. In contrast, Khorana et al. compared 190 cases of intussusceptions, solved by pneumatic and hydrostatic reduction methods, guided under sonography and fluoroscopy. They found success rate of pneumatic and hydrostatic reduction 61 % and 26 %, respectively [8, *1841*]. Lautz et al. in their study compared delayed repeat enema with immediate surgery in children with ileocolic intussusception and statistically proved that delayed repeat enemas are safe, increase success of non-operative reduction, decrease rate of bowel resection and reduce mean hospital length of stay and costs [9, *425*]. Geltzeiler et al. report about laparoscopy – assisted hydrostatic reduction of intussusception in cases of failed reduction by contrast enema under fluoroscopy as treatment modality [4, *764*]. In this study, pneumatic reduction under fluoroscopy was performed in 85 (57.4 %) patients with success rate of 82.5 %, which coincide with other authors' results. Most reviewed studies as absolute contraindications for non-surgical treatment mention only signs of peritonitis and bowel perforation, compared with the hospital's contraindications of age, length of symptoms, ileus at X-ray [7, *509*; 8, *1838*; 14, *519*].

Recurrence rate of intussusception varies from 3–20 %, with higher incidence in non-operative treatment group (3–15 %) and less than 5–8 % in operative group [3, *2*; 7, *515*]. Recurrence risk according to literature increase in first 24–48 hours after treatment episode and after 6 months [3, *3*; 7, *515*]. In the study, early recurrence was higher in non-operative group, but overall recurrence was 6.8 %, which corresponds to other reports.

## Conclusions

1. Pneumatic reduction is the main intussusception treatment method at Children's Clinical University Hospital.
2. There is no statistically significant correlation between patient's age, length of symptoms and pneumatic reduction success rate.
3. Pneumatic reduction is minimally invasive for patients, has high success rate (82.5 %) and low complication rate, decrease length of hospital stay.

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# EEG Controlled Sedation in Patients Undergoing Hand Surgery under Regional Anaesthesia: Dexmedetomidine vs. Propofol Target Controlled Infusion

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**Abstract**

The aim of the study is to compare sedations with dexmedetomidine vs. propofol controlled by *Narcotrend* electroencephalogram (EEG) in patients undergoing hand surgery under regional anaesthesia.

50 patients ASA I–II undergoing hand surgery under brachial plexus block, included in a prospective study, were randomised into 2 groups of 25.

Sedation with dexmedetomidine: a loading dose 1 μg/kg over 10 min, followed by infusion 0.1–0.6 μg/kg/h.

Sedation with propofol: Target Controlled Infusion (TCI), using *Schnider* Effect Site pharmacokinetic model, initial dose: 2.5 μg/ml.

Sedation depth was controlled with EEG index by Narcotrend.

After 10 minutes of sedation with dexmedetomidine patients' heart rate (HR) decreased from 74.9 ± 10.0 to 62.8 ± 7.9 ×/min ($p < 0.01$), systolic blood pressure (SBP) decreased from 136.7 ± 22.2 to 122.5 ± 17.7 mmHg ($p < 0.01$), diastolic blood pressure (DBP) decreased from 82.7 ± 14.3 to 72.5 ± 11.1 mmHg ($p < 0.01$).

After 10 minutes of sedation with propofol patients' HR decreased from 74.1 ± 13.1 to 71.2 ± 10.6 ×/min ($p = 0.15$), SBP decreased from 139.2 ± 19.4 to 128.6 ± 19.5 mmHg ($p < 0.01$), DBP decreased from 84.1 ± 14.6 to 76.0 ± 14.5 mmHg ($p < 0.01$).

Mean haemodynamic values during surgery in dexmedetomidine group: HR 61.7 ± 7.5, SBP 120.7 ± 38.3, DBP 70.3 ± 10.4 and in propofol group: HR 69.4 ± 11.5, SBP 121.6 ± 19.6, DBP 71.8 ± 14.7.

All patients in both groups maintained spontaneous breathing, no patient required bag-mask ventilation. To maintain $SpO_2 > 95\%$ in dexmedetomidine group 48 % patients required $O_2$, no patient required oral airway insertion or jaw thrust; in propofol group 56 % required $O_2$, no patient required oral airway insertion but 20 % required jaw thrust.

Sedation with dexmedetomidine decreased patients' heart rate more than sedation with propofol ($p < 0.01$) but did not require treatment. There was no difference in blood pressure values between both groups.

Patients sedated with dexmedetomidine required achievement of correct airway less frequently than patients sedated with propofol ($p = 0.02$).

*Keywords*: dexmedetomidine, propofol, regional anaesthesia, sedation.

## Introduction

Sedation is widely used during regional anaesthesia in order to reduce patients' stress and discomfort from being awake while lying on the operating table [17]. During sedation in patients undergoing regional anaesthesia, it is important to keep a patient drowsy, light or moderate sedated to maintain spontaneous breathing, which is a hard task.

The latest sedative in clinical practice is dexmedetomidine [12, 19, 23, 33] it is highly selective $\alpha_2$ receptor agonist with sedative, anxiolytic and analgesic effect. Dose dependent bradycardia and hypotension are the most frequently reported adverse effects of dexmedetomidine sedation [10, 11, 20, 22, 24, 27] but without respiratory depression [2, 15, 19, 24, 25, 28].

## Aim

The aim of this study was to compare sedation with dexmedetomidine vs. sedation with propofol in patients undergoing hand surgery under regional anaesthesia. We evaluated influence of two different methods of sedation on respiratory function, haemodynamics and registered side effects.

## Material and Methods

In a prospective cohort study 50 patients ASA I–II over the age of 18 undergoing brachial plexus block for hand surgery were randomly allocated in 2 groups of 25 patients to receive sedation with dexmedetomidine or propofol. The study was approved by Rīga Stradiņš University ethical committee on 26.02.2015 and Riga Eastern Clinical University Hospital ethical committee on 02.02.2015. All patients provided a written consent to participate.

The exclusion criteria we used were patients with cardiovascular diseases, liver failure, pregnancy, sleep or mental disorders.

**Anaesthesia methods.** All patients in both groups received premedication with midazolam 7.5 mg before surgery. For brachial plexus blockade 20 ml 0.5 % bupivacaine and 20 ml 1 % lidocaine were used for hand reconstructive surgeries without exceeding the maximum recommended doses of local anaesthetics.

**Sedation method with dexmedetomidine.** A loading dose of 1μg/kg over 10 min, followed by infusion of 0.1–0.6 μg/kg/h, controlled by Narcotrend electroencephalogram (EEG) index of 50–70.

**Sedation method with propofol.** Target Controlled Infusion (TCI), using *Schnider* Effect Site pharmacokinetic model with initially set dose of 2.5 μg/ml adjusted during surgery (1–4 μg/ml) controlled by Narcotrend EEG index of 50–70. TCI is a computer-driven system that manages infusion according to on-previous studies based pharmacokinetic model [4, 6].

**Monitoring.** Standard monitoring was used during sedation: heart rate (HR), non-invasive systolic (SBP) and diastolic (DBP) blood pressure, respiratory rate (RR), peripheral oxygen saturation ($SpO_2$). Bradycardia was defined as HR < 50 beats per minute for more than 5 minutes. Respiratory depression was defined as RR < 12 breaths per minute or $SpO_2$ < 90 %. For patients with decreased $SpO_2$ we used airway obstruction management algorithm (Figure 1) [8].

Electroencephalogram monitoring using Narcotrend EEG monitor was performed for all patients in both groups during sedation. The monitor recorded patients' hypnotic status and the depth of sedation, and classified EEG stages on a scale from A to F (Table 1), referring to a range of EEG indexes [5, 18].

Level of sedation was measured by Richmond Agitation Sedation Scale (RASS) (Table 2) [26] before sedation, after first 10 minutes of sedation and every 10 minutes until the end of surgery. The optimal sedation level was considered RASS −2 or −3 [26, 29].

Patients' satisfaction with the received sedation and recovery was evaluated from handed out questionnaires an hour after the end of surgery.

Data statistical analysis was performed using IBM SPSS Statistics and Microsoft Excel. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to determine normality of distribution. To evaluate data Student's T test, Chi-Square test and Mann–Whitney test were used.

*Figure 1.* Management of airway obstruction for sedation

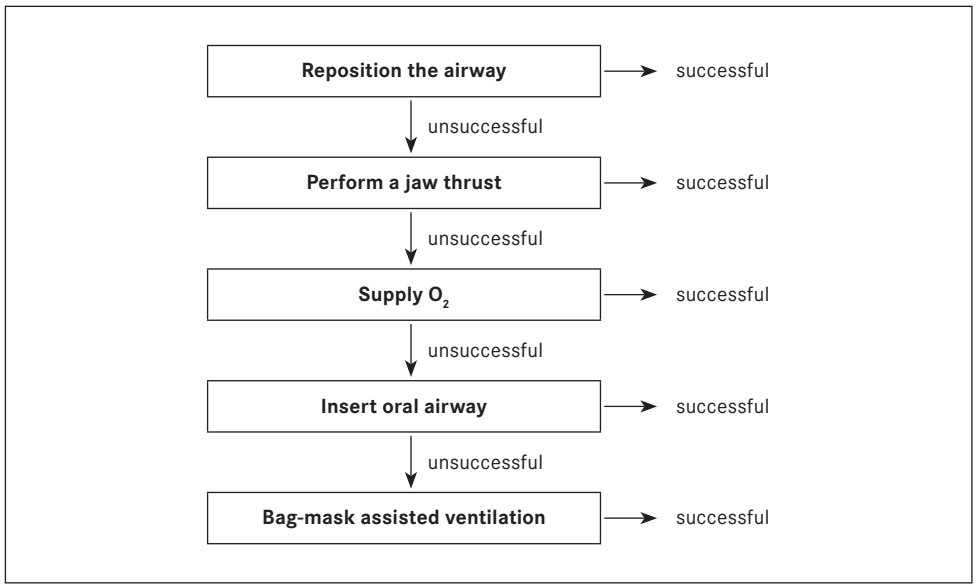



*Table 1.* Narcotrend EEG index and stages

| EEG index | EEG stage | Clinical condition |
|---|---|---|
| 95–100 | A | Awake |
| 80–94 | B | Sedated |
| 65–79 | C | Light anaesthesia |
| 37–64 | D | General anaesthesia |
| 13–36 | E | General anaesthesia with deep hypnosis |
| 0–12 | F | General anaesthesia with increasing burst suppression |

*Table 2.* Richmond Agitation Sedation Scale

| | | |
|---|---|---|
| **+4** | **Combative** | Overtly combative or violent, immediate danger to staff |
| **+3** | **Very agitated** | Pulls on or removes tubes or catheters or has aggressive behaviour towards staff |
| **+2** | **Agitated** | Frequent no purposeful movements |
| **+1** | **Restless** | Anxious or apprehensive but movements not aggressive or vigorous |
| **0** | **Alert and calm** | – |
| **–1** | **Drowsy** | Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact/eye opening to voice |
| **–2** | **Light sedation** | Briefly (less than 10 seconds) awakens with eye contact to voice |
| **–3** | **Moderate sedation** | Any movement (but no eye contact) to voice |
| **–4** | **Deep sedation** | No response to voice, but any movement to physical stimulation |
| **–5** | **Unarousable** | No response to voice or physical stimulation |

## Results

There was no significant difference in demographic and surgical characteristics between patients in both groups (Table 3).

After 10 min of sedation with dexmedetomidine patients' mean HR decreased from 74.9 ± 10.0 to 62.8 ± 7.9 ×/min (−16.2 %, $p < 0.01$), during surgery in patients sedated with dexmedetomidine mean HR value was 61.7 ± 7.5 ×/min (Table 4).

After 10 min of sedation with propofol patients' HR decreased from 74.1 ± 13.1 to 71.2 ± 10.6 ×/min (−3.9 %, $p = 0.15$), during surgery in patients sedated with propofol mean HR value was 69.4 ± 11.5 ×/min (Table 4).

No patient sedated with either dexmedetomidine or propofol had HR below 50 ×/min (Figure 2).

*Table 3.* Demographic data and surgical characteristics

| Valuable | Dexmedetomidine group | Propofol group | p value* |
|---|---|---|---|
| Gender – Female : male, n (%) | 9 (36%) : 16 (64%) | 10 (40%) : 15 (60%) | 0.77 |
| Mean age, years | 46.6 ± 15 | 52 ± 15 | 0.59 |
| Mean body mass, kg | 76.0 ± 15.4 | 74.5 ± 12.8 | 0.71 |
| Body mass index, kg/m$^2$ | 25 ± 4.3 | 25.1 ± 4.6 | 0.94 |
| Type of surgery – elective : acute | 22 (88%) : 3 (12%) | 19 (76%) : 6 (24%) | 0.27 |
| Mean duration of surgery, min | 81 ± 57.8 | 64 ± 33.4 | 0.21 |

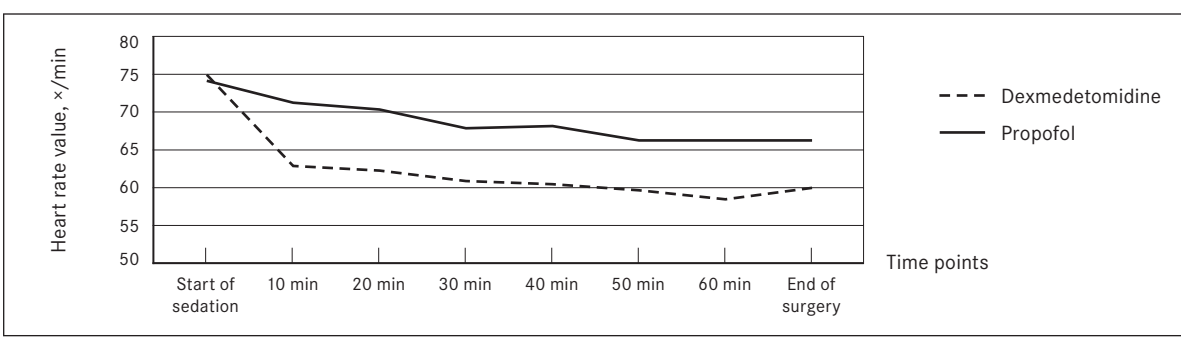
* p – significance of difference between both groups.

*Table 4.* Changes in HR during sedation

| Dexmedetomidine | n | SM | SD | Propofol | n | SM | SD | SM difference | p value |
|---|---|---|---|---|---|---|---|---|---|
| Start of sedation | 25 | 74.9 | 10.0 | Start of sedation | 25 | 74.1 | 13.1 | 0.8 | 0.81 |
| 10 min | 25 | 62.8 | 7.9 | 10 min | 25 | 71.2 | 10.6 | −8.4 | 0.00 |
| 20 min | 25 | 62.2 | 7.7 | 20 min | 25 | 70.3 | 13.0 | −8.1 | 0.01 |
| 30 min | 25 | 60.8 | 6.8 | 30 min | 23 | 67.8 | 12.0 | −6.9 | 0.02 |
| 40 min | 23 | 60.4 | 7.2 | 40 min | 22 | 68.1 | 10.6 | −7.7 | 0.01 |
| 50 min | 19 | 59.6 | 6.0 | 50 min | 17 | 66.2 | 11.8 | −6.7 | 0.04 |
| 60 min | 15 | 58.4 | 5.9 | 60 min | 12 | 66.2 | 11.1 | −7.8 | 0.04 |
| End of surgery | 25 | 59.9 | 6.7 | End of surgery | 25 | 66.2 | 10.2 | 6.2 | 0.04 |
| Mean value | 25 | 61.7 | 7.5 | Mean value | 25 | 69.4 | 11.5 | −7.5 | 0.01 |

n – number of patients; SM – statistic mean; SD – standard deviation.

*Figure 2.* Heart rate values



After 10 min of sedation with dexmedetomidine patients' mean SBP decreased from 136.7 ± 22.2 to 122.5 ± 17.7 mmHg (−10.4 %, $p < 0.01$), mean DBP decreased from 82.7 ± 14.3 to 72.5 ± 11.1 mmHg (−12.3 %, $p < 0.01$). During surgery in patients sedated with dexmedetomidine mean SBP value was 120.6 ± 38.3 mmHg (Table 5), and mean DBP value was 70.3 ± 10.4 (Table 6).

After 10 min of sedation with propofol patients' mean SBP decreased from 139.2 ± 19.4 to 128.6 ± 19.5 mmHg (−8.6 %, $p < 0.01$), mean DBP decreased from 84.1 ± 14.6 to 76.0 ± 14.5 mmHg (−9.6 %, $p < 0.01$). During surgery in patients sedated with propofol mean SBP value was 121.6 ± 19.6 mmHg (Table 5), and mean DBP value was 71.8 ± 14.7 (Table 6).

There was no significant difference between SBP (Table 5, Figure 3) and DBP (Table 6, Figure 4) values in patients sedated with dexmedetomidine and patients sedated with propofol.

*Table 5.* Changes in SBP during sedation

| Dexmedetomidine | n | SM | SD | Propofol | n | SM | SD | SM difference | p value |
|---|---|---|---|---|---|---|---|---|---|
| Start of sedation | 25 | 136.7 | 22.2 | Start of sedation | 25 | 139.2 | 19.4 | −2.5 | 0.67 |
| 10 min | 25 | 122.5 | 17.7 | 10 min | 25 | 128.6 | 19.5 | −6.2 | 0.25 |
| 20 min | 25 | 114.4 | 14.3 | 20 min | 25 | 121.4 | 18.5 | −7.0 | 0.14 |
| 30 min | 25 | 112.9 | 13.1 | 30 min | 23 | 116.0 | 16.3 | −3.0 | 0.48 |
| 40 min | 23 | 111.0 | 11.0 | 40 min | 22 | 113.7 | 15.1 | −2.7 | 0.49 |
| 50 min | 19 | 109.4 | 10.5 | 50 min | 17 | 113.4 | 14.8 | 4.0 | 0.28 |
| 60 min | 15 | 115.7 | 12.8 | 60 min | 12 | 112.5 | 9.1 | −3.2 | 0.58 |
| End of surgery | 25 | 122.5 | 17.7 | End of surgery | 25 | 118.2 | 16.6 | 3.8 | 0.34 |
| Mean value | 25 | 120.6 | 38.3 | Mean value | 25 | 121.6 | 19.6 | −1.0 | 0.79 |

n – number of patients; SM – statistic mean; SD – standard deviation.

*Figure 3.* Systolic blood pressure values

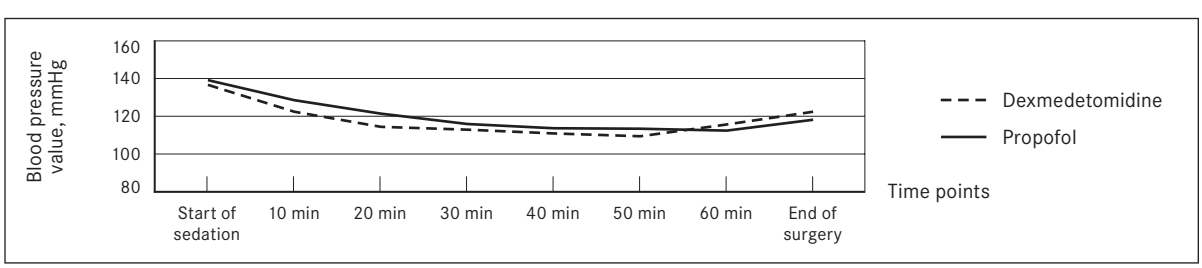
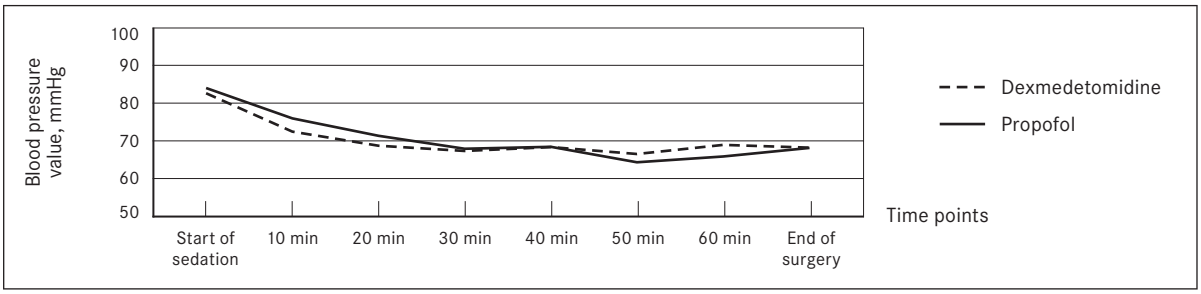



*Table 6.* Changes in DBP during sedation

| Dexmedetomidine | n | SM | SD | Propofol | n | SM | SD | SM difference | p value |
|---|---|---|---|---|---|---|---|---|---|
| Start of sedation | 25 | 82.7 | 14.3 | Start of sedation | 25 | 84.1 | 14.6 | −1.4 | 0.73 |
| 10 min | 25 | 72.5 | 11.1 | 10 min | 25 | 76.0 | 14.5 | −3.5 | 0.34 |
| 20 min | 25 | 68.8 | 10.5 | 20 min | 25 | 71.4 | 14.0 | −2.7 | 0.45 |
| 30 min | 25 | 67.4 | 9.0 | 30 min | 23 | 68.0 | 13.6 | −0.7 | 0.84 |
| 40 min | 23 | 68.4 | 8.7 | 40 min | 22 | 68.5 | 12.2 | −0.1 | 0.97 |
| 50 min | 19 | 66.6 | 7.4 | 50 min | 17 | 64.4 | 10.2 | 2.2 | 0.46 |
| 60 min | 15 | 69.0 | 7.6 | 60 min | 12 | 65.9 | 9.4 | 3.1 | 0.35 |
| End of surgery | 25 | 68.3 | 7.8 | End of surgery | 25 | 68.2 | 13.5 | 0.1 | 0.97 |
| Mean value | 25 | 70.3 | 10.4 | Mean value | 25 | 71.8 | 14.7 | −1.5 | 0.35 |

n – number of patients; SM – statistic mean; SD – standard deviation.

*Figure 4.* Diastolic blood pressure values




In patients sedated with dexmedetomidine mean RR values were similar at the start of sedation (14.8 ± 1.2 ×/min) and after 10 minutes of sedation (14.6 ± 1.4 ×/min) (Table 7).

After 10 minutes of sedation with propofol, patients' RR decreased from 16.0 ± 2.2 to 14.5 ± 1.7 ×/min (−9.4 %, $p < 0.01$), during surgery in patients sedated with propofol mean RR value was 14.6 ± 1.8 ×/min (Table 7).

There was no significant difference between RR values in patients sedated with dexmedetomidine and patients sedated with propofol (Table 7, Figure 5).

All patients in both groups maintained spontaneous breathing; no patient required bag-mask ventilation.

To maintain $SpO_2 > 95$ % in dexmedetomidine group, 48 % patients required $O_2$ supply; no patient required oral airway insertion or jaw thrust; in propofol group 56 % required $O_2$ supply; no patient required oral airway insertion, but 20 % required jaw thrust (Figure 6).

*Table 7.* Changes in RR during sedation

| Dexmedetomidine | n | SM | SD | Propofol | n | SM | SD | SM difference | p value |
|---|---|---|---|---|---|---|---|---|---|
| Start of sedation | 25 | 14.8 | 1.2 | Start of sedation | 25 | 16.0 | 2.2 | −1.20 | 0.02 |
| 10 min | 25 | 14.6 | 1.4 | 10 min | 25 | 14.5 | 1.7 | 0.12 | 0.79 |
| 20 min | 25 | 14.0 | 1.3 | 20 min | 25 | 14.5 | 1.7 | −0.48 | 0.25 |
| 30 min | 25 | 14.0 | 1.4 | 30 min | 23 | 14.6 | 1.8 | −0.56 | 0.21 |
| 40 min | 23 | 14.2 | 1.3 | 40 min | 22 | 14.7 | 1.8 | −0.41 | 0.36 |
| 50 min | 19 | 14.1 | 1.1 | 50 min | 17 | 14.3 | 1.5 | −0.14 | 0.58 |
| 60 min | 15 | 14.0 | 1.6 | 60 min | 12 | 15.0 | 2.1 | −1.00 | 0.22 |
| End of surgery | 25 | 14.1 | 1.4 | End of surgery | 25 | 14.8 | 2.7 | −0.62 | 0.86 |
| Mean value | 25 | 14.2 | 1.3 | Mean value | 25 | 14.6 | 1.8 | −0.40 | 0.40 |

n – number of patients; SM – statistic mean; SD – standard deviation.

*Figure 5.* Respiratory rate during sedation

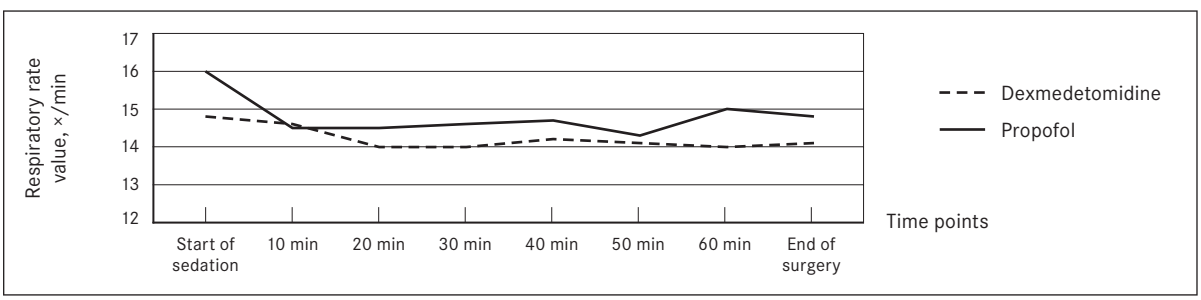
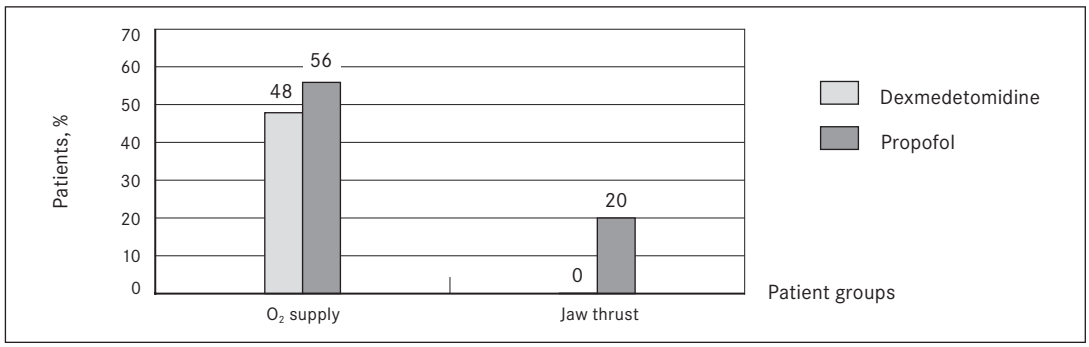


*Figure 6.* Actions required to maintain $SpO_2$ > 95 %




Patients sedated with dexmedetomidine required achievement of correct airway less frequently than patients sedated with propofol, (0 % vs. 20 %, p = 0.02).

After 10 minutes of sedation with dexmedetomidine patients' mean Narcotrend EEG Index (NI) decreased to 79.3 ± 22.4 (–20.7 %, p < 0.01), during surgery in patients sedated with dexmedetomidine mean NI value was 63.8 ± 26.3 (Table 8).

After 10 minutes of sedation with propofol patients' mean NI decreased to 78.5 ± 1.7 (–21.5 %, p < 0.01), during surgery in patients sedated with propofol mean NI value was 61.8 ± 20.2 (Table 8).

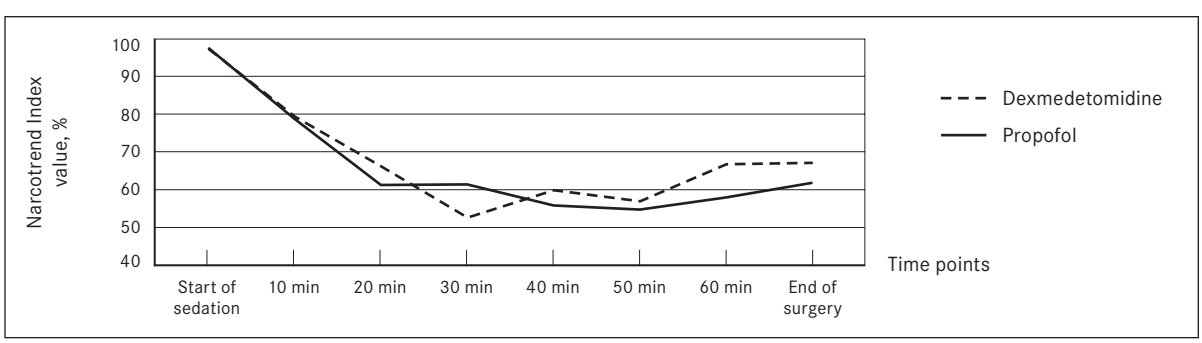
Target depth of sedation of 50–70 NI was achieved within 10 minutes and maintained in both groups (Table 8, Figure 7). There was no significant difference between NI values in patients sedated with dexmedetomidine and patients sedated with propofol within first 50 minutes of sedation.

*Table 8.* NI values during sedation

| Dexmedetomidine | n | SM | SD | Propofol | n | SM | SD | SM difference | p value |
|---|---|---|---|---|---|---|---|---|---|
| Start of sedation | 25 | 97.2 | 2.0 | Start of sedation | 25 | 97.5 | 3.6 | 0.30 | 0.98 |
| 10 min | 25 | 79.3 | 22.4 | 10 min | 25 | 78.7 | 18.8 | –0.60 | 0.56 |
| 20 min | 25 | 66.1 | 25.8 | 20 min | 25 | 61.2 | 19.5 | –4.80 | 0.46 |
| 30 min | 25 | 52.6 | 24.8 | 30 min | 23 | 58.4 | 18.7 | 5.80 | 0.32 |
| 40 min | 23 | 59.8 | 26.4 | 40 min | 22 | 61.4 | 19.4 | 1.60 | 0.80 |
| 50 min | 19 | 56.9 | 26.6 | 50 min | 17 | 55.8 | 18.8 | –1.10 | 0.86 |
| 60 min | 15 | 66.7 | 27.8 | 60 min | 12 | 54.7 | 18.3 | –12.0 | 0.01 |
| End of surgery | 25 | 67.1 | 22.8 | End of surgery | 25 | 57.9 | 18.9 | –9.20 | 0.01 |
| Mean value | 25 | 63.8 | 26.3 | Mean value | 25 | 61.8 | 20.2 | 2.0 | 0.49 |

n – number of patients; SM – statistic mean; SD – standard deviation.

*Figure 7.* Narcotrend Index during sedation



Patients sedated with Dexmedetomidine were arousable by moderate noises in operating room during surgery, they were briefly awakening and falling back asleep without necessity to increase dexmedetomidine dose; but to patients sedated with propofol, Narcotrend Index values were resistant to similar noises during surgery.

According to answers from their questionnaires, all patients in both groups were satisfied with the received sedation.

## Discussion

Different sedatives: midazolam, diazepam, propofol and barbiturates are used for sedation during regional anaesthesia in order to reduce patients' stress and discomfort from being awake while lying on the operating table [17]. During sedation, it is important keep patient sleeping and maintain spontaneous breathing, which is a difficult task. The latest sedative in clinical practice is dexmedetomidine [2, 19, 23, 28]; there are only few reports about dexmedetomidine use during regional anaesthesia.

Literature describes that dexmedetomidine is not associated with significant respiratory depression [3, 14, 31, 32], this is why it has been hypothesised for propofol sedation to be a good alternative to be widely used in clinical practice.

Dose dependent bradycardia and hypotension are the most frequently reported adverse effects of dexmedetomidine [10, 11, 20, 22, 27]. Bradycardia is mainly associated with rapid bolus dose infusion that exceeds 1 μg/kg/h over 10 minutes [22]. Dexmedetomidine causes biphasic blood pressure reaction: short hypertension phase caused by $\alpha_{2B}$ adrenal receptor activation followed by hypotension phase caused by $\alpha_{2A}$ adrenal receptor activation [19, 32].

There are different methods described of dexmedetomidine administration for sedation. All of these methods start with bolus dose over 10 minutes, to avoid bradycardia that is associated with rapid infusion of dexmedetomidine.

Arain S. R. and Ebert T. J. described dexmedetomidine bolus dose of 1 μg/kg over 10 minutes followed by infusion of 0.4–0.7 μg/kg/h, as safe and sufficient for sedation [2]. Kilic N. et al. used dexmedetomidine bolus dose of 1 μg/kg over 10 minutes followed by infusion of 0.5–0.7 μg/kg/h providing adequate sedation and suggested dexmedetomidine as a better alternative to midazolam. [21]. In the current, study sedation with either dexmedetomidine or propofol did not cause treatment requiring bradycardia. There were two patients that had a brief heart rate decrease below 50 beats per minute (not < 45 ×/min). Those were young patients without existing cardiac co morbidities. Heart rate decreases were self-limited – did not exceed 5 minutes and did not require treatment with atropine.

Some authors describe dexmedetomidine as a useful sedative because of its minimal respiratory depression [7, 9]. Belleville J. P. et al. reported a study of respiratory effects of four different doses over two-minute infusion; results showed that exceeding the maximum dose of 2.0 μg/kg irregular breathing with periods of apnoea were noticed but there was no significant arterial oxygen desaturation below 90 % [30].

In our study, the depth of sedation was controlled by Narcotrend EEG monitor, maintaining target level of Narcotrend index of 50–70 and Richmond agitation sedation scale level of −2 to −3. Although interpretation of assessment scales are subjective, and cannot be used in real time, authors describe them as an effective addition to neuromonitoring [24]. Narcotrend EEG monitoring was described effective to provide more accurate sedative dose adjustment [18].

Propofol sedation method was a target controlled infusion, which is described as superior to intermittent bolus dose infusion [16] and manual infusion [1, 16] because of its precision and safety. The most commonly used pharmacokinetic models at the moment are Marsch's and Schnider's effect site. Marsch's model infuses significantly bigger bolus dose to achieve required target concentration, which makes Schnider's effect site model to be safer especially in old patient population and for patients with impaired respiratory functions with increased risks of hypoxemia [4, 13]. We used Schnider's effect site pharmacokinetic model because it is newer, uses more patient related variables, e.g. age, allometric body mass, lean body mass and height, and provides smoother bolus dose infusion.

Patients sedated with dexmedetomidine were arousable by moderate noises in operating room during surgery, they were briefly awakening and falling back asleep without nesissity to increase dexmedetomidine dose; but to patients sedated with propofol, Narcotrend Index values were resistant to similar noises during surgery. It is described that patients sedated with dexmedetomidine are easily arousable without suppression in cognitive or motor functions [21], and results of our study confirmed this effect.

## Conclusions

1. Sedation with dexmedetomidine in patients undergoing hand surgery under regional anaesthesia decreased patients' heart rate significantly more than sedation with propofol ($p < 0.01$); however, there was no observed incidence of bradycardia or hypotension that required treatment.
2. Patients sedated with dexmedetomidine required achievement of correct airway less frequently than patients sedated with propofol ($p = 0.02$).
3. Sedation with dexmedetomidine using a loading dose 1 μg/kg over 10 minutes followed by infusion 0.1–0.6 μg/kg/h during brachial plexus block for patients undergoing hand surgery is effective and safe method allowing to keep adequate haemodynamics and spontaneous breathing.

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# Changes of Regional Cerebral Oxygen Saturation Using Near Infrared Spectroscopy during Neurosurgical Spine Operations in Prone Position

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## Abstract

Near infrared spectroscopy (NIRS) used to maintain cerebral oxygenation during surgery prevents complications such as cognitive dysfunction, organ failure improving postoperative outcome.

The aim of the study was to determine whether prone position during neurosurgical spine surgery using NIRS devices intraoperatively impacts cerebral oxygen saturation.

Fifteen patients undergoing spinal surgery were included in the study. Regional cerebral oxygen saturation ($rScO_2$) was monitored intraoperatively using INVOS 4100. Postoperative complications and days spent in intensive care unit (ICU) were monitored.

Results showed medium $rScO_2$ lying supine left side (L) 72.39 %, right side (R) 72.49 %, in prone position L 74.73 %, R 74.01 %, returning on spine L 74.11 %, R 73.15 %. Seven out of fifteen patients showed a slight up to significant $rScO_2$ decrease when turned from supine to prone position. There was no incidence of postoperative complications, no patients were admitted to ICU.

Patients in prone position intraoperatively experience decrease in cerebral oxygen saturation. Regional cerebral oxygen saturation is a valuable intraoperative measurement in patients undergoing neurosurgical spine operations in prone position to manage perioperative period.

*Keywords*: regional cerebral oxygenation, prone position, spine surgery.

## Introduction

Human brain is a very complex and fragile system. It receives about 15 % of cardiac output, consumes approximately 20 % of all oxygen having the highest metabolic rate of any organ system. Brain is highly vulnerable to desaturation. It consumes oxygen reserves in about 8–10 seconds. Cerebral hypoxia is a leading cause of adverse cerebral outcomes as well as the duration of hypoxia has a direct impact on brain survivability, activity and function. It has been proven that up to 53 % of CABG patients have such complications related to cerebral hypoxia as focal injury, stupor, coma, decrease of intellectual function, seizures, memory deficit, disorientation and death. Cerebral oxygenation cannot be detected by common monitoring devices or can only be detected after damage has already occurred.

Cerebral oximetry is a simple, non-invasive, continuous measurement which gives the ability to monitor regional cerebral oxygen saturation as well as to predict low cardiac output, being an early warning of problems developing in other organ systems. Monitoring standards set by the Association

of Anaesthetists of Great Britain and Ireland are: electrocardiography (ECG), pulse oximetry, end tidal carbon dioxide and non-invasive blood pressure; yet, they give little indication of the adequacy of oxygen delivery ($DO_2$) to the patient during surgery (Bidd, 2013). Systemic arterial and (mixed/central) venous oxygenation can be measured routinely with widely established techniques like pulse oximetry, blood gas analysis, and venous finer oximetry (e.g., in pulmonary artery catheters). However, regional measurement of tissue oxygenation was not possible on a routine clinical basis until recently. Traditionally, tissue oxygenation has been measured by experimental tools that were either invasive (e.g., Clark-type needle electrodes) or dependent on toxic dyes (e.g., palladium phosphorescence), restricting their clinical use (Scheeren, 2012).

Normal values of cerebral oximetry are between 60 % and 80 % or has been kept 20–25 % below the baseline as preoperative readings may differ from patient to patient. Unlike pulse oximetry which is based on light loss due to pulsation of arterial blood, cerebral oximetry bases on light loss due to entire non-pulsative field consisting of approximately 30 % arterial and 70 % venous blood.

The first publications about cerebral oximetry were dated about 30 years ago, but it has gained its importance as an additional monitoring technique in operating rooms and intensive care units only recently. Mostly used in cardiac surgery and for severe head injury monitoring due to high risk for cerebral desaturation because of changes in cerebral blood perfusion and association with such postoperative complications like cognitive dysfunction, stroke, seizures and even death. Lately it has been extensively investigated in association with massive blood loss, surgery in the beach-chair position, surgery in prone position, by head and neck manipulations and one-lung ventilation (Hemmerling, 2008).

Neurosurgical spinal surgery includes one level, to multiple level surgery and patients vary from healthy, stable up to decompensated, hemodynamically unstable and sever trauma patients. Prone position used in spinal surgery leads to physiological changes affecting cerebral blood flow and cerebral oxygenation. The main cause is vena cava inferior and its branches compression causing blood deposition in epidural venous plexus favouring intraoperative blood loss, reducing blood return in the systematic circulation and affecting the cerebral blood flow.

## Aim

The aim of the study was to determine whether prone position during neurosurgical spine surgery using NIRS devices intraoperatively impacts cerebral oxygen saturation.

## Material and Methods

Fifteen patients scheduled for spinal neurosurgery were included in the study. Inclusion criteria: age > 18 years, spinal surgery performed in prone position (transpedicular fixation (TPF), microdiscectomy (MDE), removal of spinal tumours); exclusion criteria: spinal surgery not performed in prone position. Cerebral oxygen saturation ($rScO_2$) was continuously monitored using INVOS 4100 (COVIDIEN, USA) near infrared spectroscopy oximeter intraoperatively. Non-invasive blood pressure (NIBP), heart rate (HR), end tidal carbon dioxide tension ($EtCO_2$), and peripheral oxygen saturation ($SpO_2$) were also monitored. All the data was fixed every five minutes. We observed cognitive dysfunction, the rate of postoperative complications – stroke, organ dysfunction, wound infection, days spent in ICU.

All patients received standard anaesthesia. Induction with fentanyl 0.1–0.2 mg, propofol 1–2 mg/kg, miorelaxation with cisatracurium 0.2 mg/kg. For maintenance, there was used fentanyl 0.03–0.06 μg/kg/min, cisatracurium 0.06–0.1 mg/kg/h. During maintenance of anaesthesia sevoflurane was used to achieve MAC 0.7–1.0. Mechanical lung ventilation with inspired oxygen concentration $FiO_2$ 0.5. Two INVOS Cerebral/Somatic Oximetry Adult cerebral oximetry sensors were placed on a patient's forehead before induction of anaesthesia. After operation all the patients were extubated in operating room.

Statistical analysis was performed using the IBM SPSS Statistics.

The study was performed with the approval of Rīga Stradiņš University ethics committee (Nr. 61/28.01.2016).

## Results

Fifteen patients (men – 9, woman – 6, mean age – 60 years) were enrolled in the study. Results showed the average regional cerebral oxygen saturation during operation for the left side (L) 79.9 %, the right side (R) 79.52 %. Lying supine before intubation L 72.39 %, R 72.49 %, in prone position L 74.73 %, R 74.01 %, returning back to spinal position L 74.11 %, R 73.15 %. Significant changes in the calculated average $rScO_2$ values between supine and prone position were not observed (Table 1). Despite the calculated average $rScO_2$ values, seven out of fifteen patients showed a slight up to significant decrease in $rScO_2$ when turned from supine to prone position (Table 2). The minimum $rScO_2$ value observed during the whole surgery was 55 % (Table 3). One patient's $rScO_2$ values decreased by 32 % from baseline values when turned to prone position (from 85.5 % supine to 58.5 % in prone position). One patient with stroke in anamnesis showed initial values lying supine 21 % lower than average (57.5 % compared to average $rScO_2$ lying supine 72 %). No cognitive dysfunction, no incidence of stroke or organ dysfunction was observed, no patients were admitted to ICU.

*Table 1.* Patient details

| Patient, No | Age/Sex | Surgery | Blood loss, ml | Mean $rScO_2$, % | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Supine 1 | | Prone position | | Supine 2 | |
| | | | | Right side | Left side | Right side | Left side | Right side | Left side |
| 1 | 62/M | TPF | 200 | 72 | 71 | 69 | 65 | 69 | 72 |
| 2 | 52/M | TPF | 200 | 85 | 85 | 80 | 80 | 89 | 89 |
| 3 | 60/M | TPF | 150 | 57 | 58 | 70 | 71 | 69 | 70 |
| 4 | 48/M | TPF | 150 | 72 | 78 | 91 | 94 | 85 | 87 |
| 5 | 27/M | MDE | 100 | 86 | 87 | 92 | 92 | 86 | 85 |
| 6 | 59/M | TPF | 300 | 61 | 61 | 75 | 78 | 64 | 66 |
| 7 | 72/M | MDE | 150 | 69 | 69 | 77 | 80 | 69 | 69 |
| 8 | 78/M | MDE | 150 | 69 | 69 | 64 | 64 | 74 | 74 |
| 9 | 72/F | MDE | 150 | 74 | 74 | 69 | 68 | 64 | 65 |
| 10 | 82/F | TPF | 500 | 70 | 70 | 73 | 73 | 70 | 70 |
| 11 | 74/M | TPF | 2000 | 85 | 86 | 56 | 61 | 71 | 70 |
| 12 | 49/F | MDE | 150 | 59 | 55 | 59 | 58 | 60 | 65 |
| 13 | 54/F | TPF | 700 | 62 | 62 | 85 | 84 | 74 | 76 |
| 14 | 37/F | MDE | 150 | 89 | 89 | 83 | 83 | 83 | 83 |
| 15 | 84/F | Th1 meningioma | 150 | 75 | 68 | 61 | 63 | 66 | 66 |
| Average $rScO_2$ (%) | | | | 72 | 72 | 74 | 74 | 73 | 74 |

M – male; F – female; TPF – transpedicular fixation; MDE – microdiscectomy.
Supine 1 – position on spine before prone position at the beginning of surgery.
Supine 2 – position on spine after prone position at the end of surgery.

*Table 2.* Medium $rScO_2$ (%) in supine and prone position

| Patient, No | Medium $rScO_2$, % | | $rScO_2$ decrease, % |
|---|---|---|---|
| | Supine position | Prone position | |
| 1 | 71.75 | 67.44 | 4.31 |
| 2 | 85.00 | 80.83 | 4.17 |
| 3 | 69.00 | 64.71 | 4.29 |
| 4 | 74.00 | 69.13 | 4.88 |
| 5 | 85.50 | 58.93 | 26.57 |
| 6 | 89.50 | 83.00 | 6.50 |
| 7 | 72.00 | 62.58 | 9.42 |

*Table 3.* Descriptive $rScO_2$ (%) values for each patient during surgery

| Patient, No | Mean $rScO_2$ value, % | Std. Deviation | 95 % Confidence Interval for mean | | Minimum $rScO_2$ value, % | Maximum $rScO_2$ value, % |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| 1 | 69.75 | 2.72 | 66.90 | 72.60 | 65.00 | 72.00 |
| 2 | 85.05 | 3.80 | 81.07 | 89.04 | 80.80 | 89.33 |
| 3 | 65.98 | 6.62 | 59.03 | 72.94 | 57.00 | 71.40 |
| 4 | 84.81 | 8.28 | 76.11 | 93.50 | 72.00 | 94.00 |
| 5 | 88.40 | 3.08 | 85.17 | 91.63 | 85.80 | 92.38 |
| 6 | 67.32 | 6.97 | 60.01 | 74.64 | 61.00 | 78.47 |
| 7 | 72.42 | 5.03 | 67.13 | 77.70 | 69.00 | 80.50 |
| 8 | 69.24 | 4.16 | 64.87 | 73.60 | 64.71 | 74.00 |
| 9 | 69.43 | 3.99 | 65.23 | 73.62 | 64.50 | 74.00 |
| 10 | 71.65 | 1.45 | 70.13 | 73.18 | 70.67 | 73.69 |
| 11 | 71.65 | 12.01 | 59.04 | 84.25 | 56.67 | 86.00 |
| 12 | 59.37 | 3.26 | 55.94 | 62.79 | 55.00 | 65.00 |
| 13 | 74.32 | 10.11 | 63.71 | 84.93 | 62.50 | 85.07 |
| 14 | 85.17 | 3.36 | 81.64 | 88.69 | 83.00 | 89.50 |
| 15 | 67.03 | 4.75 | 62.04 | 72.01 | 61.58 | 75.25 |
| Total | 73.44 | 9.94 | 71.36 | 75.52 | 55.00 | 94.00 |

## Discussion

Non-invasive cerebral oxygenation monitoring has lately gained its importance and topicality in different medical fields. Being non-invasive, it offers a possibility to use it intraoperatively as an extra monitoring device and enhances patient safety and improves surgical outcome by reducing postoperative complication rate.

According to literature, no significant changes in $rScO_2$ were observed during prone position intraoperatively which also correlates with our first 15 patients' data (Fuchs, 2000). Deiner et al. in their study showed that mild cerebral desaturation episodes were 2.3 times more frequent for elderly patients (> 68 years of age) undergoing surgery in prone position vs. supine (Deiner, 2014). In our study patients' mean age was 60 years and our average values did not show $rScO_2$ decrease when patients were turned from supine to prone position although 7 out of 15 patients $rScO_2$ medium values decreased while being in prone position.

There are studies performed regarding the monitoring of brain saturation and the interventions to restore its proper values to improve treatment outcomes, particularly in regard to the incidence of neurological complications and postoperative cognitive dysfunction as well as the intraoperative reduction of brain saturation which correlates with prolonged treatment in ICUs and increased mortality (Biedrzycka, 2016). In our study we did not observe any postoperative complications such as stroke, organ dysfunction or cognitive dysfunction after surgery which also correlates with the fact that no significant intraoperative $rScO_2$ decrease was observed.

A systematic review was undertaken to determine whether spinal surgery in prone position impacts cerebral oxygenation. Relevant publications were found using PubMed database. Search strategy included MeSH terms: (Spectroscopy) OR (Monitoring/Intraoperative) OR (Spine) OR (Prone position), in total 309 articles were found (published between 2000 and 2014). Only 3 articles met all the criteria ((Spectroscopy) and (Monitoring/Intraoperative) and (Spine) and (Prone position)) showing that cerebral oxygen saturation monitoring during neurosurgical spine surgery in prone position is still an open field for further investigations.

## Conclusion

Although our first experience revealed that the average intraoperative cerebral oxygen saturation changes during neurosurgical spine operations in prone position from baseline values is not significant, 7 out of 15 patients showed a mild to moderate decrease in cerebral oxygen saturation.

Regional cerebral oxygen saturation is a valuable intraoperative measurement in patients undergoing neurosurgical spine operations in prone position to manage perioperative period.

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# Dynamics of Bone Marrow Cellularity in Paediatric B-cell Acute Lymphoblastic Leukaemia Measured by Automated Haematology Testing

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## Abstract

Bone marrow cellularity (BMC) or total content of nucleated cells in bone marrow (BM) is one of essential features of haemopoesis. The routine method for BMC assessment is subjective and poorly reproducible evaluation of cytological samples by microscopy. Haematological analysers could provide an objective alternative, but no results of cohort-based automated BM testing have been published.

B-cell acute lymphoblastic leukaemia (B-ALL) may be a suitable model for dynamic changes of paediatric BMC: it is the most common childhood tumour and majority of patients are treated by standardised regimen with BM examination at defined time points. The aim of the study was to use routine automated haematology for assessing BMC dynamics in paediatric B-ALL in comparison to reactive benign samples.

46 primary B-ALL cases treated by standard/median risk BFM protocol in 2011–2015 at Children's Clinical University Hospital were analysed. BM samples had been routinely tested by microscopy and by haematological analysers Advia 2120i and Sysmex XN 1000. Overall, 208 representative analyses were available: 38 at diagnosis, 46 at treatment day 15, 45 at day 33, 40 at day 78 and 39 before reinduction. In addition, 37 non-neoplastic BM samples with BMC microscopically evaluated as "normal" were used for reference (median BMC 54.8 × $10^9$/L, range 31.5–73.1 × $10^9$/L, normal distribution of values).

Median BMC at diagnosis was 74.1 × $10^9$/L (significantly above normal, $p = 0.01$), at day 15 – 8.5 × $10^9$/L and at day 33 – 11.7 × $10^9$/L (both below normal, $p < 0.001$ and $p = 0.001$, respectively), at day 78 – 61.1 × $10^9$/L and before reinduction – 60.4 × $10^9$/L (both slightly above normal). BMC drop from diagnosis to day 15 was significant ($p < 0.001$); likewise, the increase from day 15 to day 33 ($p = 0.01$) and from day 33 to day 78 ($p < 0.001$).

The study demonstrated the validity of automated BMC testing and possible use of samples with cytologically normal BMC for reference. Potential limitations of the approach are further discussed.

*Keywords*: bone marrow cellularity, automatic haematology, paediatric acute lymphoblastic leukaemia.

## Introduction

After centuries of research, human haemopoesis in bone marrow (BM) is one of the most extensively studied biologic systems (Zon, 1995). Still many questions remain, some of them due to technical reasons and ethical restrictions.

Total content of nucleated cells or bone marrow cellularity (BMC) is an important basic aspect of haemopoesis, closely related to its activation, suppression and infiltration. BMC inclusion in BM analysis report is mandatory. Dynamic changes of BMC, like in myelosuppression and subsequent regeneration, are of particular clinical interest. Routinely, BMC is subjectively assessed by microscopy of histological biopsies (as percentage of BM tissue volume occupied by nucleated cells) or of cytological material (as experience-based assessment of nucleated cells' density on the slide) (Friebert et al., 1998; McKenzie et al., 2010). Besides being highly subjective, this evaluation is prone to technical artefacts of slide preparation.

Using automated haematological analysers for the task looks like a logical way to objectivity and standardisation. As a rule, modern systems have specialised programmes for testing BM, where BMC is reported in the quantitative form of cell count per volume, analogous to leukocyte count in peripheral blood. Tested BM suspension is homogenous and large number of events is recorded during the test, thus avoiding the main pitfalls of microscopy. Still, no comprehensive serial data on the automatically measured BMC have been published.

BMC assessment is even more complicated in paediatric patients. Haemopoesis in childhood differs from adults due to higher demand, high BM reactivity and still unfinished maturation, meaning that reference BMC data and experience obtained from adult patients are not entirely applicable in paediatric practice. Moreover, evaluation of BMC in children faces additional problems due to difficulties in acquiring material (Friebert et al., 1998; Lanzkowsky, 2011; Proytcheva, 2011, 2013).

Finally, since BM studies are performed as a part of diagnostic algorithm for marrow diseases, few samples of "normal" BM are obtained, particularly in children. All these factors make definitions of "normal" and "abnormal" BMC not strictly specified, the clinical demand notwithstanding.

Finding a model for studying treatment-related BMC dynamics presents additional problem, for different disorders and treatment modalities cause dissimilar marrow changes. Moreover, most paediatric disorders that involve haemopoesis are quite rare, so it is difficult to collect a homogenous representative patients' cohort. B-cell acute lymphoblastic leukaemia (B-ALL) is a reasonable solution to both problems. It is the most common paediatric tumour with sufficient number of patients available, and majority of B-ALL patients receive standardised treatment that includes several BM checks at specific time points (Hunger et al., 2015; Lanzkowsky, 2011). Latvian children with B-ALL are treated according to international BFM regimen that for standard and median risk patients requires BM sampled at diagnosis and during intensive chemotherapy on the $15^{th}$, $33^{th}$, $78^{th}$ day of treatment and before M-protocol/reinduction (Möricke et al., 2008). The purpose of these repeated checks is following-up the tumour population for therapy adjustment and evaluating restitution of normal haemopoesis.

According to common cytological experience of B-ALL follow-up, initial high cellularity of blast-infiltrated BM usually drops dramatically at day 15, remains low at day 33 with subsequent regeneration by day 78. Reasonably, the automatically measured BMC should follow the same sequence.

### Aim and Objectives

The aim of the study was to investigate BMC of paediatric B-ALL patients at diagnosis and in follow-up samples by automated haematology assay.

The results were compared to BM samples where cellularity had been cytologically evaluated as "normal" in order to test the validity of the approach and to objectively evaluate dynamics of BMC during treatment.

## Material and Methods

Fourty six paediatric patients (age from 3 months to 17 years) treated for primary standard/median risk B-ALL in 2011–2015 at Children's Clinical University Hospital Haematooncology Department were retrospectively included in the study. BM samples had been routinely analysed in the Hospital Laboratory by microscopy and by haematological analysers Advia 2120i (Siemens AG) in July 2011 – October 2014 and Sysmex XN 1000 (Sysmex Corporation) since November 2014, using manufacturer's settings for BM testing. Anonymised BMC counts and cytology reports were obtained from the Laboratory LIS "Dialab" (Diamedica SIA). 208 representative analyses were available: 38 at diagnosis (peripheral blood had been used as diagnostic material in 8 patients), 46 at day 15, 45 at day 33, 40 at day 78 and 39 before reinduction.

In addition, BMC counts from 37 non-neoplastic BM samples from the same period, where BMC had been microscopically evaluated as "normal" were used for reference.

Microsoft Excel database was created for data collection and basic statistics; IBM SPSS Statistics was used for calculating correlations (Spearman rho test), differences between checkpoints and between checkpoints and "normal" group (Wilcoxon signed rank test) and normality (Kolmogorov–Smirnov test).

## Results

BMC in the "normal" group was normally and uniformly distributed (Kolmogorov–Smirnov test $p = 0.753$ and $p = 0.167$, respectively) with median $54.8 \times 10^9$/L, mean $53.0 \times 10^9$/L and 90 % range $31.5–73.1 \times 10^9$/L.

Most important findings in B-ALL patients have been summarised in Table 1.

BMC at diagnosis was significantly above that in the "normal" group. On commencing chemotherapy, it reached nadir at day 15, remained low at day 33 and then increased during regeneration of haemopoesis at day 78 and before reinduction (Figure 1). The dynamic changes were statistically significant, BMC at therapy day 15 was significantly lower than at diagnosis, at day 33 significantly higher than at day 15, at day 78 highly significantly higher than at day 33; there was no significant difference between day 78 and before M protocol (Table 1).

BMC was significantly higher than in the "normal" group at diagnosis, significantly below "normal" at days 15 and 33 and again reached levels slightly above the "normal" group at day 78 and before reinduction (Table 1).

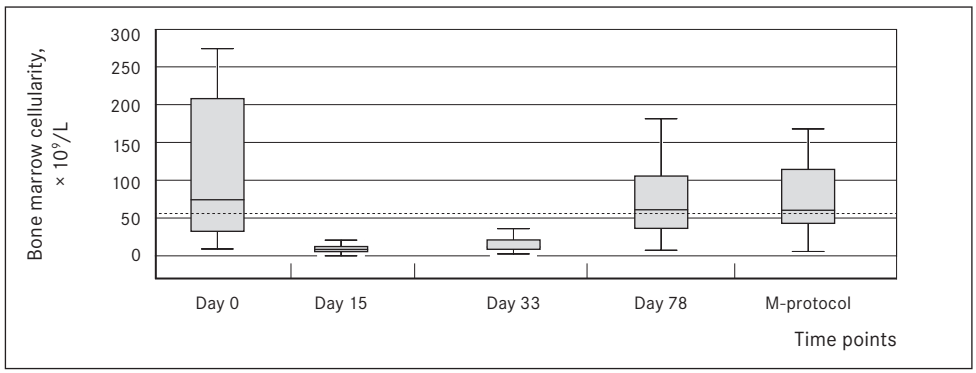
The initial BMC at diagnosis did not correlate with further BMC levels during therapy by Spearman test, the only significant correlation found was between day 15 and day 33 ($p = 0.039$).

*Table 1.* Dynamic changes of BMC during treatment of paediatric ALL

| Time point | Diagnosis | Day 15 | Day 33 | Day 78 | M-protocol |
|---|---|---|---|---|---|
| **Number of cases, n** | 38 | 46 | 45 | 40 | 39 |
| **Median BMC, × $10^9$/L** | 74.1 | 8.5 | 11.7 | 61.1 | 60.4 |
| **Difference with normal group, p* value** | 0.010 | < 0.001 | < 0.001 | NS** | 0.049 |
| **Difference with previous time point, p* value** | – | with diagnosis < 0.001 | with day 15 0.001 | with day 33 < 0.001 | with day 78 NS** |

* p – Wilcoxon signed rank test;
** NS – non-significant.

*Figure 1.* BMC at time points in relation to reference group*




* Boxes show median, 95 % confidence interval and total range in B-ALL patients. Dotted line represents median "normal" BMC.

## Discussion

Reliable assessment of BMC is necessary for diagnostics of BM diseases, as well as for tailoring therapy and performing BM transplantation (Friebert et al., 1998; McKenzie et al., 2010; Proytcheva, 2013). Still, objective evaluation of BMC remains elusive. On the one hand, in case of significantly abnormal samples, it is easily qualitatively assessed by an experienced pathologist on cytology or histology. On the other hand, this evaluation is subjective, poorly reproducible and becomes unreliable in cases of borderline BMC. The classical work of Friebert et al. (1998) that remains the most extensive quantitative study of BMC in children, used optical histometry of trephine biopsies; but paediatric trephines are notorious for being small and prone to crush artefacts, particularly in infants.

The study demonstrated another workable approach. Haematology analysers are particularly effective in counting blood cells, being designed for the purpose. In addition, besides BMC, automated haematology provides additional valuable information on BM, like preliminary assessment of main leukocyte populations, presence of optically abnormal cells, possibility of hemodilution. Actually, the test had been initially introduced at Children's Clinical University Hospital Laboratory with the sole purpose to calculate BMC for optimal dilution of the sample for flow cytometric analysis. It proved useful and was subsequently extended to all BM samples.

The results show that, in the absence of other options, BMC of non-neoplastic patients' cohort evaluated as normal by an experienced cytologist could be tentatively used as reference range. We found normal distribution of BMC values in this group. In addition, there is empirical experience of BFM treatment regimen that BMC should be "about normal" at day 78 and before reinduction (Kushwaha et al., 2014; Möricke et al., 2008), just like in the present study. Still, some caution would be advised. The studied cohort is small and should be expanded to ensure precision. Microscopy was performed by a single cytologist, a panel revision would be advised to minimise subjectivity. Finally, technical considerations should be taken into account. The smear for BM cytology is prepared directly from syringe immediately after aspiration to ensure the best morphology, the rest is mixed with anticoagulant for further analysis; sometimes, additional material is aspirated. Thus, cytological slide and suspension that is tested for BMC are not the same material, in the strict sense. The rather broad range of BMC in the "normal" group may be the result of this discordance.

The use of B-ALL as a model with well-known BMC dynamics demonstrated reliability of automated BM analysis in this setting. BMC of B-ALL patients during treatment follow the empirical experience: high cellularity at diagnosis due to blast infiltration, sharp decrease during initial treatment followed by mild regeneration at day 33, then normal levels at the next two time points (Hunger et al., 2015; Kushwaha et al., 2014; Proytcheva, 2011, 2013). Both hyperplasia at diagnosis and aplasia at day 15 and day 33 statistically significantly differed from the proposed reference cohort. BMC at day 15, day 33

and day 78 was significantly different from their respective previous checkpoints, making the changes sharp and distinctive. A larger patient cohort would be necessary to define reference values of BMC for standard time points. Study prolongation to BM status during later therapy stages and at the end of treatment may be of interest.

Very high variability of BMC at diagnosis, probably due to sampling artefacts, is noteworthy; the notion could be checked by BM histology where available.

## Conclusions

Automatically measured median BMC in samples with microscopically "normal" cellularity was 54.8 × $10^9$/L (90 % range 31.5–73.1 × $10^9$/L). Pending availability of a larger and better-defined pool, the cohort could tentatively serve for reference BMC in children. Moreover, the figure is near to B-ALL BMC at day 78 and before reinduction when (according to cytological experience) BM returns to its normal cellularity. Thus, the use of reactive BM for reference seems to be a workable approach. Additional material and expertise, probably through international cooperation, will be needed to exclude possible artefacts.

Using automated haematology for BMC evaluation in B-ALL patients demonstrated significant and consistent changes, well in accordance with subjective experience. BMC dropped almost 10-fold from high initial cellularity at diagnosis (median 74.1 × $10^9$/L) to the equivalent of cytological aplasia at day 15 (8.5 × $10^9$/L) and deep hypoplasia at day 33 (11.7 × $10^9$/L). Subsequent decrease of therapy intensity resulted in BM regeneration and restitution of BMC to "normal" levels (61.1 × $10^9$/L at day 78 and 60.4 × $10^9$/L before reinduction). Both the sharp drop of BMC and the steeper increase were statistically significant; that provided additional credibility to the model.

The study demonstrated that assessment of BMC by automated haematological analysis is an objective, quantitative, simple, fast and relatively cost-effective alternative to microscopic evaluation. Its limitations are related mostly to BM material acquisition.

The study results are of direct clinical value, being applicable for objective follow-up of patients during leukaemia treatment.

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# Use of Computed Tomography in Orbital Trauma Diagnostic: Literature Review

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## Abstract

Computed tomography (CT) is widely used in orbital trauma visualisation that provides rapid and detailed evaluation of bony structures and soft tissues of the orbit. CT is sensitive in detection of orbital foreign bodies, and often guides clinical and surgical management decisions in orbital trauma (Rehm, 1995). Depending of their location, fractures are classified into two groups: isolated (only one orbital wall is involved) and combined (more than one orbital wall is involved). Clinical and radiological findings play major role in management of orbital trauma.

The aim of this study is to summarise and analyse literature about the use of the CT in orbital structures visualisation, trauma diagnostic and compare CT with other radiological methods.

A literature search was conducted electronically in databases PubMed, EBSCO and manually in RSU scientific resources. The search was limited to articles published in the English and Latvian languages between 1990 and 2016.

In all, 141 articles were found, 44 of which met the aforementioned requirements and thus were included and analysed in the study. 97 scientific papers could not be included in the literature review due to the fact that they were written prior to 1990 or do not meet the aforementioned requirements. This article comprises and analyses materials about computed tomography role in orbital trauma diagnostic and management.

The use of high-resolution multidetector CT has become the gold standard of reference in evaluating patient with orbital trauma. Bony fractures and displacements, small comminuted fragments and radio-opaque foreign body are best seen on CT but vascular and nerve injury, and intracranial hematomas are better evaluated with MRI.

Radiological diagnostics and orbital posttraumatic clinical findings have a key role in orbital fracture diagnosis and trauma management.

*Keywords*: orbital fracture, computed tomography, midface fracture, orbit radiology, maxillofacial radiology.

## Introduction

Facial trauma currently constitutes a social and public health problem of relevance because of its frequency and magnitude as well as for its close association with car accidents and episodes of violence and insecurity (Bord, 2008). Due to anatomical proximity, craniofacial trauma often involves injury to

the eye and orbit. Orbital fractures are consequence of middle third facial trauma and occur as a result of the application of forces that overcome resistance of bone structures forming the orbital cavity (Reyes, 2013). These fractures are very frequently associated with damage to the surrounding soft tissue and they sometimes damage orbital cavity contents or communicate the orbit with adjacent structures (cranial cavity, paranasal sinuses or nasal cavity) (Cruz, 2004).

The bony orbit is a pyramidal-shaped space with a roof, medial wall, floor, and lateral wall (Aaron, 2014). The orbital walls vary considerably in their thickness. Whereas superior lateral and inferior rims tend to be rather thick, bones just posterior to these and medial rim are usually fairly thin (Frenkel, 1990). The orbit is a relatively small and anatomically complex space that contains many critical structures. This can make CT evaluation of orbital-facial injuries challenging.

Computed tomography (CT) is widely used in the initial evaluation of patients with craniomaxillofacial trauma that provides a rapid and detailed evaluation of bony structures and soft tissues of the orbit (Rehm, 1995). Other imaging modalities, such as plain radiography, reconstructed three dimensional CT, magnetic resonance imaging (MRI), ophthalmic ultrasonography, colour Doppler imaging, and angiography may provide necessary additional information in specific conditions but CT scans have become the standard of care in evaluating orbital injuries (Dunkin, 2011). A trauma CT scan series generally involves 10 mm axial cuts of the cranium and 5 mm cuts through the facial region (Miloro, 2004).

Obviously, the role of CT in orbital injuries is very important and injuries imaging is essential for proper diagnosis and treatment of orbital trauma. It is necessary to understand the treatment plan and decide to pursue immediate surgery, delayed surgery, or no operative management.

## Aim

The aim of this study is to summarise and analyse literature about the use of the CT in orbital trauma diagnostic and comparison of CT with others radiological modalities in orbital trauma diagnostics.

## Material and Methods

Literature was selected through search in PubMed (Medline), EBSCO and RSU Library scientific resources. The search was restricted to papers published in English and Latvian, in the period 1990–2016. Keywords used for search were orbital fracture, computed tomography, midface fracture, and orbit radiology. Additionally, a manual search in Latvian and European medical journals was performed. Only articles which met the requirements were included in the review. After selection of the literature, 44 articles were used: 16 controlled studies and 28 literature reviews. Different types of orbital fractures and different radiological diagnostic modalities were market.

## Results

In total, 141 articles were found. 44 met the aforementioned requirements and thus were included and analysed in the study. 97 scientific papers could not be included in the literature review due to the fact that they were written prior to 1990, contained outdated information and descriptions of obsolete methods.

Two major groups were distinguished that include orbital trauma: isolated orbital fracture and combined fractures. Isolated orbital fractures were divided in orbital floor fracture, medial wall fracture and orbital roof fracture. The combined fractures that include orbital cavity walls are zygomaticomaxillary complex fracture (ZMC), Le Fort fractures and nasoorbitoethmoid (NOE) fractures.

All orbital trauma diagnostic methods were discussed (conventional radiography, ultrasound, magnetic resonance imaging and computed tomography). Aforementioned methods were compared with each other.

### Isolated Orbital Fractures

Isolated orbital fractures are less common than combined maxillofacial trauma. In a study carried out in Latvia from 2011 to 2012, 538 patients with maxillofacial trauma were analysed. In 133 cases was diagnosed combined orbital trauma and only 32 patients had isolated orbital wall fractures (Muceniece, 2016).

**Orbital Floor Fracture.** The orbital floor is formed primarily by the orbital process of the maxilla. Anterolaterally it is formed by a portion of the zygomatic bone, and posteriorly by a small portion of the palatine bone (Som, 2003).

Orbital floor injuries may occur in isolation or in conjunction with higher level Le Fort injuries, ZMC and NOE fractures, panfacial trauma. They often occur in combination with fractures of the medial orbital wall (Bell, 2002).

The mechanism of injury typically involves direct anteroposterior blunt trauma to the globe and orbital margins. Proposed mechanisms for this fracture include hydraulic energy and buckling of the floor from impact to the inferior orbital margin (Waterhouse, 1999).

The computed tomography helps to define the displacement degree of the fracture fragment and relative area of the fracture fragment that are important discriminators in predicting the need for surgery (Schouman, 2012).

The optic nerve is the only nerve within the orbit that can be meaningfully and consistently evaluated by CT in trauma. Transverse fracture size and presence of soft tissue herniation on CT imaging can play an important role in predicting persistent diplopia in isolated orbital floor fractures (Linnau, 2003).

**Medial Wall Fracture.** After the orbital floor, the medial wall is the next most commonly fractured orbital wall. Medial wall fractures most commonly occur in association with orbital floor fractures, but can be seen as an isolated fracture (Linnau, 2003).

The medial orbital wall is composed anterior to posterior by a portion of the maxillary, lacrimal, ethmoid and sphenoid bones. Medial wall is formed by the extremely thin 0.2–0.4 mm lamina of the ethmoid bone (Miloro, 2004). Non-displaced fractures of the lamina papyracea or the ethmoid are difficult to visualise and should be considered in the presence of ethmoid air-cell opacification or herniation of orbital fat (Pelton, 1998). Orbital emphysema and diplopia are another indirect indicators of medial wall fracture (Liss, 2010). The radiologist should take an account medial wall's anatomical structures such as medial canthal tendon, lacrimal apparatus, superior oblique muscle, orbital nerves, vessels and origin of the orbital muscles (Cruz, 2004).

**Orbital Roof Fracture.** Orbital roof consists mainly of the frontal bone, with the anterior cranial fossa superior to it. In adults orbital roof fractures are more likely to be associated with complex high energy facial trauma (Aaron, 2014).

Fracture fragments of the orbital roof may be superiorly, inferiorly displaced or non-displaced and often is associated with intracranial complications. Orbital roof fractures may also extend to the orbital rim with or without frontal sinuses involvement. Involvement of the adjacent superior rectus and superior oblique muscles may lead to entrapment and impaired ocular motility (Buitrago-Tellez, 2002). Anterolaterally there is a smooth broad fossa that houses the lacrimal gland. At the most medial extent is the trochlea that has a dual insertion of the superior oblique muscle tendon (Som, 2003).

Any fracture of the orbital roof or lamina papyracea should prompt careful analysis of the optic canal and ophthalmic vein. The superior ophthalmic vein is the only vascular structure of the orbit that is consistently visualized on CT imaging (Yousem, 2010).

### Combined Fractures

Combined fractures of orbital cavity are often associated with zygomaticomaxillary complex, maxilla fractures, and nasoorbitoethmoidal complex.

**Zygomaticomaxillary Complex Fractures.** Zygomaticomaxillary complex fractures are the most common fracture with orbital involvement. Due to anatomical structures of the zygomatic bone, fractures of the lateral wall of the orbit usually present in association with more complex patterns of maxillofacial injury (Patel, 2012).

Blunt trauma to the lateral face and orbit may fracture the four legs of the ZMC. On CT imaging, this will show fractures of the lateral orbital margin, inferior orbital margin with extension into the anterior wall of the maxillary sinus, zygomatic arch, and internal lateral orbital wall (Winegar, 2010).

There may be multiple orbital or ocular sequelae of ZMC fracture. Severe lateral angulation of the internal lateral wall of the orbit increases orbital volume and leads to exophthalmos, requiring orbital exploration as part of the surgical repair (Wright, 1998). ZMC fractures are also frequently associated with orbital floor fractures. CT is critical in characterising angulation and comminution of the internal lateral orbital wall fracture, as well as determining if there is coexistent orbital floor fracture (Jamal, 2009).

**Maxillary Fractures.** Maxillary fractures are classified into Le Fort I, Le Fort II and Le Fort III types. This classification scheme describes three variants of partial or complete dissociation of the maxillary bone from the skull base (Noffze, 2011).

Le Fort II and III fractures involve orbital wall fractures, whereas a pure Le Fort I fracture does not involve the orbit. All three Le Fort fractures are presented for completeness and to emphasize that multiple variants of Le Fort fractures can coexist (Patel, 2012).

Le Fort I fracture occurs when there is horizontal fracture involving the anterior and medial walls of the maxillary sinus and the nasal septum. Coronal CT depicts interruption of the zygomaticoalveolar arch and the piriform sinus by a fracture line. Dislocation frequently occurs in a posterior or lateral direction causing a floating palate and malocclusion with an "open bite". Concomitant dental root fractures are delineated by CT, panoramic view or dental films (Manson, 1999).

In Le Fort II fracture, there is oblique fracture of the zygomaticomaxillary articulation, involving the anterior maxillary sinus wall, inferior orbital rim, and medial orbital margin. Variations in the course of fractures with regard to the maxilla, nasal bones, the anterior ethmoid and vomer or perpendicular plate are readily displayed by coronal CT images (Linnau, 2003).

A Le Fort III fracture is present when there is fracture of the medial and lateral walls of the orbit, as well as fracture of the zygomatic arch. CT is particularly important to recognize potential optic canal, cribriform plate and ethmoid roof involvement (Aaron, 2014).

**Nasoorbitoethmoidal Complex Fractures.** Nasoorbitoethmoidal fracture is a severe craniofacial injury pattern that involves high-energy impact to the nasoethmoidal region of the midface (Remmler, 2004). The blunt injury to the nasoethmoid region causes fracture of the ethmoid sinuses and medial orbital wall. Fractures through the medial orbital wall and the entire NOE complex may result in telecanthus due to medial canthal tendon injury (Sargent, 2007). Up to 20 % of patients have nasolacrimal duct involvement, and may result in abnormalities of tear drainage. Medial orbital wall fractures fragments associated with NOE complex injuries may be dislocated to the NOE complex or orbit side (Yamashita, 2007).

The degree of comminution of an NOE injury pattern describes the severity of injury and may guide clinical and surgical management (Hopper, 2006). These fractures create cosmetic deformities with a flattening of the nasal dorsum and a widening of the intercanthal distance (Miloro, 2004).

## Discussion

Common modalities for imaging the orbit and eye include radiography, ultrasound, MRI and CT. The sensitivity of CT for fractures is higher than that of radiography, and three-dimensional reformations after image acquisition can sometimes help to guide subsequent surgical treatment. For orbital trauma, the optimal protocol is thin-sliced CT scan with 1–2 mm cut through the orbit performed with a helical CT. The advantages of the high resolution orbital CT include (Winegar, 2015):

1) much shorter scanning time;
2) reduced motion artefact;
3) much lower radiation exposure.

**Conventional Radiography.** Plain radiographs may show orbital fractures but are usually of limited value due to the difficult anatomy of the region and they fail to distinguish between the various soft tissues involved. Plain radiographs are limited in assessing the degree of soft tissue injury and displacement of bony fragments. Their sensitivity for fractures is only 15–50 % (Schuknecht, 2005). Plain radiographs may reveal herniation of orbital fat into the maxillary sinus giving rise to the so called tear drop appearance on the Waters' view (Brady, 2001).

**Ultrasonography.** The use of ultrasound as an alternative to radiography of facial fractures has been explored. Its principal benefit remains in the high-resolution evaluation of superficial soft tissue injury of the face and orbit (Shah et al., 2016). Ultrasonography is an available method for the diagnosis of medial and inferior orbital wall fractures and can be used as the modality of choice for the investigation of orbital wall fracture. Ultrasonography shows normal orbital bones structure as an echogenic line. Orbital bones fracture manifests as disruption of echogenic lines and local hematoma (Johari, 2016). However, if eyeball rupture is suspected than ultrasonography should be avoided.

**Magnetic Resonance Imaging.** Magnetic resonance imaging (MRI) has a specific role in the evaluation of orbital injuries, providing additional information in cases of cranial nerve deficits, vascular and intracranial complications (Rootman, 2003). Magnetic resonance imaging is contraindicated if there is suspicion of a metallic foreign body within the globe that could potentially move in the strong magnetic field and worsen the eye damage. This diagnostic method is superior to CT in assessing the degree of damage to the globe and optic nerve and differentiation between edema and hemorrhage (Varnamkhasti, 2010).

*Table 1.* Diagnostic methods compare

| Diagnostic methods | Advantages | Disadvantages | Indications |
|---|---|---|---|
| CT | • Possible to evaluate structures in different planes<br>• Successfully visualise bony structures, in outside of the orbit, its opening and its relationship with the skull<br>• Fast image acquisition and easy patient positioning | • Less useful in imaging the ocular globe and adnexae<br>• High radiation dosage | • Isolated and complex orbital fractures<br>• Orbital haematoma<br>• Evaluation of orbital volume<br>• Orbital structure reconstruction |
| MRI | • Provide excellent images of soft tissues contained in orbital cavity<br>• Possible to evaluate structures in different planes<br>• No radiation | • Contraindicated to metal foreign body detection<br>• Less useful in imaging the orbital bones and paranasal cavities | • Vascular injuries<br>• Optic nerve visualisation<br>• Intraorbital soft tissue damages<br>• Non-metal foreign body detection<br>• Edema and haemorrhage differentiation |
| Conventional radiography | • It makes it possible to consider orbital bone structures and paranasal sinuses<br>• Low radiation dosage | • Plain radiographs are limited in assessing the degree of soft tissue injury and displacement of orbital bony fragments<br>• For diagnosis of orbital wall fracture required to do x-rays in different projections<br>• A patient must be conscious<br>• Structures overlay each other | • Isolated and non-isolated orbital fracture<br>• Metal foreign body detection |
| Ultrasono-graphy | • It allows to diagnose orbital soft tissue damage in combination with isolated fractures in real time<br>• No radiation | • One of the major limitations of ultrasonography in orbital complex fractures is the detection of the other associated fractures of the facial bone<br>• Specific knowledge and experience in working with ultrasonography<br>• Rupture of eyeball | • Foreign body detection<br>• Evaluation of orbital volume<br>• Intraorbital soft tissue damages<br>• Medial and inferior orbital wall fractures<br>• Globe disruption<br>• Lens dislocation<br>• Vitreous haemorrhage<br>• Vascular injuries |

## Conclusion

Due to anatomical proximity, craniofacial trauma often involves injury to the eye and orbit. Orbital trauma may occur as an isolated injury or in context of a more severe craniofacial injury.

The use of high resolution CT has become the gold standard of reference in evaluating patient with orbital trauma. Axial and coronal CT scans can provide information on the location and size of the orbital fracture. Use an axial CT scans allow to measure orbital volume that often is useful in orbital trauma diagnostic. With its widespread availability, fast image acquisition and easier patient positioning, it has largely replaced conventional radiographs.

Bony fractures and displacements, small comminuted fragments and foreign body are best seen on CT. Vascular and nerve injury and intracranial haematomas can be diagnosed by CT; however, MRI is superior to CT in soft tissue visualisation. MRI imaging is an alternative to CT in evaluating orbital trauma.

The imaging method of choice for orbital is thin section CT that can effectively predict prognosis and surgical indication. High resolution thin slice CT of the orbit is ideal for assessing the extent of the bony involvement and it allows three dimensional and multiplanar reformatting.

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