ISSN 2545-4366
www.e-mja.finki.ukim.mk

# MJA

## Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

**Vol. 5 No 1, March 2021**

Journal of the Macedonian Society of Anaesthesiologists
and Macedonian Society of Critical Care Medicine

**Publisher:**
Department of Anaesthesia and Reanimation, Faculty of Medicine,
"Ss. Cyril and Methodius" University, Skopje, R.N. Macedonia

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**I.V. Paracetamol**


## БЕЗБЕДНА АНАЛГЕЗИЈА

### менаџирање на болка кога сте загрижени за безбедноста

**I.V. paracetamol** за прв пат во Европа е применет во 2001 година, а денес поради неговата докажана безбедност и ефикасност е прв од избор **аналгетик и антипиретик.**

**Предоперативна и Интраоперативна Аналгезија:**
Предоперативна анелгезија е дефинирана како третман кој што започнува пред оперативниот зафат се со цел да се превенира воспоставувањето на централна сензибилизација на болка.
**i.v. paracetamol** е безбеден, добро толериран лек со докажана ефикасност како **предоперативна и интраоперативна анелгезија** за умерена до средна болка при оперативни зафати.
**Голем број на клинички студии** ја докажуваат ефикасноста на **i.v. paracetamol** како **преодоперативна и интраоперативна анелгезија**.

**КЛИНИЧКА СТУДИЈА:**
Ефект од **предоперативен i.v. paracetamol** за постоперативни аналгетски потреби кај пациенти кои се подлежни на оперативни зафати. A Sreenivasulu , R Prabhavathi, 2015
**Цел:** Да се утврди ефикасноста на **предоперативната употреба на 1000mg i.v. paracetamol** кај постоперативните болки и анелгетски потреби кај пациенти подлежни на хируршки зафати.
**Метод:** 60 пациенти беа поделени во две рандомизирани групи од по 30 пациенти.
**На I. Група** им беше администрирано **ампула од 1000mg i.v. paracetamol разредена 0,9%NaCl** р-ор 30 минути пред индукција **(ГРУПА П)**,
**На II. Група** им беше администрирано **i.v. 0,9% NaCl р-ор 100мл** 30 минути пред индукција **(ГРУПА НС)**
Сите пациенти беа индуцирани со i.v. thiopentone 5mg/kg, i.v. fentanyl 2µg/kg, i.v. vecuronium 0.1mg/kg
Постоперативниот резултат на болка беше мерен со **Визуелна Аналогна Скала (ВАС) од "0-10"**. Исто така беше забележувана и **постоперативната употреба на tramadol** како спасувачки аналгетик. Инциденцата на **постоперативно гадење и повраќање (ПОГП)** и други компликации исто така беа забележувани во пост оперативниот период.
**Резултатот** на постоперативната болка беше забележуван во интервали 15 мин, 30 мин, 1 час, 2 часа, и 6 часа.

**Резултат:**

***Табела 1:*** *Споредба на средниот резултат на болка (ВАС) помеѓу двете групи*

| Интервали | I Група П | II Група НС | *P вредност* |
|---|---|---|---|
| 15 мин | 2.06 ± 0.63 | 2.61 ± 0.56 | 0.0006 |
| 30 мин | 2.35 ± 1.17 | 3.84 ± 1.55 | 0.0001 |
| 1 час | 2.42 ± 1.12 | 2.87 ± 0.99 | 0.0989 |
| 2 часа | 2.13 ± 1.06 | 2.52 ± 0.89 | 0.1219 |
| 6 часа | 2 ± 0.52 | 2.52 ± 0.89 | 0.0549 |

***Табела 2:*** *Споредба за потребите од tramadol помеѓу двете групи*

| Интервали | I Група П | II Група НС | *P вредност* |
|---|---|---|---|
| До 1 час | 4 (12.90%) | 15 (50%) | 0.0002 |
| 1-2 часа | 3 (9.68%) | 2 (6.45%) | 0.64 |
| 2-6 часа | 1 (3.23%) | 3 (9.68%) | 0.301 |
| **Вкупно** | **8 (25.81%)** | **20 (64.52%)** | **0.002** |

***Табела3:*** *Споредба на ПОПГ помеѓу двете групи*

| ПОГП | |
|---|---|
| I Група П | II Група НС |
| 0 | 4 |

**Заклучок:** Предоперативна администрација на **1000mg i.v. paracetamol** кај пациенти подлежни на оперативен зафат обезбедува **статистички задоволителна анелегизија**, и ја **намалува постоперативната употреба на tramadol**. Оттука **1000mg i.v. paracetamol** може безбедно да се администитрира како превенција при оперативни зафати.

| | |
|---|---|
| i.v. Paracetamol + јак опоид | МНОГУ ЈАКА БОЛКА |
| i.v. Paracetamol + слаб опоид | ЈАКА БОЛКА |
| i.v. Paracetamol + NSAID<br>i.v. Paracetamol + rescue medicine | УМЕРЕНА БОЛКА |
| i.v. Paracetamol + rescue medicine | СЛАБА БОЛКА |

**Мултимодално менаџирање на постоперативна болка**
**I.V. Paracetamol е атрактивна компонента за мултиодално менаџирање на болка.**

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- **Значително намалување на болка**
- **Редукција на дозата на опоидни лекови за - 40% во првите 24 часа**
- **Намалување на несаканите ефекти поврзани со монотерапија на NSAID и опоидни лекови**
- **Ублажување на акутна и хронична болка**

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# Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

# CONTENT

# PANCREATIC CANCER: WHERE DO WE STAND?

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Less than 5% of patients diagnosed with pancreatic cancer (PC) survive for five years, and the average lifetime following the diagnosis is no more than 5 months. Although pancreatic cancer across Europe is on seventh place according to incidence rates with 100,000 new cases, every year, it is the third leading cause of cancer-related death, claiming the lives of 95,000 citizens per year. According to the data of European Cancer Information System, last year in our country pancreatic cancer was on the 6th place with incidence of 16.7 in 100,000 people. Despite these horrifying facts, there has been a little advancement in patient outcomes last five decades, and pancreatic cancer remains a disease which has been "staked" in the past. The silent killer shows no signs of conceding either, with the morbidity and mortality rates estimated to grow up to 40% by 2035 as stated by European Parliament Interest group on Digestive Health. Forecast is similar in United States, with projections disclosing that "pancreatic carcinoma will be the second cause of cancer related deaths by 2030".

Pancreatic cancer is hard to recognize in its initial phase, due to non-specific presenting symptoms. Although scientists are trying to come upon the molecular mechanisms leading to malignant transformation of healthy pancreatic cells and discover new biomarkers that can signify the presence of the disease in its early stage when is still treatable, in Europe pancreatic cancer research has limited funding of less than 2% of overall cancer funding. This actuality, in conjunction with the therapeutic resistance of pancreatic cancer, is the main reason of lowest survival rate among "the cancers" and steadily increasing incidence (1 – 9).

## The Facts

Predominant part of pancreatic carcinoma, more than 80% are caused by sporadic mutation, and minor proportion is due to germ-line mutations in BRCA2, p16, ATM, STK11, PRSS1/PRSS2, SPINK1, PALB2. Aetiology still remains unrevealed, nonetheless, a vast majority of well-known risk factors do exist like: cigarette smoking, heavy alcohol drinking, chronic pancreatitis, diabetes (especially recent onset, or longstanding diabetes with unexplained instable hyperglycaemia), obesity (central type with BMI>30), hereditary pancreatitis and hereditary pancreatic carcinoma (having two first degree relatives with PC doubles the risk of developing cancer). Lifestyle risk factors are modifiable, which offers enormous mode of prevention, if public awareness is developed. Regarding hereditary pancreatitis/ carcinoma, genetic cancer screening is recommended by International Cancer of the Pancreas Screening (CAPS) consortium in all patients with Peutz-Jeghers syndrome, all carriers of CDKN2A mutation, carriers of a germline BRCA2, BRCA1,

PALB2, ATM, MLH1, MSH2 and MSH6 gene mutation and individuals with familiar type of pancreatic carcinoma. The aim of proposed actions is prevention, early detection and decreasing of the morbidity/ mortality rates of pancreatic carcinoma. Regarding the gender, pancreatic cancer affects men and women equally, with incidence increasing after the fourth decade (10-15).

## Symptoms

Pancreatic carcinoma in initial phase is presented by non-specific or indeterminate symptoms. Loss of appetite, nausea, abdominal and back pain, a change in bowel habits or vague depression, can be frequently misleading. The appearance of alarming symptoms like jaundice, significant unexplained weight loss or cachexia usually disclose advanced disease. Symptoms depend on the location of cancer as well; tumours arising in the head of pancreas (60-70% of cases) will exhibit painless jaundice earlier in the course of the disease. Carcinomas in the body of the pancreas (that assemble with lesions in the tail and are approximately 20-25%) usually cause dreadful pain in the back, that can be deceiving for a spinal pain, while lesions in the tail can grow symptomless until display of distant metastases (16-18).

## Diagnosis

Pancreatic cancer occurs weather from exocrine or endocrine parenchyma, yet approximately 80% arise from ductal epithelium, and the most common is ductal adenocarcinoma.

At the time of diagnosis only 20% of the cases are suitable for surgical resection, i.e. 80% of patients with pancreatic carcinoma are already metastatic. Imaging methods like ultrasound for initial examination, contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI) combined with MR-cholangiopancreatography (MRCP), and endoscopic ultrasound (EUS), followed by fine needle aspiration biopsy (FNAB), are the main diagnostic tools. There is still concern over the use of EUS in detection of pancreatic cancer, considering that precision can be reached only by excellent training, in big clinical centres. Positron emission tomography scan (PET) is usually used for detecting residual cancer tissue after treatment and is not recommended for diagnosis. According to American Gastroenterology Association (AGA) updated pancreatic cancer guidelines, biopsy is recommended "only when imaging results are ambiguous" and should be performed during EUS procedure that offers lower risk of malignant seeding than percutaneous biopsy under ultrasound or CT guidance. The value of FNAB carried out by experienced pathologist adds 95% of diagnostic accuracy. Percutaneous biopsy is contraindicated in resectable lesions and is justified only for metastatic lesions. There is still lack in specific tumour markers. American Society of Clinical Oncology (ASCO) discouraged the use of Carbohydrate Antigen 19-9 (CA 19-9) as a screening or diagnostic tool, due to the absence of enzyme responsible for its production in 5-10% of patients, as well as the fact that markers can be falsely positive/negative in many other benign conditions. Nevertheless, according to the European Society for Medical Oncology (ESMO), the latest clinical pancreatic cancer guidelines, CA 19-9 has a significant value as a prognostic factor; rising levels of CA 19-9 post-operatively are recommended for predicting recurrent disease and can be used as a marker to measure disease burden after surgery and before adjuvant therapy, and potentially guide treatment decisions (19,20).

## Treatment

Staging procedure allows classification of pancreatic carcinoma as resectable, borderline resectable and locally advanced or metastatic disease. A treatment decision must be taken by multidisciplinary team and consistent with diagnostic findings, including performance status and comorbidities. According to ESMO recommendations, radical surgery is the only curative therapy, and is defined on small percent of patients (those in stage I and a little proportion in stage II). Even so, the latest understanding of pancreatic cancer as a systemic disease with micro-metastases at the time of diagnosis, suggests use of multimodality therapy, involving combination of treatments rather than resection alone. Nowadays, neoadjuvant therapy given as a first line therapy in order to shrink tumor size before surgery and downsize larger tumors, has been announced as a first treatment choice, permitting safer and clearer resection lines, hence improving survival rates.

Considering that at the time of diagnosis only 20% of patients are acceptable for surgical resection and taking into account poor results of surgery alone (out of these 20%, only 20% will reach five-years survival), adjuvant chemotherapy, chemoradiotherapy (CRT) or stereotactic body radiotherapy (SBRT) may be offered alone or in combination, after radical surgery in order to improve 5-years survival rates. According to 2016 ASCO guidelines: multiphase CT scan of thorax, abdomen and pelvis, should be performed to assess extent of disease in patients with locally advanced, unresectable tumor. The first line treatment with FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin) or gemcitabine plus nab-paclitaxel is recommended for patients who have Eastern Cooperative Oncology Group performance status (ECOG PG) of 0 to 1, and favorable comorbidity profile. Gemcitabine alone is recommended for patients who have either an ECOG PS of 2 or a comorbidity profile that prevents more aggressive treatments. Patients with an ECOG PS≥3 or with inadequately controlled comorbidities, despite active medical care, should be offered cancer-directed therapy only on a case-by-case basis. Second-line therapy with PD-1 immune checkpoint inhibitor pembrolizumab is recommended only for patients who have tested positive for deficient Mis Match Repair (dMMR) or High levels of Micro Satellite Instability (MSI-H). Patients with metastatic pancreatic cancer need a palliative care and ESMO guidelines recommend morphine as a drug of choice for pain management (21-25).

## Future

Regarding the fact that pancreatic cancer has the lowest survival rate among other more frequent cancers, and there has not been any visible advance in patient's outcome almost five decades, it

is of utmost importance urgently and coordinatively to set the collaboration between academia, industry and healthcare providers. Specific microenvironmental properties of tumor tissue that makes it resistant to chemo and immunotherapy, newly detected connections with microbiota, and biomarkers that may accurately detect pancreatic cancer in early stages, when it's the most likely to respond to treatment, are few provocative scientific fields which can fill up the gap in better understanding of this complex disease. Boosting the knowledge of pancreatic cancer's nature, is a big step forward in fighting the cancer.

Broad public awareness of existence and early diagnosis of the fatal disease is needed, in order to improve patient's outcome. Since screening is still not recommended except in individuals with known germline mutations associated to pancreatic cancer, resourcefulness and cooperation among all interested parties like patients' groups, clinical experts and legislative, should be initiated as soon as possible with one clear aim: defeating the deadliest cancer (26).

**Conflict of interest:** none

**Funding:** none

## References

1. European Commission (2018). European Cancer Information System. Available: http://ecis.jrc.ec.europa.eu/php.http://encr.eu/images/docs/factsheets/ENCR_ Factsheet_Pancreas_2016_References.pdf.
2. Ilic M, Ilic I. Epidemiology of pancreatic cancer. World J Gastroenterol 2016 Nov 28;22(44):9694-9705.
3. Tavakkoli A, Singal, Waljee AK et al. Racial Disparities and Trends in Pancreatic Cancer Incidence and Mortality in the United States Clin Gastroenterol Hepatol 2020 Jan;18(1):171-178.
4. Ferlay J, Partensky C, Bray F et al. More deaths from pancreatic cancer than the breast cancer in EU by 2017. Acta Oncologica. August 2016.
5. L. Rahi. BD, Smith R, Aeizenberg et al. Projecting Cancer Incidence and Deaths to 2030: The Unexpected Burden of Thyroid, Liver, and Pancreas Cancers in the United States. May 2014 Cancer Research 74(11)DOI:10.1158/0008-5472. CAN-14-0155.
6. Pancreatic cancer Research Fund. (2018). Why do we exist. Available: http//www.prcf.org.uk/pages/why-we-exist.html.
7. Malvezzi, M. et al. European cancer mortality predictions for the year 2019 with focus on breast cancer. Ann. Oncol. 30, 781 – 787 (2019).
8. Carrato et al, 2015. "A Systematic Review of the Burden of Pancreatic Cancer in Europe: Real-World Impact on Survival, Quality of Life and Costs." DOI 10.1007/s12029-015-9724-1.
9. Bray F, Ren JS, Masuyer E et al. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer 2013; 132:1133-45.
10. Pancreatic Cancer Action – Risk factors for pancreatic cancer – https://pancreaticcanceraction.org/about-pancreatic-cancer/causes-and-risks/ – Retrieved September 2015 6 "15 facts on Pancreatic Cancer", European Cancer Patient Coalition (ECPC) http://www.ecpc.org/edu/pancreas/249-15-key-facts-on-pancreatic-cancer [Retrieved September 2015].
11. Pancreatic Cancer Action – Research Funding – https://pancreaticcanceraction.org/pancreatic-cancer/stats-facts/research-funding/.
12. Goggins M, Overbeek K.A., R. Brand et al., Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Gut 2020;69:7 – 17. doi:10.1136/gutjnl-2019-319352.
13. Hu C, Hart SN, Polley EC, et al. Association between inherited germline mutations in cancer predisposition genes and risk of pancreatic cancer. JAMA. 2018; 319:2401-2409.
14. Murphy KM, Brune KA, Griffin C, et al. Evaluation of candidate genes MAP2K4, MADH4, ACVR1B, and BRCA2 in familial pancreatic cancer: deleterious BRCA2 mutations in 17%. Cancer Res. 2002; 62: 3789-3793.
15. Sharma A, Smyrk TC, Levy MJ Et al. Fasting Blood Glucose Levels Provide Estimate of Duration and Progression of Pancreatic Cancer Before Diagnosis. Gastroenterology 2018 Aug;155(2):490-500. e2.
16. Khalaf N, Wolpin MB. Metabolic Alterations as a Signpost to Early Pancreatic Cancer Gastroenterology 2019 May; (6): 1560-1563.
17. Gupta S et al. Risk of pancreatic cancer by alcohol dose, duration and pattern of consumption, including binge drinking; a population based study. Cancer Causes Control 2010 21(7);1047-1059.
18. Evans J, Chapel A, Salisbary H et al. "It can't be very important because it comes and goes" — patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: a qualitative study. BMJ Open 2014;4:e004215. doi:10.1136/bmjopen-2013-0042.
19. Chu L, Goggins M, Fishman EK. Diagnosis et Detection of Pancreatic Cancer. The Cancer Journal: 11/12 2017 – Volume 23 – Issue 6 – p 333-342.
20. Locker Gy, Hamilton S, Harris J et al. ASCO 2006 update of recommendations of the use of tumour markers in gastroenterology cancer. J Clin Oncol 2006 Nov 24(33):5313-27.
21. Asianian HR, Lee JA, Canto M et al. AGA Clinical Practice Update on Pancreas Cancer Screening in High Risk Individuals: Expert Review: Gastroenterology 2020 May 13:S0016-5085(20)30657-0. doi: 10.1053/j.gastro.2020.03.088.
22. Ducreux M, Sa Cuhna A, Caramella C, et al. cancer of the Pancreas. ESMO Clinical practice guidelines Ann Oncol (2015) 26 (suppl 5): v56-v68.eUpdate 15 march 2019.
23. Sohal PSD, Kennedy E. B, Khorana A et al. Metastatic Pancreatic Cancer: ASCO Clinical Practice Guideline Update. Journal of Clinical Oncology 2018 August 36:N24.
24. Dragovich T. Pancreatic Cancer Guidelines – Guidelines summary https://emedicine.medscape.com/article/280605-guidelines.
25. Evans DB, George B, Tsai S et al. Non-metastatis Pancreatic Cancer-resectable, Border line resectable and locally advanced-Definition of increasing importance for the optimal Delivery of Multimodality Therapy. Ann Surg Oncol 2015; 2(11): 3409-3413.
26. Pushalkar S, Hundeyin M, Daley D et al. The Pancreatic Cancer Microbiome Promotes Oncogenesis by Inductionof Innate and Adaptive Innate Suppression. Cancer Discov 2018; 403 (4):403-415.

UDK: 616-022.7:579.841.1]:614.2:616-083.98

# SEASONALITY OF PSEUDOMONAS SPECIES IN SURGICAL INTENSIVE UNIT

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## SUMMARY

*Pseudomonas* strains are frequent microorganisms associated to healthcare-acquired infections. *Pseudomonas aeruginosa* is one of the leading intra-hospital pathogens in the intensive care units. *Pseudomonas* infections usually present wide antimicrobial resistance in treatment and they are important public health problem. Medical devices are the most often responsible for nosocomial infections in the intensive care centers. *Pseudomonas* colonization and its ability to form *biofilm on medical devices highlights this organism as emergent pathogen at* the Clinic for Anesthesiology, Resuscitation and Intensive Care in Skopje. Multidrug-resistant *Pseudomonas aeruginosa* is an *endemic* problem in the intensive care units. Also, *Pseudomonas* spp. strains demonstrate seasonality. This research will investigate its existence on respiratory medical devices (endotracheal tubes and nasal cannulas). The study will determine its seasonal variation and it will indicate preventive medical measures in critical seasons.

***Key Words:*** *intensive care, nosocomial infection, Pseudomonas, seasonality.*

## Introduction

Intra-hospital infections in intensive care units are important public health problem. The most common nosocomial infections in intensive care centers are lower respiratory tract infections, surgical wound infections, urinary tract infections and bacteremia. These infections complicate the underlying disease, prolong the period of hospitalization (number of hospital days) and increase the hospital costs (1). Intra-hospital infections in the intensive care wards are mostly related to the use of medical equipment. In these units, the use of medical devices is the greatest, while the patients are severely immunocompromised (2). *Pseudomonas* strains are one of the most common nosocomial pathogens that often cause life-threatening infections. The most commonly isolated member of the genus is *Pseudomonas aeruginosa*, which is the most common cause of nosocomial lower respiratory infections and has been shown to be an endemic microorganism in the intensive care units worldwide (3). *Pseudomonas* species is genus with considerable medical importance, because it is a ubiquitous pathogen that is resistant to multiple groups of drugs and it is associated to serious diseases mostly with nosocomial pneumonia – associated with respiratory devices (ventilator-associated pneumonia). *Pseudomonas* is generally responsible for infections in immunocompromised individuals but can also cause disease in immunocompetent patients. Healthcare-acquired *Pseudomonas* infections cause inflammation and devitalization of healthy tissues (4). *Pseudomonas* spp. has an affinity for tissues with increased humidity, such as respiratory and genitourinary tract. This microorganism can be found on wet surfaces and medical equipment, including respirators and catheters, causing cross-infections in the hospital environment. Treatment of *Pseudomonas* infections can be difficult due to its natural resistance to antibiotics and especially due to its ability to form a lasting biofilm. *Pseudomonas* spp. has an affinity for a humid environment, which allows it to spread in hospital ecosystems. Climate parameters interfere with the isolation rate of *Pseudomonas* spp. (5). The aim of the study was to detect *Pseudomonas* strains colonization of respiratory medical devices in patients at the Clinic for Anesthesiology, Resuscitation and Intensive Care (CARIC) in Skopje and to recognize their seasonality.

## Material and methods

The retrospective study included period of eight years (2010 – 2017). This research reviewed microbiological examined materials from medical respiratory devices (endotracheal tubes and nasal cannulas) of the patients at the Clinic for Anesthesiology, Resuscitation and Intensive Care. Routinely obtained materials were sent to the Institute of Microbiology and Parasitology at the Faculty of Medicine of "Ss. Cyril and Methodius" University in Skopje for microbiological analysis. The laboratory data findings were obtained by laboratory software for daily routine work (LabIS-Codex), owned by the Institute. The *Pseudomonas* spp. isolation rate was observed and then compared to the average humidity of the air. Official climate data from the National Hydrometeorological Service was used.

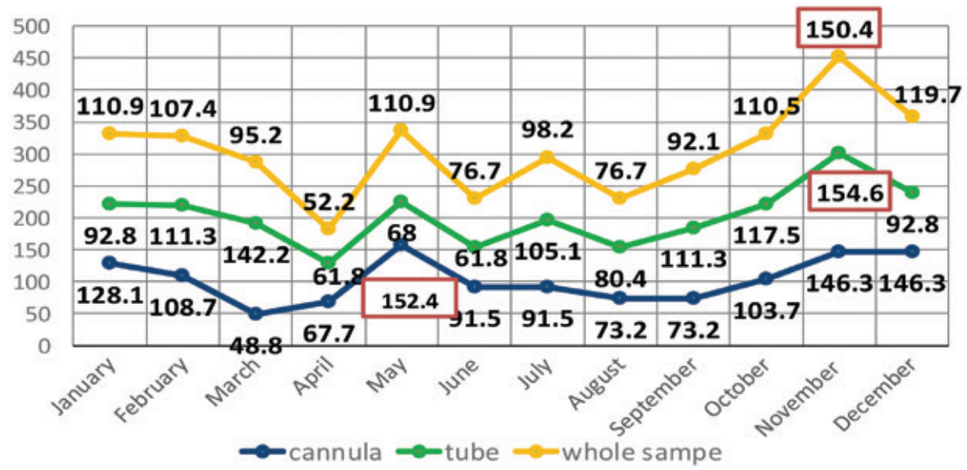
## Results and discussion

The most common nosocomial pathogens for the examined period in the whole sample of positive isolates were *Acinetobacter* spp. – 36.96% and *Pseudomonas* spp. – 20.07%. The results of the findings approached to the literature data. *Pseudomonas* has an affinity to both respiratory medical devices (tubes and cannulas), but the percentage difference of *Pseudomonas aeruginosa* presence in the cannula by $p<0.05$, was significantly larger compared to its presence in the tube (Difference test: Difference 12.03% [(8.21-15.94) CI 95%]; Chi-square=40.7; df =1; p=0.0001). *Pseudomonas* spp. has an ability to develop and to maintain itself in a wet and humid environment, so these bacteria make rapid invasion of medical respiratory devices (6, 7). The presence of *Pseudomonas* spp. in the whole sample of positive isolates (endotracheal tubes and nasal cannulas), for the period of eight years, was the highest in 2010 (25.3%), followed by 2011 (22.1%) and 2013 (21.7%). The monthly variations for the presence of *Pseudomonas* in the whole samples of positive isolates, as well as individually in the positive isolates from tubes and cannulas were performed. The analysis presented values of positive isolates for each month,

individually for both places of isolation. The highest monthly isolation rate of *Pseudomonas* spp. from tubes and cannulas was determined in 2012 (October – 46.15%) and 2013 (36.36% – June) followed by 2017 (35.29% – July). The analysis of the positive isolates from tubes due to the monthly distribution of *Pseudomonas* strains indicated that for the examined period they were mostly isolated in October 2012 (50%). The analysis of the monthly distribution of *Pseudomonas aeruginosa* in the positive cannula isolates indicated the highest isolation in September 2010 (62.5%), followed by November 2012 (55.6%). Conditions of elevated humidity have a positive effect on the development of this bacterium (8, 9). Representation of 50% was generally recorded in autumn/winter season (more precisely in December – 2012, January and February in 2013 and 2016, respectively) and summer season or June and July 2015 (10-12).

Additionally, for the period of interest, the seasonal index for *Pseudomonas* was determined. The analysis of the total sample, according to the values of the seasonal index above 100% (above the monthly average), indicated that *Pseudomonas aeruginosa* was the most isolated in November – 150.4% and in December – 119.71%, followed by January – 110.5%, February – 107.43%, May – 110.5% and October – 110.5%. The highest value of the seasonal index for *Pseudomonas* from tubes was in November – 154.61%, followed by March – 142.24%. Values of the seasonal index above the monthly average, were also registered in February – 111.31%, July – 105.13%, and September/October consequently 111.32% vs.117.50%. Additional analysis for cannula indicated the highest value of the seasonal index for *Pseudomonas aeruginosa* above 100% in May – 152.44%. We registered high values of this index continuously from October to February. Seasonal index values have shown that months with high air humidity positively affected the development of these bacteria. In a hospital setting, during periods of high humidity, this bacterium increased the number of respiratory tract infections (especially in people connected to mechanical ventilation) (9, 13). The seasonal variations of *Pseudomonas aeruginosa* in the positive isolates from the whole sample, tube and cannula were analyzed through the seasonal index given in Figure 1.

**Figure 1**. *Seasonal index of Pseudomonas aeruginosa, CARIC, 2010-2017.*




These findings correspond to foreign studies, which highlight seasons mentioned above as the most critical for the development of *Pseudomonas* spp. In a seven-years study in the United States, children with cystic fibrosis were found to have a respiratory invasion of *Pseudomonas aeruginosa* during the summer and fall months, with lower isolation in the spring than in the winter months. In the general immunocompetent population in England, the number of external ear infections (otitis externa) caused by *Pseudomonas* spp. were higher during the summer months and early autumn (August to October). This is due to the increased contact with water (in the warmer months, in the period of holidays and the periods of increased precipitation) (14, 15).

Associations of *Pseudomonas aeruginosa* strains isolated from intubated CARIC patients with humidity of the air, have shown interesting results. Between the average monthly humidity and the presence of *Pseudomonas* in the sample of positive isolates from tubes and cannulas, we noticed the existence of a non-significant positive linear correlation (Spearman Rank Order Correlations: $R(192)=0.1392$; $p=0.0541$). With the increase of air humidity, for $p>0.05$ – the presence of *Pseudomonas aeruginosa* increased slightly.

## Conclusions

The results of this study indicate that detection of *Pseudomonas* strains acquisition on respiratory medical devices can predict and diagnose nosocomial ventilator-associated pneumonia, reduce its occurrence and decrease outbreaks of healthcare-acquired cross-infections. Determining the seasonality of *Pseudomonas* spp. in the intensive care units will contribute to detecting potential reservoirs, including environmental sources, patients and health care workers in critical seasons. Increasing awareness in development seasons with specific hospital preventive measures will reduce nosocomial infections with *Pseudomonas* species.

**Declaration of interest**

None declared.

## References

1. Kritsotakis E, Kontopidou F, Astrinaki E, et al. Prevalence, incidence burden, and clinical impact of healthcare-associated infections and antimicrobial resistance: a national prevalent cohort study in acute care hospitals in Greece. Infect Drug Resist. 2017;10:317 – 28.
2. Safdar N, Crnich CJ, Maki DG. Nosocomial Infections in the Intensive Care Unit Associated with Invasive Medical Devices. Curr Infect Dis Rep. 2001;3(6):487 – 95.
3. Foca M, Jakob K, Whittier S, et al. Endemic *Pseudomonas aeruginosa* infection in a neonatal intensive care unit. N Engl J Med. 2000 Sep 7;343(10):695-700.
4. Rossolini GM, Mantengoli E. Treatment and control of severe infections caused by multi-resistant *Pseudomonas aeruginosa*. Clin Microbiol Infect. 2005 Jul;11 Suppl 4:17-32.
5. Kerr KG, Snelling AM. *Pseudomonas aeruginosa:* a formidable and ever-present adversary. J Hosp Infect. 2009 Dec;73(4):338-44.
6. Maurice NM, Bedi B, Sadikot RT. *Pseudomonas aeruginosa* Biofilms: Host Response and Clinical Implications in Lung Infections. Am J Respir Cell Mol Biol. 2018 Apr;58(4):428-439.

7. Jadhav S, Sahasrabudhe T, Kalley V, et al. The microbial colonization profile of respiratory devices and the significance of the role of disinfection: a blinded study. J Clin Diagn Res. 2013 Jun;7(6):1021-6.
8. Ramos GP, Rocha JL, Tuon FF. Seasonal humidity may influence *Pseudomonas aeruginosa* hospital-acquired infection rates. Int J Infect Dis. 2013; 17(9):e757 – 61.
9. De Abreu PM, Farias PG, Paiva GS, et al. Persistence of microbial communities including *Pseudomonas aeruginosa* in a hospital environment: a potential health hazard. BMC Microbiol. 2014 May 8; 14:118.
10. Pericolini E, Colombari B, Ferretti G, et al. Real-time monitoring of *Pseudomonas aeruginosa* biofilm formation on endotracheal tubes in vitro. BMC Microbiol. 2018 Aug 14;18(1):84.
11. Aloush V, Navon-Venezia S, Seigman-Igra Y, et al. Multidrug-resistant *Pseudomonas aeruginosa:* risk factors and clinical impact. Antimicrob Agents Chemother. 2006 Jan;50(1):43-8.
12. Davies G, Wells AU, Doffman S, et al. The effect of *Pseudomonas aeruginosa* on pulmonary function in patients with bronchiectasis. Eur Respir J. 2006 Nov;28(5):974-9.
13. Hoffman MA, Finberg L. *Pseudomonas* infections in infants associated with high-humidity environments. J Pediatr. 1955 Jun;46(6):626-30.
14. Psoter KJ, De Roos AJ, Wakefield J, et al. Season is associated with *Pseudomonas aeruginosa* acquisition in young children with cystic fibrosis. Clin Microbiol Infect. 2013 Nov;19(11): E483-9.
15. Villedieu A, Papesh E, Weinberg SE, et al. Seasonal variation of *Pseudomonas aeruginosa* in culture positive otitis externa in South East England. Epidemiology and Infection. Cambridge University Press; 2018;146(14):1811 – 2.





# COMMON COMPUTED TOMOGRAPHY FINDINGS AND ASSOCIATION OF THEIR EXTENT TO THE DEMOGRAPHIC FEATURES OF 47 COVID-19 PATIENTS IN NORTH MACEDONIA

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## ABSTRACT

**Introduction and Purpose:** There was an unprecedentedly rapid and worldwide spread of the coronavirus after the acknowledgement of several cases of unusual pneumonia that were defined as coronavirus disease 19 (COVID-19) and reported in December 2019 in Wuhan, China. As of March 12th, 2021, there are more than 119 million confirmed cases, 2.63 million deaths due to the disease, and 67.1 million recovered. In the Republic of North Macedonia as of March 11th, 2021, we have 110.209 confirmed cases, 3.265 deaths and 96.570 recovered.

The purpose of this study was to perform a thorough evaluation of the CTs in COVID-19 patients with the focus on the type, extent and common distribution of the parenchymal findings, as well as to make an assessment of the relationship between the extent of the parenchymal findings and different demographic features of the patients by using a visual volumetric grading of the parenchymal involvement and administering an appropriate CT score.

**Material and Methods:** CT radiological findings of 47 patients from North Macedonia, enrolled in the study, were analyzed and summarized, and all of whom had positive RT – PCR tests for 2019 – nCoV. The CTs in all patients were performed with 1.25 mm and 5 mm slice thickness on 16-slice Somatom Definition AS+ computed tomography (Siemens Healthineers, USA). The main focus was put on identifying the lesions, evaluating their most common type, distribution and scoring their extent in the lung parenchyma. While applying an appropriate CT score, we made a correlation with the demographic characteristics, such as age, gender and body weight.

**Results and Discussion:** The most common CT finding in almost all 47 patients was the ground glass opacities (GGO) diffusely scattered in both lungs with a dominant peripheral and posterior distribution. We found that age and weight are significant risk factors for predicting the severity and outcome of COVID-19 disease.

**Conclusion:** Chest CT is an important diagnostic and predictive tool in patients with COVID-19. There should be a consensus in the definite diagnosis of COVID-19 based on clinical findings, positive nCov PCR tests and radiological findings. Demographic features can aid in the prediction of severity and outcome of the disease.

***Key Words:*** *computed tomography (CT), consolidation, COVID-9, ground glass opacity (GGO), North Macedonia.*

## Introduction

The COVID-19 pandemic is a worldwide, rapidly spreading viral infection that so far, has provoked a huge impact upon the healthcare systems and the socio-economic circumstances of the countries affected (1). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19), as named by the World Health Organization (WHO), was first described in a series of 41 individuals presenting with undetermined forms of pneumonia in Wuhan, China, during December 2019. There was a new type of coronavirus isolated from the epithelial cells of the airways of infected patients (2, 3).

The first case of COVID-19 in North Macedonia was confirmed on 26th of February 2020. It was a Macedonian citizen who returned ill from Italy – the epicenter of the coronavirus in Europe. She was meanwhile cured and discharged from hospital, but the general view remained that the initial clusters of the disease in our country were formed by returnees from abroad. In North Macedonia as of March 11th, 2021, there are 110.209 confirmed cases, 3.265 deaths and 96.570 recovered.

Our method of choice for the radiological assessment of the extent of lung involvement is non-contrast, low dose chest CT. The computed tomography plays an important role in the early detection of lung changes, especially with RT-PCR negative patients who have positive clinical findings, as well as the management and follow-up of the disease. Chest CT also helps with assessment of the severity, risk stratification and predicting the outcome of the disease. In that manner, we have accepted a visual and semi quantitative CT scoring system for the extent of lung involvement that has been proposed by Pan et al., and described by many other authors in multiple studies (4 – 6).

## Purpose

The purpose of this study was to analyze the radiological CT findings of the lung parenchyma in detail, and semi-quantitatively, visually score the extent of lung involvement in our coronavirus infected patients, and to explore the relationship between the CT score and different demographic features.

## Material and Methods

This is a cross-sectional prospective study. We summarized the most common CT radiological features of randomly picked 47 patients with positive RT PCR tests and various clinical symptoms for COVID-19 in North Macedonia, from December 2020 to February 2021, and we evaluated the relationship between the demographic features and the radiological findings. 47 CTs of the patients with COVID-19 taken at the Institute of Radiology were retrospectively analyzed with the main focus on identification, characterization, distribution and extent of the most common findings, visually and semi-quantitatively calculating the CT score, as well as correlating the CT score with the demographic features of the patients.



The CTs in all patients were performed with 1.25 mm and 5 mm slice thickness on 16-slice Somatom Definition AS+ Computed Tomography (Siemens Healthineers, USA). Images were reconstructed with a 1-mm slice thickness in all cases with a soft tissue kernel of B20 and a lung kernel of B60. There were also multiplanar reconstructions for each patient.

Appropriate infection prevention and control measures were arranged for all CT exams, consisting of prompt sanitation of the CT facility, as well as proper protective measures for the radiology technicians and nurses on site. All chest CT images were reviewed and interpreted by an experienced radiologist with a subspecialty in thoracic imaging.

Positive CTs of each of the patients were evaluated for the presence or absence of the following signs:

1. Ground glass opacities (GGO),
2. Consolidation,
3. Number and extent of lobes involved with GGO and Consolidation,
4. Nodules,
5. Linear opacities,
6. Present or absent peripheral distribution of findings, and
7. Other findings such as pleural effusion, pneumomediastinum, pulmonary embolism, atelectasis, pericarditis, emphysema, fibrosis and mediastinal lymphadenopathy, whereas negative CTs were defined by the absence of GGO and consolidation in the lung parenchyma.

Then a CT severity score was calculated for each patient, as proposed by Pan et al., by summing all the scores for each individual lobe involved, Table 1. Each lobe was graded: $0^0$-no involvement; $1^0$-<5% involvement; $2^0$-5-25% involvement; $3^0$-26-49% involvement; $4^0$-50-75% involvement; $5^0$->75% involvement. Thus, the total score of all lobes involved would range from 0 to 25. Descriptive statistics of patients' demographics were reported as numbers and relative frequencies. Frequencies of CT scores were calculated and reported with other clinical variables. The Pearson correlation coefficient test was used for correlations, and p value less than 0.05 was defined statistically significant.

**Table 1.** *Individual lobar score and total CT severity score.*

| **Lobar involvement** | **Score** |
|---|---|
| 5% or less | 1 |
| 5-25% | 2 |
| 26-49% | 3 |
| 50-75% | 4 |
| >75% | 5 |
| **Total Score (numerical)** | **Severity** |
| **7 or less** | **Mild** |
| **8-17** | **Moderate** |
| **18 or more** | **Severe** |

## Results and Discussion

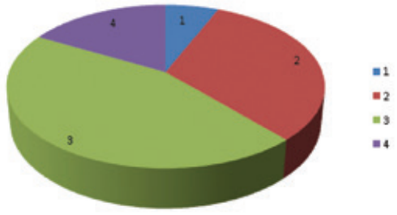
The study included a total of 47 patients, of both genders, aged 26 to 89 years, with an average age of 55.23% ± 14.8. Out of 47 respondents, 17 were women (36.17%) and 30 men (63.83%). Patients were divided into 5 age groups, 25-40, 40-55, 55-70, 70-85, 85-100 years.

Three patients (6.4%) died as a result of complications from coronavirus infection. Two of the deceased patients (66.7%), had a severe CT score of 20 and 23 points each, and one of the deceased patients manifested pneumomediastinum and pulmonary embolism as complications of the disease, that depicts the important predictive value of the severe CT score for the possible fatal outcome of the patients. The third deceased patient had a moderate CT score of 14. Two of the deceased patients were women (66.7%), and the average age of the deceased patients was 76.67±4.04. The three deceased patients were of Macedonian nationality. Three patients (6.4%), had positive nCov PCR tests for the presence of corona virus in the specimens, but negative radiological CT findings.

The body weight of patients ranged from 69 to 105 kg, and the average weight was 85.81± 8.6 kg.

The CT score ranging from 0 to 25 points, had an average of 10.6 ± 7.0, Table 2 and Figure 1.

**Figure 1.** *Frequency distribution of CT score.*




*Negative CT score (3); 2. Mild CT score (15), Moderate CT score (21), 4. Severe CT score (8).*

**Table 2.** *Average values for age, body weight and CT score.*

| | Mean | Median | St. deviation |
|---|---|---|---|
| **Age** | 55. 23 | 53 | 14. 8 |
| **Body weight** | 85. 81 | 87 | 8. 6 |
| **CT score** | 10. 6 | 10. 0 | 7. 0 |

In 18 patients there was a mild CT score of up to 7 points, in 21 patients moderately severe CT score of up to 18 points, and in 8 patients there was severe CT score of above 18 points. The mean values in terms of the extent of CT changes, their appearance and location are presented in Tables 3 and 4. Bilateral pneumonia was found in 44 patients, and in 43 the most common findings were peripheral and posteriorly distributed ground glass opacities, GGO. Pleural effusion as a complication occurred in 6 patients (12.76%). From Table 4, we can conclude that the highest prevalence of changes is observed in the lower left lobe with 91.50%, and lower right lobe with 89.36%, Figures 2-9.

**Table 3**. *Average values for extent, appearance and location.*

| | No | Mean (%) |
|---|---|---|
| **Bilateral pneumonia** | 44 | 93. 62 |
| **More than 1 lobe** | 44 | 93. 62 |
| **Peripheral and posterior GGO** | 43 | 91. 49 |
| **GGO** | 41 | 87. 23 |
| **Consolidation** | 28 | 59. 57 |
| **Nodules** | 22 | 46. 81 |
| **Linear opacities** | 36 | 76. 59 |
| **Dilated vascular structures** | 29 | 61. 70 |
| **Pleural effusion** | 6 | 12. 76 |

**Table 4.** *% involvement of each individual lobe.*

| URL | MRL | LRL | ULL | LLL | |
|---|---|---|---|---|---|
| 41 | 36 | 42 | 40 | 43 | |
| 87. 23 | 76. 59 | 89. 36 | 85. 11 | 91. 50 | Mean (%) |

*URL-upper right lobe, MRL-medial right lobe, LRL-lower right lobe, ULL-upper left lobe, LLL-lower left lobe.*

**Figure 2 and 3**. *GGO with peripheral, posterior distribution as the most common CT finding.*

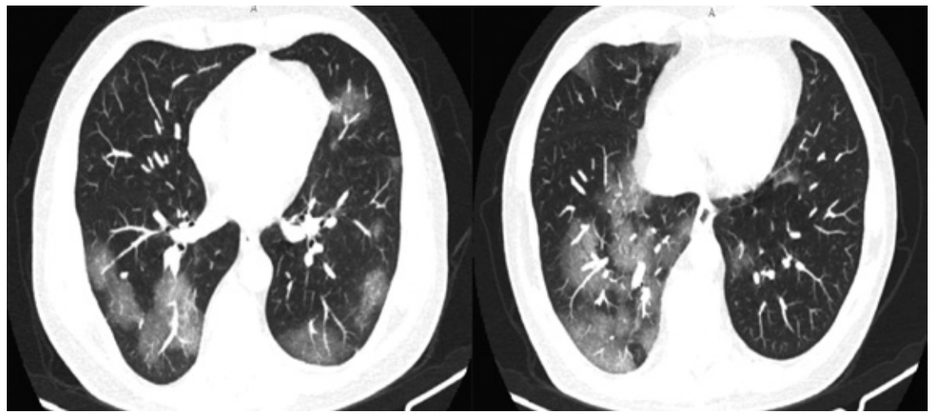


**Figure 4, 5 and 6**. *GGO with/ without consolidation and dilated vascular markings on CT.*

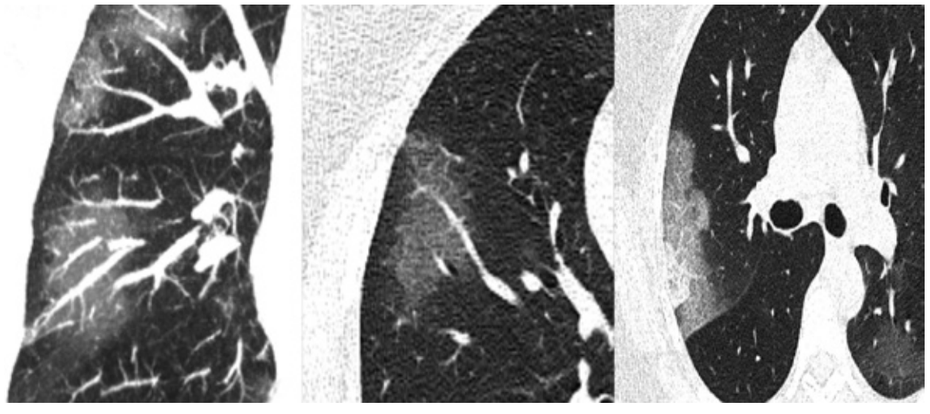


**Figure 7**. *Extensive parenchymal consolidation.*

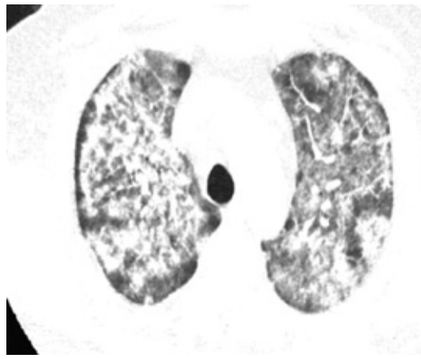


**Figure 8**. *GGO, subpleural consolidation, bands and reticulations.*

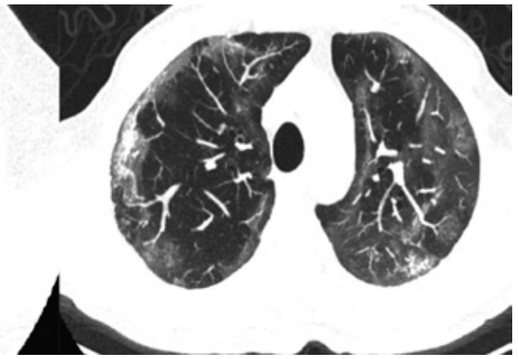
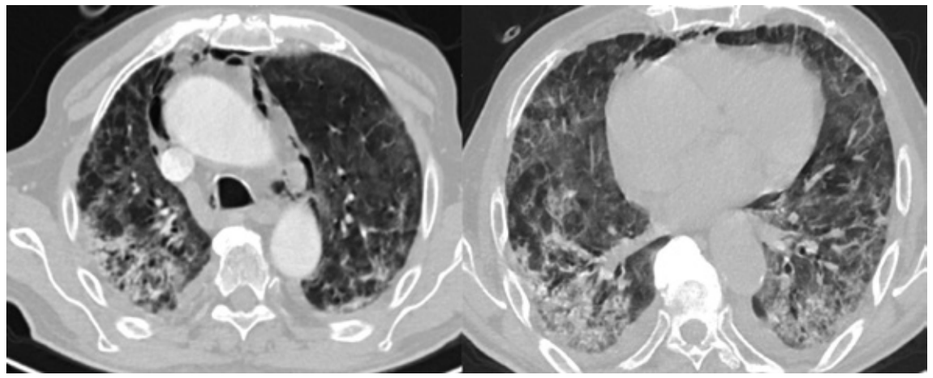


**Figure 9**. *Pneumomediastinum and pleural effusion as complications of corona infection in the same patient.*



We can conclude that moderately severe degrees of CT changes are observed in the age group of 40-55 and 55-70 years, while more severe CT changes are the most commonly observed in the age group 70-85 years. A mild degree of CT changes is observed in the age group of 40-55 years, Table 5 and 6, and Figure 10.

**Table 5**. *Mean values of the CT score in all patients*.

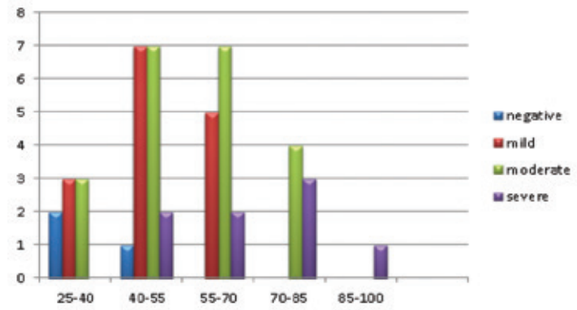
| | No | % | Median | SD | Men | Women |
|---|---|---|---|---|---|---|
| **Score 0** | 3 | 6. 4 | | | 2 | 1 |
| **Mild Score <7** | 15 | 4. 13 | 4 | 1. 5 | 10 | 5 |
| **Moderate Score <17** | 21 | 12. 5 | 13 | 2. 7 | 13 | 8 |
| **Severe Score >18** | 8 | 21. 8 | 21. 5 | 2. 5 | 4 | 4 |

**Table 6.** *CT score by age groups*

| Age group | No. | Mild Score | Moderate Score | Severe Score |
|---|---|---|---|---|
| **25-40** | 8 | 5 | 3 | 0 |
| **40-55** | 17 | 8 | 7 | 2 |
| **55-70** | 14 | 5 | 7 | 2 |
| **70-85** | 7 | 0 | 4 | 3 |
| **85-100** | 1 | 0 | 0 | 1 |



**Figure 10.** *The distribution of CT scores by age groups.*




There is a moderately positive and statistically significant correlation between the CT score and patient's age, $p<0.05$, while we found a weak and statistically insignificant positive correlation between the CT score and body weight, and statistically insignificant positive correlation between the CT score and patient's gender, Table 7.

**Table 7.** *Correlation between CT score and age, gender and weight.*

| | |
|---|---|
| **Age** | R= 0.531<br>p= 0.001 |
| **Weight** | R= 0.1633<br>p= 0.273 |
| **Gender** | R= 0.1782<br>p= 0.231 |
| **CT score/ gender** | Rs= 0.199<br>p= 0.179 |
| **CT score/ age** | Rs= 0.5346<br>p= 0.0001 |
| **CT score/ weight** | Rs= 0.18021<br>p=0.225 |

## Conclusion

In conclusion we can summarize that the most common findings on our CT exams were round ground glass opacities and subpleural linear opacities with a posterior peripheral distribution and lower left and right lobe predilection. The most common other findings, classified as complications of the disease, were pleural effusions, pneumomediastinum and pulmonary embolism that were noted in 8 patients (17.02%), all of which had a severe CT score above 18 points. Mild and moderately severe degrees of CT changes were observed in the age group of 40-55 and 55-70 years, while more severe CT changes were the most commonly observed in the age group 70-85 years. There was a moderately positive and statistically significant correlation between the CT score and patient's age, while there was a weak and statistically insignificant positive correlation between the CT score and body weight, as well as the patient's gender. We can conclude with the importance of chest CT as a diagnostic and predictive tool in patients with COVID-19. There should be a consensus in the definite diagnosis of COVID-19 based on clinical findings, positive

nCov PCR tests and radiological findings. Demographic features can aid in the prediction of severity and outcome of the disease.

## References


1. https://www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=Cj0KCQjwi7y-CBhDJARIsAMWFScNwvxOPPeXrRGZDnLuegxzGSPQUPYtx0Nx-VVCsk-LYqs5SmDJQYIaAijUEALw_wcBCoronavirus Disease (COVID-19)-World Health Organization. Accessed February 15th, 2021.
2. Wuhan Municipal Health Commission website. Report of clustering pneumonia of unknown etiology in Wuhan City. Available at: Wjw.wuhan.gov.en/front/web/showDetail/2020011109035. Accessed February 15th, 2021.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in Lancet. 2020 Jan 30;:]. *Lancet*. 2020;395 (10223):497-506. doi:10.1016/S0140-6736(20)30183-5.
4. K. Li, Y. Fang, W. Li et al., CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19); European Radiology, 2020; vol. 30, no. 8, pp. 4407-4416.
5. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol*. 2020;30(12):6808-6817. doi:10.1007/s00330-020-07033-y.
6. Pan F, Ye T, Sun P et al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology. 2020 Jun;295(3):715-721. doi: 10.1148/radiol. 2020200370. Epub 2020 Feb 13. PMID: 32053470; PMCID: PMC7233367. Available at: https://pubmed.ncbi.nlm.nih.gov/32053470/.




*ORIGINAL ARTICLE* UDK: 614.253.1/.5:616-089.5

# HEALTH BEHAVIOURS AND THEIR RELATIONSHIPS WITH JOB DEMANDS AND BURNOUT IN ANAESTHESIA HEALTH WORKERS

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## ABSTRACT

The **aim** of this study was to examine the associations between burnout and health behaviours in a sample of anaesthesia health workers (HWs).

**Material and Method**

79 anaesthesia HWs (29 physicians, 50 nurses) participated in this cross-sectional study (aged 40.2±10.8 years, 81% females). For the evaluation of health behaviours, the questionnaire constructed for the study of Moustou et al. was used. Job demands and burnout were measured by Hospital Experience Scale and Maslach Burnout Inventory, respectively. A series of multiple regression models were tested to examine the associations of burnout to health behaviours, whereby controlling of age, hospital's and unit's tenure, as well as job demands.

**Results**

Only 57% of the participants had breakfast every day or almost every day. Anaesthesia HWs consumed fast food on average of 2.47 (SD=2) times a week. Even 63.3% of the respondents didn't exercise at all. Out of 79 respondents, 29 (36.7%) were smokers. Average scores of emotional exhaustion and depersonalization were 25.34±12.95 and 4.7±5.57, respectively. Results showed that emotional exhaustion positively predicted number of cigarettes smoked per day, frequency of using pills in order to relax and painkillers. Additionally, depersonalization positively predicted number of cigarettes smoked per day, frequency of using pills in order to relax and non-pharmaceutical remedies in order to relax/sleep, and number of drink units per time after leaving work and when going out.

**Conclusion**

Job demands and burnout predicted health behaviours in anaesthesia HWs. Preventive strategy has to be developed in order to improve health and safety of anaesthesia HWs.

***Key Words:*** *anaesthesia, burnout, health behaviours, health workers, job demands.*

## Introduction

Job stress usually involves different reactions of the human organism to the detrimental physical or emotional hazards at the workplace. It is important to notice that workplace pressures and job demands are not always hazardous. They are particularly effective when job resources are insufficient and when there is a gap between the job demands and the knowledge, skills and needs of the worker (1,2). Burnout syndrome, characterized mostly by emotional exhaustion and depersonalization, develops as a result of the chronic workplace exposure to physical, emotional, cognitive, organizational, and interpersonal psycho-social hazardous determinants (3,4). Psycho-social workplace factors could be related either to high job demands that require emotional and cognitive efforts in workers, or to reduced job resources which could lead to withdrawal behavior (depersonalization) and disengagement (5,6,7,8,9). The aforementioned relationships are the main elements of the proposed Job Demands-Resources (JD-R) Model of burnout development. However, the actual study puts focus on job demands and burnout and their associations to health behaviors.

Why health behaviors? Burnout has been linked to a variety of organizational (e.g. or enterprise-related or organization-related) and personal (e.g. worker-related) effects. The organization could be affected in terms of increased absenteeism and turnover of workers, reduced effectiveness and quality of work, as well as affected image of the company. Personal effects of burnout could be manifested as health-related problems, mostly recognized as cardiovascular and musculoskeletal problems or psychosomatic discomfort (10,11,12). Emotional changes, such as anxiety and depression, cognitive difficulties in working or learning, and practicing risky health behaviors are well documented in scientific literature on burnout predictors and consequences. Health behaviors are actions taken by the individuals (either risky or protective behaviors) and they could affect individuals' health. Protective behaviors, such as sleeping enough hours per night or regular practicing of exercise, could improve the health of individuals, while risky behaviors, such as smoking, fast food or alcohol consumption could result in disease development. Despite the importance of health behaviors in the etiology of non-communicable diseases, the associations between burnout and health behaviors have been rarely studied in our country (13).

Anesthesia, including intensive care medicine, is characterized by high job demands and workplace pressures. The health workers (HWs) in anesthesia department administer anesthetics to eliminate or reduce pain in patients during surgery or another healthcare procedure, either diagnostic or therapeutic. They also provide special care to critically ill patients and have tasks to prepare the patients before surgical interventions. Anesthesia HWs deal with long working hours, under time-pressure, during rotating and night shifts, sometimes giving care to critically ill patients in high-risk working context leading to high incidence of burnout in this healthcare sector (14,15,16,17).

The aim of this actual study was to examine the associations between burnout and health behaviors in a sample of anesthesia HWs. Scientific data obtained from studies conducted in HWs have shown that burnout decreases with age and working experience, while it increases with increased job demands. Therefore, age, hospital and unit tenure, as well as job demands, were examined as potential confounders (18,19).

## Material and Method

The actual survey was conducted during June-September 2018 within regular preventive medical examinations of anaesthesia HWs. The study instrument together with an invitation letter and information about the study was sent to anaesthesia HWs working in a tertiary-level clinic that is a part of the Faculty of Medicine in Skopje.

A questionnaire constructed for the purposes of the study of Moustou et al. was used for the assessment of both high-risk behaviors (drinking - frequency of drinking, drink - units consumed, smoking - frequency of smokers and number of cigarettes per day, and unhealthy eating - fast food meals per week) and protective health behaviors (exercise - frequency of exercise per week, healthy eating - number of breakfasts per week, number of regular meals per day, and sleeping - hours of sleeping per night) (10).

The Hospital Experience Scale (HES) was constructed and developed for the evaluation of job demands (http://orcab.web.auth.gr/). HWs noted the level of agreement with items focusing on physical (seven items, $\alpha$=0.71), organizational (six items, $\alpha$=0.73), emotional (six items, $\alpha$=0.72) and cognitive (five items, $\alpha$=0.71) job demands using a 5-point Likert scale (1=never to 5=always). We calculated mean score for each of the four types of job demands.

Maslach Burnout Inventory (MBI) (20) was used for the assessment of burnout. Emotional exhaustion (nine items, $\alpha$=0.91) and depersonalization (five items, $\alpha$=0.76) were measured on a 7-point Likert scale (0=never to 6=every day). The sum score was calculated for each burnout dimension.

The final sample consisted of 79 anaesthesia HWs (29 physicians and 50 nurses, aged 40.2±10.8 years, 81% females) who have returned filled-in questionnaires. They worked for an average of 200.71 (SD=143.29) months at the same hospital and 168.25 (SD=127.45) months within the same unit. 56 (70.9%) of all respondents were married or lived together with their partner and 71 (89.9%) of them reported full-time contract as a type of employment. They worked for in average of 38.46 hours per week (SD=2.98).

Bivariate analyses were used to evaluate the associations between health behaviours, job demands, and burnout dimensions. Additionally, in order to examine the role of emotional exhaustion and depersonalization, controlling for age, hospital tenure, unit tenure and job demands, a hierarchical multiple regression model was tested for each health behaviour that was shown to be significantly associated to at least one burnout dimension. Age, hospital tenure and unit tenure were entered in the first step, four types of job demands were entered in the second step, while emotional exhaustion or depersonalization was entered in the third step.

## Results

### Descriptive Data

Only 45 (57%) of the participants had breakfast every day or almost every day. The same frequency of examinees had at least three regular meals in a day. Anaesthesia HWs consumed fast food on average of 2.47 (SD=2.003, range 0-7) times a week. Even 50 (63.3%) of the respondents didn't exercise at all. On average, HWs slept 6.37 (SD=1.4) hours per night. Out of 79 respondents, 29 (36.7%) were smokers. The mean number of cigarettes smoked per day was 4.9 (SD=7.66). Anaesthesia HWs consumed alcohol, regardless of the quantity, on average 1.03 times per week (SD=1.52) and consumed on average 1.11 drink units (SD=1.15) per time. Finally, they consumed on average 0.2 (SD=0.52), 0.18 (SD=0.58), 1.2 (SD=1.29) drink units per time in each of the following occasions: after leaving work, before going to bed at night, and when going out, respectively. Data showed that 16.5%, 13.9%, 16.5%, and 50.6% of all participants, at least once a week, used sleeping pills, pills in order to relax, non-pharmaceutical remedies in order to relax/sleep, and painkillers, respectively.

The average score of emotional exhaustion was 25.34 (SD=12.95), while the average score of depersonalization was 4.7 (SD=5.57). The mean scores of physical, organizational, emotional, and cognitive job demands were 3.99 (SD=0.6, range: 2-5), 3.02 (SD=0.73, range: 1.5-5), 2.32 (SD=0.76, range: 1-5), and 2.75 (SD=0.85, range: 1-5).

### Findings of Bivariate Analyses

Bivariate analyses revealed significant associations between emotional exhaustion and:

- number of regular meals per day ($r$=-.23, $p$=0.04),
- number of cigarettes smoked per day ($r$=.31, $p$=0.006),
- frequency of exercises per week ($r$=-.25, $p$=0.028), as well as
- frequency of using pills in order to relax ($r$=.34, $p$=0.003), non-pharmaceutical remedies in order to relax/sleep ($r$=.27, $p$=0.019), and painkillers ($r$=.35, $p$=0.00) per week.

Depersonalization demonstrated significant correlations to:

- number of cigarettes smoked per day ($r$=.29, $p$=0.011),
- frequency of alcohol consumption (regardless of the quantity) per week ($r$=.25, $p$=0.033),
- number of drink units per time after leaving work ($r$=.31, $p$=0.006) and when going out ($r$=.37, $p$=0.001), as well as
- frequency of using pills in order to relax ($r$=.27, $p$=0.018) and non-pharmaceutical remedies in order to relax/sleep ($r$=.42, $p$<0.001) per week.



### Findings Obtained by Testing Hierarchical Multiple Regression Models

Table 1 shows the standardized beta coefficients for the independent predictors of certain health behaviours.

**Table 1.** *Standardized beta coefficients for the independent predictors of health behaviours*

| | Number of regular meals per day | Number of cigarettes per day | | Frequency of exercise per week | Pills in order to relax | | Non-pharmaceutical remedies in order to relax/ sleep | Pain-killers | Drink units after leaving work | Drink units when going out |
|---|---|---|---|---|---|---|---|---|---|---|
| **Emotional exhaustion** | -.075 | .288* | / | -.24 | .355* | / | -.174 | .254* | / | / |
| **Depersonalization** | / | / | .304* | / | / | .322* | .478** | / | .31* | .376** |
| **Age** | .592 | -.394 | -.377 | -.332 | .224 | .184 | -.017 | .242 | -.145 | -.341 |
| **Hospital tenure** | -.661* | .729 | .762* | .214 | .193 | .3 | .881* | .856* | .68 | .304 |
| **Unit tenure** | mc | -.221 | -.183 | .017 | -.3 | -.274 | .609* | .861** | .582* | -.273 |
| **Physical JDs** | -.275* | -.008 | .047 | .091 | .107 | .155 | -.113 | .06 | .203 | .092 |
| **Organizational JDs** | .02 | .275 | .289 | -.124 | .026 | .046 | -.018 | .044 | .039 | -.032 |
| **Emotional JDs** | .005 | -.111 | -.056 | -.179 | -.012 | .043 | .003 | -.065 | -.24 | -.143 |
| **Cognitive JDs** | .041 | -.312 | -.381 | .251 | -.147 | -.191 | .076 | -.014 | .018 | -.05 |
| **$R^2$ for the Model** | .196 | .242 | .256 | .106 | .179 | .177 | .365 | .353 | .228 | .285 |
| **$\Delta R^2$ for Step 3** | .004 | .054* | .068* | .037 | .08* | .078* | .122** | .052* | .072* | .106** |

*$p<0.05$, **$p<0.01$
*mc - removed due to possible multicollinearity (standardized beta above 1)*

The results showed that emotional exhaustion positively predicted number of cigarettes smoked per day ($\beta$=.288, $p$<0.05) ($R^2$ for the model=.242), frequency of using pills in order to relax ($\beta$=.355, $p$<0.05) ($R^2$ for the model=.179), and frequency of using painkillers ($\beta$=.254, $p$<0.05) ($R^2$ for the model=.353). The frequency of using painkillers was also predicted by hospital ($\beta$=.856, $p$<0.05) and unit ($\beta$=.861, $p$<0.01) tenure.

Additionally, results demonstrated that depersonalization positively predicted number of cigarettes smoked per day ($\beta$=.304, $p$<0.05) ($R^2$ for the model=.256), frequency of using pills in order to relax ($\beta$=.322, $p$<0.05) ($R^2$ for the model=.177), frequency of using non-pharmaceutical remedies in order to relax/sleep ($\beta$=.478, $p$<0.01) ($R^2$ for the model=.365), and number of drink units per time after leaving work ($\beta$=.31, $p$<0.05) ($R^2$ for the model=.228) and when going out ($\beta$=.376, $p$<0.01) ($R^2$ for the model=.285). The number of cigarettes smoked per day was also predicted by hospital tenure ($\beta$=.762, $p$<0.05), the frequency of using non-pharmaceutical remedies in order to relax/sleep by hospital ($\beta$=.881, $p$<0.05) and unit ($\beta$=.609, $p$<0.05) tenure, while the number of drink units per time after leaving work was positively predicted by unit tenure ($\beta$=.582, $p$<0.05).

Apart from burnout dimensions, the number of regular meals per day was negatively predicted by hospital tenure ($\beta$=-.661, $p$<0.05) and physical job demands ($\beta$=-.275, $p$<0.05) ($R^2$ for the model=.196).

## Discussion

Data obtained from this study showed high emotional exhaustion (average 25.3) and depersonalisation (average 4.7) scores which is comparable to previous studies conducted in HWs (21). However, our previous studies in hospital HWs demonstrated lower burnout levels (22). To our knowledge, compensatory efforts that are effective in the early stages of burnout development

and which are stemming from high job demands were less effective in this group of workers (23). Those psychological processes are developed in each individual with a purpose of increasing the level of the performance. Another goal of the compensatory efforts is to reduce the associated psychological costs in workers and to prevent the individuals from depersonalisation.

Job resources according to the JD-R Model are important hospital protective factors, but they've also been presented as less effective in the HWs from the actual survey. Our previous study in HWs working in a general hospital demonstrated that the mean values of emotional exhaustion and depersonalization were significantly higher when the follow-up was conducted three years later from the baseline survey (24). It was concluded that high job demands (namely, job demands were also significantly increased between baseline and follow-up evaluation), consume workers' mental and physical resources, resulting in emotional exhaustion (25).

In the actual study, it was found that anaesthesia HWs mostly followed sedentary lifestyle and even 63.3% didn't exercise at all. These data showed that HWs didn't practise the recommended regular physical activities (26). They also experienced unhealthy diet showing that fast food was consumed on average 2.47 times per week (27). Additionally, only 57% of the participants had breakfast every day or almost every day and only 57% of them had at least three regular meals in a day. Cigarette smoking seemed to be frequent (36.7% HWs were smokers). While alcohol consumption was infrequent, participants frequently used pills and painkillers.

These findings demonstrate the potential risk for anaesthesia HWs' health and well-being due to their unhealthy lifestyle (e.g. physical inactivity, fast food consumption, smoking and frequent use of pills and painkillers) (26,27). The inappropriate use of painkillers increases the risk of other disease, damages, and interactions with other drugs (28,29,30).

The actual study demonstrated that emotional exhaustion was related to increased quantity of smoking and increased frequency of using pills and painkillers. Quantity of smoking was also positively predicted by depersonalization. Depersonalization itself was related to increased frequency of using pills and non-pharmaceutical remedies, and increased quantity of drinking after leaving work and when going out. The more that anaesthesia HWs experienced job burnout, the more they tended to smoke, to use pills and to drink socially. Additionally, less frequent regular meals per day were predicted by physical job demands. The more that participants felt that there was excessive workload at the hospital, the more that they felt time pressures or lack of staff and supplies, the more they tended to have irregularly meals per day.

The relationships of health behaviours with burnout and job demands have been detected in other studies conducted in HWs' (28). Associations between burnout and smoking were shown in the nursing staff in intensive care units and mental health professionals (31,32). Burnout predicted more frequent painkiller use in human service workers, including HWs (33). Burnout was also related to increased alcohol consumption in dentists, emergency physicians, surgeons and ambulance workers (10, 34-37). Finally, working more than 40 hours per week was associated to time-related barriers to healthy eating in young adult men (38).



The relationships of health behaviours with job demands and burnout are part of the pathological process that affects workers' health. Job demands exhaust employees' psychological and physical resources and lead to health problems via burnout. The findings of the actual study are in line with the theoretical and empirical data concerning the existence of an energetic process involving job demands - burnout - poor health (38,39). Within this process, high risk behaviours are one of the potential mechanisms that link burnout with poor health (40).

However, this study was cross-sectional with a reduced capacity to make causal conclusions. Besides that, we included several confounding factors (age, tenure, job demands), it is possible that some were missed in the models. Particular response bias is also possible, because HWs with high levels of burnout tend to have reduced motivation for participation in surveys of this type. Also, a "healthy worker effect" may have under-estimated the levels of burnout in the total sample.

## Conclusion

Job demands and burnout predicted several health behaviours in anaesthesia HWs. These associations remained significant after inclusion of some confounding factors. Moreover, the study of risk behaviours in HWs is important because the health behaviours can have a negative impact on health and wellbeing and also in the context of HWs' roles as healthcare providers. Risk health behaviours are known factors that could contribute to medical errors and inadequate patient safety. Therefore, they could be erosive for occupational performance, wellbeing at work and quality of care provided to the patients.

As a conclusion, a preventive strategy has to be developed in order to improve health and safety of anaesthesia HWs. Occupational health services have to be focussed on early detection of burnout in HWs, as well as development and implementation of specific action research interventions in hospital settings. The action research process should take into account the findings that job demand and burnout predicted unhealthy behaviours in anaesthesia HWs. Those interventions together with appropriate management of job demands could effectively improve the health of HWs, as well as to improve quality of patients' care.

## Author Contributions

DM and PK gave the idea and created the design of the study. DB, IM, and ZM were involved in the data collection. DM and SS performed the statistical data analysis. All authors equally contributed to the writing of the manuscript.

## References

1. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Stress at Work. DHHS (NIOSH) Publication No. 99–101. Cincinnati, OH: National Institute for Occupational Safety and Health (NIOSH); 1999.

2. Leka S, Griffiths A, Cox T, Institute of Work, Health & Organizations. Work Organization and stress: systematic problem approaches for employers, managers and trade union representatives. Geneva: World Health Organization (WHO); 2004.
3. Maslach C, Leiter MP. The truth about burnout. San Francisco, CA: Jossey-Bass; 1997.
4. Leiter MP, Maslach C. Burnout and health. In: Baum A, Revenson T, Singer J, Eds. Handbook of health psychology. Hillsdale, NJ: Lawrence Earlbaum; 2000.
5. Demerouti E, Bakker AB, Nachreiner F, et al. The job demands-resources model of burnout. J Appl Psychol. 2001; 86:499-512. https://doi.org/10.1037/0021-9010.86.3.499
6. Demerouti E, Bakker A. The Job demands-resources model: Challenges for future research. SA Journal of Industrial Psychology. 2011; 37(2):1-9.doi:10.4102/sajip.v37i2.974
7. European Heart Network. Social factors, work, stress and cardiovascular disease prevention. Brussels: European Heart Network; 1998.
8. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Proposed National Strategy for the Prevention of Psychological Disorders. DHHS (NIOSH) Publication No. 89-137. Cincinnati, OH: National Institute for Occupational Safety and Health (NIOSH); 1988. Available at: http://www.cdc.gov/niosh/docs/89-137/pdfs/89-137.pdf (Accessed 02.01.2020).
9. Maslach C, Schaufeli WB, Leiter MP. Job Burnout. Annu Rev Psychol. 2001; 52:397-422. doi:10.1146/annurev.psych.52.1.397.
10. Moustou I, Panagopoulou E, Montgomery AJ, et al. Burnout predicts health behaviors in ambulance workers. The Open Occupational Health & Safety Journal. 2010; 2: 16-18.
11. Faragher EB, Cass M, Cooper CL. The relationship between job satisfaction and health: a meta-analysis. Occup Environ Med. 2000; 62: 105-112.
12. Mijakoski D, Karadzinska-Bislimovska J, Bislimovska D, et al. Associations between burnout and subjective musculoskeletal complaints in surgery health professionals. Mac Med Review. 2019; 73(3): 140-149.
13. Bislimovska D, Pazheska-Dimitrioski E, Andonov G, et al. Health behaviours and burnout in pediatric health workers. Книга на апстракти на 20ти Конгрес на МЛД, Скопје (онлајн), 10-20 ноември 2020.
14. Wong AV, Olusanya O, Burnout and resilience in anaesthesia and intensive care medicine. BJA Education. 2017; 17(10): 334-340. https://doi.org/10.1093/bjaed/mkx020 .
15. Van Der Wal R, Bucx M, Hendriks J, et al. Psychological distress, burnout and personality traits in Dutch anaesthesiologists: a survey. Eur J Anaesthesiol. 2016; 33: 179-186.
16. Milenovic M, Matejic B, Vasic V, et al. High rate of burnout among anaesthesiologists in Belgrade teaching hospitals: results of a cross-sectional survey. Eur J Anaesthesiol. 2016; 33: 187-94.
17. Embriaco N, Azoulay E, Barrau K, et al. High levels of burnout in intensivists. Prevalence and associated factors. Am J Resp Crit Care Med. 2007; 175: 686-696.
18. Panagopoulou E, Montgomery A, Benos A. Burnout in internal medicine physicians: Differences between residents and specialists. Eur J Int Med. 2006; 17: 195-200.
19. Steptoe A, Wardle J, Pollard TM, et al. Stress, social support and health-related behavior: a study of smoking, alcohol consumption and physical exercise. J Psychosom Res. 1996;41: 171-180.
20. Maslach C, Schaufeli WB, Leiter MP. Job burnout. Annu Rev Psychol. 2001; 52: 397-422.
21. Vahey DC, Aiken LH, Sloane DM, et al. Nurse burnout and patient satisfaction. Med Care. 2004; 42(2): II57–II66.
22. Mijakoski D, Karadzinska-Bislimovska J, Basarovska V, et al. Burnout and work demands predict reduced job satisfaction in health professionals working in a surgery clinic. OA Maced J Med Sci. 2015 Mar 15; 3(1):166-173.
23. Schaufeli WB, Bakker AB, Van Rhenen W. How changes in job demands and resources predict burnout, work engagement, and sickness absenteeism. Journal of Organizational Behavior. 2009; 30: 893-917.
24. Mijakoski D, Karadzhinska-Bislimovska J, Stoleski S, et al. Job Demands, burnout, and teamwork in healthcare professionals working in a general hospital that was analysed at two points in time. Open Access Maced J Med Sci. 2018; 6(4): 723-729.
25. Innstrand ST, Langballe EM, Espnes GA, et al. Positive and negative work–family interaction and burnout: A longitudinal study of reciprocal relations. Work & Stress. 2008; 22 (1): 1-15.
26. WHO. Global recommendations on physical activity for health. Geneva: WHO Press, Geneva; 2010.
27. Odegaard AO, Koh WP, Yuan JM, et al. Western-style fast food intake and cardiometabolic risk in an Eastern country. Circulation. 2012; 126:182–188.
28. Alexandrova-Karamanova A, Todorova I, Montgomery A, et al. Burnout and health behaviors in health professionals from seven European countries. Int Arch Occup Environ Health. 2016; 89(7): 1059-1075.
29. Dale O, Borchgrevink PC, Fredheim OMS, et al. Prevalence of use of non-prescription analgesics in the Norwegian HUNT3 population: impact of gender, age, exercise and prescription of opioids. BMC Public Health. 2015; 15: 461.
30. Samuelsen PJ, Slordal L, Mathisen UD, et al. (2015) Analgesic use in a Norwegian general population: change over time and high-risk use - The Tromso Study. BMC Pharmacol Toxicol. 2015; 16: 16.
31. Fernandes LS, Nitsche MJT, Godoy I. Association between burnout syndrome, harmful use of alcohol and smoking in nursing in the ICU of a university hospital. Cien Saude Colet. 2018; 23(1): 203-214.
32. Xia L, Jiang F, Rakofsky J, et al. Cigarette smoking, health-related behaviors, and burnout among mental health professionals in China: a nationwide survey. Front Psychiatry. 2020; 11: 706.
33. Kristensen TS, Borritz M, Villadsen E, et al. The Copenhagen burnout inventory: a new tool for the assessment of burnout. Work Stress. 2005; 19: 192-207.
34. Gorter RC, Eijkman MAJ, Hoogstraten J. Burnout and health among Dutch dentists. Eur J Oral Sci. 2000; 108: 261-267.
35. Winwood PC, Winefield AH, Lushington K. The role of occupational stress in the maladaptive use of alcohol by dentists: a study of South Australian general dental practitioners. Aust Dent J. 2003; 48:102-109.
36. Goldberg R, Boss RW, Chan L, et al. Burnout and its correlates in emergency physicians: four years' experience with a wellness booth. Acad Emerg Med. 1996; 3: 1156-1164.
37. Oreskovich MR, Kaups KL, Balch CM, et al. Prevalence of alcohol use disorders among American surgeons. Arch Surg. 2012; 147: 168-174.
38. Schaufeli WB, Bakker AB. Job demands, job resources, and their relationship with burnout and engagement: a multi-sample study. J Organiz Behav. 2004; 25: 293-315.
39. Schaufeli WB, Bakker AB. Werk en welbevinden: Naar een positieve benadering in de Arbeidsen Gezondheidspsychologie (Work and well-being: Towards a positive occupational health psychology). Gedrag & Organisatie. 2001; 14: 229-253.
40. Melamed S, Shirom A, Toker S, et al. Burnout and risk of cardiovascular disease: evidence, possible causal paths, and promising research directions. Psychol B. 2006; 132: 327-353.

# POSTERIOR MALLEOLUS FRACTURES – REVIEW OF THE CURRENT KNOWLEDGE AND SINGLE CENTER EXPERIENCE

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## SUMMARY

Posterior malleolar component of the ankle fractures has gained increased interest during the past decade. Several studies emphasized enormous variety of patterns of the fracture of the posterior malleolus and suggested the necessity of the recognition of its importance. Furthermore, the intimate relation of the posterior malleolar fracture with the distal tibiofibular syndesmosis has been elucidated. The traditional approach to fix the posterior malleolus based on its size as measured on the lateral x-rays, has also been questioned – radiographs have been demonstrated as inadequate for determining the size of the fracture fragment. Direct open reduction and internal fixation of the posterior malleolus via posterolateral or posteromedial approach has been recommended. Currently, in the most of the hospitals worldwide new treatment recommendations are not widely used. Also, CT scans are not routine work up for malleolar fractures. The goal of obtaining the best functional result following surgery should always be a subject of reevaluation. New achievements in a theory of surgery gain their real practical meaning in terms of patient's benefit, only when diligently applied in practice.

***Key Words:*** *ankle, classification, posterior malleolus, reduction, stability*

## Introduction

Fractures of the posterior malleolus represent about 46% of displaced Weber B and C ankle fractures (1-3). Anatomically, those are fractures of the posterior edge of the tibia, and they still represent one of the controversial aspects in relation to the treatment of the fractures of the ankle (4,5). This problem has been investigated for more than 200 years, but despite the increased interest, significant number of published studies and widespread use of the CT scans that allow for precise morphological description of the injury, there is still no consensus on the classification and treatment of these injuries (6-8).

Historically, Earle, in 1828, was the first to describe the injury to the posterior edge of the distal tibia with displaced ankle fracture (9). Chaput's radiographic examinations in 1907 and Destot in 1911 practically introduced the term posterior malleolus in the literature (10). Handerson in 1932 introduced the term trimalleolar fracture – terminology that is still generally accepted today (11).





There is a dilemma in defining the anatomical localization, i.e. the precise description of the injury. The question is still present, whether it is a fracture of the posterior malleolus or a posterior pilon fracture. In the last decade, a significant step forward has been made in understanding the nature of this injury. However, it is not always easy to answer the question and differentiate between a posterior malleolar fracture, posterior edge of the distal tibial plateau with dislocation and a posterior tibial plafond fracture or pilon fracture caused by compressive forces. It is difficult to explain the mechanism of occurrence of these fractures using the standard Lauge-Hansen classification. Posterior malleolar fractures the most commonly occur as a result of a combination of tension, compression and shearing forces. The forces that cause trimalleolar fractures with significant dislocation, as well as multifragmentary fractures caused by compressive forces where the bone fragments occupy a large part of the articular surface already represent a transition towards posterior pilon fractures. Hence, it is quite challenging to make a precise distinction, but most of the authors recommend using the transmalleolar line as a dividing line.

The subject of the classification, as well as the treatment choice are still controversial. Opinions are divided on which fracture of the posterior malleolus should be addressed surgically. The first published case of fixation of posterior malleolus via posterior approach dates back in 1920 (4, 12, 13). However, what is still somehow a practice in today's routine work, is probably from the Nelson and Jensen classification, published in 1940, which classifies the fractures in two types: so called classic type – fractures that include more than a third of the articular surface in a profile view, and minimal – fractures that occupy less than a third of the articular surface (14). Hence, surgical treatment has been recommended for the classic type. The classic type should be operatively fixed with a screw through a posteromedial approach. The rest do not need to be fixed separately. This so-called one-third rule is still in practice worldwide, and many surgeons are still guided by this classification and recommendation. However, in order to determine the right treatment of this particular entity, a detailed analysis of the type of injury is needed. Today, using modern radiological techniques, especially CT and 3D CT, the anatomical specificity of the posterior malleolus can be accurately determined (8, 15). These techniques also allow us to determine the type of fracture with great precision, and thus to find the correct treatment.

The anatomical and biomechanical aspects of this injury should be considered first. The medial malleolus is not part of the tibial pilon, hence, it does not present the articular surface through which axial compression forces are transmitted. The movement and position of the talus are limited by the posterior malleolus (15-17). The anatomical features are also important by the fact that in the lateral view, the posterior articulating edge of the distal tibial plafond extends more distally than the anterior. The medial part of the posterior malleolus is the malleolar groove in which the posterior tibial tendon is situated (18, 19). The posterior tubercle of the distal tibia forms the posterior part of the tibial notch (incisura fibularis tibiae), an important element for

the stability, as well as correct placement of the malleolar fork (tibiofibular mortise). The posterior tubercle of the distal tibia is also the origin for the posterior tibiofibular ligament, which is important for the joint stability. Here are also the attachments to the posterior joint capsule and the intermalleolar ligament. These anatomical features give the importance of the posterior malleolus in the transmission of forces as well as the stability of the ankle (20, 21).

Several cadaveric studies have been performed to demonstrate the role of the engaged articular surface in posterior malleolar fracture and its importance on stability. The results are again inconclusive, although it seems that the inclusion of the posterior tubercle and fibular notch, have impact on the stability of the ankle, and represent a relevant factor for the stability and should not be disregarded during the treatment (20, 22, 23).

## Investigations

Initial radiological examinations of the injured ankle include standard imaging in anterior-posterior, lateral and mortise views, and posterior malleolus is the most commonly seen on lateral view, but can also be indirectly detected on anterior-posterior view. However, the most accurate and precise diagnosis is made with CT on which, the medial propagation of the fragment, i.e. the intra-fragmentary depression, is clearly visualized. 3D reconstruction can give additional information and even better visualization.

## Classification

The first classification of these injuries is practically related to the clinical use of the radiographs and this historical classification in many ways does not differ from the newer radiological classifications (24).

The AO Radiological Classification, published in 1987, distinguishes three types of posterior malleolar fractures depending on the involved articular surface (25):

- Extra-articular fracture;
- Fractures with a small fragment of the articular surface;
- Fractures with large fragment of the articular surface.

This is the basis of the modern modifications of the original AO classification which are surgically acceptable and probably the most widely used.

There are classifications that are based on the analysis of data obtained from CT. The first so-called two-dimensional CT classification was published in 2006 by Haraguchi and distinguishes three types of these fractures in which data are analyzed only from transverse sections without analysis of 2D and 3D CT reconstructions (15).

In 2015, a new, so-called 3D classification by Bartonicek and Rammelt was published, which analyzed data from transverse, sagittal and frontal planes, as well as 3D reconstruction in patients with Weber B and C ankle fractures with dislocation with a posterior malleolar fracture (26). In this classification, the fractures of the posterior malleolus are divided into four basic types with particular reference to the fibular notch:

- Type 1 – extraincisural fragment;
- Type 2 – posterolateral fragment;
- Type 3 – posteromedial, two-parts fragment;
- Type 4 – large posterolateral triangular fragment;
- Type 5 was also determined, i.e. irregular osteoporotic fracture, which was rarely observed, in 3% of the study group.

The most common type is type 2, seen in 52% of the study group.

It is noteworthy that in this study, no cases of extraarticular fragments were observed in posterior malleolus fractures. This is practically contrary to the recommended AO classification which is still widely used in clinical practice. These studies show that in all, including those of type 1 i.e. extraincisural, the part of the articular surface of the distal tibia is involved, which contributes to the severity of the injury, i.e. even in the most simple injuries according to the present classification stability of the ankle is compromised. In other words, these injuries should be carefully analyzed and treated in order to prevent late possible complications. This should be taken into account when referring to widely used AO classification.

## Indications for Surgical Treatment

The first reports for operative treatment of posterior malleolus fractures due to ankle instability, dated from the 1920 s and 1930 s (4, 12, 14, 27).

However, the real basis for surgical treatment, the principles for restoration of the articular surface of the distal tibial plafond as a basis for good postoperative results in the long term were established by the AO group, i.e. the Association for the Study of Internal Fixation (ASIF) (28-31). The basis for the indication for surgical fixation in clinical practice for a long time was, and still remains the size of the articular surface of the fractured posterior malleolus. According to this principle, posterior malleolus fracture should be fixed, if one quarter to one third of the articulating surface is involved and displacement of the fragment is greater than 2 mm, detected on the lateral view x-rays. However, recent studies using CT diagnostics show that it is virtually impossible to determine the true size of the bone fragment and articular zone involved in the fracture only by lateral radiograph view and even on 2D CT scans. Only 3D CT examination of the fracture can delineate its true nature and determine the critical size of the bone fragment and the necessity for reduction and fixation.

Using the classification of Bartonicek et al. of the posterior malleolus, based on 3D CT diagnostics of the injury, the following treatment is recommended (26):

- Type 1 (extraincisural) fractures – non-operative treatment of posterior malleolus;
- Type 2 (posterolateral) fractures – anatomical reduction and fixation of the posterior malleolar fracture, in part due to impacted intercalary fragment (Weber C), to reconstruct the

fibular notch and to provide anatomical reduction of the distal fibula to secure the stability of the tibiofibular syndesmosis;
- Type 3 (two-parts) – open reduction and internal fixation of the displaced fragments to restore tibiotalar joint congruence and stability, integrity of the fibular notch, syndesmotic stability, and medial malleolar congruence with medial fracture propagation;
- Type 4 (large triangular) – open reduction and internal fixation to restore the articular surface and ensure joint stability.

However, it should be emphasized that the choice of surgical treatment also depends on the nature of the ankle injury, which is the type of lateral malleolus fracture as well as the nature of the injury to the medial structures. This can be done through several surgical approaches and methods of open reduction and internal fixation techniques. Internal fixation can be performed with direct and indirect technique.

Overall, several surgical approaches and techniques are recommended: indirect reduction and anterior to posterior screw fixation, transfibular reduction according to Weber, direct reduction and fixation via posterolateral approach, direct reduction and fixation by posteromedial approach (32-35).

However, the choice of the surgical approach should always depend on an accurate assessment of the type of fracture. The optimal treatment for each case individually is the one that is defined by the exact morphology of the fracture based on the CT diagnosis.

Studies show that direct operative reduction and fixation of the posterior malleolus with a posterolateral and posteromedial approach is a biomechanically superior, compared to the indirect reduction and anteroposterior fixation with a screw.

## Postoperative Treatment

Postoperative treatment should be performed individually, according to the nature of the injury, type of fixation, quality of the bone and soft tissues, and the needs and expectations of the patients.

## Complications and Their Treatment

The most often the complications are related to poor reduction, regardless of the surgical approach and implant. It is necessary to make a control CT on which the position of the fixed fragments will be assessed. If the position is unsatisfactory, re-reduction should be performed to ensure a good position of the articular surface of the distal tibial plafond or correction in the presence of poor reduction of the fractured fibula which may result in poor position and impaired tibiofibular space.

Symptomatic malunion or nonunion of the posterior malleolar fragments may also occur and can be treated with a preservative osteotomy and secondary anatomical fixation if there is no or mild post-traumatic arthritis (36, 37).



In cases of severe post-traumatic arthritis, joint fusion with correction of the axis may be appropriate surgical procedure.

Post-traumatic arthritis can occur as a consequence of damage to the articular cartilage at the time of injury, or secondary, due to incongruence, when the posterior malleolus fracture has not been reduced and fixed (38-40).

## Our experience

Ankle fractures remain one of the most common injuries addressed by the skeletal surgeons worldwide. Despite significant scientific volume, treatment protocols still differ from one hospital to another. At the author's institution, total of 168 patients with ankle fractures have been operatively treated in a period of 2 years (2019 and 2020). This represents 1.28% of all operatively treated patients in the hospital. Mean age was 49.18 (range 21-76) years (46.6 years males and 49.60 years females). There was no gender predominance. In 86.2% of all cases, the ankle fracture was the consequence of a simple fall, while in the others, the injury was caused by high energy trauma. In those 13.8%, other injuries were present in 18 patients, while in 5 patients, ankle fracture was isolated injury. All the patients were operated within first 12 hours following hospital admission. According to our practice, routine preoperative CT scans were not performed, and in most of the cases, the decision on the treatment choice and type of osteosynthesis was made solely based on the x-rays. The surgery itself was performed in accordance to the AO principles. The fibular fracture was initially reduced and fixed with one-third semitubular plate, followed by the medial malleolar fracture, which was addressed with one/two malleolar screws. Posterior malleolar fractures were reduced and fixed only if the posterior fragment represented more than one-third on the profile view. Posterior malleolar fracture was reduced in indirect manner and it was fixed with one or two compression screws, placed in antero-posterior way through stab incisions (percutaneously). Once the fractures have been reduced and fixed, we checked for syndesmotic disruption demonstrated by the lateral stress test under fluoroscopic imaging; we considered the disruption to be present if there was a difference >2mm in the clear spaces (medial and tibiofibular) on the mortise views when two ankles were compared. The syndesmotic reduction was achieved with a clamp placed over the medial and lateral malleolus under fluoroscopic control and fixed with one fully threaded tricortical 3.5 mm screw.

The review of the postoperative x-rays demonstrated that of all malleolar fractures, the fracture of the posterior malleolus was present in 26% of cases (43 patients). Based on the abovementioned criterion of thirds, posterior malleolus was fixed in 28% of them (12 patients).

For the purposes of the present study, we evaluated the functional result at the minimum of 12 months post injury of the patients in whom the analysis of the preoperative x-rays demonstrated posterior malleolus fracture. We used the American Orthopedic Foot and Ankle society Score (AOFAS), which consists of three subcategories of questions related to pain, function and alignment. The best possible score presents of 100 points. The questions of alignment and range of motion are completed by the examiner.

In the group in which the posterior malleolus was fixed, the mean value of the AOFAS score was 85.33±6.7 points. In those in whom the posterior malleolus was left unfixed, the value of the score was 81.30±8.5 points. In order to compare the results, we used Student t – test, that demonstrated better result in the group in which the posterior malleolus was fixed, and the difference was presented to be statistically significant (Student t=0.43, p=0.67).

With regard to the technique used to fix the posterior malleolus, we found that in 3 out of 12 patients, the posterolateral approach with direct visualization of the fracture of the posterior malleolus and plate fixation was used, while in the others indirect reduction under fluoroscopic guidance and anterior to posterior percutaneous screw fixation was performed. The small number of those in whom direct reduction and posterior plate fixation was used, did not allow for analysis of the functional result; however, the knowledge of the significance of the posterior malleolar component of the ankle fractures will increase the rate of surgeries with direct approach.

The basic analysis of the types of malleolar fractures and the decision to operate on the posterior malleolus fractures in a single center, demonstrated low rate of fixation of the posterior malleolus fractures. New insights in the treatment of the posterior malleolar component clearly demonstrated its importance in obtaining anatomical reconstruction of the complex relationship of the anatomical structures at the level of the syndesmosis.

## Conclusion

The advancement of X-ray diagnostics, the introduction of CT into the clinical routine for the diagnosis of articular fractures, including ankle fractures, has increased interest in posterior malleolus fractures, as well as their practical significance for the final outcome of the injury.

Preoperative CT examination should become standard i.e. part of the algorithm for diagnosis of ankle fractures. Standard native radiographs are no longer sufficient for an adequate diagnosis of these injuries. Analysis of CT, 2D, and preferably in 3D, will contribute to set adequate diagnosis, and thus classification and treatment that will ultimately mean better outcomes. The 3D reconstruction will help in the differentiation of the injury, determining the main fragments for the fracture of the posterior malleolus, the involvement of the fibular notch, i.e. the fibular incisure of the distal tibia, as well as the presence of depression of the intercalary fragments. This appears to be of a greater therapeutic importance than separately observing the size of the fragment and the involvement of the articular surface. Because of this, the morphology of the injury should be carefully assessed, and surgical treatment indicated with the main goal of reconstructing the posterior tibial plafond and the fibular notch, providing adequate tibiofibular reduction, as well as ensuring the integrity of the distal posterior tibiofibular syndesmosis.

However, it is imperative to provide an individual approach i.e. choice of surgical approach and method of fixation according to the type of fracture of the posterior malleolus, but certainly as part of the treatment of ankle injury, i.e. the associated lateral and medial malleolus. The main goal is to ensure biomechanically stable fixation, which is the basis of good functional outcome.





## References


1. Jehlička D, Bartoníček J, Svatoš F, et al. Fracture-dislocations of the ankle in adults. Part I: Epidemiological evaluation of one-year group of patients. Acta Chir Orthop Tramatol Cech 2002; 69:243 – 7 [in Czech].
2. Van den Bekerom MPJ, Haverkamp D, Kloen P. Biomechanical and clinical evaluation of posterior malleolar fractures. A systematic review of the literature. J Trauma 2009;66: 279 – 84.
3. Irwin TA, Lien J, Kadakia AR. Posterior malleolus fracture. J Am Acad Orthop Surg 2013; 21:32 – 40.
4. Bartoníček J, Kostlivý K. The history of fractures of the posterior lip of the tibia in fracture-dislocations of the ankle [in Czech]. Ortopedie 2014; 8:132 – 6.
5. Bartoníček J, Rammelt S, Tuček M, et al. Posterior malleolar fractures of the ankle. Eur J Trauma Emerg Surg 2015; 41:587 – 600.
6. Yao L, Zhang W, Yang G, et al. Morphologic characteristics of the posterior malleolar fragment: a 3-D computer tomography based study. Arch Orthop Trauma Surg 2014; 134:389 – 94.
7. Magnus L, Meijer DT, Stufkens SA, et al. Posterior malleolar fracture patterns. J Orthop Trauma 2015; 29:428 – 35.
8. Meijer DT, de Muinck Keizer RJO, Doornberg JN, et al. Diagnostic accuracy of 2-dimensional computed tomography for articular involvement and fracture pattern of posterior malleolar fractures. Foot Ankle Int 2016; 37:75 – 82.
9. Earle H. Simple, succeeded by compound dislocation forwards, of the inferior extremity of the tibia, with fracture of its posterior edge, comminuted fracture of the fibula, amputation of the leg, and death. Lancet 1828 – 29; II/6:346 – 8.
10. Chaput V. Les fractures malléolaires du cou-de-pieds et les accidents du travail. Paris: Masson; 1907.
11. Henderson MS. Trimalleolar fractures of the ankle. Surg Clin North Am 1932; 12:867 – 72.
12. Ludloff K. Zur Frage der Knöchelbrüche mit Heraussprengung eines hinteren Volkmann'schen Dreiecks. Zentralbl Chir 1926; 53:390 – 1.
13. Lounsbury BF, Metz AR. Lipping fracture of lower articular end of tibia. Arch Surg 1922; 5:678 – 90.
14. Nelson MC, Jensen NK. The treatment of trimalleolar fractures of the ankle. Surg Gynec Obst 1940; 71:509 – 14.
15. Haraguchi N, Haruyama H, Toga H, et al. Pathoanatomy of posterior malleolar fractures of the ankle. J Bone Joint Surg 2006;88-A:1085 – 92.
16. Lauge-Hansen N. Fractures of the ankle. Part 2. Combined experimental-surgical and experimental-roentgenologic investigations. Arch Surg 1950; 60:957 – 87.
17. Switaj PJ, Weatherford B, Fuchs D, et al. Evaluation of posterior malleolar fractures and the posterior pilon in operatively treated ankle fractures. Foot Ankle Int 2014; 35:886 – 95.
18. Bartoníček J. Anatomy of the tibiofibular syndesmosis and its clinical relevance. Surg Radiol Anat 2003; 25:379 – 86.
19. Harper MC. Talar shift. The stabilizing role of the medial, lateral, and posterior ankle structures. Clin Orthop Relat Res 1990; 257:177 – 83.
20. Fitzpatrick DC, Otto JK, McKinley TO, et al. Kinematic and contact stress analysis of posterior malleolus fractures of the ankle. J Orthop Trauma 2004; 18:271 – 8.
21. Gardner MJ, Brodsky A, Briggs SM, et al. Fixation of posterior malleolar fractures provides greater syndesmotic stability. Clin Orthop Relat Res 2006; 447:165 – 71.

22. Hartford JM, Gorczyca JT, McNamara JL, et al. Tibiotalar contact area. Contribution of posterior malleolus and deltoid ligament. Clin Orthop Relat Res 1995; 20:182 – 7.
23. Papachristou G, Efstathopoulos N, Levidiotis C, et al. Early weightbearing after posterior malleolus: an experimental and prospective clinical study. J Foot Ankle Surg 2003; 42:99 – 104.
24. Ashhurst APC, Bromer RS. Classification and mechanism of fractures of the leg bones involving the ankle. Arch Surg 1922; 4:51 – 129.
25. Müller ME, Nazarian S, Koch P, et al. The comprehensive classification of long bones. Berlin: Springer; 1987.
26. Bartoníček J, Rammelt S, Kostlivý K, et al. Anatomy and classification of the posterior tibial fragment in ankle fractures. Arch Orthop Trauma Surg 2015; 135:506 – 16.
27. Leveuf J. Traitment des fractures et luxations des membres. Paris: Masson; 1925.
28. Weber BG. Die Verletzungen des oberen Sprunggelenkes. Bern (Switzerland): Huber; 1966.
29. Müller ME, Allgöwer M, Schneider R, et al, editors. Manual der Osteosynthese. 3. Aufl. Berlin: Springer; 1991. p. 595 – 612.
30. Zenker H, Nerlich M. Prognostic aspects in operated ankle fractures. Arch Orthop Trauma Surg 1982; 100:237 – 41.
31. Heim U. Trimalleoar fractures: late results after fixation of the posterior fragment. Orthopedics 1989; 12:1053 – 9.
32. Bois AJ, Dust W. Posterior fracture dislocation of the ankle: technique and clinical experience using a posteromedial surgical approach. J Orthop Trauma 2008; 22:629 – 36.
33. Amorosa LF, Brown GD, Greisberg J. A surgical approach to posterior pilon fractures. J Orthop Trauma 2010; 24:188 – 93.
34. Rammelt S, Heim D, Hofbauer LC, et al. Problems and controversies in the treatment of ankle fractures. Unfallchirurg 2011; 114:847 – 60.
35. Kim MB, Lee YH, Kim JH, et al. Lateral transmalleolar approach and miniscrews fixation for displaced posterolateral fragments of posterior malleolus fractures in adults: a consecutive study. J Orthop Trauma 2015; 29:105 – 11.
36. Weber M, Ganz R. Malunion following trimalleolar fracture with posterolateral subluxation of the talus: reconstruction including the posterior malleolus. Foot Ankle Int 2003; 24:338 – 44.
37. Rammelt S, Zwipp H. Intra-articular osteotomy for correction of malunions and nonunions of the tibial pilon. Foot Ankle Clin 2016; 21:63 – 76.
38. Leed HC, Ehrlich MG. Instability of the distal tibiofibular syndesmosis after bimalleolar and trimalleolar ankle fractures. J Bone Joint Surg 1984; 66-A:490 – 503.
39. Lindsjø U. Operative treatment of ankle fracture-dislocations. A follow-up study of 306/321 consecutive cases. Clin Orthop Relat Res 1985; 199:28 – 38.
40. Jaskulka RA, Ittner G, Schedl R. Fractures of the posterior tibial margin: their role in the prognosis of malleolar fractures. J Trauma 1989; 29:1565 – 70.



*ORIGINAL ARTICLE* UDK: 616.711-007.55-053.2/.6

# POSTERIOR SEGMENTAL INSTRUMENTATION AND FUSION WITH HIGH DENSITY ALL POLYAXIAL PEDICLE SCREW CONSTRUCT IN THE TREATMENT OF ADOLESCENT IDIOPATHIC SCOLIOSIS – SINGLE CENTER STUDY

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## SUMMARY

Idiopathic scoliosis is the most common type of spinal deformity in children and adolescents. This type of spinal deformity accounts for about 65% of cases. In contrast, about 15% are congenital and about 10% are secondary to neuromuscular disease. The rest are rare cases of spinal deformities as part of some syndromes. This retrospective study of 14 adolescent idiopathic scoliosis patients was performed to analyze the effectiveness of high density thoracic and lumbar all-polyaxial pedicle screws and rods construct in patients undergoing surgical correction of adolescent idiopathic scoliosis (AIS).

The studied group of patients included 12 female and 2 male patients, average age 16.8 years (12-25 at the age of surgery). The used implants were polyaxial pedicle screws and titanium-alloy rods. A combination of scoliosis correction maneuvers (rod translation, rod derotation, segmental direct vertebral derotation, compression-distraction and in-situ bending) were used depending on the individual case. Standard preoperative and postoperative scoliosis x-ray films with PA and lateral views were used for assessment of radiographic parameters. The follow-up period was in average 22.5 months (6-48 months).

We analyzed preoperative and postoperative Cobb angle, coronal balance, thoracic trunk shift, apical vertebral translation, clavicle angle, shoulder height, thoracic kyphosis, lumbar lordosis and overall sagittal balance. The initial results showed that the obtained correction of the scoliotic curve was significant. This was reflected through improvement of the analyzed radiographic parameters.

***Key Words:*** *high density construction, idiopathic scoliosis, polyaxial pedicle screw*

## Introduction

Idiopathic scoliosis is the most common type of spinal deformity in children and adolescents. This type of spinal deformity accounts for about 65% of cases. In contrast, about 15% are congenital and about 10% are secondary to neuromuscular disease. The rest are rare cases of spinal deformities as part of some syndromes.

Idiopathic scoliosis is a complex three-dimensional spinal deformity, with curvature on the side of a part of the spine, in the shape of the letter "S" or "C", greater than 10 degrees (measured radiographically according to Cobb's method), with simultaneous rotation of the vertebrae around the vertical axis. This type of spinal deformity lacks congenital anomalies in the formation and segmentation of the vertebrae.

The present rotation of the vertebrae makes the difference between the so-called structural curves and compensatory curves of the other parts of the spine.

Although the exact cause of this deformity cannot be confirmed (idiopathic scoliosis), in recent years, in the framework of basic research on the possible causes of this deformity, a genetic basis was being evaluated. About 30% of patients have a family history of spinal deformity.

Multiple gene loci have been proven to recur in patients with idiopathic scoliosis. Therefore, genetic tests are already underway to help in the early diagnosis and prognosis of the course of spinal deformity (Scoliscore test).

It occurs the most often in the period of 10-14 years of age, in the pre-pubertal and early pubertal period, therefore marked as adolescent idiopathic scoliosis. During this period, due to the active hormonal status of developing children, rapid progression of the deformity occurs. In girls, this is associated to the first menarche and there is usually a gradual progression of the deformity to the period of stunting. In boys, progression is usually faster and occurs over a shorter period of time, usually before growth stops.

Juvenile idiopathic scoliosis occurs between the ages of 4 and 10 years and accounts for about 10-15% of cases of idiopathic scoliosis. Early onset is usually associated to greater curve magnitude in adolescence.

Infantile idiopathic scoliosis occurs before 4 years of age. Over 90% of them are spontaneously corrected. For the remaining 10%, regular monitoring of the condition and assessment of possible neuraxial anomalies is required.

The clinical examination shows:

- Asymmetry of the shoulder or pelvic girdle, depending on the type of curvature;
- Positive Adams test – if vertebral rotation is present;
- Ligament laxity – in case of collagenopathy;
- Superficial sensory deficit is being exacerbated in case of neurological disorders associated to neuraxial anomalies (Figure 1).



**Figure 1**. *Characteristics of the presence of scoliosis in a patient on clinical examination.*

For radiographic assessment of the type of deformity, morphology, magnitude and growth potential, an X-ray of the spine in the PA and lateral projection are performed. The flexibility of the spine is assessed by lateral bending radiographs.

Magnetic resonance imaging is not routinely performed in these patients. It is reserved for patients with present neurological signs or atypical curves.

This retrospective cohort study of 14 patients with adolescent idiopathic scoliosis is performed to analyze the efficacy of a of high-density all polyaxial pedicle screw construct in the surgical correction of adolescent idiopathic scoliosis (AIS).

## Patients and Methods

The study analyzed the cases of 14 patients, 12 females, 2 males, with a mean age of 16.8 years (12-25 years in the period of surgery). The median follow-up period was 22.5 months (6 to 48 months). According to the Lenke Classification (1) the patients' curves were as follows (1):

**Table 1**

| Lenke classification | No. of patients | Lenke classification | No. of patients |
|---|---|---|---|
| **1A** | 1 | 3B | 1 |
| **1B** | 3 | 3C | 2 |
| **1C** | 3 | 5C | 1 |
| **2C** | 2 | 6C | 1 |

Preoperative and postoperative full spine panorama radiographs were analyzed according to the recommendations of the Spinal Deformity Study Group Guidelines, analyzed by the surgeon (2).

The following parameters were analyzed:

- Cobb angle,
- Coronal balance,
- Thoracic trunk shift,

- Apical vertebral translation,
- Clavicle angle,
- Shoulder height,
- Thoracic kyphosis,
- Lumbar lordosis,
- Sagittal balance,

The average preoperative values of the parameters were compared to the average postoperative values using the SPS 13 program.

All patients underwent posterior segmental instrumentation and fusion with a high-density construct (two implants at each instrumented level), entirely constructed of titanium polyaxial pedicle screws and titanium alloy rods. A combination of maneuvers was used to correct the deformity (rod translation, rod derotation, direct segmental derotation, compression-distraction and in-situ banding) depending on the individual case.

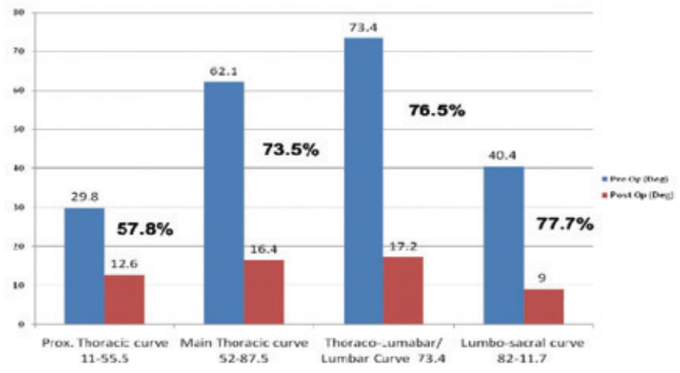
The surgeries were performed at the University Clinic for Orthopedic Surgery, Skopje.

The conduction of this study was approved form the Ethical Committee of the Medical Faculty, University "Ss. Cyril and Methodius", Skopje.

## Results

The initial analysis showed Cobb angle correction of 57.8% for proximal thoracic curves, 73.5% correction for major thoracic curves, 76.5% for thoraco-lumbar curves, and 77.7% for limbo-sacral curves (Chart 1).

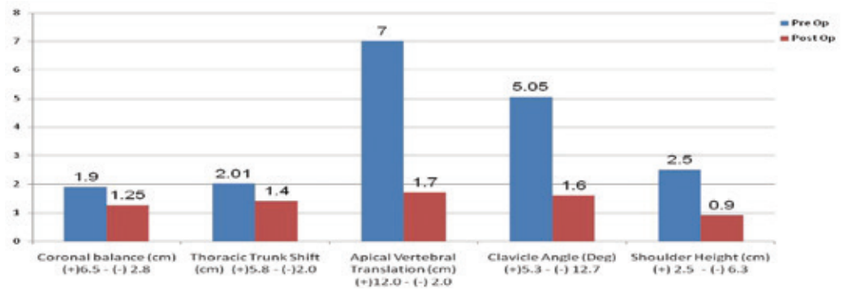
**Chart 1**. *Cobb angle correction of parts of the spine.*




The other parameters are the following:

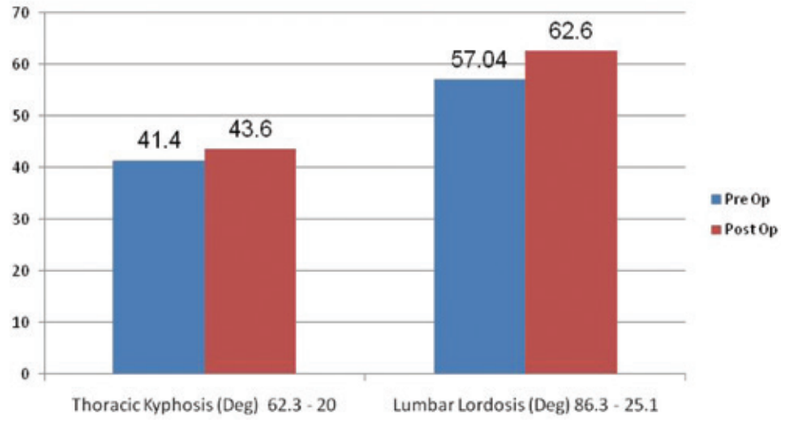
- The coronal balance preoperatively is 1.9 cm, postoperatively – 1.25 cm (+ 6.5 cm to-2.5 cm).
- Thoracic trunk shift on average preoperatively is 2.01 cm, postoperatively – 1.4 cm (+ 5.8 cm to-2.0 cm).
- Apical vertebra translation preoperatively on average is 7 cm, postoperatively – 1.7 cm (+ 12 cm to-2.0 cm).
- The clavicle angle preoperatively average is 5.05 degrees, postoperatively 1.6 degrees (+ 5.3 deg to-12.7 deg).
- Shoulder height preoperatively on average is 2.5 cm, postoperatively 0.9 cm (+ 2.5 cm to-6.3 cm) (Chart 2).

**Chart 2**. *Coronal balance correction, thoracic trunk shift, apical vertebral translation, clavicle angle, and shoulder height.*



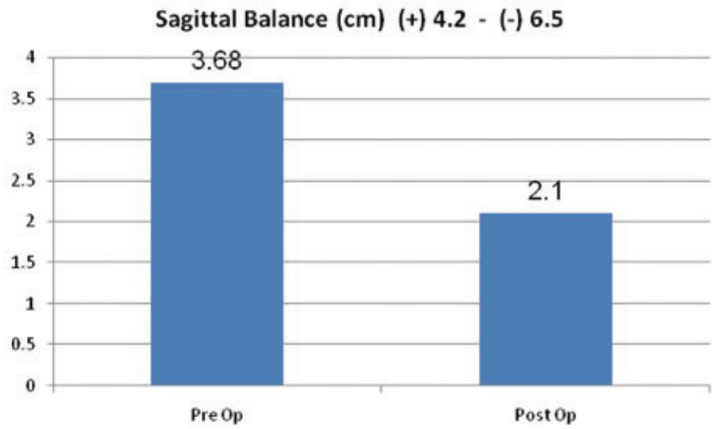

Thoracic kyphosis was corrected from an average of 41.4 degrees preoperatively, to 43.6 degrees postoperatively (20-62.3 degrees). The lumbar lordosis was on average 57.04 degrees preoperatively, to 62.6 degrees postoperatively (25.1 – 86.3 degrees). (Chart 3)

**Chart 3**. *Correction of thoracic kyphosis and lumbar lordosis.*




The average value of the sagittal balance preoperatively was 3.68 cm, postoperatively 2.1 cm (+ 4.2 cm to – 6.5 cm) (Chart 4).

**Chart 4**. *Correction of sagittal balance.*




## Discussion

Unlike in the past, today we should not focus only on the correction of the coronary deformity. The surgical strategy should be also aimed at effective correction of the sagittal and coronary alignment and balance of the spine because the closer we bring them to the normal parameters, the greater the patients' satisfaction of the surgical intervention is. Ilharebrod in his study from 2018 indicates that the current literature regarding the correction of spinal deformities does not support the preservation of mobile segments (selective fusion) and that no association has been found between distal fusion level and low back pain as a consequence of the fusion (3). The same study showed that sagittal positioning of the spine is more important than the distal instrumental level to avoid disc degeneration at adjacent non-instrumental levels.

Numerous studies on the quality of life of patients with spinal deformities have shown that scoliosis causes mental dysfunction and psychosocial problems of the patient and family that are not commensurate with the severity of the deformity (4,5). Gandehari et al. in their extensive study of 135 patients who were surgically treated, followed for two years postoperatively and evaluated with the SRS-30 questionnaire, showed that aesthetic experience and appearance is the most important factor determining patient's satisfaction and quality of life related to the health condition (6). Therefore, special attention must be paid to maximize the gibbus correction and shoulder asymmetry.

The initial analysis of the parameters in our series, as well as the "behavior" of the curves of the parts of the spine, showed consistency with the change of the parameters, and their correction in the published large series of patients treated with the same method. In a study by Lehman et al., who analyzed 114 cases of operated patients with adolescent idiopathic scoliosis, they obtained an average correction of 68% for major thoracic curve, 50% for proximal thoracic curve, and 66% for thoraco-lumbar / lumbar curve (7). In our study the correction rate is higher, but it remains to be seen whether this higher correction rate will be consistent with a larger number of patients treated.



The design of pedicle screws, whether they are polyaxial, monoaxial or uniplanar, as well as their use for the correction of spinal deformities, is a topic of constant debate. Kuklo et al. in their study comparing correction performed with monoaxial versus polyaxial pedicle screws in 35 operated patients with the most common Lenke Type 1 scoliosis, showed that the constructs with both monoaxial and polyaxial pedicle screws showed excellent coronal correction, but the monoaxial screws achieved better derotation and restoration of the thoracic symmetry (8).

A study by Blondel, Lafage et al. showed that polyaxial pedicle screws achieved significantly greater correction of thoracic kyphosis (9). This is an important fact because one of the most important features of idiopathic scoliosis is the applanation of thoracic kyphosis (hypokyphosis), which is important to correct within the sagittal positioning of the spine postoperatively.

Uniplanar pedicle screws have been presented in recent years. Although they have been shown to achieve greater apical vertebral derotation compared to polyaxial in Lenke Type 5 curves, according to a study by Tao Lin et al., no studies are yet available to confirm their efficacy in a larger series of patients with other types of curves and compared to polyaxial implants (10).

There is still debate about whether to focus on low-or high-density structures. High-density structures provide greater power of correction but are associated to longer duration of surgery and greater blood loss.

A very important element in the correction of spinal deformities is its retention. In the study by Hwang, Samdani and co-workers analyzed 800 patients regarding the reduction of the correction postoperatively (11). Decreased correction postoperatively is usually associated to the presence of pseudoarthrosis, loosening of the instrumentation, or an "adding-on" phenomenon. In their study, these factors were excluded as a reason for postoperative reduction of correction. They associated the reduced correction to a positive correlation with a greater magnitude of the thoracic curves, as well as with the use of hybrid constructs (laminar hooks in combination with the pedicle screws or sublaminar wires, which are essentially low-density structures). On the other hand, they have proven that the use of pedicle screws reduces the incidence of loss of correction.

In lower-density construct, the duration of the surgery is shorter and blood loss is lower as shown in the study by Shen et al. The important issue with low-density constructs is that they can be associated to implant loosening, and also to the possibility of "Crankshaft" phenomenon in skeletally immature patients (12,13).

## Conclusion

The analysis of our series of operated patients with adolescent idiopathic scoliosis, as well as a review of the literature on this topic, shows that the high-density construction made entirely of polyaxial pedicle screws and rods, is a powerful tool for three-dimensional correction of the adolescent idiopathic scoliosis.

## References

1. The Lenke Classification of Adolescent Idiopathic Scoliosis: How It Organizes Curve Patterns as a Template to Perform Selective Fusions of the Spine, Lawrence G Lenke 1, Charles C Edwards 2nd, Keith H Bridwell, Spine (Phila Pa 1976) 2003 Oct 15;28(20):S199-207. doi: 10.1097/01.BRS.0000092216.16155.33.
2. Spinal deformity Study Group Guildinies Radiographic Measurement Manual Medtronic Sofamor Danek; 2008 Medtronic Sofamar Danek USA, Inc. edition (2005).
3. Sagittal balance and idiopathic scoliosis: does final sagittal alignment influence outcomes, degeneration rate or failure rate?, Ilharreborde B, Eur Spine J. 2018 Feb;27(Suppl 1):48-58. doi: 10.1007/s00586-018-5472-9. Epub 2018 Jan 24.
4. A review of quality of life and psychosocial issues in scoliosis, Tones M, Moss N, Polly DW Jr. Spine (Phila Pa 1976). 2006;31(26):3027-38.
5. Health-related quality of life in patients with adolescent idiopathic scoliosis: a matched follow-up at least 20 years after treatment with brace or surgery, Danielsson AJ, Wiklund I, Pehrsson K, et al. Eur Spine J. 2001;10(4):278-88.
6. Evaluation of Patient Outcome and Satisfaction after Surgical Treatment of Adolescent Idiopathic Scoliosis Using Scoliosis Research Society-30, Hasan Ghandehari, MD, Maryam Ameri Mahabadi, MD, Seyed Mani Mahdavi, MD, et al. Arch Bone Jt Surg. 2015 Apr; 3(2): 109 – 113. Published online 2015 Apr.
7. Operative treatment of adolescent idiopathic scoliosis with posterior pedicle screw-only constructs: minimum three-year follow-up of one hundred fourteen cases, Lehman RA Jr, Lenke LG, Keeler KA, et al. Spine (Phila Pa 1976). 2008 Jun 15;33(14):1598-604. doi: 10.1097/BRS.0b013e318178872a.
8. Monaxial versus multiaxial thoracic pedicle screws in the correction of adolescent idiopathic scoliosis, T.R. Kuklo, B.K. Potter, D.W. Polly Jr. et al. Spine, 30 (2005), pp. 2113-2120.
9. Influence of screw type on initial coronal and sagittal radiological correction with hybrid constructs in adolescent idiopathic scoliosis. Correction priorities, B. Blondel, V. Lafage, J.-P. Farcy, et al. Orthop Traumatol Surg Res. 2012 Dec;98(8):873-8.
10. Comparing Uniplanar and Multiaxial Pedicle Screws in the Derotation of Apical Vertebrae for Lenke V Adolescent Idiopathic Scoliosis: A Case-Controlled Study, Tao Lin, Tangbo Li, Heng Jiang, et al. World Neurosurgery Volume 111, March 2018, Pages e608-e615.
11. Impact of Pedicle Screw Fixation on Loss of Deformity Correction in Patients With Adolescent Idiopathic Scoliosis, Steven W Hwang, Amer F Samdani, Paul Stanton, et al. Pediatr Orthop. 2013 Jun;33(4):377-82. doi: 10.1097/BPO.0b013e31828800e9.
12. Comparison of low density and high density pedicle screw instrumentation in Lenke 1 adolescent idiopathic scoliosis. Mingkui Shen, Honghui Jiang, Ming Luo, et al. BMC Musculoskeletal Disorders (2017) 18:336, DOI 10.1186/s12891-017-1695-x.
13. The effect of differing spinal fusion instrumentation on the occurrence of postoperative crankshaft phenomenon in adolescent idiopathic scoliosis. Tao F, Zhao Y, Wu Y, et al. Spinal Disord Tech. 2010 Dec;23(8):e75-80.




*CASE REPORT* UDK: 616.72-002-089:616.151.5

# FIRST MAJOR ELECTIVE ORTHOPEDIC SURGERY IN A PATIENT WITH SEVERE HEMOPHILIA A AND FACTOR VIII INHIBITORS IN MACEDONIA

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## ABSTRACT

Orthopedic surgery in patients with hemophilia and inhibitors is not straightforward due to the increased bleeding risk compared to the patients without inhibitors during the surgical procedure. We describe the use of rFVIIa using the Giangrande protocol for the first elective orthopedic surgery in a patient with severe hemophilia A and inhibitors performed in Macedonia, a country with limited resources.

***Key Words:*** *hemophilia, inhibitors, orthopedic surgery, rFVIIa*

## Introduction

Plasma-derived factor VIII (FVIII) concentrates and the subsequent development of recombinant FVIII (rFVIII) products have advanced care and contributed to better outcomes in patients with hemophilia A (1-3). An adverse consequence of exposure to FVIII replacement therapy is the risk of developing anti-FVIII neutralizing antibodies (inhibitors) that markedly reduce the effectiveness of the treatment, with consequent bleeding events (3). Inhibitor incidence rates of up to 30% have been reported in patients with severe hemophilia A (3).

Repeated bleeding into joints may lead to synovitis, joint instability and progressive arthropathy in people with hemophilia (4-7). Patients with inhibitors have a greater incidence of joint abnormalities and more rapid progression of arthropathy than those without inhibitors and they experience a greater range of joint motion limitations and joint pain at an earlier age (8). Furthermore, patients with high-titres of inhibitors have substantially worse clinical and radiological joint scores than patients without inhibitors, and a three-fold increased risk of disability due to joint disease progressing more rapidly (8,9).

Corrective orthopedic surgery may be the best option to improve quality of life for some patients with hemophilic arthropathy (4). However, orthopedic surgery in patients with inhibitors is not straightforward due to an increased bleeding risk compared to the patients without inhibitors (4,10). The presence of inhibitors in patients with hemophilia was previously considered as a contraindication to elective surgery (4). However, bypassing agents (i.e., rFVIIa or

plasma-derived activated prothrombin complex concentrate [pd-aPCC]) have been shown to be effective in hemostatic control in surgery and wound healing (4,10).

A consensus protocol was published in 2009 (Giangrande protocol) for elective orthopedic surgery (EOS) in patients with hemophilia with inhibitors using rFVIIa as initial treatment to control hemostasis during surgery (4). Guidance on the planning of surgery and pre-operative testing were outlined, in addition to recommendations for the bolus schedule for rFVIIa pre-surgery and 2-h follow-up doses of rFVIIa throughout surgery; advice was also provided on administration of rFVIIa following surgery and dosing prior to removal of sutures, as well as on the concomitant use of antifibrinolytic agents and fibrin sealants.

Financial resources in Macedonia are limited; therefore, it is important to secure an excellent outcome that minimizes costs when planning for and embarking on a major EOS procedure in a patient with inhibitors. Here, we report a case study of the first EOS procedure performed in Macedonia using the Giangrande protocol on a patient with severe hemophilia A and inhibitors.

## Case Report

The patient was a 53-years-old man with severe hemophilia A and a history of FVIII inhibitors. His body weight was 78 kg and height – 170 cm. He was hepatitis C antibody positive. The FVIII genetic mutation status was not known for this patient.

The patient presented with pain, decreased range of motion and instability in his left knee. This joint had been affected by numerous bleeding episodes over 30 years. In the last 2 years, the patient had experienced difficulty walking and climbing stairs because of a fixed flexed deformity of the left knee (flexion contracture with – 25°extension), but walked without aid and only occasionally used crutches.

Until the patient developed inhibitors, his hemophilia had been mainly treated with plasma cryoprecipitate and, sometimes, depending on availability, plasma-derived FVIII. Twenty years ago, he had an episode of bleeding from the oesophagus and developed inhibitors against FVIII during this episode. The bleeding was stopped with abdominal surgery and use of rFVIIa (eptacog alfa, NovoSeven, Novo Nordisk A/S, Bagsvaerd, Denmark). After the development of inhibitors, the patient was treated on-demand with bypassing therapy with rFVIIa, to which he had a good response.

Six months prior to EOS on his left knee, the patient's inhibitor titre was 12 Bethesda Units (BU). He received advice to minimize risk for bleeding episodes during this period, including more frequent use of crutches, performing minimal household activities and abstinence from alcohol. He was also advised on how to manage bleeding episodes, but there were none during this period.

As the patient had no inhibitors (0 BU) on admission to hospital, it was decided that this would be the appropriate time for him to undergo his EOS, which was a cruciate-retaining total knee endoprosthesis (cemented) to the left knee.





Although the patient had no inhibitors at this stage, the Giangrande protocol with rFVIIa, rather than FVIII, was used prior to, during and also after the procedure in order to reduce the risk of post-surgery hematoma or an anamnestic response (4). The re-occurrence of inhibitors to FVIII therapy was a particular concern because of the anamnestic response the patient had experienced twenty years ago. Another factor influencing the choice of rFVIIa was the patient's history of gastrointestinal bleeding. Furthermore, although the center had excellent clinical experience with rFVIIa, it had restricted quantities of rFVIIa to manage any potential inhibitor recurrence, and insufficient was available to provide coverage for rehabilitation after the patient was discharged from the hospital. The limited amount of rFVIIa was to be used over the period when the patient was receiving physical therapy in hospital and during the removal of sutures, and given to the patient for home use in the event of a bleed. Therefore, a modification was made to the Giangrande protocol (i.e., a higher dose of rFVIIa during and after surgery), with the hope of reducing the overall amount of hemostatic therapy.

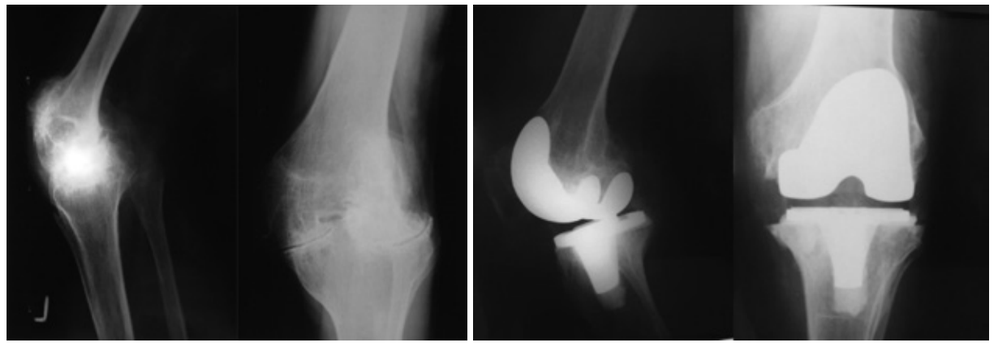
Five minutes before the surgical incision, 120 μg/kg rFVIIa was administered. Tranexamic acid (antifibrinolytic agent) was administered (750mg every 8 hours). During and after surgery rFVIIa (120μg/kg) was administered at 2-h intervals to obtain and maintain good hemostasis. The duration of surgery was 2 h 5 min (110 min to skin closure and 125 min to extubation). In the first 2 days after surgery, rFVIIa (120μg/kg) was given every 2 h; on the third and fourth day, it was given every 4 h. On the fifth day, rFVIIa (120μg/kg) was given with a 6-hours regimen with the interval increasing until discharge (day 10).

Physical therapy was started on the fourth postoperative day with only slight exercises (as tolerated by the patient) and was closely monitored by the surgeon for signs of bleeding. Antibiotic prophylaxis with ceftriaxone (2g per day) was used for the first 4 days. There was no thromboprophylactic treatment.

Pre-and post-surgery images (6 weeks after surgery) of the patient's left knee are shown in Figure 1. Pre-and post-surgery X-ray images (a day after surgery) of the patient's left knee are shown in Figure 2.

**Figure 1**. *Pre-surgery (A) and 6 weeks post-surgery (B and C) images of the patient's left knee.*

**Figure 2**. *X-ray Images of the left knee pre-surgery (A and B) and 1 day post-surgery (C and D)*



The patient made an uneventful recovery after the operation. He is walking without aid and with no pain; by one year post-surgery, he had no bleeding episodes in his left knee. The range of motion in the knee was 95° of flexion with full extension.

## Discussion

Orthopedic surgery in patients with hemophilia complicated by inhibitors is challenging and it is recommended that such procedures should only be carried out in comprehensive care centers with the requisite multidisciplinary experience and facilities (4). The advent of pd-aPCCs and rFVIIa as bypassing treatments to control hemostasis has made major orthopedic surgery possible for patients with hemophilia with inhibitors (11,12). Studies in major surgery, including orthopedic procedures, have found that rFVIIa provides consistently high hemostatic efficacy rates. Importantly, the data do not raise any unexpected safety concerns surrounding rFVIIa use. Use of rFVIIa has been a major step towards narrowing the gap in outcomes between those patients with or without inhibitors (13).

Cruciate-retaining total knee endoprosthesis was successfully carried out in this case using the Giangrande consensus protocol recommendations for use of rFVIIa to control of hemostasis. An exception from the Giangrande protocol was the use of a higher-dose regimen of rFVIIa (120 μg/kg rather than 90 μg/kg) during and after surgery (4). Due to limited resources in the center, there was little rFVIIa available for post-hospital rehabilitation. Therefore, the higher dose was used to maximize hemostasis and wound healing; thereby shortening the time to full mobility while in hospital. We considered that reducing the likelihood of a bleed with the higher dose during postoperative rehabilitation would potentially reduce the amount of hemostatic therapy required, as a bleed with a lower rFVIIa dose would necessitate an immediate dose increase and return to a decreased dosing interval.

## Conclusion

The implantation of a total knee endoprosthesis as an elective surgery was performed for the first time in the country. The success of this first EOS procedure carried out in Macedonia in the setting of limited resources opens the way for improved care for patients with hemophilia who have arthropathy in this country.

## References


1. Darby SC, Kan SW, Spooner RJ, *et al*. Mortality rates, life expectancy, and causes of death in people with hemophilia A or B in the United Kingdom who were not infected with HIV. *Blood* 2007; 110: 815-25.
2. Plug I, van der Bom JG, Peters M, *et al*. Mortality and causes of death in patients with hemophilia, 1992-2001: a prospective cohort study. *J Thromb Haemost* 2006; 4: 510-6.
3. Hermans C, Brackmann HH, Schinco P, et al. The case for wider use of recombinant factor VIII concentrates. *Crit Rev Oncol Hematol* 2012; 83: 11-20.
4. Giangrande PL, Wilde JT, Madan B, et al Consensus protocol for the use of recombinant activated factor VII [eptacog alfa (activated); NovoSeven] in elective orthopaedic surgery in haemophilic patients with inhibitors. *Haemophilia* 2009; 15: 501-8.
5. Ozcan Z. Radiosynovectomy in hemophilic synovitis. *Mol Imaging Radionucl Ther* 2014; 23: 1-4.
6. Blobel CP, Haxaire C, Kalliolias GD et al. Blood-Induced Arthropathy in Hemophilia: Mechanisms and Heterogeneity. *Semin Thromb Hemost* 2015.
7. Silva M, Luck JV, Leissinger C. Opinions on radiosynovectomy for chronic haemophilic synovitis: point/counterpoint. *Haemophilia* 2012; 18: 836-42.
8. Morfini M, Haya S, Tagariello G, *et al*. European study on orthopaedic status of haemophilia patients with inhibitors. *Haemophilia* 2007; 13: 606-12.
9. Du Treil S. Physical and psychological challenges in adult hemophilia patients with inhibitors. *J Blood Med;* 115-22.
10. Van Veen JJ, Maclean RM, Hampton KK, et al. Major surgery in severe haemophilia A with inhibitors using a recombinant factor VIIa and activated prothrombin complex concentrate hybrid regimen. *Haemophilia* 2014; 20: 587-92.
11. Ju HY, Jang HL, Park YS. The efficacy of bypassing agents in surgery of hemophilia patients with inhibitors. *Blood Res* 2015; 50: 173-8.
12. Rodriguez-Merchan EC. Aspects of current management: orthopaedic surgery in haemophilia. *Haemophilia* 2012; 18: 8-16.
13. Santagostino E, Escobar M, Ozelo M, *et al*. Recombinant activated factor VII in the treatment of bleeds and for the prevention of surgery-related bleeding in congenital haemophilia with inhibitors. *Blood Rev* 2015; 29 Suppl **1:** S9-18.

# CARPAL TUNNEL SYNDROME CAUSED BY LIPOMA

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## ABSTRACT

Carpal tunnel syndrome as a result of space occupying masses is very rare. Lipomas located in the carpal tunnel were found in small number of cases. In this case report, we present a case of a middle-aged woman with progressive muscle atrophy of the thenar and loss of sensation on the right hand innervated by the median nerve. Clinical examinations, electromyography and MRI were done, and a soft tissue mass, the most likely lipoma, was found in the carpal tunnel making pressure to the median nerve. Surgery was performed, decompression of the median nerve was provided, and results after two months showed complete improvement of the motor end sensory function of the hand.

***Key Words:*** *carpal tunnel syndrome, lipoma, median nerve.*

## Background

Lipomas were firstly described by Sir James Paget in 1856 and are one of the most common soft tissue tumors found in adults. The true incidence of lipomas is unknown, mostly because of their asymptomatic presence that doesn't obtain any medical attention (1). They are mesenchymal tumors, formed from mature adipose tissue that is slow growing and have minimal connective tissue, lying in the subcutaneous layer in the most of the cases. They can be found at every part of the human body, although is very rare in the hand, between 1 and 3.8% of all the benign tumors in the hand (2). Carpal tunnel syndrome is the most common nerve entrapment neuropathy, presented with pain, usually during nights at the beginning, numbness and paresthesia in the thumb, index, middle finger and radial side of the ring finger (3). It is a result of the median nerve compression in the carpal tunnel, caused due to the increased pressure in the carpal tunnel. Space-occupying lesions are rarely a reason for pressure to the median nerve. We present a case report of a 50-years old woman, that have been operated in our department because of the CTS caused by lipoma.

## Case Report

A 50-years-old right-handed woman was admitted to our clinic, presented with a 2-years history of right-hand numbness and pain that affect thumb, index and middle finger accompanied with the decreased grip strength. Thenar muscle atrophy was noted during the examination. She complained to us for a progression of nocturnal acroparaesthesia in the last few months. She was also

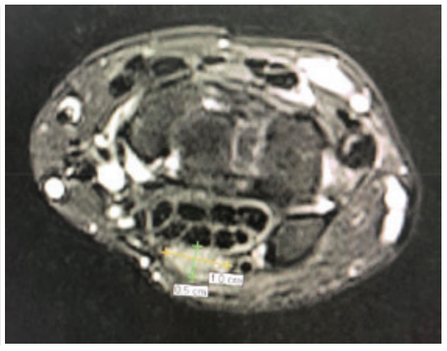




having pain in the neck region, dating for 15 years ago, and a weakness in the muscle strength also from the left side, but not as much as in her right hand. On palpation, a soft tissue mass was not found in the distal forearm, and normal range of movement was found in the wrist. In the region of median nerve innervations, decrease in the sensitivity have been noted on the both sides, more decreased in the right hand (Picture 1). Tinel's sign was positive, and electromyography of upper limb was also positive, so the diagnosis of the CTS was confirmed. MRI investigation was done, and scans of the right hand showed a perineural lipoma (1×0.5cm) that was increasing the pressure in the carpal tunnel and making pressure on the median nerve (Picture 2).

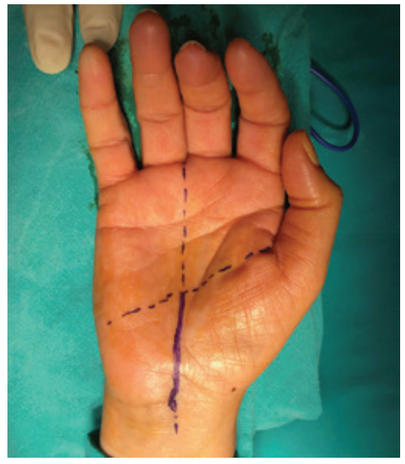
**Picture 1**

**Picture 2**



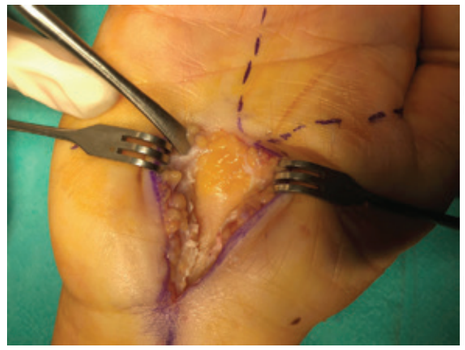
An axillary block and a tourniquet were applied while the patient was arranged in supine position. Conventional approach for skin incision (Picture 3) was used and the transversal carpal ligament was cut, and the tumor was carefully removed, releasing the median nerve from the pressure inside the carpal tunnel (Picture 4 and 5), ending with releasing the nerve from the pressure inside the carpal tunnel.

**Picture 3**

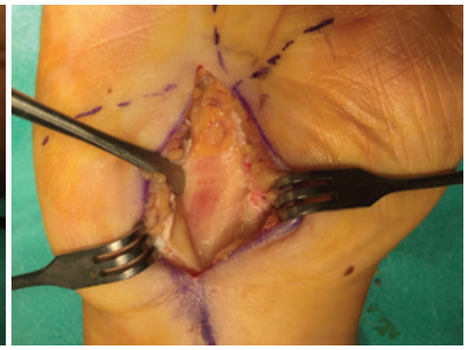


Skin was closed, light dressing with small compression have been applied, and no drainage or immobilization was used. No antibiotics was prescribed, the first check up on the first post-operative day have been done, with no sighs for inflammation or bleeding. The stitches were removed after 12 days, and in two months she has recovered full hand sensitivity and motor function without presence of the nocturnal acroparaesthesia. After two months a complete recovery of motor and sensory function was noted.

**Picture 4**



**Picture 5**



## Discussion

Tumors formed by mature adipocyte cells are known as lipomas. They are usually slow growing, encapsulated and can be infiltrating (4). When they are located superficially, can be palpated as a movable soft mass. These types of tumors are rarely located in the hand and sometimes they can cause different types of nerve compression syndromes, including interosseous nerve compression, the Gyon tunnel compression to the ulnar nerve and digital nerve compression in the palmar region (5). Lipomas, as a space occupying mass causing CTS, are very rare (6). Therefore, every unilateral CTS presented with no changes in the nerve conduction tests in the contralateral side, needs to be investigated for a space occupying masses. Preoperative investigation includes ultrasonography and MRI as a diagnostic tool. On MRI lipomas are found as a homogenous mass and provide information for size and its relations to the surrounding nerves and vessels, ensuring excellent preoperative planning. MRI suspected masses for lipomas, in the most cases were confirmed with histological findings (7). Endoscopic approach is contraindicated in cases of unilateral CTS as a result of space occupying masses. Open approach is indicated, with careful dissection and preservation of the neurovascular bundle, avoiding iatrogenic injuries of the nerve.

## Conclusion

Unilateral, secondary CTS, needed to be examined for any space occupying lesions, including lipomas, even it was rare. Clinical examination and nerve conduction tests without anomalies in the contralateral side, alerted us for possible space occupying mass, so MRI or ultrasonography needed to be done. Surgical resection of the mass had to be performed in order to remove the pressure on the median nerve and to recover motor and sensory function of the hand.

**Picture 6**

## References


1. Johnson CN, Ha AS, Chen E, et al. Lipomatous Soft-tissue Tumors. J Am Acad Orthop Surg. 2018 Nov 15;26(22):779-788. doi: 10.5435/JAAOS-D-17-00045. PMID: 30192249.
2. Amar MF, Benjelloun H, Ammoumri O, et al. Lipome compressif de la tabatière anatomique. À propos d'un cas [Anatomical snuffbox lipoma causing nervous compression. A case report]. Ann Chir Plast Esthet. 2012 Aug;57(4):409-11. French. doi: 10.1016/j.anplas.2010.07.001. Epub 2010 Aug 16. PMID: 20719424.
3. Peters S, Page MJ, Coppieters MW, et al. Rehabilitation following carpal tunnel release. Cochrane Database Syst Rev. 2016 Feb 17;2:CD004158. doi: 10.1002/14651858.CD004158.pub3. PMID: 26884379.
4. Cristofaro RL, Maher JO 3rd. Digital lipoma of the foot in a child. A case report. J Bone Joint Surg Am. 1988 Jan;70(1):128-30. PMID: 3335561.
5. Zahrawi F. Acute compression ulnar neuropathy at Guyon's canal resulting from lipoma. J Hand Surg Am. 1984 Mar;9(2):238-9. doi: 10.1016/s0363-5023(84)80149-5. PMID: 6715832.
6. Chen CH, Wu T, Sun JS, et al. Unusual causes of carpal tunnel syndrome: space occupying lesions. J Hand Surg Eur Vol. 2012 Jan;37(1):14-9. doi: 10.1177/1753193411414352. Epub 2011 Aug 8. PMID: 21825010.
7. Capelastegui A, Astigarraga E, Fernandez-Canton G, et al. Masses and pseudomasses of the hand and wrist: MR findings in 134 cases. Skeletal Radiol. 1999 Sep;28(9):498-507. doi: 10.1007/s002560050553. PMID: 10525793.

*CASE REPORT*

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# SUCCESSFUL TREATMENT OF MASSIVE PULMONARY EMBOLISM WITH CARDIOGENIC SHOCK AS A FIRST MANIFESTATION OF COVID-19 INFECTION

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## ABSTRACT

COVID-19 infected patients have increased the risk for thromboembolic complications which can cause many organ dysfunctions that leads to premature patient's mortality (1). Our patient was admitted because of sudden chest pain and shortness of breath. In order to establish the cause of hemodynamic instability urgent bed site echocardiography was performed with showed indirect signs of pulmonary embolism with right ventricular dysfunction. Pulmonary CT angiography showed the presence of massive pulmonary embolism (PE) which was complicated by right ventricular dysfunction and hemodynamic instability. The patient was successfully treated with fibrinolysis. The PCR analysis was positive for COVID-19. This is case of pulmonary embolism complicated with cardiogenic shock as a first manifestation of COVID-19 – infection at our clinic since the start of the pandemic.

***Key Words:*** *cardiogenic shock, COVID-19, pulmonary embolism.*

## Introduction

Inflammation and hypercoagulability are ones of the mechanisms responsible for thrombotic complications in patients with COVID-19 infection (1). Additionally, generalized endothelial dysfunction is also one of the main causes of increased thrombotic burden in these patients. We present a case with acute pulmonary embolism as complication of COVID-19 infection. Our patient was admitted because of sudden chest pain and dyspnea. Urgent bed site echocardiography showed indirect signs of pulmonary embolism, which was confirmed by pulmonary CT angiography and diagnosis of massive pulmonary embolism (PE) complicated by right heart failure and cardiogenic shock was established. Patient had Polymerase Chain Reaction (PCR) analysis positive for COVID-19. This case is an example of thrombotic cardiovascular complication as a first manifestation of COVID-19 – infection, where cardiovascular imaging adds to fast diagnosis and successful treatment. Focused echocardiography is very useful noninvasive widely available method, particularly when evaluating patients with undifferentiated hypotension or acute dyspnea.

## Case Report

Our patient is 73-years-old man who was examined at cardiology clinic emergency department with symptoms of sudden dyspnea, syncope and chest pain. He denied past history of cardiovascular or respiratory disease, previous PE or deep vein thrombosis (DVT). Chest pain and dyspnea started four hours before arrival at our clinic. The patient had diabetes mellitus type 2 and treated hypertension. The patient was afebrile (36.4C). Physical examination showed irregular heart rhythm, with peripheral and basal crepitation on the right lung and no heart murmurs. ECG showed atrial fibrillation with HR 120bpm and incomplete RBBB. Blood pressure was 85/45 mmHg with cold periphery. Epidemiologic questionnaire for COVID-19 infection was negative (no contacts with SARS CoV2 positive patients, no increased temperature, respiratory symptoms or recent respiratory infection). Patient did not report any PE risk factor (injury, recent surgery, prolonged bed rest, absent cancer history, no signs of DVT or previous known PE).

Immediately after the hospitalization, bed site echocardiography was performed aimed to assess the cause of patient's symptoms and hemodynamic instability. Echocardiography findings showed several signs of RV dysfunction: increased right ventricle (RV) size with D shaped left ventricle (Figure 1A), reduced RV function (TAPSE 13, TDI S' 9), presence of McConnell's sign, severe tricuspid regurgitation and presence of pulmonary hypertension (SPAP 65 mmHg) (Figure 1B). Left ventricular ejection fraction was 65%, with no wall motion abnormalities found. We did not see any thrombus in the RV cavities or pulmonary artery. We have obtained all indirect signs of the presence of pulmonary embolism with right ventricular dysfunction.

Due to hemodynamically unstable patient with cardiogenic shock fibrinolysis with Actilyse, 100 mg infusion for two hours was applied. The patient faced significant hemodynamic improvement after the first hour of Actilyse infusion, with normalization of blood pressure to 110/70 mmHg, HR 100bpm, oxygen saturation increased to 92% on room air, and respiratory rate decreased to 11/min. Patient continued with Heparin 25.000 IE infusion for 24 hours and remained clinically stable with no further episodes of dyspnea or hypoxia.

CT angiography was performed on the same day of hospital admission in order to definitely confirm PE. CT result showed large intraluminal thrombus in the right pulmonary artery with dimensions 50×12mm. Thrombotic mases were found riding over the pulmonary trunk, extending to the left pulmonary artery up to subsegmental level (Figure 2A, B). Lung parenchyma showed 4-5 pneumonic focuses with ground glass pattern located subcostally in the upper and basal paracardial zones (Figure 2C). Calculated sPESI score was 2, which implied increased 30-days mortality risk (10.9%).

Base on the hemodynamic profile, echocardiography findings of RV dysfunction, sPESI score >1 and elevated troponin levels, patient was initially assessed as high risk for early mortality.

Laboratory results showed increased leucocytes level of $15\times10^9$/l (ref $4\text{-}9\times10^9$/l), Hgb 110 g/l (ref 120-180 g/l), platelet counts $285 \times 10^9$/l (ref $150\text{-}450 \times 10^9$), leukopenia (6.8%) – range 15-50%, elevated lactate dehydrogenase of 436 U/l – range (up to 248 U/L), C-reactive protein of 99.5 mg/l (ref up to 6 mg/l), creatinine 188ng/l (range 45-109nmol/l), ferritin 476.51 mg/l (ref up to 300 mg/l). Other laboratory analyzes were within normal range. Hs-Troponin I (ABBOT Essay) was elevated – 420.6ng/l (referent values for men 0-34.2ng/l), D-dimer levels were increased – 10.000ng/ml (cut off value <500ng/ml).

After the PE was confirmed, nasopharyngeal smear for SARV CoV-2 was taken due to ongoing pandemic and result come out positive for virus RNK (real-time fluorescence polymerase chain reaction – PCR).

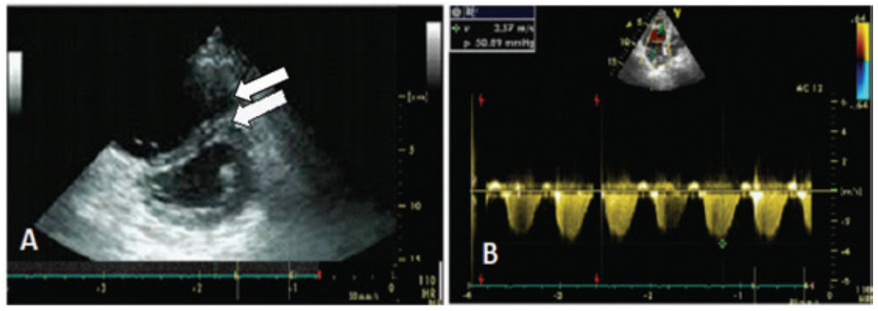
**Gas Analyses**

Gas analyses were within normal limits, with slightly decreased pCO2 levels (pH 7,41, $pCO_2$ 26 mmHg, pO2 74 mmHg, HCO3 16.5 mmol/l, S02 95%, lactate 1,5 mmol/).

## Treatment and Complication

After fibrinolytic therapy, patient continued with Heparin 25.000 IE infusion for 24 hours. Antibiotic therapy with Azithromycin 500 mg bid and Dexamethasone 4 mg intravenously was given upon laboratory and SARV CoV-2 smear results. Patient was clinically stable, without additional episodes of dyspnea or reduced oxygen saturation. The next hospital day patient was transferred to the Infectious Disease Clinic for further treatment in clinical stable condition. Patient was clinically stable and treated at the Infectious Disease Clinic for additional two weeks. He was discharged with recommendation for oral anticoagulant therapy with Rivaroxaban for the next three months. Patient was called for outpatient visit at cardiology clinic after four months. He was in stable condition with completely normalized echocardiography result and no additional thrombotic complications.

**Figure 1**. *Bedside Transthoracic Echocardiography*




*(A) Parasternal short-axis view of the heart showing a dilated right ventricle and D shape of the left ventricle. (B) Doppler echocardiographic view of severe tricuspid regurgitation.*

**Figure 2**. *CT of the Chest and CT Pulmonary Angiography.*


*(A, B) Computed tomography pulmonary angiography demonstrates multiple filling defects involving lobar and segmental branches of the right pulmonary artery and a linear saddle pulmonary embolus. (C) Axial unenhanced chest computed tomography (CT) scan shows areas of ground-glass interstitial opacities in the subcostal upper and basal paracardial zones.*





## Discussion

Over the last year, we are globally facing major health challenge caused by COVID-19 pandemic. COVID-19 infection increases patient's risk for arteriosus and venous thrombotic complications, due to several prothrombotic mechanism, which includes severe inflammatory reaction, blood stasis and generalized endothelial dysfunction (2). Clinical data report the presence of severe interstitial pneumonia in up to 15% of patients, which can cause acute respiratory distress syndrome, and in more severe cases – multiorgan failure and death (2). Scientific literature data incidence the presence of DVT or PE in approximately 30% of COVID-19 diseased patients. It is assumed that around 50% of infected patients have elevated D-dimer levels during disease progression, which is related to the increased thrombosis risk (3). Literature data showed increased intra hospital death in patients with elevated D-dimer values over 1000ng/ml (3,4). Significant correlation is found between thrombosis risk and disease severity, the fact that supports the recommendation for the use of therapeutic anticoagulation in patients with COVID-19 with elevated D-dimer levels (4). Respiratory failure associated to COVID-19 infection leads to high morbidity and mortality, with microvascular pulmonary thrombosis, playing an important pathophysiological role. Among risk factors, obesity is associated to more severe form of the disease and complications (5).

One of the explained mechanisms for COVID-19 induced thrombosis involves cytokine-mediated generalized microvascular disfunction, hypercoagulable state, tissue hypoxia, prolonged bed rest and increased platelets number (6). The risk of pulmonary embolism is additionally increased by obesity, older age, and immobilization. Our patient had increased C-reactive protein and D-dimer values with no additional PE risk factors reported, which lead us to assume that a COVID-19 infection triggered hypercoagulable state that finally resulted in massive PE. Generalized endotheliopathy induced by COVID-19 infection is assumed to persist even after the infection recovery, which also predispose the patients to increased thrombotic risk.

Heparin and LMWH have also anti-inflammatory effects, which may offer additional clinical benefits. Factor Xa inhibitors anti-viral mechanisms have been found in several researches with animals (7). Application of the therapeutic anticoagulation in selected hospitalized COVID patients without established PE/DVT has been advized. The population with specifically increased PE risks are patients with cardiovascular disease, cancer and several other comorbidities (8). The risk of major bleeding proportionally increased in older patients, patients with hepatic and renal insufficiency and known bleeding history. Fibrinolytic therapy is lifesaving for management of PE in patients with cardiogenic shock. Our patient is an example of successful treatment of massive PE with COVID-19 infection. The European Society of Cardiology's recommendation for treatment of cardiovascular disease in COVID-19 infection indicated the use of anticoagulant therapy in patients hospitalized with COVID-19. The use of therapeutic doses is indicated in high-risk patients and patients with confirmed PE (1). COVID-19 infected patients with confirmed PE who are treated with therapeutic anticoagulation should continue with anticoagulation therapy for minimum 3 months (depending on the patient's treatment tolerance and bleeding risk).

Some interesting data come from the latest publications showing no significant difference in ICU admissions, the need and duration of intubation between patients with and without PE development. Almost two thirds of the patients with diagnosed PEs did not require treatment in the ICU, which is quite opposite to the actual published study that underlines that PE is associated to ICU hospitalization and invasive ventilation (9). Our case is an example of PE as a first manifestation of COVID-19 infection, which lead to severe hemodynamic compromise. Fibrinolytic therapy leads to hemodynamic stabilization. Our patient did not require ventilatory support and he had good short-term outcome.

## Conclusions

Hospitalized patients with COVID-19 infection are population with increased risk for thrombotic events. Sudden worsening of respiratory function accompanied with high D-dimers values should raise clinical alert for pulmonary embolism as a first manifestation of the disease which requires prompt diagnosis and proper management. In hemodynamically unstable patients with massive PE, fibrinolytic therapy is lifesaving treatment option.

## References


1. ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic [Internet]. [cited 2020 Apr 27]. Available from: www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance.
2. Behnood Bikdeli, Mahesh V. Madhavan, David Jimenez et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: *JACC* State-of-the-Art Review. Journal of the American College of Cardiology. Volume 75, Issue 23, 16 June 2020: 2950-2973.
3. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of Venous Thromboembolism in Hospitalized Patients with COVID-19.2020.
4. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up. J Am Coll Cardiol 2020: S0735-1097(20): 35008-7.
5. Lin L, Lu L, Cao W, et al. Hypothesis for potential pathogenesis of SARS-CoV-2 infection-a review of immune changes in patients with viral pneumonia. Emerg Microbes Infect 2020; 9: 727 – 732.
6. Neo Poyiadji, Peter Cormier, Parth Y. Patel et al. Acute Pulmonary Embolism and COVID-19. Radiology, 2020 Dec;297(3): E335-E338.
7. Zhu N., Zhang D., Wang W., et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382:727 – 733.
8. Tang N., Bai H., Chen X., et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J ThrombHaemost, [E-pub ahead of print]. 2020 Mar 27.
9. Franck Grillet, Julien Behr, Paul Calame, et al. Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography. *Radiology*. April 2020.




*ORIGINAL ARTICLE*

UDK: 616.24-002-085.216.2:[616.98:578.834
616.98:578.834]:616.24-002-085.216.2

# EVALUATION OF THE EFFECT OF THE NEBULIZED LOCAL ANESTHETIC FOR INHALATION IN PATIENTS WITH CONFIRMED COVID-19 PNEUMONIA IN SERIES OF CASES

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## ABSTRACT

The aim of this study was to evaluate the data in 12 patients with Covid-19 pneumonia and different types of hypoxemia (mild, moderate and severe) in whom nebulized lidocaine was given and to analyze the efficiency of the lidocaine in the improvement of the oxygenation.

**Material and Methods**

12 patients with confirmed COVID-19 pneumonia aged between 22 and 72 years (mean age 53), who had dyspnea admitted to the City General Hospital "8th of September", Skopje, Macedonia were enrolled in the study. In all patients nebulized lidocaine was given at doses of 2.85 mg/kg via inhalation, four times daily. Patients' demographic, clinical data, body mass index and average number of days between illness and inhalation were collected for each of the patients.

We analyzed the level of the partial pressure of oxygen (Pao2) and level of blood saturation 5 minutes before the treatment and 30 minutes after inhalation.

**Results**

12 patients with COVID-19 pneumonia have been enrolled in this study: 9 patients (75%) were male and 3 (25%) were female. Most of the patients presented with shortness of breath (50%), 9 patients (75%) have co-morbidities and 66.7% were obese. 9 (75%) patients had opacity while 3 (25%) patients had pattern on radiological findings. At the time of presentation, the hypoxemia was mild (85-90%) in 4 patients, 3 patients had moderate hypoxemia (75-85%) and 5 patients had severe hypoxemia (50-75%). The average number of the days was 6.5 days.

**Conclusion**

We observed improvement in oxygen saturation after inhalation in all patients.

***Key Words:*** *hypoxemia, lidocaine, nabulisator, oxygenation.*

## Introduction

Large number of studies show that local anesthetics and, among them, lidocaine have effects that prevent cellular damage caused by inflammation of the lungs (1). Based on John Hopkins University Report on COVID-19 for Macedonia, there were a total of 586 new confirmed cases until November 16, 2020 (2). Since the start of the pandemic, many medicaments, even older ones, have been researched and tested for possible efficacy against COVID-19 (3). Accumulating data suggest that local anesthetics possess a wide range of anti-inflammatory effects, due to their effects on cells of the immune system (4). Additionally, lidocaine has shown beneficial role in reducing cytokine storm (5).

The aim of this study was to evaluate the data in 12 COVID-19 positive patients with interstitial pneumonia and different types of hypoxemia (mild, moderate and severe) to whom nebulized lidocaine was given in a dose of 2.85 mg/kg via inhalation, and to analyze the efficiency of the lidocaine in the improving of the oxygenation.

## Material and Methods

12 patients with confirmed COVID-19 pneumonia, aged between 22 and 72 years (mean age 53), who had dyspnea and difficult breathing and have been admitted to the City General Hospital "8th September" Skopje, Macedonia were enrolled in the study. All patients regardless of the type of disease who were admitted for hospitalization, were inhaled with lidocaine. The Ethical Committee of the hospital approved this report according to the situations for emergency infected diseases. We included patients with different stages of illness (4 patients had mild type, 3 were with moderate type of COVID-19 pneumonia and in 5 patients COVID-19 pneumonia was severe). All patients had clinical symptoms for respiratory failure with hypoxemia and supplementary oxygen requirement at the time of presentation. One patient required life support with inotropic medicaments from the first day of hospitalization. All patients had hypoxemia with partial pressure of oxygen between 25 and 89 mmHg when nebulized lidocaine was given. Ventilation support was ongoing from the first day of admission in all 12 patients. Out of the 12 cases, 3 patients were intubated immediately after hospitalization, and noninvasive ventilation with cpap mask was ongoing in the other 9 patients. Out of the 12 cases, only one had preexisting respiratory complain before the COVID-19 pneumonia and only one was smoker. All patients had therapy with antibiotic (Beta lactam antibiotic in dose 1 gram every 8 hours), corticosteroids (methylprednisolone in dose 4 mg/kg/daily), anticoagulant (nadroparin calcium administered on a daily basis according body weight and hemostasis), vitamins and antihistaminic ha2 receptor antagonist for intravenous use in dose 40 mg two times daily.

In purpose to improve oxygenation in all 12 patients nebulized lidocaine was given as supportive drug. In all patients nebulized lidocaine was given in a dose of 2.85 mg/kg, diluted as a 1% solution, via inhalation, four times daily. Inhalation was performed using a ventilator with nebulizer. We analyzed the level of the partial pressure of oxygen (PaO2) measured by the gas analyzer Gem premier 3000 from the radial artery blood 5 minutes before the treatment and 30 minutes after nebulized lidocaine was given. Level of blood saturation measured by pulse oximeter put on point finger was also analyzed, 5 minutes before the inhalation and 30 minutes after nebulized lidocaine was given. Patients were analyzed at hospital admission for demographics data (gender, age), presence of clinical anamnestic data for symptoms (temperature, shortness of breath, dyspnea, cough, fever, pain, renal problems, general weakness), the present co-morbidities (diabetes mellitus, hypertension, chronic renal failure, chronic obstructive pulmonary disease, chronic cardiomyopathy, stenting), x-ray specificities (opacity, pattern) and degree of hypoxemia (mild, moderate, severe). Body fat assessment was performed within 48 hours of admission using measures of height and weight. For each patient, we calculated body mass index (BMI). BMI was calculated by using on-line calculator (htts://www.calculator.net/bmi-calculator.html) entering patients' weight and height. Patients were classified, according to World Health Organization Classification, in correlation to BMI, into following groups: normal BMI (18.5-24.9), overweight (25-29.9), obesity class (>30) (6).

Average number of days from the beginning of the symptoms to the introduction of inhalation was filled latter after admission, using medical records.

## Results

12 patients with COVID-19 pneumonia have been enrolled in this study. Patients' demographics characteristics are shown in Table 1.

Out of them, 9 patients (75%) were male and 3 (25%) were female. Most of the patients presented with shortness of breath (50%), dyspnea (41.6%) and cough (41.67%), and 9 patients (75%) had co-morbidities. Among the various co-morbidities, hypertension has been the most common disease.

**Table 1**. *Patient's demographic and clinical characteristics*

| **Characteristics** | **N (%)** |
|---|---|
| Gender | |
| Male | 9 (75%) |
| Female | 3 (25%) |
| **Symptoms** | |
| Shortness of breath | 6 (50%) |
| Dyspnea | 5 (41.67%) |
| Cough | 5 (41.67%) |
| Fever | 4 (3.34%) |
| Pain | 2 (16%) |
| Anuria/oliguria | 1 (8.33%) |
| General weakness | 1 (8.33%) |
| **Co-morbidities**<br>With comorbidities<br>Without comorbidities | <br>9 (75%)<br>3 (25%) |
| Diabetes mellitus | 3 (25%) |
| Hypertension | 6 (50%) |
| Chronic renal failure | 2 (16%) |
| Chronic obstructive pulmonary disease | 1 (8.33%) |
| Cardiomyopathy chronic heart failure | 1 (8.33%) |
| Stenting on coronary arteries | 1 (8.33%) |

Examination with x-ray showed that all patients had radiological findings and opacity was found in 9 (75%) patients and 3 (25%) patients had pattern.

**Table 2**. *Chests' x-ray findings*

| CHEST X RAY | N (%) |
|---|---|
| Opacity | 9 (75%) |
| Pattern | 3 (25%) |

Out of 12 patients, 16% had normal BMI, 16.67% were overweight and 66.67% were obese.

**Table 3**. *Body mass index in patients*

| BODY MASS INDEX | N (%) |
|---|---|
| Normal 18.5-24.9 | 2 (16.67%) |
| Overweight 25-29.9 | 2 (16.67%) |
| Obesity class 1 (>30) | 8 (66.66%) |

Table 4 showed type of ventilator support according the type of disease. 3 patients were on mechanical ventilation. Non-invasive ventilation was ongoing in 4 patients with mild type of disease, in 3 patients with moderate and in 5 patients with severe type.

**Table 4**. *Type of ventilation support according the type of disease*

| | Mild type of disease N (%) | Moderate type of disease N (%) | Severe type of disease N (%) |
|---|---|---|---|
| Invasive ventilation | / | / | 3 (25%) |
| Non-invasive ventilation | 4 (33.33%) | 3 (25%) | 5 (41.67%) |

Level of oxygen saturation shows hypoxemia at the time of presentation in each patient. The hypoxemia was mild (85-90% of oxygen saturation) in 4 patients, 3 patients had moderate hypoxemia (75-85%) and severe hypoxemia (50-75%) was noticed in 5 patients (Table 5). The average number of days from the beginning of the disease to the introduction of our therapeutic strategy with lidocaine was 6.5 days. Seven patients had experienced a rapid improvement of hypoxemia from the day of admission to the day of treatment.

**Table 5**. *Oxygen level on admission, before and after inhalation*

| | Oxygen saturation ($SaO_2$) on admission | Oxygen saturation ($SaO_2$) before the treatment with lidocaine | Partial pressure of oxygen ($PaO_2$) before the treatment with lidocaine | Oxygen saturation ($SaO_2$) after the treatment with lidocaine | Partial pressure of oxygen ($PaO_2$) after the treatment with lidocaine |
|---|---|---|---|---|---|
| Case 1 | 87% | 49% | 30 mmHg | 87% | 60 mmHg |
| Case 2 | 65% | 25% | 18 mmHg | 80% | 48 mmHg |
| Case 3 | 60% | 66% | 45 mmHg | 99% | 162 mmHg |
| Case 4 | 87% | 84% | 64 mmHg | 100% | 96 mmHg |
| Case 5 | 83% | 80% | 32 mmHg | 100% | 90 mmHg |
| Case 6 | 60% | 61% | 30 mmHg | 69% | 36 mmHg |
| Case 7 | 85% | 60% | 50 mmHg | 80% | 90 mmHg |
| Case 8 | 60% | 85% | 48 mmHg | 87% | 90 mmHg |
| Case 9 | 80% | 61% | 33 mmHg | 69% | 35 mmHg |
| Case 10 | 82% | 79% | 52 mmHg | 100% | 246 mmHg |
| Case 11 | 86% | 89% | 83 mmHg | 99% | 102 mmHg |
| Case 12 | 68% | 86% | 54 mmHg | 87% | 60 mmHg |





In all 12 patients who had mild (4 patients) or moderate hypoxemia (5 patients) at admission, we observed significantly improvement in oxygen saturation after inhalation. Even in severe group with 5 patients we noticed improvement in all of the 5 patients.

## Discussion

COVID-19 patients can experience respiratory failure associated to profound hypoxemia (7). Clinical indicators of respiratory failure include increase in respiratory rate, decrease of oxygen level or increasing supplementary oxygen requirement (8). The main goal of dealing with respiratory failure is to improve oxygenation. Our study reported twelve patients with mild, moderate and severe hypoxemia in whom nebulized lidocaine was used as additional therapy for the improvement of oxygenation. After inhalation with nebulized lidocaine SaO2 and PaO2 have higher values. In comparison to the moderate and severe group of patients, the group with mild hypoxemia had the most significant improvements.

Lidocaine has been continuously used for decades, and it has a long history of practice (9). Recently lidocaine has been shown to reduce cytokines storm and suppresses the development of netosis as a form of cell death (10). It was confirmed that cytokines are involved in viral propagation to respiratory failure (11). Another mechanism of acting of lidocaine is blocking the voltage of Na and Ca channels (12).

Virus induced disruption in Epithelial Sodium Channel (ENAC) or amiloride-sensitive sodium channel which is selective permeable to the sodium ions. This ion channel modulation regulates the alveolar fluid clearance (13). Thus, decreasing in this ion-channel function leads to accumulation of fluid across already inflamed lung epithelium. By using lidocaine and by blocking the voltage of Na and Ca channel, the progression of fluid accumulation across ENAC may be stopped, even in the patients with severe conditions. However, there have been identified some risk factors for poor outcomes, such as preexisting co-morbidities, obesity, and male gender (14). In our study we identified some risk factors for poor outcomes.

Extent of radiology changes is also negatively associated to prognosis (15) and this was also presented in our patients. Many studies demonstrated improvement in airway obstruction and oxygenation when asthmatic patients were treated with nebulized lidocaine (16). In our data nebulized lidocaine was also associated to increasing level of partial pressure of oxygen and oxygen saturation. But, there are limited studies for the use of nebulized lidocaine and the most of them hypothesize the role of lidocaine in COVID-19. Searching in the literature for the nebulized lidocaine, many studies showed a promising efficacy in improving pulmonary function and reducing cough in asthmatic patients (17). Additional investigation is warranted for the beneficial effects in COVID-19.

These results are obtained from one day application. Secondly, the number of the patients is small, although the role of nebulized lidocaine in improving the oxygenation was our focus.

## Conclusion

In this case series, we used nebulized lidocaine as a supportive drug. In all 12 patients who had different types of hypoxemia (mild, moderate, severe) we observed improvement in oxygen saturation after inhalation.

## References


1. Schmidt W, Schmid H, Martin E. Influence of lidocaine on endotoxin-induced leukocyte-endothelial cell adhesion and macromolecular Leakage in vivo. Anesthesiology. 1997: Vol 87, 617-624.
2. John Hopkins Coronavirus Resource Center Covid-19 Dashboard repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU): Global cases https://systems.jhu.edu.
3. Scriabine A, Alexander. Discovery and development of major drugs currently in use. Pharmaceutical innovation: Revolutionizing human health. 1999; 148.
4. Cassuto J, Sinclair R, Bonderovic M. Anti-inflamatory properties of local anesthetics and their present and potential clinical implications. Acta Anaesthesiol Scandinavica. 2006; 50(3):265-82.
5. Ali ZA, El-Mallakh RS. Nebulized Lidocain in Covid-19, An Hypotheses. Medical Hypotheses. 2020nov; 144:109947.
6. World Health Organization/Europe/ Nutrition https://euro.who.int/en/helth-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi.
7. Dylan T, Finnerty and Donal J, Buggy. A novel role for lidocaine in COVID-19 patients. BJA British Journal of Anaesthesia. 2020; 124(4): e391-e394.
8. Thomas W Nicholson, Nick P Talbot, Annabel N, et al. Respiratory failure and non-invasive respiratory support during the COVID-19 pandemic: an update for re-deployed hospital doctors and primary care physicians. The BMJ British Medical Journal. 2020; 369.
9. Torsten G, Torsten E, Kjell L, et al. Lidocaine: The origin of a Modern Local Anesthetic. Anesthesiology. 2010; Vol. 113, 1433-1437.
10. Elena V G, et all. Neutrophil extracellular trapping and angiogenesis biomarkers after intravenous or inhalation anaesthesia with or without intravenous lidocaine for breast cancer surgery: a prospective, randomized trial. BJA British Journal of Anaesthesia. 2020; Nov; 125(5): 712-721.
11. Seung Hye H, Rama K. The acute respiratory distress syndrome from mechanism to translation. Journal of Immunology. 2015 Fev 1; 194(3): 855-60.
12. Nasser A M, Hammodi A, Dayanidhi R J. Lignocaine's substantial role in COVID-19 management: Potential remedial and therapeutic implications. Anaesthesia, Pain and Intensive Care. 2020; 24(1): 59-63.
13. Mossel EC, Wang J, Jeffers S, et al. SARS-CoV replicates in primary human alveolar type 2 cell cultures but not in type 1-like cells. Virology. 2008; Mar 1; 372 (1): 127-35.
14. Xiaochen Li et al. Risk factors for severity and mortality in adult Covid-19 in patients in Wuhan. Allergy Clinical Immunology. 2020; 146 (1):110-118.
15. Nanshan C, Min Z, Huan D, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020; 95(10223).
16. Rosario NA, Riedi CA, Farias L. Lidocaine nebulization for treatment of asthma. Ann Alergy Astma Immunology. 2000 Sep; 85(3): 245-6.
17. Loren W, Huntet el al. Treatment of asthma with nebulized lidocaine: a randomized, placebo-controlled study. Journal of Allergy Clinical Immunology. 2004 May; 113(5): 853-9.




*CASE REPORT*

UDK: 616-007.41:[616.98:578.834
616.98:578.834]:616-007.41

# SITUS INVERSUS TOTALIS: PATIENT WITH POST COVID-19 INFECTION

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## ABSTRACT

Situs inversus totalis (SIT) is an especially rare congenital condition with complete reverse location of the thoracic and abdominal organs. People with situs inversus totalis sometimes are unaware of their unusual anatomy condition until the moment they need some medical diagnostic procedures or some surgical interventions. We present the case of the 41-years-old female, with post COVID-19 infection in November 2020, with long lasting cough for two months, who was referred to the Radiology Department for CT examination of the lungs. CT scan without contrast was performed. We discovered a situs inversus totalis, where the heart was located on the right side of the thorax, the stomach and spleen were situated on the right side of the abdomen and the liver, gallbladder and duodenum were on the left side. CT scans of the lungs showed normal lung density, without sign of the consolidation, pulmonary fibrosis or pleural effusion. The thoracic and abdominal organs and the viscera were complementary inversed, as a mirror image of the normal position of the internal organs. All laboratory tests were normal. No previous radio diagnostic exams of the thorax or abdomen existed. Patient had the pregnancy and she gave a birth in 2018, with no evidence of the situs inversus totalis. It is very important to make an evidence and inform the patient and medical professionals of the diagnosis of situs inversus totalis in the direction to prevent future complications which can arise from patient's assessment and care, especially in cases of the accidental abdominal or thoracic organs trauma or in cases with acute infection condition as cholecystitis, appendicitis.

***Key Words:*** *Situs Inversus Totalis (SIT)*

**CONFLICT OF INTERESTS:** None declared.

## Introduction

Situs inversus totalis (SIT) is a rare condition of congenital anomaly, which are characterize by the transposition of the thoracic and abdominal organs, viscera and vascular structures, with the incidence of the 0,01% of the population, or about 1 person in 10,000 births. The term situs inversus derives from the Latin phrase: "situs inverses viscerum", which means "inverted position of

the internal organs". It may include complete transposition of the thoracic and abdominal viscera in general or transposition of only one of them. The term "situs inversus" denotes the position or location of an organ specifically and abdominal viscera in relation to the midline of the body through the sagittal plane. Dextrocardia as a condition was seen on the pictures drown by Leonardo da Vinci. In the year of 1600 Fabricius, the first reported the known case of reversal position of the liver and spleen in a male patient. Kuchmeister in the year of 1824 was the first who recognized this condition in a living person. Vehsemeyer in the year of 1897 was the first who demonstrated, transposition of the viscesra, by roentgen with X-ray. Situs inversus is an autosomal recessive genetic condition and may or may not be associated to dextro cardia. The 25% of the cases with situs inversus might have a primary ciliary dyskinesia, within a condition known as a Kartagener syndrome, which is characterized by the triad of chronic sinusitis, bronchiectasis a situs inversus (1). SIT is the most often diagnosed by ultrasound, radiographic, CT scans or MRI exams. The imaging features on radiograph that need to be evaluated are the following: location of the apex of the heart; location of the aortic arch and locations of the stomach bubble and liver. Situs inversus is diagnosed incidentally after acute thoracic or abdominal trauma and in cases where radio diagnostic examination is required for some acute infections. In the cases of isolated type of situs inversus totalis, many affected people have no associated other health issues (2). There are three types of situs: situs solitus, situs inversus and situs ambiguous. Situs solitus is a normal location and position of organs, with right atrium, liver, gallbladder, three lobed right lung and inferior vena cava located on the right side and atrium, stomach, spleen, two lobed left lung and descending aorta located on the left side. Situs inversus totalis indicates a complete mirror-reversal image of the normal position of the internal organs, with normal anterior-posterior symmetry (3). The heart is located on the right side of the thorax. The right lung has two lobes, and the left lung has tree lobes. Aorta and great blood vessels, lymphatics and nerves are also transposed. The liver, gallbladder and duodenum are located on the left side and the stomach and the spleen are on the right side. Intestines are transposed too. Position with sinstro cardia is known as a situs inversus incomplitus. Situs ambiguous is the random arrangement of the internal organs, well known as heterotaxia, which can be associated in many cases to congenital heart disease and other abnormalities. Situs ambiguus has been field of scientific research since 1973. In some cases, such as situs ambiguous, situs cannot be well determined. In these patients, the liver might be located at midline, the spleen might be multiple or absent, and the bowel might be malrotated. In many cases, some of the structures are duplicated or completely absent. In cases of such abnormal positioning of organs in situs ambiguus, orientation across the left-right axis of the body is disrupted much earlier in fetal development, as a result of which severely cardiac abnormalities may develop, with impaired function in 50 – 80% of the cases. There are many complications with systemic and pulmonary vessels, accompanied with severe morbidity and sometimes even death (4). Heterotaxy syndrome with atrial isomerism is associated to approximately 3% of congenital heart disease cases (5).

In cases of absence of congenital heart defects, many individuals with situs inversus are unrecognized and they can live a long life as healthy persons, without any future complications related to their specific unusual medical condition. Situs inversus totalis in the 3%-5% of the cases occurs with dextro cardia, usually with transposition of the great vessels. In 80% of these patients right-sided aortic arch can be found. Situs inversus with sinistro cardia position is rare condition, associated to congenital heart disease in 95% of the patients. Isolated sinistro cardia is a rare type of the situs inversus in which the heart is still in normal position, but other viscera are transposed (6).

## Case Report

We report a case of a 41-years-old female patient who came at the Department of radiology in the University Clinic of Surgery, with anamnesis of positive COVID-19 test and post COVID infection in November 2020, with compliance of long-lasting cough for two months. The patient had no other symptoms or complains of other organs. The laboratory tests were normal (CRP = 4.8, D-Dimer = 235ng/mL, Gly=5.6), with normal blood test and blood pressure (135/87Hg). MDCT multislice (GE Somatom Bright Speed)) native scan (slice thickness 2.5 mm), of the lung and mediastinum was performed. MDCT allowed detection of the complete transposition of the thoracic and upper abdominal organs, viscera and vessels. The heart was located on the right side of the thorax (Fig. 1). The right lung with two lobes was on the left and the left lung with three lobes was located on the right (2,3,4). Great blood vessels such aorta, pulmonary trunc, lymphatics were also transposed (fig. 5,6). The liver, gall bladder, duodenum were located on the left side and the stomach and the spleen were on the right side (Fig. 7). Intestines were transposed too. There was no evidence of consolidation of the lung or residual pulmonary fibrosis. Pleural effusion was not detected.

**Figure 1**. *Radiography of the lung and CT of the lung (coronal view): reverse location of the thoracic and abdominal organs.*

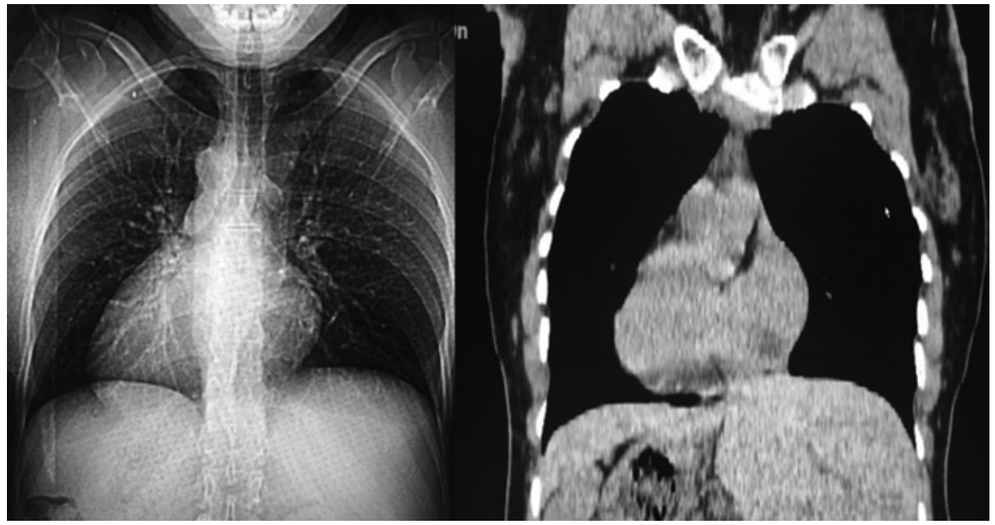


**Figure 2**. *Axial CT scan slice of situs inversus with right-sided heart.*

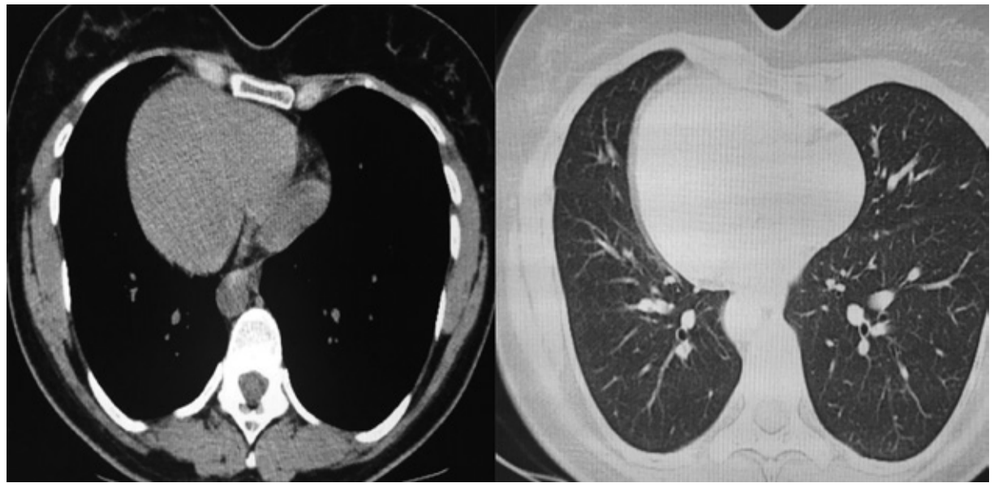


**Figure 3**. *CT scans of the lung (coronal view) in situs inversus totalis.*

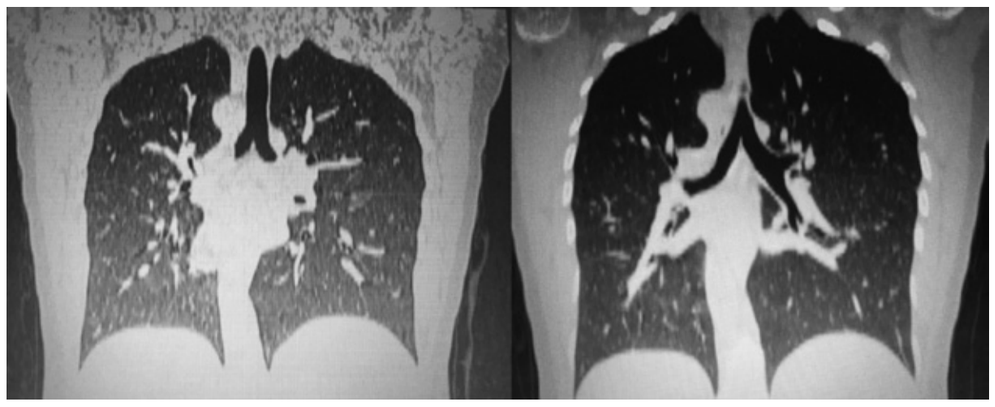


**Figure 4**. *CT scans (sagittal view) of the right lung and right hilla.*

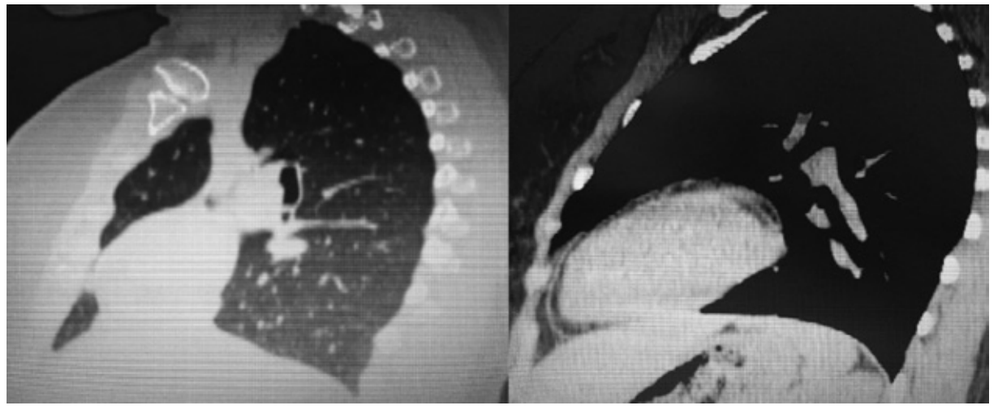


**Figure 5**. *Axial CT scans: transposition of the main vessels in the upper mediastinum: aorta, v.cava sup. et pulmonary trunc.*

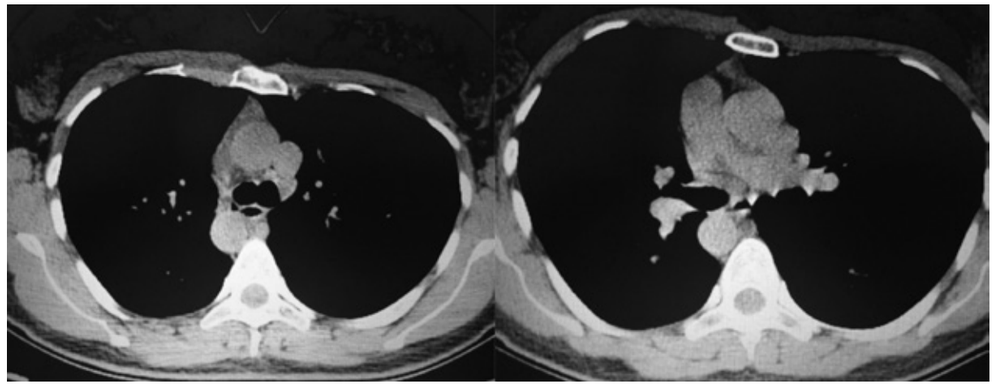


**Figure 6**. *Axial CT scan slice of situs inversus with right-side aortic arch, pulmonary trunk and descending aorta.*

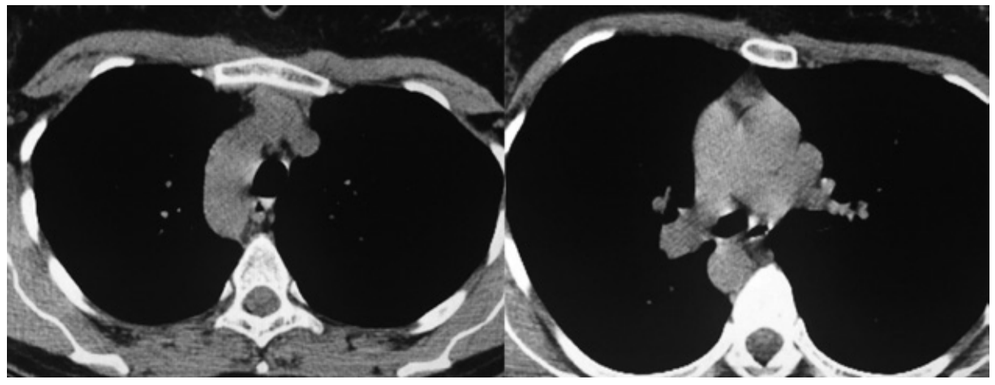
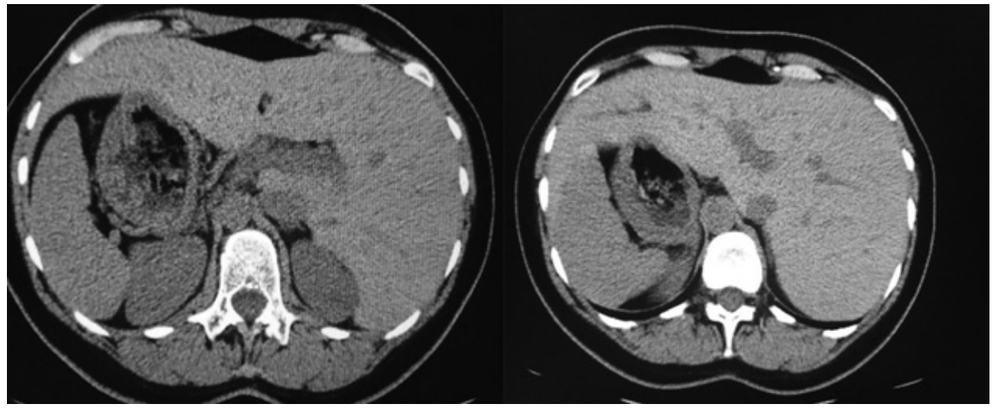


**Figure 7**. *Axial CT scans: inversion of the abdominal organs – upper abdomen.*



## Discussion

Situs inversus is an exceedingly rare autosomal recessive genetic condition and positional anomaly, with reverse of the thoracic and abdominal internal viscera, with an incidence in the population of only 0.001 to 0.1, with a male/female ratio of 3:2. Transmission mode of the situs inversus totalis is autosomal recessive, but its precise genetic mechanism remains complex and still unknown well. Different genetic factors or genesis may cause this condition among different people or some families (7, 8). Situs inversus occurs as a result of a rotation of the viscera and organs to the opposite side, during the organogenesis of the embrio. Shigenori et al. suggested that some conditions as immobility of nodal cilia inhibits the flow of extraembryonic fluid during embryogenesis, which can lead to a development of situs inversusus totalis (9,10). Situs inversus totalis is not actually a structural heart disease and it is normally not associated to congenital heart disease. In situs inversus with sinistro cardia and situs solitus with dextro cardia, structural heart condition is much commoner, such as double outlet right ventricle, pulmonary atresia or stenosis, single ventricle, transposition of the great vessels, atrial and ventricular septal defect (11,12,13). Cardiovascular abnormalities (septal defects, tetralogy of Fallot, transposition of the great arteries, pulmonary arterial stenosis) and problems with intestinal tract may be seen very often (14). Up to 20% of patients with situs inversus can have a Kartagener syndrome as a subgroup of primary ciliary dyskinesia manifesting with bronchiectasis, chronic sinusitis and male infertility (15). About 60% of the patients with situs inversus totalis have other congenital anomalies such as a biliary atresia, small bowel atresia, duplication, colon aganglionarius, splenic agenesis and etc. Situs inversus totalis with normo cardia (situs inversus incomplete) is more often acompanied with cardiac abnormalities (15). Many different type of cancers have been reported in the patients with situs inversus totalis, including pancreatic, hepatocellular, gastric and colo-rectal cancers. In the year 1936 Allen was the first who reported a gastrectomy on a 30-years-old male with gastric cancer (16,17). Besides that, the incidence of intraabdominal malignancies in the patients with SIT are very rare, but the surgeon must consider on the complexity of the anatomy when planning surgery in the patients with SIT, especially when dissection of the lymph node is needed. Despite the fact that in many cases, situs inversus totalis with dextrocardia does not affect normal health or longevity, this condition is very important to be recognizied for treating many other diseases which can appear during life, even they are unrelated to situs inversus, especially for those who need surgical intervention (18). Situs inversus totalis is very often incidentally recognized during some screening procedures. In some cases, the reversal of the organs may cause some confusion because many signs and symptoms will be on the wrong side and the surgical procedures also can be difficult to perform due to the totally different anatomic position of the organs. Preoperative recognition of the anatomic variations of SIT may be needed and referral to preoperative diagnostic procedures in a patient with SIT. The preoperative evaluation for situs inversus has two main objectives: evaluation of cardiac, pulmonar and gastrointestinal anomalies and orientation of the viscera. In some cases, it is especially useful to perform a three-dimensional CT angiography with 3D reconstruction prior operation, to see exact placement of vascular and organ structures. The risk of occurrence of intraoperative complications is much higher in patients with situs inversus totalis in comparison to procedures of the patient without SIT (18). In some special conditions when transplantation is needed, the situation can be complicated because donor organs will come from situs solitus (normal donors) with different orientation of the vessels. This situation requires more previous planning and more surgical steps that blood vessels can join properly. Diagnostic procedure as chest X-Ray, chest and abdomino-pelvic Computed Tomography and positron emission tomography (PET), ECG and ultrasound can recognized SIT. These procedures allow early recognition and well management of this condition and guidance for the best approaches. In order to predict the long-term outlook for people with situs inversus, it is important to consider if the condition is isolated, or is associated to additional abnormalities which can affecting the heart, lung or other parts of the body. Only isolated situs transversus totalis cases with dextrocardia have an excellent prognosis. When situs inversus is associated to another condition or syndrome, the prognosis may depend on that – of the underlying condition with which this condition is present (19).

## Conclusion

The reversal of the organs can make many confusions in diagnosing, because many signs and symptoms will be on the contralateral “wrong” side, so early diagnosis of this condition with X-ray, CT or PET scan is particularly important. People with situs inversus must inform their physicians before the examination or operation about their condition. But in a condition when a patient is in coma in the medical Emergency Department, they must wear a medical identification card or note, which can help to inform health care clinicians in the event the person is unable to communicate, and it can help to ensure proper treatment in the assigned emergency medical situation. To know that person has situs inversus is especially important to prevent surgical errors or side effects and all medical problems that can result in a case of unrecognized reversed anatomy.

**Acknowledgment**

This work was performed in the University Clinic of Surgery “St. Naum Ohridski” Skopje. We express our gratitude and appreciation to our staff for the excellent collaboration.

## References

1. Mayo CW, Rice RG. SITUS INVERSUS TOTALIS: A Statistical Review of Data on Seventy-Six Cases with Special Reference to Disease of the Biliary Tract. *Arch Surg*. 1949; 58 (5):724 – 730. doi:10.1001/archsurg.1949.01240030734014.
2. G. Supriya, S. Saritha, and S. Madan, “Situs inversus totalis – a case report,” IOSR International Journal of Applied Physics, vol. 3, no. 6, pp. 2278 – 4861, 2013. View at: Publisher Site | Google Scholar.
3. Tonkin IL, Tonkin AK. Visceroatrial situs abnormalities: sonographic and computed tomographic appearance. *AJR* 1982; 138:509-515

4. Lowenthal, A.; et al. (September 26, 2015). “Anatomy, clinical manifestations and diagnosis of heterotaxy (isomerism of the atrial appendages)”. Up To Date. Retrieved November 4, 2015.
5. Kim, Soo-Jin (2011). Heterotaxy Syndrome. Korean Circulation Journal. 41 (5): 227 – 32.
6. Tiller GE, Hamid R Situs Inversus, NORD Guide to rare Disorders. 2003;https://rarediseases.org/rare-diseases/dextrocardia-with-situs-inversus/.
7. Huang SM, Yao CC, Tsai TP, et al. Acute appendicitis in situs inversus totalis. J Am Coll Surg 2008;207:954.
8. Reza A, Hadi Sh. Two Case Reports of Situs Inversus Totalis, Anatomical Science Journal 2013, Vo.l10, No2, 111-116.
9. Nonaka S, Tanaka Y, Okada Y, et al: Randomization of the leftiright asymmetry due loss of nodal cilia generating leftward flow of extraembryonic fluid in mice lacking kIF3B motor protein. Cell 1998;95 Suh B. J: A case of Gastric Cancer with Situs Inversus Totalis. Case Rep Oncol 2017;10:130-135.
10. Suh B. J: A case of Gastric Cancer with Situs Inversus Totalis. Case Rep Oncol 2017;10:130-135.413679-overview. Accessed August 26, 2013.
11. Wilhelm A, et al. Situs Inversus Imaging. Medscape. Published May 25, 2011. Available online at emedicine.medscape.com/article.
12. Perloff JK, Marelli AJ. *Perloff’s Clinical Recognition of Congenital Heart Disease, 6th Edition*. Philadelphia, PA: Elsevier Inc. 2012.
13. Annamaria Wilhelm. Situs Inversus Imaging. Medscape. October 7, 2013;
14. Peters R, de Jonge G. Kartagener’s Syndrome: Situs Inversus, Chronic Sinusitis and Bronchiectasis. Journal of the Belgian Society of Radiology. 2016;100(1):25. DOI.
15. F: A Case of malignant tumour of the stomach in male with transposition of the viscera. Indian Med Gaz 1936; 71:3.
16. Haruki T, Maeta Y, Nakamura S, et al: Advanced cancer with situs inversus totalis associated with KIF3 complex deficiency: report of two cases. Surg Today 2010;40:162-166.
17. (Blegen HM: Surgery in situs inversus. Ann Surg a949;12:244-599).
18. Alfred Z. Abuhamad, Rabih Chaouri. Fetal heterotaxy, Left Atrial Isomerism, Right Atrial Isomerism, and Situs inversus. A Practical Guide to Fetal echography: Normal and Abnormal Hearts. Philadelphia, PA: Lippincot Williams&Wilkins; 2010.



*CASE REPORT* UDK: 616.127-02:616.432-008.61]-055.2

# PROLONGED RECOVERY IN A CASE OF ACROMEGALIC PATIENT WITH DILATED CARDIOMYOPATHY: POINTS TO PONDER

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## ABSTRACT

Acromegalic cardiomyopathy has a very high mortality. Patients can develop a lot of cardiovascular complications. The incidence of acromegaly in females is rare and usually the disease is missed during early phases because of its slow progression. Therefore, it is crucial to identify and treat it at an early stage, as it is potentially reversible if the patient is young. We report a case of acromegaly presenting as dilated cardiomyopathy in a 33-years old female patient taken in emergency owing to the progressive diminishing of vision for trans-sphenoidal resection of pituitary macroadenoma. Dopamine infusion was used throughout the procedure and post-procedure patient was ventilated for 2 hours then extubated uneventfully.

***Key words:*** *acromegaly, dilated cardiomyopathy, pituitary macroadenoma, prolonged recovery*

## Introduction

Acromegalic cardiomyopathy has a very high mortality, up to 60% (1). Patients can develop a lot of cardiovascular complications like hypertension, arrhythmias, systolic and diastolic dysfunction, heart failure (2,3,4). The incidence of Acromegaly in females is very rare and usually the disease is missed during early phases because of its slow progression. Patients presenting with cardiovascular symptoms should be identified as early as possible, as it is potentially reversible if the patient is young (2,3). We report a case of acromegaly presenting as dilated cardiomyopathy in a 33-years old Indian female patient taken in emergency.

## Case Report

A 33-years old female patient was admitted with complaints of breathlessness on exertion for 10 days and progressive decrease of vision since past 6 months, accompanied by anorexia, nausea and vomiting for the last 3 days. Family history was not significant and with no comorbidities. Her blood pressure was 110/60, pulse was 98/min and respiratory rate was 16/min. General examination showed coarse facial features and pedal edema. Cardiovascular examination revealed normal heart sounds with tachycardia and S3 gallop. Respiratory system had decreased bilateral

air entry and crepitations. 12 lead Electrocardiogram showed sinus tachycardia, QRS prolongation. A 2D Echocardiography was carried out. The findings were of dilated cardiomyopathy, Ejection Fraction (LVEF) of 18%, Global left ventricle hypokinesia, dilated left atrium and ventricle, severe Tricuspid Regurgitation, moderate Mitral Regurgitation, Mild PH (30mmHg). Patient was started on Digoxin, ACE inhibitors, Diuretics, Statins and beta-blocker.

Other hormonal tests were also sent: Growth hormone level was 68, IGF-1 level: 376 ng/ml (range 68-225ng/ml), Pituitary hormone profiling showed an increase in Prolactin level 68.46, Free T4: 0.6ng/dl (Normal range 0.8-2), Serum electrolytes, renal and liver function tests and lipid profile were normal.

Magnetic resonance imaging revealed a pituitary macroadenoma. The final diagnosis of acromegaly with dilated cardiomyopathy was made. But there was severely compromised vision owing to the pressure effects on optic chiasma, the patient was taken for emergency trans-sphenoidal excision after 2 days of starting of the medical treatment.

A detailed pre anesthesia checkup was carried out. Airway was Mallampatti class II. High risk consent was taken, and the patient and her relatives were explained about the possibility of cardiovascular events and post-operative ventilator and/or Intensive care unit (ICU) stay.

In operating room, after all preparation, patient was taken inside, a 16G peripheral line and arterial line was put in the left radial artery and a right sided subclavian PICC (peripherally inserted central catheter) line was inserted. Electrocardiogram, pulse oximeter and capnography were attached. Anesthesia was induced with 2 mcg/kg Injection Fentanyl, 0.2 mg/kg Etomidate given slowly and 1 mg/kg of Rocuronium. Airway was secured with 7 mm cuffed endotracheal tube and a throat pack was inserted. There was no stress response to intubation. Anesthesia was maintained with oxygen: nitrous oxide (50:50), sevoflurane titrated to MAC 0.8-1 by adjusting dial concentration and Atracurium 0.25 mg/kg. In view of low ejection fraction Inj. Dopamine infusion was started with 5 mcg/kg/min and continued throughout the procedure.

500 ml of normal saline was infused intraoperatively. Blood loss was 100 ml, urine output was 100 ml. After 2 hours of surgery patient was reversed with injection Neostigmine 0.05 mg/kg and Glycopyrrolate 0.5 mg. However, owing to poor neuromuscular tone and poor breathing efforts, the patient was electively ventilated for 2 hours. After 2 hours she was extubated uneventfully. For post-operative analgesia, she was prescribed 50 mg of Tramadol intravenously 8 hourly and tablet paracetamol 1 g orally 4 times a day. She was made to resume her scheduled medications.

## Discussion

Patient with acromegaly pose multitude of challenges to anesthesiologists in terms of preoperative optimization, airway management, cardiovascular complications and perioperative care (1,2,3). Early diagnosis and prompt treatment is required to increase the likelihood of reversibility of patient having dilated cardiomyopathy due to acromegaly. Acromegalic dilated cardiomyopathy (DCM) is associated to a poor outcome and has an increased mortality rate (1,4). In our case the patient did not present with typical features of acromegaly and airway management was uneventful, however they were anticipated difficult for airway due to their coarse facial features and the difficult cart should be ready. These patients may have glottis or subglottic stenosis, turbinate enlargement, vocal cord thickening and recurrent laryngeal nerve involvement.

In view of dilated cardiomyopathy and decreased ejection, fraction minimal and titrated use of cardio-stable anesthetic agents (Etomidate) should be used and preoperative optimization of patient with anti-failure medications should be done. In our case, as it was emergency in terms of severely compromised vision, the patient has to be taken in without optimization. Use of the ionotropic agents (Dopamine, Dobutamine, Levosimendan or Milrinone) may be warranted, in cases when there is probability of myocardial depression (1). Young patients with short duration of disease have a relatively better outcome compared to the late diagnosed old patients, especially once heart failure manifests. Treatment is usually supportive in the form of diuretics, Angiotensin converting enzyme (ACE) inhibitors, Beta blockers, and nitrates (1,2,4).

Principles remain the same with acromegaly too – avoid tachycardia and myocardial depression, precipitous fall in blood pressure, patient should be euvolemic, prevent increase in afterload, maintain preload and maintain sinus rhythm (1). These patients may require ICU and elective ventilation post-operatively, more so when they are not optimized as was in our case. The patient was electively ventilated for 2 hours then was extubated, this is because of low ejection fraction hence delay in metabolization and washout of relaxants from the body.

**Conclusion:** Acromegaly with DCM is rare in females and can be missed at early stages. They pose multiple challenge for anesthesiologists in terms of difficult airway management and an impaired heart, it can be managed by vigilant airway examination, preoperative optimization, and a difficult airway cart peri-operatively. By following the principles of anesthesia, worsening of myocardial function and heart failure can be prevented. Hence, adequate preoperative optimization and ICU care will definitely help in improving post-operative outcomes in acromegaly patients with DCM.

**Acknowledgements:** None.

**Declaration conflict of interest:** No potential conflict of interest relevant to this article was reported.

**Funding source:** None.

## References

1. Nair AS, Nirale AM, Sriprakash K, et al. Dilated cardiomyopathy in acromegaly: Case report and anesthesia management. Anesth Essays Res 2013; 7:411-4.
2. Dargad RR, Parekh JD, Dargad RR. Acromegaly with Dilated Cardiomyopathy. Journal of The Association of Physicians of India. Vol. 64. June 2016.
3. Devoitille A, Beckers A, Piérard LA. Rev Med Liege. Clinical case of the month. Cardiac complications of acromegaly: A rare cause of dilated cardiomyopathy 2012; 67:174-8.
4. Doshi SR, Punatar SB. A case of reversible dilated cardiomyopathy due to acromegaly with partial empty sella. *Indian Heart J*. 2012; 64(2):209-210. doi:10.1016/S0019-4832(12)60065-0.

# CARDIAC ARREST IN THE EARLY POSTOPERATIVE PERIOD

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## ABSTRACT

In-hospital cardiac arrest (IHCA) is determined as acute circulatory loss which requires fast resuscitation with chest compressions and/or defibrillation. Despite that it is a common condition, little research is done in this area, and many data are extracted from out-hospital cardiac arrest guidelines and researches. Perioperative cardiac arrest patients are a subclass of surgical patients who need CPR on the day of surgery.

In this article, through a case report about successful reanimation, the in-hospital and perioperative cardiac arrest characteristics are discussed. A young female patient presented with cardiac arrest, 30 minutes after arriving in PACU and acute pulmonary embolism was the most suspected cause of the arrest. She was reanimated for around 30 minutes and she recovered without any neurological impairment.

Perioperative cardiac arrest must be distinguished from other cardiac arrests and ACLS guidelines should be targeted according to particular situations. These patients require rapid evaluation and quick management, because usually there is a potentially reversible cause. As quickly as the cause is identified, as much the chances of ROSC are bigger.

***Key Words:*** *cardiopulmonary resuscitation, perioperative cardiac arrest, pulmonary embolism.*

***A special appreciation to all the stuff members of the University Clinic of Anesthesiology, Reanimation and Intensive care, who made a huge effort for successful recovery of this patient***.

## Introduction

In-hospital cardiac arrest (IHCA) is determined as acute circulatory loss which requires fast resuscitation with chest compressions and/or defibrillation (1). The data from European Resuscitation Council, particularly from UK National Cardiac Arrest Audit and Danish In-Hospital Cardiac Arrest Registry, present with incidence of IHCA of 1.6 and 1.8 per 1000 admissions, very lower compared to American Heart Association (AHA) incidence of 6 to 7 IHCA per 1000 admissions (2). Despite that it is a common condition, little research is done in this area, and many data are extracted from out-hospital cardiac arrest guidelines and researches.

Perioperative cardiac arrest patients are a subclass of surgical patients who need CPR on the day of surgery. Cardiac arrest in the perioperative period is certainly a less frequent condition than overall IHCA. According to some reports, the incidence of perioperative cardiac arrest as a special entity is 4.3 per 10000 anesthetics and the mortality rate is 1 death per 100000 anesthetics (3).

## Case Report

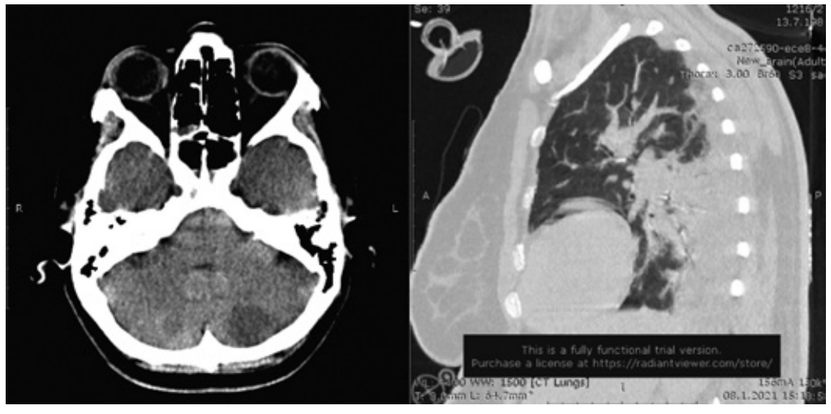
A 39 years old female patient was admitted to our hospital for elective laparoscopic repair of ventral hernia. Her preoperative examination showed that she had no allergies, did not take any daily drugs, was obese, and had four Caesarean sections and one laparoscopic tube ligation without any uneventful conditions and was classified as ASA II. Preoperative laboratory, coagulation tests and X-ray were without abnormalities. After routine monitoring, she was preoxygenated, and she received 2 mg Midazolam, 150 mcg Fentanyl, 60 mg Lidocaine, 150 mg Propofol and 50 mg Roccuronium and was intubated. Sequential Compression Device (SCD) was placed at the beginning as a prevention of thromboembolism. During the laparoscopy, which lasted for 70 minutes only in supine position, no adverse events occurred. Patient was hemodynamically stable maintaining BP around 130/70 mmHg, HR 60-80bpm, SaO2 100% and ETCO2 36-41 mmHg. She was extubated in the OR and transferred to PACU. After 30 minutes in the PACU, she complained having an urge to vomit, and she stopped breathing, and she had no palpable pulse. She was immediately intubated and 1 mg Atropine and 1 mg Adrenaline were given intravenously, while she was only monitored with Rad-8 Pulse Oximeter. When the ECG monitoring was placed the rhythm was polymorphic ventricular fibrillation. Immediately CPR was started, while the defibrillator was getting ready. She was defibrillated twice with energy 150 J and 200 J, with continuous cardiac massage between the defibrillations. Then she had a brief episode of supraventricular tachycardia and then polymorphic ventricular fibrillation again. CPR was resumed, and she was shocked four more times in the next period with maximal energy of 360 J, receiving many boluses of Adrenalin between with total dose of 20 mg. She also received 5000+5000 IU Heparin, Calcium gluconate 2 g, NaHCO3 100 ml. Finally, after around 30 minutes, she stabilized into rhythm of supraventricular tachycardia, with marked hypotension, despite Gelofundine 500 ml and Normal Saline 1000 ml, so inotropic support with Dopamine and Adrenaline were initiated along with continuous Heparin infusion. Portable capnography device was not available in the first part of reanimation. Central venous line and arterial line were placed, and at the initial CVP at that period was 19cmH2O. She manifested with pulmonary edema, SaO2 no more than 70% despite FiO2 1, ETCO2 39 mmHg and pCO2 89 mmHg, with wet crackles bilaterally. She was given Furosemide total dose 140 mg, Methylprednisolone 250 mg and Pantoprazole 40 mg. Blood gas analysis were done few times during resuscitation showing mixed severe acidosis (Table 1). Cardiology consultation and echocardiography revealed a right heart dilatation. She was stabilized and transferred to ICU where she remained mechanically ventilated and sedated for few days and extubated after 7 days. During this period, she was on inotropic support which was gradually reduced, with gradual improvement of the blood gas analysis, and few times of awakening trials to monitor her level of alertness. Neuroprotective therapy with mannitol 50

g total daily dose and PK Merz was initiated on the same day of the arrest. Many laboratory analyses were done on a daily basis showing high D dimer levels at the beginning (9000ng/ml), increased Troponin I 545.14 ng/L, Myoglobin 426.97 ng/ml and CK-MB 88U/L. A lung and brain CT scan with contrast were done on day 5 and revealed small cerebellar hypo density zone and bilateral lung consolidations (Picture 1,2,3 and 4). After 10 days she was discharged from ICU without any disability and with ongoing physical therapy.

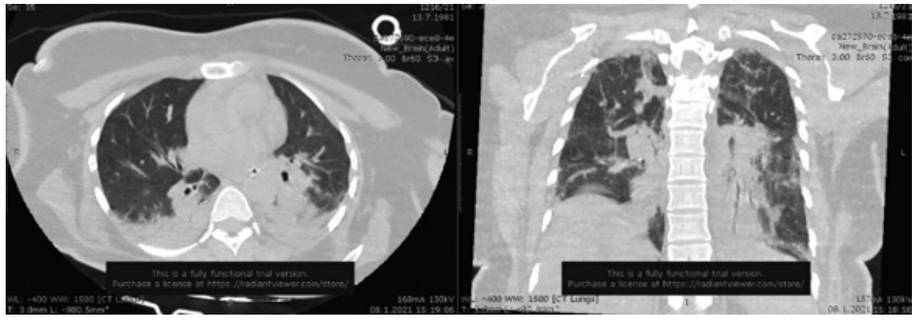
***Table* 1**. *Blood gas analysis in the first 3 days*

| | **Day 1** | | | | | | **Day 2** | | | **Day 3** |
|---|---|---|---|---|---|---|---|---|---|---|
| **pH** | 6.94 | 6.85 | 7.01 | 6.97 | 7.142 | 7.168 | 7.14 | 7.252 | 7.202 | 7.304 |
| **pCO2** | 8.66 | 11.86 | 8.53 | 10.72 | 6.19 | 5.64 | 4.88 | 3.53 | 7.14 | 6.5 |
| **pO2** | 8.39 | 7.33 | 9.46 | 7.61 | 15.10 | 16.3 | 24.70 | 27.83 | 26.66 | 24.2 |
| **HCO3** | 14 | 15.5 | 16.2 | 18.1 | 15.5 | 15.0 | 12.2 | 11.4 | 20.6 | 23.7 |
| **BE** | - 17.7 | - 18.2 | - 15.7 | - 15.3 | - 13.2 | - 13 | - 15.9 | - 14.3 | - 7.4 | - 2.6 |
| **SaO2** | 73 | 57 | 83 | 79 | 97 | 97 | 98 | 98 | 98 | 98 |
| **AnGap** | | | | 24.9 | 20.5 | 20.6 | 21.1 | 18 | 10.0 | 9.4 |
| **Lactate** | 11.0 | 9.0 | 6.0 | 4.84 | 4.80 | 5.32 | 5.62 | 2.21 | 1.71 | 1.53 |

**Picture 1 and 2.** *CT scan of the brain and lungs*




**Picture 3 and 4.** *CT scan of the lungs*








## Discussion

Perioperative cardiac arrest patients are divided in 3 groups: anesthesia-attributable, anesthesia-contributory and not related to anesthesia cases (3). The most of the anesthesia-attributed cardiac arrests are due to airway management and ventilation problems, complications due to placement of central venous lines or accidental application of medications (for example during peripheral nerve blocks). Anesthesia-contributory cardiac arrest patients are usually with some cardiovascular comorbidities, with difficulties in intraoperative management or postoperative respiratory depression. The last group, cardiac arrests not related to anesthesia, includes patients with surgical factor as a reason for deterioration or who have disease or condition which leads to cardiac arrest, for example myocardial infarction, pulmonary embolism, major trauma, ruptured aneurysm, sepsis or multiple organ failure.

Perioperative cardiac arrest must be distinguished from other cardiac arrests and ACLS guidelines should be targeted according to particular situations (4). During this perioperative period many additional factors can contribute to circulatory destabilization and consecutive cardiac arrest, like vagal reaction to surgical stress, vagotonic effects and sympatholysis by anesthetics, neuroaxial suppression, difficulties in airway management, hypovolemia due to massive hemorrhage or inadequate volume replacement, malignant hyperthermia, air embolism, QT prolonged syndrome, tension pneumothorax, transfusion and anaphylactic reactions (3,5). This is why anesthesia provider must be familiar with the patient's condition and also the surgical procedure and all the risks that particular procedure carries. According to studies and statistics, cardiac arrests more often occur in ASA IV and V subclasses and they usually don't survive to discharge; the most of the patients are older, under general anesthesia and with performed emergency surgery (3,5,7). Data show that laparoscopic procedures of the upper or lower abdomen carry additional risk because of the gas inflation with $CO_2$ and patient's positioning during the procedure (8).

Despite all the protocols and improvement in care, the survival rates vary around 20% and are almost double in patients with shockable rhythm (1,4). Fast identification, initialization of CPR, detection and treatment of the cause and post-cardiac arrest care are the most crucial elements in the chain of survival (4). These patients need rapid assessment and quick management, because there is commonly a potentially reversible cause. As quickly as the cause is identified, as much the chances of recovery of spontaneous circulation (ROSC) are bigger (1,9). These events differ from other IHCA because are always witnessed as they occur in the period when the patient is the most closely monitored (5). Unlike other patients, these are already oxygenated, monitored and have venous access. Continuous chest compressions with rate of 100-120/min and minimizing the hands-off period only to the time for delivery of the shock, will improve the chance of survival and lower the possible disabilities. Good coordination between the individual who operates the defibrillator and the individual who performs chest compressions is of a great importance. The algorithm should be followed, by giving 2 minutes of CPR, and then defibrillating the heart to stop the unwilling electrical activity and resume CPR for another 2 minutes. Adrenalin and Amiodarone are the drugs of choice. According to few trials, steroid use during CPR for IHCA patients improved survival

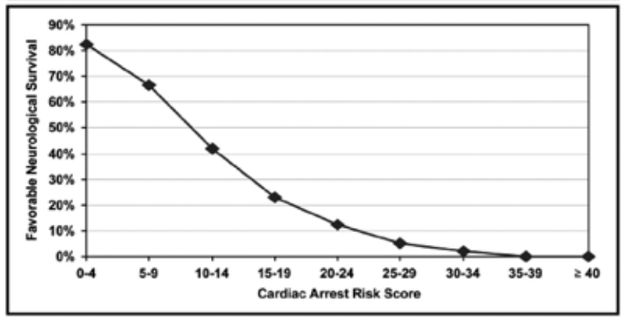
to hospital discharge, but there is no clear recommendation for its routine use (10). Escalating of care is often necessary to guide the resuscitation, like invasive monitoring strategy or point of care ultrasound (4,5). Echocardiography is recommended as a useful tool for myocardial contractility assessment, to detect hypovolemia, tamponade or pulmonary thromboembolism (10).

It is necessary to properly manage the ischemia and also the reperfusion injury after the recovery of spontaneous circulation, to avoid multi organ failure which is a very common complication and a cause for death in prolonged cardiac arrest for more than 30 minutes (1,10). Cerebral protective strategy is very important, alongside with cardio-respiratory support. The most of the recovered patients seem to be discharged to a rehabilitation facility because they have a permanent neurological or functional impairment. Scoring systems, like CASPRI score, are a useful tool to predict post cardiac arrest neurological outcome and survival, and to help in setting the goals of care (Figure 1) (11).

**Figure 1**. *The Cardiac Arrest Survival Post-Resuscitation In-hospital (CASPRI) Score Card and Nomogram for Favorable Neurological Survival.*

| Predictor | Points | Predictor | Points |
|---|---|---|---|
| 1) Age Group, yrs | | 4) Hospital Location | |
| < 50 | 0 | Telemetry unit | 0 |
| 50 to 59 | 0 | Intensive Care unit | 1 |
| 60 to 69 | 1 | Non-monitored unit | 3 |
| 70 to 79 | 2 | 5) Duration of Resuscitation, min | |
| ≥ 80 | 4 | < 2 | 0 |
| 2) Initial Arrest Rhythm | | 2 to 4 | 0 |
| VF / VT, Time to Defibrillation | | 5 to 9 | 3 |
| ≤ 2 minutes | 0 | 10 to 14 | 5 |
| 3 minutes | 0 | 15 to 19 | 6 |
| 4 - 5 minutes | 2 | 20 to 24 | 6 |
| > 5 minutes | 3 | 25 to 29 | 6 |
| Pulseless Electrical Activity | 6 | ≥ 30 | 8 |
| Asystole | 7 | **Factors Present Prior to Arrest** (items 6-11) | |
| 3) Pre-Arrest CPC Score | | 6) Mechanical Ventilation | 3 |
| 1 | 0 | 7) Renal Insufficiency | 2 |
| 2 | 2 | 8) Hepatic Insufficiency | 4 |
| 3 | 9 | 9) Sepsis | 3 |
| ≥ 4 | 9 | 10) Malignancy | 4 |
| | | 11) Hypotension | 3 |

| Points | Cardiac Arrest Survival Score | No. Alive / Total N | Mean Survival (95% CI) | Proportion of Observations in Cohort |
|---|---|---|---|---|
| 1) | 0 to 4 | 303/367 | 82.6% (78.7% - 86.5%) | 2.6% |
| 2) | 5 to 9 | 707/1061 | 66.6% (63.8% - 69.5%) | 7.4% |
| 3) | 10 to 14 | 1023/2434 | 42.0% (40.1% - 44.0%) | 17.0% |
| 4) | 15 to 19 | 946/4092 | 23.1% (21.8% - 24.4%) | 28.6% |
| 5) | 20 to 24 | 403/3291 | 12.3% (11.1% - 13.4%) | 23.0% |
| 6) | 25 to 29 | 112/2158 | 5.2% (4.3% - 6.1%) | 15.1% |
| 7) | 30 to 34 | 16/751 | 2.1% (1.1% - 3.2%) | 5.2% |
| 8) | 35 to 40 | 0/158 | 0.0% | 1.1% |
| 9) | ≥ 40 | 0/16 | 0.0% | 0.0% |
| 10) | | | | |
| 11) | | | | |
| **Cardiac Arrest Survival Score =** | | | | |




*Our patient was scored 9 with 66% favorable neurological survival (11).*

A brief overview of European Society of Cardiology Guidelines for acute pulmonary embolism was done, as it was the most suspected cause of the arrest. It's a very frequent condition, especially in elderly population, and presented as DVT or PE. 34% of patients dies immediately or within few hours, and only 7% were diagnosed before death (12). A very important measure in hospital care is to consider the risk factors and to make a decision about a suitable therapy. Many of the hospitalized patients pose strong or moderated risk factors like a major trauma, spinal cord injury, lower limb fracture, atrial fibrillation/flutter, central venous line, cancer, infection, stroke, and many more. It is necessary in regular practice to identify the condition, to understand the pathophysiology and to manage it urgently and properly. Acute PE has issues with both circulation and gas exchange, leading to a rise in pulmonary artery pressure and consecutive RV failure. Next, this RV dysfunction leads to impaired LV filling and hemodynamic instability and a condition of "induced" myocarditis with elevated levels of cardiac biomarkers. In the lungs, there is a ventilation – perfusion mismatch leading to marked hypoxemia and hypercapnia, which additionally worsens the acidosis caused by the circulatory insufficiency. The diagnosis is based on several steps: clinical presentation and assessment of risk factors, D-dimers level and imaging techniques. For performing an imaging diagnosis, patient should be hemodynamically stable and transportable. Few imaging tests are available: Computed Tomographic Pulmonary Angiography (CTPA), pulmonary angiography, Lung scintigraphy (Planar V/Q scan), Magnetic resonance angiography and echocardiography. Each of them has different sensitivity and specificity influenced by the pre-test risk stratification category. Laboratory biomarkers also contribute to the diagnosis and prognosis, for example: troponins, heart-type fatty acid-binding protein (H-FABP), B-type natriuretic peptide (BNP) and N-terminal (NT)-pro BNP, lactate levels and serum creatinine. In the acute phase, the treatment plan takes care of hemodynamic and respiratory support, carefully treating RV failure. Initial anticoagulation should be applied even before getting the results except when there is a risk for major bleeding. Medications used include low-molecular weight heparin (LMWH) subcutaneously, fondaparinux or intravenous unfractionated heparin (UFH). Dose should be weight-adjusted and adapted according to creatinine clearance (CrCl). For obese patients or with CrCl<30ml/min, UFH is more recommended and controlled by activated partial thromboplastin time (aPTT). Reperfusion treatment with systemic thrombolytic therapy should be initiated if there is further deterioration despite anticoagulation medications. The best results are noted in the first 48 hours, but caution should be paid on the contraindications for this treatment. After the recovery oral anticoagulation with NOACs or VKA is recommended as a long-term treatment option (12).

## Conclusion

The aim of all studies and proposed risk stratification scores, like ASA score and Risk Calculator by the National Surgical Quality Improvement Program, is to identify the high risk patients, to optimize them preoperatively, to monitor them properly and to minimize complications or

death (13). Medical personnel should be qualified to know how to monitor vital signs correctly, warn for irregularities, use multiple scoring systems to predict early deterioration and intervene according to protocols. It is very important to register and to analyze all the cases, to determine all the complications due to anesthesia during the perioperative period and to make a suitable prevention and treatment strategy for future events.

## References


1. Andersen L., Holmberg M., Berg K., et al. In-Hospital Cardiac Arrest: A Review. JAMA. 2019; 321(12):1200-1210.
2. Gräsner J. T., Herlitz J., Wnent J. et al. Epidemiology of cardiac arrest in Europe. Draft guidelines by European Resuscitation Council October 2020.
3. Sheila J. Ellis, Myrna C. Newland, Jean A. Simonson, et al. Anesthesia-related Cardiac Arrest. Anesthesiology 2014; 120:829 – 838.
4. Soar J., Nolanb J.P., Böttiger B. W. et al. European Resuscitation Council Guidelines for Resuscitation 2015. Section 3. Adult advanced life support. Resuscitation Journal 95 (2015) 100-147.
5. Moitra V., Einav S., Thies, Karl-Christian et al. Cardiac Arrest in the Operating Room: Resuscitation and Management for the Anesthesiologist: Part 1. Anesthesia & Analgesia: March 2018 – Volume 126 – Issue 3 – p 876-888.
6. McEvoy M., Thies, Karl-Christian, Einav S. et al. Cardiac Arrest in the Operating Room: Part 2 — Special Situations in the Perioperative Period. Anesthesia & Analgesia: March 2018 – Volume 126 – Issue 3 – p 889-903.
7. Ahmed A, Ali M, Khan EA, Khan MU. An audit of perioperative cardiac arrests in a Southeast Asian university teaching hospital over 15 years. Anaesth Intensive Care. 2008 Sep;36(5):710-6.
8. Nunnally ME, O'Connor MF, Kordylewski H, et al. The incidence and risk factors for perioperative cardiac arrest observed in the national anesthesia clinical outcomes registry. Anesth Analg. 2015 Feb;120(2):364-70.
9. Moezzi M, Afshari G, Rahim F, et al. Outcomes of Cardiopulmonary Resuscitation and its Predictors in Hospitalized Patients. Clin Med Rev Case Rep 2020; 7:309.
10. American Heart Association. Advanced Cardiovascular Life Support Provider Manial 2016, Pages 92-109.
11. Chan S. P., Spertus J. A., Krumholz H. M., et al. A Validated Prediction Tool for Initial Survivors of In-Hospital Cardiac Arrest. Archives of internal medicine 2012; 172(12). 947-953.
12. Konstantinides S., Meyer G., Becattini C., et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). European Heart Journal, Volume 41, Issue 4, 21 January 2020, Pages 543 – 603.
13. Kaiser HA, Saied NN, Kokoefer AS, et al. Incidence and prediction of intraoperative and postoperative cardiac arrest requiring cardiopulmonary resuscitation and 30-day mortality in non-cardiac surgical patients. PLoS ONE 2020; 15(1): e0225939.




*CASE REPORT* UDK: 616.342-007.43-089.819

# LEFT PARADUODENAL HERNIA

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## ABSTRACT

Internal hernias are relatively rare condition and are a rare type of intestinal obstruction. Paraduodenal hernias are considered to be the most common cause of obstruction and are a challenge for diagnostics.

We present the case of a 29-years-old young man with several episodes of abdominal pain, accompanied by vomiting, which was examined in the emergency department. The patient was generally a healthy person.

Among the other examinations, a computed tomography scan of the abdomen was performed where tumor-like mass was seen between the stomach and pancreas, with characteristic CT signs of paraduodenal hernia. On CT of the abdomen with i.v. contrast medium, a mass of thin cervical vertebrae was seen in the space between the stomach and pancreas, placed in a ball with a visible hydroaeric level at the height of the ligament of Treitz. The mesentery is on the jejunum is drawn to the left.

***Key Words:*** *abdominal pain, CT abdomen, internal hernia, paraduodenal hernia.*

## Introduction

Intra-abdominal hernias are rare condition, accounting for 0.9% of all intestinal obstructions (1). The half of all internal abdominal hernias are paraduodenal hernias. They occur when part of the small intestine herniates occurs into the paraduodenal fossa and is manifested by intestinal obstruction. The herniation may occur in the paraduodenal fossa Landzert on the left or in the right paraduodenal fossa Kolb.

The Landzert paraduodenal fossa is located to the left of the 4th part of duodenum, behind v. mesenterica inferior and the ascending branch of the a. colica sin., where three edges of the hernia form directly below the posterior parietal peritoneum (3). At autopsy, this pit was found in 2% of cases. In recent examinations, paraduodenal recess was found in 12% of the cases (4).

The clinical diagnosis is difficult. We present a case of left paraduodenal hernia, in a patient admitted due to severe pain, vomiting and palpable mass in the left hypochondrium.

## Case Report

A 29-years-old patient was admitted as an emergency patient with intermittent left hypochondrium pain. The patient was a frequent patient in the emergency department last year. Admission pain was associated to nausea and vomiting.

During the clinical examination, an oval palpable tumor in the left hypochondrium was found. The laboratory findings were without special deviations. Native abdominal X-rays showed no signs of ileus and no signs of pneumoperitoneum. On CT of the abdomen with iv contrast, a mass of thin cervical vertebrae was seen in the space between the stomach and pancreas, placed in a ball with a visible hydroaeric level at the height of the lig. Treitz. The mesentery was on the jejunum, drawn to the left. Free fluid in the abdomen was not monitored.

**Figure 1.** *Schematic presentation of a paraduodenal hernia, the small intestine prolapsing into the fossa Landzert, (curve arrow) localized behind the v. inferior mesentery a. colica sinistra (arrow).*

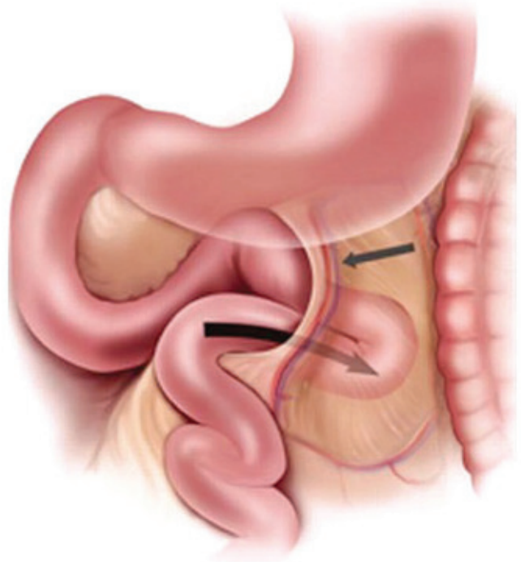


**Figure2**. *Plane abdominal x-ray shows intestinal loops grouped in the left hypochondrium.*





**Figure 3**. *Axial CT of abdomen with contrast-arterial phase follows a round mass prerenal between the stomach and pancreas that pushes the stomach forward*

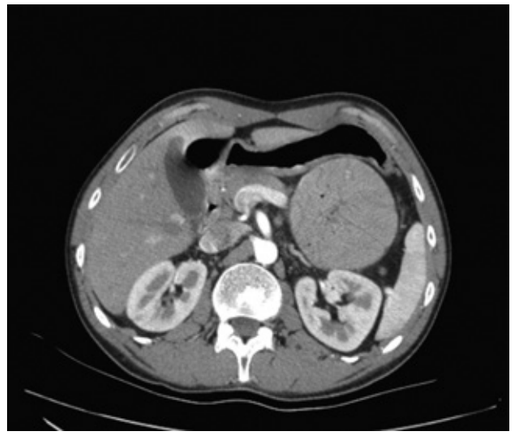


***Figure 4***. *Axial CT of abdomen with contrast – Mesenteric blood vessels burst to the right and front of a stagnant small intestine.*

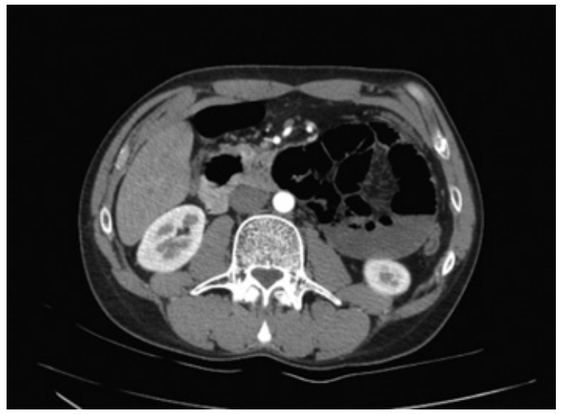
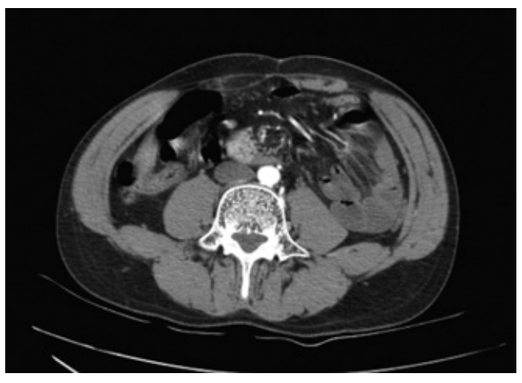


**Figure 5**. *Axial CT of abdomen with contrast – Branches of the mesenteric blood vessels are drawn and designated.*



After a few hours in Emergency Unit, the patient's pain was reduced, the abdomen was softened, and the patient was sent for home treatment with an indication for further monitoring of the condition.

## Discussion

Internal hernias are defined as hernias formed by intestinal protrusion through a peritoneal or mesenteric opening, leading to the formation of a closed, encapsulated vein in the abdomen. This type of hernia accounts for 0.2% – 0.9% of all intestinal obstructions. The most often these hernias in 10-50% are accidental findings of surgery or autopsy.

The classification of hernias according to Hansmann and Morton, which analyzed 467 cases of hernias, are grouped into 7 groups: paraduodenal (53%), through foramen Winslowi (8%), pericecal (13%), intersigmoid (6%), transmesentric (8%), trans ometric (1-4%) or retroanastomotic (2).

According to Liew and colleagues 25 types of internal hernias are classified. Paraduodenal hernias are rare but can account for 30-50% of all internal hernias. Left-sided paraduodenal hernias are more common (75%) than right-sided (25%) (2). They are more common in men and are the most often congenital (1). It is a congenital defect that occurs due to malrotation and abnormal mesenteric adhesion (2). In the most cases, it is presented up to the 4th or 5th decade of life. The clinical picture may range from asymptomatic to acute or chronic intestinal pain, which can be emphasized after a hearty meal.

The clinical finding may range from a normal finding to a palpable mass or signs of intestinal obstruction.

Computed tomography as well as a passage with barium porridge show the site of prolapse. Preoperative diagnosis in asymptomatic patients with a paraduodenal hernia is difficult, but imaging methods can help with asymptomatic paraduodenal hernia. Out of the 45 cases reported so far, 19 have been diagnosed.

The plain x-ray of the abdomen may sometimes show signs of ileus by moving the surrounding organs from the herniated part of the bowel. CT of the abdomen is followed by a "cluster" of intestinal vesicles encapsulated in a hernia near the lig. Treitz, depression of the duodenum-jejunal junction, displacement of the mesenteric vessels to the right and elevation of the mesenteric vein, and depression of the transverse colon. Angiography is presented by displacement or curvature of blood vessels.

Laparoscopy gives a definitive diagnosis (4).

Treatment is usually laparoscopic investigation because of the risk of mesenteric vascular ischemia.

## Conclusion

Paraduodenal hernias are an extremely rare and difficult condition to diagnose. Radiological methods can help diagnose these rare conditions. In the presence of acute suffering with signs of ileus, urgent surgical treatment is necessary.

The method of choice is laparoscopic surgery.





## References

1. Kuzinkovas V, Haghighi K, Singhal R, et al. Paraduodenal hernia: a rare cause of abdominal pain. Can J Surg. 2008; 51(6): E127-E128.
2. Assenza M, Rossi D, Rossi G, et al. Laparoscopic management of left paraduodenal hernia. Case report and review of literature. G Chir. 2014;35(7-8):185-189.
3. Kadhem S, Ali MH, Al-Dera FH, et al. Left Paraduodenal Hernia: Case Report of Rare Cause of Recurrent Abdominal Pain. Cureus. 2020;12(3): e7156. Published 2020 Mar 2. doi:10.7759/cureus. 7156.
4. Moussa MB, Nouhi I, Lachguar T, et al. A paraduodenal hernia revealed by bowel obstruction: case report and literature review. Pan Afr Med J. 2018; 31:120. Published 2018 Oct 17. doi:10.11604/pamj.2018.31.120.13538.
5. A. Blachar, M.P. Federle, S.F. DodsonInternal hernia: clinical and imaging findings in 17 patients with emphasis on CT criteria Radiology, 218 (2001), pp. 68-74.
6. Hassani KI, Aggouri Y, Laalim SA, et al. Left paraduodenal hernia: A rare cause of acute abdomen. Pan Afr Med J. 2014; 17:230. Published 2014 Mar 27. doi:10.11604/pamj.2014.17.230.3546.

# INTERNAL INCARCERATION OF THE SMALL INTESTINE

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## ABSTRACT

Incarcerated hernia is often accompanied by strangulation and subsequent necrosis of the strangulated tissue. Incarcerations through visible natural openings in the abdominal wall or at the incision sites of previous surgeries, are much easier to diagnose. In contrast, incarcerated internal hernias with the same danger and risk to the patient are often much more difficult to diagnose preoperatively.

Often, computed tomography cannot confirm internal incarceration with complete certainty (3). Such a diagnosis should be suspected especially in any patient who has had previous abdominal surgery and it occurs in a state of intestinal obstruction or acute abdomen, with no signs of pneumoperitoneum.

This case report describes a 73-years-old male with internal incarcerated hernia with small intestine obstruction, who was found an opening – defect of the gastrocolic ligament in which was herniated and strangulated part from the small intestine.

***Key Words:*** *abdominal surgery, iIleus, internal incarceration, intestinal obstruction, strangulation*,

## Introduction

During the strangulation of the small intestine, its circulation is disturbed and its vitality is endangered. Firstly, venous return is compromised. As a result, capillary pressure increases, and loss of intravascular fluid and erythrocytes occurs in the intestinal wall (edema) and its lumen. Deterioration of the arterial blood supply leads to intestinal infarction. Translocation of anaerobic microorganisms and their toxins follows. The strangulation morbidity in internal incarceration is much higher than in external incarceration due to much larger absorbent surface. Potential sites of internal incarceration include the Winslow foramen, an opening in the mesentery, an opening in the mesocolon transversus, a congenital or acquired diaphragmatic hernia, and of course, postoperative unclosed openings in the meso or some intra-abdominal ligaments (1).

When the patient complains of severe pain, which is often resistant to analgesics, it is indicative of ischemic pain that is also present during strangulation. For example, such pain is not found in paralytic ileus. Strangulation may be associated to elevated levels of K, amylase and lactate dehydrogenase. There may be leukocytosis or leukopenia. Clinical symptoms of strangulation include:

- Persistent pain despite conservative treatment,
- Localized pain in the abdomen,
- Shock (4).





In the case of intestinal obstruction, conservative treatment should not be longer than 72 hours, but in the case of strangulation, surgical treatment should be instituted very soon. In the case described below, due to an opening in the gastrocolic ligament, the small intestine-penetrated through it, filled the omental bursa, and then pierced the hepatogastric ligament. After penetrating the hepatogastric ligament, it passes along the hepatoduodenal ligament, incarcerates, and then strangulates, bringing the patient to an acute abdominal condition (2).

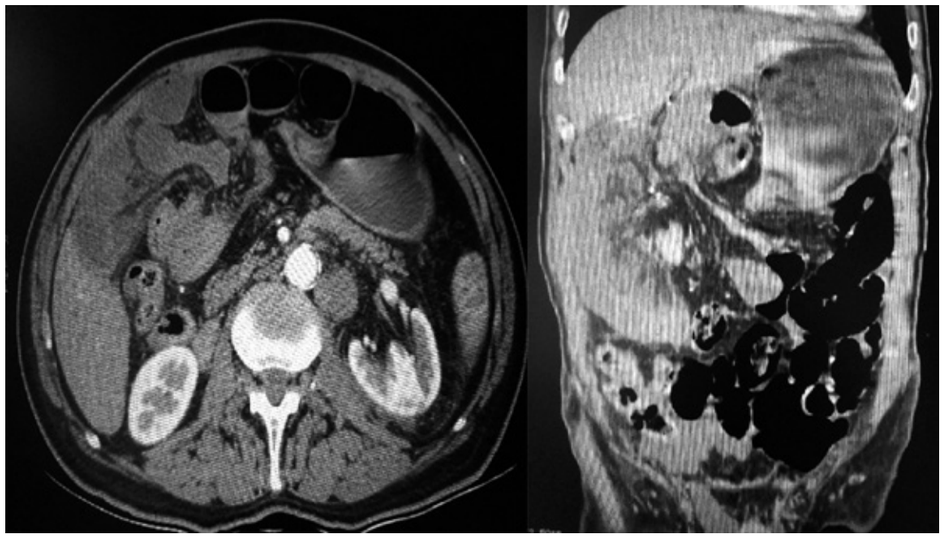
## Case Report

A 73 years old patient, was brought to our clinic as an emergency case, with severe abdominal pain, especially epigastric. He was also afebrile and tachycardic with a pulse of 108. The pain started that day and was sudden and persistent, followed by multiple vomiting. On palpation the abdomen was tense, especially painful in the epigastric region. No contents were obtained during nasogastric tube placement. From laboratory findings, there were elevated leukocytes 12.70 (reference value 3.5-10.00). Elevated platelets 568.00 (reference value 150.00-390.00). The other values of the parameters were normal (even CRP).

Anamnestic, he has previously had problems with epigastric difficulties and the appearance of heartburn. The patient was operated more than 20 years ago from acute appendicitis, and immediately afterwards from ileus, with a partial resection of the small intestine and T-T anastomosis (we noticed the same during the operation).

We made native abdominal X-ray and CT of the abdomen – non contrast and contrast enhanced. On the CT a cluster of dilated small bowel loops with wall thickening was seen, feces sign and mesenteric edema. After application of contrast medium, the thickened wall was with lack of enhancement (6). There was also ascites in the abdominal cavity (transudate).

**Figure 1** **Figure 2**



The first picture shows a group of dilated small bowel loops with an edematous, thickened wall and mesenteric edema, and lack of enhancement of the wall after application of contrast. The same can be seen in the second image with a picture of a distended stomach and ascites.

So, we decided on surgery without a definite preoperative diagnosis. On operation was encountered a gangrenous altered small intestine about 1.5 m long as a result of its strangulation. That part of the small intestine was resected and was made T-T anastomosis. The opening of the gastrocolic ligament was sewn (closed). A lavage of the abdominal cavity was performed and a drain was placed in the douglas. More than 1 m from the small intestine, mostly the jejunum, remained after resection. The postoperative course went smoothly, without complications and the patient was released home on the 9th day postoperatively, with a proper diet and stool.

**Figure 3**. *The picture shows the part of the small intestine where it penetrates the hepatogastric ligament and strangulates*

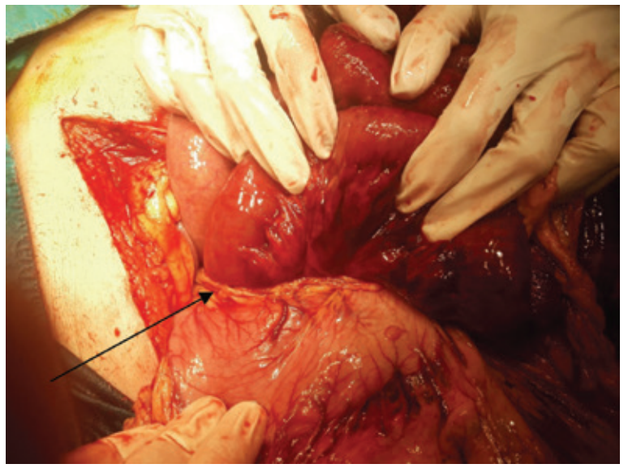


**Figure 4**. *The image shows where the small intestine enters the gastrocolic ligament and omental bursa.*

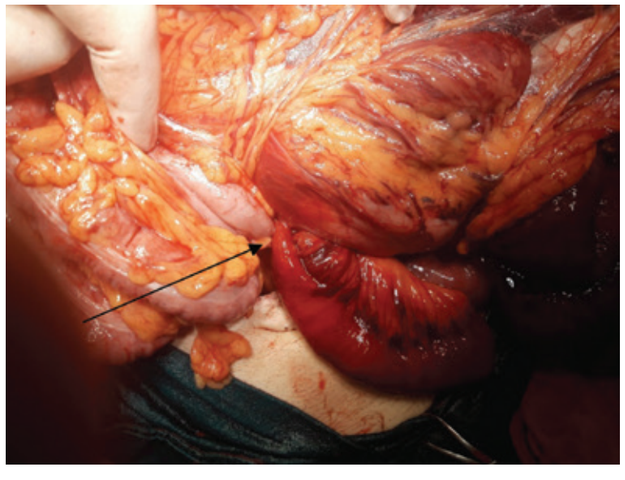


**Figure 5**. *Gangrenous changes in the small intestine after release from strangulation.*

**Figure 6**. *Resected part of the small intestine, mostly ileum (about 1.5 m).*

## Discussion

Internal hernias can be the cause of acute, life-threatening conditions, and often with difficulty, a preoperative diagnosis can be made with certainty. Therefore, in any patient with an acute abdomen, especially if he has previously had abdominal surgery, the possible cause of internal hernia and its incarceration should be considered. The importance of the presence of congenital

openings in the mesentery, abdominal ligaments or non-closure of newly created openings in the mesentery, omentum or other intra-abdominal openings of ligaments during surgery can also be confirmed in this case (1. 2. 5). In addition, it turns out that even after a very long period (in which the body compensates), the problem of internal incarceration can occur, followed by all possible complications.

The condition of the acute abdomen does not always allow enough time for a reliable diagnosis preoperatively and as in our case the operation was necessary without a definite preoperative diagnosis. In this case, it was assumed that during one of the previous two surgeries that the patient had several years ago (probably the second), an iatrogenic opening was created in the gastrocolic ligament and this led to the small intestine entering it after a long period and gradually leading to a state of incarceration, ileus and strangulation. Of course, in such emergencies, one should not wait too long to make a reliable diagnosis, but an urgent operation is needed, which in this case was performed about 3.5 hours after the arrival of the patient in our institution.

## Conclusion

Incarceration of internal hernias are rarer cases in clinical practice and their preoperative diagnosis is difficult to establish with certainty. They are often accompanied by strangulation. In order to maximally expect a good outcome of the disease, short preoperative preparation of the patient and prompt surgical intervention are required.

## References


1. Michael J. Zinner and Stanley W. Ashley, Maingot's abdominal operatons. 12th edition (2013).
2. George G. Zuldema, Charles J. Yeo. Shackelford's Surgery of the Alimentary Tract – Small Bowel Obstruction, 5th ed., Chapter 23 (2002).
3. Fausto Catena, Salomone Di Saverio, Luca Ansaloni, et al. CT Scan in Abdominal Emergency Surgery, 371-358 (2018).
4. Ang Li, Renwang Hu, Dong Zhou, et al. Internal herniation through lesser omentum hiatus and gastrocolic ligament with malrotation: a case report. *Journal of Medical Case Reports* volume 11, Article number: 344 (2017).
5. Jan Philipp Ramspott, Tarkan Jäger MD, Klaus Emmanuel, et al. *European Surgery*, First description of an acquired internal hernia: a case report, volume 51, pages 217 – 219 (2019).
6. Heiken J. P. and Smithius, R. Closed loop in small bowel obstruction H. Radiology Assistant, https://radiologyassistant.nl/abdomen/bowel/closed-loop-in-small-bowel-obstruction (2012).



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Manuscripts that are published should have not been published previously. Manuscripts that have been previously published only in form of abstracts are eligible for publishing in the journal but should be followed by additional letter send to the Editor, where the abstract details are noted (abstract number, which book of proceeding or doi, date and place).

The authors are responsible for respecting the ethical guidelines for medical researches, as well as for all that is explained, attitudes, analyses and shown results.

The redaction sends the manuscripts to anonymous reviewing process from international or domestic reviewers and the Editors determine the definitive categorization of the manuscript. Once reviewed manuscript together with the reviewers' remarks is send back to the corresponding author, after what the author is omitted to deliver the final form of the manuscript to the Editorial board within one week.

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## *MANUSCRIPT PREPARATION*

Manuscript should be sent together with the accompanying letter from the corresponding authors where declaration that the text has not been published previously is signed. Additional conflict of interests and confirmation by all the authors should be declared in this letter (example: Annex no. 1).

The guidelines for authors adhere to the uniform Requirements for Manuscripts submitted to Biomedical Journals: www.nlm.nih.gov.

**Language and style** of the manuscripts should be clear, simple to according the language, anesthesiological and medical taxonomy.

The manuscript has to be written in **English Manuscripts** should be written in **Microsoft Word** (*.doc format) with **Times New Roman** font and **size 12.** Margins on left, up and bottom should be 3 cm and right margin should be 2,5 cm.

The inline space should be 2. Do not use Bold or Italic letters for the whole text (only for parts that have to be emphasized). Manuscript should not exceed 10 pages (without the references).

**Abbreviations and correct medical terms** should be used according to the International Committee of Editors of Medical Journals (http://www.icmje.org). Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

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- Manuscript should be organized in:
- Title page
- Text organized in IMRaD
- Acknowledgments
- Authors Contribution
- References

Review articles, case reports, therapeutic and technological innovation, discussions, critics, impressions from meetings, information for international conferences and reviews of new books or variate may be written in different sequences and manners.

## *TITLE PAGE*

**The title** of the manuscript written in CAPITAL LETTERS.

**Authors Surname and Name initial** (Jovanov J, maximum 6 authors), without academic or other titles.

**Name and address of the institution** where the authors come from whit the subscribed digits

**Abstract in English.** Abstract should include up to 250 words and should contain goals of the paper, important elements from the methodology, concisely displayed results and conclusion. Each abstract at the end must have **Key words:** in alphabetical order.

## *TEXT*

- Introduction,
- Matherial and Method,
- Results
- Discussion
- Conclusion

Review articles, case reports, therapeutic and technological innovation, discussions, critics, impressions from meetings, information for international conferences and reviews of new books or variate may be written in different sequences and manners.





**Introduction** section should include a literature overview in relevance to the elaborated problem. In this sections 3-5 key references are citied and this section should not be longer than 2 pages.

**Material and method** sections includes detailed description of the performances in the research as well as the statistical analyses used. This section should include: time during what the research was conducted, type of the study, place of where the research was undertaken, randomization or stratification used (clear description of the examined groups), exclusion and inclusion criteria, method, analysis types, apparatus and instruments used and referent values of the examined features (in SI-International System units).

**Results** are displayed in simple manner with text, images, tables and charts that are submitted in the text where author wants to stand, titled and numbered appropriately. Additionally, on separate document all carts images and tables are send together with the manuscript.

Title and the number of the charts and tables are placed above them while the explanations, abbreviations and comments are placed below. Images title and number is placed below and the image should include proper explanation.

**Discussion** section emphasize the key finding of the actual research and compares these result to other relevant literature data.

**Conclusion** section should not include more than 150 words and shoul be drown from the relevant elaborated results.

**Acknowledgment and Author contributions** sections are displayed after the conclusion and before the reference section.

## *REFFERENCES*

This sections include only the citied references. **The references** are listed in order of appearance in the paper and the citation is standard numbers enclosed in small brackets in the same line with the text ( ).

For each reference if more than three authors appear provide the names of the first three authors and followed by **et al.**

**Examples:**

Journal references:

Nirmala BC, Kumari G. Foot drop after spinal anaesthesia: a rare complication. Indian J Anaesth. 2011; 55: 78 – 79.

Lynch EP, Lazor MA, Gellius JE, et al. The Impact of Posoperative Pain on the Development of Postoperative Delirium. Anesth Analg 1998; 86:781-785.

**2. Journal supplements:**

AzmanJ, Frkovic V, Bilic L, et al. Korelacija I regresija. Acta Med Croat 2006;60 (suppl I):81-89.| 70 |

**3. Books**

Brown, D.L. Spinal, epidural, and caudal anesthesia. In R.D. Miller Miller's Anesthesia, 6th edition. Philadelphia: Elsevier Churchill Livingstone; 2005.p 98-198

**4. Doctoral or master thesis**

Jelisavac Cosic S. Urokinazni I tkivni aktivator plazminogena i njihov inhibitor u raku dojke (Master thesis). Zagreb: Farmaceutsko-biohemijski fakultet 2004, p.50

**5. Electronic reference**

Dag Stat. Mackinnon A. Available from: http//www.mhri.cdu.au/biostats.Accessed May 5th 2006.

Webster NR. The anaesthetist as peri-operative physician. Anaesthesia. http://dx.doi.org/10.1046/j.1365-2044.2000.01722.x

References used from abstracts are marked as **(abstr).,** and from letters with **(letter)**

## *MANUSCRIPT SUBMISSION*

Prepared manuscript should be submitted electronically to:

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**All manuscripts that don't fulfill the above criteria will not be accepted for reviewing**

## *Accompany letter ANNEX no. 1*

I _____. Here by declare that the article _____ (NAME OF THE ARTICLE) has not been previously published (fully or partialy) previously.

We autors_____

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I _____ (THE FIRST AUTHOR FULL NAME) declare Conflict of interest or declare non Conflict of interest.

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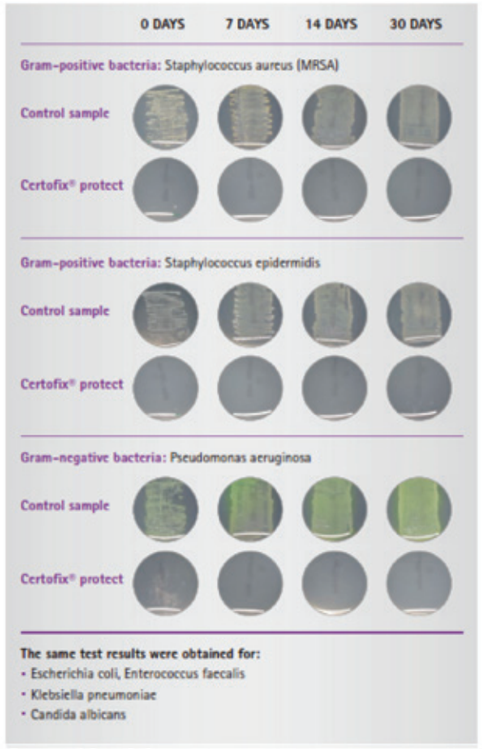


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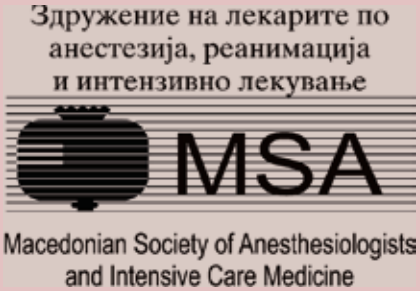
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