

# 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

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Department of Anaesthesia and Reanimation, Faculty of Medicine,  
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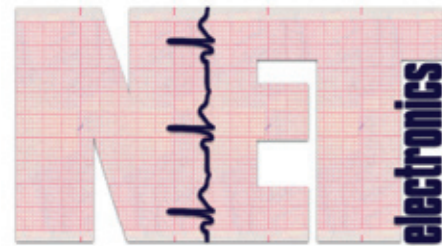
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## PANCREATIC CANCER: WHERE DO WE STAND?

*Meri Trajkovska, MD, PhD*

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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,



## 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.

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## 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 inverted, 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 drawn 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 ambiguous 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.

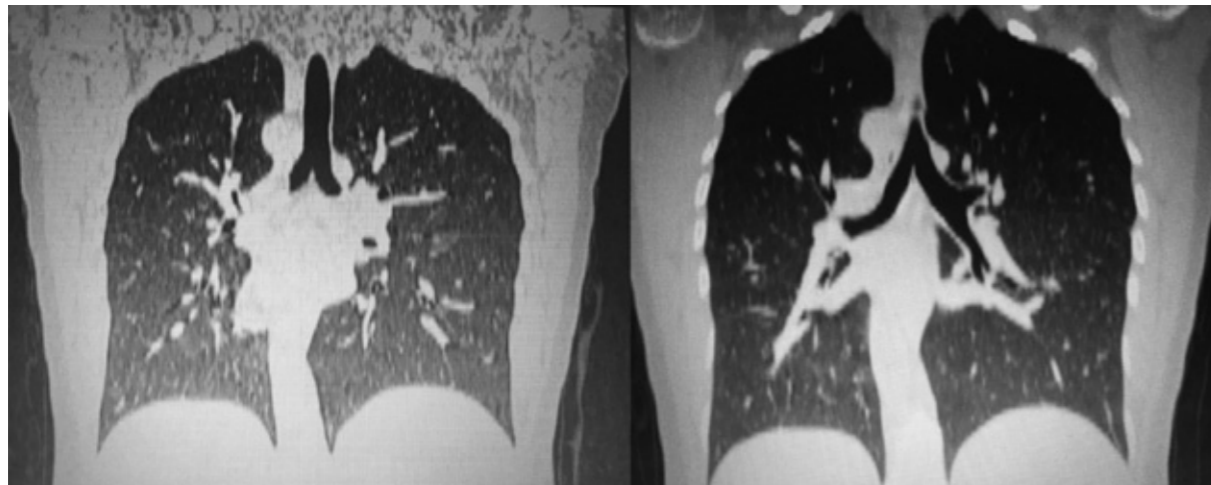




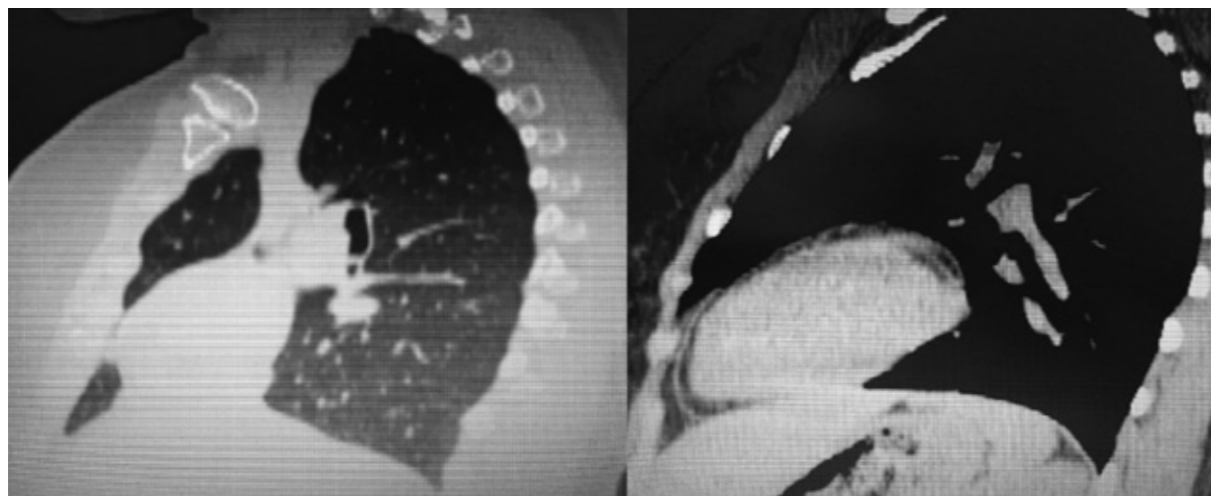
**Figure 2.** Axial CT scan slice of situs inversus with right-sided heart.



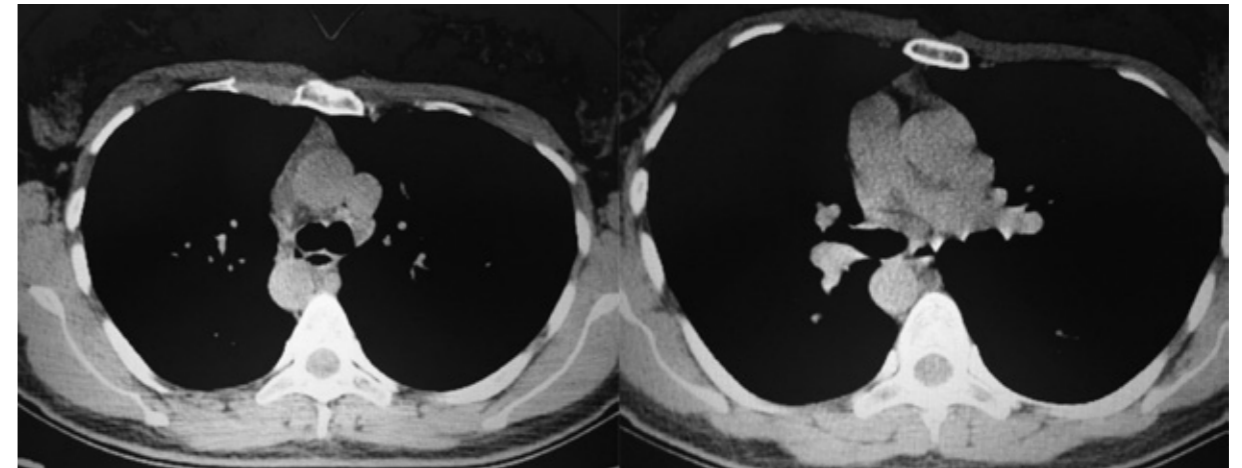
**Figure 3.** CT scans of the lung (coronal view) in situs inversus totalis.



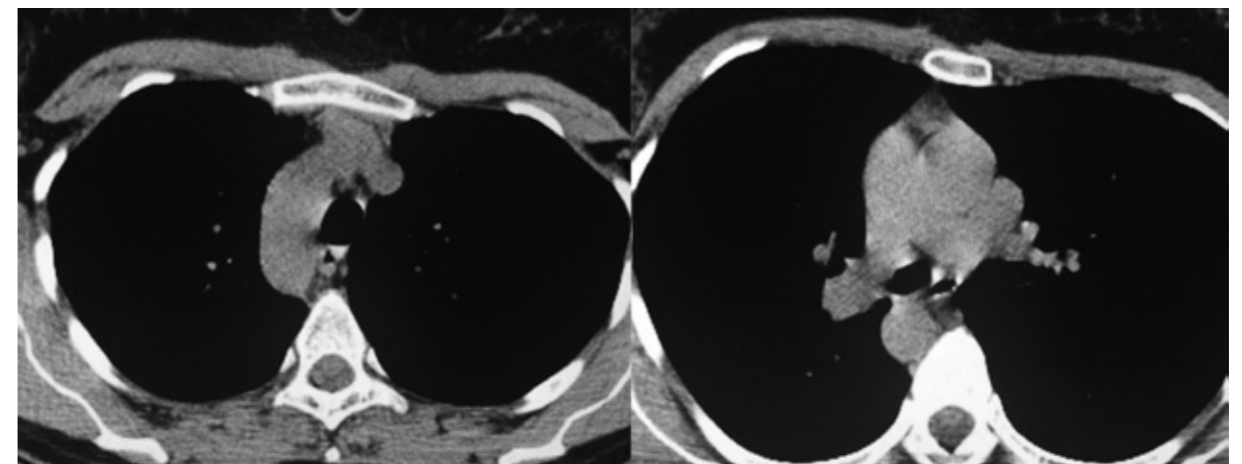
**Figure 4.** CT scans (sagittal view) of the right lung and right hilla.



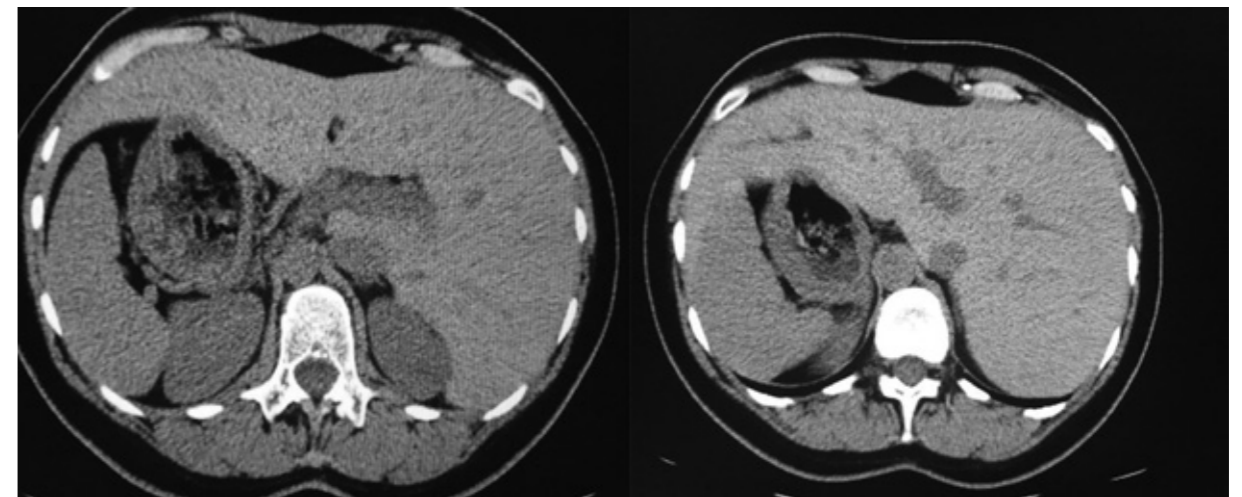
**Figure 5.** Axial CT scans: transposition of the main vessels in the upper mediastinum: aorta, v.cava sup. et pulmonary trunc.



**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 embryo. 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 inversus 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 accompanied 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 recognized 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, pulmonary 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 recognize 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 affect 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.

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## 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