

Evidences on the clinical and anatomical aspects of situs inversus

Evidências sobre os aspectos clínicos e anatômicos da situs inversus

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Abstract

Introduction: situs *inversus* is a rare congenital anomaly characterized by the transposition of the abdominal organs, viscera and vasculature, in relation to the sagittal direction, offering an image called “mirror image”. It is classified as total when associated with dextrocardia, while partial *situs inversus* affects only one or more organs. Objective: to answer what is the evidence about the clinical and anatomical aspects of situs *inversus*. Methodology: this is an integrative literature review. The research was carried out through online access to the *National Library of Medicine* (PubMed MEDLINE), *Scientific Electronic Library Online* (SciELO), Cochrane Database of Systematic Reviews (CDSR), Google Scholar, Virtual Health Library (BVS) and EBSCO databases. *Information Services Results and Discussion*: In situs *solitus*, the right lung has three lobes and an eparterial bronchus (bronchi above the pulmonary artery), while the left lung has two lobes with a hyarterial bronchus (bronchi below the pulmonary artery), the stomach and the spleen are on the left and the greater lobe of the liver is on the right. The morphological left atrium is to the left of the morphological right atrium. With situs *inversus*, the left lung has three lobes with an eparterial bronchus and the right lung has two lobes with a hyperarterial bronchus, the stomach and spleen are on the right side of the body, the larger lobe of the liver is on the left, and the morphological left atrium is to the right of the morphological right atrium. Final considerations: it is known that this anatomical asymmetry is established during embryonic formation, specifically, in organ rotation. However, it is worth noting that individuals with total *situs*

inversus alone do not have clinical repercussions, with the exception of cases associated with heart disease. Therefore, almost always, its diagnosis is a finding in imaging tests, such as radiographs, CT scans and ultrasounds.

Keywords: *Situs inversus*; Dextrocardia; Congenital anomaly.

Resumo

Introdução: *situs inversus* é uma rara anomalia congênita caracterizada pela transposição dos órgãos abdominais, vísceras e vasculatura, em relação ao sentido sagital, oferecendo uma imagem denominada “imagem em espelho”. É classificada como total quando associada à dextrocardia, enquanto *situs inversus* parcial afeta apenas um ou mais órgãos. Objetivo: responder quais são as evidências sobre os aspectos clínicos e anatômicos do *situs inversus*. Metodologia: trata-se de uma revisão integrativa da literatura. A pesquisa foi realizada por meio de acesso online à National Library of Medicine (PubMed MEDLINE), Scientific Electronic Library Online (Scielo), Cochrane Database of Systematic Reviews (CDSR), Google Scholar, Virtual Health Library (BVS) e bases de dados EBSCO. Resultados e Discussão dos Serviços de Informação: In *situs solitus*, o pulmão direito possui três lobos e um brônquio eparterial (brônquios acima da artéria pulmonar), enquanto o pulmão esquerdo possui dois lobos com um brônquio hiarterial (brônquios abaixo da artéria pulmonar), o estômago e o baço está à esquerda e o lobo maior do fígado está à direita. O átrio esquerdo morfológico está à esquerda do átrio direito morfológico. Com *situs inversus*, o pulmão esquerdo tem três lobos com um brônquio eparterial e o pulmão direito tem dois lobos com um brônquio hiperarterial, o estômago e o baço estão no lado direito do corpo, o lobo maior do fígado está no lado esquerdo, e o átrio esquerdo morfológico está à direita do átrio direito morfológico. Considerações finais: sabe-se que essa assimetria anatômica se estabelece durante a formação embrionária, especificamente, na rotação dos órgãos. Entretanto, vale ressaltar que indivíduos com *situs inversus* total isoladamente não apresentam repercussão clínica, com exceção dos casos associados a cardiopatias. Por isso, quase sempre, seu diagnóstico é um achado em exames de imagem, como radiografias, tomografias e ultrassonografias.

Palavras-chave: *Situs inversus*; Dextrocardia; Anomalia congênita.

Resumen

Introducción: el *situs inversus* es una rara anomalía congénita caracterizada por la transposición de los órganos abdominales, vísceras y vasculatura, en relación con la dirección sagital, ofreciendo una imagen denominada “imagen en espejo”. Se clasifica como total cuando se asocia a dextrocardia, mientras que el *situs inversus* parcial afecta solo a uno o más órganos. Objetivo: responder cuál es la evidencia sobre los aspectos clínicos y anatómicos del *situs inversus*. Metodología: se trata de una revisión integrativa de la literatura. La investigación se llevó a cabo a través del acceso en línea a la Biblioteca Nacional de Medicina (PubMed MEDLINE), Scientific Electronic Library Online (Scielo), Cochrane Database of Systematic Reviews (CDSR), Google Scholar, Virtual Health Library (BVS) y bases de datos EBSCO. Servicios de Información. Resultados y Discusión: En *situs solitus*, el pulmón derecho tiene tres lóbulos y un bronquio eparterial (bronquios arriba de la arteria pulmonar), mientras que el pulmón izquierdo tiene dos lóbulos con un bronquio hiarterial (bronquios debajo de la arteria pulmonar), el estómago y el bazo está a la izquierda y el lóbulo mayor del hígado está a la derecha. La aurícula izquierda morfológica está a la izquierda de la aurícula derecha morfológica. Con *situs inversus*, el pulmón izquierdo tiene tres lóbulos con un bronquio eparterial y el pulmón derecho tiene dos lóbulos con un bronquio hiperarterial, el estómago y el bazo están en el lado derecho del cuerpo, el lóbulo más grande del hígado está en el izquierdo, y la aurícula izquierda morfológica está a la derecha de la aurícula derecha morfológica. Consideraciones finales: se sabe que esta asimetría anatómica se establece durante la formación embrionaria, específicamente, en la rotación de órganos. Sin embargo, cabe señalar que los individuos con *situs inversus* total por sí solos no tienen repercusión clínica, a excepción de los casos asociados a cardiopatías. Por ello, casi siempre, su diagnóstico es un hallazgo en pruebas de imagen, como radiografías, tomografías computarizadas y ecografías.

Palabras clave: *Situs inversus*; Dextrocardia; Anomalia congénita.

1. Introduction

Situs inversus is a rare congenital anomaly characterized by the transposition of the abdominal organs, viscera and vasculature, in relation to the sagittal direction, offering an image called “mirror image”. It is classified as total when associated with dextrocardia, while partial *situs inversus* affects only one or more organs. Its incidence is 1:10,000 in the world population and only 5-10% of patients have associated heart diseases and cardiovascular malformations, with the rest of patients generally asymptomatic (Lima et al., 2019). In view of this, total *situs inversus* is an uncommon congenital condition, characterized by dextrocardia with complete reversal of the heart chambers, the aorta turned to the right, the left lung with three lobes and the right lung with only two.

In partial situs *inversus*, at the level of the abdomen, the stomach, spleen and pancreas are on the right, while the liver and gallbladder are on the left side and the colonic flexures are inverted (Wu et al., 2017). This rare genetic anomaly is usually discovered incidentally, often when an evaluation of a patient is performed to investigate trauma or abdominal disease, by imaging tests, and most cases are detected during medical examinations using simple chest radiography or in other imaging tests such as ultrasound and computed tomography, when requested to evaluate a clinical complaint or when there is a strong suspicion of the presence of the pathology. In addition, and recent studies state that there is the possibility of being detected by prenatal ultrasound as well (Lima et al., 2019).

Thus, dextrocardia results from anomalies in the rotation of the heart tube during the embryonic period. Abnormal bending of the embryonic heart tube to the left instead of the right causes complete inversion of the position of the heart, so that the apex faces the right instead of the left. It is believed that this is usually an autosomal recessive genetic condition, although it can be linked to the X chromosome (Moore et al., 2019). In dextrocardia with *situs inversus*, the incidence of associated cardiac defects is low, and cardiac function is usually normal. In isolated dextrocardia, however, the congenital anomaly can be complicated by severe cardiac anomalies, such as transposition of the great arteries (Moore et al., 2019). Furthermore, there may be double right ventricular outflow tract with ventricular septal defect and right ventricular outflow tract obstruction, atrioventricular valve atresia, single ventricle and tetralogy of Fallot. Other vascular anomalies are variation of the celiac trunk and superior mesenteric artery (Wu et al., 2017).

There are also records of gastrointestinal system anomalies that include: biliary atresia, duodenal atresia, preduodenal portal vein, intestinal malrotation, polysplenia/asplenia, annular pancreas, diaphragmatic hernia, and others. In addition, situs *inversus* associated with clinical syndromes such as Kartagener-situs inversus, chronic rhinosinusitis and bronchiectasis (Basso et al., 2014). Furthermore, the condition is closely associated with another pathology called primary ciliary dyskinesia (PCD). In this condition, the cilia are not functioning properly, which leads to recurrent respiratory infections and bronchiectasis seen in childhood that can present with noticeable lung damage in adulthood. Also, men may suffer from infertility secondary to sperm dyskinesia (Devera et al., 2021).

Individuals with *situs inversus* should be instructed to inform the physician of their situation, in order to prevent any medical misdiagnosis due to the altered positioning of the organs. Furthermore, surgical procedures are considered more difficult in patients with *situs inversus* than in other patients, due to the different anatomical position of organs, especially in laparoscopic operations (Basso et al., 2014; Akbulut et al., 2019). Allied to this, the diagnosis of total *situs inversus* is an important finding, because even if the patient does not have any congenital anomaly and has a normal life expectancy, the presentation of common diseases of the patient can become difficult, such as For example, if a patient with unknown total *situs inversus* had appendicitis, most clinicians would rule it out based on location alone, which could lead to a harmful outcome (Dastouri et al., 2022; Estorillo, 2016). From this perspective, the present study aims to answer the evidence on the clinical and anatomical aspects of situs *inversus*.

2. Methodology

This is a descriptive research of the integrative literature review type, which sought to answer the evidence on the clinical and anatomical aspects of situs *inversus*. The research was carried out through online access to the *National Library of Medicine* (PubMed MEDLINE), *Scientific Electronic Library Online* (SciELO), Cochrane Database of Systematic Reviews (CDSR), Google Scholar, Virtual Health Library (BVS) and EBSCO databases. *Information Services*, in March and April 2022. To search for works, the keywords present in the descriptors in Health Sciences (DeCS) were used: in English: "*situs inversus*", "*anatomy*", "*dextrocardia*", "*congenital anomaly*", and in Portuguese: "*situs inversus*", "*anatomia*", "*dextrocardia*", "*congenital anomaly*".

As inclusion criteria, original articles were considered, which addressed the researched topic and allowed full access to the study content, published in the period from 2005 to 2022, in English and Portuguese. The exclusion criterion was imposed on those works that were not in English or Portuguese, that had not gone through the Peer-View process and that were not related to the proposed theme. The article selection strategy followed the following steps: search in the selected databases; reading the titles of all articles found and excluding those that did not address the subject; critical reading of the abstracts of the articles and full reading of the articles selected in the previous steps. After careful reading of the publications, 2 articles were not used due to exclusion criteria. Thus, there were a total of 14 scientific articles for the integrative literature review, with the descriptors presented above.

3. Results and Discussion

With regard to the placement of the cardiac apex, the placement of the heart can be classified into the conditions of levocardia, dextrocardia and mesocardia (Wilhelm, 2009). Dextrocardia is a congenital anomaly in which abnormal bending of the embryonic heart tube to the left instead of to the right results in complete inversion of the position of the heart, so that its base-apex axis is inferiorly oriented to the right. It can be an intrinsic condition of the heart or extrinsic, when it presents anatomical alterations in other structures (Fulton, 2008). Dextrocardia in *situs solitus* (isolated dextrocardia) occurs due to congenital malposition, which affects only the heart and maintains the normal arrangement of the other viscera. This condition is often accompanied by other defects. Dextrocardia in *situs inversus* (total dextrocardia - DSI) is the general transposition of the thoracic and abdominal viscera, but maintaining their respective relationships (Moore et al., 2019; Yilmaz et al., 2019).

Situs refers to the pattern of the viscera and each abnormality itself, such as the lung, liver, spleen, and gastrointestinal tract, and the term also applies to the heart and each of the cardiac chambers because each is asymmetrical. In *situs solitus*, the right lung has three lobes and an eparterial bronchus (bronchi above the pulmonary artery), while the left lung has two lobes with a hyarterial bronchus (bronchi below the pulmonary artery), the stomach and spleen are on the left and the larger lobe of the liver is on the right. The morphological left atrium is to the left of the morphological right atrium. With *situs inversus*, the left lung has three lobes with an eparterial bronchus and the right lung has two lobes with a hyperarterial bronchus, the stomach and spleen are on the right side of the body, the larger lobe of the liver is on the left, and the morphological left atrium is to the right of the morphological right atrium (van Praagh, 2005).

It is a condition transmitted by autosomal recessive genes, which are located on the long arm of chromosome 14, affecting the genetic cascade responsible for left-right differentiation. It is important to note that most individuals can lead normal lives (Saadi et al., 2007). This anatomical disagreement does not make ISD a pathological condition, even though the frequency of congenital heart defects is higher than in patients with *situs solitus*, at a rate of 3% versus 0.08% (Yilmaz et al., 2019). This is justified by the fact that most patients do not have other birth defects and life expectancy is the same as that of the general population (Rossi et al., 2015).

In addition, $\frac{1}{4}$ of cases of ISD are associated with Kartagener syndrome, a rare genetic disease defined by the clinical triad *situs inversus total*, chronic sinusitis and bronchiectasis. The prevalence is 1/15000 – 1/30000 individuals, although more recent studies place it at 1/10000 live births (Yilmaz et al., 2019). DSI is rare, accounting for 0.2% of all congenital heart defects (Romero et al., 2017). However, it can cause difficulties in the treatment of abdominal diseases, especially in laparoscopic procedures, due to its mirror image (Barros et al., 2010). Most reports of laparoscopic surgery in patients with SIT have involved cholecystomy. A review of the English literature showed that laparoscopic colectomy was only reported in 8 patients with SIT. No complications were reported in these cases (Yaegashi et al., 2015).

The importance of early diagnosis is debated in some case reports in the literature, as it can prevent inappropriate conduct and procedures in these patients. The most frequent forms of detection are physical examination, anamnesis,

radiological investigations and ECG (electrocardiogram), with computed tomography as the preferred test for definitive diagnosis (Liu et al., 2017; Fuchs et al., 2020). Generally, situs *inversus* remains unknown unless it is associated with other abnormalities. Furthermore, even if associated, it is difficult to recognize this condition in a timely manner because the etiologies of abdominal pain are multiple and diverse (Kashiwagi et al., 2013).

There are no reports of the etiological relationship between total *situs inversus* and cancer (Ozben et al., 2010), but the condition may be associated with other congenital anomalies such as duodenal atresia, asplenism, multiple spleens, ectopic kidney, horseshoe kidney and various pulmonary and pulmonary abnormalities. vascular. In *situs inversus complications* associated with the cardiovascular system, coronary atherosclerotic diseases have incidences similar to those of the general population (Ylmar et al., 2019). In the case report found in the literature, an anomaly in the right coronary artery was shown, which originates from the left coronary sinus and the anomalous pathway, a rare congenital coronary anomaly. In this case, the therapeutic approach divides opinions due to the complexity of the procedure and the need for certain modifications. There are more reports of coronary artery bypass grafting than percutaneous coronary intervention (Fuchs et al., 2020).

In these specific cases, early identification and the importance of clinical reasoning stand out. For this to happen, the electrocardiogram is essential. When the rhythm is sinus and the P wave is negative in D1 and V6, positive in D2, D3, and aVF, if aVL looks like aVR and vice versa, there is sufficient evidence to recognize atrial *situs inversus* on the ECG. This characteristic results from atrial inversion in which the sinus node is located to the left of the left atrium, resulting in the mean P vector moving from left to right and inferiorly, in the opposite direction to normal. Likewise, the main forces of the QRS in the thorax point to the right. In this way, the repositioning of the electrodes on the arms and chest produces a virtual normalization of the electrocardiographic tracing (Ylmar et al., 2019). In addition, case reports demonstrate the importance of careful surgical planning and the multidisciplinary contribution to deal with serious pathologies in the setting of total *situs inversus*, due to the anatomical changes present, but also taking into account the physiological inadequacies that the patient may present (Ylmar et al., 2019).

4. Final Considerations

This study made it possible to understand about of the evidence regarding the clinical and anatomical aspects of *situs inversus*. With this, it is possible to perceive the variations of presentation of this unusual congenital condition depending on the level of anomaly in the formation and arrangement of organs. In order to reach this understanding, it was defined that depending on the level of anomaly in the formation and disposition of the organs, the perception is, clinically and anatomically, differentiated. It was noticed that the total *situs inversus* is marked by a dextrocardia with complete reversal of the cardiac chambers, the aorta rotated to the right, the left lung with three lobes and the right lung with only two and that, in the partial *situs inversus*, both the stomach, the spleen and pancreas are on the right, but the liver and gallbladder are on the left, and the colonic flexures are reversed.

Therefore, the importance of this finding lies in the fact that the clinical manifestations will be directed and, if necessary, the surgical planning of a pathology arising from total *situs inversus* must be more cautious, given the more pronounced anatomical and physiological variations. Regarding the diagnosis, its importance is clear in order to avoid improper management of patients and that the tools for this detection are focused on physical examination, anamnesis, ECG and imaging investigations that consider computed tomography as the primary examination. However, the present study concluded that the discovery of this condition is usually associated with an accidental finding, closely related to other abnormalities and difficult to distinguish, given the wide range of etiologies linked to abdominal pain. In addition, even though *situs inversus* has a higher frequency of congenital heart defects, considering total dextrocardia, when compared to patients with other anomalies, such as *situs solitus*, the occurrence of serious complications is not common. Finally, it is noted that

from the information discussed that most individuals with this condition are not aware of it and have great chances of having normal lives, since most do not have other birth defects and that the epidemiology related to the life expectancy is roughly equivalent to that of the general population.

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