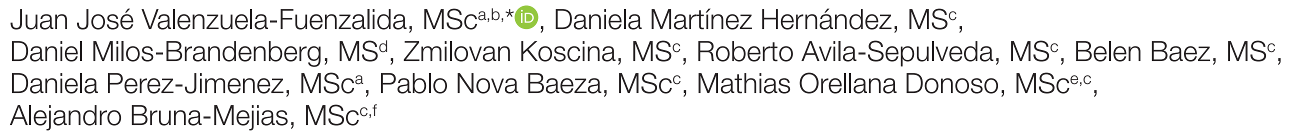
Systematic Review and Meta-Analysis

Medicine®

OPEN

Association between types of abdominopelvic cancer in patients with situs inversus total

Systematic review



Juan José Valenzuela-Fuenzalida, MSc[a,b,*], Daniela Martínez Hernández, MS[c], Daniel Milos-Brandenberg, MS[d], Zmilovan Koscina, MS[c], Roberto Avila-Sepulveda, MS[c], Belen Baez, MS[c], Daniela Perez-Jimenez, MSc[a], Pablo Nova Baeza, MSc[c], Mathias Orellana Donoso, MSc[e,c], Alejandro Bruna-Mejias, MSc[c,f]

Abstract

Background: Situs inversus is a rare congenital anatomical variant that involves a group of anomalies regarding the arrangement of intrathoracic and intraabdominal organs. Being able to find in the abdominal region the liver, gallbladder, inferior vena cava, and head of the pancreas and ascending colon on the left side of the abdomen, while on the right side there is the spleen, the stomach, the body of the pancreas, the ligament of Treitz, descending colon among others. In this same way, the thoracic organs, lungs and heart, are changed in their position in a mirror translocation.

Methods: We systematically searched MEDLINE, Web of Science, Google Scholar, CINAHL, Scopus, and LILACS; the search strategy included a combination of the following terms: "Situs inversus," "Situs inversus totalis," "Cancer," "Neoplasm," "Abdominopelvic regions," and "clinical anatomy."

Results: Within the 41 included studies, 46 patients with situs inversus who had cancer, in addition to being found in this organ and in these regions, we also found as a result that the majority of the studies in the research were in stage II; finally, no one study could assert the direct relationship between the situs inversus totalis and the cancer.

Conclusion: If our hallmarks could make us think that more exhaustive follow-up of the stomach and other organs should be carried out in these patients, there could also be other predisposing factors for cancer, which is why more studies are suggested to give future diagnostic and treatment guidelines treatment.

Abbreviations: CT = computed tomography, SIT = situs inversus totalis.

Keywords: abdominopelvic region, anatomy abdominal, cancer, clinical anatomy, neoplasm, situs inversus, situs inversus totalis

1. Introduction

Situs inversus is a rare congenital anatomical variant that involves a group of abnormalities regarding the disposition of intrathoracic and intraabdominal organs. This is opposed to situs solitus, which is the normal anatomical disposition of all bodily organs.[1] There are 2 types of situs inversus: situs inversus totalis (SIT) which corresponds to the mirror image of situs solitus, including the heart (dextrocardia), and partial situs inversus, where intraabdominal and thoracic organs are seen in mirror image. However, the heart is in a normal arrangement (levocardia). In the SIT we find the cardiac apex, stomach, spleen, ligament of Treitz, descending colon, and aorta in the right side of the abdomen, while the inferior vena cava, liver, gallbladder, and ascending colon are found in the left side of the abdomen (Fig. 1). Besides, it presents a bilobed right lung. SIT differs from *situs ambiguous* in that the latter corresponds to any other abnormality in the development of the left-right axis of the organs, and is characterized by right or left isomerism, heteroataxia, and multiple thoracoabdominal malformations. Among

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

Supplemental Digital Content is available for this article.

[a] Department of Morphology and Function, Faculty of Health and Social Sciences, Universidad de las Américas, Santiago, Chile, [b] Departamento de Ciencias Química y Biológicas, Facultad de Ciencias de la Salud, Universidad Bernardo O'Higgins, Santiago, Chile, [c] Departamento de Morfología, Facultad de Medicina, Universidad Andrés Bello, Santiago, Chile, [d] Escuela de Medicina, Facultad Ciencias de la Salud, Universidad del Alba, Santiago, Chile, [e] Escuela de Medicina, Universidad Finis Terrae, Santiago, Chile, [f] Departamento de Ciencias y Geografía, Facultad de Ciencias Naturales y Exactas, Universidad de Playa Ancha, Valparaíso 2360072, Chile.

* Correspondence: Juan José Valenzuela-Fuenzalida, Department of Morphology and Function, Faculty of Health and Social Sciences, Universidad de las Américas, Santiago, Chile (e-mail: juan.valenzuela.f@unab.cl).

Copyright © 2024 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Valenzuela-Fuenzalida JJ, Martínez Hernández D, Milos-Brandenberg D, Koscina Z, Avila-Sepulveda R, Baez B, Perez-Jimenez D, Nova Baeza P, Orellana Donoso M, Bruna-Mejias A. Association between types of abdominopelvic cancer in patients with situs inversus total: Systematic review. Medicine 2024;103:8(e37093).

Received: 19 October 2023 / Received in final form: 14 December 2023 / Accepted: 5 January 2024

http://dx.doi.org/10.1097/MD.0000000000037093

its subdivisions we find: *situs ambiguous* with polysplenia, *situs ambiguous* with asplenia, and Ivemark syndrome.[2] Classically, *situs inversus totalis* is asymptomatic, although a third of the cases are associated with a recessive genetic condition: primary ciliary dyskinesia.[2] Other concomitant pathologies are increasingly being reported, including: cardiovascular malformations (tetralogy of Fallot, pulmonary stenosis, defects in the development of the atrial or ventricular septum), lung adenocarcinoma, metastasis of gallbladder carcinoma, and biliary atresia.[2,3] The pathogenesis of SIT is still not well established. The involvement of an autosomal recessive gene on the long arm of chromosome 14 and deletions on chromosomes 7 and 8 have been established.[2] The correlation with deletions of KIF3-A and KIF3-B, 2 microtubule-dependent motor kinesins involved in cancer development, and whose nonfunctional forms prevent the transport of the cell adhesion factors N-cadherin and β-catenin to the cell surface has also been studied.[4] The epidemiology of these anatomical variations differs according to the literature. One review estimates that the incidence of *situs inversus totalis* in general population is 1:10,000.[5] The most current reviews estimate an incidence of 1:20,000 to 1:25,000 at a general level.[4] In addition, it tends to occur commonly in men (1.5:1) and there is no racial predilection.[2,4]

The objective of this study was to know the characteristics of SIT and its relationship with different types of cancer of the abdominopelvic region.

2. Methodology

This systematic review was performed and reported according to the Preferred Reporting Items for Systematic Reviews statement.[6]

2.1. Eligibility criteria

Studies on the presence of SIT associated with cancer of the abdominopelvic region were considered eligible for inclusion if they met the following criteria: (1) population: cadaveric case reports or imaging reports of subjects with SIT; (2) results: presence of SIT, with presence of cancer diagnosed at any stage. In addition, SIT was classified and described based on normal anatomy and the classifications proposed in the literature; (3) studies: This systematic review included research articles, research reports, or original research published in English in peer-reviewed journals and indexed in some of the reviewed databases. On the contrary, the exclusion criteria were the following: (1) population: animal studies; (2) presence of situs inversus without cancer; (3) presence of situs inversus with cancer of a region other than the abdominopelvic region; (4) studies: letters to the editor or comments.

2.2. Electronic search

We systematically searched MEDLINE (via PubMed), Web of Science, Google Scholar, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, and the Latin American and the Caribbean Literature in Health Sciences (LILACS) from inception until August 2023 (Fig. 2).

The search strategy included a combination of the following terms: "Situs inversus" (No Mesh), "Situs inversus totalis" (No Mesh), "Cancer" (Mesh terms), "Neoplasm" (No Mesh), "Abdominopelvic organs" (No Mesh), and "clinical anatomy" (No Mesh) using the Boolean connectors "AND," "OR," and "NOT." The search strategies for each database are available in Table S1, Supplemental Digital Content, http://links.lww.com/MD/L595.

2.3. Study selection

Two authors (JJV and DM) independently screened the titles and abstracts of references retrieved from the searches. We obtained the full text for references that either author considered to be potentially relevant. We involved a third reviewer (RA) if consensus could not be reached.

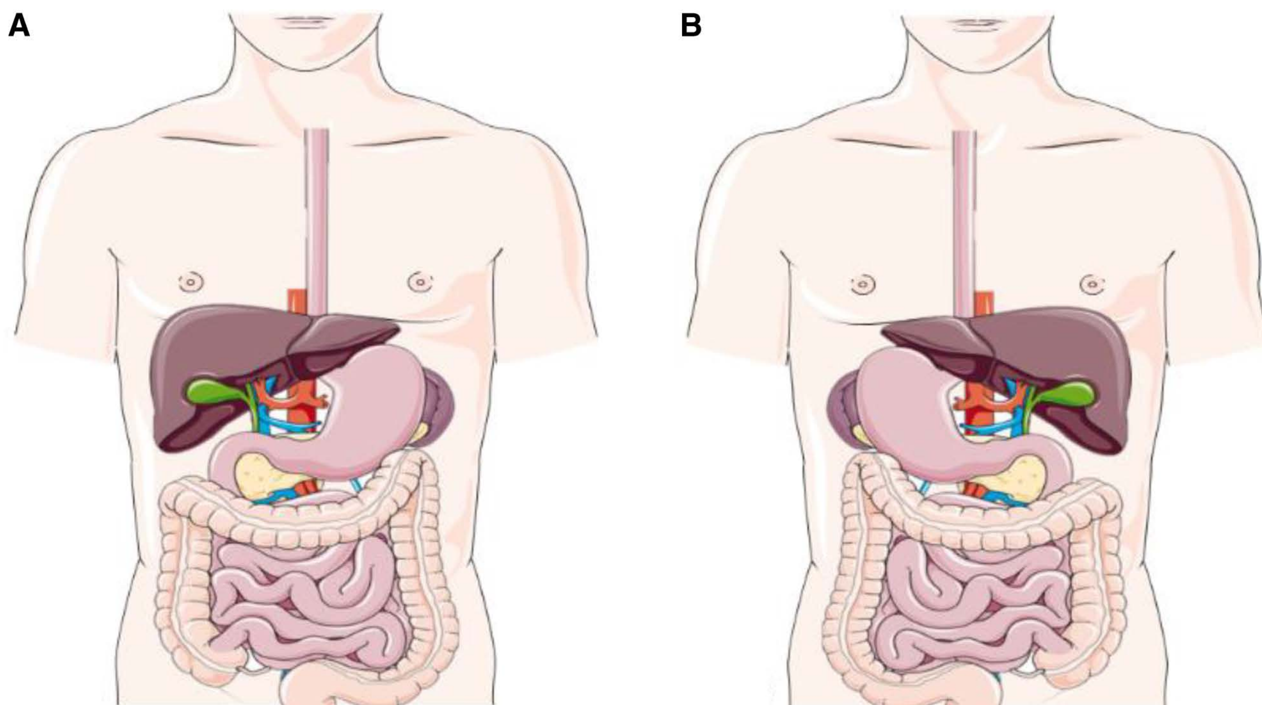


Figure 1. Representation of a patient with his normal arrangement of abdominal organs (A) and a patient with situs inversus totalis (B); note that in image (B) the liver and gallbladder are present in the left hypochondrium. On the contrary, the spleen and gastric fundus in the right hypochondrium.

2.4. Data collection process

Two authors (PN and MO) independently extracted data on the outcomes of each study. The following data were extracted from the original reports: (1) authors and year of publication, (2) country, (3) type of study, (4) sample characteristic, (5) gender and age, (6) reported pathology associates, (7) diagnostics methods, and (8) cancer stage.

2.5. Assessment of risk of bias in included studies

Two authors (JJV and MO) independently assessed the risk of bias in included studies, and one author acted as arbitrator (MK). To assess for risk of bias for case reports belonging to the descriptive studies category, we used the Joanna Briggs Institute (JBI) critical appraisal checklist for case reports (last amended in 2017; Table 1). Each article was assessed using 8 questions by selecting answers "yes," "unclear," "no," or "not applicable." Articles were evaluated using the criteria: low risk of bias—more than 70% "yes" score, moderate risk of bias—50% to 69% "yes" score, and high risk of bias—<49% "yes" score. Two authors independently applied this tool to each case report to reach an overall appraisal judgment with supporting justifications for each article (Table 2).

3. Results

In the present study, 41[7–47] case reports that included SIT and some type of cancer in the abdominal-pelvic region were analyzed. In the 41 reports, a total of 46 patients were analyzed, of which 19 (41.30%) correspond to female patients and 27 (58.70%) correspond to male patients. Regarding the ages, the total age range among those reported was from 29 to 84 years of age, for the female sex from 41 to 80 years, of which 6 are between 40 and 59 years, and the remaining 13 are between 60 and 80 years of age. For the male sex, the range was from 29 to 84 years, of which only one was between 20 and 39 years, 11 between 40 and 59 years of age, and 15 patients between 60 and 80 years. Geographically, the majority corresponded to the Asian continent with 42 patients, mainly from Japan followed by China and South Korea, only one patient was from the African continent, likewise only one is from the European continent, one from North America, and one from Oceania (Table 3 and Fig. 3).

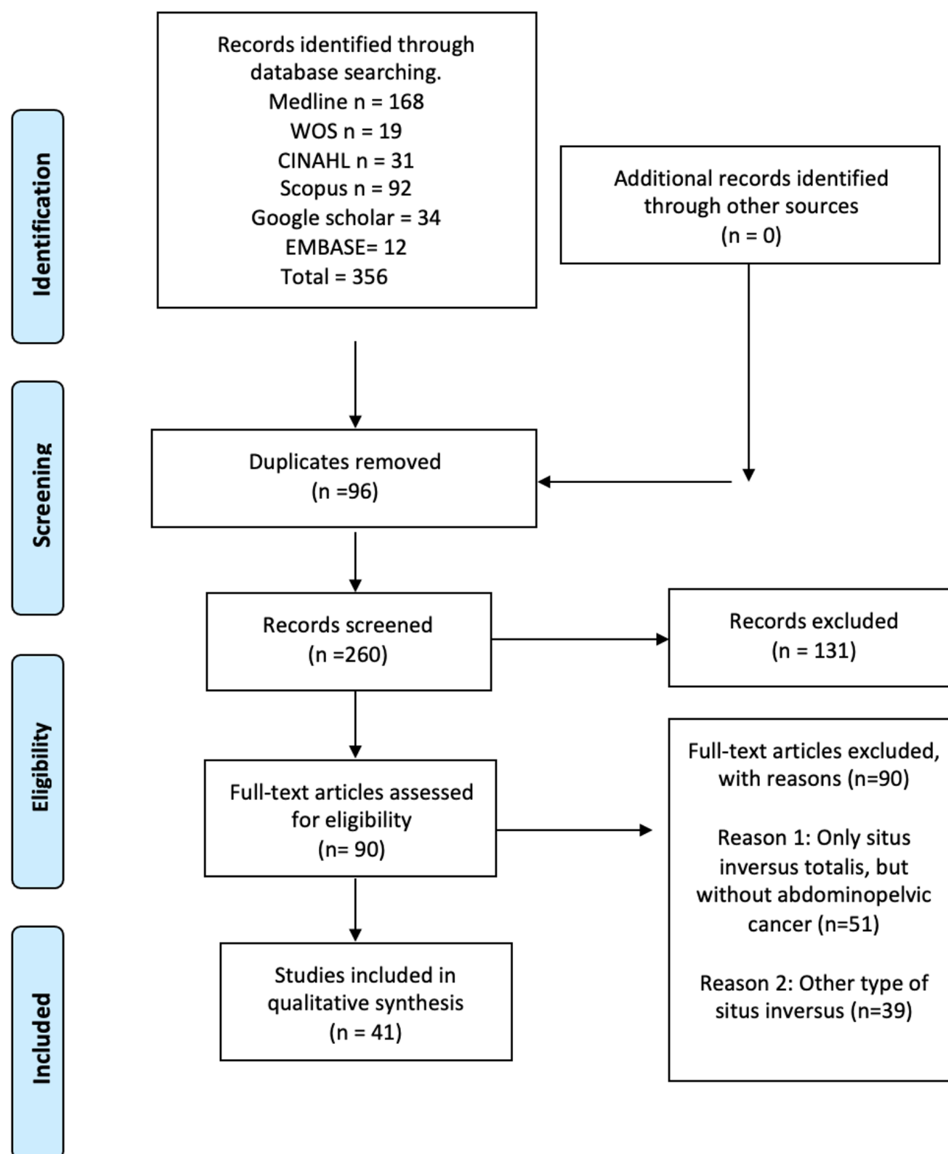


Figure 2. Flow chart—search strategy.

Table 1

Risk of bias of included studies (risk of bias assessment according to the JBI critical appraisal check-list).

Author	JBI Q1	JBI Q2	JBI Q3	JBI Q4	JBI Q5	JBI Q6	JBI Q7	JBI Q8	Bias risk
Gao YK et al, 2022									Low
Kitasato A et al, 2022									Low
Zhang C et al, 2022									Low
Abbey E et al, 2021									Low
Namikawa T et al, 2021									Low
Sivakumar J et al, 2021									Low
Takeno A et al, 2021									Low
Yoshimoto T et al, 2021									Low
Koyama Y et al, 2020									Low
Oh CH, 2020									Low
Ojima T et al, 2019									Low
Dai HB et al, 2018									Low
Gündes E et al, 2018									Low
Shibata K et al, 2018									Low
Xiang D et al, 2018									Low
Alhossaini R et al, 2017									Low
Cao Y et al, 2017									Low
Kigasawa Y et al, 2017									Low
Martinez L et al, 2017									Low
Suh B et al, 2017									Low
Isobe T et al, 2015									Low
Morimoto M et al, 2015									Low
Yaegashi M et al, 2015									Low
Ye MF et al, 2015									
Zhu H et al, 2015									Low
Sumi Y et al, 2014									Low
Fujikawa H et al, 2013									Low
Kyuno D et al, 2013									Low
Min SH et al, 2013									Low
Kim H et al, 2012									Low
Pan K et al, 2012									Low
Kim YW et al, 2011									Low
Seo K et al, 2011									Low
Futawari N et al, 2010									Low
Huh JW et al, 2010									Low
Benjelloun E et al, 2008									Low
Fujiwara Y et al, 2007									Low
Murakami S et al, 2003									Low
Kamikee W et al, 1996									Low
Yoshida Y et al, 1992									Low
Organ B et al, 1991									Low

JBI = Joanna Briggs Institute.

Table 2

Items to evaluate risk of bias (the Joanna Briggs Institute (JBI) critical appraisal checklist for case reports).

(1) Were patient's demographic characteristics clearly described?	Yes	No	Unclear	Not applicable
(2) Was the patient's history clearly described and presented as a timeline?	Yes	No	Unclear	Not applicable
(3) Was the current clinical condition of the patient on presentation clearly described?	Yes	No	Unclear	Not applicable
(4) Were diagnostic tests or assessment methods results clearly described?	Yes	No	Unclear	Not applicable
(5) Was the intervention(s) or treatment procedure(s) clearly described?	Yes	No	Unclear	Not applicable
(6) Was the postintervention clinical condition clearly described?	Yes	No	Unclear	Not applicable
(7) Were adverse events (harms) or unanticipated events identified and described?	Yes	No	Unclear	Not applicable
(8) Does the case report provide takeaway lessons?	Yes	No	Unclear	Not applicable

Overall appraisal: Include ☐ exclude ☐ seek further info ☐.

For the diagnosis of SIT, 15 patients underwent a chest X-ray and an abdominal computed tomography (CT) scan, 11 patients only an abdominal CT, 4 patients a chest X-ray and thoracoabdominal CT, 3 patients were subjected to cardiac ultrasound, chest X-ray, and abdominal CT, 2 patients an abdominal ultrasound and chest X-ray, one patient underwent electrocardiogram, chest X-ray, and abdominal CT, one patient was exposed to abdominal and CT, and finally 3 studies did not specify the diagnostic method for SIT.

3.1. Characteristics of cancers and state

Of a total of 46 patients, 39 presented a neoplastic pathology in the supramesocolic region, 5 in the inframesocolic region, 1 in the retroperitoneal region, and 1 in the subperitoneal region. Within the supramesocolic region, 30 had different degrees of neoplasms in the stomach, 3 in the liver, and 6 in the gallbladder or bile ducts. Regarding the inframesocolic region, there were 2 cases in the ascending colon, 1 case in the transverse colon, 1 case in the sigmoid colon, and 1 case in the rectosigmoid junction. On the other hand, in the retroperitoneal region, 1 case

Table 3

Characteristics of the included studies.

Author and year	Country	Type of study	N	Gender/age	Associated pathology	SIT diagnostic method	Type of procedure	Cancer stage
Gao Y et al, 2022 [7]	China	Case report	2	M/51 F/63	Gallbladder carcinoma with SIT	-Chest X-ray -Abdominal CT scan	-ERCP -Percutaneous transhepatic cholangial drainage (PTCD)	T3NxM0
Kitasato A et al, 2022[8]	Japan	Case report	1	M/57	Hepatocellular carcinoma with SIT	-X-ray chest -Thoracic and abdominal CT	Caudate lobectomy	NA
Zhang C et al, 2022[9]	China	Case report	1	F/62	SIT with local metastasis of gallbladder carcinoma and common hepatic artery variation	-Thoracic and abdominal CT scan	-Radical cholecystectomy, total pancreatectomy, splenectomy, hepatic artery-splenic artery reconstruction	T3N1M1 (stage IVb)
Abbey E et al, 2021[10]	China	Case report	1	M/69	Gastric carcinoma with SIT	-Thoracic and abdominal CT scan	Robotic distal gastrectomy	T3N3aM0 (stage IIIb)
Namikawa T et al, 2021[11]	Japan	Case report	1	F/66	Gastric cancer and gastrointestinal stromal tumor (GIST) with SIT	-Chest X-ray -Electrocardiography -Abdominal CT scan	Total gastrectomy	T1aN0M0 (stage IA)
Sivakumar J et al, 2021[12]	Australia	Case report	1	M/29	Hereditary gastric cancer with SIT	-Thoracic and abdominal CT scan	Laparoscopic total gastrectomy	pT1aN0M0 (stage IA)
Takeno A et al, 2021[13]	Japan	Case report	1	F/71	Gastric cancer with SIT	-Thoracic and abdominal CT scan	Robotic-assisted proximal gastrectomy	cT1bN0M0 (stage IA)
Yoshimoto T et al, 2021[14]	Japan	Case report	1	M/84	advanced gastric cancer with SIT	-Thoracic and abdominal CT scan	Robotic-assisted total gastrectomy	T3N2M0 (stage IIIA)
Koyama, Y et al, 2020[15]	Japan	Case report	1	M/74	Gastric cancer with SIT	-Thoracic and abdominal CT scan	Endoscopic submucosal dissection	NA
Oh, C et al, 2020[16]	South Korea	Case report	1	M/60	Hepatocellular carcinoma with SIT	-Thoracic and abdominal CT scan	ERCP	NA
Ojima T et al, 2019[17]	Japan	Case report	1	F/80	Gastric cancer with SIT	-NE	Robotic distal gastrectomy	pT1bN0M0 (stage IB)
Dai, H et al, 2018[18]	China	Case report	1	F/59	Gastric cancer with SIT	-Chest X-ray -Abdominal CT scan	Robotic radical gastrectomy	pT4aN2M0 (stage IIIB)
Gündeş E et al, 2018[19]	Turkey	Case report and literature review	22	M: 12 F: 9	Gastric cancer with SIT	-Chest X-ray -Thoracic and abdominal CT scan	Laparoscopy-assisted distal subtotal gastrectomy	T1bN0M0 (stage IA)
Shibata K et al, 2018[20]	Japan	Case report	1	M/79	Gastric cancer with SIT	-NE	Laparoscopic total gastrectomy	T3N0M0 (stage IIB)
Xiang D et al, 2018[21]	China	Case report and literature review	1	F/45	SIT with solid pseudopapillary pancreatic tumor	-Heart ultrasonography, chest X-ray and abdominal CT scan	Laparoscopic splenectomy of the pancreatic body and tail	Benign/low-grade malignancy
Alhossaini R et al, 2017[22]	South Korea	Case report	1	M/64	Gastric cancer with SIT	-NE	Robotic distal gastrectomy	T1bN0M0 (stage IA)
Cao Y et al, 2017[23]	China	Case report and literature review	1	M/60	Gastroesophageal junction adenocarcinoma with SIT	-Chest X-ray -Abdominal CT scan	Robotic total gastrectomy	pT3N1M0 (stage IIB)
Kigasawa Y et al, 2017[24]	Japan	Case report	1	M/40	Gastric cancer with SIT	-Thoracic and abdominal CT scan	Laparoscopy-assisted distal gastrectomy	pT1b1pN1sM0) (stage IB)
Martínez L et al, 2017[25]	Spain	Case report	1	M/67	Ascending colon cancer with SIT	-Chest X-ray -Abdominal CT scan	Laparoscopic hemicolectomy with radical lymphadenectomy.	pT3N0M0 (stage IIA)
Suh B et al, 2017[26]	South Korea	Case report	1	M/50	Gastric cancer with SIT	-Chest X-ray -Abdominal CT scan	Radical subtotal gastrectomy	Early gastric cancer Paris type IIc
Isobe T et al, 2015[27]	Japan	Case report	1	F/79	Gastric adenocarcinoma with SIT	-Chest X-ray -Thoracic and abdominal CT scan	Total gastrectomy	T4aN2H0P0M0 stage IIIB Japanese Classification of Gastric Carcinoma

(*Continued*)

Table 3

(*Continued*)

Author and year	Country	Type of study	N	Gender/age	Associated pathology	SIT diagnostic method	Type of procedure	Cancer stage
Morimoto M et al, 2015[28]	Japan	Case report	1	M/58	Gastric cancer with SIT	-Chest X-ray -Abdominal CT scan	Laparoscopic-assisted distal gastrectomy	T1bN0M0 (stage IA)
Yaegashi M et al, 2015[29]	Japan	Case report	1	F/71	Sigmoid colon adenocarcinoma with SIT	-Chest X-ray -Abdominal CT scan	Laparoscopic sigmoidectomy	type II, Japanese classification of colorectal carcinoma
Ye M et al, 2015[30]	China	Case report	1	F/60	Gastric cancer with SIT	-Thoracic and abdominal CT scan	Laparoscopy-assisted distal gastrectomy	pT4aN0M0 (stage IIB)
Zhu H et al, 2015[31]	China	Case report	1	F/66	Gastric cancer with SIT	-Thoracic and abdominal CT scan	Distal gastrectomy	pT4aN1M0 (stage IIIa)
Sumi Y et al, 2014[32]	Japan	Case report	1	M/42	Gastric cancer with SIT	-Chest X-ray -Abdominal CT scan	Laparoscopy-assisted distal gastrectomy	pT1b1N1M0 (stage IB)
Fujikawa H et al, 2013[33]	Japan	Case report	1	F/60	Gastric cancer with SIT	-Chest X-ray -Abdominal CT scan	Laparoscopic assisted distal gastrectomy	cT1acN0cM0 (stage IA, Japanese Classification of Gastric Carcinoma)
Kyuno D et al, 2013[34]	Japan	Case report	2	M/74 M/67	Biliary tract carcinoma with SIT	Chest X-ray Abdominal CT scan	Pancreaticoduodenectomy	1:pT3N1M0 (stage IIB) 2:pT1N0M0 (stage IA)
Min S et al, 2013[35]	South Korea	Case report	2	M/52 M/68	Gastric cancer with SIT	Chest X-ray Abdominal CT scan	Laparoscopic-assisted distal gastrectomy and total laparoscopic distal gastrectomy resp.	pT2N0M0 (stage IB) and pT1aN0M0 (stage IA) resp.
Kim H et al, 2012[36]	South Korea	Case report	1	M/47	Gastric cancer with SIT	Thoracic and abdominal CT scan	Robotic-assisted distal gastrectomy	pT3N3aM0 (stage IIIB)
Pan K et al, 2012[37]	China	Case report	1	M/52	Gastric adenocarcinoma with SIT	Chest X-ray Electrocardiography	Proximal gastrectomy	NA
Kim Y et al, 2011[38]	South Korea	Case report	2	M/66 F/71	1:Proximal and Sigmoid Transverse Colon Cancer with SIT 2: cancer rectosigmoid junction with SIT	Echocardiography Chest X-ray Abdominal CT scan	Total colectomy and distal gastrectomy resp.	1:T3N2M0 (stage IIIA) 2:T3N0M0 (stage IIA) resp.
Seo K et al, 2011[39]	South Korea	Case report	1	M/60	Gastric cancer with SIT	Chest X-ray Abdominal CT scan	Laparoscopy-assisted distal gastrectomy and laparoscopic cholecystectomy	pT1pN0sM0 (stage IA)
Futawatari N et al, 2010[40]	Japan	Case report	1	M/53	Gastric cancer with SIT	Chest X-ray Abdominal CT scan	Laparoscopy-assisted distal gastrectomy	cT1, cN0, cH0, cP0, cM0, (Stage IA, Japanese Classification of Gastric Carcinoma)
Huh, J et al, 2010[41]	South Korea	Case report	1	F/41	Rectal cancer with SIT	Chest X-ray Abdominal CT scan	Laparoscopic total mesorectal excision	pT3N0M0 (stage IIA)
Benjelloun E et al, 2008[42]	Morocco	Case report	1	M/70	Gastric cancer with SIT	Chest X-ray Abdominal CT scan	Subtotal gastrectomy	T3N3M0 (stage IIIB)
Fujiwara, Y et al, 2007[43]	Japan	Case report	1	F/53	Ascending colon adenocarcinoma with SIT	Abdominal ultrasonography, chest X-ray and abdominal CT scan	Laparoscopic hemicolectomy	NA
Murakami S et al, 2003[44]	Japan	Case report	1	F/51	Gastric lymphoma with SIT	Chest X-ray - Ultrasonography Abdominal CT scan	Total gastrectomy Splenectomy	NA
Kamiike W et al, 1996[45]	Japan	Case report	1	F/69	liver cancer with SIT	-Chest X-ray -Abdominal ultrasonography	Right hepatic segmentectomy	NA
Yoshida Y et al, 1992[46]	Japan	Case report	2	F/54 M/69	Gastric cancer with SIT	NA	NA	NA
Organ B et al, 1991[47]	The United States	Case report	1	F/38	Adenocarcinoma of the distal common bile duct with SIT	Chest X-ray Abdominal ultrasonography	Pancreaticoduodenectomy and antecolic gastrojejunostomy	NA

CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography, NA = not available, SIT = situs inversus totalis.

Figure 3. Continental map that includes studies and samples obtained from each continent. The continents separated by color are the following: Asia (Orange), Europe (Magenta), Oceania (Light blue), Africa (Light purple), North America (Yellow), and South America (Green).

was reported in the pancreas, and in the subperitoneal region, 1 case of rectal cancer was reported (Table 4).

Due to their higher proportion, stomach neoplasms were classified according to their location in the organ. The pyloric region, mainly in the pyloric antrum, represented the majority of reported cases, with a total of 17 cases; the next most affected portion was the body of the stomach, where it was more frequent in the lesser curvature of this, with a total of 6 reported cases, the fundus portion and the cardia both had a total of 2 reported cases for each one. However, in 3 reported patients the region of the stomach in which the neoplastic lesion was not specified. These results were grouped in Table 5. Regarding the stage of cancer for each organ according to the TNM classification following The American Joint Committee on Cancer 8th edition, 9 patients with stage IA cancer, 5 IB patients, 3 IIA patients, 3 IIB patients, 3 IIIA patients, 4 IIIB patients, and 1 patient in stage IV. No patients in stage IIIC were reported. Those studies which did not specify the stage of the cancer or were classified according to another scale (i.e. Japanese Classification of Gastric Carcinoma, Paris Classification of Early Gastric Cancer), in this study, they were classified as NA ("not available"), and of these, 18 patients correspond to this category. These results were summarized in Table 6.

3.2. Risk of bias of included studies

All the case studies included in this review were subjected to risk of bias assessment, of which the following results are reported; in the accumulated all the studies presented a low risk of bias; the highest risk of bias was presented in item 2 which refers to "Was the patient's history clearly described and presented as a timeline?"; in this item 17 studies presented high risk of bias; the second was item 8 which refers to "Does the case report provide takeaway lessons?"; in this item 10 studies presented a high risk of bias; finally, the 3rd item with the greatest bias was item 7, which refers to "Were adverse events (harms) or unanticipated events identified and described?"; in this item 9 studies presented a high risk of bias.

4. Discussion

This systematic review aimed to report the relationship between SIT and the presence of cancer in the abdominopelvic region, as well as being able to define cancer points in the affected organ, as well as the cancer stage, its association with geographic location or age, and the evolution of cancer in this type of patients. Only case reports were included since the sample in this relationship always occurred by chance; the aforementioned indicates that cancer, although it is a pathology that many people can have and is multifactorial, this association agrees to have a periodic follow-up in the diagnosis of possible malignant lesions in the abdominal and pelvic organs, because early detection of cancer could help to better treat these patients; this becomes a predictor of good response to treatment in the patients of the included studies.

We have not found any review in our search that makes the relationship we did in this study; we have only found case report studies with a review of the literature, but no systematic review studies. This study shows that the largest number of patients reported with cancer in the abdominopelvic region, predominantly gastric, and situs inversus is in the Asian continent, mainly in the countries of Japan, China, and South Korea; this agrees with Csendes and Figueroa.[48] The countries of Japan, China, and South Korea are the countries that concentrate 60% of gastric cancers worldwide, and this affects more men than women; according to Karimi et al[49] may be due to the greater exposure to carcinogens due to the occupation of men, in turn women would have a protective effect due to the production of estrogens, protection that decreases with menopause. Also, this condition is associated with eating habits in the region, such as the excessive use of salt and the intake of products with a large amount of preservatives, as indicated by Csendes and Figueroa[48] in their study. However, there are other risk factors such as the use of tobacco and alcohol, consumption of smoked food, low intake of fruits and vegetables, the use of drugs to lower cholesterol such as statins, and the presence of *Helicobacter pylori* and Epstein-Barr virus.[50] In the present review, it was found that in most of the studies whose patients presented some neoplastic pathology and SIT,

Table 4

Diagnostic method to detect cancer in patients with situs inversus.

Diagnostic method of SIT	Studies
Chest X-ray and abdominal CT scan	Gao Y et al, 2022
	Dai H et al, 2018
	Cao Y et al, 2017
	Martínez L et al, 2017
	Suh B et al, 2017
	Morimoto M et al, 2015
	Yaegashi M et al, 2015
	Sumi Y et al, 2014
	Fujikawa H et al, 2013
	Kyuno D et al, 2013
	Min S et al, 2013
	Seo K et al, 2011
	Futawatari N et al, 2010
	Huh J et al, 2010
	Benjelloun E et al, 2008
Chest X-ray and thoracoabdominal CT scan	Kitasato A et al, 2022
	Gündeş E et al, 2018
	Isobe T et al, 2015
Thoracoabdominal CT scan	Zhang C et al, 2022
	Abbey E et al, 2021
	Sivakumar J et al, 2021
	Takeno A et al, 2021
	Yoshimoto T et al, 2021
	Koyama Y et al, 2020
	Oh C et al, 2020
	Kigasawa Y et al, 2017
	Ye M et al, 2015
	Zhu H et al, 2015
	Kim H et al, 2012
Electrocardiography, chest X-ray and abdominal CT scan	Namikawa T et al, 2021
Electrocardiography and chest X-ray	Pan K et al, 2012
Abdominal ultrasonography and chest X-ray	Kamiike W et al, 1996
	Organ B et al, 1991
Abdominal ultrasonography, chest X-ray and abdominal CT scan	Murakami S et al, 2003
Heart ultrasonography, chest X-ray and abdominal CT scan	Xiang D et al, 2018
	Kim Y et al, 2011
	Fujiwara Y et al, 2007
Not specified	Ojima T et al, 2019
	Shibata K et al, 2018
	Alhossaini R et al, 2017
	Yoshida Y et al, 1992

Table 5

Types of intrasurgical diagnoses of patients with cancer associated with situs inversus totalis.

Type of procedure	Studies
Laparoscopic-assisted distal gastrectomy	Gündeş E et al, 2018
	Kigasawa Y et al, 2017
	Morimoto M et al, 2015
	Ye M et al, 2015
	Sumi Y et al, 2014
	Fujikawa H et al, 2013
	Min S et al, 2013
	Kim H et al, 2012
	Seo K et al, 2011
	Futawatari N et al, 2010
Robotic-assisted distal gastrectomy	Abbey E et al, 2021
	Ojima T et al, 2019
	Alhossaini R et al, 2017
Robotic-assisted proximal gastrectomy	Takeno A et al, 2021
Robotic-assisted total gastrectomy	Yoshimoto T et al, 2021
	Cao Y et al, 2017
Radical subtotal gastrectomy	Dai H et al, 2018
	Suh B et al, 2017
	Benjelloun E et al, 2008
Laparoscopic-assisted total gastrectomy	Sivakumar J et al, 2021
	Shibata K et al, 2018
	Min S et al, 2013
Total gastrectomy	Namikawa T et al, 2021
	Isobe T et al, 2015
	Murakami S et al, 2003
	Yoshida Y et al, 1992
Proximal gastrectomy	Pan K et al, 2012
Distal gastrectomy	Zhu H et al, 2015
	Kim Y et al, 2011
Total colectomy	Kim Y et al, 2011
Laparoscopic sigmoidectomy	Yaegashi M et al, 2015
Laparoscopic total mesorectal excision	Huh J et al, 2010
Laparoscopic hemicolectomy	Martínez L et al, 2017
	Fujiwara Y et al, 2007
Hepatic segmentectomy	Kamikee W et al, 1996
Caudate hepatic lobectomy	Kitasato A et al, 2022
Pancreaticoduodenectomy	Kyuno D et al, 2013
	Organ B et al, 1991
Total pancreatectomy	Zhang C et al, 2022
Gastrojejunostomy	Organ B et al, 1991
Laparoscopic splenectomy	Xiang D et al, 2018
Splenectomy	Zhang C et al, 2022
	Murakami S et al, 2003
Lymphadenectomy	Martínez L et al, 2017
ERCP	Gao Y et al, 2022
	Oh C et al, 2020
PTCD	Gao Y et al, 2022
Endoscopic submucosal dissection	Koyama, Y et al, 2020
Radical cholecystectomy	Zhang C et al, 2022

ERCP = endoscopic retrograde cholangiopancreatography, PTCD = percutaneous transhepatic cholangial drainage.

the cancer was detected in early stages, and not in stages of metastasis to regional lymph nodes or to other distant organs. This can be explained by the increased use of *screening tools*, such as endoscopy, particularly in areas where there is a higher incidence of cancer, such as East Asia and South America.[51] The largest number of reported cases of cancer and SIT were gastric cancer, mainly in the antropyloric region, and although the literature has not elucidated a pathophysiological relationship between said anatomical area and the concomitant presence of SIT by itself, it can be established. The majority of the included reports that associated with cancer and SIT were from Japan, which is one of the countries with the highest prevalence of stomach cancer.[52] Among the risk factors for developing stomach cancer is *H pylori*, which in early stages usually colonizes the antrum and the lesser curvature of the stomach, favored in part by the presence of a high number of mucin-secreting glands (Fig. 4).[53] The diagnosis of SIT in patients with cancer of any abdominopelvic origin has been rather an imaging finding, either sporadically or during the course of symptoms that suggest neoplasia. For the analysis of the overall risk of bias, all the studies included in this review had a low risk of bias, so this suggests that the studies were of good quality and did not present any type of manipulation in the data presented in the studies included in this review. We believe that more details could only have been mentioned in the description of the clinical history of the patients in the case reports, since there were many studies that showed a high bias in that evaluated characteristic. Finally, this study proposes continuous follow-up of patients with SIT in order to be able to investigate early any incentive or predisposing cancer.

Table 6

Stage of cancer and organ involved in patients with situs inversus.

TNM stage of cancer		Studies	Organ involved					
			S	L	P	G/BT	SI	LI
I	IA	Namikawa T et al, 2021	✓					
		Sivakumar J et al, 2021	✓					
		Takeno A et al, 2021	✓					
		Gündeş E et al, 2018	✓					
		Alhossaini R et al, 2017	✓					
		Morimoto M et al, 2015	✓					
		Kyuno D et al, 2013				✓		
		Min S et al, 2013	✓					
		Seo K et al, 2011	✓					
	IB	Ojima T et al, 2019	✓					
		Kigasawa Y et al, 2017	✓					
		Sumi Y et al, 2014	✓					
		Kyuno D et al, 2013				✓		
		Min S et al, 2013	✓					
II	IIA	Martínez L et al, 2017						✓
		Kim Y et al, 2011						✓
		Huh J et al, 2010						✓
	IIB	Shibata K et al, 2018	✓					
		Cao Y et al, 2017	✓					
		Ye M et al, 2015	✓					
III	IIIA	Yoshimoto T et al, 2021	✓					
		Zhu H et al, 2015	✓					
		Kim Y et al, 2011						✓
	IIIB	Abbey E et al, 2021	✓					
		Dai H et al, 2018	✓					
		Kim H et al, 2012	✓					
		Benjelloun E et al, 2008	✓					
	IIIC	–						
IV		Zhang C et al, 2022				✓		
NA		Gao Y et al, 2022				✓		
		Gao Y et al, 2022				✓		
		Kitasato A et al, 2022		✓				
		Koyama Y et al, 2020	✓					
		Oh C et al, 2020		✓				
		Xiang D et al, 2018			✓			
		Suh B et al, 2017	✓					
		Isobe T et al, 2015	✓					
		Yaegashi M et al, 2015						✓
		Fujikawa H et al, 2013	✓					
		Pan K et al, 2012	✓					
		Futawatari N et al, 2010	✓					
		Fujiwara Y et al, 2007						✓
		Murakami S et al, 2003	✓					
		Kamiike W et al, 1996		✓				
		Yoshida Y et al, 1992	✓					
		Yoshida Y et al, 1992	✓					
		Organ B et al, 1991				✓		

G/BT = gallbladder/bilia, L = liver, LI = large intestine, NA = not available, P = pancreas, S = stomach, SI = small intestine.

5. Limitations

The limitations of this review are the publication bias of the included studies, since studies with different results may have been omitted that were found in the non-indexed literature in the selected databases; the probability of not having carried out the most sensitive and specific search regarding the topic to be studied; and, finally, personal preference of the authors for the selection of the articles, the previous ones have been tried to minimize as much as possible.

6. Conclusion

The SIT is a rare condition, for which there are no studies with a high number of subjects that show their detailed morphological characteristics; in this review we aimed to demonstrate the relationship between the SIT and the cancer of the abdominopelvic region. The most common cancer is the one that affects the stomach and the most common stage is II; although these findings could suggest the need for a more exhaustive monitoring of the stomach in patients with SIT, it is also conceivable that this cancer could be attributed to dietary or environmental factors of the patient who presented this pathology; so although periodic monitoring should be done, there may be patients who never develop cancer, and could also be in another organs and not necessarily in the abdominal region; some prospective or retrospective primary investigations could help to give clearer guidelines to see if there is any kind of direct or indirect relationship between situs inversus and cancer.

Acknowledgments

The figures were generated by combining and modifying various images from Servier Medical Art, provided by Servier, licensed

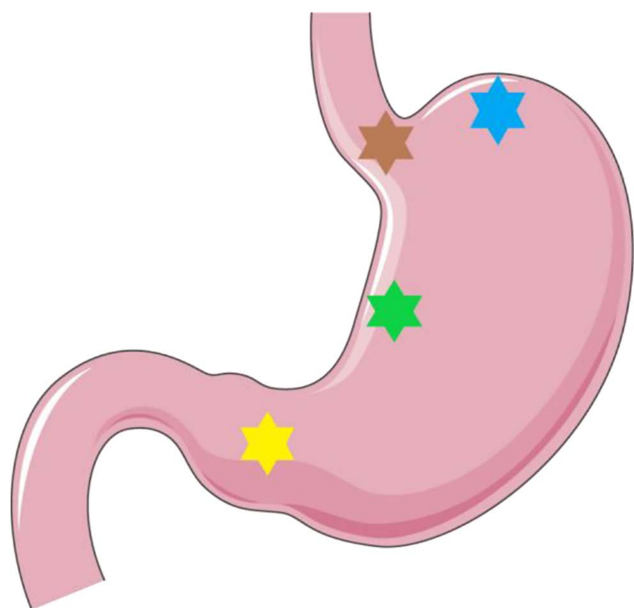


Figure 4. Representation of the most frequent locations in which gastric neoplastic lesions were reported, being the pyloric region yellow, the body close to the lesser curvature in green, the cardia brown, and finally the gastric fundus blue.

under a Creative Commons Attribution 3.0 unported license. (https://creativecommons.org/licenses/by/3.0/).

Author contributions

Conceptualization: Daniela Martínez Hernández, Pablo Nova Baeza.
Data curation: Juan José Valenzuela-Fuenzalida, Daniel Milos-Brandenberg.
Formal analysis: Daniel Milos-Brandenberg, Alejandro Bruna-Mejias.
Funding acquisition: Daniela Martínez Hernández, Daniel Milos-Brandenberg, Mathias Orellana Donoso, Alejandro Bruna-Mejias.
Investigation: Zmilovan Koscina.
Methodology: Zmilovan Koscina.
Project administration: Daniela Martínez Hernández, Zmilovan Koscina, Mathias Orellana Donoso.
Resources: Juan José Valenzuela-Fuenzalida, Zmilovan Koscina, Pablo Nova Baeza.
Software: Roberto Avila-Sepulveda, Pablo Nova Baeza.
Supervision: Roberto Avila-Sepulveda, Mathias Orellana Donoso.
Validation: Juan José Valenzuela-Fuenzalida, Roberto Avila-Sepulveda, Mathias Orellana Donoso.
Visualization: Roberto Avila-Sepulveda, Daniela Perez-Jimenez.
Writing – review & editing: Belen Baez, Daniela Perez-Jimenez.
Writing – original draft: Daniela Perez-Jimenez.

References

[1] Dastouri D, McSweeney W, Sivananthan S. Situs inversus: an interesting case of spontaneous splenic rupture. J Surg Case Rep. 2022;2022:rjac033.
[2] Aljure V, Álvarez G, Ávila N, et al. Situs inversus totalis: revisión de tema con aproximación a la Genética y reporte de casos. Rev Colomb Cardiol. 2017;24:40–7. Available at: https://www.sciencedirect.com/science/article/pii/S0120563316301929.
[3] Chen L, Qiu X, Sun H, et al. Two types of lung cancer with situs inversus totalis: a case report and review of the literature. J Int Med Res. 2020;48:300060520944107.
[4] Eitler K, Bibok A, Telkes G. Situs inversus totalis: a clinical review. Int J Gen Med. 2022;15:2437–49.
[5] Gálvez Valdovinos R, Funes Rodríguez JF, Funes Curiel ME. Situs inversus totalis: su importancia en la cirugía laparoscópica. Acta Méd Grupo Ángeles. 2019;17:91–91. Available at: https://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S1870-72032019000100091.
[6] Page M, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
[7] Gao Y, Liu S, Xie S, et al. Successful endoscopic drainage of malignant obstructive jaundice in patients with situs inversus totalis: two cases report. Int J Surg Case Rep. 2022;93:106873.
[8] Kitasato A, Miyoshi T, Okamoto T, et al. Hepatocellular carcinoma with situs inversus totalis treated by caudate lobectomy: a case report. Int J Surg Case Rep. 2022;95:107204.
[9] Zhang C, Zhang B, Huang H, et al. Situs inversus totalis with local metastasis of gallbladder carcinoma and variation of the common hepatic artery. BMC Gastroenterol. 2022;22:357. Published 2022 Jul 26.
[10] Abbey E, Yang F, Qi L, et al. Situs inversus totalis patients with gastric cancer: robotic surgery the standard of treatment?—a case report. Int J Surg Case Rep. 2021;81:105818.
[11] Namikawa T, Maeda M, Yokota K, et al. Laparoscopic distal gastrectomy for synchronous gastric cancer and gastrointestinal stromal tumor with situs inversus totalis. In Vivo. 2021;35:913–8.
[12] Sivakumar J, Crosthwaite G. Prophylactic laparoscopic total gastrectomy in a patient with situs inversus totalis. J Surg Case Rep. 2021;2021:rjaa475. Published 2021 May 15.
[13] Takeno A, Masuzawa T, Katsuyama S, et al. Robotic-assisted proximal gastrectomy using the double-flap technique for early gastric cancer with situs inversus totalis: a case report. Surg Case Rep. 2021;7:172. Published 2021 Aug 2.
[14] Yoshimoto T, Yoshikawa K, Tokunaga T, et al. Robotic-assisted total gastrectomy in a patient with gastric cancer associated with situs inversus totalis: With video. Asian J Endosc Surg. 2021;14:297–300.
[15] Koyama Y, Kawai T, Matsumoto T, et al. Endoscopic submucosal dissection of early gastric cancer in a patient with situs inversus totalis. VideoGIE. 2020;5:347–9.
[16] Oh C. Successful endoscopic retrograde cholangiopancreatography and bilateral stenting in a patient with situs inversus totalis. Dig Liver Dis. 2022;54:136–7.
[17] Ojima T, Nakamura M, Nakamori M, et al. Robotic distal gastrectomy with D2 lymphadenectomy for gastric cancer in a patient with situs inversus totalis. Surg Oncol. 2019;30:98–9.
[18] Dai H, Wang Z, Feng X, et al. Case report about a successful full robotic radical gastric cancer surgery with intracorporeal robot-sewn anastomosis in a patient with situs inversus totalis and a two-and-a-half-year follow-up study. World J Surg Oncol. 2018;16:41.
[19] Gündeş E, Çetin DA, Aday U, et al. Gastric cancer with situs inversus totalis: does it really create difficulties for surgeons? Prz Gastroenterol. 2018;13:47–51.
[20] Shibata K, Kawamura H, Ichikawa N, et al. Laparoscopic total gastrectomy for advanced gastric cancer in a patient with situs inversus totalis. Asian J Endosc Surg. 2018;11:39–42.
[21] Xiang D, He J, Fan Z, et al. Situs inversus totalis with solid pseudopapillary pancreatic tumor: a case report and review of literature. Medicine (Baltimore). 2018;97:e0205.
[22] Alhossaini R, Hyung W. Robotic assisted distal gastrectomy for gastric cancer in a patient with situs inversus totalis: with video. J Gastrointest Surg. 2017;21:2144–5.
[23] Cao Y, Li J, Shen L, et al. Gastric cancer in a situs inversus totalis patient with multiple intestinal and vessel variations related to gastrectomy surgery: a case report and literature review. Medicine (Baltimore). 2017;96:e8209.
[24] Kigasawa Y, Takeuchi H, Kawakubo H, et al. Laparoscopy-assisted distal gastrectomy in a case of gastric cancer with situs inversus totalis: a case report. Asian J Endosc Surg. 2017;10:47–50.
[25] Martínez M, Veguillas P, Carlin J, et al. Laparoscopic hemicolectomy for a patient with situs inversus totalis and colorectal cancer. J Coloproctology. 2017;37:147–51.
[26] Suh B. A case of gastric cancer with situs inversus totalis. Case Rep Oncol. 2017;10:130–5.
[27] Isobe T, Ogata S, Kaku H, et al. A patient with advanced gastric cancer and situs inversus totalis: report of a case. Kurume Med J. 2015;61:73–6.
[28] Morimoto M, Hayakawa T, Kitagami H, et al. Laparoscopic-assisted total gastrectomy for early gastric cancer with situs inversus totalis: report of a first case. BMC Surg. 2015;15:75.
[29] Yaegashi M, Kimura T, Sakamoto T, et al. Laparoscopic sigmoidectomy for a patient with situs inversus totalis: effect of changing operator position. Int Surg. 2015;100:638–42.

[30] Ye M, Tao F, Xu G, et al. Laparoscopy-assisted distal gastrectomy for advanced gastric cancer with situs inversus totalis: a case report. World J Gastroenterol. 2015;21:10246–50.
[31] Zhu H, Yang K, Hu J. Gastrectomy for gastric carcinoma with situs inversus totalis: case report and literature review. Hippokratia. 2015;19:360–2.
[32] Sumi Y, Maehara R, Matsuda Y, et al. Laparoscopy-assisted distal gastrectomy in a patient with situs inversus totalis. JSLS. 2014;18:314–8.
[33] Fujikawa H, Yoshikawa T, Aoyama T, et al. Laparoscopy-assisted distal gastrectomy for an early gastric cancer patient with situs inversus totalis. Int Surg. 2013;98:266–70.
[34] Kyuno D, Kimura Y, Imamura M, et al. Pancreaticoduodenectomy for biliary tract carcinoma with situs inversus totalis: difficulties and technical notes based on two cases. World J Surg Oncol. 2013;11:312.
[35] Min S, Lee C, Jung H, et al. Laparoscopic distal gastrectomy in a patient with situs inversus totalis: a case report. J Gastric Cancer. 2013;13:266–72.
[36] Kim H, Lee J, Park D, et al. Robot-assisted distal gastrectomy for gastric cancer in a situs inversus totalis patient. J Korean Surg Soc. 2012;82:321–4.
[37] Pan K, Zhong D, Miao X, et al. Situs inversus totalis with carcinoma of gastric cardia: a case report. World J Surg Oncol. 2012;10:263.
[38] Kim Y, Ryu H, Kim D, et al. Double primary malignancies associated with colon cancer in patients with situs inversus totalis: two case reports. World J Surg Oncol. 2011;9:109.
[39] Seo K, Yoon K. Laparoscopy-assisted distal gastrectomy for early gastric cancer and laparoscopic cholecystectomy for gallstone with situs inversus totalis: a case report. J Korean Surg Soc. 2011;81 (suppl 1):S34–8.
[40] Futawatari N, Kikuchi S, Moriya H, et al. Laparoscopy-assisted distal gastrectomy for early gastric cancer with complete situs inversus: report of a case. Surg Today. 2010;40:64–7.
[41] Huh J, Kim H, Cho S, et al. Laparoscopic total mesorectal excision in a rectal cancer patient with situs inversus totalis. J Korean Med Sci. 2010;25:790–3.
[42] Benjelloun B, Zahid FE, Ousadden A, et al. A case of gastric cancer associated to situs inversus totalis. Cases J. 2008;1:391.
[43] Fujiwara Y, Fukunaga Y, Higashino M, et al. Laparoscopic hemicolectomy in a patient with situs inversus totalis. World J Gastroenterol. 2007;13:5035–7.
[44] Murakami S, Terakado M, Misumi M, et al. Situs inversus totalis with malignant lymphoma of the stomach: report of a case. Surg Today. 2003;33:533–6.
[45] Kamiike W, Itakura T, Tanaka H, et al. Hepatic segmentectomy on primary liver cancer with situs inversus totalis. HPB Surg. 1996;9:169–72;discussion 172.
[46] Yoshida Y, Saku M, Masuda Y, et al. Total gastrectomy for gastric cancer associated with situs inversus totalis. A report of 2 cases. S Afr J Surg. 1992;30:156–8.
[47] Organ B, Skandalakis L, Gray S, et al. Cancer of bile duct with situs inversus. Arch Surg. 1991;126:1150–3.
[48] Csendes A, Figueroa M. Situación del cáncer gástrico en el mundo y en Chile. Rev Chil Cir. 2017;69:502–7. Available at: https://www.sciencedirect.com/science/article/pii/S0379389316301533.
[49] Karimi P, Islami F, Anandasabapathy S, et al. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev. 2014;23:700–13.
[50] Machlowska J, Baj J, Sitarz M, et al. Gastric cancer: epidemiology, risk factors, classification, genomic characteristics and treatment strategies. Int J Mol Sci . 2020;21:4012.
[51] Chan A, Wong B. Epidemiology of gastric cancer. Uptodate. 2023 [cited 2023 Aug 7]. Available at: https://www.uptodate.com/contents/epidemiology-of-gastric-cancer [access date October 15, 2023].
[52] Hooi J, Lai W, Ng W, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology. 2017;153:420–9.
[53] Kim S, Choi C. common locations of gastric cancer: review of research from the endoscopic submucosal dissection era. J Korean Med Sci. 2019;34:e231.