

# World Journal of *Gastrointestinal Oncology*

*World J Gastrointest Oncol* 2023 August 15; 15(8): 1317-1504



### REVIEW

- 1317** Update and latest advances in mechanisms and management of colitis-associated colorectal cancer  
*Dan WY, Zhou GZ, Peng LH, Pan F*

### MINIREVIEWS

- 1332** Breast cancer metastasizing to the upper gastrointestinal tract (the esophagus and the stomach): A comprehensive review of the literature  
*Da Cunha T, Restrepo D, Abi-Saleh S, Dharan M*
- 1342** Research progress on drug delivery systems for curcumin in the treatment of gastrointestinal tumors  
*Wu X, Yang Y*

### ORIGINAL ARTICLE

#### Basic Study

- 1349** Potential of damage associated molecular patterns in synergising radiation and the immune response in oesophageal cancer  
*Donlon NE, Davern M, Sheppard A, O'Connell F, Moran B, Nugent TS, Heeran A, Phelan JJ, Bhardwaj A, Butler C, Ravi N, Donohoe CL, Lynam-Lennon N, Maher S, Reynolds JV, Lysaght J*
- 1366** LINC01268 promotes epithelial-mesenchymal transition, invasion and metastasis of gastric cancer *via* the PI3K/Akt signaling pathway and targeting MARCKS  
*Tang LH, Ye PC, Yao L, Luo YJ, Tan W, Xiang WP, Liu ZL, Tan L, Xiao JW*
- 1384** Antitumor activity of miR-188-3p in gastric cancer is achieved by targeting CBL expression and inactivating the AKT/mTOR signaling  
*Lin JJ, Luo BH, Su T, Yang Q, Zhang QF, Dai WY, Liu Y, Xiang L*
- 1400** Physcion increases the sensitivity of hepatocellular carcinoma to sorafenib through miRNA-370/PIM1 axis-regulated glycolysis  
*Pan XP, Jiya BR, Wang F, Lan Z*

#### Clinical and Translational Research

- 1412** Expression patterns of cluster of differentiation 147 impact the prognosis of hepatocellular carcinoma  
*Xu YJ, He HJ, Wu P, Li WB*

#### Case Control Study

- 1424** Fecal microbial biomarkers combined with multi-target stool DNA test improve diagnostic accuracy for colorectal cancer  
*Fan JQ, Zhao WF, Lu QW, Zha FR, Lv LB, Ye GL, Gao HL*

**Retrospective Cohort Study**

- 1436** Comparison of clinicopathological characteristics and survival outcomes between gallbladder mucinous adenocarcinoma and gallbladder adenocarcinoma: A propensity score-matched study

*Yang WW, Fang YT, Niu YR, Sun YK*

- 1451** Incidence and prevalence of gastric neuroendocrine tumors in patients with chronic atrophic autoimmune gastritis

*Massironi S, Gallo C, Elvevi A, Stegagnini M, Coltro LA, Invernizzi P*

**Retrospective Study**

- 1461** Epidemiologic characteristics and risk factors associated with overall survival for patients with mucinous colorectal cancer: A population-based study

*Jiang J, Tang XW, Huang S, Hu N, Chen Y, Luo B, Ren WS, Peng Y, Yang WX, Lü MH*

- 1475** Carcinoembryonic antigen, carbohydrate antigen 199 and carbohydrate antigen 724 in gastric cancer and their relationship with clinical prognosis

*Wang R, Zuo CL, Zhang R, Zhu LM*

**Observational Study**

- 1486** Development and application of hepatocellular carcinoma risk prediction model based on clinical characteristics and liver related indexes

*Liu ZJ, Xu Y, Wang WX, Guo B, Zhang GY, Luo GC, Wang Q*

**CASE REPORT**

- 1497** Gastric neuroendocrine tumors in a BRCA2 germline mutation carrier: A case report

*Zhang HF, Zheng Y, Wen X, Zhao J, Li J*

## Contents

*World Journal of Gastrointestinal Oncology*  
Monthly Volume 15 Number 8 August 15, 2023

### ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Tomohide Hori, FACS, MD, PhD, Chief Doctor, Director, Doctor, Surgeon, Department of Gastroenterology and Hepatology, Nagai Hospital, Tsu 514-8508, Mie, Japan. tomohidehori@yahoo.co.jp

### AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (WJGO, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

### INDEXING/ABSTRACTING

The WJGO is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJGO as 3.0; IF without journal self cites: 2.9; 5-year IF: 3.0; Journal Citation Indicator: 0.49; Ranking: 157 among 241 journals in oncology; Quartile category: Q3; Ranking: 58 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO's CiteScore for 2022 is 4.1 and Scopus CiteScore rank 2022: Gastroenterology is 71/149; Oncology is 197/366.

### RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Xiang-Di Zhang; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ru Fan.

#### NAME OF JOURNAL

*World Journal of Gastrointestinal Oncology*

#### ISSN

ISSN 1948-5204 (online)

#### LAUNCH DATE

February 15, 2009

#### FREQUENCY

Monthly

#### EDITORS-IN-CHIEF

Monjur Ahmed, Florin Burada

#### EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

#### PUBLICATION DATE

August 15, 2023

#### COPYRIGHT

© 2023 Baishideng Publishing Group Inc

#### INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

#### GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

#### GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

#### PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

#### PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

#### ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

#### STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

#### ONLINE SUBMISSION

<https://www.f6publishing.com>

© 2023 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com) <https://www.wjgnet.com>



## Breast cancer metastasizing to the upper gastrointestinal tract (the esophagus and the stomach): A comprehensive review of the literature

Teresa Da Cunha, David Restrepo, Simon Abi-Saleh, Murali Dharan

**Specialty type:** Oncology

**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Gao SG, China; Hou L, China

**Received:** March 14, 2023

**Peer-review started:** March 14, 2023

**First decision:** May 16, 2023

**Revised:** June 1, 2023

**Accepted:** July 5, 2023

**Article in press:** July 5, 2023

**Published online:** August 15, 2023



**Teresa Da Cunha, Murali Dharan**, Department of Gastroenterology and Hepatology, University of Connecticut Health Center, Farmington, CT 06030, United States

**David Restrepo, Simon Abi-Saleh**, Department of Internal Medicine, University of Connecticut Health Center, Farmington, CT 06030, United States

**Corresponding author:** Murali Dharan, AGAF, FASGE, MRCP, Assistant Professor, Department of Gastroenterology and Hepatology, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030, United States. [dharan@uchc.edu](mailto:dharan@uchc.edu)

### Abstract

Breast cancer can infrequently metastasize to the upper gastrointestinal (GI) tract but the exact incidence is not well established-there is considerable variation between incidence reported from clinical studies and incidence noted in autopsy series. Clinical presentation can be very non-specific and often mimics primary gastrointestinal conditions. Endoscopy alone may not be sufficient to make a diagnosis and misdiagnosis is also common. A high degree of awareness and clinical suspicion is required to establish metastases to the upper GI tract. We undertook a comprehensive review of the available literature on breast cancer metastases to the esophagus and stomach including the clinical symptoms and presentation, endoscopic features, additional diagnostic imaging modalities, treatment and outcomes.

**Key Words:** Metastatic breast cancer; Esophagus; Stomach; Endoscopy

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Diagnosis of breast cancer metastasizing to the upper gastrointestinal (GI) tract requires a high index of suspicion and multi-modal approach to establish the diagnosis. GI symptoms are often non-specific and endoscopic findings can be subtle. We performed a comprehensive review of the available literature on this topic.

**Citation:** Da Cunha T, Restrepo D, Abi-Saleh S, Dharam M. Breast cancer metastasizing to the upper gastrointestinal tract (the esophagus and the stomach): A comprehensive review of the literature. *World J Gastrointest Oncol* 2023; 15(8): 1332-1341

**URL:** <https://www.wjgnet.com/1948-5204/full/v15/i8/1332.htm>

**DOI:** <https://dx.doi.org/10.4251/wjgo.v15.i8.1332>

## INTRODUCTION

Breast cancer is the second leading cause of death by cancer in women, after lung cancer[1]. The incidence of breast cancer has been increasing and the associated mortality rate is high (12.8 and 15 per 100000 in developed and developing countries, respectively)[2]. Approximately 6.8 million women were living with breast cancer in 2018, and there were an estimated 2.3 million new cases in 2020, surpassing the incidence of lung cancer[2]. Moreover, metastatic breast cancer is associated with a five-year survival of less than 30%[3].

This type of tumor commonly metastasizes to the bone, liver, and lungs[4]. However, different histological types demonstrate different metastatic patterns[4]. Breast cancer metastasizing to the gastrointestinal tract is less common, but an incidence of up to 16.4% has been reported in autopsy studies[5]. However, clinical studies suggest a much lower incidence. A study from Montagna *et al*[6] identified 2588 patients with metastatic breast cancer from these, 1.55% had metastasis to the gastrointestinal (GI) tract[6]. In another study of 12001 patients with metastatic breast cancer, only 0.34% had GI metastases[7].

The reported frequency of the location of the metastases along the GI tract is conflicting. One study reported a higher frequency of metastases in the stomach and esophagus and the lowest in the colon[5]. Another retrospective study revealed a higher number of metastases in the colon, followed by the stomach, small bowel, and esophagus[7]. However, an extensive review of breast cancer metastasis revealed that the stomach was the most affected site[8].

Histologically, the lobular type of breast cancer has a higher association with GI metastases when compared to other types of breast cancer[6,7,9]. The clinical signs and symptoms are usually nonspecific. Moreover, the endoscopic findings can mimic gastritis, and the biopsies retrieved *via* endoscopy are often negative. These factors make the diagnosis of GI metastases from breast cancer highly challenging and lead to delays in management.

The aim of this work was to comprehensively review the literature on breast cancer metastases to the esophagus and stomach and understand the clinical symptoms and presentation, endoscopic features, additional diagnostic imaging modalities, treatment, and outcomes.

In September 2022, the authors searched for articles concerning breast cancer metastasizing to the esophagus and stomach using PubMed databases. Only the articles written in English were selected, and those articles in which the patients were individually characterized and contained enough information regarding age, symptomatology, diagnostic, and treatment modalities were analyzed. No autopsy studies were included. From the articles obtained, the references were reviewed to retrieve additional articles.

For each study, the following parameters were assessed when available: Patient age, the time interval from index breast cancer diagnosis to the diagnosis of esophageal/gastric metastases, histological type of breast cancer, the hormone receptor status of the primary tumor, the type of treatment of the primary tumor, the clinical presentation preceding the diagnosis of the metastatic lesions, misdiagnosis, the anatomical location of the metastatic lesions, the endoscopic findings, the use of additional imaging, the diagnostic modality that provided the final confirmatory biopsies, the histological findings and hormonal status and specific markers of the esophageal/gastric metastases, the type of treatment for the metastatic lesions, the presence of other metastatic sites and finally the clinical outcome.

We extracted the data from each study, one parameter at a time. The data was entered into an Excel database which was used for the descriptive statistical analysis.

### Esophagus

We found 74 studies individually describing and characterizing patients with breast cancer metastasizing to the esophagus. A total of 77 patients were included. The median age at diagnosis of esophageal metastases from breast cancer was 64 years, and all patients were female. The median time interval from the diagnosis of breast cancer to the diagnosis of metastases was 10 years. One patient was diagnosed with esophageal metastases before the diagnosis of breast cancer.

In 14 patients, the type of breast cancer was reported-4 (29%) were lobular, 9 (64%) were ductal, and one patient had both types (Table 1). Six studies reported the hormone receptor status of the primary tumor individually. Estrogen receptors (ER) were positive in four (67%) patients and negative in three (50%). Progesterone receptors (PR) were positive in two patients and negative in four (67%). Human epidermal growth factor receptor 2 (HER2) was not positive in any of the cases, and it was negative in three cases (50%). The treatment of the primary tumor was individually reported in 67 patients. Mastectomy was performed in 97% ( $n = 65$ ) of cases, radiotherapy in 49% ( $n = 33$ ), chemotherapy in 30% ( $n = 20$ ), and hormonal therapy in 19% ( $n = 13$ ). Ten percent ( $n = 7$ ) of patients had surgery, chemotherapy, and hormonal therapy, and 6% ( $n = 4$ ) underwent all 4 treatment modalities.

The clinical presentation was reported in 52 patients (Table 2). Patients most commonly presented with dysphagia (96%,  $n = 50$ ) or weight loss (31%,  $n = 16$ ), and 27% ( $n = 14$ ) reported both. The site of esophageal involvement was described in 61 cases. The middle third of the esophagus was affected in 66% ( $n = 40$ ) of cases, followed by the lower third (21%,  $n = 13$ ) and the upper third (13%,  $n = 8$ ). Moreover, in 16 cases there were no other reported sites of metastases, 20 patients had one more site of metastases, and 8 patients had more than two additional sites of metastases.

**Table 1 Clinical characteristics of patients with metastatic breast cancer to upper gastrointestinal tract**

	Esophagus (%)	Stomach (%)
Age (years)	64	57.3
Breast cancer type		
Lobular	4 (29)	135 (72)
Ductal	9 (64)	49 (36)
Initial treatment of breast cancer		
Surgery	65 (97)	70 (80)
Radiotherapy	33 (49)	28 (32)
Chemotherapy	20 (30)	42 (48)
Hormonal Therapy	13 (19)	33 (38)
Median time between diagnosis of primary breast cancer and GI metastases (years)	10	4

GI: Gastrointestinal.

**Table 2 Clinical symptoms of patients with metastatic breast cancer to upper gastrointestinal tract**

	Esophagus (%)	Stomach (%)
Symptoms		
Dysphagia	50 (96)	-
Weight loss/anorexia	16 (31)	80 (42)
Abdominal pain	-	108 (57)
Nausea/vomiting	-	82 (43)
Gastrointestinal bleed	-	22 (12)

Endoscopic features were reported in 67 patients (Table 3). The majority (84%,  $n = 56$ ) had intact esophageal mucosa, and 9% ( $n = 6$ ) had mucosal changes. These included hyperemic mucosa, mucosal edema, and mucosal erosions. Esophageal stenosis was identified through endoscopy in 61% ( $n = 41$ ) of patients, whereas a mass was observed in only 3% ( $n = 2$ ) of patients. A computed tomography (CT) scan showed abnormal findings in 32 patients. These were described as esophageal wall thickening. For all 12 patients in whom an endoscopic ultrasound (EUS) was performed, the findings were abnormal and were also described as thickening of the esophageal wall.

The diagnostic procedure that resulted in confirmatory biopsy was reported in 46 individual cases. The biopsies that established the final diagnosis were retrieved during surgery in 67% ( $n = 31$ ) of cases, esophagogastroduodenoscopy (EGD) in 15% ( $n = 7$ ), EUS in 7% ( $n = 3$ ), autopsy in 4% ( $n = 2$ ), and endoscopic mucosal resection in 2% ( $n = 1$ ). Moreover, the first biopsy retrieved by EGD was reportedly negative in at least 52 patients (68%). Only 13 cases had the hormonal receptor status of the metastatic lesions reported. All of them were ER+, 69% ( $n = 9$ ) were PRG+ and 8% ( $n = 1$ ) were HER+ (Table 4).

The treatment modalities for esophageal metastases were reported in 66 patients (Table 5). Surgery alone (in the form of partial esophagectomy or esophageal myotomy) was performed in 20 (30%) of cases, 15 (23%) patients received hormonal therapy and/or chemotherapy alone, and radiation alone was reported in 6 (9%) patients. Twelve (18%) patients had surgery combined with chemotherapy and/or hormonal therapy, and 10 (15%) patients had radiation combined with chemotherapy and/or hormonal therapy. In addition, thirty-two patients (48%) underwent esophageal dilation, and nine (14%) had a stent placed for symptomatic relief of dysphagia.

Esophageal perforation occurred in 11 patients as a complication of symptomatic treatment with either dilation or stent. In one patient, the perforation occurred secondary to tumor evasion.

The outcome was reported in 55 patients (Table 5). Twenty-four (44%) patients died within one year, 9 (16%) patients died within 5 years, and 19 (35%) patients were alive at one year follow-up. In 7 patients, the follow-up was reported at 1 mo, and they were alive.

From the patients that were alive at 1 year ( $n = 19$ ), 16% ( $n = 3$ ) had surgery only, 32% ( $n = 6$ ) had surgery and chemotherapy and/or hormonal therapy, 32% ( $n = 6$ ) had only chemotherapy and/or hormonal therapy, 16% ( $n = 3$ ) had radiation combined with chemotherapy and/or hormonal therapy, and 5% ( $n = 1$ ) had radiation alone.



**Table 3 Endoscopic characteristics of patients with metastatic breast cancer to upper gastrointestinal tract**

	Esophagus (%)	Stomach (%)
Location		
Upper third of the esophagus	8 (13)	-
Middle third of the esophagus	40 (66)	-
Lower third of the esophagus	13 (21)	-
Proximal stomach	-	24 (21)
Middle stomach	-	13 (11)
Distal stomach	-	38 (32)
Diffuse in the stomach	-	42 (36)
Endoscopic findings		
Normal mucosa	56 (84)	-
Mucosal changes	6 (9)	-
Stenosis	41 (61)	-
Mass	2 (3)	4(3)
Linitis plastica	-	44 (36)
Ulcer	-	30 (25)
Polyps	-	7 (6)
Nodularity	-	7 (6)
External compression	-	23 (19)

**Table 4 Hormone status and immunohistochemistry markers for patients with metastatic breast cancer to upper gastrointestinal tract**

	Esophagus (%)	Stomach (%)
Tumor receptors of primary breast tumor		
ER+	4 (67)	37 (88)
ER-	3 (50)	5 (12)
PRG+	2 (33)	29 (69)
PRG-	4 (67)	12 (29)
HER+	0 (0)	2 (5)
HER-	3 (50)	23 (55)
Tumor receptors and markers of gastrointestinal metastases		
ER+	13 (100)	86 (57)
ER-	-	39 (26)
PRG+	9 (69)	30 (20)
PRG-	-	18 (12)
HER+	1 (8)	8 (5)
HER-	1 (8)	38 (25)
CK7+	3 (23)	25 (17)
CK20+	-	1 (1)
CK20-	3 (23)	18 (12)

### Stomach

In our literature review, we found 51 studies describing and characterizing patients with breast cancer that had



**Table 5 Treatment and outcomes of patients with metastatic breast cancer to the upper gastrointestinal tract**

	Esophagus (%)	Stomach (%)
Treatment of primary tumor		
Surgery	65 (97)	70 (80)
Radiotherapy	33 (49)	28 (32)
Hormonal therapy	13 (19)	33 (38)
Chemotherapy	20 (30)	42 (48)
Treatment of metastases		
Surgery	20 (30)	12 (11)
Surgery and chemotherapy/hormonal therapy	13 (20)	15 (15)
Chemotherapy/hormonal therapy	15 (23)	74 (70)
Radiotherapy only	6 (9)	3 (3)
Radiation and chemotherapy/hormonal therapy	10 (15)	-
Dilation	32 (48)	-
Stent placement	9 (14)	-
Outcome		
Alive at one month	7 (13)	-
Alive at one year	19 (35)	13 (24)
Dead at 1 yr	24 (44)	20 (37)
Dead at 2 yr	-	18 (33)
Dead at 5 yr	9 (16)	-
Dead at 10 yr	-	1 (2)

metastasized to the stomach. These included a total of 210 patients. Of these, 208 were female, and two were male; the mean age was 57 years. The median time from breast cancer diagnosis to gastric metastases detection was 4 years (Table 1). Some patients had both primary cancer and metastases diagnosed simultaneously while others were diagnosed with gastric metastasis almost two decades after the diagnosis of the primary malignancy. Moreover, five patients had gastric metastasis identified before the diagnosis of primary cancer. Among 188 patients, 135 (72%) had lobular breast cancer, 49 (36%) had ductal, 3 had both lobular and ductal, and one had a phyllodes tumor. The presence of hormone receptors in the primary tumor was individually described in 42 patients. ER were positive in 37 (88%) patients and negative in five (12%). Twenty-nine (69%) patients had positive PR receptors; negative PR receptors were reported in 12 (29%) patients. In 23 (55%) patients, HER2 was negative, whereas this receptor was reportedly positive in only two patients (5%). In 28 (67%) patients, the primary tumor was positive for ER and PR. The treatment for the primary breast cancer was described in 87 patients. Breast surgery (radical mastectomy or lumpectomy) was performed in 80% ( $n = 70$ ) of patients, 32% ( $n = 28$ ) of patients received radiotherapy, 48% ( $n = 42$ ) received chemotherapy, and 38% ( $n = 33$ ) received hormonal therapy. Moreover, 14 (16%) patients received all treatment modalities, and six (7%) patients only received chemotherapy and hormonal therapy.

The clinical presentation was reported in 189 patients (Table 2). The most common symptoms were abdominal pain (57%;  $n = 108$ ), nausea and/or vomiting (43%;  $n = 82$ ), weight loss and/or anorexia (42%;  $n = 80$ ), and gastrointestinal bleeding (GIB) (12%;  $n = 22$ ). The GIB was described as hematemesis (3 patients), melena (3 patients) or non-specific bleed (16 patients). The most common location of abdominal pain was the epigastrium. Other clinical features included dysphagia, early satiety and anemia.

The reported location of the gastric was most commonly diffuse (36%,  $n = 42$ ) and distal (32%,  $n = 38$ ), followed by proximal (21%,  $n = 24$ ) and mid stomach (11%,  $n = 13$ ). The endoscopic findings were described in 122 patients (Table 3). These included linitis-plastica-like features ( $n = 44$ , 36%), ulceration ( $n = 30$ , 25%), nodularity ( $n = 7$ , 6%), polyps ( $n = 7$ , 6%), and mass ( $n = 4$ , 3%). Moreover, external compression/stenosis was described in 23 patients (19%).

In 26 patients, additional imaging was reported. The CT scan abnormal findings in 17 (65%) patients and was normal in two (8%) patients and. The abnormal findings included thickening of a portion of the gastric wall and/or the presence of a mass in the stomach. Three patients underwent EUS with findings of gastric mucosal thickening in 2 patients and a rounded submucosal hypoechoic lesion in another patient [who also had an unremarkable positron emission tomography (PET) scan]. Finally, PET was done in 4 patients and the results showed no abnormal findings in 2.

Twelve patients were initially misdiagnosed. The misdiagnoses included primary gastric cancer (7 patients), Crohn's disease (2 patients with widespread GI involvement), gastric lymphoma (1 patient), gastric neuroendocrine tumor (1 patient) and Ménétrier disease (1 patient).

The biopsies obtained from the initial EGD were positive for malignancy in 88 patients and negative in 19. Moreover, in 64 patients, the modality that provided the confirmatory biopsy establishing the correct diagnosis was reported individually. Confirmatory biopsies were obtained by EGD in 35 (55%) patients, surgery in 23 (36%) patients, autopsy in five (8%) patients, and EUS with fine-needle aspiration (FNA) in one (2%) patient.

The hormonal receptors of gastric metastases were reported in 150 patients (Table 4). ER was positive in 57% ( $n = 86$ ) of patients and negative in 26% ( $n = 39$ ), PR+ in 20% ( $n = 30$ ), and HER+ in 5% ( $n = 8$ ). In addition, in 25 patients the gastric metastases were CK7+, in 18 patients were CK20-, and in nine patients were CK7+/CK20-. Signet ring cell morphology was reported in 10 patients.

Among 38 patients reported as having breast cancer metastases involving other organs, 17 (44%) patients had one additional site of metastases, 18 (46%) patients had two or more sites, and four (10%) patients only had gastric involvement.

The treatment modalities for the gastric metastases were grouped into surgery, surgery with chemotherapy and/or hormonal therapy, chemotherapy and/or hormonal therapy only (Table 5). The choice of treatment of gastric metastases was reported in 105 patients. Twenty-eight patients underwent surgery, from which 16 (16%) also received adjuvant chemotherapy and/or hormonal therapy. Seventy-four patients (70%) only received chemotherapy and/or hormonal therapy, and three (3%) received radiotherapy.

The outcome was described in 54 patients. Death was reported in 39 (72%) patients, 20 (37%) patients died within one year of the diagnosis of metastases, 18 (33%) patients died within two years and one (2%) patient died within 10 years. Thirteen (24%) patients were stable at 1 year follow up and 2 (4%) patients were stable at an unknown follow-up time.

## EPIDEMIOLOGY

Metastatic breast cancer affecting the esophagus and the stomach is rare compared to other organs[10,11]. However, the actual incidence is difficult to assess. Autopsy studies have reported an incidence of metastases to the esophagus and stomach of around 0.3%-6.1% and 0.2%-5.4%, respectively[10-14].

The most commonly reported sites of the primary tumors metastasizing to the esophagus are the lung, the stomach, the breast, and the liver[10]. Whereas primary cancers commonly metastasizing to the stomach include the lung, the breast, and the skin (melanoma) cancers[11]. In one study of gastric metastases, melanoma was the most common primary tumor (38%), followed by breast cancer (33%) and lung cancer (6%)[15]. However, in another study, breast cancer was the primary tumor in only 5.7% of patients, whereas lung cancer was the primary tumor in 18.9% of patients with gastric metastases[16].

Given the rarity of occurrence and diagnostic challenges, the true incidence of breast cancer metastases in the esophagus and stomach is hard to establish, and studies have shown varying results. Moreover, the results from clinical studies are much lower than those from autopsy studies[5,7,10,12,17].

The autopsy study of Mizobuchi *et al*[10] included 188 cadavers from patients with metastatic breast cancer, and 14 (7.4%) had esophageal metastases[10].

In the study by Mclemore *et al*[7], 12001 patients with metastatic breast cancer were identified[7]. Four (0.03%) patients had esophageal metastases, and 15 (0.12%) had stomach metastases. Similarly, Ellis *et al*[17] reviewed 19049 breast cancer cases, and only four (0.02%) patients had gastric metastatic lesions[17]. On the other hand, Oda *et al*[12] observed a much higher number-from 526 autopsies of the breast, 61 (11.6%) patients had gastric metastasis[12]. These differences in rates between autopsy studies and studies in live individuals point towards an underdiagnosis and emphasize the challenges in establishing diagnosis of breast cancer metastases to the upper GI tract.

The most reported type of breast cancer metastasizing to the gastrointestinal tract is the lobular type[4,7,18]. We observed a similar finding with respect to gastric metastases (73%). Nevertheless, in the esophageal metastases group, we observed the inverse. However, the sample size of patient with reported sub-type of breast cancer among those with esophageal metastases was too small.

The median age for the esophageal and gastric groups was 59 and 64, respectively. These were similar to those from other studies[7,19]. Overall, only two patients were male (0.7%), and both had gastric metastases[20,21].

## CLINICAL FEATURES

The clinical signs and symptoms of metastases are very nonspecific. In the case of esophageal metastasis, dysphagia is undoubtedly the most common symptom. However, patients with gastric metastasis can have a wider variety of symptoms, including abdominal pain (most commonly), nausea and/or vomiting, weight loss and/or anorexia, and GIB. Fulminant hematemesis[22] and gastric perforation[23,24] occurred in isolated reports of patients with gastric metastases.

In the esophagus, the middle third was the most common location of metastases. This finding was also described in the case series of Rampado *et al*[25] and could be due to the anatomical location of mediastinal lymph nodes[25]. On the other hand, the location of gastric metastases was more variable. For instance, in the study of Almubarak *et al*[18] ( $n = 35$ ), the distal and proximal portions were equally involved ( $n = 15$ ), whereas in the study of Taal *et al*[19] ( $n = 51$ ), a higher proportion of patients had diffuse gastric metastases ( $n = 23$ )[18,19].

## DIAGNOSTIC CHALLENGE

The diagnosis of breast cancer metastatic to the upper GI tract is challenging, and misdiagnosis is not uncommon, especially with stomach involvement. From our results, misdiagnosis of primary gastric cancer occurred in several cases [21,23,26-30]. In addition, a misdiagnosis of a benign esophageal stricture has been reported more than once [31,32]. The time interval between the diagnosis of primary tumor and the diagnosis of either esophageal or stomach metastases can be several decades. Consistent with the findings of Taal *et al* [19] and Almubarak *et al* [18], our study also showed a median interval between the primary tumor and the diagnosis of stomach metastases to be 4 years. Interestingly, the median time in the esophageal group was much higher, 13 years. Importantly, gastrointestinal metastases can be the first manifestation of breast cancer [22,26,30,33-35].

Depending on the patient's symptoms, an EGD is often part of the first steps of the initial evaluation. Interestingly, mucosal changes are rare in the esophageal group but very frequent in the gastric. Similar to the findings in our article, in the study by Rampado *et al* [25], 96% ( $n = 25$ ) of the patients had a normal esophageal mucosa on EGD [25]. The common abnormal finding was esophageal stenosis.

Although gastric mucosal changes are common, they are nonspecific. The most common mucosal appearances are linitis plastica, ulceration, and polyps [19,23]. However, rarely, the mucosal features might mimic other diseases such as lymphoma [36].

A CT scan is an important diagnostic tool as it frequently reveals thickening of the wall of the esophagus and the stomach over the affected areas. Hence, we recommend it to be part of the diagnostic workup, especially because an EGD might be unrevealing. The utilization of a EUS should be considered as it can show changes in the esophageal and gastric wall and can facilitate the use of FNA, which might serve as a better device to retrieve a biopsy [25,37,38].

Surprisingly, in four gastric cases that reported the use of PET scans, two did not show an increased fluorodeoxyglucose (FDG) uptake [39,40]. However, the other two patients had an increased FDG activity in the exact location of the metastatic lesions [21,27]. Further information is warranted regarding its sensitivity in detecting metastases to the gastrointestinal tract.

A tissue biopsy is required to make a diagnosis which can be obtained through endoscopy, EUS/FNA, or surgery. Since mucosal changes in the esophagus are rare, using EGD may lead to negative biopsy results, as seen in our study (68%). A similar finding was emphasized in the studies of Taal *et al* [19], where seventeen patients with gastric metastases had a negative first biopsy [19,23]. However, only one additional study reported this. Nonetheless, the reliability of the biopsies retrieved by EGD is higher when the metastases occur in the stomach compared to the esophagus. This could be due to the frequent mucosal changes observed in the gastric group compared to the esophageal group. Although more invasive, EUS with FNA might be a better option to obtain the tissue specimens in the esophagus as it detects submucosal changes and can also collect submucosal tissue [38,41,42].

The histological findings are most often those of an undifferentiated adenocarcinoma, and signet ring cell morphology is often seen [43]. For that reason, it can lead to a misdiagnosis of gastrointestinal signet ring cell carcinoma. Lobular breast cancer and gastrointestinal signet ring cell carcinoma are the most common sources of metastatic signet ring cells. Hence, immunohistochemical staining to differentiate these entities is crucial [44]. Cytokeratin 20 (CK20) is strongly associated with gastrointestinal signet ring cell carcinoma, whereas cytokeratin 7 (CK7) is strongly associated with lobular carcinoma of the breast. As suggested by Tot *et al* [44], CK20 and ER can differentiate gastrointestinal signet ring cell carcinoma and lobular breast cancer [44]. Their study identified 33 of 34 metastases as gastrointestinal (CK20+) and mammary (CK20-). Moreover, the CK20+/ER- pattern correctly identified all the gastrointestinal metastases. In our study, only 17 cases reported the CK20 status, and only one was CK20+, but it was simultaneously positive for CK7. The latter is highly associated with invasive breast cancer; but, it can still be positive in metastases of gastrointestinal origin [45]. In addition, the presence of hormonal receptors is suggestive of breast cancer. Unfortunately, in the esophageal group, there was not enough individual data regarding the presence of hormonal receptors on both the primary breast tumor and the esophageal metastases. However, in the stomach group, 18 cases reported the hormonal status of both primary and metastatic tumors. The concordance rate of ER receptors was 81%, and that of the PRG receptors was 53%. These results are aligned with results from a large study by Grinda *et al* [46] in which the authors found that the ER concordance rate was 84.9% and that of PR was 68.9% between primary breast cancer and breast cancer metastases to the brain, lymph nodes, lungs, pleura, liver, skin, and bones [46].

## TREATMENT AND OUTCOME

The treatment modalities for both esophageal and gastric metastases range between surgery, radiation, chemotherapy with or without hormonal therapy, and radiation therapy. These can be used alone or in combination. Moreover, palliation with esophageal dilation or placement of a stent can confer improvement of the dysphagia. However, there is a considerable risk of esophageal perforation, as noted in several reports [25,47-50].

From the 59 cases of esophageal metastasis that provided information on the treatment and outcome, patients who received chemotherapy and/or hormonal therapy had a better outcome. However, there was no significant difference in the outcome between the group that had surgery combined with chemotherapy and/or hormonal therapy and those who had chemotherapy and/or hormonal therapy alone. These findings were similar in the gastric group.

The fact that the esophageal group had a higher percentage and number of patients having surgery might be due to several factors. One is that only in a few numbers of cases was the EGD able to retrieve diagnostic tissue biopsies, and for that reason, many patients ended up having an esophagectomy for both diagnostic and treatment purposes. In addition,

the fact that the metastatic lesions are often localized to one segment of the esophagus can also make the feasibility of surgery more manageable, whereas, in the stomach, diffuse involvement is frequently observed.

## CONCLUSION

Breast cancer metastasizing to the esophagus and stomach is rare. However, differences in frequency seen between autopsy and clinical studies indicate that it is underdiagnosed. This could be due to the lack of specific symptoms and the challenge of establishing the diagnosis. It is essential to have a high degree of suspicion when a patient with a history of breast cancer develops dysphagia, weight loss, and other gastrointestinal symptoms. The endoscopic features vary considerably between patients, and initial biopsies might be negative for malignancy, especially in the esophagus. For this reason, a multimodal diagnostic approach using additional imaging, preferably a CT scan, should be considered. In addition, endoscopic surveillance with a lower time interval should be contemplated in breast cancer survivors.

## FOOTNOTES

**Author contributions:** Da Cunha T proposed concept for review, collected data, wrote and revised the manuscript with critical revisions; Restrepo D and Abi-Saleh S collected data, helped write manuscript; Dharan M edited the article, critical revision of the article, and final approval.

**Conflict-of-interest statement:** The authors have no conflicts of interest to disclose.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** United States

**ORCID number:** Teresa Da Cunha 0000-0002-8319-7608; David Restrepo 0000-0002-3841-0895; Simon Abi-Saleh 0000-0003-2166-6488; Murali Dharan 0000-0002-9764-0068.

**Corresponding Author's Membership in Professional Societies:** American Gastroenterological Association; American Society for Gastrointestinal Endoscopy.

**S-Editor:** Fan JR

**L-Editor:** A

**P-Editor:** Yu HG

## REFERENCES

- 1 Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin* 2022; **72**: 7-33 [PMID: 35020204 DOI: 10.3322/caac.21708]
- 2 Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]
- 3 Kashyap D, Pal D, Sharma R, Garg VK, Goel N, Koundal D, Zaguia A, Koundal S, Belay A. Global Increase in Breast Cancer Incidence: Risk Factors and Preventive Measures. *Biomed Res Int* 2022; **2022**: 9605439 [PMID: 35480139 DOI: 10.1155/2022/9605439]
- 4 Korhonen T, Kuukasjärvi T, Huhtala H, Alarmo EL, Holli K, Kallioniemi A, Pylkkänen L. The impact of lobular and ductal breast cancer histology on the metastatic behavior and long term survival of breast cancer patients. *Breast* 2013; **22**: 1119-1124 [PMID: 23863867 DOI: 10.1016/j.breast.2013.06.001]
- 5 Asch MJ, Wiedel PD, Habif DV. Gastrointestinal metastases from carcinoma of the breast. Autopsy study and 18 cases requiring operative intervention. *Arch Surg* 1968; **96**: 840-843 [PMID: 5647555 DOI: 10.1001/archsurg.1968.01330230148023]
- 6 Montagna E, Pirola S, Maisonneuve P, De Roberto G, Cancelli G, Palazzo A, Viale G, Colleoni M. Lobular Metastatic Breast Cancer Patients With Gastrointestinal Involvement: Features and Outcomes. *Clin Breast Cancer* 2018; **18**: e401-e405 [PMID: 28778379 DOI: 10.1016/j.clbc.2017.07.003]
- 7 McLemore EC, Pockaj BA, Reynolds C, Gray RJ, Hernandez JL, Grant CS, Donohue JH. Breast cancer: presentation and intervention in women with gastrointestinal metastasis and carcinomatosis. *Ann Surg Oncol* 2005; **12**: 886-894 [PMID: 16177864 DOI: 10.1245/ASO.2005.03.030]
- 8 Di Micco R, Santurro L, Gasparri ML, Zuber V, Fiocco E, Gazzetta G, Smart CE, Valentini A, Gentilini OD. Rare sites of breast cancer metastasis: a review. *Transl Cancer Res* 2019; **8**: S518-S552 [PMID: 35117130 DOI: 10.21037/tcr.2019.07.24]
- 9 Borst MJ, Ingold JA. Metastatic patterns of invasive lobular vs invasive ductal carcinoma of the breast. *Surgery* 1993; **114**: 637-41; discussion 641 [PMID: 8211676]
- 10 Mizobuchi S, Tachimori Y, Kato H, Watanabe H, Nakanishi Y, Ochiai A. Metastatic esophageal tumors from distant primary lesions: report of



- three esophagectomies and study of 1835 autopsy cases. *Jpn J Clin Oncol* 1997; **27**: 410-414 [PMID: 9438004 DOI: 10.1093/jjco/27.6.410]
- 11 **Menuck LS**, Amberg JR. Metastatic disease involving the stomach. *Am J Dig Dis* 1975; **20**: 903-913 [PMID: 1190198 DOI: 10.1007/BF01070875]
  - 12 **Oda**, Kondo H, Yamao T, Saito D, Ono H, Gotoda T, Yamaguchi H, Yoshida S, Shimoda T. Metastatic tumors to the stomach: analysis of 54 patients diagnosed at endoscopy and 347 autopsy cases. *Endoscopy* 2001; **33**: 507-510 [PMID: 11437044 DOI: 10.1055/s-2001-14960]
  - 13 **Neoplasms of the Stomach**. Cancer Research/American Association for Cancer Research. Available from: <https://aacrjournals.org/cancerres/article/28/2/388/657592/Neoplasms-of-the-StomachGordon-McNeer-and-George-T>
  - 14 **Weigt J**, Malfertheiner P. Metastatic Disease in the Stomach. *Gastrointest Tumors* 2015; **2**: 61-64 [PMID: 26674003 DOI: 10.1159/000431304]
  - 15 **Willis RA**, Pp FRCP. The Spread of Tumours in the Human Body. *Postgrad Med J* 1953; **29**: 160
  - 16 **Davis GH**, Zollinger RW. Metastatic melanoma of the stomach. *Am J Surg* 1960; **99**: 94-96 [PMID: 13814449 DOI: 10.1016/0002-9610(60)90258-0]
  - 17 **Ellis MC**, Mason T, Barnett J, Kiesow LL, Vetto JT. Gastric malignancies in breast cancer survivors: pathology and outcomes. *Am J Surg* 2009; **197**: 633-636 [PMID: 19306975 DOI: 10.1016/j.amjsurg.2008.12.015]
  - 18 **Almubarak MM**, Laé M, Cacheux W, de Cremoux P, Pierga JY, Reyat F, Bennett SP, Falcou MC, Salmon RJ, Baranger B, Mariani P. Gastric metastasis of breast cancer: a single centre retrospective study. *Dig Liver Dis* 2011; **43**: 823-827 [PMID: 21616731 DOI: 10.1016/j.dld.2011.04.009]
  - 19 **Taal BG**, Peterse H, Boot H. Clinical presentation, endoscopic features, and treatment of gastric metastases from breast carcinoma. *Cancer* 2000; **89**: 2214-2221 [PMID: 11147591]
  - 20 **Davis HL Jr**, Murray RK, Korbitz BC. Breast carcinoma metastatic to the stomach. Report of a case in a male and review of an autopsy series. *Am J Dig Dis* 1968; **13**: 868-873 [PMID: 5303029 DOI: 10.1007/BF02237571]
  - 21 **Ricciuti B**, Leonardi GC, Ravaoli N, De Giglio A, Brambilla M, Properi E, Ribacchi F, Meacci M, Crinò L, Maiettini D, Chiari R, Metro G. Ductal Breast Carcinoma Metastatic to the Stomach Resembling Primary Linitis Plastica in a Male Patient. *J Breast Cancer* 2016; **19**: 324-329 [PMID: 27721883 DOI: 10.4048/jbc.2016.19.3.324]
  - 22 **Gurzu S**, Baniyas L, Bara T, Feher I, Jung I. The Epithelial-Mesenchymal Transition Pathway in Two Cases with Gastric Metastasis Originating from Breast Carcinoma. One with a Metachronous Primary Gastric Cancer. *Recent Pat Anticancer Drug Discov* 2018; **13**: 118-124 [PMID: 29090670 DOI: 10.2174/2212798409666171101121108]
  - 23 **Taal BG**, den Hartog Jager FC, Steinmetz R, Peterse H. The spectrum of gastrointestinal metastases of breast carcinoma: I. Stomach. *Gastrointest Endosc* 1992; **38**: 130-135 [PMID: 1568608 DOI: 10.1016/s0016-5107(92)70377-0]
  - 24 **Güler SA**, Şimşek T, Pösteği G, Güreşin A, Çınar S, Onbaşlı U, Cantürk NZ. A Very Rare Reason for Gastric Perforation, Caused by Gastric Metastasis of Breast Cancer: Case Presentation. *Eur J Breast Health* 2019; **15**: 59-62 [PMID: 30816356 DOI: 10.5152/ejbh.2018.4285]
  - 25 **Rampado S**, Ruol A, Guido M, Zaninotto G, Battaglia G, Costantini M, Portale G, Amico A, Ancona E. Mediastinal carcinosis involving the esophagus in breast cancer: the "breast-esophagus" syndrome: report on 25 cases and guidelines for diagnosis and treatment. *Ann Surg* 2007; **246**: 316-322 [PMID: 17667512 DOI: 10.1097/01.sla.0000263507.11053.26]
  - 26 **Bushan K**, Kammar P, Singh C, Advani S, Mahajan P. Infiltrating Lobular Breast Cancer Presenting as Isolated Gastric Metastasis: a Case Report. *Indian J Surg Oncol* 2018; **9**: 318-322 [PMID: 30287990 DOI: 10.1007/s13193-017-0705-7]
  - 27 **Geredeli C**, Dogru O, Omeroglu E, Yilmaz F, Cicekci F. Gastric Metastasis of Triple Negative Invasive Lobular Carcinoma. *Rare Tumors* 2015; **7**: 5764 [PMID: 26266010 DOI: 10.4081/rt.2015.5764]
  - 28 **Pera M**, Riera E, Lopez R, Viñolas N, Romagosa C, Miquel R. Metastatic carcinoma of the breast resembling early gastric carcinoma. *Mayo Clin Proc* 2001; **76**: 205-207 [PMID: 11213310 DOI: 10.1016/S0025-6196(11)63129-7]
  - 29 **Yim K**, Ro SM, Lee J. Breast cancer metastasizing to the stomach mimicking primary gastric cancer: A case report. *World J Gastroenterol* 2017; **23**: 2251-2257 [PMID: 28405154 DOI: 10.3748/wjg.v23.i12.2251]
  - 30 **Woo J**, Lee JH, Lee KE, Sung SH, Lim W. Gastric Metastasis as the First Presentation One Year Before Diagnosis of Primary Breast Cancer. *Am J Case Rep* 2018; **19**: 354-359 [PMID: 29576606 DOI: 10.12659/ajcr.908039]
  - 31 **Wilson MA**, Shah N, O'Donnell ME, Jaroszewski DE. An unusual presentation of esophageal metastasis from breast cancer. *J Thorac Cardiovasc Surg* 2015; **149**: e110-e112 [PMID: 25816959 DOI: 10.1016/j.jtcvs.2015.02.038]
  - 32 **Anaya DA**, Yu M, Karmy-Jones R. Esophageal perforation in a patient with metastatic breast cancer to esophagus. *Ann Thorac Surg* 2006; **81**: 1136-1138 [PMID: 16488749 DOI: 10.1016/j.athoracsur.2005.01.052]
  - 33 **Khan I**, Malik R, Khan A, Assad S, Zahid M, Sohail MS, Yasin F, Qavi AH. Breast Cancer Metastases to the Gastrointestinal Tract Presenting with Anemia and Intra-abdominal Bleed. *Cureus* 2017; **9**: e1429 [PMID: 28924517 DOI: 10.7759/cureus.1429]
  - 34 **Dória MT**, Maesaka JY, Martins SN Filho, Silveira TP, Boufelli G, Siqueira SA, Baracat EC, Filassi JR. Gastric metastasis as the first manifestation of an invasive lobular carcinoma of the breast. *Autops Case Rep* 2015; **5**: 49-53 [PMID: 26558248 DOI: 10.4322/acr.2015.018]
  - 35 **Ciulla A**, Castronovo G, Tomasello G, Maiorana AM, Russo L, Daniele E, Genova G. Gastric metastases originating from occult breast lobular carcinoma: diagnostic and therapeutic problems. *World J Surg Oncol* 2008; **6**: 78 [PMID: 18652707 DOI: 10.1186/1477-7819-6-78]
  - 36 **Ghirarduzzi A**, Sivelli R, Martella E, Bella M, De Simone B, Arcuri MF, Zannoni M, Del Rio P, Sianesi M. Gastric metastasis from breast carcinoma. Report of three cases, diagnostic-therapeutic critical close examination and literature review. *Ann Ital Chir* 2010; **81**: 141-146 [PMID: 20726393]
  - 37 **Ulmer LL**, Cormier I, Jha LK, Singh S, Fisher KW, Hewlett AT. Use of Endoscopic Ultrasound in a Diagnostic Dilemma: Metastatic Breast Cancer to the Stomach. *Case Rep Gastrointest Med* 2018; **2018**: 2820352 [PMID: 29850292 DOI: 10.1155/2018/2820352]
  - 38 **Koike M**, Akiyama S, Kodera Y, Nakao A. Breast carcinoma metastasis to the esophagus: report of two cases. *Hepatogastroenterology* 2005; **52**: 1116-1118 [PMID: 16001642]
  - 39 **Whitty LA**, Crawford DL, Woodland JH, Patel JC, Nattier B, Thomas CR Jr. Metastatic breast cancer presenting as linitis plastica of the stomach. *Gastric Cancer* 2005; **8**: 193-197 [PMID: 16086123 DOI: 10.1007/s10120-005-0334-7]
  - 40 **Hara F**, Kiyoto S, Takabatake D, Takashima S, Aogi K, Ohsumi S, Teramoto N, Nishimura R. Metastatic Breast Cancer to the Stomach Resembling Early Gastric Cancer. *Case Rep Oncol* 2010; **3**: 142-147 [PMID: 20740187 DOI: 10.1159/000313923]
  - 41 **Talanow R**, Vieweg H, Andresen R. Solitary breast cancer metastasis to the esophagus - a multimodal diagnostic approach. *Z Gastroenterol* 2013; **51**: 635-637 [PMID: 23839916 DOI: 10.1055/s-0033-1335262]
  - 42 **Liu A**, Feng Y, Chen B, Li L, Wu D, Qian J, Yang A. A case report of metastatic breast cancer initially presenting with esophageal dysphagia.

- Medicine (Baltimore)* 2018; **97**: e13184 [PMID: [30407355](#) DOI: [10.1097/MD.00000000000013184](#)]
- 43 **Washington K**, McDonagh D. Secondary tumors of the gastrointestinal tract: surgical pathologic findings and comparison with autopsy survey. *Mod Pathol* 1995; **8**: 427-433 [PMID: [7567944](#)]
  - 44 **Tot T**. The role of cytokeratins 20 and 7 and estrogen receptor analysis in separation of metastatic lobular carcinoma of the breast and metastatic signet ring cell carcinoma of the gastrointestinal tract. *APMIS* 2000; **108**: 467-472 [PMID: [11028811](#) DOI: [10.1034/j.1600-0463.2000.d01-84.x](#)]
  - 45 **Dum D**, Menz A, Völkel C, De Wispelaere N, Hinsch A, Gorbokon N, Lennartz M, Luebke AM, Hube-Magg C, Kluth M, Fraune C, Möller K, Bernreuther C, Lebok P, Clauditz TS, Jacobsen F, Sauter G, Uhlig R, Wilczak W, Steurer S, Minner S, Marx AH, Simon R, Burandt E, Krech T. Cytokeratin 7 and cytokeratin 20 expression in cancer: A tissue microarray study on 15,424 cancers. *Exp Mol Pathol* 2022; **126**: 104762 [PMID: [35390310](#) DOI: [10.1016/j.yexmp.2022.104762](#)]
  - 46 **Grinda T**, Joyon N, Lusque A, Lefèvre S, Arnould L, Penault-Llorca F, Macgrogan G, Treilleux I, Vincent-Salomon A, Haudebourg J, Maran-Gonzalez A, Charafe-Jauffret E, Courtinard C, Franchet C, Verrielle V, Brain E, Tas P, Blanc-Fournier C, Leroux A, Loussouarn D, Berghian A, Brabencova E, Ghnassia JP, Scoazec JY, Delalogue S, Filleron T, Lacroix-Triki M. Phenotypic discordance between primary and metastatic breast cancer in the large-scale real-life multicenter French ESME cohort. *NPJ Breast Cancer* 2021; **7**: 41 [PMID: [33863896](#) DOI: [10.1038/s41523-021-00252-6](#)]
  - 47 **Stallone RJ**, Roe BB. Breast carcinoma as a cause of dysphagia. *Dis Chest* 1969; **56**: 449-451 [PMID: [5347254](#) DOI: [10.1378/chest.56.5.449](#)]
  - 48 **Varanasi RV**, Saltzman JR, Krims P, Crimaldi A, Colby J. Breast carcinoma metastatic to the esophagus: clinicopathological and management features of four cases, and literature review. *Am J Gastroenterol* 1995; **90**: 1495-1499 [PMID: [7661177](#)]
  - 49 **Wu CM**, Hruban RH, Fishman EK. Breast carcinoma metastatic to the esophagus. CT findings with pathologic correlation. *Clin Imaging* 1998; **22**: 343-345 [PMID: [9755397](#) DOI: [10.1016/s0899-7071\(98\)00027-8](#)]
  - 50 **Atkins JP**. Metastatic carcinoma to the esophagus. Endoscopic considerations with special reference to carcinoma of the breast. *Ann Otol Rhinol Laryngol* 1966; **75**: 356-367 [PMID: [5912892](#) DOI: [10.1177/000348946607500205](#)]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

