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Beyond gastric adenocarcinoma: Multimodality assessment of common and uncommon gastric neoplasms

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Abstract

Despite advances in molecular biology, imaging, and treatment, gastric neoplasms remain a significant cause of morbidity and mortality; gastric adenocarcinoma is the fifth most common malignancy and third most common cause of death worldwide (Brenner et al., Methods Mol Biol 472:467–477, 2009; Howson et al. Epidemiol Rev 8:1–27, 1986; Roder, Gastric Cancer 5(Suppl 1):5–11, 2002; Ferlay et al., GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. International Agency for Research on Cancer, 2013). Because of both the frequency at which malignant gastric tumors occur as well as the worldwide impact, gastric neoplasms remain important lesions to identify and characterize on all imaging modalities. Despite the varied histologies and behaviors of these neoplasms, many have similar imaging features. Nonetheless, the treatment, management, and prognosis of gastric neoplasms vary by pathology, so it is essential for the radiologist to make every effort to differentiate between these lesions and raise the less common entities as differential diagnostic considerations when appropriate.

Key words: Gastric cancer—Benign gastric neoplasms—Malignant gastric neoplasms—Metastasis

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Epidemiology

"Gastric cancer" is a term that most commonly refers to gastric adenocarcinoma, which represents 90–95 % of all malignant gastric neoplasms [1, 2]. Less common gastric malignancies comprising the remaining 5–10 % of cancers include lymphoma, gastrointestinal stromal tumor, and neuroendocrine tumor, as well as very rare malignant tumors such as leiomyosarcoma, choriocarcinoma, angiosarcoma, and Kaposi sarcoma. While these lesions can appear similar on imaging, there are some characteristic imaging features and behaviors that can help differentiate them.

Benign lesions make up 85–90% of all lesions found within the stomach [5]. Of these benign lesions, approximately 50% are fundic gland, hyperplastic, or adenomatous polyps. The remaining 50% of benign lesions are mesenchymal in nature, including lipoma, schwannoma, leiomyoma, and glomus tumors. In addition to both benign and malignant primary gastric lesions, metastases also commonly occur to the stomach, with the most common metastases arising from breast cancer, melanoma, and lung cancer.

There has been a significant decrease in the number of cases of gastric cancer in the 21st century with the improvement in sanitary conditions, diet, and medical advances. However, gastric cancer remains a significant cause of morbidity and mortality worldwide. The incidence varies dramatically, with greater than two-thirds of all cases occurring in developing countries and reports of up to 43% of cases occurring in China, with a similar geographical variability that is also seen in other cancers [1]. The areas with the greatest incidence include East Asia, Eastern Europe, and parts of Central and South

America. On the contrary, the lowest incidence rates occur in Southern Asia, North and East Africa, North America, Australia, and New Zealand.

Being the most common gastric malignancy, gastric adenocarcinoma is typically diagnosed between 60–80 years of age, with men approximately twice as likely to be affected. Significant mortality is associated with gastric adenocarcinoma: The 5-year overall survival rate is 20–30 % overall, with higher survival rates in Japan (52 % 5-year survival) that have been attributed to early screening programs [1, 3, 6]. Gastric adenocarcinoma tends to be diagnosed at later stages secondary to non-specific early symptoms such as dyspepsia, which commonly progress to abdominal pain. Cited risk factors include *H. pylori* infection, male sex, dietary factors, environmental factors, and smoking.

Table 1. WHO classification of gastric tumors

WHO classification of malignant tumors	
Epithelial type	Non-epithelial type
Adenocarcinoma-diffuse type, intestinal type	Leiomyoma
Papillary adenocarcinoma	Schwannoma
Tubular adenocarcinoma	Granular cell tumor
Mucinous adenocarcinoma	Glomus tumor
Signet ring cell carcinoma	Leiomyosarcoma
Squamous cell carcinoma	Gastrointestinal stromal tumor
Small cell carcinoma	Kaposi sarcoma
Undifferentiated carcinoma	Malignant lymphoma
Carcinoid (well-differentiated)	

Classification of gastric tumors

The World Health Organization (WHO) classification of gastric tumors divides malignant tumors into epithelial or non-epithelial subtypes (Table 1). The epithelial subtypes include adenomas, neuroendocrine neoplasms, and carcinomas, with carcinomas including the various types of adenocarcinoma and rare carcinoma types for this site, such as squamous cell carcinoma, carcinoma with lymphoid stroma, and undifferentiated carcinoma. Neuroendocrine neoplasms include grade 1 (and grade 2) neuroendocrine tumors (also known as carcinoid tumors) and neuroendocrine carcinomas of large cell or small cell type. The mesenchymal tumors include gastrointestinal stromal tumor (GIST), leiomyoma, schwannoma, glomus tumor, and several other rare tumor types. The most common gastric lymphomas are diffuse large B-cell lymphoma and MALT lymphoma (marginal zone lymphoma of mucosa-associated lymphoid tissue) [4, 7].

Imaging of known or suspected gastric neoplasms

When a patient presents with a known or suspected gastric lesion, the optimal imaging strategy strongly depends upon the clinical context. Computed tomography

Table 2. 7th edition AJCC TNM staging for gastric neoplasms with suggested imaging for staging

AJCC gastric cancer TNM staging	Definition	Imaging features
T		
TX	Primary tumor cannot be assessed	Based on depth of invasion on endoscopic ultrasound
T0	No evidence of primary tumor	
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria	
T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa	
T1a	Tumor invades the lamina propria or muscularis mucosae	
T1b	Tumor invades the lamina propria	
T2	Tumor invades the muscularis propria	
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures.	
T4	Tumor invades serosa or adjacent structures	Tumor nodularity outside of the stomach on CT of the abdomen and/or PET–CT, or invasion of adjacent organs.
T4a	Tumor invades serosa	
T4b	Tumor invades adjacent structures	
N		
NX	Regional nodes cannot be assessed	Significantly enlarged lymph nodes with short-axis measuring greater 1 cm on CT of the abdomen or PET–CT, and/or FDG-avid lymph nodes on PET–CT
N0	No regional lymph nodes	
N1	Metastasis in 1 to 2 regional lymph nodes	
N2	Metastasis in 3 to 6 regional lymph nodes	
N3	Metastasis in 7 or more regional lymph nodes	
M		
M0	No metastatic disease	Metastatic disease seen on CT or PET–CT, most commonly involving the peritoneum, liver, and lungs.
M1	Metastatic disease	

Adapted from Washington [8]

(CT) with oral and intravenous contrast is commonly used in the assessment of non-specific left upper quadrant or epigastric pain and can detect and characterize some gastric neoplasms. Fluoroscopic upper GI series can provide excellent characterization of mucosal contours but has limited utility for alternative diagnoses, so its use is typically limited to patients who require dynamic imaging or who cannot have CT scans. Endoscopic evaluation via esophagogastroduodenoscopy (EGD) plays a crucial role in the initial diagnosis of many gastric lesions due to its ability to both characterize and sample gastric lesions.

Once the presence of a lesion has been established, additional imaging may be needed to characterize and stage the lesion of interest. Magnetic resonance imaging (MRI) can provide superior soft tissue contrast and is very useful for characterizing cystic or lipomatous lesions, for assessing direct involvement of adjacent viscera, and for characterizing potential metastatic lesions in the liver. Contrast-enhanced CT and PET–CT both play important roles in the staging of proven gastric malignancies using the AJCC system (see Table 2) [8]; PET–CT offers superior sensitivity for regional and systemic metastases [9], while contrast-enhanced CT offers lower cost, radiation dose, and superior spatial resolution for local staging, particularly for locally advanced T4 disease [10]. Endoscopic ultrasound (EUS) is the best modality for evaluating the depth of involvement of the stomach wall (T1–T3 tumors) and for assessing the perigastric lymph nodes.

Benign gastric neoplasms

Mucosal polyps

Mucosal polyps are incidentally discovered in 2–4% of patients undergoing upper endoscopic evaluation and by one report, 1.7 % of all patients undergoing radiological exams [11, 12]. The most common type of polyp (by far) is the fundic gland polyp, followed in incidence by hyperplastic polyps [13]; adenomas and hamartomatous polyps are rare, with the latter most commonly occurring in genetic cancer syndromes. Overall, polyps have similar imaging characteristics that include their mucosal location, intraluminal protrusion, and well-circumscribed boundaries. These lesions are best identified radiographically on double-contrast barium fluoroscopic studies, which have the highest sensitivity and specificity in diagnosis, but can also be identified using positive or negative contrast agents on CT [12].

Fundic gland polyps

By far, the most common type of gastric polyp is the fundic gland polyp, which makes up 77% of gastric polyps [13]. Fundic gland polyps are typically sessile in appearance and on histological examination demonstrate cystic dilated oxyntic glands. These are often associated with proton pump inhibitor usage, but can also be sporadic. Additionally, patients with familial adenomatous polyposis (FAP) can develop hundreds of fundic gland polyps (Fig. 1).

Hyperplastic polyps

Hyperplastic polyps are the second most common type of gastric polyp. These lesions are smooth, round or oval, sessile or pedunculated polyps identified during barium swallow or CT. These benign polyps are essentially localized forms of foveolar hyperplasia and are composed of elongated pits lined by foveolar epithelium. These polyps tend to be randomly distributed in the stomach, with females aged 65.5–75 years most commonly affected [11]. Two-thirds of hyperplastic polyps

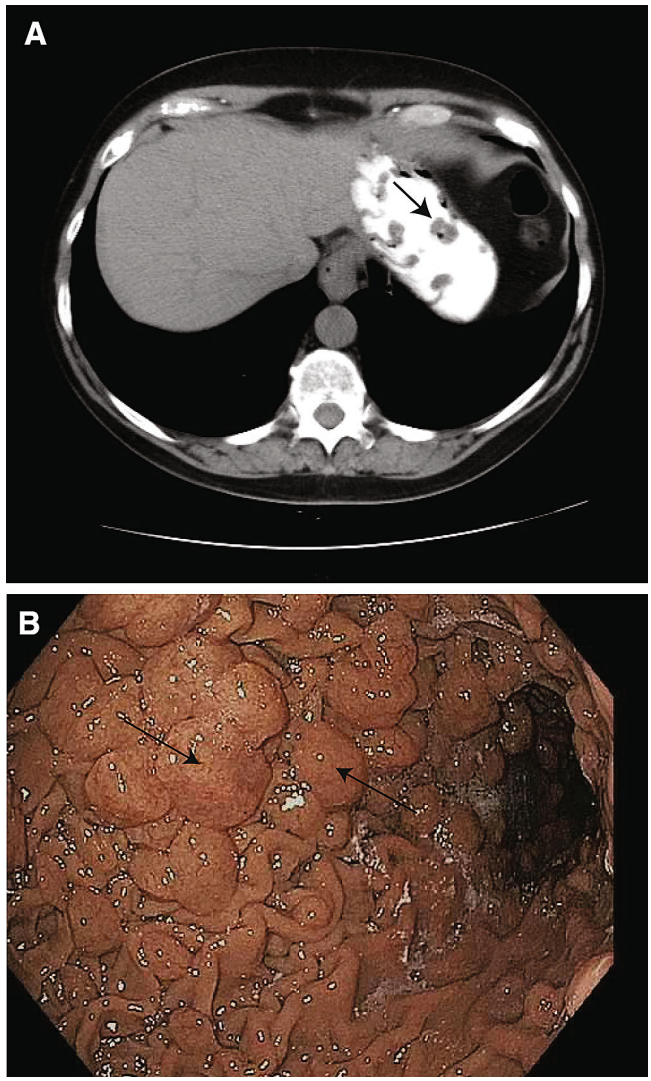


Fig. 1. Fundic gland polyp. **A** CT images demonstrating multiple polypoid lesions in the fundus of the stomach (*arrow*). **B** Endoscopic images of the fundic gland polyps (*arrow*).

occur singly and are typically around 1 cm or less in size, but multiple polyps can occur [11, 14].

Hamartomas

Hamartomas most commonly occur in syndromes such as Peutz–Jeghers and Cowden syndrome. Hamartomas can be found throughout the gastrointestinal tract, with the stomach being the least common location. These polyps typically vary in size and can be either sessile or pedunculated. A solitary hamartoma is rare; hamartomatous polyps more commonly appear as a cluster of lobulated lesions identified on fluoroscopic studies [15].

Adenomatous polyps

Adenomatous polyps are variable in size and may reach 2 cm or larger [14]. As compared to the previously described polyps, adenomatous polyps tend to occur in the antrum of the stomach, are associated with atrophic gastritis, and have the potential to transform into adenocarcinoma.

Mesenchymal tumors

Schwannoma

Gastrointestinal schwannomas are rare overall, but when they do occur within the gastrointestinal tract the stomach is the most common location. These benign tumors are composed of fascicles of elongated spindle cells that are immunoreactive for S-100 protein in a collagenous stroma. On CT imaging, they present as well-circumscribed, non-encapsulated, relatively homogenous lesions with delayed enhancement and are most commonly located in the gastric body [16–18]. Cystic degeneration, hemorrhage, necrosis, or cavity formation is uncommon in gastric schwannomas [16]. Double-contrast upper gastrointestinal series demonstrates features of a submucosal mass with a smooth, well-demarcated margin in the body of the stomach [18].

Glomus tumors

Glomus tumors are composed of modified smooth muscle cells of the glomus body. Histologically, glomus tumors comprise rounded cells with sharply defined cell borders growing in sheets, typically associated with thin-walled, variably dilated blood vessels. On CT imaging, these lesions are typically circumscribed, oval or spherical, hypervascular lesions arising from the antrum of the stomach (Fig. 2), with an average size of 2 cm [17, 19, 20]. Reports suggest that lesions measuring greater than 5 cm may have an increased malignant potential [20]. Hemangioma-like imaging characteristics have been reported, including peripheral contrast enhancement and progressive filling [19]. These benign lesions are more easily identified by their contrast enhancement pattern on CT. In contrast, on double-contrast upper gastrointestinal series these lesions have similar characteristics to other submucosal lesions like lipomas.

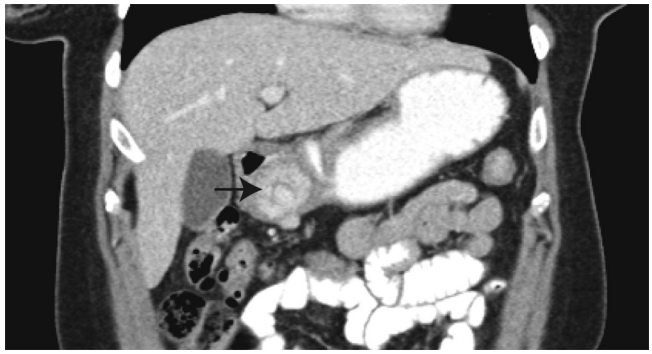


Fig. 2. Glomus tumor. **A** CT image demonstrating hyperenhancing glomus tumor in the antrum and pylorus of the stomach (*arrow*).

Lipomas

Lipomas are composed of well-differentiated adipose tissue and are often incidentally found in the stomach on imaging. Most lesions are asymptomatic, but lesions greater than 2 cm can produce symptoms such as abdominal pain, intussusception, or gastrointestinal bleeding secondary to mucosal ulceration [21]. Lipomas typically appear as solitary, smooth, round, fat-attenuating intramural lesions on CT (Fig. 3A) and show characteristic decreases in signal on fat-suppressed and out-of-phase MR sequences (Fig. 3B). They can also be incidentally picked on abdominal radiograph as a relatively lucent shadow. On fluoroscopy, lipomas are smooth, round, oval, sharply marginated submucosal masses that compress on exam and change shape during fluoroscopic palpation and peristalsis [17, 21].

Leiomyoma

Leiomyomas are rare benign tumors with low cellularity and are composed of fascicles of bland spindle cells with brightly eosinophilic cytoplasm. In older literature, these tumors were mistakenly referred to as GISTs. However, unlike GISTs these tumors are negative for KIT; rather they are immunoreactive for desmin [17]. These benign lesions typically appear as lobulated, hypoattenuating, and non-enhancing lesions in the cardia that arise within the muscularis propria and project into the lumen; they have a mean size of 36 mm [22]. On fluoroscopic imaging with barium, these lesions appear as lobulated submucosal filling defects along the wall of the cardia.

Hemangioma

Hemangiomas are solitary, polypoid, vascular lesions that can occur anywhere in the gastrointestinal tract, most commonly in the small intestine, accounting for 1.6% of benign tumors in the stomach [23]. Gastrointestinal bleeding and/or symptoms of anemia are the most common presentations. Multiple lesions, in combination with cutaneous or liver hemangiomas, are suggestive of syndromes such as Osler–Weber–Rendu disease, Maffucci syndrome, Klippel–Trénaunay syndrome, or congenital blue rubber bleb nevus syndrome [23]. Barium studies demonstrate a compressible polypoid intraluminal lesion. The presence of phleboliths within lesions is pathognomonic for the diagnosis of hemangioma [23]. Contrast-enhanced CT typically demonstrates an enhancing lobulated, intraluminal mass. Because of the risk of hemorrhage, these lesions are often resected.

Miscellaneous benign tumors

Heterotopic pancreas

Heterotopic pancreas in the stomach is a very rare lesion that can manifest with epigastric pain, gastrointestinal symptoms, or obstruction. Heterotopic pancreas is ectopic pancreatic tissue that is not anatomically connected to the normal pancreas, but contains the normal cellular components. As such, heterotopic pancreas can rarely show the same pathology as the normal pancreas, including pancreatitis, pseudocyst formation, neuroendocrine tumors, and other malignancies [24]. Pancreatic heterotopia most commonly occurs in the antrum, ranging in size from 1 to 3 cm [24, 25]. On CT, heterotopic pancreas appears as a solitary, round or oval solid lesion, with more than half of lesions demonstrating enhancement characteristics similar to pancreas (Fig. 4).

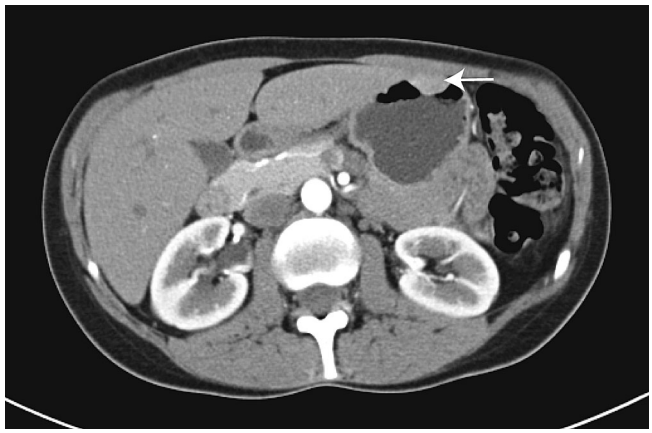


Fig. 4. Heterotopic Pancreas. **A** CT demonstrating nodular focus within the stomach with similar enhancement characteristics as the pancreas (*arrow*).

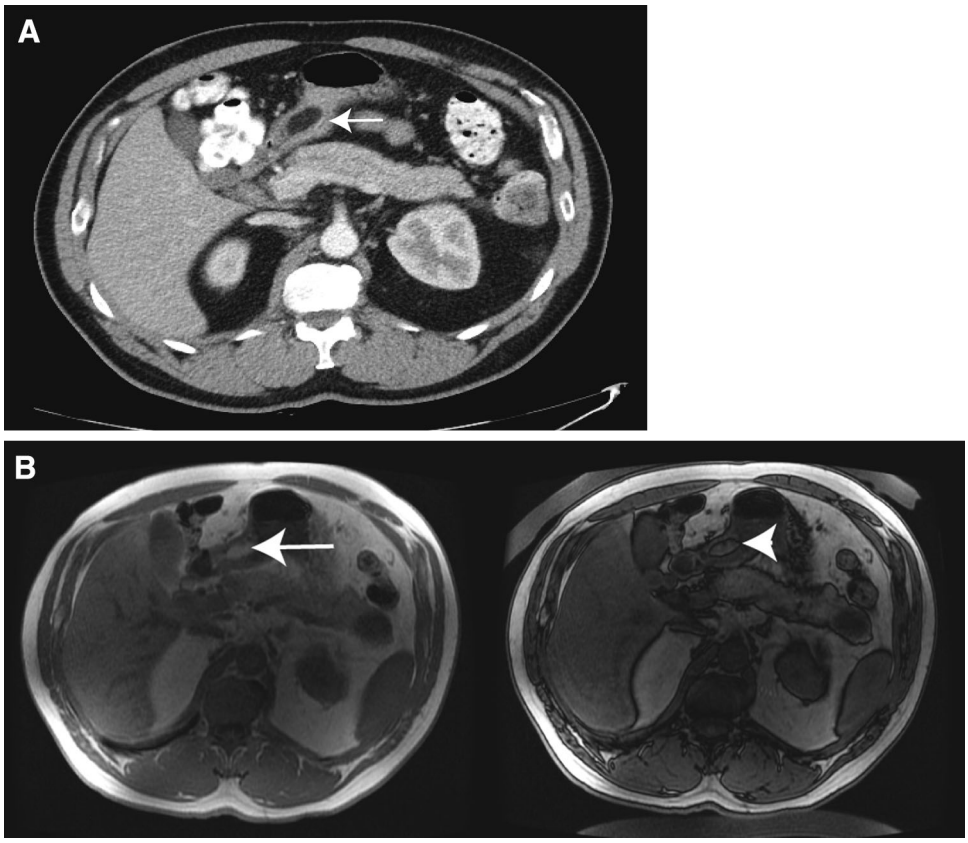


Fig. 3. Gastric Lipoma. **A** Polypoid fat-attenuating lesion (*arrow*). **B** In- (*arrow*) and out-of-phase (*arrowhead*) imaging demonstrating loss of signal consistent with fat.

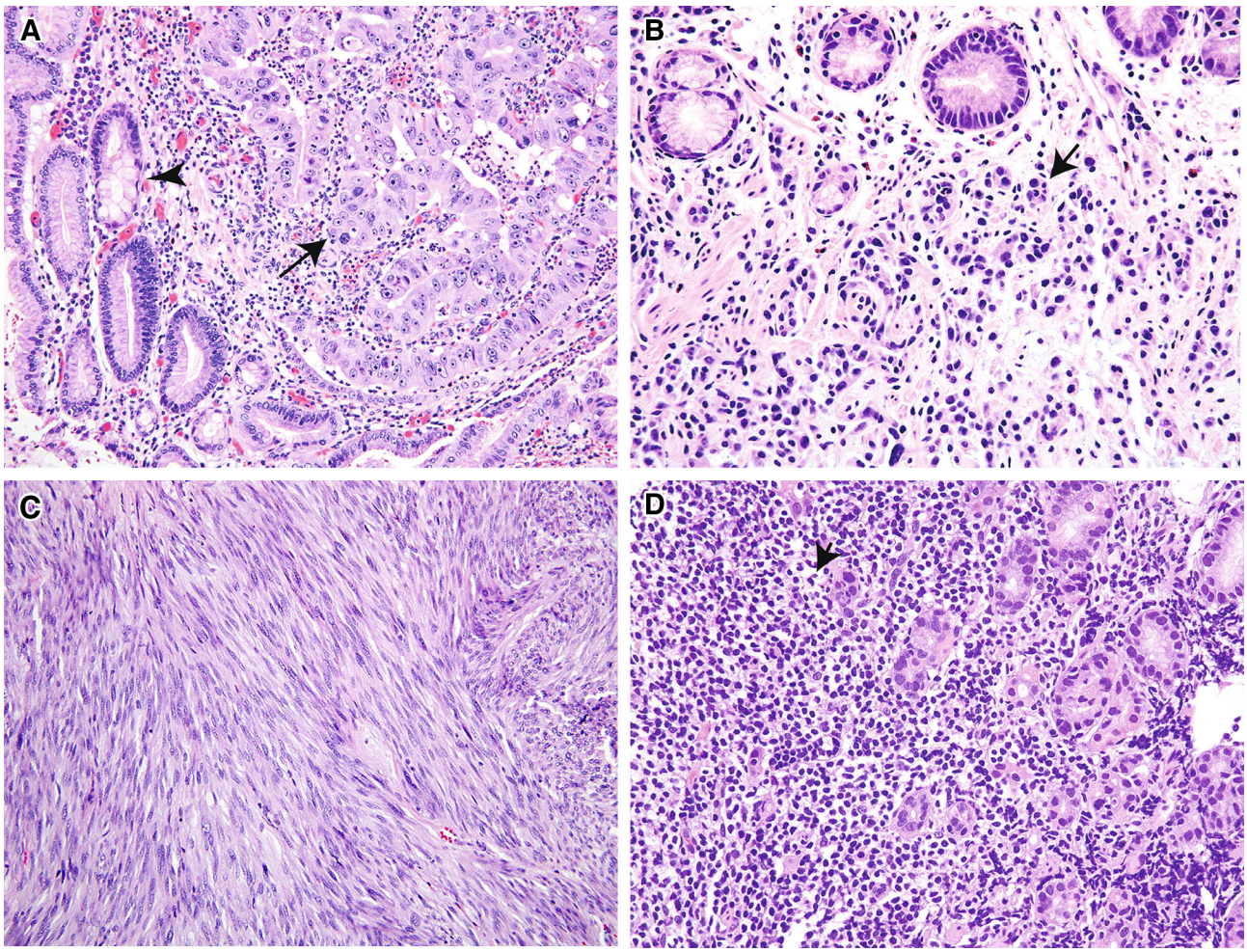


Fig. 5. Pathology of gastric tumors. **A** Papillary adenocarcinoma. The tumor is composed of papillary structures lined by large tumors cells with prominent nucleoli (*arrow*). Note the intestinal metaplasia in the background gastric mucosa (*arrowhead*). **B** Well-differentiated neuroendocrine tumor (carcinoid tumor). The tumor shows a nested growth pattern and consists of relatively uniform cells with hyperchromatic nuclei and moderate amounts of cytoplasm (*arrow*). This tumor arose in a background of chronic atrophic autoimmune gastritis (type I carcinoid). **C** Gastrointestinal stromal tumor, spindle cell type. The tumor is composed of fascicles of elongated spindle cells with tapering nuclei and palely eosinophilic cytoplasm. **D** Extranodal marginal zone lymphoma (MALT lymphoma). The tumor is composed of sheets of small lymphoid cells with variably clear cytoplasm, infiltrating gastric glands (*arrow*).

A key imaging feature on CT is endoluminal growth with associated enhancement of the overlying mucosa [26]. However, some lesions do not demonstrate enhancement and can have cystic degeneration [24, 25].

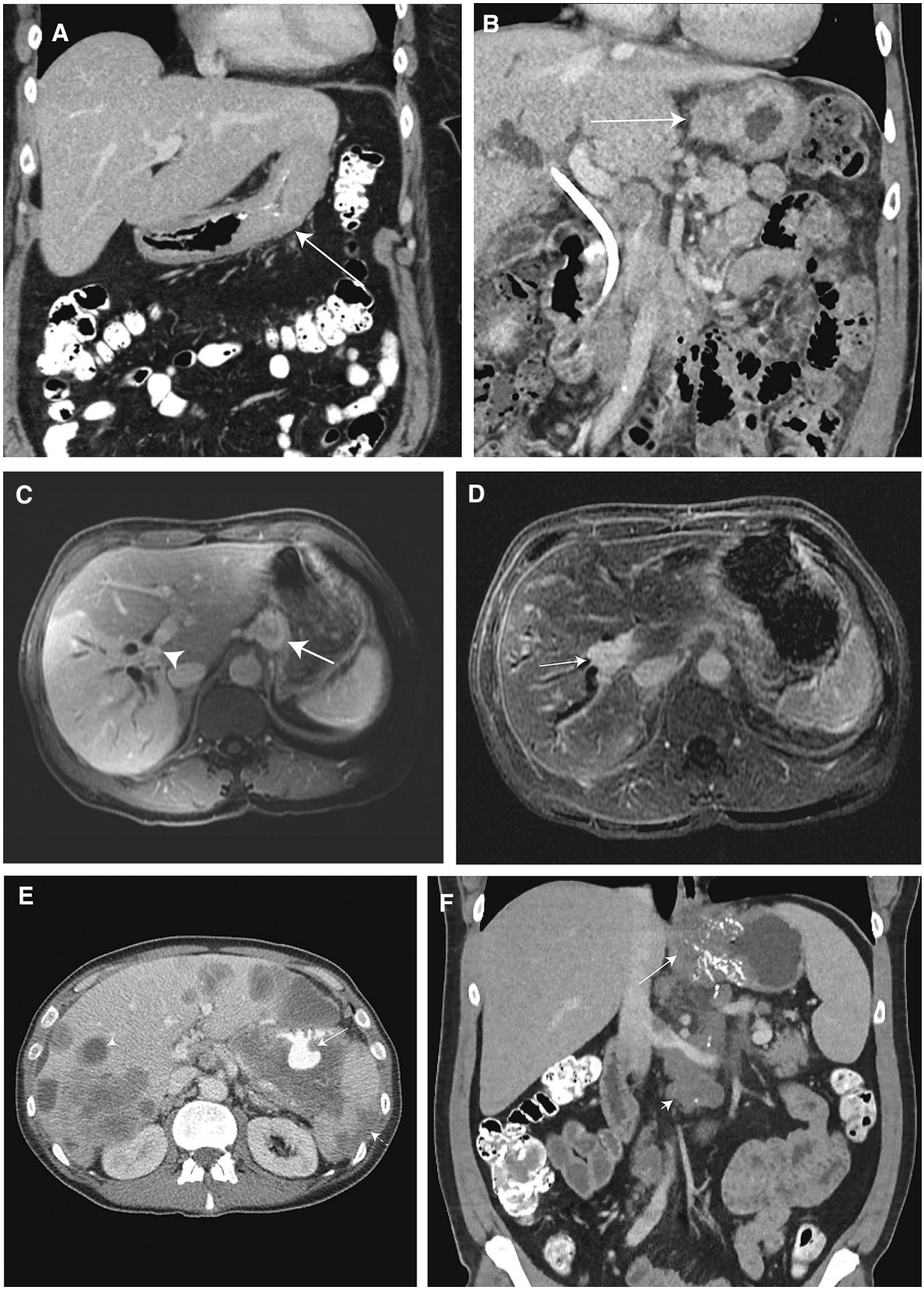
Malignant gastric lesions

Epithelial lesions

Adenocarcinoma

Adenocarcinoma is the most common gastric malignancy, accounting for 95% of malignant gastric tumors. There are several different subtypes of adenocarcinoma, including papillary (Fig 5A), tubular, mucinous, and signet ring cell. The imaging appearance of adenocarcinoma is variable. Adenocarcinoma can appear as a bulky

Fig. 6. Gastric adenocarcinoma. **A** Linitis plastica with diffuse gastric wall thickening (*arrow*). **B** Coronal image of gastric adenocarcinoma with marked gastric wall thickening at the gastric fundus and tumor extension to the gastrohepatic ligament. **C** T1 post-contrast images demonstrating enhancing gastric adenocarcinoma in the fundus extending to the gastrohepatic ligament. An associated liver metastasis causes a right-sided perfusion abnormality (*arrowhead*) and mild intrahepatic biliary ductal dilatation. **D** T1 post-contrast subtraction MR image from the same patient in Fig. 6C showing an enhancing lesion at the bifurcation of the right hepatic vein (*arrow*). **E** Ulcerated gastric adenocarcinoma (*arrow*) with hepatic (*arrowhead*) and peritoneal metastases (*dashed arrow*). **F** CT demonstrating thickening and calcification in the antrum of the stomach consistent with signet ring gastric cancer. ►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mass with or without ulceration, as gastric wall thickening, or as diffuse infiltration without a visible lesion (linitis plastica) [26] (Fig. 6A–D). One distinctive but uncommon appearance of gastric adenocarcinoma is that of mucinous adenocarcinoma, which can partially calcify [27] (Fig. 6F).

CT is most commonly used to stage the extent of disease and can detect both local invasion and metastases (Table 2). Local T staging of gastric cancers is based on the depth of invasion of the cancer through the gastric wall [8]. Early T-stage disease (T1–T3) is typically characterized using endoscopic ultrasound. CT has insufficient spatial resolution and soft tissue contrast to distinguish the layers of the gastric wall, but it is useful in identifying extragastric invasion (T4) and regional nodal dissemination. There have been efforts to using MRI for T staging, but the technical challenges of MRI in the relatively mobile stomach and the availability of endoscopic ultrasound have limited its adoption [28].

Regional and distant metastases are common, including metastases to the gastrohepatic ligament (Fig. 6B), lymph nodes, and liver (Fig. 6D–E). Regional lymph nodes are often adjacent or in the vicinity of the primary tumor, most commonly in the lymph nodes along the distribution of the celiac artery. Pathologically involved lymph nodes inferior to the level of the renal veins are treated as systemic metastases for the purposes of staging [8]. More distant "drop metastases" can occur in the pelvis with metastases to the sigmoid, rectum, or ovaries (Krukenberg tumors). Pelvic metastases can grow up to 20 cm in size and are heterogeneous in appearance, with both solid and cystic components on CT and MRI [27].

Linitis plastica is poorly seen on cross-sectional imaging due to its infiltrative growth pattern and is typically discovered via EGD and biopsy, or via secondary signs of metastasis in the absence of a well-defined gastric mass. CT and MRI often show no gastric abnormality in this disease process, but PET–CT can sometimes show diffusely increased gastric uptake.

Neuroendocrine Tumor (Carcinoid)

Well-differentiated gastric neuroendocrine tumors (carcinoid tumors) most often originate from the epithelial enterochromaffin-like cells of the gastric mucosa (Fig. 5B). Overall, the majority of well-differentiated neuroendocrine tumors are found in the gastrointestinal tract followed by the tracheobronchial tree. In the gastrointestinal tract, the small bowel is the most common location, whereas the stomach is the least common with gastric carcinoid tumors comprising 1.8% of all gastric malignancies [17]. Indium 111 pentetreotide (Octreoscan) can help confirm the diagnosis of well-differentiated neuroendocrine tumor, as such tumors will have avid uptake of this radiotracer. Upper gastrointestinal endoscopy remains an important tool for evaluating the prior tumor, the surrounding gastric epithelium and for tissue sampling.

There are 3 types of well-differentiated neuroendocrine tumors, all of which are hyperenhancing on postcontrast imaging (Fig. 7A). Type I tumors are associated with hypergastrinemia, chronic atrophic gastritis (usually autoimmune gastritis), with or without pernicious anemia, and resultant enterochromaffin-like cell hyperplasia [29]. These tumors are typically multicentric, occurring in the body or fundus of the stomach and are less than 2 cm in size. Lymph node or hepatic metastases are rare in type 1.

Type 2 is less common and is also secondary to hypergastrinemia. Type 2 is associated with gastrinomas in patients with MEN1, with approximately 30% of MEN1 patients developing well-differentiated neuroendocrine tumors. These lesions tend to be 2 cm in size with associated gastric thickening from the hypergastrinemia (Fig. 7B–C). Lymph node metastases are more common. Type 3 is slightly more common than Type 2, most often presenting as a solitary lesion without associated hypergastrinemia. These lesions tend to ulcerate and are more clinically aggressive with distant metastases and frequent recurrences.

The imaging appearance of neuroendocrine tumor varies by type; knowledge of the patient's medical history is important. Imaging findings consistent with atrophic gastritis in the setting of multiple enhancing lesions is more consistent with Type 1. In contrast, Type 2 neuroendocrine tumors typically demonstrate gastric thickening in addition to the multiple small enhancing polyps in a patient with known or suspected MEN1. A large, solitary, irregular, ulcerated enhancing mass on CT with associated large lymph nodes is suggestive of Type 3.

Mesenchymal tumors

Gastrointestinal stromal tumor (GIST)

GISTs are the most common mesenchymal tumors of the stomach with either spindle cell or epithelioid morphology (Fig. 5C), making up 2–3 % of gastric tumors. Before the molecular genetics underlying GISTs was discovered, GISTs were classified as smooth muscle tumors (leiomyosarcoma, leiomyoma, or "leiomyoblastoma"). The vast majority of GISTs express KIT (CD117), a tyrosine kinase growth factor receptor involved in cellular signaling pathways [30]. These tumors primarily involve the outermost layer of muscle and demonstrate either exophytic or intramural growth. GIST can be found throughout the gastrointestinal tract, but the most common site is the stomach. Within the stomach, GISTs can occur at any location, but are most commonly found in the body (75%), followed by the cardia and fundus (14%) [31].

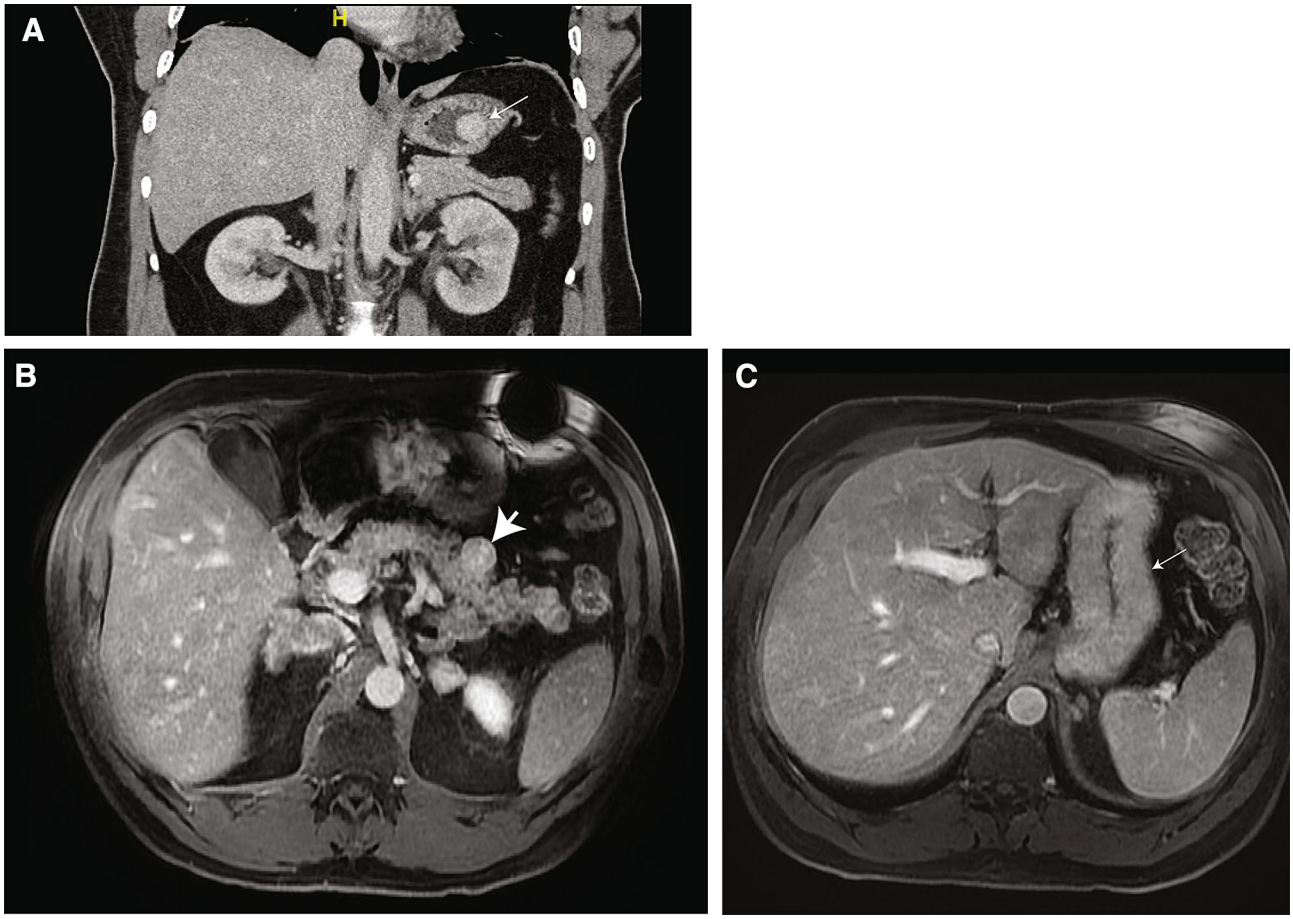


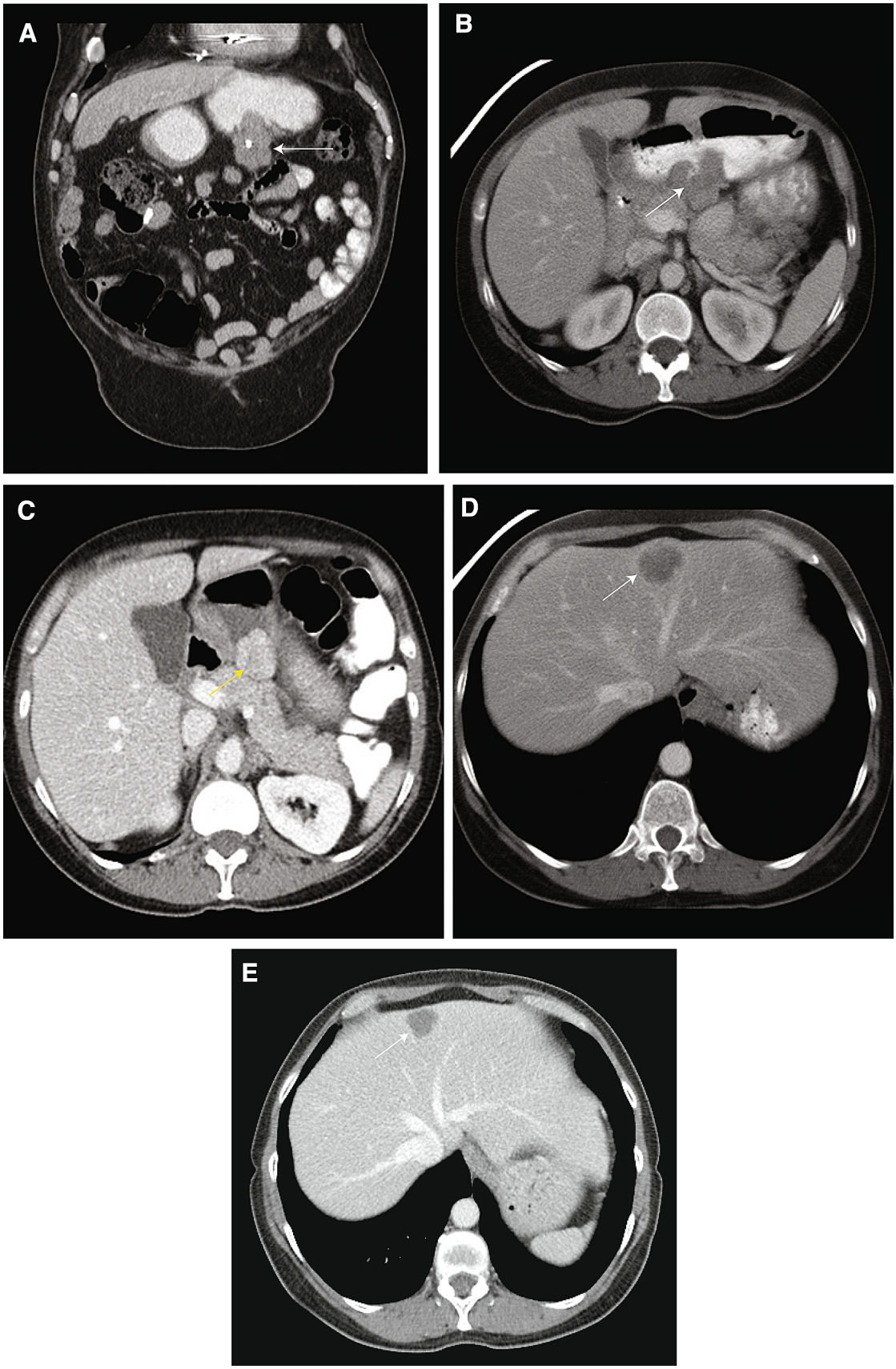
Fig. 7. Neuroendocrine tumors (carcinoid tumors). **A** Hypervascular gastric neuroendocrine tumor in the fundus, unclassified subtype (*arrow*). **B** Hyperenhancing gastrinoma (*arrow*) in the pancreatic body in a patient with MEN1. **C** The same patient as in Fig. 2 with resultant hypertrophic gastritis (*arrow*) in Zollinger–Ellison syndrome and gastrinomas. This is the substrate for type II neuroendocrine tumors.

The malignant potential of GISTs is variable. Imaging can be a useful tool in assessing the malignant potential of suspected or known GISTs. In general, tumors less than 5 cm with lower mitotic rates (5 or fewer mitoses per 5 mm^2) have less malignant potential than tumors greater than 5 cm or showing higher mitotic rates (more than 5 mitoses per 5 mm^2). If a tumor is found to be less than 5 cm with less than 5 mitoses per 5 mm^2, it is considered to have low risk for malignant behavior. In general, gastric GISTs have a better prognosis than small bowel GISTs [31].

Additionally, the pattern of spread is important for the radiologist to understand. Aggressive GIST rarely spreads to lymph nodes and more commonly demonstrates locally aggressive behavior with invasion of the adjacent organs and metastases to the omentum, peritoneum, and liver [31, 32]. However, lymph node metastases are relatively common in a distinctive subset of tumors known as succinate dehydrogenase-deficient GISTs, which have a predilection for younger patients [33–35].

The multimodality appearance of GISTs has been well described. The radiographic appearance of GISTs is non-specific, but if the mass is large enough, radiographs can demonstrate a soft tissue mass with associated displacement of the gastric bubble [31]. Barium studies can demonstrate a smoothly circumscribed mass with obtuse angles on barium studies, although this is a less common appearance for GIST than for other gastric lesions. On CT, lesions tend to be exophytic and appear to be arising from the stomach and extending into the peritoneum. The majority of GISTs demonstrate heterogeneous appearance on contrast-enhanced CT with a central region of hypoattenuation, which correlates to regions of necrosis, hemorrhage, or cyst or cavity formation pathologically [31]. Formed cavities may communicate with the gastric lumen and accordingly contain gas, air-fluid levels, or oral contrast [31]. Calcification is rare, but can be seen on radiographs or CT (Fig. 8A).

MR findings are similar to CT findings. MR allows better soft tissue delineation as compared to CT. The typical GIST on MR is low signal intensity on T1-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◀**Fig. 8.** Gastrointestinal stromal tumors (GISTs). **A** Gastric GIST with endoluminal and exophytic components and calcification (*arrow*). **B** Pretreatment appearance of another gastric GIST with associated ulceration (*arrow*). **C** Post-treatment appearance of the tumor from B showing marked response to imatinib. **D** GIST metastasis to the liver showing central hypodensity on CT (*arrow*). **E** Post-treatment contrast-enhanced CT demonstrates decreased attenuation of GIST liver metastasis (*arrow*) measuring 37 Hounsfield Units (HU); pretreatment liver metastasis measured 64 HU.

weighted images, high signal intensity on T2 images, and shows post-contrast enhancement. The imaging appearance of the central region of the tumor is more variable since it is prone to hemorrhage, areas of necrosis and cyst formation; therefore, the signal can vary depending on whether it is primarily cystic and the age of the hemorrhage [31].

Imaging during the treatment of GIST can be challenging for radiologists. Initial tumor response to treatment with imatinib, a tyrosine kinase inhibitor, often demonstrates a more hypoattenuating lesion on contrast-enhanced CT with decreased SUVMax values and no significant change in the bidimensional size [36, 37] (Fig. 8B–C). Specifically, Choi et al. evaluated 173 GIST tumors on contrast-enhanced CT and FDG PET and found that the tumor density decreased by 16.5% and the SUVMax decreased by 64.9% [36] Size alone was not accurate in demonstrating treatment response [36]. The decrease in attenuation on contrast-enhanced CT is also seen in metastatic lesions (Fig. 8D–E). Additionally, these findings can result in the unmasking of isoattenuating liver lesions as 'new' metastases, which complicates the assessment of treatment response. Recurrent GIST often presents as new soft tissue within treated lesions or as new hepatic or peritoneal metastases. Therefore, it is essential that the radiologist is aware of the post-treatment imaging appearance of GIST so that attention can be paid to subtle changes in the tumor on follow-up imaging.

Leiomyosarcoma

Leiomyosarcoma is a rare gastric malignancy of smooth muscle origin [27]. Tumors tend to be large spherical masses with an average diameter of 15 cm [27]. Similar to GISTs, they tend to be exophytic masses with areas of necrosis or can appear as asymmetric thickening on CT (Fig. 9). Leiomyosarcomas have a similar pattern of spread regardless of anatomical location with spread to the peritoneum, direct invasion of adjacent organs, and systemic metastases to the lungs.

Angiosarcoma

Primary angiosarcoma in the stomach is exceptionally rare. The pathology of the lesion is variable, ranging from vasoformative structures to sheets of poorly differentiated epithelioid or spindle cells [38]. Angiosarcoma can present as a primary gastric lesion with symptoms of gastrointestinal bleeding, abdominal pain, and anemia. On CT, angiosarcoma presents as a large mass with gastric wall thickening. Few case reports have been published, so there are currently no known distinguishing features that uniquely identify angiosarcomas.

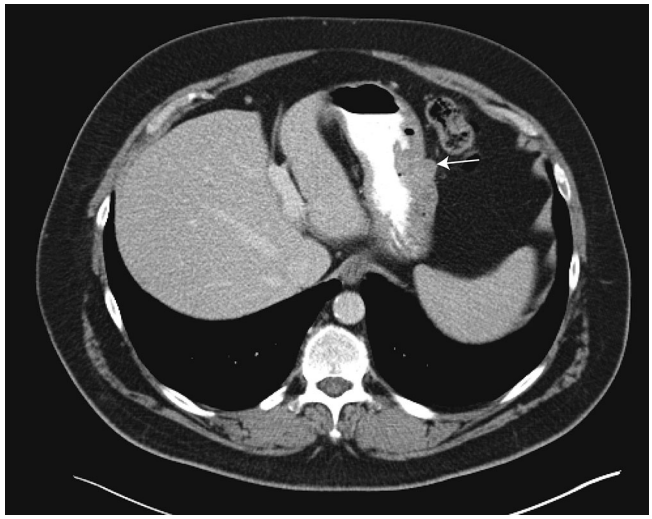

Fig. 9. Leiomyosarcoma. **A** Axial CT demonstrating asymmetrical thickening in the body of the stomach (*arrow*).

Kaposi sarcoma

Kaposi sarcoma is a low-grade malignant endothelial lesion primarily affecting the skin, but lesions can become disseminated. Acquired Immunodeficiency Syndrome (AIDS)-related Kaposi sarcoma is much less prevalent with the advent of effective antiretroviral therapy. In one study, 48% of patients affected by AIDS-related Kaposi sarcoma had gastrointestinal involvement [39]. Gastrointestinal involvement consists of small flat to polypoid lesions that frequently ulcerate. Double-contrast barium studies can demonstrate small polypoid lesions or may be negative if the lesions are flat. On CT, there is a typical "bulls-eye" or targetoid appearance of the small 0.5- to 3-cm polypoid lesions secondary to the central necrosis [39].

Lymphoma

Primary gastrointestinal lymphoma comprises 0.9% of all gastrointestinal tumors and 1–5% of gastric tumors with the majority of primary gastrointestinal lymphomas occurring in the stomach [40]. Risk factors for developing primary gastrointestinal lymphoma include *Helicobacter pylori* infection, immunosuppression after transplantation of solid organs, celiac disease, inflam-

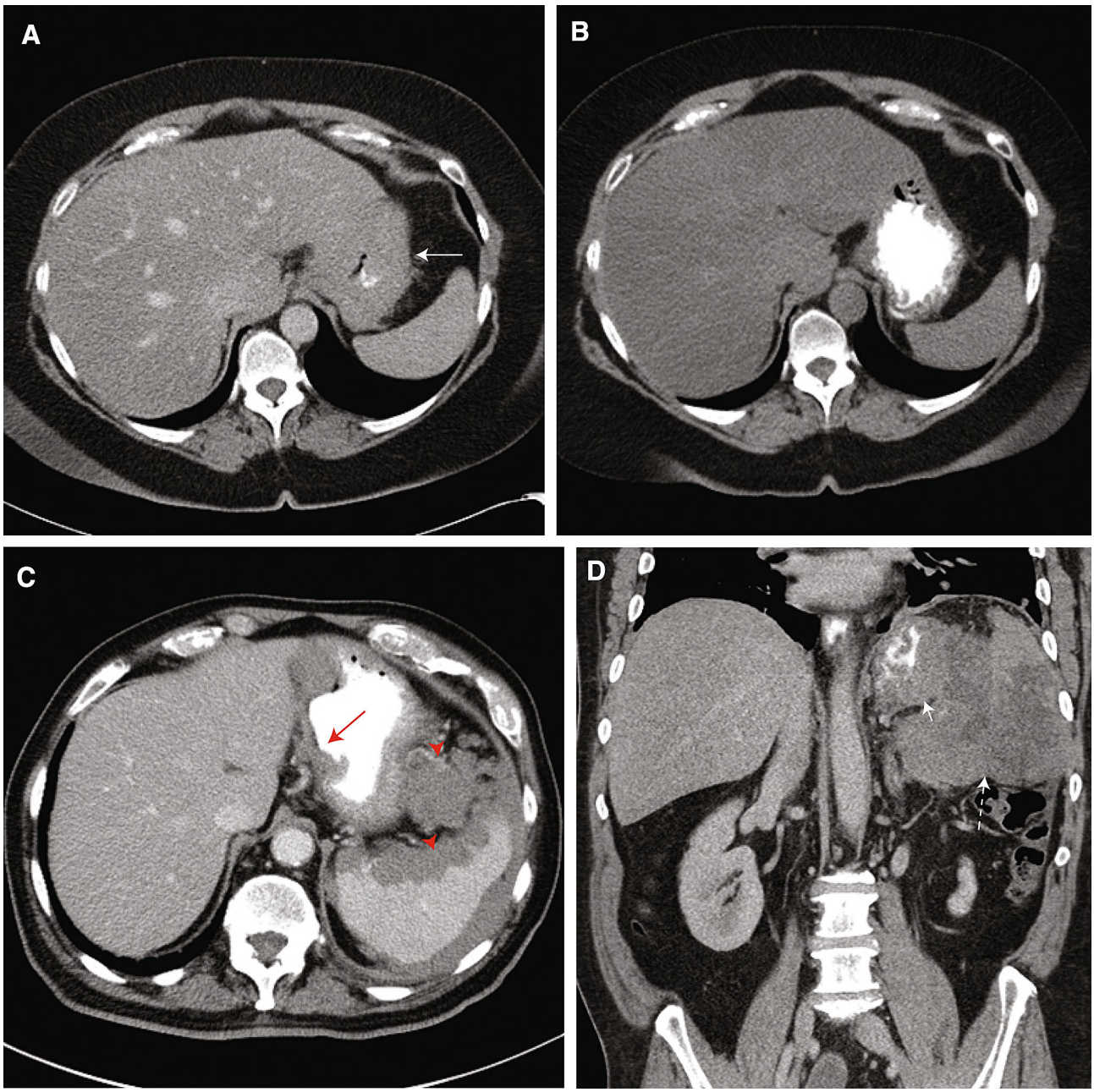

Fig. 10. Lymphomas. **A** CT with oral contrast demonstrating MALT (*marginal zone*) lymphoma with marked gastric wall thickening (*arrow*) before treatment. **B** MALT lymphoma from A shows decreased gastric wall thickening after treatment. **C** Ulcerated diffuse large B-cell lymphoma (*arrow*) with peritoneal dissemination (*arrowhead*). **D** Diffuse large B-cell lymphoma (*arrow*) with local spread to the spleen and pancreas (*dashed arrow*).

matory bowel disease, and human immunodeficiency syndrome [40]. Of the gastric lymphomas, a low-grade lymphoma known as mucosa-associated lymphoid tissue (MALT) lymphoma (marginal zone lymphoma) most commonly occurs secondary to chronic inflammation from *H. pylori* infection. Diffuse large B-cell lymphoma is another common gastric lymphoma that pursues an aggressive clinical course. Other B-cell lymphoma subtypes and T-cell lymphomas rarely arise primarily in the stomach (Fig. 5D).

On imaging, gastric lymphoma appears as single or multiple ulcers or masses of varying size, gastric rugal thickening (most commonly associated with a mass), or mucosal nodularity (Fig. 10A–D). In general, gastric wall thickening correlates with the grade of the lymphoma, with more severe gastric wall thickening being a feature of diffuse large B-cell lymphoma. Gastric wall thickening tends to be very homogenous in appearance and thicker than the gastric wall thickening in gastric adenocarcinoma [26].

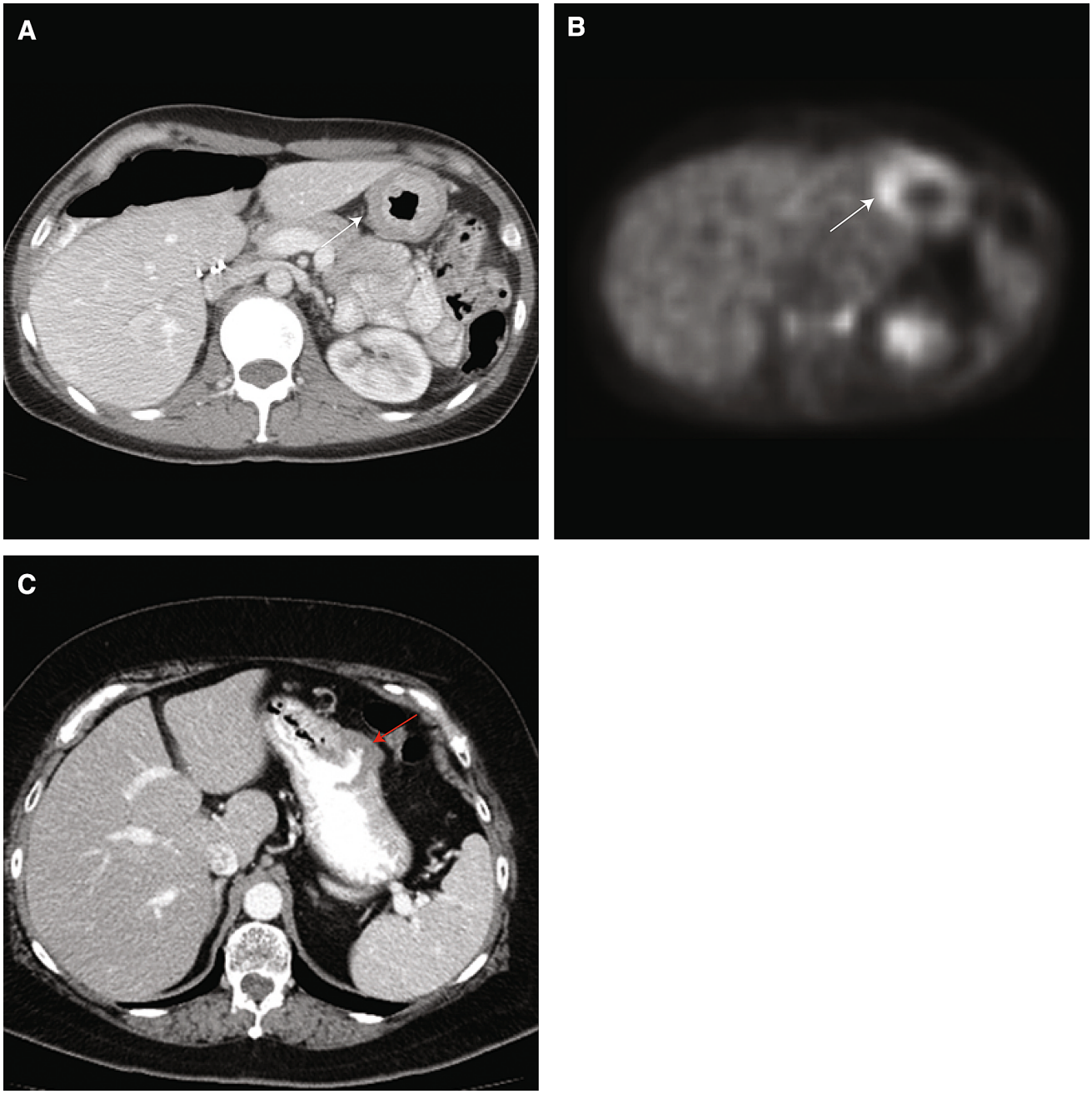

Fig. 11. Gastric metastases. Metastases from lobular breast cancer cause diffuse wall thickening on CT (*arrow*) (**A**) and marked FDG avidity on PET–CT (*arrow*) (**B**). Melanoma metastasis in the stomach shows deep ulceration on CT (*arrowhead*) (**C**).

A common feature in gastric lymphoma is preservation of the gastric fat planes with large masses, whereas the fat planes in an equally sized adenocarcinoma are more likely to show invasion. Additionally, bulky lymphadenopathy often extends below the renal hilum, as compared to gastric adenocarcinoma where lymphadenopathy is typically more local [40].

Treatment for gastric lymphoma depends on the type of lymphoma. Most MALT lymphomas are successfully treated with antibiotics for *H. pylori,* whereas treatment for diffuse large B-cell lymphoma typically includes systemic chemotherapy with or without radiation therapy [41].

Miscellaneous malignant tumors

Metastases

Metastases to the stomach are rare, with the most common cancers metastasizing to the stomach being breast and lung cancers and melanoma [42]. The most common

presenting clinical symptoms are gastrointestinal bleeding or dysphagia. The multi-modality appearance of metastatic lesions can have very similar appearances to primary gastric cancers, and the patient's clinical history plays an important role. The imaging appearance can also be variable, with lobular breast cancer demonstrating diffuse gastric wall thickening (Fig. 11A–B), whereas melanoma metastases often have a bulls-eye appearance with central ulceration [27] (Fig. 11C).

Rarely, gastric metastases arise as the initial presentation of testicular seminoma. A few case reports in the literature describe gastric metastases with a "burned out" testicular primary lesion. CT features of such metastases are non-specific and could demonstrate an ulcerated lesion or gastric thickening [43, 44].

Germ cell tumor

Primary germ cell tumors of the stomach are exceedingly rare and are indistinguishable from other aggressive primary and metastatic gastric neoplasms. For example, there are approximately 64 cases of extragonadal gastric choriocarcinoma reported in the literature [45]. Figure 12 shows an example of a gastric seminoma without evidence of a synchronous testicular primary.

Cancer syndromes with gastric neoplasms

Hereditary diffuse gastric cancer

Initially described by Guilford et al. in 1998, hereditary diffuse gastric cancer is an inherited disease that results in development of diffuse gastric cancer (linitis plastica) at an early age [46]. This disease is caused by a germline mutation in *CDH1* (encoding e-cadherin) with an autosomal dominant inheritance pattern, and an associated high degree of penetrance results in patients developing linitis plastica at an average age of 38 [46, 47]. Women with *CDH1* mutations are also at a higher risk of developing lobular breast cancer [48]. Imaging can be helpful in evaluating the extent of disease in symptomatic patients with diffuse gastric cancer, but is not helpful in screening for early foci of gastric cancer. A study by Rogers et al. evaluated the gastrectomy specimens of asymptomatic patients with a negative screening endoscopy and found that all of the asymptomatic patients had microscopic foci of signet ring cell carcinoma [47]. This is an important disease entity for radiologists to be aware of so that they can raise this as a possibility in a diagnosis of linitis plastica in patients under the age of 40.

Juvenile polyposis syndrome

Juvenile polyposis syndrome is another rare autosomal dominant syndrome characterized by multiple juvenile polyps in the gastrointestinal tract and an increased risk of colorectal cancer. More than half of cases are related to germline mutations in the *SMAD4* or *BMPR1A* gene, with an increased risk of gastric cancer and an increased number of upper gastrointestinal polyps associated with mutations in the *BMPR1A* gene [49].

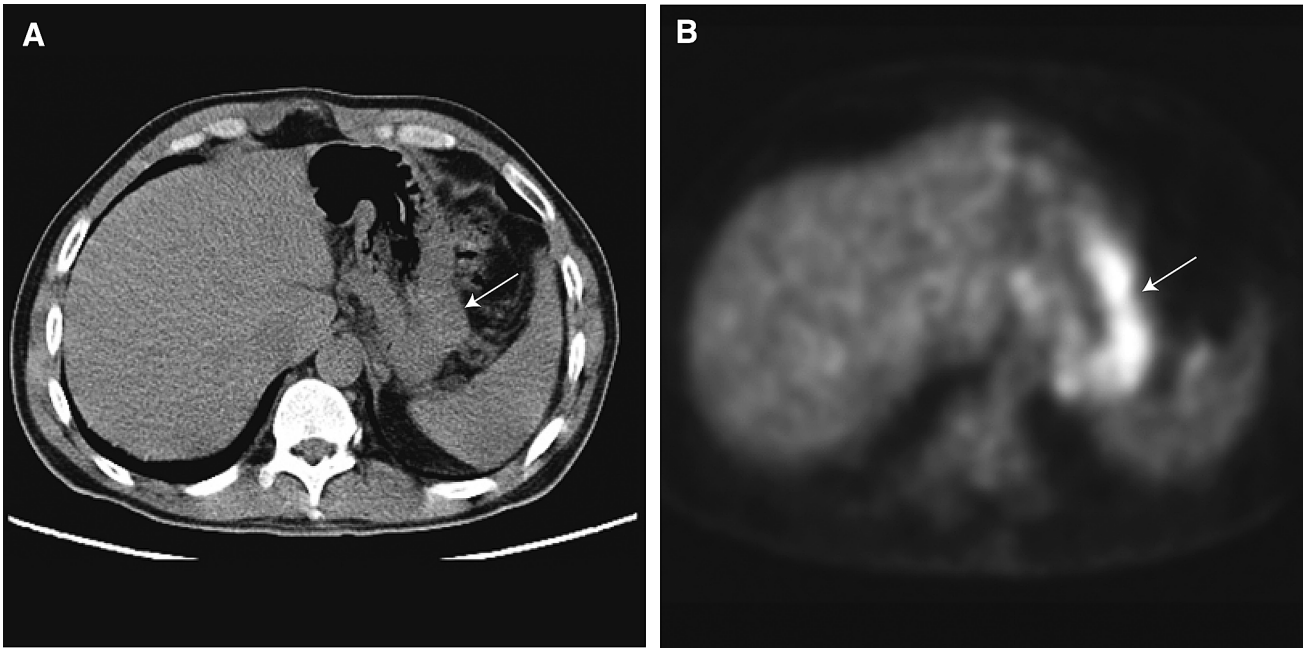

Fig. 12. Gastric seminoma. FDG-PET-CT (**A**–**B**) shows diffusely increased FDG uptake in the thickened gastric fundus and body (*arrow*). Biopsy demonstrated seminoma. Testicular ultrasound showed no primary tumor.

Table 3. Approach to the gastric unknown. The heuristic table of features below can be helpful in developing a weighted differential diagnosis for an unknown gastric neoplasm based on the presence or absence of specific characteristics

Feature	Adenocarcinoma	Carcinoid/Neuroendocrine	GIST	Lymphoma	Metastasis	Benign
Diffuse wall thickening	+ (Linitis Plastica)	– (except in Zollinger-Ellison)	–	++	+ (Lobular breast cancer)	–
Ulceration	++	–	+	+ (aggressive)	+	–
Well-defined intramural mass	–	++	–	–	+	++
Purely exophytic	–	–	++	+	–	–
Dumbbell shaped	+	–	++	–	–	–
Cystic	–	–	+	–	–	–
Hypervascular	–	++	+	–	++ (melanoma)	–
Calcifications	+	–	+	–	–	–
Nodal involvement	++	–	+ (SDHD)	++	+	–

Features of different types of malignant gastric lesions as well as benign lesions
–, uncommon; +, common; ++, very common; SDHD, succinate dehydrogenase deficient

Peutz–Jeghers syndrome

Peutz–Jeghers syndrome is a rare autosomal dominant inherited disorder, characterized by gastrointestinal hamartomas and mucocutaneous pigmentations. Affected patients harbor germline mutations in *STK11* (*LKB1*). Patients develop hamartomatous polyps (as described above) and are at an increased risk of developing cancer, including gastric cancer [50].

Lynch syndrome

Lynch syndrome (formerly known as hereditary nonpolyposis colorectal cancer) is the most common dominantly inherited colorectal cancer predisposition syndrome. This syndrome is caused by germline mutations in 4 mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, and *PMS2*). A study by Capelle et al. demonstrated that patients with a mutation in the *MLH1* or *MSH2* genes are at higher risk for developing gastric adenocarcinoma with 4.8% and 9.1% ultimately developing gastric adenocarcinoma, respectively [51].

Management

Treatment of gastric neoplasms varies by histology and, for adenocarcinoma, depends on the T, N, and M staging. For localized disease, surgery is the treatment of choice. If there is local nodal involvement, the treatment of choice is resection of the tumor with the addition of either neoadjuvant chemotherapy or chemoradiation. For unresectable tumors, treatment of choice is palliative chemotherapy and/or chemoradiation. If there is suggestion of T3 or node-positive disease by imaging, then there should be consideration of diagnostic laparoscopy for complete staging prior to surgical resection. As with other tumors, an accurate assessment of disease burden is required to direct therapeutic options.

Surgical planning and extent of gastric resection rely heavily on tumor margins. In general, adequate gastric resection to achieve negative margins, typically greater than 4 cm, will determine whether the patient has a distal, subtotal, or total gastrectomy [48]. Post-operative management of tumors depends heavily on the resection margins of the tumor. If the tumor resection margins are negative, deemed R0, the primary follow-up is surveillance if the tumor is T2 N0, or chemotherapy and surveillance if there is nodal involvement or if the tumor is T3 or greater. If there is microscopic, R1, or macroscopic, R2, positive surgical margins, then the recommendation is for adjuvant chemoradiation therapy.

When presented with an unknown gastric lesion, the radiologist can contribute to the patient's care by helping to order and direct the differential diagnosis based on the observed imaging features of the lesion. Table 3 describes a heuristic approach to assessing the relative likelihood of the most common gastric neoplasms based on a set of eight important imaging characteristics. For example, the presence of a purely exophytic hypervascular mass with cystic components and internal calcification would strongly favor GIST over lymphoma, while the presence of an ulcerated mass would favor gastric adenocarcinoma, aggressive lymphoma, or metastasis from a systemic source.

Conclusion

Gastric lesions include a broad spectrum of benign and malignant neoplasms. It is important for the radiologist to be able to distinguish and raise the possibility of uncommon malignant lesions while being able to recognize more common neoplasms that occur in the stomach. Imaging features such as gastric wall thickening, ulceration, calcification, characteristics of the mass (cystic, hypervascular, etc.), and nodal involvement should help direct the radiologist toward the correct diagnosis (Table 2).

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Compliance with Ethical Standards

Conflict of Interest None of the other authors have declared any conflicts of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Brenner H, Rothenbacher D, Arndt V (2009) Epidemiology of stomach cancer. Methods Mol Biol 472:467–477. doi:10.1007/978-1-60327-492-0_23
2. Howson CP, Hiyama T, Wynder EL (1986) The decline in gastric cancer: epidemiology of an unplanned triumph. Epidemiol Rev 8:1–27
3. Roder DM (2002) The epidemiology of gastric cancer. Gastric Cancer 5(Suppl 1):5–11
4. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin D, Bray F (2013) GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. International Agency for Research on Cancer. http://globocan.iarc.fr. Accessed on October 28, 2014
5. Park SH, Han JK, Kim TK, Lee JW, Kim SH, Kim YI, Choi BI, Yeon KM, Han MC (1999) Unusual gastric tumors: radiologic-pathologic correlation. Radiographics 19(6):1435–1446. doi:10.1148/radiographics.19.6.g99no051435
6. Bosman FT, Carneiro F, Hruban RH, Theise ND (2010) WHO classification of tumours of the digestive system. Classification of tumours of the digestive system, 4th edn. IARC Press, Lyon
7. Hamilton SR, Aaltonen LA (eds) (2000) World Health Organization classification of tumours. Pathology and genetics of tumours of the digestive system. IARC Press, Lyon
8. Washington K (2010) 7th edition of the AJCC cancer staging manual: stomach. Ann Surg Oncol 17(12):3077–3079. doi:10.1245/s10434-010-1362-z
9. Yoon H, Lee DH (2014) New approaches to gastric cancer staging: beyond endoscopic ultrasound, computed tomography and positron emission tomography. World J Gastroenterol 20(38):13783–13790. doi:10.3748/wjg.v20.i38.13783
10. Bentley-Hibbert S, Schwartz L (2015) Use of Imaging for GI Cancers. J Clin Oncol 33(16):1729–1736. doi:10.1200/JCO.2014.60.2847
11. Park do Y, Lauwers GY (2008) Gastric polyps: classification and management. Arch Pathol Lab Med 132(4):633–640. doi:10.1043/1543-2165(2008)132[633:GPCAM]2.0.CO;2
12. Feczko PJ, Halpert RD, Ackerman LV (1985) Gastric polyps: radiological evaluation and clinical significance. Radiology 155(3):581–584. doi:10.1148/radiology.155.3.4001357
13. Carmack SW, Genta RM, Schuler CM, Saboorian MH (2009) The current spectrum of gastric polyps: a 1-year national study of over 120,000 patients. Am J Gastroenterol 104(6):1524–1532. doi:10.1038/ajg.2009.139
14. Ba-Ssalamah A, Prokop M, Uffmann M, Pokieser P, Teleky B, Lechner G (2003) Dedicated multidetector CT of the stomach: spectrum of diseases. Radiographics 23(3):625–644. doi:10.1148/rg.233025127
15. Harned RK, Buck JL, Sobin LH (1995) The hamartomatous polyposis syndromes: clinical and radiologic features. AJR Am J Roentgenol 164(3):565–571. doi:10.2214/ajr.164.3.7863873
16. Levy AD, Quiles AM, Miettinen M, Sobin LH (2005) Gastrointestinal schwannomas: CT features with clinicopathologic correlation. AJR Am J Roentgenol 184(3):797–802. doi:10.2214/ajr.184.3.01840797
17. Kang HC, Menias CO, Gaballah AH, Shroff S, Taggart MW, Garg N, Elsayes KM (2013) Beyond the GIST: mesenchymal tumors of the stomach. Radiographics 33(6):1673–1690. doi:10.1148/rg.336135507
18. Hong HS, Ha HK, Won HJ, Byun JH, Shin YM, Kim AY, Kim PN, Lee MG, Lee GH, Kim MJ (2008) Gastric schwannomas: radiological features with endoscopic and pathological correlation. Clin Radiol 63(5):536–542. doi:10.1016/j.crad.2007.05.026
19. Hur BY, Kim SH, Choi JY, Rha SE, Lee MW, Kim SY, Han JK, Choi BI (2011) Gastroduodenal glomus tumors: differentiation from other subepithelial lesions based on dynamic contrast-enhanced CT findings. AJR Am J Roentgenol 197(6):1351–1359. doi:10.2214/AJR.10.6360
20. Miettinen M, Paal E, Lasota J, Sobin LH (2002) Gastrointestinal glomus tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 32 cases. Am J Surg Pathol 26(3):301–311
21. Taylor AJ, Stewart ET, Dodds WJ (1990) Gastrointestinal lipomas: a radiologic and pathologic review. AJR Am J Roentgenol 155(6):1205–1210. doi:10.2214/ajr.155.6.2122666
22. Lee MH, Choi D, Park MJ, Lee MW (2012) Gastric cancer: imaging and staging with MDCT based on the 7th AJCC guidelines. Abdom Imaging 37(4):531–540. doi:10.1007/s00261-011-9780-3
23. Levy AD, Abbott RM, Rohrmann CA Jr, Frazier AA, Kende A (2001) Gastrointestinal hemangiomas: imaging findings with pathologic correlation in pediatric and adult patients. AJR Am J Roentgenol 177(5):1073–1081. doi:10.2214/ajr.177.5.1771073
24. Park SH, Han JK, Choi BI, Kim M, Kim YI, Yeon KM, Han MC (2000) Heterotopic pancreas of the stomach: CT findings correlated with pathologic findings in six patients. Abdom Imaging 25(2):119–123
25. Cho JS, Shin KS, Kwon ST, Kim JW, Song CJ, Noh SM, Kang DY, Kim HY, Kang HK (2000) Heterotopic pancreas in the stomach: CT findings. Radiology 217(1):139–144. doi:10.1148/radiology.217.1.r00oc09139
26. Kim JY, Lee JM, Kim KW, Park HS, Choi JY, Kim SH, Kim MA, Lee JY, Han JK, Choi BI (2009) Ectopic pancreas: CT findings with emphasis on differentiation from small gastrointestinal stromal tumor and leiomyoma. Radiology 252(1):92–100. doi:10.1148/radiol.2521081441
27. Fishman EK, Urban BA, Hruban RH (1996) CT of the stomach: spectrum of disease. Radiographics 16(5):1035–1054. doi:10.1148/radiographics.16.5.8888389
28. Motohara T, Semelka RC (2002) MRI in staging of gastric cancer. Abdom Imaging 27(4):376–383. doi:10.1107/s00261-001-0118-4
29. Binstock AJ, Johnson CD, Stephens DH, Lloyd RV, Fletcher JG (2001) Carcinoid tumors of the stomach: a clinical and radiographic study. AJR Am J Roentgenol 176(4):947–951. doi:10.2214/ajr.176.4.1760947
30. Sarlomo-Rikala M, Kovatich AJ, Barusevicius A, Miettinen M (1998) CD117: a sensitive marker for gastrointestinal stromal tumors that is more specific than CD34. Modern Pathol 11(8):728–734
31. Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M (2003) Gastrointestinal stromal tumors: radiologic features with pathologic correlation. Radiographics 23(2):283–304, 456; quiz 532. doi:10.1148/rg.232025146
32. Burkill GJ, Badran M, Al-Muderis O, Meirion Thomas J, Judson IR, Fisher C, Moskovic EC (2003) Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. Radiology 226(2):527–532. doi:10.1148/radiol.2262011880
33. Agaimy A, Wunsch PH (2009) Lymph node metastasis in gastrointestinal stromal tumours (GIST) occurs preferentially in young patients < or = 40 years: an overview based on our case material and the literature. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie 394(2):375–381. doi:10.1007/s00423-008-0449-5
34. Miettinen M, Wang ZF, Sarlomo-Rikala M, Osuch C, Rutkowski P, Lasota J (2011) Succinate dehydrogenase-deficient GISTs: a clinicopathologic, immunohistochemical, and molecular genetic study of 66 gastric GISTs with predilection to young age. Am J Surg Pathol 35(11):1712–1721. doi:10.1097/PAS.0b013e3182260752
35. Doyle LA, Hornick JL (2014) Gastrointestinal stromal tumours: from KIT to succinate dehydrogenase. Histopathology 64(1):53–67. doi:10.1111/his.12302
36. Choi H, Charnsangavej C, de Castro Faria S, Tamm EP, Benjamin RS, Johnson MM, Macapinlac HA, Podoloff DA (2004) CT evaluation of the response of gastrointestinal stromal tumors after imatinib mesylate treatment: a quantitative analysis correlated with FDG PET findings. AJR Am J Roentgenol 183(6):1619–1628. doi:10.2214/ajr.183.6.01831619
37. Holdsworth CH, Badawi RD, Manola JB, Kijewski MF, Israel DA, Demetri GD, Van den Abbeele AD (2007) CT and PET: early prognostic indicators of response to imatinib mesylate in patients with gastrointestinal stromal tumor. AJR Am J Roentgenol 189(6):W324–330. doi:10.2214/AJR.07.2496
38. Taxy JB, Battifora H (1988) Angiosarcoma of the gastrointestinal tract. A report of three cases. Cancer 62(1):210–216

39. Restrepo CS, Martinez S, Lemos JA, Carrillo JA, Lemos DF, Ojeda P, Koshy P (2006) Imaging manifestations of Kaposi sarcoma. Radiographics 26(4):1169–1185. doi:10.1148/rg.264055129
40. Ghai S, Pattison J, Ghai S, O'Malley ME, Khalili K, Stephens M (2007) Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation. Radiographics 27(5):1371–1388. doi:10.1148/rg.275065151
41. Ferrucci PF, Zucca E (2007) Primary gastric lymphoma pathogenesis and treatment: what has changed over the past 10 years? Br J Haematol 136(4):521–538. doi:10.1111/j.1365-2141.2006.06444.x
42. Campoli PM, Ejima FH, Cardoso DM, Silva OQ, Santana Filho JB, Queiroz Barreto PA, Machado MM, Mota ED, Araujo Filho JA, Alencar Rde C, Mota OM (2006) Metastatic cancer to the stomach. Gastric Cancer 9(1):19–25. doi:10.1007/s10120-005-0352-5
43. Mesa H, Rawal A, Rezcallah A, Iwamoto C, Niehans GA, Druck P, Gupta P (2009) ''Burned out'' testicular seminoma presenting as a primary gastric malignancy. Int J Clin Oncol 14(1):74–77. doi:10.1007/s10147-008-0804-0
44. Yamamoto H, Deshmukh N, Gourevitch D, Taniere P, Wallace M, Cullen MH (2007) Upper gastrointestinal hemorrhage as a rare extragonadal presentation of seminoma of testis. Int J Urol 14(3):261–263. doi:10.1111/j.1442-2042.2007.01685.x
45. Coskun M, Agildere AM, Boyvat F, Tarhan C, Niron EA (1998) Primary choriocarcinoma of the stomach and pancreas: CT findings. Eur Radiol 8(8):1425–1428
46. Guilford P, Hopkins J, Harraway J, McLeod M, McLeod N, Harawira P, Taite H, Scoular R, Miller A, Reeve AE (1998) E-cadherin germline mutations in familial gastric cancer. Nature 392(6674):402–405. doi:10.1038/32918
47. Rogers WM, Dobo E, Norton JA, Van Dam J, Jeffrey RB, Huntsman DG, Kingham K, Chun N, Ford JM, Longacre TA (2008) Risk-reducing total gastrectomy for germline mutations in E-cadherin (CDH1): pathologic findings with clinical implications. Am J Surg Pathol 32(6):799–809. doi:10.1097/PAS.0b013e31815e7f1a
48. National Comprehensive Cancer Network (NCCN) Gastric Cancer (Version 1.2014). 2014
49. Brosens LA, Langeveld D, van Hattem WA, Giardiello FM, Offerhaus GJ (2011) Juvenile polyposis syndrome. World J Gastroenterol WJG 17(44):4839–4844. doi:10.3748/wjg.v17.i44.4839
50. van Lier MG, Wagner A, Mathus-Vliegen EM, Kuipers EJ, Steyerberg EW, van Leerdam ME (2010) High cancer risk in Peutz-Jeghers syndrome: a systematic review and surveillance recommendations. Am J Gastroenterol 105(6):1258–1264; author reply 1265. doi:10.1038/ajg.2009.725
51. Capelle LG, Van Grieken NC, Lingsma HF, Steyerberg EW, Klokman WJ, Bruno MJ, Vasen HF, Kuipers EJ (2010) Risk and epidemiological time trends of gastric cancer in Lynch syndrome carriers in the Netherlands. Gastroenterology 138(2):487–492. doi:10.1053/j.gastro.2009.10.051