Computed Tomography-Based Diagnosis of Gastric Vein Invasion in Patients with Gastric Cancer

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ABSTRACT

Objective: The objective of this study was to demonstrate computed tomography (CT)-based diagnosis of venous invasion in patients with gastric cancer and its prognostic value.

Materials and Methods: Medical records and CT examinations of 530 patients with gastric cancer diagnosed after biopsy from February 2003 to December 2015 were included in this retrospective study. An imaging-based diagnosis of venous invasion was established when one of the following criteria were satisfied: 1) tumoral enhancement in the lumen of the vein, 2) tumor protruding through the course of a vein, and 3) distention of the vein due to extension of the gastric tumor. CT-based diagnosis of gastric vein invasion was established in 11/530 patients.

Results: Histopathological examination revealed poorly differentiated gastric adenocarcinoma (n=10) and neuroendocrine carcinoma (n=1). The median survival of the patients after the initial CT was 153.5 (range: 6–1275) days. Tumor invasion was observed at the aberrant left gastric vein (n=2), right gastroepiploic and superior mesenteric vein (n=2), gastric vein (n=4), and short gastric vein (n=3). Two of the three patients with short gastric vein invasion died 6 and 7 days after the initial CT, respectively.

Conclusion: All draining veins of the stomach can be invaded by gastric cancer; CT can enable diagnosis that may be important for prognosis and surgical planning. The presence of short gastric vein invasion detected by CT may be associated with poor prognosis.

Keywords: Gastric cancer, prognosis, venous invasion, CT, gastric vein

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Introduction

Gastric cancer is still the cause for a considerable amount of cancer-related deaths worldwide [1-3]. Surgery is the main treatment option for patients with gastric cancer, and for almost 2 decades, laparoscopic surgery has gained great interest, particularly for early-stage gastric cancer [4-9]. Complex perigastric vascular anatomy can be a challenging issue during surgery [6-8]. Moreover, a high rate of anomalous course of the perigastric vessels may distress surgeons. However, recent advances in multidetector computed tomography (MDCT) scanners have enabled visualization of the precise course of perigastric vessels. The efficacy of computed tomography (CT) in assessing perigastric vascular anatomy and its application in the preoperative period has been indicated by several studies [5-10]. Despite curative and successful surgery, there are several tumor-related prognostic factors affecting survival. In a study by Nakanishi et al. [11], histological differentiation, depth of tumor invasion, presence of metastases, and venous invasion were found to be main prognostic factors of overall survival in patients with gastric carcinoma. Although the usual late presentation of the disease is also responsible for the poor survival rate, the presence of venous invasion is further reported to be a reliable independent prognostic factor in early-stage gastric cancer [12, 13]. Lee et al. [12] reported that lymphovascular invasion was an independent negative prognostic factor in node-negative patients, and the prognosis was similar to that of the N1 group (involvement of 1 to 2 nodes). Araki et al. [13] concluded that moderate or marked venous invasion was an independent predictor of relapse-free and overall survival in patients with stage IB node-negative gastric cancer. Moreover, several molecular markers have been found to be useful in predicting poor prognostic factors related with venous invasion in gastric cancer [14-16]. Previous studies have been based on histopathological/surgical findings, and there has been no study regarding CT-based diagnosis of venous invasion in gastric cancer. Histopathological diagnosis

of venous invasion is a well-recognized prognostic factor in patients with gastric cancer; however, CT-based diagnosis of venous invasion by gastric cancer is a rare entity. In this study, we aimed to demonstrate CT-based diagnosis of venous invasion in patients with gastric cancer and its prognostic value.

Materials and Methods

Ethics

This retrospective study has been approved by the local ethics committee of Hacettepe University (GO 16/112-17). Informed consent was waived because of the retrospective nature of the study.

Patients

Medical records and CT examinations of 530 patients diagnosed with gastric cancer from February 2003 to December 2015 were retrospectively reviewed in the study. This was a retrospective analysis of a prospectively collected database of patients with gastric cancer from a single tertiary care institution. The exclusion criterion was lack of CT-based diagnosis of gastric vein invasion according to imaging criteria given below. Imaging-based diagnosis of venous invasion was established in 11 patients. CT findings and clinical data of the patients are summarized in Table 1.

CT Technique and Image Analysis

Abdominal CT was performed using a 16-detector row CT scanner (Somatom Sensation 16, Siemens, Germany). All patients received 100 ml of iodinated contrast material (Ultravist 300/100 mg/mL; Bayer Schering Pharma, Berlin, Germany) at a flow rate of 4 mL/s using a power injector. CT images were obtained 70 s after the injection of the contrast.

The location of the gastric cancer, extension of the tumor, and tumoral invasion through the course of draining veins of the stomach were reviewed on CT images. An imaging-based diagnosis of venous invasion was established when one of the following criteria were satisfied: 1) tumoral enhancement in the lumen of the vein, 2) tumor protruding through the course of a vein, and 3) distention of the vein due to extension of the gastric tumor. Right and left gastric veins, aberrant left gastric vein (ALGV), right and left gastroepiploic veins, superior mesenteric vein (SMV), short gastric veins, and the portal vein were evaluated for tumoral invasion (Figure 1). Right and left gastric veins were evaluated as a gastric vein because the mass located at the lesser curvature of the stomach prevented assessment (Figure 2). Pathology reports of the patients were retrieved from the hospital information system.

Statistical Analysis

Statistical Package for Social Sciences version 15.0 (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. Descriptive statistics are provided as median (minimum-maximum). Statistical significance is deemed to occur when a p value is <0.05.

Results

The study cohort comprised six men and five women, with a median age of 60 (range: 48-83) years. In all patients, diagnosis of gastric carcinoma was established by histopathological examination. Only three patients (27%) underwent surgical treatment. In two of the three patients, bland thrombus was observed at follow-up after chemotherapy, whereas residual tumoral thrombus was detected in the remaining one patient. The median survival of the patients after the initial CT was 153.5 (range: 6-1275) days. One patient was still alive 6 months after the initial CT, i.e., at the time of the study. Although no postmortem examination was performed to verify the cause of death, there was no evidence in any of the patients supporting the presence of a metastasis that could be the cause of sudden cardiopulmonary arrest (e.g., brain, mediastinal, and heart metastases). In addition, none of the patients had advanced stage of comorbid diseases (e.g., severe cardiac arrhythmia and significant heart-kidney-lung-

Table 1. CT findings and clinical data of the study cohort

Age (years)	Gender	Pathology	Dissemination	Invaded vein	Survival (days)	Surgery
58	M	Poorly differentiated adenocarcinoma	Liver–bone left adrenal metastases, perigastric and periportal lymphadenopathy	Short gastric vein	6	-
53	F	Poorly differentiated adenocarcinoma with signet ring cell formation	Disseminated lymphadenopathy	Short gastric vein	7	-
66	F	Poorly differentiated adenocarcinoma	Disseminated lymphadenopathy	Gastric veina	60	-
60	F	Poorly differentiated adenocarcinoma	Liver invasion, disseminated lymphadenopathy, and peritoneal involvement	ALGV	105	-
83	F	Poorly differentiated adenocarcinoma	No sign of metastases	SMV via the right gastroepiploic vein	120	Distal gastrectomy
48	M	Poorly differentiated adenocarcinoma	Liver invasion, perigastric and periportal lymphadenopathy	ALGV	187	-
66	M	Poorly differentiated adenocarcinoma	Pancreatic invasion and perigastric lymphadenopathy	Short gastric vein	256	-
78	M	Poorly differentiated adenocarcinoma	Disseminated lymphadenopathy and peritoneal involvement	Gastric veina	439	-
74	M	Large-cell neuroendocrine carcinoma	Perigastric and periportal lymphadenopathy	Portal vein via the gastric veina	537	Total gastrectomy
58	F	Poorly differentiated adenocarcinoma	Perigastric and periportal lymphadenopathy	SMV via the right gastroepiploic vein	1275b	-
54	M	Poorly differentiated adenocarcinoma	Perigastric and periportal lymphadenopathy	Portal vein via the gastric veina	N/Ac	Total gastrectomy

ALGV: aberrant left gastric vein; SMV: superior mesenteric vein
[a]Differentiation of right and left gastric veins from each other was not possible, [b]The only patient with regression, [c]Alive at the time of the study.

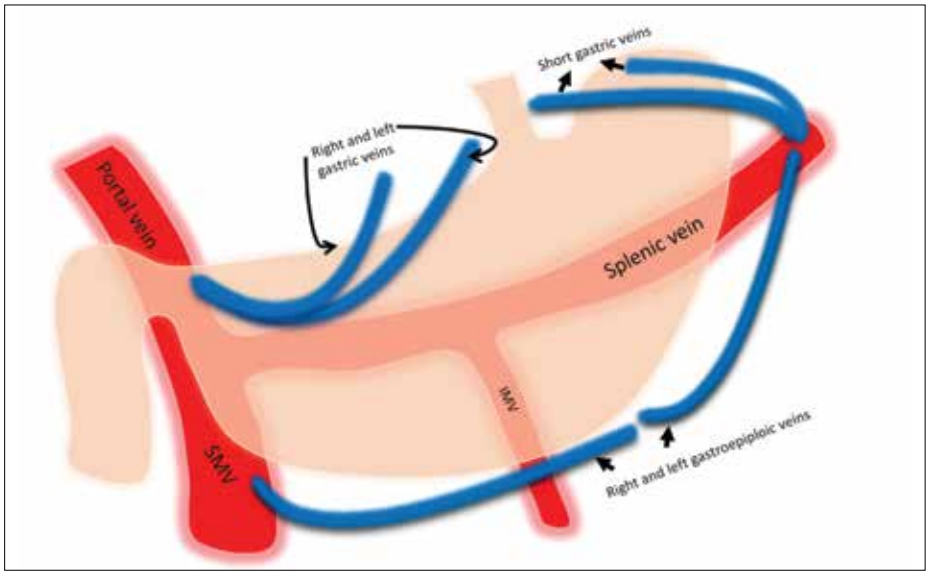

Figure 1. Schematic drawing showing courses of primary veins of the stomach
SMV: superior mesenteric vein, IMV: inferior mesenteric vein

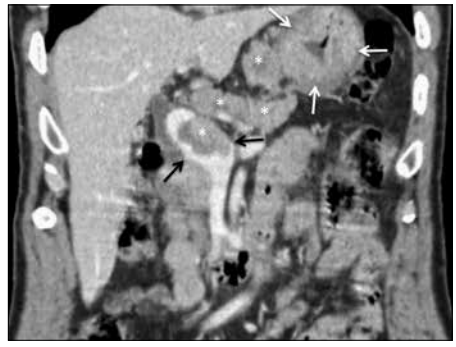

Figure 2. A 74-year-old man with gastric cancer invading the gastric veins. Coronal reformatted contrast-enhanced computed tomography (CT) image showing malignant thickening of the stomach wall (white arrows) and tumoral invasion through the course of the gastric vein (asterisks). Marked portal vein dilatation is seen at the site of gastric vein drainage because of luminal filling of the main portal vein with tumor (black arrows)

Figure 3. A 48-year-old man with gastric cancer invading the liver. Axial contrast-enhanced CT image demonstrating gastric cancer (asterisk) invading the left lobe of the liver via an aberrant left gastric vein (ALGV). Tumoral invasion of ALGV (arrows) and multiple liver metastases are seen

liver failure). Therefore, deaths of these patients were primarily attributed to gastric cancer.

Pathological examination revealed poorly differentiated adenocarcinoma in 10 out of the 11 patients (91%). Of these 10 patients, one had signet ring cell formation. In the remaining one patient, a large-cell neuroendocrine carcinoma was diagnosed. Although statistical analysis could not be achieved because of the small patient group of our study, survival rates of the patients with ALGV (Figure 3) and short gastric vein (Figure 4) invasion were low. Two patients with ALGV invasion died 105 and 187 days after the initial CT, respectively. Furthermore, two of the three patients with short gastric vein invasion died 6 and 7 days after the initial CT, respectively. These four patients had poorly differentiated adenocarcinoma, and the patient who died 7 days after CT had signet ring cell formation. The patient who died 1275 days after diagnosis had poorly differentiated adenocarcinoma invading SMV via the right gastroepiploic vein and the tumor in SMV almost totally regressed after chemotherapy; this was the only patient who was responsive to chemotherapy (Figure 5).

Discussion

The present study evaluated the value of CT-based diagnosis of venous invasion in patients with gastric cancer. Although our study had a small patient cohort as a major drawback for further analysis, survival rates of patients with ALGV and short gastric vein invasion were significantly low. Therefore, we can argue that the presence of ALGV or short gastric vein invasion on CT of a patient with gastric cancer may indicate poor prognosis. Advanced gastric cancer has a poor prognosis with a median survival time of 3-5 months in patients who are untreated and<12 months in those who have undergone the current chemotherapy protocols [2, 3]. In the present study, the median survival of patients after the initial CT was 153.5 days despite chemotherapy, and in seven patients, survival was <9 months, suggesting that venous invasion detected on CT is a poor prognostic factor of gastric cancer. One patient was still alive 6 months after the initial CT, i.e., at the time of the study.

Surgery is the main accepted treatment option for patients with operable gastric cancer with or without adjuvant chemotherapy depending on the stage of the disease [2, 3, 12, 13]. However, there is still a debate regarding the treatment of gastric cancer with venous invasion. Lee et al. [12] suggested that an individualized and comprehensive treatment approach should be considered in the presence of lymphovascular invasion because they found out that lymphovascular invasion was an independent negative prognostic factor of node-negative gastric cancer. Moreover, Araki et al. [13] determined that venous invasion was the only independent prognostic factor of relapse-free and overall survival in stage IB node-negative gastric cancer. They further concluded that adjuvant chemotherapy could be used for improving outcomes in patients with early-stage gastric cancer, particularly in the presence of venous invasion [13]. Nevertheless, authors of both studies also pointed out that further clinical trials are needed for confirming their results. In the present study, two patients had SMV invasion via the right gastroepiploic vein. One of these two patients underwent distal gastrectomy because there was no evidence of any metastases and pathological examination also revealed lack of lymph node metastasis. On the other hand, the other patient was followed up with chemotherapy. The patient who underwent distal gastrectomy was 83 years old and died 3 months postoperatively because of postoperative complications. However, the other patient who had inoperable gastric cancer responded to the treatment, and the main tumor and venous invasion were significantly reduced in size at follow-up. The anomalous course of the left gastric vein (LGV) has been recently described [17]. The efficacy of MDCT in depicting the perigastric vessel anatomy was investigated in several studies; authors have reported that MDCT is a useful and effective method for preoperative visualization of the

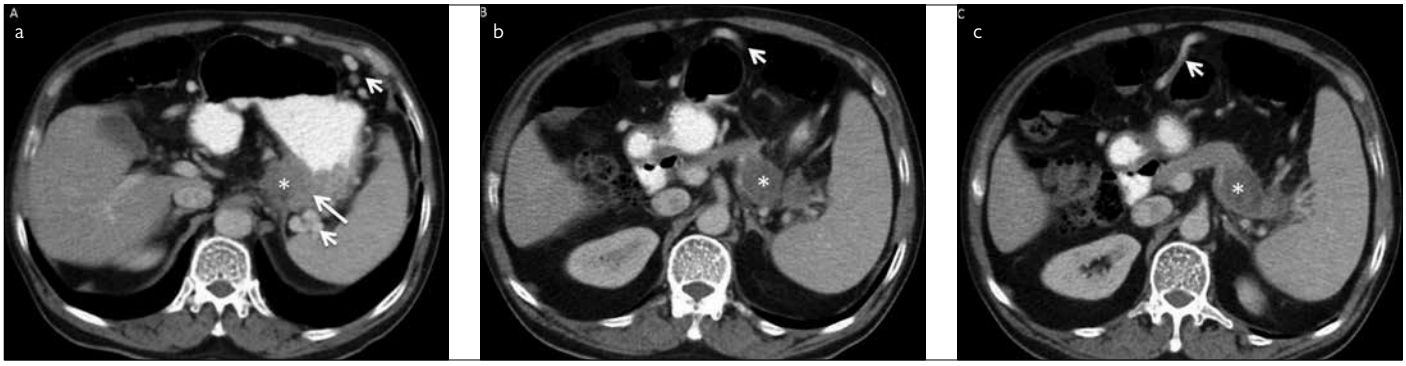

Figure 4. a-c. A 66-year-old man with gastric cancer extending through the course of short gastric veins. Serial axial contrast-enhanced CT images demonstrating the main tumor (long arrow, a), and tumor infiltrating through the course of short gastric veins (asterisks, a-c). Tumoral occlusion of the splenic vein is clearly seen (asterisk, c). Dilated collateral veins due to splenic vein occlusion (short arrows, a-c)

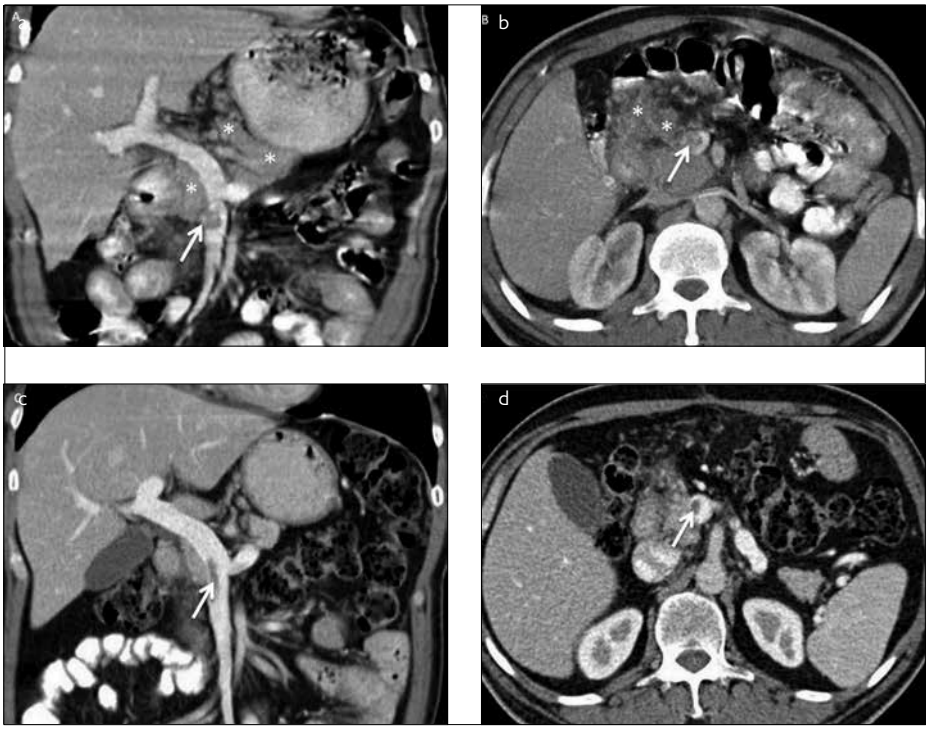

Figure 5. a-d. A 58-year-old woman with gastric cancer invading the superior mesenteric vein. Coronal (a) and axial (b) CT images demonstrating tumoral infiltration through the course of the right gastroepiploic vein (asterisks, a, b). Superior mesenteric vein invasion is also seen at the side of gastroepiploic vein drainage (arrows, a, b). Follow-up CT (c, d) after chemotherapy reveals marked tumoral regression at the course of the right gastroepiploic vein. Residual bland thrombus is seen without any sign of enhancing the soft tissue mass (arrows, c, d)

perigastric vessel anatomy [5-10]. Furthermore, preoperative demonstration of the vascular anatomy by MDCT can contribute to reduction of intraoperative blood loss, particularly during laparoscopic surgery [5, 6]. Identifying the course of LGV is important because LGV may demonstrate variations in the course, and injury to LGV may lead to significant blood loss [6]. On the other hand, ALGV develops because of morphogenetic changes during the developmental process in early embryonic life and has a unique course through the ligamentum venosum [17]. ALGV directly connects the stomach and liver, leading to venous drainage of lesser curvature into the liver. Therefore, direct spread of gastric cancer into the liver can occur in the presence of ALGV. In the present study 2 of 11 patients had ALGV invasion.

The most significant finding in our study was the survival time of patients with short gastric vein invasion; two of the three patients with short gastric vein invasion died within 1 week after CT. Perineural invasion was significantly associated with lymphatic venous invasion [12, 18]. Short gastric veins are adjacent to more important nerves (e.g., vagus nerve, phrenic nerve, and sympathetic-parasympathetic nervous system adjacent to the upper one third of the stomach) than the other veins of the stomach. Moreover, Jiang et al. [18] also reported that the incidence of perineural invasion was higher in the upper one third of the stomach. They considered that the presence of larger autonomic nerves and larger perineural spaces located in this area could be responsible [18]. In light of this information, we speculate that sudden cardiopulmonary arrest because of perineural invasion could be the cause of death, particularly in two patients with short gastric vein invasion. We acknowledge that the small sample size of our study prevents further analysis; thus, further studies are warranted for confirming our results. Nevertheless, our findings tend to agree with the above-mentioned studies that individual treatment options rather than standard protocols are more appropriate for managing gastric cancer, particularly in patients with venous invasion.

One of the major reasons for poor survival rates of gastric cancer is the late presentation of the disease. Nevertheless, it has also been reported that the presence of venous invasion on pathological examination could be used as a reliable prognostic marker in the early stage of the disease, particularly in patients with node-negative gastric cancer [12, 13]. Routine histopathological examination is occasionally insufficient for evaluating the presence of lymphatic and venous involvement in gastric cancer; therefore, researchers investigated the significance of molecular marker expression in predicting the presence of venous invasion [14-16]. However, Sekiguchi et al. [4] suggested that using immunohistochemistry in routine practice was not feasible in terms of the cost and workload. They reported that deeper invasion, the presence of an undifferentiated-type adenocarcinoma component, and a macroscopically elevated type were independent risk factors of venous involvement in gastric cancer. They also found out that a larger size (>20 mm), deeper invasion, the presence of a papillary

adenocarcinoma component, and the presence of an undifferentiated-type adenocarcinoma component were independent risk factors of lymphatic involvement as well [4]. Based on their results, Sekiguchi et al. [4] suggested that identification of these risk factors contributes to efficient use of immunohistochemistry stains in high-risk patients. On the other hand, it should be emphasized that CT can miss microscopic venous invasion. Moreover, smaller size of RGV and metastatic lymph node compression of LGV may result in non-visualization of these veins [9].

Our study had several limitations. First, the study cohort was small. However, CT-based diagnosis of venous invasion in gastric cancer is an uncommon finding in daily routine practice. Second, it was a retrospective, case-control study performed at a single institution. Third, pathological examination information regarding the presence of venous invasion was not available for patients who did not undergo surgery.

In conclusion, venous invasion of gastric cancer can be detected on CT and the presence of short gastric vein and ALGV invasion may be associated with poor prognosis.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Hacettepe University (GO 16/112-17).

Informed Consent: Written informed consent was waived because of the retrospective nature of the study.

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Author Contributions: Concept - E.U., M.K., D.A.; Design - E.U., M.K., A.D.K., M.N.O.; Supervision - M.K., D.A., M.N.O.; Resources - E.U., A.D.K., M.K.; Materials - E.U., D.A., M.K.; Data Collection and/or Processing - E.U., A.D.K., M.K.; Analysis and/or Interpretation - D.A., M.N.O., M.K.; Literature Search - E.U., A.D.K., M.K.; Writing Manuscript - E.U., A.D.K, M.N.O., D.A., M.K.; Critical Review - E.U., D.A., M.K.

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