Evaluating the Sensitivity of Arterial Phase CT Images for Detection of Hepatic GIST Metastases

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Abbreviations: Gastrointestinal stromal tumor (GIST), computed tomography (CT), portal venous (PV), multidetector computed tomography (MDCT)

ABSTRACT

Gastrointestinal stromal tumor (GIST) frequently metastasizes to the liver, and conventional staging computed tomography (CT) protocols use multiphasic contrast enhancement for detection of hepatic lesions. We evaluated the sensitivity of arterial phase CT imaging for hepatic GIST metastases compared with that of standard (portal venous [PV]) phase imaging. We conducted a retrospective review of patients who presented with hepatic GIST metastases identified on staging CT examinations between 2005 and 2015. Arterial and PV phase CT images were randomized and reviewed by 2 radiologists blinded to clinical history, correlative imaging, and number of controls. In total, 32 patients had hepatic metastases identified on multiphasic (arterial and PV) staging CT examinations. There was no significant difference in identification of metastases between arterial and PV phase imaging (31 vs 32, $P = .32$). Lesion size measurements did not significantly differ ($P = .58$). Arterial phase CT imaging did not significantly increase the sensitivity for hepatic GIST metastases compared with PV phase imaging alone.

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) account for 90% of mesenchymal tumors in the gastrointestinal tract with incidence of 14–20 cases per million and prevalence of 130 cases per million (1-3). GISTs most commonly occur in the stomach accounting for 2%–3% of all gastric malignancies and most commonly metastasize to the liver and peritoneum (4, 5). GISTs are generally considered to be hypervascular tumors (6, 7). Accordingly, the literature suggests that arterial phase computed tomography (CT) imaging may be helpful for detection of hypervascular liver metastases (1, 8). Conventional literature also states that GIST metastases can become isoattenuating to liver parenchyma and therefore occult on portal venous (PV) phase imaging, necessitating multiphasic enhanced CT imaging for detection (9-14). Current consensus guidelines support the use of multiphasic enhanced CT to stage newly diagnosed GISTs but state that monophasic studies are adequate for follow-up evaluations (9-15).

However, outside of anecdotal support for the practice, there is a paucity of data showing the necessity of arterial phase imaging for detection of hepatic GIST metastases. In fact, large series have characterized primary and metastatic GIST with only PV phase imaging (16). Some literature studies state CT imaging during PV phase is adequate for detection of primary GIST, vascular encasement, and hepatic metastases (17). Even advocates of multiphasic CT for evaluation of GIST acknowledge that further study is necessary to support its use (11). This study aims to determine whether arterial phase imaging augments the sensitivity of standard PV phase imaging when evaluating for hepatic GIST metastases.

MATERIALS AND METHODS

A retrospective review of all patients with new diagnosis of GIST at a single academic institution between September 1, 2005 and August 31, 2015, was performed. Of these, 61 patients had hepatic metastases identified on initial staging CT. After exclusion of patients with monophasic staging CT, 32 patients were included. All procedures were in accordance with the ethical standards of the Institutional Review Board, and the waiver of need for informed consent was approved.

All CT examinations were performed on either 16-multidetector computed tomography (MDCT) or 64-MDCT scanners (Brilliance, Philips Healthcare, Amsterdam, Netherlands). The institutional protocol for CT staging of GIST includes PV phase images (reconstructed section thickness = 3 mm) of the entire abdomen and pelvis with additional arterial phase images (section thickness = 3 mm) of the liver, which are optional and obtained as per the physician's discretion. Iohexal (120 mL; 4–5 mL/s through peripheral venous access; Omnipaque 350; GE Healthcare) was administered to the patients. Arterial phase

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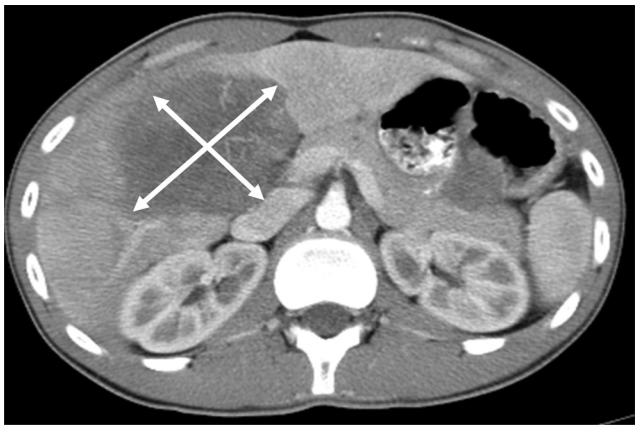

Figure 1. Measurement of hepatic lesions. The largest hepatic lesion identified in each series was measured to the nearest millimeter in axial long and short axes.

images were obtained 35 seconds after injection and PV phase images were obtained 75 seconds after injection. A fixed 120-kVP technique was used for all phases, with the automated tube current modulation varying between 100 and 500 mA. Reformatted axial, sagittal, and coronal images of all patients were available.

Two radiologists (senior residents, each with over 2 years of experience interpreting cross-sectional imaging) were blinded to patient history and any correlative imaging. Arterial and PV phase images of the 32 patients were separated and each of the 64 series was independently reviewed. The readers recorded the presence and number of hepatic lesions for each series. Readers were asked to annotate any image in which the same number of lesions were identified on arterial and PV phases but with a difference in the location of the lesions. For patient who >5 lesions, the number of lesions was recorded as "multiple". The largest lesion identified for each patient was measured in both long and short axes on axial images (Figure 1). PACS (picture archiving and communication system; iSite, version 3.6.150, Philips Medical Systems) was used for reviewing images, and electronic calipers to the nearest millimeter were used for measurements.

In addition to the 32 patients with hepatic GIST metastases, 16 patients with GIST but no hepatic metastases on multiphasic staging CT were included in our series. Follow-up imaging was reviewed for these patients (mean follow-up period = 4.1 years, range, 1.2–7.1 years), and no patient developed lesions suspicious for hepatic GIST metastases on follow-up. To prevent the readers from being overly sensitive to subtle findings and identifying them as metastases, the blinded readers were kept unaware of the number of patients with metastases. The readers declared that not all patients may have hepatic metastases.

Medical records were reviewed to obtain patient demographic data. Available pathology results from subsequent liver biopsy or resection were recorded and considered the gold standard for diagnosis. Follow-up CT imaging of all 16 patients without hepatic metastases was reviewed to evaluate for metastases that may have been missed on the initial staging CT.

Table 1. Demographics and Technical Data

	Control	Study Cases with Metastases	*P* Value
Age (years)	59	66.7	.15
Gender			.99
Male	8	18	
Female	8	14	
CT scanner			.12
16-MDCT	7	22	
64-MDCT	9	10	

Statistical analysis was performed using the STATA software package (Version 12.0, 1985-2011, StataCorp LP). Patient demographics between groups were compared using 2-sample t tests and χ^2 tests. The Cohen kappa coefficient was used to measure interobserver agreement, and the Fischer exact test was used to compare identification of lesions between arterial and PV imaging. Sensitivity and specificity of arterial and PV phase imaging were calculated. Paired t test was used to compare both long- and short-axes measurements between arterial and PV imaging. Statistical significance was denoted by $P < .05$.

RESULTS

Initial multiphasic staging CT from 48 patients, 32 patients with hepatic GIST metastases and 16 without, was evaluated. Interobserver agreement regarding the presence or absence of hepatic metastases was very good ($\kappa = 0.98$). In total, 29 (60%) and 19 (40%) examinations were performed on 16-MDCT and 64-MDCT scanners, respectively. Demographical or technical parameters were not significantly different between the 32 patients with hepatic GIST metastases and the 16 controls with GIST but no hepatic metastases (Table 1).

In patients with hepatic GIST metastases, lesions were identified on 31 (97%) arterial series and 32 (100%) PV series. One observer identified a metastasis on a single arterial series in a patient without hepatic metastasis. This examination was performed on a 64-MDCT scanner; however, there was no significant difference in detection of metastasis between types of scanners ($P = .31$). No additional hepatic lesions were identified on arterial or PV series in the 16 controls.

Pathology results were available and confirmed hepatic GIST metastasis in 17 patients (53%). Both the patients in whom lesions were seen on PV but not on arterial phase and the patient in whom more lesions were detected on arterial than PV phase images had pathological confirmation of hepatic GIST metastases. On comparing CT interpretation with pathological results and known controls, arterial phase imaging had sensitivity of 94.1% and specificity of 93.8%–100% for hepatic metastases. PV phase imaging had sensitivity of 100% and specificity of 100% for hepatic metastases.

The average axial measurements of the largest lesions did not differ between arterial and PV phases (38.1 vs 37.6 mm, $P = .96$), and there was no difference when comparing only the long- (41.9 vs 42.3 mm, $P = .62$) or short- (34.1 vs 34.2 mm,

Table 2. Sensitivity for and Measurements of Lesions on Arterial and PV Image Series

	Control Arterial	Control PV	Study Cases Arterial	Study Cases PV	*P* Value (Art vs PV)
Presence of hepatic lesions	1	0	31 (97%)	32 (100%)	.32
Average axial measurement (mm)	7.0	0	38.1 (SD = 35.1)	37.6 (SD = 35.0)	.96
Long-axis measurement (mm)	8.0	0	41.9 (SD = 38.3)	42.3 (SD = 38.1)	.62
Short-axis measurement (mm)	6.0	0	34.1 (SD = 32.2)	34.2 (SD = 32.0)	.77

$P = .77$) axes measurements (Table 2). There was 1 patient in whom more lesions were detected on arterial phase images than on PV phase images, otherwise the number of lesions detected did not differ.

DISCUSSION

Conventional literature and guidelines support the inclusion of arterial phase imaging for identification of hepatic metastases when staging GIST (9-15). These sources report decreased conspicuity of GIST metastases on PV phase imaging of the liver, but these reports rely on expert opinion rather than formal analysis of imaging examinations. To the best of our knowledge, the value of arterial phase imaging in addition to standard PV phase imaging is yet to be formally studied (11).

Our results suggest that arterial phase imaging may not be more sensitive for hepatic GIST metastases than PV phase imaging (94.1% vs 100%). In 1 patient, a hepatic lesion was detected on PV phase images but not on arterial phase (Figure 2). This lesion measured 18 mm in the long axis and appeared to be hypovascular, becoming more conspicuous as the attenuation of the liver parenchyma exceeded that of the lesion.

In another patient in our study, a number of GIST metastases were isoattenuating to the liver parenchyma on PV phase but visible on arterial phase (Figure 3). However, this patient had other conspicuously hypoattenuating and heterogeneous hepatic lesions that were compatible with metastases. Our study also found no significant difference between arterial and PV phase imaging in terms of average lesion size or by the individual axes of measurement. Overall, these results support the previously suggested notion that PV phase imaging may be adequate for detecting hepatic metastases on initial staging CT (17).

Of note, in our study, patients with GIST metastases to the liver had large lesions, with the largest lesions measuring an average of 37–38 mm. We hypothesize that the large lesion size on initial staging study may be because of the intrinsic rapid growth of GIST once metastasized to the liver. Certainly, this large lesion size contributes to the conspicuity of lesions on both arterial and PV phase imaging. Nevertheless, the largest visible lesion measured <1 cm in 5 patients (15.6%) from our series, and, in each of these patients, the presence of metastases was identified on both arterial and PV phases of imaging. Further study may be useful to formally determine whether PV phase imaging is sufficient to identify subcentimeter hepatic GIST metastases.

This study has a number of limitations. The number of patients included was relatively small, partially because of the study's retrospective nature and because of the fewer available multiphasic staging CT examinations for GIST with hepatic metastases. The standard for calculating sensitivity and specificity was based on pathology, which was only available for 53% of the patients and follow-up imaging.

This study only evaluated the use of arterial phase images for detection of hepatic metastases. Other potential reasons for arterial phase imaging include preoperative evaluation of arte-

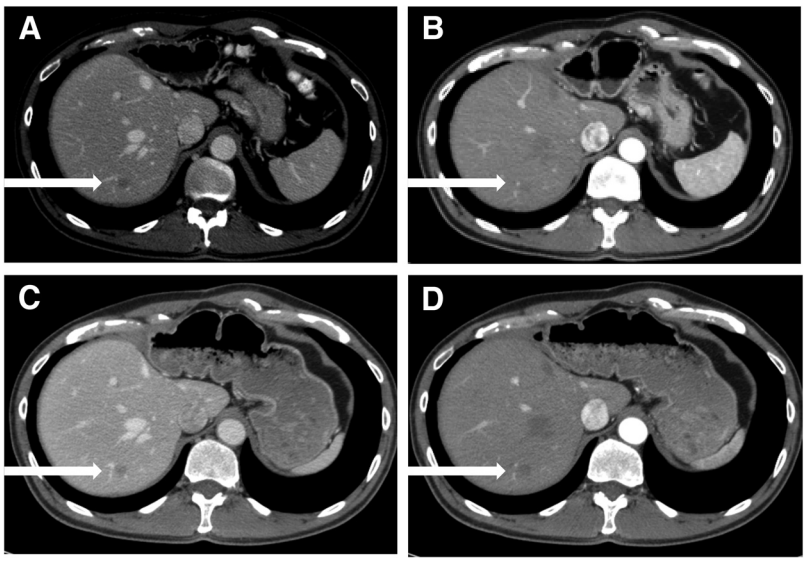

Figure 2. Lesion detected on portal venous but not on arterial phase. In 1 patient, a single lesion was identified on portal venous (PV) phase images (A) but not on arterial phase (B). At 3-month follow-up, this lesion is visible on both PV (C) and arterial phase (D) images.

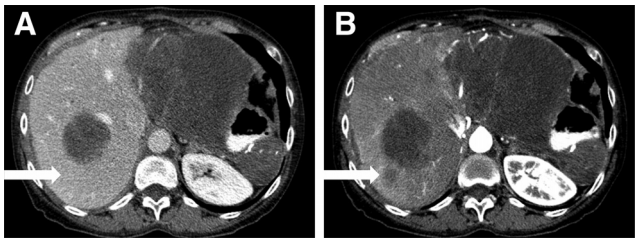

Figure 3. Case in which more lesions were identified on arterial than PV phase. In 1 patient, 3 hepatic lesions were identified on PV phase images (A) but >5 lesions were seen on arterial images (B).

rial anatomy and assessment of tumor vascularity. In total, 27 patients (84%) with hepatic metastases completed follow-up CT examinations; however, the focus of this study was on the initial staging examinations, so these examinations were not evaluated. Nevertheless, lesion attenuation and vascularity have been shown to be important factors in evaluating the treatment response of GIST, and our study did not evaluate the value of arterial phase imaging in establishing the baseline values for these parameters (6, 7, 13). Indeed, the literature anecdotally supports the use of multiphase CT imaging to evaluate tumor vascularity on follow-up studies of patients on treatment (10-12).

The findings of this study are important to patients and care providers for multiple reasons. Inappropriate multiphase CT examinations may be a more important source of medically unnecessary radiation exposure than nonoptimized technical scanner parameters (18). Furthermore, the addition of arterial phase images increases technologist processing and radiologist interpretation time. There is a discrete cost to patient and provider from the use of arterial phase imaging in staging GIST, which must be balanced with the value it provides.

Further study may evaluate the use of multiphasic CT for assessing baseline tumor vascularity for assessing response to treatment. Further studies can also investigate the value of arterial phase imaging for staging other classically hypervascular tumors (eg, carcinoid, pancreatic islet cell, renal cell). Results from our small retrospective cohort, however, suggest that arterial phase imaging may not offer increased sensitivity for the detection of hepatic GIST metastases on initial staging CT.

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Conflict of Interest: None reported.

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