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Comparison between the deconvolution and maximum slope 64-MDCT perfusion analysis of the esophageal cancer: Is conversion possible?

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ABSTRACT

Purpose: To estimate if CT perfusion parameter values of the esophageal cancer, which were obtained with the deconvolution-based software and maximum slope algorithm are in agreement, or at least interchangeable.

Methods: 278 esophageal tumor ROIs, derived from 35 CT perfusion studies that were performed with a 64-MDCT, were analyzed. "Slice-by-slice" and average "whole-covered-tumor-volume" analysis was performed. Tumor blood flow and blood volume were manually calculated from the arterial tumor-time–density graphs, according to the maximum slope methodology (BF_{ms} and BV_{ms}), and compared with the corresponding perfusion values, which were automatically computed by commercial deconvolution-based software ($BF_{deconvolution}$ and $BV_{deconvolution}$), for the same tumor ROIs. Statistical analysis was performed using Wilcoxon matched-pairs test, paired-samples *t*-test, Spearman and Pearson correlation coefficients, and Bland–Altman agreement plots.

Results: $BF_{deconvolution}$ (median: 74.75 ml/min/100 g, range, 18.00–230.5) significantly exceeded the BF_{ms} (25.39 ml/min/100 g, range, 7.13–96.41) ($Z = -14.390$, $p < 0.001$), while $BV_{deconvolution}$ (median: 5.70 ml/100 g, range: 2.10–15.90) descended the BV_{ms} (9.37 ml/100 g, range: 3.44–19.40) ($Z = -13.868$, $p < 0.001$).

Both pairs of perfusion measurements significantly correlated with each other: $BF_{deconvolution}$, versus BF_{ms} ($r_S = 0.585$, $p < 0.001$), and $BV_{deconvolution}$, versus BV_{ms} ($r_S = 0.602$, $p < 0.001$). Geometric mean $BF_{deconvolution}/BF_{ms}$ ratio was 2.8 (range, 1.1–6.8), while geometric mean $BV_{deconvolution}/BV_{ms}$ ratio was 0.6 (range, 0.3–1.1), within 95% limits of agreement.

Conclusions: Significantly different CT perfusion values of the esophageal cancer blood flow and blood volume were obtained by deconvolution-based and maximum slope-based algorithms, although they correlated significantly with each other. Two perfusion-measuring algorithms are not interchangeable because too wide ranges of the conversion factors were found.

1. Introduction

The analysis of the tumor vascularization has been actual for a long time [1]. Histological assessment of the microvessel density (MVD) is restricted to few spots of the tumor tissue specimens (biopsy or postoperative), which might not definitely reflect the whole tumor vascularization [2].

Dynamic contrast-enhanced computed tomography (DCE-CT) has been recognized as an effective tool in assessing the tumor perfusion in vivo [3,4]. The multi-detector computed tomography (MDCT) enables the analysis of the whole tumor or near whole tumor volume perfusion, depending on the available CT equipment [3–6]. The MDCT perfusion studies were used for the diagnosis of the neoplastic lesions, prognosis of the neoplasm aggressiveness and overall patient's survival, prediction and monitoring of the tumor response to radiotherapy and chemotherapy [6–14]. The cut-off values of the available perfusion parameters, which discriminate the neoplasm from the normal tissues, malignant from benign lesions, high-aggressive from low-aggressive tumors, potential or

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actual responders to the anticancer therapy from non-responders, were provided in the available studies [6–15]. However, problem is that wide range of perfusion parameter values were reported in the literature, probably due to various CT perfusion protocols and different kinetic models implemented in the commercial CT perfusion software packages provided by the manufacturers [3,4,6–15].

For the esophageal and gastric cancer, quantitative assessment of the first-pass perfusion and correlation of the perfusion parameters with the tumor MVD, VEGF expression, histological grade and pathological stage, were performed in the majority of studies available in literature using the maximum slope based CT perfusion software [16–19]. However, in two reported studies, in which the predictive value of the baseline CT perfusion parameter values of the esophageal carcinoma to tumor response to the neoadjuvant chemo radiotherapy was assessed, the deconvolution-based commercial CT perfusion software was used [10,11]. Since CT perfusion measurement is potentially useful functional imaging tool for predicting, monitoring and assessing the esophageal cancer response to radiation and chemotherapy, we think that it could be of clinical importance to estimate if different CT perfusion algorithms provided interchangeable perfusion parameter values. It will also enable inter-studies data comparison.

Only few studies compared the values of the tumor perfusion measurements using different CT perfusion software [20–22]. We could not find any data in literature that the agreement between two most frequently used CT perfusion algorithms was assessed: deconvolution and maximum slope. Therefore, the aim of this study was to compare the 64-MDCT perfusion measurements of the blood flow and blood volume of the esophageal carcinoma, using the deconvolution-based software, with the corresponding perfusion values calculated according to the maximum slope methodology in the same tumor volume samples and to estimate if these values were in agreement, or at least interchangeable.

2. Materials and methods

2.1. Selection of patients

Thirty-five consecutive patients (31 men, 4 women; mean age 63; range, 44–78 years) with the endoscopic biopsy-confirmed esophageal cancer, who were untreated (i.e. no previous surgery or chemo-radiation therapy), were enrolled in this prospective study. The CT perfusion study was incorporated in the conventional CT examination of patients with the esophageal cancer, for the pretreatment staging purposes. The institutional Ethics Board approved this study, and written informed consent was obtained from each subject. Exclusion criteria were defined as follows: the impossibility of intravenous iodinated contrast injection due to inability of vein cannulation, allergy to iodine, renal impairment, prior radio and/or chemotherapy, and impossibility to locate the esophageal tumor if esophageal wall thickening was not visible on the unenhanced CT scan.

Thirty esophageal tumors were squamous cell carcinomas and five were adenocarcinomas. According to the CT criteria of staging, two patients had T2, 24 had T3, and nine had T4 neoplasm. The tumors were located in the cervical and the upper thoracic portion of the esophagus in 2 patients, the upper thoracic portion in 4, the upper and the middle thoracic portion in 2, the midthoracic portion in 11, the middle and the lower thoracic portion in 7, the lower thoracic portion in 5, and the lower esophagus and the cardia in 4 patients. The mean length of tumors (±SD), assessed by computed tomography, was 7.43 ± 2.47 cm (range, 3–13 cm), and the mean transverse diameter of tumors was 36.92 ± 13.27 mm (range, 21–75 mm).

The mean weight and maximum transverse diameter of patients were 68 ± 14 kg (range, 37–102 kg), and 33.2 ± 3.3 cm (range, 25.2–41.1 cm), respectively.

2.2. Perfusion CT scans

CT was performed with the 64-detector row CT (LightSpeed VCT, GE Health-care Technologies). Immediately before the CT scanning, the patients drank 250–500 ml of water as an oral negative contrast material in order to opacify and distend the lumen of the esophagus and the stomach. First series was an unenhanced low-dose thoracic CT scan, which was performed to identify the tumor and plan the CT perfusion study, and was restricted to the expected region of tumor extension (axial-mode, 5 mm-section thickness, 1-s rotation time, detector coverage 40 mm: 8 images per rotation, 80 kV, 40 mAs, 25-cm scan field of view, 16–24 slices, 2–3 s total exposure time). This series was viewed, and, after identification of the tumor as localized segmental esophageal wall thickening, eight contagious sections at the level of the greatest tumor area were chosen for the following perfusion study and spatial coordinates were recorded. Second series was a low-dose CT perfusion study. For the perfusion CT study, 50 ml of the non-ionic iodinated contrast (iopromide, 370 mg/ml iodine; Ultravist 370, Bayer Schering Pharma, Berlin, Germany), followed by 30 ml of saline, was administrated intravenously using the pump injector (Urlich-Missuri, Urlich, Germany), at a flow rate of 7 ml/s, through a 16-gauge cannula that was placed in the ante-cubital vein [23]. Although slower flow rate, minimum 4 ml/s, is allowed for deconvolution-based analysis of the CT perfusion study, we applied faster injection rate of 7 ml/s in order to enable appropriate calculation of the perfusion parameters values using the maximum slope methodology [3,23,27]. Using the cine-mode acquisition, eight contagious sections with 5-mm axial thickness (totally 40 mm *z*-axis coverage), which were previously chosen in the unenhanced series, were scanned at 1-s intervals (80 kV, 40 mAs, 25-cm scan field of view, 512×512 matrix) (Fig. 1a). Scanning started 5 s after the beginning of the intravenous contrast administration, and total scan duration was 50 s (400 images per study). Prior to examination, the patients were forewarned that they would feel a sensation of warmth during the contrast administration, and advised to stay motionless, not to swallow, and breathe quietly during the dynamic CT scanning. Third series was a conventional portal venous phase CT of the neck, thorax and abdomen, after the intravenous administration of 60–100 ml of iodinated contrast, performed for the staging purposes (helical-mode, 5-mm section thickness, 5-mm section interval, 120 kV, 120–750 mAs in tube current modulation mode, 39.5 mm/s table speed, 0.7 s rotation time, 50-cm scan field of view, scan delay 55 s, reconstructed sections 0.625 mm).

2.3. Imaging data analysis

All CT series were transferred to the workstation (Advantage Windows 4.3, GE Health-care Technologies), and analyzed by one radiologist (corresponding author, fourteen years of experience in the thoracic-abdominal radiology and five years in the perfusion CT). CT perfusion series were analyzed with the commercial deconvolution-based perfusion software (Perfusion 3.0, GE Healthcare Technologies). A threshold range of 0–120 HU was chosen, according to the Manufacturer's recommendations. Arterial input was defined by the circular region of interest (ROI), area of which 4–6 mm^2 was placed in the center of the largest-diameter artery presented in the CT perfusion series, depending on the esophageal neoplasm localization, as was recommended in the literature [4]. In patients with tumors in the middle thoracic, lower thoracic esophagus, and cardia, the arterial input ROI was placed in the descending aorta (29 patients (pts)), in patients with tumors in the upper

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