Pancreatology xxx (2017) 1–6

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Transarterial chemoembolization in pancreatic adenocarcinoma with liver metastases: MR-based tumor response evaluation, apparent diffusion coefficient (ADC) patterns, and survival rates

Thomas J. Vogl [a, 1], Sherif A. Mohamed [a, *, 1], Moritz H. Albrecht [a, b], Tatjana Gruber-Roh [a], Han Lin [b], Nour Eldin A. Nour Eldin [a], Iliana Bednarova [a, c], Nagy N. Naguib [a], Bita Panahi [a]

[a] University Hospital Frankfurt, Department of Diagnostic and Interventional Radiology, Frankfurt, Germany
[b] Medical University of South Carolina, Department of Radiology and Radiological Science, Charleston SC, USA
[c] Institute of Diagnostic Radiology, Department of Medical and Biological Science, Udine, Italy

ARTICLE INFO

Article history:
Received 6 August 2017
Received in revised form
26 November 2017
Accepted 28 November 2017
Available online xxx

Keywords:
Transarterial chemoembolization
Liver metastasis
Pancreatic adenocarcinoma
Diffusion-weighted MRI
ADC

ABSTRACT

Purpose: To retrospectively investigate the effectiveness of triple drug combination transarterial chemoembolization (TACE) on local tumor response and survival in patients with liver metastases from pancreatic cancer. Also, this study will evaluate the variances in response regarding the number of metastases, assess the correlation between tumor response and the changes in the apparent diffusion coefficients (ADC) in diffusion weighted (DW) MRI.

Materials and methods: One hundred and twelve patients (58 men and 54 women; mean age 57) with malignant liver metastases from pancreatic adenocarcinoma underwent at least one session of TACE with a chemotherapeutic combination of mitomycin C, cisplatin, and gemcitabine. A size-based evaluation of tumor response (response evaluation criteria in solid tumors (RECIST)) was conducted, along with ADC values, and survival indices as related to treatment pattern.

Results: Four weeks following the end of the treatment, 78.26% of patients showed stable disease and 11.59% showed partial response. The median survival time was 19 months and for the stable disease group, 26 months. Low pretreatment ADC values showed no significant correlation to poor response to treatment ($r = 0.347$,$p = 0.146$).

Conclusion: The triple drug TACE technique showed improvements in median survival times in patients with hepatic metastases from pancreatic carcinoma and helped control disease progression, whereas the number of hepatic lesions was not a statistically significant factor in patients' response to TACE. The data suggest that pre-treatment ADC values in DW-MRI have no statistical correlation with tumor response.

Introduction

Pancreatic cancer is a major world health problem, currently representing the 12th most common cancer worldwide and the 7th most common cause of cancer-related deaths [1]. The disease carries a poor prognosis, as it is usually diagnosed at a late stage when the tumor has already metastasized to distant organs.

The most common pancreatic tumor is adenocarcinoma, which originates in the ductal system and constitutes about 80% of all malignant pancreatic tumors [2]. The presence of liver metastases negatively impacts the prognosis and reduces the 5-year survival rate; it also causes additional symptoms that further deteriorate the quality of life of cancer patients [3].

Although there are different approaches to the treatment of pancreatic cancer, surgical resection remains the only potentially curative treatment. However, only 15–20% of patients are eligible for such treatment [4]. Hepatic metastases is associated with shortening the survival time, therefore in patients with advanced disease controlling of liver metastases is a major therapeutic goal [5]. Interventional, loco-regional treatment methods are used in cases of liver metastasis either as a palliative, neoadjuvant treatment or for symptomatic relief [6].

Transcatheter arterial chemoembolization (TACE) has proven to

* Corresponding author.
E-mail address: sherifabdou90@gmail.com (S.A. Mohamed).
[1] These authors share first authorship and have provided equal contribution.

https://doi.org/10.1016/j.pan.2017.11.014
1424-3903/

be an effective treatment of liver metastases from different primary neoplasms [7]. Early assessment of the effectiveness of TACE is paramount to the identification of procedure failure, to guide future therapy, and to determine the interval for repetitive treatment [8]. In addition to tumor response monitoring, functional imaging as diffusion-weighted magnetic resonance imaging (DW-MRI) reveals microstructural changes related to treatment effects over time that usually precedes changes in size [9]. Functional imaging, unlike anatomic imaging, provides information on tumor viability, cellularity, vascularity, and metabolism. These changes can be detected earlier than anatomic changes and are more applicable in assessing treatment response after TACE [10]. However, there is a paucity of evidence regarding the predictive value of DW-MRI concerning tumor response after TACE in patients with liver metastases from pancreatic cancer.

Therefore, the purpose of this study is to evaluate the effectiveness of TACE in patients with pancreatic liver metastasis regarding local tumor response, overall patient survival and show the variances in response concerning the number of lesions and to evaluate the correlation between tumor response and the changes in the apparent diffusion coefficient (ADC) in DW-MRI.

Materials and methods

The study was approved by the ethical committee of our university hospital and conducted retrospectively on patients who had received TACE for metastatic pancreatic cancer between 1999 and 2015.

Patients

One hundred and twelve patients (54 females and 58 males; mean age 57) were enrolled. TACE treatment was considered for the patients who demonstrated signs of tumor progression in terms of an increase in lesion size or the occurrence of new hepatic metastasis despite systemic chemotherapy. A multidisciplinary committee consensus decided who received treatment. Inclusion criteria were: histologically documented pancreatic carcinoma with liver metastasis, administration of FOLFIRINOX as first or second line treatment, nonsurgical candidates or failure to respond to systemic chemotherapy, the age of 18 years or older and have disease measurable according to the Response Evaluation Criteria In Solid Tumors (RECIST) criteria (11). Patients were excluded if they were undergoing concomitant chemotherapy or radiation therapy, tumor burden involved more than 70% of the liver, had metastases to organs other than the liver, or did not have adequate follow-up data available. Other exclusion criteria were severe or uncontrolled medical conditions, anticipated receiving major surgery during treatment, were pregnant or breastfeeding, or showed evidence of a bleeding diathesis.

There were two different treatment trends for these patients. For patients with unresectable diseases, the goal of palliative treatment is to control symptoms, improve life quality and prolong survival. For patients with end-stage advanced disease the main aim is controlling pain as a symptomatic treatment only for improving quality of life. Seventy patients had TACE for symptomatic treatment of pain from tumor stretching the liver capsule.(Only one or two treatment sessions), and the other 42 patients underwent TACE as palliative therapy (more than two treatment sessions). Both groups received the same treatment protocol; the only difference is the number of TACE sessions. On average, patients underwent 2.8 sessions TACE (range 1–14) at 4–8 week intervals. All patients were treated consecutively.

From the symptomatically treated patients, 43 patients had only one session. These patients lacked imaging at the four-week post-treatment interval, excluding them in the response evaluation (Table 1).

Intervention technique

A radiologist with over 20 years of experience performed all TACE procedures. Assessment of anatomy, tumor burden, and vascularity was performed through endo-luminal superior mesenteric and celiac arteriography. In patients with bilobar involvement of the liver, the dominant lobe with higher tumor load was treated first. A catheter was advanced into the target lesion's segmental artery and used to introduce the triple regimen drugs mitomycin C (8 mg/m2; Medac GmbH, Germany), cisplatin (40 mg/m2; Gry Pharma GmbH, Germany), and gemcitabine (1000 mg/m2; Gemzar, Lilly Pharma, Giessen, Germany). After the drugs had been injected via the catheter, a maximum of 15 mL/m2 of iodized oil (lipiodol) and 200–450 mg of degradable 50 μm diameter starch microspheres (EmboCept, PharmaCept, Berlin, Germany) were injected as the embolizing agents to achieve complete stasis. Additional angiographic study of the hepatic artery was performed to confirm devascularization.

Image evaluation

Two radiologists with three and six years of experience respectively in abdominal imaging independently performed all of the assessments. MRI was done using a conventional 1.5-T system (Magnetom symphony; Siemens, Erlangen, Germany). The MRI protocol included T1-weighted unenhanced with transverse and sagittal section orientation, in addition to unenhanced T2-weighted turbo spin-echo sequences and dynamic volume interpolated breath-hold examination sequences. Measurable metastatic lesions greater than 10 mm and the primary tumor were assessed at 24 h pretreatment, directly after each session and four weeks after each session. The mean follow-up time was four months. Tumor response data for all patients; palliatively and symptomatically treated, males and females, with oligo-metastatic ($n < 5$) or multi-metastatic ($n \geq 5$) lesions were considered. Response evaluations were based on the RECIST [11] applied to the findings of MRI. Axial imaging was used to measure the cross-sectional diameters of the tumors as length and their associated perpendicular diameters as width. Coronal imaging was used to measure the longest diameter of the lesion as height.

Target lesions were selected based on their size (longest diameter) and suitability for accuracy in repeated imaging. The baseline sum of the longest diameters of all target lesions was calculated and reported, and the ellipsoid volume formula was used to analyze

Table 1
Demographic and characteristic data of the studied patients.

Variables	Value (n = 112)
Age	
Range	32–82
Mean Age ±S.D.	57.0 ± 22.3
Sex	
Male	58 (51.8%)
Female	54 (48.2%)
Type of treatment	
Symptomatic treatment	70 (62.5%)
Palliative treatment	42 (37.5%)
Number of session	
1 session	43 (38.4%)
2 sessions	27 (24.1%)
>2session	42 (37.5%)
Mean number of sessions (Range)	2.8 (1–14)

Please cite this article in press as: Vogl TJ, et al., Transarterial chemoembolization in pancreatic adenocarcinoma with liver metastases: MR-based tumor response evaluation, apparent diffusion coefficient (ADC) patterns, and survival rates, Pancreatology (2017), https://doi.org/10.1016/j.pan.2017.11.014