CLINICAL STUDY

Yttrium-90 Radioembolization of Advanced, Unresectable Breast Cancer Liver Metastases—A Single-Center Experience

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ABSTRACT

Purpose: To determine value of transarterial radioembolization (TARE) for palliative treatment of unresectable liver-dominant breast metastases (LdBM) and to determine prognostic parameters.

Materials and Methods: Records of patients undergoing TARE for progressing LdBM between June 2006 and March 2015 were retrospectively reviewed; 44 female patients (mean age 56.1 y; range, 34.9–85.3 y) underwent 69 TAREs (56 resin-based, 13 glass-based). Of 44 patients, 42 had bilobar disease. Mean administered activity was 1.35 GBq ± 0.71. Median clinical and imaging follow-up times were 121 days (range, 26–870 d; n = 42 patients) and 93 days (range, 26–2,037 d; n = 38 patients). Clinical and biochemical toxicities, imaging response (according to Response Evaluation Criteria In Solid Tumors), time to progression, and overall survival (OS) were evaluated. Data were analyzed with stratification according to clinical and procedural parameters.

Results: Toxicities included 1 cholecystitis (grade 2) and 1 duodenal ulceration (grade 3); no grade ≥ 4 clinical toxicities were noted. Objective response rate (complete + partial response) was 28.9% (11/38); disease control rate (response + stable disease) was 71.1% (27/38). Median time to progression of treated liver lobe was 101 days (range, 30–2,037 d). During follow-up, 34/42 patients died (median OS after first TARE: 184 d [range 29–2,331 d]). On multivariate analysis, baseline Eastern Cooperative Oncology Group (ECOG) status of 0 ($P < .0001$, hazard ratio [HR] = 0.146) and low baseline γ-glutamyltransferase (GGT) levels ($P = .0146$, HR = 0.999) were predictors of longer OS.

Conclusions: TARE can successfully delay progression of therapy-refractory LdBM with low complication rate. Nonelevated baseline ECOG status and low GGT levels were identified as prognostic factors.

ABBREVIATIONS

ECOG = Eastern Cooperative Oncology Group, GGT = γ-glutamyltransferase, HR = hazard ratio, LdBM = Liver dominant breast metastases, OS = overall survival, RECIST = Response Evaluation Criteria In Solid Tumors, TARE = transarterial radioembolization, TTEP = time to extrahepatic progression, TTHP = time to hepatic progression, $TTHP_{treated}$ = time to hepatic progression of treated part of the liver, $TTHP_{untreated}$ = time to hepatic progression of untreated part of the liver

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Breast cancer is the most common malignant tumor in women with a lifetime risk of 10%–15% (1). Liver-dominant breast metastases (LdBM) are associated with a particularly poor prognosis with a median survival of 1–20 months (2). Surgery as the only curative treatment option of LdBM is feasible in only 10%–20% of patients (3). Yttrium-90 transarterial radioembolization (TARE) has been evaluated for palliative treatment of therapy-refractory LdBM in several studies with promising results (4–10). However, both imaging response and survival rates vary between 26%–75% and 2–14 months, respectively (4–6). To date, the Eastern Cooperative Oncology Group (ECOG) status, imaging response assessment after 3 months rated by Response Evaluation Criteria In Solid Tumors

(RECIST) (11), hepatic tumor burden, presence of extrahepatic disease, and changes in the maximum standardized uptake value on fluorodeoxyglucose positron emission tomography combined with computed tomography (CT) have been suggested as prognostic factors after TARE (4–8). However, although ECOG status was identified as a prognostic factor in most studies, other parameters, such as the presence of extrahepatic disease, were not associated with survival in numerous studies (5,7–9). The clinical value of these parameters remains uncertain and warrants further investigation. The aim of this study was to analyze the value of TARE for palliative treatment of advanced, unresectable, therapy-refractory LdBM and to determine prognostic parameters.

MATERIALS AND METHODS

Patient Cohort

Patients with LdBM who underwent yttrium-90 TARE from June 2006 to March 2015 were retrospectively identified. Indications for TARE were discussed in interdisciplinary conferences according to general inclusion and exclusion criteria for TARE (12,13). All patients had progressive liver metastases after failure of at least 2 lines of chemotherapy. Patients showing disease progression after primary TARE were offered repeat TARE in interdisciplinary consensus. The study was approved by the local institutional review board with a waiver for informed patient consent.

Inclusion criteria of the study were histologically confirmed breast cancer, availability of imaging of the liver (contrast-enhanced magnetic resonance [MR] imaging or CT) before embolization, TARE performed at our institution, and accessible procedural and clinical data. Patients were also included if extrahepatic metastatic disease was present that was stable at the time of evaluation. Patients were excluded if no follow-up information was available.

There were 44 female patients (mean age 56.1 y ± 10.5) who underwent TARE for LdBM. Patient characteristics are listed in **Table 1**. At the time of first TARE, 39 patients presented with extrahepatic disease that had been stable for at least 3 months before TARE. In 1 patient, brain metastases had been treated with stereotactic radiotherapy, and the patient showed complete remission for 18 months.

Baseline clinical and laboratory parameters, procedural data, and results of follow-up examinations were reviewed in the clinical electronic archiving system (C.M. and C.C.P. with 13 and 5 years of experience in abdominal imaging, respectively). The relative liver tumor burden was estimated on baseline cross-sectional imaging by 2 radiologists in consensus. Tumor vascularity was determined on multiphasic contrast-enhanced MR or CT images in comparison to normal liver tissue (hypovascular tumors were hypointense/hypodense on arterial phase imaging; hypervascular tumors were hyperintense/hyperdense on arterial phase imaging).

Radioembolization

Workup before treatment and TARE were performed according to published clinical standards (4 interventionalists with 9 to >30 years of interventional experience) (13,14). TARE was usually performed at least 4 weeks after last administration of systemic chemotherapy (especially bevacizumab). TARE with concomitant systemic chemotherapy was performed only after interdisciplinary discussion in patients with good extrahepatic response to chemotherapy and no signs of compromised liver function. Extrahepatic or excessive pulmonary sphere deposition was excluded by angiography before treatment with injection of technetium-99m macroaggregated albumin and subsequent single photon emission computed tomography combined with CT. Coil embolization of nontarget vessels was performed if necessary. Treatment was performed either in a single session (whole liver/unilobar) or via a sequential lobar approach. Calculation of the prescribed activity was performed in compliance with international consensus guidelines (13) using the body surface area method for resin microspheres (SIR-Spheres; Sirtex Medical Ltd, North Sydney, Australia) and using the medical internal radiation dose equation as provided by the manufacturer of glass microspheres (TheraSphere; BTG International, London, United Kingdom). Microsphere administration was performed with a microcatheter, Renegade (Boston Scientific, Marlborough, Massachusetts) or MicroFerret (Cook, Inc, Bloomington, Indiana). Application of resin microspheres was stopped if imminent stasis (marked reduction of forward flow on angiography not resolving within 5 min) was observed. Medication administered during the procedure included 24 mg dexamethasone, 8 mg ondansetron, and 40 mg pantoprazole. In accordance with local regulations, all patients were admitted for 2 days after TARE.

Toxicity and Adverse Events

Toxicities were evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03 (15) for biochemical parameters (bilirubin, aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase [GGT]), presence of ascites, and procedure-related complications.

Follow-up

Follow-up protocol included physical examination, contrast-enhanced MR imaging or CT, and laboratory liver function tests. Patients underwent early follow-up after 4–6 weeks and a second follow-up examination