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ORIGINAL ARTICLE

Early arterial stasis during resin-based yttrium-90 radioembolization: incidence and preliminary outcomes

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Abstract

Objectives: This study was conducted to determine the incidence of early stasis in radioembolization using resin yttrium-90 (Y-90) microspheres, to evaluate potential contributing factors, and to review initial imaging outcomes.

Methods: Patients in whom early stasis occurred were compared with those in whom complete delivery was achieved for tumour type and vascularity, tumour : normal liver ratio (T : N ratio) at technetium-99m-macroaggregated albumin (Tc-99m-MAA) angiography, previous intra-arterial therapy, and infusion site (left, right or whole liver). Tumour response was evaluated at 3 months and defined according to whether a partial response and stable disease versus progressive disease were demonstrated.

Results: A total of 71 patients underwent 128 Y-90 infusions in which 26 (20.3%) stasis events occurred. Hypervascular and hypovascular tumours had similar rates of stasis (17.4% versus 27.8%; P = NS). The mean ± standard deviation T : N ratio was 3.03 ± 1.54 and 3.66 ± 2.79 in patients with and without stasis, respectively (P = NS). Stasis occurred in 14 of 81 (17.3%) and 12 of 47 (25.5%) infusions following previous intra-arterial therapy and in therapy-naïve territories, respectively (P = NS). Early stasis occurred in 15 of 41 (36.6%) left, 10 of 65 (15.4%) right and one of 22 (4.5%) whole liver infusions ($P < 0.001$). Rates of partial response and stable disease were similar in the stasis (88.3%) and non-stasis (76.0%) groups (P = NS).

Conclusions: Early stasis occurred in approximately 20% of infusions with similar incidences in hyper- and hypovascular tumours. Whole-liver therapy reduced the incidence of stasis. Stasis did not appear to affect initial imaging outcomes.

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Introduction

There are two yttrium-90 (Y-90) radioembolization devices commonly used in clinical practice. The TheraSphere® (MDS Nordion, Inc., Ottawa, ON, Canada) is a glass microsphere which is US Food and Drug Administration (FDA)-approved for the treatment of hepatocellular carcinoma (HCC).[1] SIR-Spheres® (Sirtex Medical Ltd, North Sydney, NSW, Australia) are resin microspheres which are FDA-approved for the treatment of metastatic colorectal carcinoma with concomitant fludarabine.[2] Although these devices both emit beta radiation to induce tumour necrosis following locoregional delivery, they are quite different: most importantly, the glass microspheres contain a much greater density of Y-90 per bead than do the resin microspheres. The net result is that complete dose delivery is always accomplished with glass microspheres without detectable angiographic evidence of embolization.[3] Given the lower density of Y-90 per bead afforded by resin microspheres, full delivery is not always possible as the target artery can develop stasis prior to the completion of infusion.[4]

Although stasis with resin microspheres is an anecdotally known phenomenon, the exact incidence of this event and the factors that contribute to it are not described in the literature. Greater understanding of this event is valuable for multiple reasons. Stasis prevents the delivery of the prescribed activity and can result in non-target infusion with toxic dose administration to extrahepatic tissues.[5,6] As with other types of radiation therapy, resin microspheres are ordered at a specified activity level with the goal of administering a prescribed dose to the targeted tumour(s). The brachytherapy effect of Y-90 microspheres allows the delivery of a greater dose to the targeted liver tumour(s) than does external beam radiation.[7] However, early stasis may potentially lead to early tumour progression secondary to suboptimal dose delivery. The primary goals of this study were to define the incidence of stasis in the study patient population and to evaluate potential contributing factors. Secondary goals were to evaluate imaging responses following treatment and to compare findings in the groups in which complete dose delivery was and was not achieved.

Materials and methods

This study was approved by the institutional review board of Thomas Jefferson University (Philadelphia, PA, USA). All patients treated with resin Y-90 microspheres between January 2007 and February 2010 were included. The criteria for treatment with Y-90 microspheres required that patients demonstrated: (i) confirmed unresectable liver-dominant disease; (ii) an East Coast Oncology Group performance status of 0–2; (iii) adequate liver function (bilirubin of <1.8 mg/dL), haematologic parameters (granulocyte and platelet counts of >1500/microliter and >50 000/microliter, respectively, per μL blood) and renal function (creatinine of <2.5 mg/dL), and (iv) the ability to undergo selective hepatic angiography.

Criteria that excluded patients from treatment included: (i) a life expectancy of <2 months; (ii) a side branch flow to the gastrointestinal tract that could not be avoided or embolized, and (iii) an estimated lung dose of ≥30 Gy.

Yttrium-90 treatment

Baseline cross-sectional imaging, including computed tomography (CT), magnetic resonance imaging (MRI) and/or positron emission tomography (PET)-CT, was obtained based on the primary tumour aetiology. All patients underwent mapping arteriography with side-branch embolization performed as previously described.[6,8] Following side-branch embolization, technetium-99m-macroaggregated albumin (Tc-99m-MAA) was infused into the target arteries to estimate the lung-shunt fraction and evaluate for extrahepatic flow. If outcomes were satisfactory, the first treatment was administered 10–21 days later. The dose prescribed was based on body surface area (BSA) and calculated as:

$$A\,(\mathrm{GBq}) = (\mathrm{BSA} - 0.2) + V_{\mathrm{tumour}}/V_{\mathrm{liver}}$$

where V_{tumour} and V_{liver} represent the volume of tumour and total liver, respectively, and A represents radioactivity in GBq (gigabecquerel). Body surface area in square metres was calculated as $0.20247 \times \mathrm{height\ (m)}^{0.725} \times \mathrm{weight\ (kg)}^{0.425}$.

Prescribed activity was calculated according to the patient's weight, height and tumour volume, and in line with the patient's history of previous therapy. In patients who had previously received either systemic chemotherapy or intra-arterial liver-directed therapy (chemo- or immunoembolization), the dose was reduced by 25%.[9,10] Patients were treated with lobar or whole-liver infusion based on anatomy and tumour burden. If untreated liver remained or if patients underwent whole-liver therapy in multiple fractions, the second treatment was performed 4–6 weeks after the initial infusion.

A standard practice for resin microsphere infusion was followed by all operators. Infusions were performed by four board-certified interventional radiologists with 5–17 years of experience (DJE, JWM, CFG, DBB). The radioactive microsphere dose was pushed through the proprietary delivery kit with small aliquots of sterile water. After flushing the line clear, 2–3-mL aliquots of non-ionic contrast [Ioversol 320 (Covidien, Inc., Hazelwood, MO, USA) or Iodixanol 320 (GE Healthcare, Inc., Waukesha, WI, USA) in patients with a glomerular filtration rate of <60 mL/min] were injected and cleared with sterile water to ensure continued antegrade flow after each pulse of radioactive microsphere delivery. Sterile water infusions were limited to the volume necessary to infuse and clear the microspheres and contrast. When the delivery vial was clear, the vial was emptied by priming the inlet line with air (the 'air shot'). For the purpose of this study, early stasis was defined as an infusion in which the delivery of resin microspheres was halted as a result of a lack of antegrade flow at angiography during infusion. In all cases of early stasis, residual microspheres remained in the delivery vial and the infusion was halted prior to the air shot. Standard post-procedure measurements of the residual dose within the vial were obtained in all patients using a survey meter (portable ion chamber radiation monitor model TBM-IC-AJI; Technical Associates, Canoga Park, CA, USA).

Factors contributing to stasis

Factors that might potentially contribute to early stasis were identified and evaluated. Relationships were tested using chi-squared, Fisher's exact or *t*-tests. Factors included: (i) tumour type; (ii) vascularity (hypo- versus hypervascular)[11] based on angiographic appearance; (iii) a low tumour : normal liver ratio (T : N ratio) at scintigraphic imaging following Tc-99m-MAA angiography; (iv) previous intra-arterial therapy, and (v) infusion site (left, right or whole liver).

Potential effect of stasis on early outcomes

The delivery of an incomplete dose could potentially lead to the failure of treatment and the early progression of disease. The earliest time at which a measurable response to Y-90 therapy can be obtained is at 3 months following treatment.[12,13] As a primary goal