The Role of Transarterial Radioembolization (TARE) in the Management of Hepatocellular Carcinoma

Raj Ayyagari  M.D.
Assistant Professor of Radiology
Section of Interventional Radiology
Yale University School of Medicine
raj.ayyagari@yale.edu
Disclosures

• I do not have any financial interest or other relationship with the manufacturers of any products or providers of services I intend to discuss.
Overview

- TARE Treatment Rationale
- Patient selection
- Technique
- Dosimetry
- Side Effects, Complications
- Clinical Outcomes

Wang EA, Broadwell SR, Bellavia RJ, Stein JP. J Gastrointest Oncol. 2017;8(2):266-278.
TARE Treatment Rationale

- Transarterial radioembolization (TARE) is the hepatic intra-arterial injection of the radioisotope \textit{Yttrium-90} to treat \textit{unresectable HCC}.

- \textit{Yttrium-90}, a $\beta$-emitter with a $\frac{1}{2}$-life of 64.2h and tissue penetration of 2.5-11 mm, is incorporated into glass (\textit{TheraSphere}) or resin (\textit{SIR-Spheres}) microspheres 20-60$\mu$m in diameter.

- By delivering an internal radiation source, TARE is a \textit{form of brachytherapy}. Allows safe administration of therapeutically high radiation doses (up to 150 Gy) with lower risk of radiation-induced liver damage than external beam radiation (at 35-40 Gy).
TARE Treatment Rationale

- High tumoricidal doses achieved by preferential deposit of particles in tumor due to differential perfusion.

- Treatments can be...
  - Whole liver (higher risk)
  - Lobar
  - Segmental (“Radiation Segmentectomy”)
  - Sequential
  - Repeated?

SIRTex, Incorporated
Patient Selection for TARE

- Multifactoral assessment involving disease burden, biochemical profile, and performance status.

- Unresectable, with large majority of tumor burden (if not all of it) in the liver, with <70% of the liver involved.

- Adequate functional liver reserve needed: total bilirubin $\leq 2$ mg/dL, albumin $>3$ g/dL, and a normal INR.

- ECOG performance status score of 0-1, maybe 2.

- Extreme caution when treating patients with ampulla of Vater manipulations due to increased risk of liver abscess.

- Portal vein patency not required, and in fact tumoral portal thrombus cannot be treated any other way.
TARE Technique
TARE Technique

- Outpatient procedure involving an initial mapping mesenteric angiogram combined with a liver-lung shunt scan, followed by dose planning and a subsequent angiographic treatment procedure.

- If radioactive particles embolize anywhere but the targeted liver (via shunts, collaterals, reflux)...
  - Lungs: Radiation pneumonitis
  - Stomach/Bowel: Ulcers, bleeding, perforation
  - Can be DEVASTATING.
TARE Technique

• Mapping mesenteric angiogram goals:
  – embolize collaterals (GDA, right gastric artery) ...hepatic arterial variants are common!
  – evaluate arterial anatomy to plan catheter placement
  – obtain liver lobar/segmental/tumoral volumes ...needed for dosimetry.
  – inject ~4 mCi technetium-99m MAA test dose ...arteriovenous shunting can be extensive!
TARE Technique
TARE Technique
TARE Dosimetry

- Lobar or segmental liver volumes are calculated using diagnostic MRI/CT, axial SPECT-CT, or even better, cone-beam CTA images.
- Liver tumor volumes are calculated using a diagnostic MRI/CT.
- BSA is calculated using patient height and weight.
- Lung shunt fraction is calculated by a nuclear medicine scan that measures the amount of $^{99m}$Tc-MAA that gets to the lungs.

Treatment Dose calculation method differs based on whether glass TheraSpheres (2500 Bq/sphere) or resin SIR-Spheres (50 Bq/sphere) are being used.
TARE Dosimetry

• TheraSpheres:

Activity = \text{Absorbed Dose (Gy)} \times \text{Mass of Liver} \times 50 \times (1-%\text{LSF}/100) \times (1-%\text{R}/100)

Target delivered activity is typically 80-150 Gy

• SIR-Spheres:

Activity = BSA – 0.2 + %\text{Tumor}

LSF <10\% = no dose reduction; LSF 10-15\% = 20\% reduction; LSF 15-20\% = 40\% reduction
SIDE EFFECTS:

- Fatigue – 50-60% patients in first 1-2 weeks after.
- Low grade abdominal pain, nausea/vomiting – 20%.

COMPLICATIONS:

- **Radiation-induced GI ulcers** often refractory to conservative management.
- Biliary complications (10%): dyskinesia, cholecystitis (2.7%), stricture (2.4%), necrosis (3.9%), biloma (1%).
- Radiation-induced liver disease – sinusoidal congestion, venous occlusion, hepatic fibrosis; 4-8 weeks after; 4-7%, but in a series including liver metastatic lesions previously treated with chemotherapy; *no predictive model for RILD*.
TARE Clinical Outcomes

• 1-year survival rates of untreated HCC patients are ~50% among intermediate stage (BCLC-B) patients and ~25% among advanced stage (BCLC-C) patients.

• Salem et al reported TARE results in 291 intermediate and advanced stage patients. Response rates were 42% (WHO) and 57% (EASL). TTP was 7.9 mo. CP-A patients had median survival of 17.2 mo, CP-B 7.7 mo, and CP-B with PVT 5.6 mo.

• Hilgard et al validated these results in 108 patients, and showed outcomes equivalent to cTACE and DEB-TACE.

• A 325 patient study by Sangro et al showed TARE patients to have median survival of 24.4 mo (BCLC-A), 16.9 mo (BCLC-B), and 10.0 mo (BCLC-C).
TARE Clinical Outcomes

- As yet, no RCT comparing TARE and TACE in HCC.

- Salem et al’s “comparative effectiveness report” of a 245 patient cohort (123 TARE, 122 cTACE) described adverse events, toxicities, response rates, and TTP to be improved in TARE, with no difference in overall survival.

- TARE has also been shown to superior favorable rate of down-staging HCC patients to transplantation.

- TARE also seems to cause less hepatotoxicity than TACE in patients with a TIPS in place, likely due to the minimal embolic effect of TARE.
REFERENCES

THANK YOU!

ANY QUESTIONS OR COMMENTS?

Raj.Ayyagari@yale.edu
Cell: 206-853-0197