Follow up After Locoregional Liver Treatments in Patients with Cancer

Introduction:
Over the last several decades interventional radiology has consciously established itself as a clinically oriented specialty. At the same time, the specialty has demonstrated its value in oncology care. Liver-directed therapy is perhaps one of the greatest examples of the benefits interventional radiology locoregional therapies can provide for patients. Treatment of these patients also requires and highlights the importance of a robust clinical service to provide adequate follow-up.

Follow up after locoregional liver treatments in patients with cancer is beyond question. However, patients can be lost to follow-up, which can lead to delays in care and worse outcomes. Ensuring that patients receive timely follow-up appointments and have the appropriate information, such as labs and imaging, available for these visits can be a challenge. This subject can make for an excellent topic for quality improvement (QI) projects, as it is both significant to patient care and measurable.

This toolkit, developed by the Society of Interventional Radiology’s (SIR’s) Practice Improvement and Change Committee (PICC), reviews this subject and provides an example of how interventional radiologists may go about evaluating their own practice in a systematic and critical way.

Data collection planning
In the early stage of project development, the IR should consider what type of data they will be analyzing throughout the process. Data collection planning will ensure that collected data will be useful and reliable for performance improvement without excessive resource investment, either cost or time.

When determining what data to collect consider the following:

- Why are we collecting the data?
- What data analysis tools will be used to display the data (e.g., run chart, control chart)
- What type of data is needed?
- Where in the process can we get this data and from whom?

Keep in mind that the goal is to collect data with minimum effort, minimum chance for error, and with periodic audits to ensure accuracy and completeness.
CASE STUDY

Dr. Linda Johnson is participating in tumor board when a familiar patient is presented. The 72-year-old patient was treated by Dr. Johnson 4 years ago with transarterial radioembolization (TARE) of a 5 cm right lobe hepatocellular carcinoma (HCC). The patient now has a 12 cm left lobe lesion with portal vein invasion. On review of the case Dr. Johnson realizes that the patient was not followed in clinic after the treatment, with the last communication coming on day 2 after treatment when she called to ask how the patient was doing. The patient lives in a small community 2 hours away and was referred to Dr. Johnson’s larger medical center by a local hepatologist. That hepatologist has since retired and the patient has only received periodic care from his primary care physician. A similar case was presented 4 months ago at tumor board, where a patient had been lost to follow-up after microwave ablation (MWA). Dr. Johnson decides to do a quality improvement (QI) project to determine how frequently she is losing patients to follow-up.

Current evidence and analysis

Follow-up imaging for liver directed therapy is important in evaluating treatment response and allowing prompt treatment of recurrent or residual disease, particularly as early detection of residual tumor has been correlated with better outcomes. It is important to remember that imaging response does not perfectly reflect pathologic response. Furthermore, determining response in the first month after TARE may be more difficult than with other locoregional therapies such as thermal ablation and transarterial chemoembolization (TACE). Several authors have questioned the utility of 1 month post TARE imaging, with one study finding that it rarely changed management in patients with HCC but did change management in up to 16.7% of patients being treated with metastatic disease. The difficulty, particularly with magnetic resonance imaging (MRI), is secondary to the fact that expected post treatment changes at 1 month after TARE can appear very similar to residual disease.

Several authors have attempted to evaluate the ideal follow-up schedule. For instance, Boas et al evaluated follow-up imaging for hepatocellular carcinoma in chemoembolization, radioembolization and radiofrequency ablation (RFA), and found recurrence is most likely in the first year after treatment and proposed imaging to be done 2, 4, 6, 8, 11, 14 and 18 months post-treatment. Alternatively, a consensus publication of the European Conference on Interventional Oncology-European Society of Oncologic Imaging (ECIO-ESOI) recommended follow-up multiphasic imaging at 1, 3, 6, 9 and 12 months and every 6 months thereafter following liver-directed therapy. While recommendations vary, as indicated above, the importance of close follow-up in the year following treatment is widely recognized.

While the modality of follow-up imaging has been debated, the commonly discussed options include multiphasic computed tomography (CT), multiphasic MRI and positron emission tomography (PET) CT. Each modality has positives and negatives when it comes to the unique nature of TARE, especially in the setting of HCC, MRI is often felt to be the ideal modality. MRI is superior to CT in terms of being able to diagnose HCC by imaging. However, there is ongoing research into improvements in response assessment, particularly in the early post-procedural period.

Follow-up recommendations: locoregional treatments for HCC

- Imaging with multiphasic MRI or CT every 3–6 months for 2 years, then every 6 months.

- Serum AFP every 3–6 months for 2 years, then every 6 months. Sensitivity for detecting disease progression increases with the additional measurement of AFP-L3 and DCP.

- Surveillance imaging and laboratory measurement should continue for at least 5 years and thereafter screening dependent on HCC risk factors.
Recurrence is 6.5 times more likely in the first year after treatment than in the subsequent year. Therefore, screening should be frequent in the first year. A suggested, optimal schedule for follow-up within the first two years would be: 2, 4, 6, 8, 11, 14, 18 and 24 months post-treatment.\cite{17}

Multiphasic contrast-enhanced MRI or CT of the abdomen and pelvis are the preferred modalities of assessment, as they reliably evaluate intranodular arterial vascularity, a key feature of residual or recurrent tumor.\cite{16} Multiple consensus panels support the utilization of gadoxetic acid as the preferred MRI contrast medium.\cite{18,19} CT imaging should include a quadruple-phase protocol, which includes unenhanced images as well as arterial, portal venous and delayed phases. Sufficient evidence is lacking on new techniques such as diffusion-weighted imaging, dynamic contrast-enhanced magnetic resonance imaging (DWI/DCE-MRI) as well as perfusion CT, but these techniques are promising.\cite{20} PET/CT has limited sensitivity but high specificity and may be considered when there is an equivocal finding on MRI.\cite{21}

The Liver Reporting & Data System (LI-RADS\textsuperscript{®}) treatment response (LR-TR) classification system is well-suited for the assessment of lesions after radioembolization therapy.\cite{22} Briefly, post-treatment lesions can be classified as non-evaluable, viable, nonviable or equivocal. Common nonviable findings include lack of lesional enhancement or a treatment-specific, expected enhancement pattern (e.g., peripheral nodules, which may represent slowly developing necrosis).\cite{23} Viable residual disease features nodular, mass like or thickened tissue along the margin of the treated region, with findings of arterial phase hyperenhancement, washout appearance and/or enhancement similar to pre-treatment. Nodular arterial phase enhancement or washout appearance along the margin of a treated lesion which persists on serial imaging is most suspicious for recurrence or residual viable tumor. Again, after radiation-based treatment, intralesional enhancement and washout appearance may persist for months, but should eventually regress.\cite{24}

Studies using histopathological correlates suggest that LR-TR is effective at predicting residual tumor with a sensitivity of 40–77\% and nonviable tumor with complete lesional necrosis with a sensitivity of 81–85\%.\cite{25} In comparative analysis, the LR-TR has proven to have greater specificity but comparable sensitivity relative to mRECIST.\cite{26}

Overall, nodule size does not reliably indicate treatment response since a variety of factors may cause a successfully treated lesion to appear stable in size or even larger after treatment. Therefore, mRECIST or EASL criteria are preferred. Response evaluations that use the mRECIST provide more accurate prognoses than those that use the RECIST 1.1 in HCC patients treated with TARE.\cite{27}

Serum tumor markers can effectively supplement imaging analysis of treatment response. The combined elevation of alpha-fetoprotein (AFP), \textit{Lens culinaris} agglutinin-reactive fraction of alpha-fetoprotein (AFP-L3) and des-gamma-carboxy prothrombin (DCP) has been shown to effectively predict disease progression. Specifically, when elevations of all three tumor markers are considered together, studies have reported a comparative increase in the size of the largest tumor, the overall number of tumors, and the prevalence of portal vein thrombosis.\cite{28} Elevation in AFP-L3 has been associated with microsatellite lesions and hypervascularity of HCC.\cite{29,30,31} Elevated DCP has been associated with portal vein invasion.\cite{32}

**Key driver diagram**

- **AIM**: All patients receive appropriate laboratory and imaging follow-up following locoregional therapy.
  - **PRIMARY DRIVERS**:
    - Improve clinic follow-up
    - Dictation templates
    - Staff communication
  - **SECONDARY DRIVERS**:
    - Improve clinic follow-up
    - Dictation templates
    - Staff communication
  - **SPECIFIC IDEAS TO TEST / CHANGE CONCEPTS**:
    - Communication with referring providers
    - Utilize SIR standardized report template
    - Review follow-up guidelines with referring providers
    - Provide education at Tumor board
    - Confirm up-to-date patient contact information at procedure appointment
    - Create and utilize standard procedure letter for referring providers

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Society of Interventional Radiology (SIR) - Follow up After Locoregional Liver Treatments in Patients with Cancer
Follow-up laboratory and imaging evaluation of patients who have undergone locoregional therapy for primary or secondary hepatic malignancies has been inconsistent and has led to patients not receiving appropriate follow-up.

Our plan is to establish and institute a systematic process to improve follow-up after hepatic locoregional therapy with the goal of 100% of patients receiving timely clinic follow-up appointments with appropriate laboratory and imaging testing. To achieve this endpoint, we need to ensure:

- IRs agree on consistent post-locoregional therapy follow-up for the entire practice.
- Medical assistants and/or ancillary staff is maintaining good communication with patients and referring providers to emphasize the importance of follow-up.
- Patients are counseled appropriately at time of discharge and given educational resources (in discharge paperwork along with clinic visit) to facilitate their understanding of appropriate follow-up.

**PDSA (plan, do, study, act) cycle**

**PLAN**

Meet with all relevant parties (IRs, referring providers and clinic staff) and agree on follow-up interval for imaging and laboratory tests.

Data points:

- Hospital (city, state)
- Date of birth/Name
- Contact information (phone numbers, email)
- Medical Record Number
- SIR standardized report template used? (Y/N)
- Follow-up (specifically mentioned in dictation)
- Patient provided with patient handout at discharge? (Y/N)
- Date of follow-up imaging and laboratory tests

**DO**

Implement the plan and keep track of patient data.

- Tabulate the data from the registry
- Analyze trends and/or specific instances where breakdown(s) may have occurred
- Use SIR standardized report templates
- Educate the patients before and after the procedure
- Disseminate the information to consulting physicians, specifically mentioning the planned follow-up
- Follow-up (specifically mentioned in dictation)
- Patient provided with patient handout at discharge? (Y/N)
- Date of follow-up imaging and laboratory tests

**STUDY**

Collect data, begin analyzing trends and try to identify major issues with patient follow-up.

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**ACT**

- Use information gained from the “Study” portion of the PDSA cycle to analyze current strategies and implement modifications to the current plan(s) or update the plan altogether based on the deficient areas leading to lack of timely follow-up and imaging.
- Discuss trends and assess improvement of patient and imaging follow-up compared to the historical data.
Locoregional liver treatments are an integral component of many interventional radiology practices, and this toolkit provides a valuable framework for interventional radiologists to optimize their oncology service line. By conducting studies, employing PDSA cycles, and using tools like the key driver diagram, interventional radiologists can systematically evaluate patient care at every step. This toolkit enables IRs to refine follow-up techniques, promote patient education, improve overall outcomes, and provide exceptional patient-centered care.
References:


16. American College of Radiology ACR Appropriateness Criteria Chronic Liver Disease https://acsearch.acr.org/docs/3098416/Narrative/


