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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Understanding Recurrence Patterns and Time Courses of Intrahepatic Cholangiocarcinoma After Surgery Helps in Postoperative Surveillance and Treatment

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PAST

Surgical resection is the optimal curative treatment for intrahepatic cholangiocarcinoma (ICC); however, the high incidence of tumor recurrence after surgery remains the major reason for unfavorable outcomes.[1] As such, some investigators have reported benefits of re-treatment of recurrence disease after surgical resection for ICC,[1,2] even though management of recurrent disease is clinically challenging as many patients have extrahepatic recurrence or unresectable intrahepatic recurrent disease. In fact, recurrence of ICC after surgical resection of primary disease can occur at the surgical margin, an intrahepatic site away from the margin, and/or extrahepatic organs, which indicates different disease biology and progression. Previous data have demonstrated that a 2-year cut-off value could be used to differentiate overall early versus late recurrence; early recurrence was defined as recurrence of the primary tumor as a result of aggressive tumor biology and inadequate resection, whereas late recurrence was defined as a de novo tumor associated with liver cirrhosis only.[3] Therefore, understanding different recurrence patterns, timing course, and risk factors is important to tailor postoperative surveillance and perioperative adjuvant treatment strategies.

PRESENT

In the current multi-institutional study,[4] 920 patients undergoing curative-intent resection for ICC were included. With a median follow-up of 38 months, 607 (66.0%) patients experienced tumor recurrence following resection. Among patients who recurred, 145 (23.9%) recurred at the surgical margin, while 178 (29.3%) recurred at a different site within the liver. In contrast, 90 (14.8%) patients had extrahepatic-only recurrence and 194 (32.0%) patients developed both intra- and extrahepatic recurrence. Of note, each recurrence pattern had different timing courses. Specifically, intrahepatic margin recurrence (median 6.0 m) and extrahepatic-only recurrence (median 8.0 m) occurred earlier, while intrahepatic recurrence at non-margin sites occurred later (median 14.0 m). In addition, different recurrence patterns were associated with different risk factors. For example, margin recurrence was only associated with inadequate margin < 10 mm, intrahepatic recurrence at other sites was associated with female sex and liver cirrhosis, while tumor size > 5 cm was associated with extrahepatic-only recurrence. Repeat curative resection of recurrent disease can improve the outcome of a select subset of patients who recurred.

FUTURE

Treatment of ICC and recurrent disease is still challenging. While margin recurrence was mostly a consequent of inadequate margin, ensuring a surgical margin wider than 10 mm might be important to decrease this type of recurrence. Inadequate margin is not always a technical

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issue, but due to aggressive tumor characteristics, such as larger size, compromised liver function as well as major vascular invasion. As such, postoperative adjuvant therapies should be indicated for these patients.[5] Underlying liver cirrhosis secondary to hepatitis B/C virus infection, alcoholic or non-alcoholic liver disease might also be a risk factor for the development of ICC and de novo recurrence of ICC.[3] As such, strict postoperative surveillance should be obeyed, even during a long period of time after initial surgery, among these patients, for early detection as well as re-treatment of recurred disease. Due to the heterogeneity of ICC, future studies should be important to identify specific biomarkers or genetic signatures for the prediction of different patterns of recurrence.

DISCLOSURES Timothy M. Pawlik has no conflicts of interest to disclose.

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