

# CRC IN FOCUS

Current Developments in the Management of Colorectal Cancer

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## Liver Transplant in Patients With Metastatic Colorectal Cancer



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### H&O How common are liver-limited metastases in colorectal cancer (CRC)?

**BA** Approximately one-third of patients with metastatic CRC (mCRC) have metastases that are isolated to the liver. Of these patients, about 10% have nonresectable disease and are potential candidates for a liver transplant. Annually, less than 2% of liver transplants in the United States are for patients with isolated metastases to the liver in CRC.

### H&O What are the other treatment options for liver-limited mCRC?

**BA** Most people with liver-limited mCRC can undergo resection successfully. Patients who have nonresectable disease will typically receive locoregional therapy and/or chemotherapy, both of which can also be used in patients who have experienced recurrence after resection. Locoregional therapy options include ablation therapy, radioembolization, and chemoembolization. All these options can be effective, but they can also have a negative effect on the liver. In some cases, the treatments lead to liver dysfunction and the need for a liver transplant. One of the drawbacks of chemotherapy, which has many side effects, is that it may need to be continued for the rest of the patient's life.

### H&O What is the history of liver transplant in mCRC?

**BA** Early attempts at liver transplant in mCRC in this country occurred in the 1980s and were associated with poor survival and high rates of recurrence. Based on the poor outcomes and the shortage of donor organs, the

practice was abandoned, and liver transplant was used primarily for liver failure. That changed again with the publication of the landmark SECA-I and SECA-II studies from Norway.

### H&O Could you describe these studies?

**BA** These studies enrolled a highly selected population of patients with CRC and unresectable liver-limited metastases. The SECA-I study enrolled 21 patients with mCRC who had good clinical performance (Eastern Cooperative Oncology Group score of 0 or 1), had undergone complete resection of the primary tumor, and received a minimum of 6 weeks of chemotherapy.<sup>1</sup> The 5-year overall survival (OS) rate with liver transplant was 60%, which represented a major improvement over the 5-year OS rate of 10% that was seen with palliative chemotherapy for unresectable mCRC. That was when transplant for mCRC started to be a viable option.

That finding led to the SECA-II study, which enrolled 15 CRC patients with nonresectable liver-only metastases as determined by imaging who had a response to chemotherapy of at least 10%.<sup>2</sup> Thanks to improved selection criteria, the patients in SECA-II had a significantly better prognosis than those in SECA-I. As a result, the 5-year OS rate was 83%.

The investigators behind the SECA-I and SECA-II studies published long-term results on 61 patients who underwent liver transplants for isolated colorectal metastases, the 10-year overall survival was close to 40%.<sup>3</sup> The studies also found 4 clinical variables associated with a worse prognosis: (1) tumor diameter greater than 5.5 cm; (2) carcinoembryonic antigen level greater than 80 ng/mL;

(3) interval between resection and liver transplant of less than 2 years; and (4) disease progression during chemotherapy. Patients with no more than 2 of these clinical variables were far more likely to survive 5 years after liver transplant than those who had 3 or 4 variables. This scoring system is known as the Oslo score.

### H&O Which patients with mCRC are eligible for a liver transplant?

**BA** We are looking for mCRC with metastases that are limited to the liver and are not resectable. The patient should have had a response to chemotherapy of at least 10%, and a time lag of approximately 1 year between the resection of the primary tumor and the transplant without any significant progression of disease. In some studies, the OS rate is as high as 80% for patients who meet all these criteria.

We are continuing to refine these criteria to improve outcomes. For example, we have learned that results are better in patients whose CRC began in the left side of the colon rather than in the right side. That does not mean that we will not perform a liver transplant on a patient whose CRC began on the right side, but this factor is something that we now take into consideration when we evaluate patients.

We are also learning more about the genetics of CRC and how it affects prognosis. For example, a patient whose CRC has a *BRAF* mutation should not receive a transplant because the recurrence rate is so high. A *RAS* mutation is also associated with an increased risk for recurrence but is not considered an absolute contraindication to liver transplant.

Patients whose histology shows undifferentiated cancer are poor candidates for liver transplant because the recurrence rate is so high. Disease stage at the time of resection is also important; we prefer to see a tumor stage no greater than T4 and a lymph node stage no greater than N2.

### H&O What other studies have looked at the use of liver transplant in mCRC?

**BA** A cohort study was recently published that combined results from 3 leading North American transplant centers: the University of Rochester Medical Center in Rochester, New York; the Cleveland Clinic in Cleveland, Ohio; and the University Health Network in Toronto, Canada. Of 91 patients who were evaluated for transplant, just 10 made it to the transplant list and underwent a living-donor liver transplant. The results were excellent, with 1.5-year recurrence-free survival and OS rates of 62% and 100%, respectively.<sup>4</sup>

A few caveats about the existing research: these studies have small numbers of patients, they do not include

a comparison group, and the entry criteria continue to evolve. When we compare the results with those of historical control groups, however, we see major improvements. As a result, the International Hepato-Pancreato-Biliary Association published a consensus document in 2021 specifying which patients with mCRC can benefit from a liver transplant.<sup>5</sup>

There are approximately 10 transplant centers in North America that are performing liver transplants for mCRC at this time, but we can expect this number to expand as the success rates continue to improve. Patients with liver metastases from CRC are not prioritized on the transplant list because livers are typically allocated based on the severity of the liver disease, but this procedure is a good candidate to be an exception to that rule. We expect this priority status to be granted so we can offer transplants to more and more patients with mCRC.

### H&O What has been the experience of your institution with liver transplant for mCRC?

**BA** We have performed this procedure in fewer than 10 patients, and our experience has mirrored what we see in the literature. We do not yet have long-term data, but we are seeing a 3-year OS rate of approximately 50%.

### H&O Is there anything you would like to add?

**BA** As we talk about the outcome of transplant in those patients, OS and recurrence-free survival are both important. Achieving acceptable OS rates in these patients, even if some have limited recurrence after transplant, should be considered a success—especially if it has helped the patient maintain a good quality of life without the need for systemic chemotherapy.

### Disclosures

*Dr Aqel has no disclosures to report.*

### References

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