Liver resection post-selective internal radiation therapy – an overview

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1. Introduction

Surgical resection of primary and secondary liver tumours or liver transplantation are the only potentially curative options. However, only a minority of patients (15–25%) with primary hepatocellular carcinoma, intrahepatic cholangiocarcinoma, colorectal liver metastases, neuroendocrine metastases and non-colorectal and non-neuroendocrine metastases are suitable for surgical resection. There remains debate about the definition of resectability, but this is broadly acknowledged to be complete removal of all tumour (R0 resection) whilst leaving sufficient functioning liver remnant (approximately 25% of the liver) for post-operative survival. The balance of tumour clearance and residual liver parenchyma is dictated by the anatomical distribution of the tumours and the function of the underlying liver parenchyma.

The value of liver resection for colorectal metastases is reported by the Liver Met Survey database (www.livermetssurvey.com). There is however, wide variation in the rates of hepatic resection. In the UK for example, a four-fold difference in liver resection rate following resection of primary colorectal cancers was recorded between Cancer Networks and a seven-fold difference between hospital Trusts. To expand the pool of potentially resectable patients, adjuvant chemotherapy has been popularised by the work of several groups demonstrating that even initially unresectable liver metastases can be downstaged/downsized to resectability with a 33% five-year survival. More recent studies of cetuximab (EGFR inhibitor) combined with oxaliplatin- or irinotecan-based chemotherapy have again proved to be effective in downstaging patients with liver-dominant colorectal cancer with subsequent improvements in progression-free survival and overall survival after liver resection. These reports of improvement in outcomes of patients with initially unresectable disease are supported in principle by the CLOCC Trial data which suggest an improvement in progression-free survival after ablation of colorectal metastases when compared with control.

2. Downstaging for resection with SIRT

It would seem reasonable therefore, that downstaging with other modalities such as selective internal radio-
therapy (SIRT) might confer a similar survival advantage. SIRT is a liver-directed therapy that delivers significant intra-hepatic radiation doses to the tumours while minimising the risks of radiation exposure to the normal parenchyma. A number of randomised controlled trials and single-arm studies have reported characteristically high objective response rates with SIRT varying between 90% in the first-line setting,4,5 45% in the second-line setting6 and 25−35% in chemorefractory patients.7 Combining SIRT and modern oxaliplatin-based chemotherapy regimens first-line, Sharma et al. (2007)5 showed that 80% of patients responded (by RECIST criteria) and two of the twenty patients were downstaged to resection.8 Of interest will be the data now being collated in over 900 patients from two large phase III studies [FOXFIRE (UK) and SIRFLOX (multinational)] on the proportion of patients downstaged for resection following first-line chemotherapy with mFOLFOX and SIRT.

Analyses of the published data on SIRT suggest that approximately 10% of patients with liver metastases are downstaged for resection. Unfortunately, most of the currently published studies are of mixed tumour populations and it is difficult to ascertain the true value of SIRT. Certainly, the conversion rate to resection in HCC and other primary liver cancers is lower and this probably reflects the concomitant underlying chronic liver disease in these patients.9

3. Radiation lobectomy

The concept of radiation lobectomy with SIRT was first reported by Gulec and colleagues in 2009.10 This technique relies on the embolisation of one hemi-liver such that atrophy of the treated liver occurs with compensatory hypertrophy of the contralateral side. This form of hypertrophy has the added advantage of simultaneous tumour control and may represent an advantage over traditional portal vein embolisation.

4. Findings in resected livers post-SIRT

With regard to the pathological findings after liver resection, 90Y microspheres are mainly localised in the tumour vasculature. The non-tumour bearing liver showed evidence of portal triaditis with portal and periportal fibrosis but without cirrhosis in reported cases.11

5. Conclusions

In conclusion, interpretation of data following liver resection in patients who were downstaged with SIRT is difficult due to the small number and size of studies. There appears to be minimal additional morbidity over and above that expected from liver resection with approximately a 10% conversion rate of inoperable metastases to R0 resection, but with fewer conversions where there is underlying chronic liver disease. There are no reports of specific post-SIRT hepatotoxicity after resection in the literature and neither is there any evidence of cirrhosis in the resected specimens. The time lag to surgery after SIRT should be at least 8 weeks after treatment and, indeed, most data report maximal effect of SIRT at 3−6 months. It remains to be proven whether there are long-term associated benefits of downstaging tumours with SIRT prior to resection, but there seems no reason why results with this technique should not mimic those of adjuvant chemotherapy.

Conflict of interest statement

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References

