neuroendocrine tumors, breast cancer, and melanoma. However, currently available data in patients with liver metastases from melanoma is quite heterogeneous with some data being obtained in a salvage situation. Kennedy et al. reported their experience treating a small number of patients with hepatic metastasis of uveal melanoma using \(^{90}\)Y radioembropheres. In that retrospective multicenter study, 11 patients underwent 12 SIRT procedures with a median activity of 1.55 GBq delivered per treatment. Only one patient experienced a grade 3 event, a gastric ulcer that healed uneventfully within 6 weeks with supportive care. No radiation-induced liver disease (RILD) was detected. CT and PET of hepatic metastatic lesions 3 months after treatment showed one complete response, six partial responses, one case of stable disease, and one case of disease progression in nine evaluable patients. Among the 10 patients with available clinical follow-up information, the 1-year survival rate was 80%. The relatively low response rate (one complete response, one partial response, and 8 cases of stable disease in 32 patients) in the study of Gonsalves et al. study compared with that found by Kennedy et al. may be explained in part by the inclusion of previously treated patients with bulky progressive hepatic metastatic lesions (from Gonsalves CF et al, AJR 2011; 196:468–473).

**Literature:**

and mortality. Intra- and/or extrahepatic recurrent disease after resection of BCLM were common, and recurrence rates (RR) of 33–78% were reported (available in 15/30 studies).

2. Prognostic factors after liver resection: Patient age was generally without significance, except in one study by Lubrano et al. General features of the primary breast cancer (site, procedure, grade, TN-stage, presence of axillary glands) have generally not been found significant for the prognosis after resection of BCLM. In some studies, the presence of hormone receptors indicated a better prognosis. Her2-status has not been associated with better prognosis.

“Disease interval” (between primary breast cancer and occurrence of BCLM) was studied in 12/30 studies of liver resection. It was a prognostic factor in five studies, but failed to be significant in several other studies, which used cut-offs at 6 months, 12 months and 24 months, respectively. The reasons for these differences are not obvious. A possible explanation may be statistical error, as most studies include few patients with synchronous BCLM.

Sizes and number of BCLM were not found significant for the prognosis in most studies, although two studies found that more than one BCLM indicated a worse outcome. Invasion of the liver vasculature was a negative prognostic factor in one study by Thelen et al.

The presence of extrahepatic metastases (EHD) was a negative factor in the studies by Sakamoto et al. and Thelen et al., but was found non-significant in the studies by Selzner et al., Yoshimoto et al., and Adam et al. Hilar lymph node metastases were found without importance in the studies by Selzner et al., Elias et al., Sakamoto et al., and Adam et al., as were “abdominal gland metastases” in the study by Yoshimoto et al.

3. Therapy-related prognostic factors: Major liver resection was done in 6–82% of cases. Type of liver resection (minor vs. major) was not significant for the prognosis in most studies; only one study by Lubrano et al. found major resection linked to worse prognosis.

The reported rates of R0-resection were 65–100%, and it was a positive prognostic factor in four studies by Lang et al., Adam et al., Thelen et al., and Hoffman et al., although it was non-significant in the studies by Elias et al., Belda et al., Abbott et al., van Walsum et al. Repeat hepatectomy was rarely performed, but was linked to positive prognosis by Adam et al.

The importance of an objective response to chemotherapy before liver resection has been stressed by some authors. Adam et al. found that a partial response to chemotherapy predicted better survival. This agrees with a recent study by Abbott et al. who found that disease progression just before hepatectomy was linked to poor survival. However, chemotherapy response was without significance in some other studies by Pocard et al., Vlastos et al., and Elias et al. However, a clear-cut disease progression during preoperative chemotherapy was an adverse factor in two studies [Treska et al., Selzner et al.], which agrees also with a previous study by Elias [Elias et al.1991]. Taken together, the literature indicates that the response to chemotherapy will influence on the prognosis.

4. Selection of patients for liver resection: Few patients with BCLM are currently candidates for liver resection; two studies reported that they made liver resection in <1% of a breast cancer cohort. Consequently, nearly all studies reviewed were accumulated over more than a decade. Two institutions only made more than (average) five resections per year, and most of them considerably less.

Features of the primary BC were generally not stated as criteria of selection. “Disease interval” (between primary cancer and occurrence of metastases) is widely believed to reflect tumour biology, but it was rarely mentioned among the inclusion criteria. However, most studies had a low rate of synchronous metastasis (disease interval <6 months); the range being 0–31%, and it may be suspected that “disease interval” was inexplicably included in the preoperative selection process in many studies. Some studies stated that they resected only patients with less than 3–5 BCLM, although several studies made liver resection also of multiple BCLM. As a consequence, the size of the largest BCLM resected also varied greatly between the studies; BCLM well exceeding 10 cm were included in several studies. However, the mean diameters of the largest BCLM were mostly in the range 3–5 cm. Liver resection in patients with extrahepatic metastases (EHD) remains a controversial issue, but the criteria varied widely. Eight studies excluded patients with EHD, while three studies accepted stable bone metastases. Ten studies accepted various EHD, as long as they were deemed resectable and/or stable on treatment.

5. Outcome after local ablation: The studies of local ablation reported post-treatment 2-, 3- and 5-year survivals of 42–80%, 43–75% and 27–41%, respectively. Post-treatment MOS was 11–60 months. The rate of synchronous metastases was similar to the studies of liver resection, 0–19% (reported in 4/8 studies). The maximum number of BCLM was generally restricted to <5, although two studies accepted a maximum number of 8 and 13, respectively. Likewise, mean sizes of the largest BCLM were in the same range as in the studies of liver resection. However, three studies included BCLM up to a maximum diameter of 7 cm. Further, patients with EHD were accepted in all but one of the studies using local ablation. The largest study, using LITT, reported MOS 52 months, and 2-, 3-, and 5-year survivals were 80%, 63% and 41%, respectively, although this study included patients 1) unetectable; 2) unfit for or refusing resection; 3) with recurrent BCLM; 4) with bilateral BCLM; 5) with stable bone metastases; 6) with multiple (up till 13) BCLM.

Conclusions: The available literature supports use of liver resection in the selected subset (<5%) of patients with isolated BCLM, if an R0-resection is possible and if the procedure adheres to current standards regarding postoperative morbidity and mortality. Also local ablation was associated with good long-term outcome, and may be a relevant alternative for small BCLM or in patients unsuited for liver resection. The coagulation necrosis caused by RF is usually not larger than 3 cm, however, which increases the risk of local recurrence. Meloni et al. have found that RF of BCLM >2.5 cm increased the risk of death by a factor 2.1. So far resection of BCLM remains the first choice, but the less invasive nature and a lower risk of complications make RF a relevant alternative for unresectable or otherwise “surgically unfit” patients. The long-term outcome, and may be a relevant alternative for small BCLM or in patients unsuited for liver resection.

“Disease interval” is generally believed to reflect tumour biology. Although, several studies show that it is a positive prognostic factor, the results are for unknown reasons divergent. We conclude that a clear-cut recommendation on disease interval cannot presently be given, and the issue needs further study.

Sizes and number of BCLM were not part of the selection of patients in most studies, although strict limits were seemingly rarely applied. Although one may hypothesize that especially the number of metastases may be linked to prognosis, both biologically (“biological behaviour”) and statistically (increased risk of reoccurring additional, tiny metastases), data corroborating its use is lacking. More obvious, sizes and number as well as distribution are important for the planning of the surgical procedure. However, the type of hepatectomy seems to be without prognostic significance, as long as an R0-resection is possible. Escolani et al. found that involvement <25% of liver volume and tumour volume <125 ml were positive prognostic factors, which indicates the importance of R0-resection as well as leaving a sufficient future liver remnant. Repeat hepatectomy has been associated with better survival, which supports not using larger than necessary resections. Although liver resection was associated with a good outcome of quod ad vitam, a substantial rate of the patients suffer relapse from their disease. In a previous analysis, we concluded that the cumulated RR was dependent on the length of follow-up, and may well exceed 70% [1]. A study by Pocard et al. supports this observation. Thus, current data support the use of adjuvant chemo- and/or hormone therapy, probably as perioperative therapy. A strategy evaluating the effect of preoperative chemotherapy before proceeding to surgery seems well motivated. Further, the response to the preoperative regimen may serve to guide postoperative, adjuvant therapy. In any case, surgery of BCLM in a situation with progressive BCLM should best be avoided.

Although some studies including EHD had good results, the series are small, and the rate of patients with EHD was generally low also in studies accepting such patients. In conclusion, liver resection in the presence of EHD remains an unsettled issue. Bone metastases of BC may represent a special situation. They are known to have a more indolent course, which could indicate that they should be managed differently than other EHD.

To conclude: Although rarely curative, the combined use of surgery and medical oncology gives hope for prolonged survival for patients with isolated BCLM. In this context, surgery may best be described as “palliative” or an “adjunct to medical therapy”. The choice between liver resection and local ablation as well as the importance of different prognostic indicators merit further study.

References: