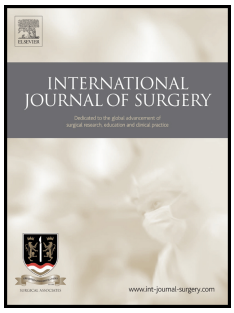
DOI:
10.1016/j.ijsu.2017.06.049

Document Version
Peer reviewed version

Accepted Manuscript



Breast cancer liver metastases in a UK tertiary centre: outcomes following referral to tumour board meeting

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PII: S1743-9191(17)30512-5

DOI: 10.1016/j.ijsu.2017.06.049

Reference: IJSU 3916

To appear in: *International Journal of Surgery*

Received Date: 21 March 2017

Revised Date: 16 June 2017

Accepted Date: 17 June 2017

Please cite this article as: Abbas H, Erridge S, Sodergren MH, Papoulas M, Nawaz A, Menon K, Heaton ND, Prachalias AA, Srinivasan P, Breast cancer liver metastases in a UK tertiary centre: outcomes following referral to tumour board meeting, *International Journal of Surgery* (2017), doi: 10.1016/j.ijsu.2017.06.049.

Breast cancer liver metastases in a UK tertiary centre: outcomes following referral to tumour board meeting

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All authors have read and approved the final manuscript.
All authors have read the journals guidelines on financial disclosures and have no disclosures to declare.
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
This manuscript is based upon previous correspondence to the AHPBA Conference in Miami, March 29-April 2 2017

Word count: 3,305
Table count: 3
Figure count: 4

Abstract

Introduction: To assess the outcomes from multidisciplinary board meetings (MDM) for patients with breast cancer liver metastases (BCLM) and identify prognostic factors for survival.

Materials and Methods: A retrospective review of MDM records for patients referred with BCLM to a tertiary centre between 2005-2016. Patient demographics, clinicopathological factors and intervention type were analysed to find predictive factors for overall survival.

Results: 61 patients with BCLM were referred to the MDM. Treatment pathways included surgical resection (n=23), radiofrequency ablation (RFA, n=11), or chemotherapy (n=27).

Surgical resection patients had an improved median overall survival compared to chemotherapy (49 v 20mo; p<0.001). RFA showed comparable survival benefit (37 v 20mo; p=0.011). Resection and RFA showed no significant difference in survival over one another (49 v 37mo; p=0.854). Survival analysis identified that resection (p=0.002) and RFA (p=0.001) were associated with improved overall survival compared to chemotherapy.

Multivariate analysis identified extrahepatic disease (HR=14.21; p=0.044) and R0 resection (HR=0.068; p=0.023) as prognostic factors.

Conclusions: Surgical resection of BCLM may improve the overall survival in selected patient groups. This study identifies a cohort of patients, without extrahepatic disease and responsive to chemotherapy, who may particularly benefit from surgery.

Keywords: Liver; Hepatic; Metastases; Resection; RFA; Chemotherapy

1. Introduction

Breast cancer is the most prevalent female cancer. The most recent epidemiological study conducted by the World Health Organisation on cancer identified that there were 1.67 million new diagnoses of breast cancer in 2012(1). The global incidence of breast cancer has risen substantially over the past 30 years and continues to rise due to increased pervasiveness of risk factors(1-3). The survival of patients with breast cancer has improved over a similar time period. This has been attributed to the development of better systemic therapies and earlier diagnosis(4-6). The prevalence of distant metastases in invasive breast cancer can range from 29.0% to 53.2%(2). The 5-year overall survival (OS) for localised breast cancer is 98.6%, which is prolonged, compared to 24.3% with distant metastases(7).

The liver is the 3rd most common site for breast metastases(8,9). Approximately 50% of patients with metastatic breast cancer will eventually develop breast cancer liver metastases (BCLM) (10). Patients with solitary BCLM have a median survival of approximately 25 months with chemotherapy(11,12). The 2nd international consensus guidelines for advanced breast cancer (ABC2) outlined that systemic therapy, with chemotherapy and hormone therapy, is the current first line treatment modality in patients with BCLM(13). However, there is a lack of knowledge as to the best treatment modalities in BCLM due to a paucity of randomised data for the use of loco-regional treatments. It is therefore currently recommended that both surgery and radio-frequency ablation (RFA) of liver deposits are carried out in a highly selective patient cohort. The most recent systematic review of resection and ablation identified that these treatments may, however, have the potential to improve survival producing 5-year OS rates between 21-61% and 27-41% respectfully(14).

Resection and ablation are both used with curative intent in the treatment of both colorectal liver metastases (CLM) and neuroendocrine liver metastases. Guidelines for both diseases indicate that hepatic resection is best indicated when it is possible to obtain a clear-margin resection with acceptable residual functioning volume, and controllable extrahepatic

disease(15,16). These provide favourable OS at 5-years compared to medical treatment(17,18). In the most recent systematic review for BCLM, however, no prognostic factors for survival were identified(14). Consequently there is a paucity of guidelines available to advise treatment in this cohort. Howlander et al. produced the only identified published guidelines in 2011(19). In the absence of randomised data on treatment for BCLM, a report on outcomes and identification of prognostic factors for OS in patients with BCLM would be valuable.

The primary aim of this study is to compare the survival outcomes for patients with BCLM discussed at multidisciplinary board meetings (MDMs). Additionally, this study hoped to identify prognostic factors for OS in patients with BCLM.

2. Materials and Methods

A retrospective review was conducted for patients referred for treatment of BCLM at King's College Hospital, a tertiary centre for liver disease, between January 2005 and August 2016. The review utilised MDM and clinical records for all consecutive patients referred in this time period. Confirmation of BCLM was made via radiological criteria and clinical evaluation with/without percutaneous core liver biopsy. The study cohort included patients who underwent resection, radiofrequency ablation (RFA) or chemotherapy as their definitive treatment for BCLM. Patients with concurrent extrahepatic metastases were also included.

Patient demographics, clinicopathological characteristics, intervention type and survival data were collected. The estrogen receptor (ER), progesterone receptor (PR) and HER2 status were assessed for both primary tumour and BCLM. Staging was based upon the most up-to-date guidelines from the American Joint Committee on Cancer(20). Synchronous presentation was defined as a time interval between the diagnosis of the primary breast cancer and development of BCLM within 6 months. The disease free interval was calculated as the

difference in time between treatment for primary cancer and diagnosis of BCLM. Response to chemotherapy was calculated according to RECIST criteria(21). Disease free survival (DFS) and OS were calculated from the date of commencement of chemotherapy regimen or surgery, as applicable. DFS was calculated by presence of recurrence by the latest follow-up recorded.

2.1 Treatment algorithm

Case-by-case based discussion at the MDM was carried out to reach a consensus with regards to treatment modality. All patients were discussed in a MDM with surgeons and oncologists present. Prior to discussion at the MDM it was established whether patients demonstrated systemic dissemination via staging. If patients had systemic disease they were treated with first line chemotherapy and subsequently evaluated in the MDM to identify if systemic control had been obtained. A treatment algorithm, outlined in figure 1, was used to aid management decision. Patients with unresectable disease were offered chemotherapy. If these patients had a good or partial response they were restaged for discussion at a future MDM. Those who had resectable metastases underwent positron emission tomography-computed tomography (PET-CT) to determine the presence of extrahepatic disease. For those with isolated BCLM, they underwent hepatectomy or RFA. Those patients with BCLM and a single bony metastasis were treated using the same algorithm as those with isolated BCLM on a case-by-case consideration. Otherwise, those with extrahepatic disease had chemotherapy.

Liver Resections were performed either via laparoscopic or open techniques. Major resections were defined as those consisting of 3 or more liver segments. Data regarding postoperative morbidity and mortality, R0 resection, and repeat liver resections were collected. Postoperative morbidity was defined as complications within 90 days of surgery according to the Clavien-Dindo classification(22).

2.2 Follow up

Follow up schedule was dependent on MDM outcome. Those who underwent surgery were followed up within one month post-operatively following MDM discussion with regards to histopathological findings and the resection margins of the tumour. Those who had RFA had a follow up interval CT scan at 6 weeks post-RFA with MDM discussion of the scan the following week and clinic review at 8 weeks. Those who were referred to oncology for systemic chemotherapy were discussed in the MDM after completion of their intended treatment course and assessment of their response to treatment.

2.3 Data Analysis:

Continuous variables were analysed using one-way ANOVA and Kruskal-Wallis tests according to whether the data was parametric. The type of distribution was confirmed by a Shapiro-Wilk test. Analysis of categorical variables was carried out using either χ^2 test or Fischer's exact test. Statistical significance was set a $p<0.05$.

Survival data were estimated using the Kaplan-Meier method and were compared using a stratified log-rank test. Univariate analysis was used to identify prognostic factors for OS. Prognostic factors with a p-value<0.05 were included in a cox regression model. A cox regression model of univariate factors of $p<0.1$ and $p<0.2$ was constructed to further investigate importance of prognostic factors. In multivariate analysis, significance was determined by $p<0.05$. All statistical analysis was carried out using SPSS (v.24.0.0.0, IBM, Armonk, NY, USA).

3. Results

A total of 80 consecutive patients were treated for breast cancer liver metastases (BCLM) at KCH between 2005 and 2016. KCH is a tertiary care centre and consequently follow-up for a

number of patients was carried out in their home institution. 19 patients were excluded from analysis (followed up at home institution, n=8; MDM outcome different to included treatments, n=11). The study cohort comprised of 61 patients; 23(38%) underwent hepatectomy, 11(18%) underwent RFA, and 27(44%) had chemotherapy only. The median follow-up for patients was 34 months(range: 1-91).

The median age of the study population at primary diagnosis was 54yrs(range: 26-94). There was no significant difference between the ages of the treatment arms. Those who underwent hepatectomy (median 54yrs; range 26-77), RFA (53yrs; 46-60) and chemotherapy (54yrs; 40-92; p=0.201) were of similar ages (Table 1). The primary cancer was typically intraductal carcinoma (hepatectomy 100%, RFA 89%; chemotherapy 88%; p=0.348). There were no significant differences in the prevalence of positive ER(p=0.127), PR(p=0.287) or HER2 receptors(p=0.647). Those who underwent hepatectomy (13 months; range: 0-90 months) as treatment for their BCLM had a shorter disease free interval from breast cancer diagnosis to BCLM diagnosis than RFA (36 months; range: 0-168 months) or chemotherapy (55 months; range: 0-192 months; p=0.010).

The clinical and pathological features of BCLM are summarised in Table 2. The number of liver metastases was fewer in the hepatectomy patients (1.6 ±1.0) compared to RFA (2.6 ±2.7) and chemotherapy (5.5 ± 2.9; p<0.001). Chemotherapy patients (n=17, 63%) had a significantly greater number of BCLM with bilobar distribution than RFA (n=4, 36%) or hepatectomy (n=4, 17%; p=0.002). Concomitant extrahepatic disease was most prevalent in chemotherapy patients (n=17, 63%; p=0.005). A higher proportion of patients who underwent hepatectomy (n=19, 95%) and RFA (n=7, 88%) as their definitive treatment had either a good or partial response to chemotherapy than for those who chemotherapy was the definitive treatment (n=6, 33%; p<0.001).

3.1 Outcomes

The median DFS for hepatectomy, RFA and chemotherapy was 25, 28 and 0 months respectfully ($p<0.001$). Surgical resection patients had an improved median OS compared to chemotherapy (49 v 20 months; $p<0.001$). RFA showed comparable survival benefit (37 v 20 months; $p=0.011$). Resection and RFA patients had no significant difference in overall survival (49 v 37; $p=0.854$). Survival analysis is displayed graphically via Kaplan-Meier curves (Figure 2). This identified that resection($p=0.002$) and RFA($p=0.001$) were associated with improved OS compared to chemotherapy. 1-, 3- and 5-year OS rates were 100%, 95% and 56% for the hepatectomy cohort, 100%, 100% 100% for the RFA cohort and 81%, 51% and 25% for the chemotherapy group. In comparison of hepatectomy and RFA subgroups neither groups suffered post-operative mortality. Postoperative morbidity was nil in the RFA group. There were 4 incidences(17%) of 90-day morbidity in the hepatectomy group (bile leak and narrowing of the common bile duct n=1; subdural haematoma n=1; seizure activity due to cerebral metastases n=1; not recorded n=1).

3.2 Prognostic Factors

Table 3 outlines the variables that were examined as possible predictive markers for OS. The following factors were identified as being associated with reduced survival: extrahepatic metastases (HR=2.47; $p=0.043$), lack of response to chemotherapy (HR=6.06; $p=0.003$) and chemotherapeutic treatment compared to resection (HR=4.49; $p=0.003$). There was no statistically significant correlation between bone metastases and reduced survival (HR=2.37; $p=0.051$). R0 resection was found to be associated with improved survival (HR=0.18; $p=0.038$). Multivariate analysis found extrahepatic disease to be associated with a poorer prognosis (HR=14.21; 95% confidence interval 1.08-186.94; $p=0.044$) and R0 resection to be associated with improved prognosis (HR=0.068; 95% CI 0.01-0.69; $p=0.023$). It was not possible to perform a reliable multivariate analysis using factors with significance $p<0.1$ or $p<0.2$ at univariate analysis due to the presence of linearly dependent covariables.

4. Discussion

It is currently unclear as to optimum treatment strategy for patients with BCLM due to an absence of randomised data comparing treatment modalities. The results of this study showed that hepatectomy and RFA were associated with 56% and 100% 5-year OS respectively. This compared to 25% overall survival in patients who received chemotherapy. In addition to this there were no peri-operative deaths following hepatectomy or RFA. Moreover, the incidence of morbidity following invasive treatment was 17% in hepatectomy patients and 0% in RFA patients. These results indicate that hepatectomy and RFA are safe to use and are associated with improved survival in comparison to medical treatment for BCLM. The most recent systematic review on resection and ablation in BCLM treatment demonstrated 5-year OS of 21-61% and 24-41% respectively(14). The findings for our study compare favourably in comparison to these results.

The improved 5-year OS data may be attributed to the implementation of the treatment algorithm. The algorithm aims to guide MDM decision making to utilise both surgical therapy alongside best medical therapy where safe to do so. Cytoreductive surgery has been shown in other metastatic disease to improve OS in select patient cohorts, despite limitations with disease recurrence(23,24). Resection of cancer cells may provide an immunological benefit. Cancer cells have been demonstrated to reduce the patient immune response either by disabling the response directly or by recruitment or immunosuppressive factors(25). Evasion of the immune system has been identified as one of the emerging hallmarks of cancer(26). Clear surgical margins may therefore provide additional immunological benefit to improve OS. Moreover, chemotherapy kills cancer cells via log-kill hypothesis. Surgical resection or RFA with best medical therapy, especially in chemotherapy responsive cancers, increases the likelihood of effective cancer cell clearance(27). Moreover, surgical therapy helps to reduce the development of chemotherapy resistance. Resistance to medical therapy can occur through a number of mechanisms, one of which is associated with tumour size. Tumours can outstrip their blood supply, preventing adequate concentrations of chemotherapeutic agents

infiltrating the tumour(28). Surgery and RFA therefore can help prevent chemotherapy resistance and eventual treatment failure.

These differences may also be explained by the comparison in timeframes between studies. The systematic review included patients treated from 1978-2008, whilst the patients in this observational series were treated between 2005 and 2016. There is a a trend towards improved overall survival in patients diagnosed with breast cancer more recently compared to their historical counterparts(4-6). Moreover, treatment was based at KCH, a tertiary liver disease centre. Studies have consecutively shown that increased specialisation and volume of procedures carried out by both individual surgeons and the centres themselves result in improved outcomes(29,30). This is integral in identifying the most appropriate treatment algorithms for individual centres and indeed regional workforce planning.

Hepatectomy and RFA have only previously been compared to medical treatment in a 2016 case-control study. This found no statistically significant differences between the 5-year OS of patients who underwent hepatectomy or RFA(38%) or had medical therapy(39%)(31). These differences may be as a result of the difference between responses to chemotherapy in the patients reported in this study. Both hepatectomy(94%) and RFA(86%) had a high proportion of patients who had disease regression as a result of chemotherapy, according to RECIST criteria(21). Univariate analysis found lack of response to chemotherapy to be a predictive factor for poor prognosis, which might have contributed to the poorer OS outcomes in the chemotherapy group. Combination therapy of chemotherapy and surgery will have allowed for complete clearance of BCLM and simultaneous treatment of micrometastases in those that were responsive. This highlights the potential for the use of medical therapy for downstaging BCLM. Utilising surgery in patients with tumours who are responsive to chemotherapy can also help to prevent significant sequelae associated with long-term chemotherapy treatment, especially in the liver(32). Medical therapy has previously been shown to improve survival in CLM by downstaging hepatic disease to allow resection(33,34).

However, no studies have examined this effect in BCLM treatment. Future studies analysing the survival benefits of resection following downstaging of BCLM will help in the production of management guidelines. In the downstaging of tumours it is also important to consider at which point it becomes appropriate to introduce locoregional treatments. In order to ensure that resection is conducted in a timely manner tumours should be reassessed frequently for response to medical therapy. It is recommended that if response is not achieved within 6 months then the treatment strategy should be reassessed to optimise quality of life(35). Moreover, in analysis of the data presented in this study we note that 18% patients treated with RFA had more than 5 metastases. RFA in patients with greater than 5 metastases has previously been recommended against, however the recent CIRSE guidelines indicate that this should no longer be an absolute contraindication providing complete ablation of all lesions can be completed(36). Utilisation of this approach in theory will also allow for more patients to be treated with curative intent.

The presence of extrahepatic metastases was found to be predictive of poor survival on multivariate analysis(HR=14.21). Two previous studies have also found extrahepatic disease to worsen prognosis in BCLM(37,38). The manifestation of coexisting extrahepatic disease is indicative of more aggressive disease and limits the ability for resection and RFA to provide clearance of metastatic deposits. In CLM, extrahepatic disease no longer precludes a patient from surgery so long as there is good response to chemotherapy and the disease is resectable(33). CLM however are as a result of haematogenous spread though the portal tract, whilst BCLM indicate further systemic spread and the presence of micro-metastases, possibly contraindication curative resection or RFA. On univariate analysis bone metastases were not found to reduce OS to statistically significant levels(HR=2.37), indicating that isolated bone metastases may not contraindicate surgical resection. Bone metastases in breast cancer may be the result of local invasion from the primary cancer. Prospective trials should be implemented to identify if ablation or resection in combination with adjuvant chemotherapy can be utilised to achieve complete metastatic clearance in this cohort.

It is important to analyse these results in light of the methodological limitations. As a retrospective cohort study, these results are subject to selection bias. Moreover, some patients were not included in the present study due to being followed up at their home institution, compounding the selection bias. The sample size of this study was limited and the methodology would have been improved by including a higher number of patients. This study has however analysed RFA and resection as separate therapies. This reduced the sample sizes of the group, however, as genuine clinical equipoise exists between the effectiveness of these treatments in BCLM it is beneficial to examine the differences between these cohorts. Moreover, the patients included in this study were treated over a short time period. Whilst increasing the time period would have increased the sample size it may have biased the results due to continuing development of improved therapies to treat breast cancer(4-6). Additionally, these patients were all treated after 2005, indicating that the treatments used are in line with current beliefs on best practice. Finally, in regards to treatment subgroups, it is important to be aware of the differences in clinicopathological characteristics of each patient cohort and that cox regression analysis cannot completely exclude this bias. As highlighted by the recent consensus on the treatment of advanced breast cancer, randomised controlled trials are urgently needed to guide best practice according to these characteristics(13).

4.1 Conclusions

Resection of BCLM appears to improve OS in selected patients with BCLM compared to medical therapy alone. However, no differences were distinguished in OS between RFA and resection cohorts. Extrahepatic disease was found to be associated with reduced OS. This indicates that BCLM patients are most likely to benefit from resection or RFA in the absence of macroscopic extrahepatic disease. Nevertheless, randomised controlled trials are required in the future to elicit which patients would most benefit from liver directed therapies.

Acknowledgements

None

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Tables

Table 1 – *Clinicopathological characteristics of primary breast cancer*

Treatment	Hepatectomy (n=23)	RFA (n=11)	Chemotherapy (n=27)	P-value
Age at diagnosis of primary breast cancer	54 (26-77)	53 (36-60)	54 (40-94)	0.201
Follow up period from BCLM to last follow up, months	48 (4-77)	43 (17-91)	16 (1-48)	-
Time interval from breast cancer diagnosis to BCLM diagnosis, months	13 (0-90)	36 (0-168)	55 (0-192)	0.010
American Joint Committee on Cancer (AJCC) staging (7th edition)				0.179
0	0	1 (25%)	3 (30%)	
I	1 (10%)	0	3 (30%)	
II	3 (30%)	2 (50%)	2 (20%)	
III	2 (20%)	1 (25%)	2 (20%)	
IV	4 (40%)	0	0	
Tumour grade				0.406
I	0	0	0	
II	8 (53%)	2 (33%)	11 (65%)	
III	7 (47%)	4 (67%)	6 (35%)	
Histological subtype				0.348
Intraductal carcinoma	17 (100%)	8 (89%)	15 (88%)	
Intralobular carcinoma	0	1 (11%)	2 (12%)	
Receptor status				
Estrogen Receptor (ER) positive	17 (94%)	5 (63%)	12 (80%)	0.127
Progesterone Receptor (PR) positive	9 (50%)	2 (25%)	4 (27%)	0.287
Human Epidermal Growth Factor Receptor 2 (HER2) positive	5 (28%)	1 (14%)	5 (33%)	0.647
Neoadjuvant chemotherapy before breast surgery	9 (43%)	4 (44%)	6 (29%)	0.560
Adjuvant chemotherapy after breast surgery	11 (48%)	5 (50%)	14 (61%)	0.654
Adjuvant hormone therapy after breast surgery	16 (73%)	5 (50%)	17 (74%)	0.351
Adjuvant herceptin treatment after breast surgery	6 (27%)	1 (10%)	4 (17%)	0.484
Type of breast surgery				0.747
Breast conserving surgery	4 (20%)	3 (30%)	7 (29%)	
Mastectomy	16 (80%)	7 (70%)	17 (71%)	

BCLM – Breast Cancer Liver Metastases
RFA – Radiofrequency Ablation

Table 2 – *Clinicopathological features of BCLM and survival*

Treatment	Hepatectomy (n=23)	RFA (n=11)	Chemotherapy (n=27)	P-value
Synchronous presentation	8 (35%)	3 (27%)	4 (15%)	0.256
Number of liver metastases	1.6 ± 1.0	2.6 ± 2.7	5.5 ± 2.9	<0.001
Number of liver metastases >5	0	2 (18%)	17 (65%)	<0.001
Solitary liver metastases	15 (65%)	5 (45%)	3 (11%)	<0.001
Bilobar distribution	4 (17%)	4 (36%)	17 (63%)	0.002
Largest liver metastasis, mm	46.7 ± 31.2	10.8 ± 1.1	23.7 ± 56.2	0.045
Largest tumour size >50mm	1 (14%)	0	1 (10%)	0.842
Receptor status				
Estrogen Receptor (ER) positive	6 (46%)	0	1 (100%)	0.364
Progesterone Receptor (PR) positive	5 (38%)	0	0	0.562
Human Epidermal Growth Factor Receptor 2 (HER2) positive	3 (21%)	0	0	0.768
Response to chemotherapy	19 (95%)	7 (88%)	6 (33%)	<0.001
Extra-hepatic disease				
Any	4 (17%)	4 (36%)	17 (63%)	0.005
Bone	4 (17%)	3 (27%)	14 (52%)	0.068
Lung	0	3 (27%)	7 (26%)	0.027
Major resection	14 (64%)	0	-	0.037
R0 resection	16 (73%)	2 (100%)	-	0.394
90-day mortality	0	0	-	-
90-day morbidity	4 (17%)	0	-	0.432
Hospital stay, days	9.5 ± 7.9	5.3 ± 3.8	-	0.639
Disease free survival (DFS), months	25 (0-72)	28 (15-91)	0 (0-33)	<0.001
Overall survival (OS)				
Median OS, months	49 (4-77)	37 (17-91)	20 (1-48)	<0.001
1-year OS	100%	100%	81%	
3-year OS	95%	100%	51%	
5-year OS	56%	100%	25%	

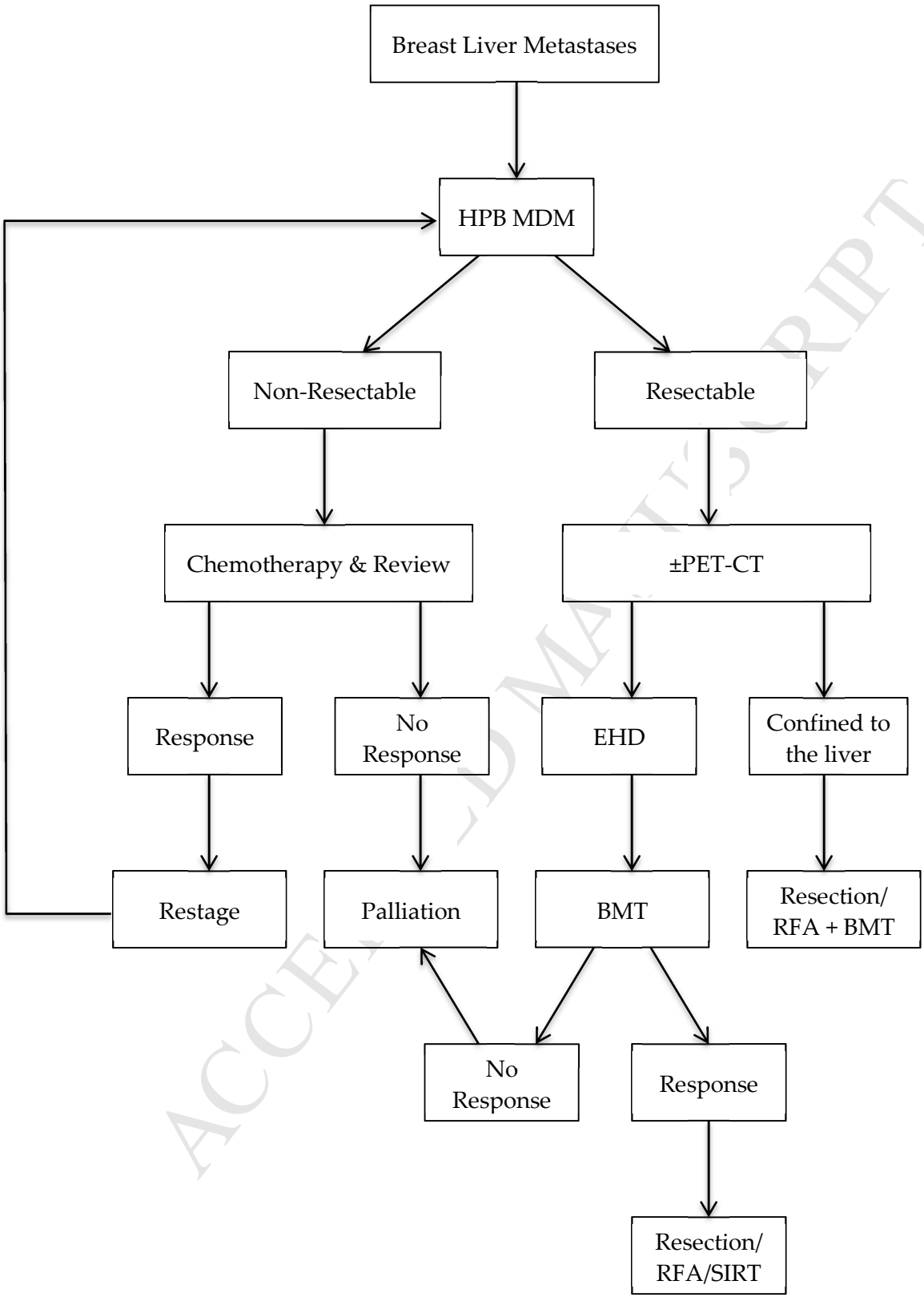
RFA – Radiofrequency Ablation

Table 3 – *Univariate analyses*

Variable	n	HR (95% CI)	P-value
Disease Free Interval			
≤36 months	36	1	
>36 months	24	1.32 (0.54-3.26)	0.547
Synchronicity			
Metachronous	45	1	
Synchronous	15	1.37 (0.49-3.81)	0.547
Tumour Number			
Single	24	1	
Multiple	37	1.97 (0.75-5.13)	0.166
Distribution			
Unilobar	31	1	
Bilobar	29	2.09 (0.85-5.16)	0.110
Tumour Size			
≤30mm	10	1	
>30mm	9	0.67 (0.13-3.49)	0.636
Response to Chemotherapy			
Response	32	1	
Stable/Regression	14	6.06 (1.87-19.64)	0.003
Extrahepatic Disease			
Absent	36	1	
Present	25	2.47 (1.03-5.94)	0.043
Bone Metastases			
Absent	40	1	
Present	21	2.37 (0.99-5.63)	0.051
Resection			
Minor	11	1	
Major	14	4.38 (0.51-37.59)	0.178
Resection Margin			
R1/R2	5	1	
R0	18	0.18 (0.04-0.91)	0.038
ER Receptor Status			
Positive	7	1	
Negative	8	7.77 (0.78-77.24)	0.080
PR Receptor Status			
Positive	5	1	
Negative	10	2.78 (0.39-20.07)	0.310
HER2 Receptor Status			
Positive	3	1	
Negative	13	0.79 (0.08-7.80)	0.839
Treatment			
Hepatectomy	23	1	
RFA	11	0.18 (0.00-1.55)	0.077
Chemotherapy	27	4.49 (1.66-12.09)	0.003

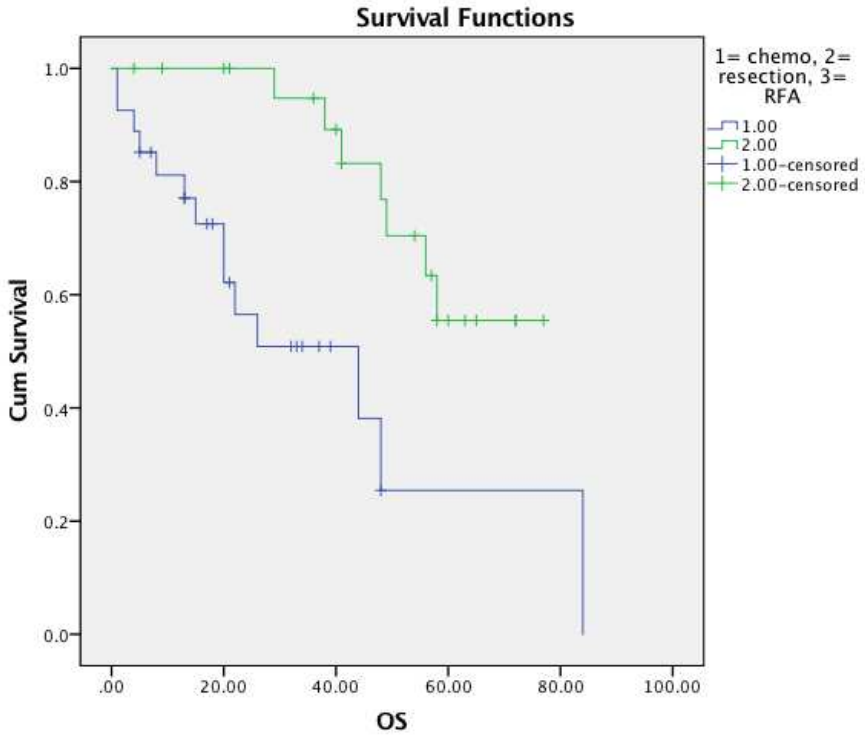
HR – Hazard Ratio; RFA – Radiofrequency Ablation

Figure 1 – Multidisciplinary Board Meeting Treatment Algorithm



HPB MDM – Hepatopancreatobiliary multidisciplinary board meeting
EHD – Extrahepatic disease
BMT – Best Medical Treatment
RFA – Radiofrequency Ablation
SIRT – Selective internal radiation therapy

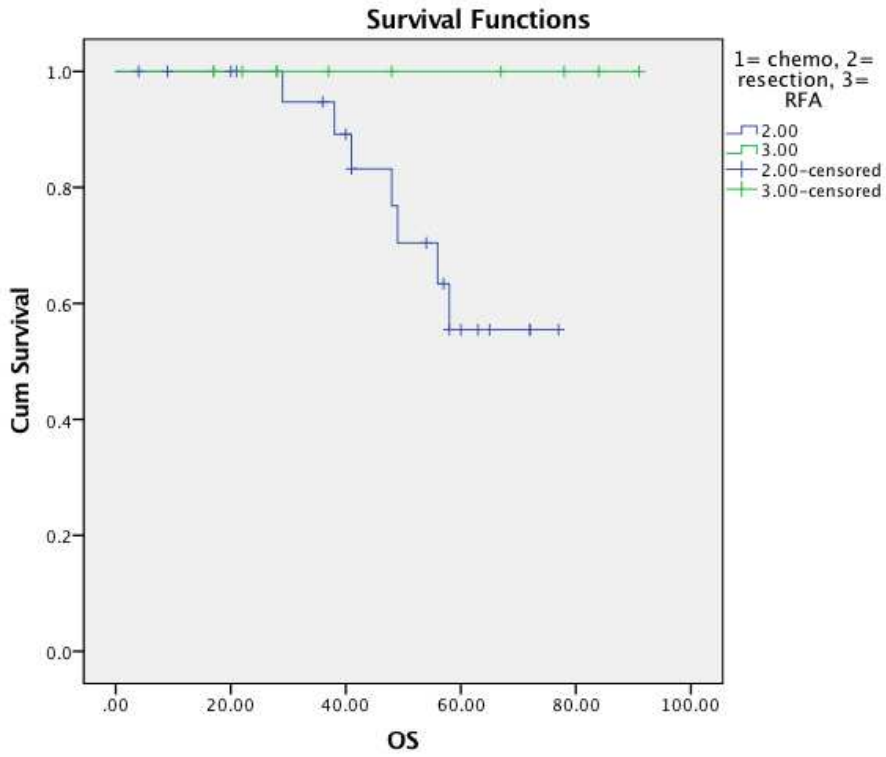
Figure 2a – *Kaplan-Meier survival curve – Chemotherapy vs Hepatectomy*



Months	6	12	18	24	30	36	42	48	54	60
Chemotherapy	22	20	14	10	9	6	4	1	1	1
Hepatectomy	22	22	22	19	18	17	13	12	10	5

1 – Chemotherapy, 2 – Hepatectomy, p=0.002

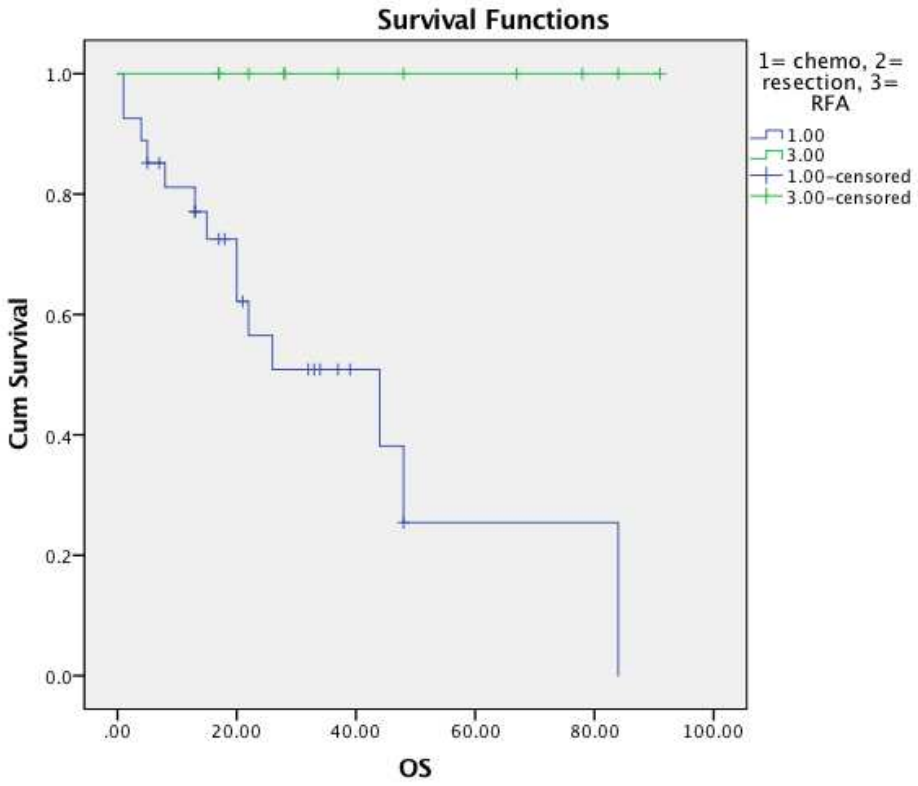
Figure 2b – *Kaplan-Meier survival curve – Hepatectomy vs RFA*



Months	6	12	18	24	30	36	42	48	54	60
Hepatectomy	22	22	22	19	18	17	13	12	10	5
RFA	11	11	9	8	6	6	5	4	4	4

2 – Hepatectomy, 3- Radiofrequency Ablation, p=0.110

Figure 2c – *Kaplan-Meier survival curve – Chemotherapy vs RFA*



Months	6	12	18	24	30	36	42	48	54	60
Chemotherapy	22	20	14	10	9	6	4	1	1	1
RFA	11	11	9	8	6	6	5	4	4	4

1 – Chemotherapy, 3 – Radiofrequency Ablation, p=0.001

Highlights

- Patients who underwent locoregional treatment for BCLM had improved overall survival.
- Extrahepatic disease and R0 resection were identified as prognostic factors for overall survival
- Presence of bony metastases was not a prognostic factor of overall survival.