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Review

Systematic review of early and long-term outcome of liver resection for metastatic breast cancer: Is there a survival benefit?

Tae Gon Yoo [a, *], Isaac Cranshaw [b], Reuben Broom [c], Sanjay Pandanaboyana [a, d], Adam Bartlett [a, d]

[a] Department of Surgery, University of Auckland, 85 Park Road, Grafton, Auckland 1023, New Zealand
[b] Breast Unit, Department of General Surgery, Auckland City Hospital, 2 Park Rd, Grafton, Auckland 1023, New Zealand
[c] Department of Medical Oncology, Auckland City Hospital, 2 Park Rd, Grafton, Auckland 1023, New Zealand
[d] HPB/UGI Unit, Department of General Surgery, Auckland City Hospital, 2 Park Rd, Grafton, Auckland 1023, New Zealand

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ABSTRACT

Background: Isolated liver metastases occur rarely in patients with metastatic breast cancer. The success of liver resection (LR) for other metastatic disease has led centres to explore the option of LR for patients with isolated breast cancer liver metastases (BCLM). A number of small series have been published in the literature, however the evidence is conflicting. This study aimed to systematically review the literature to determine the perioperative outcome and survival of patients undergoing LR for BCLM.

Methods: An electronic search of Medline and Embase databases was performed to identify all published series. Patient demographics, management, peri-operative outcome and overall survival (OS) were obtained.

Results: A total of 1705 articles were identified of which 531 included patients with non-colorectal and non-neuroendocrine metastases. 43 articles including 1686 patients, met all the inclusion and exclusion criteria. R0 resection was achieved in 83% (683/825). Morbidity and 30-day mortality rates were 20% (174/852) and 0.7% (6/918), respectively. The median OS was 36 months (12–58 months). The median 1-, 3-and 5-year OS were 90%, 56% and 37%, respectively.

Conclusions: LR for BCLM can be carried out with acceptable peri-operative risks in selected patients with survival outcomes that appear to be superior to chemotherapy alone.

1. Introduction

Breast cancer is the most common cancer affecting females, with a life time risk of 12% [1]. If diagnosed early, the prognosis remains excellent. However, approximately 25–40% will develop metastatic disease [2,3]. Metastatic breast cancer is generally regarded as a systemic disease and has historically been treated with a palliative intent. However, over the course of time, the mortality rate from metastatic breast cancer is decreasing at 1–2% every year [4] which could be associated with the development of accurate diagnostic tools, identifying metastatic diseases at an earlier stage which are more responsive to treatment and the improvement of adjuvant systemic therapies. Recent figures have shown that 70–92% of patients with metastatic breast cancer have an ECOG score of one or less meaning that the aim of treatment is no longer about palliating symptoms but rather about prolonging life [5–7].

In patients with isolated metastatic disease, it remains debatable whether surgical resection alters patient survival. Isolated breast cancer liver metastases (BCLM) are reported in 2–12% of all patients with metastatic breast cancer [8–10]. If untreated it is associated with a survival limited to a few months [11,12]. Treatment with systemic chemotherapy leads to a prolongation of survival to 8–27 months and a 5-yr survival of 8–12% [10,13–16]. The outcome of surgical resection of BCLM is not well defined.

Improvements in patient evaluation, surgical technique and adjuvant treatments have enabled liver resection (LR) to be performed with low postoperative morbidity (22%) and mortality (2–4%) [17,18]. LR is regarded as a standard treatment for a number of cancers, including metastatic colorectal cancer. The biology of metastatic colorectal cancer differs in that the liver is the first site of

* Corresponding author. Faculty of Medical and Health Sciences, University of Auckland, Auckland 1023, New Zealand.
E-mail address: taegon51@hotmail.com (T.G. Yoo).

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drainage of the splanchnic circulation. In contrast, liver metastases from breast cancer would have travelled through the systemic circulation to reach the liver. It is likely that the breast cancer is disseminated by the time liver metastases are diagnosed. It is therefore questionable whether LR of BCLM influences patient survival.

The current literature only reports single centered retrospective studies. The number of patients in each series is small, and the majority have included patients operated on during the infancy of LR. Earlier systematic reviews have demonstrated that LR is a suitable treatment for a specific group of patients. However, these reviews include a small number of patients and describe a narrow range of disease and treatment details [19,20]. The aim of this study is to systematically review the literature to determine the perioperative morbidity and mortality and survival of patients undergoing LR for metastatic breast cancer.

2. Methods

This systematic review was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21].

2.1. Literature search strategy

A systematic literature search was conducted using: Medline and Embase since inception of the databases until July 2015. No restrictions were applied with regard to language or publication date. The search was carried out to identify all manuscripts describing patients undergoing LR of non-colorectal and non-neuroendocrine (NCRNNE) metastases using the following keywords and Medical Subject Headings: 'liver or hepatic resection', 'hepatectomy', 'liver neoplasms [Surgery]' combined with 'liver neoplasms [Secondary]' whilst excluding 'colorectal', 'hepatocellular carcinoma', 'neuroendocrine carcinoma', 'cholangiocarcinoma', 'biliary tract neoplasms' and 'liver neoplasms [Radiotherapy]'. Titles were then electronically searched, and abstracts were obtained for all manuscripts that included patients undergoing LR for BCLM. Articles were included if they were original research containing data on patient survival following resection, excluding single case reports, systematic reviews, letters to editor and editorials. An assessment of risk of bias was not carried out due to the fact that the current literature regarding this topic has only shown retrospective, non-randomized articles.

2.2. Data extraction

A reviewer (TY) appraised each article using a standard proforma which was then cross-checked by a second reviewer (AB). Discrepancies between the two reviewers were resolved by discussion and consensus. The data extracted from the articles' texts, tables and figures, included number of patients, age, patient selection criteria, characteristics of the breast cancer and its treatment, characteristics of the BCLM and treatment, presence of extrahepatic metastases, postoperative hospital stay, postoperative morbidity, follow-up, prognostic factors and the primary outcome being the overall survival. The data was extracted manually and electronically tabulated into Microsoft Excel spread sheet for analysis.

3. Results

An initial search identified 1150 and 781 citations from Medline and Embase, respectively (Fig. 1). After exclusion of duplicates, the remaining citations were screened by reviewing the title and abstract to identify relevant articles. Of the 1705 potentially relevant citations, 1174 were excluded due to content not being relevant (n = 1085; colorectal or neuroendocrine metastases, ablative treatment methods, radiological imaging), patient survival not stated (n = 76), manuscripts could not be obtained (n = 3) or the article was not original research (n = 10; letters, editorials and commentaries). A total of 531 articles remained that included patients with metastases from adrenal (n = 9), breast (n = 44), gastric (n = 80), gastrointestinal stromal (n = 34), gynecological and germ cell (n = 41), lung (n = 7), melanoma (n = 43), esophagus (n = 3), pancreas (n = 50), renal (n = 32), sarcoma (n = 25) and other (n = 163). All these articles were searched electronically and a further 8 manuscripts were identified that described outcome of patients undergoing LR for BCLM. A total of 52 articles were obtained in print and read in detail. Nineteen articles were excluded due to being single case reports (n = 5), reviews (n = 11) and studies with duplicate data (n = 3). A further 10 articles were identified from reviewing the reference list. Forty-three articles met the study criteria and formed the basis of this systematic review.

The 43 studies contained data on 1686 patients (Table 1). The studies were published between 1988 and 2014. All were retrospective studies; 1 was a case control study [22], and 88% (38/43) were single center reviews. The median number of patients in each of the studies was 25 (range, 3–454). Only 6 studies reported results for more than 50 patients [22–27]. The median age at diagnosis of BCLM was 51 years (range, 43–63) and all were female.

Operative details were provided by 15 studies, including 452 patients. Fifty-eight percent (264/452) of patients underwent mastectomy while the remainder, 42% (188/452), had breast conserving surgery (lumpectomy, quadrantectomy or wide local excision). Chemotherapy was administered prior to breast cancer surgery in 23% (38/168) of the patients and following breast cancer surgery in 57% (144/254) of the patients.

3.1. Primary breast cancer histopathology

Twenty-nine studies describing 902 patients reported data on the breast cancer primary, stage and pathology (Table 2).

The TNM staging system was used by the majority of studies (17/29; 59%). Eighty-two percent of primary tumors were staged as T1 or T2 (445/541). There was no lymph node involvement (N0) in approximately half the patients (314/557; 56%). The M status was infrequently reported, being described in only 4 studies (n = 121) [24,28–30]. Seven studies gave the overall stage (n = 229); 72% were either stage I or stage II (165/229), 15% were stage III (35/229) and 13% were stage IV (29/229) [31–37].

The majority of tumors were invasive ductal carcinoma (525/611; 85.9%) and 12.8% (78/611) were lobular carcinomas. There were 5 patients (0.8%) with 'mixed' tumors and 3 (0.5%) patients were described as 'other' and excluded from the analysis [24,34,38,39].

Hormone receptor status was reported in 20 studies, involving 632 patients. Sixty-seven percent were estrogen receptor positive (231/346) and 40% were progesterone receptor positive (98/244). Six studies reported the presence of hormone receptors however they did not specify whether they were estrogen or progesterone (n = 285). Data on HER-2 receptor status was provided in 9 studies (n = 268) all of which were published after 2008. Thirty-seven percent (100/268) were positive for HER-2.

3.2. Characteristics of BCLM

The details of the BCLM was described in 35/43 studies (81%), involving 1084 patients (Table 3).

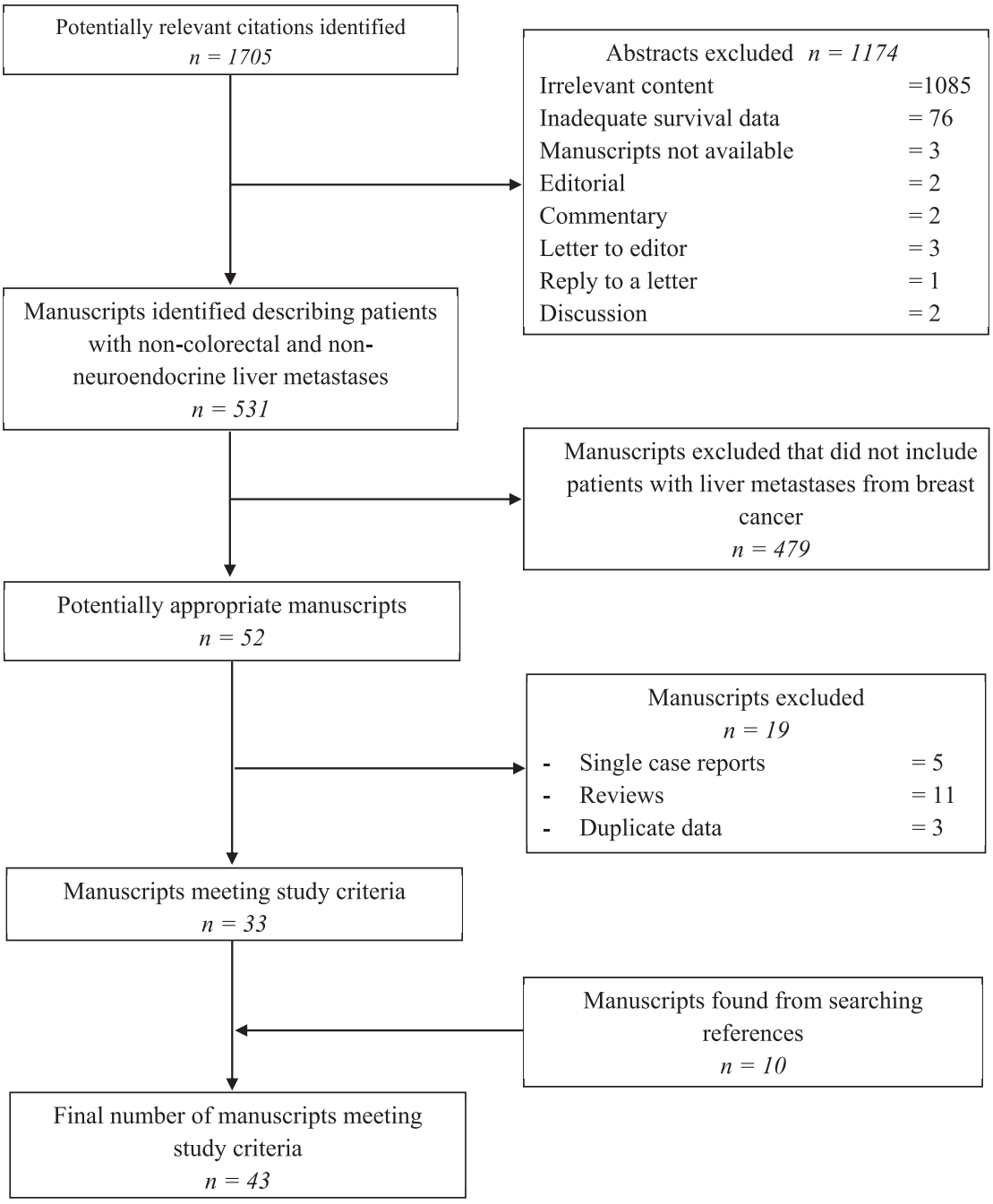

Fig. 1. Quorum diagram.

The median time between breast cancer surgery and diagnosis of BCLM was 35 months (range, 11–71 months). The definition of synchronous metastases was stated in 7 studies, which were metastases appearing <3 months [40,41], <6 months [33,38], <12 months [27] following surgery on the primary or prior to completion of chemotherapy [24]. The occurrence of BCLM was described as synchronous in 13% (123/933) of patients.

BCLM were defined as solitary and unilobar in 55% (503/913) and 64% (263/412) of patients, respectively. The median tumor size was 3.8 cm (range, 1.8–5.3 cm) with the largest tumor reported to be 19 cm [26].

Extrahepatic metastases were identified in 18% (151/843) of patients. The site of extrahepatic disease was specified in 142 patients; bone (80/142; 56%), lung (17/142; 12%) and lymph nodes (16/142; 11%) [22,24,26,29,32,33,35,38,39,41–44].

The hormone receptor status of the BCLM was reported in 25% of the patients (268/1084), compared to 70% (623/902) in the primary breast cancer. Fifty-nine percent were estrogen receptor positive (82/139) and 48% (61/127) were progesterone receptor positive similar proportion to what was seen in the primary. HER-2 receptor expression was positive in 28% (32/116) of patients.

3.3. LR and adjuvant treatment

Thirty-three studies (33/43; 77%) described the operative details of the BCLM in 1078 patients (Table 4).

Table 1
Patient demographics and treatment of included manuscripts.

First author	No. of patients	Median age (range) [years]	Breast surgery		Chemotherapy	
			M	WLE	Neoadjuvant	Adjuvant
Treska [39]	13	51[a, b, c]	NS	NS	NS	NS
Dittmar [40]	34	53 (32–74)[d]	NS	NS	NS	NS
Ehrl [32]	29	58 (39–75)[a]	NS	NS	3% (1/29)	31% (9/29)
Kostov [41]	39	58 (39–69)[a, e]	33% (14/42)[e]	67% (28/42)[e]	33% (14/42)[e, f]	
Mariani [22]	100	52 (30–72)	NS	NS	NS	NS
Polistina [28]	12	63 (44–77)[g]	25% (3/12)	75% (9/12)	0% (0/12)	67% (8/12)
Zegarac [55]	30	49 (29–73)[h]	NS	NS	NS	28% (9/32)[h]
Abbott [24]	86	NS[i]	70% (60/86)	30% (26/86)	33% (28/86)	NS
Groeschl [23]	115	NS	NS	NS	NS	NS
van Walsum [38]	32	50 (31–37)	NS	NS	NS	59% (19/32)
Bresadola [66]	13	NS	NS	NS	NS	NS
Bockhorn [31]	26	55 (35–77)[j]	58% (22/38)[j]	42% (16/38)[j]	NS	100% (38/38)[j]
Hoffman [33]	41	NS[k]	53% (21/40)[l]	48% (19/40)	22% (9/41)	59% (24/41)
Ercolani [67]	44	NS	NS	NS	NS	NS
Caralt [29]	12	58 (36–76)	58% (7/12)	42% (5/12)	NS	100% (12/12)
Furka [48]	17	56 (47–64)[g]	NS	NS	NS	NS
Kollmar [68]	27	NS	NS	NS	NS	NS
Lubrano [30]	16	54 (38–68)[g]	NS	NS	NS	NS
Thelen [43]	39	NS[m]	NS	NS	92% (36/39)[f]	
Lendoire [69]	19	NS	NS	NS	NS	NS
Adam [26]	85	47 (27–70)[g]	43% (35/82)	57% (47/82)	NS	NS
Adam [25]	454	NS	NS	NS	NS	NS
d'Annibale [34]	18	56 (36–76)[n]	59% (10/17)	41% (7/17)[o]	NS	NS
Okaro [45]	6	47 (36–58)[p]	50% (3/6)	50% (3/6)	NS	NS
Sakamoto [35]	34	51 (27–71)[g]	82% (28/34)	18% (6/34)	NS	NS
Weitz [70]	29	NS	NS	NS	NS	NS
Yedibela[71] [q]	17	NS	NS	NS	NS	NS
Arena [46]	17	49 (35–70)	NS	NS	NS	53% (9/17)
Gomez [72]	3	53 (51–59)[g]	100% (3/3)	0% (0/3)	NS	NS
Vlastos [37]	31	46 (31–70)[p]	81% (25/31)	19% (6/31)	81% (25/31)[f]	
Elias [27]	54	49 (31–73)[a, g]	NS	NS	NS	NS
Carlini [47]	17	55 (41–72)	53% (9/17)	47% (8/17)	NS	35% (6/17)
Karavias [73]	4	59 (52–64)	NS	NS	NS	NS
van Ruth [74]	3	NS	NS	NS	NS	NS
Kondo [49]	6	43 (39–58)	NS	NS	NS	NS
Maksan [50]	9	44 (26–65)	NS	NS	NS	56% (5/9)
Pocard [53]	49	47 (30–70)[a, p, r]	NS	NS	NS	NS
Selzner [42]	17	48 (32–72)[p]	94% (16/17)	6% (1/17)	NS	NS
Yoshimoto [44]	25	50 (27–70)	NS	NS	NS	NS
Seifert [51]	15	52 (43–70)	53% (8/15)	47% (7/15)	NS	33% (5/15)
Raab [36]	34	47 (36–63)	NS	NS	NS	NS
Schneebaum [54]	6	NS	NS	NS	NS	NS
Stehlin [75]	9	NS	NS	NS	NS	NS
Median (range)	25 (3–454)	51 (43–63)	58% (25–100%)	42% (0–75%)	13% (0–33%)	56% (28–100%)
Percentage (n/t)			58% (264/452)	42% (188/452)	23% (38/168)	57% (144/254)

NS = Not stated.
M = mastectomy, modified radical mastectomy, radical mastectomy.
WLE = wide local excision, breast conserving surgery, lumpectomy, quadrantectomy, breast preserving therapy.
[a] Mean.
[b] No range.
[c] Includes 24 patients, as an additional 11 patients underwent thermal ablation.
[d] Includes 50 patients, as an additional 10 patients underwent explorative laparotomy and 6 patients underwent thermal ablation.
[e] Includes 42 patients, as an additional 3 patients underwent thermal ablation.
[f] Timing of chemotherapy not specified as either before or after breast surgery.
[g] Study does not state whether the age is at diagnosis of breast cancer or BCLM.
[h] Includes 32 patients, as an additional 2 patients underwent thermal ablation.
[i] 60% of patients (52/86) were ≤50.
[j] Includes 38 patients, as an additional 12 patients underwent explorative laparotomy.
[k] 34% of patients (14/41) were ≤50.
[l] Excludes a patient who had definitive radiotherapy only.
[m] 33% of patients (13/39) were ≤50.
[n] Includes 26 patients as 8 patients did not undergo LR.
[o] Excludes a resection described as a tumorectomy.
[p] Age is at diagnosis of breast cancer.
[q] Only including patients treated after 1990.
[r] Includes 52 patients, as an additional 3 patients received a biopsy.

The number of liver segments resected was reported in 15 studies involving 305 patients. The median number of segments resected was 3 ranging from 1 to 4 segments. Major resection, defined as 3 or more segments, was performed in 53% (534/1017) of patients.

The median hospital stay was reported in 13 studies (30%), involving 391 patients, was 11 days (range, 6–16 days).

Histological margin status was reported in 22 studies involving

Table 2
Summary of primary breast cancer pathology and stage.

First author	Invasive ductal carcinoma	TNM staging					Hormone receptors		
		T1-T2	T3-T4	N0	N+	M1	Estrogen	Progesterone	HER-2
Treska [39]	71% (15/21)[a, b]	NS	NS	NS	NS	NS	63% (15/24)[a]	42% (10/24)[a]	NS
Dittmar [40]	NS	88% (42/48)[c]	12% (6/48)[c]	64% (49/77)[c, d]	36% (28/77)[c, d]	NS	81% (25/31)[c]	72% (23/32)[c]	43% (9/21)[c]
Ehrl [32]	NS	NS	NS	NS	NS	NS	86% (25/29)	NS	40% (8/20)
Kostov [41]	88% (37/42)[e]	NS	NS	NS	NS	NS	45% (19/42)[e]	10% (4/42)[e]	21% (9/42)[e]
Mariani [22]	83% (80/96)	82% (80/97)	18% (17/97)	67% (62/92)	33% (30/92)	NS	76% (55/72)[f]		NS
Polistina [28]	NS	83% (10/12)	17% (2/12)	33% (4/12)	67% (8/12)	0% (0/12)	75% (9/12)	42% (5/12)	14% (1/7)
Zegarac [55]	59% (19/32)[g]	88% (28/32)[g]	13% (4/32)[g]	31% (10/32)[g]	69% (22/32)[g]	NS	63% (20/32)[f, g]		28% (9/32)[g]
Abbott [24]	92% (73/79)[h]	76% (61/80)	24% (19/80)	62% (52/84)[i]	38% (32/84)	32% (27/85)	74% (59/80)[f]		44% (32/72)
van Walsum [38]	84% (21/25)[j]	NS	NS	28% (9/32)	72% (23/32)	NS	80% (20/25)	44% (11/25)	73% (8/11)
Bockhorn [31]	95% (36/38)[k]	NS	NS	NS	NS	NS	61% (23/38)[f, k]		NS
Hoffman [33]	98% (40/41)	NS	NS	NS	NS	NS	41% (10/24)	41% (10/24)	42% (10/24)
Caralt [29]	92% (11/12)	100% (8/8)	0% (0/8)	44% (4/9)	56% (5/9)	25% (2/8)	100% (9/9)[f]		NS
Lubrano [30]	88% (14/16)	63% (10/16)	38% (6/16)	81% (13/16)	19% (3/16)	0% (0/16)	69% (11/16)	50% (8/16)	NS
Thelen [43]	NS	82% (32/39)	18% (7/39)	38% (15/39)	62% (24/39)	NS	NS	NS	36% (14/39)
Adam [26]	86% (73/85)	88% (57/65)	12% (8/65)	52% (39/75)	48% (36/75)	NS	75% (33/44)	27% (12/44)	NS
d'Annibale [34]	88% (15/17)[j]	NS	NS	NS	NS	NS	28% (5/18)	NS	NS
Okaro [45]	NS	50% (3/6)	50% (3/6)	33% (2/6)	67% (4/6)	NS	NS	NS	NS
Sakamoto [35]	88% (30/34)[l]	NS	NS	NS	NS	NS	63% (17/27)	NS	NS
Arena [46]	NS	94% (16/17)[m]	6% (1/17)	NS	NS	NS	100% (11/11)	70% (7/10)	NS
Gomez [72]	NS	NS	NS	NS	NS	NS	NS	NS	NS
Vlastos [37]	93% (25/27)	NS	NS	NS	NS	NS	NS	NS	NS
Elias [27]	NS	82% (32/39)	18% (7/39)	NS	NS	NS	59% (32/54)[f, n]		NS
Carlini [47]	88% (15/17)	82% (14/17)	18% (3/17)	71% (12/17)	29% (5/17)	NS	80% (12/15)	53% (8/15)	NS
Karavias [73]	100% (4/4)	NS	NS	NS	NS	NS	NS	NS	NS
Maksan [50]	NS	100% (9/9)	0% (0/9)	44% (4/9)	56% (5/9)	NS	NS	NS	NS
Pocard [53]	NS	74% (32/43)[o]	26% (11/43)[o]	68% (30/44)[o, p]	32% (14/44)[o]	NS	68% (19/28)[o]	NS	NS
Selzner [42]	100% (17/17)	NS	NS	NS	NS	NS	NS	NS	NS
Seifert [51]	NS	85% (11/13)	15% (2/13)	69% (9/13)	31% (4/13)	NS	NS	NS	NS
Raab [36]	NS	NS	NS	NS	NS	NS	NS	NS	NS
Median (range)	88% (59–100%)	83% (50–100%)	17% (0–50%)	52% (28–81%)	48% (19–72%)	13% (0–32%)	72% (28–100%)	43% (10–72%)	40% (14–73%)
Percentage (n/t)	87% (525/603)	82% (445/541)	18% (96/541)	56% (314/557)	44% (243/557)	24% (29/121)	67% (231/346)	40% (98/244)	37% (100/268)

NS = Not stated.
HER-2 = Human epidermal growth factor receptor 2.
[a] Includes 24 patients, as an additional 11 patients underwent thermal ablation.
[b] Exclusion of 3 patients described as having an 'other' tumor histology.
[c] Includes 50 patients, as an additional 10 patients underwent explorative laparotomy and 6 patients underwent thermal ablation.
[d] Potential arithmetic problems as the total number of patients exceed 50.
[e] Includes 42 patients, as an additional 3 patients underwent thermal ablation.
[f] Patients have either hormone receptors.
[g] Includes 32 patients, as an additional 2 patients underwent thermal ablation.
[h] Exclusion of 3 patients described as having a 'mixed' tumor histology.
[i] Includes patients with N1.
[j] Exclusion of a patient described as having a 'mixed' tumor histology.
[k] Includes 38 patients, as an additional 12 patients underwent explorative laparotomy.
[l] Mucinous carcinoma in 6% (2/34) and medullary carcinoma in 3% (1/34) of patients.
[m] Includes T0 in 12% (2/17) of patients.
[n] Study does not state whether the receptors are from the primary breast tumor or the BCLM.
[o] Includes 52 patients, as an additional 3 patients received a biopsy.
[p] Includes patients with N1a.

825 patients. Microscopic negative margins (R0) were achieved in 83% (683/825) of resections. Five of twenty-two studies reported that R0 resection was achieved in 100% of their patients [30,32,42,45,46].

Chemotherapy was administered prior to LR in 74% (523/705) of the patients and following LR in 66% (486/733) of patients. There was insufficient detail to determine the number of patients who had also received chemotherapy around the time of their primary cancer treatment.

3.4. Postoperative morbidity and survival following LR

All 43 studies reported data on postoperative survival (Table 5). The median follow-up for all studies was 29 months (range, 12–72 months).

Tumor recurrence following LR was reported in 62% (325/523) of patients. The site of tumor recurrence was specified in 284 patients. The most common site of recurrence was in the liver (197/325; 61%), followed by skeletal (n = 36), lungs (n = 24), brain (n = 17) and pleura (n = 6) [23,26,27,29–31,35,37,38,42,44–51].

The median disease free survival and overall survival was 22 months (range, 5–29 months) and 36 months (range, 12–58 months), respectively. The longest duration of disease free period survival and overall survival were 144 [42] and 240 months [35], respectively. The median 1-, 3- and 5-year survival was 90% (range, 77%–100%), 56% (range, 31%–79%) and 37% (range, 11%–61%), respectively.

Postoperative mortality, defined as death within 30 days of surgery, was reported in 6 out of 918 (0.7%) patients from 32 studies. There were no standard criteria used to define post-operative morbidity. Twenty-six studies, involving 852 patients reported post-operative morbidity in 174 (20%) of patients that underwent LR. There was sufficient data for 93 of the 180 complications to allow for the complications to be classified according to

Table 3
Summary of pathology, stage and time to diagnosis of breast cancer liver metastases.

First author	Hormone receptor status			Percentage with synchronous BCLM	Percentage with solitary BCLM	Percentage with unilobar BCLM	Median maximal tumor size (cm)	Percentage of patients with extrahepatic metastases	Median time to diagnosis of liver metastases (months)
	Estrogen	Progesterone	HER-2						
Treska [39]	NS	NS	NS	NS	67% (16/24)[a]	NS	NS	25% (6/24)	48[a, b]
Dittmar [40]	58% (19/33)	61% (20/33)	42% (14/33)	12% (6/50)[c]	24% (12/50)[c]	62% (31/50)[c]	NS	35% (12/34)	34 (0–211)[c]
Ehrl [32]	NS	NS	NS	14% (4/29)	45% (13/29)	NS	NS	55% (16/29)	71 (0–224)
Kostov [41]	NS	NS	NS	0% (0/42)[d]	51% (20/39)	74% (29/39)	5.1 (1.4–9)	49% (19/39)	NS
Mariani [22]	NS	NS	NS	5% (5/92)	65% (65/100)	NS	1.8 (0.5–11)	7% (7/100)	38 (0–225)
Polistina [28]	67% (9/12)	NS	17% (2/12)	NS	42% (5/12)	100% (12/12)	4 (2–11)	NS	23 (0–77)[e]
Zegarac [55]	22% (7/32)[f, g]		22% (7/32)[f]	9% (3/32)[f]	50% (16/32)[f]	NS	NS	0% (0/30)	25 (8–120)[f, h]
Abbott [24]	NS	NS	NS	29% (25/86)	62% (53/86)	NS	NS	28% (24/86)	NS
Groeschl [23]	NS	NS	NS	21% (24/114)	NS	NS	NS	NS	NS
van Walsum [38]	NS	NS	NS	19% (6/32)	69% (22/32)	97% (31/32)	2.5 (0.7–9)	16% (5/31)	33 (0–219)
Bresadola [66]	NS	NS	NS	0% (0/13)	NS	NS	NS	NS	NS
Bockhorn [31]	54% (19/35)[g, i]		NS	3% (1/38)[i]	34% (13/38)[i]	61% (23/38)[i]	NS	0% (0/26)	59 (0–228)[i, j]
Hoffman [33]	46% (18/39)	36% (14/39)	23% (9/39)	10% (4/41)	49% (20/41)	46% (19/41)	NS	30% (12/41)	41
Caralt [29]	63% (5/8)[g]		NS	17% (2/12)	NS	NS	NS	8% (1/12)	54 (0–220)
Furka [48]	NS	NS	NS	NS	88% (15/17)	NS	(1.5–16)[k]	0% (0/17)	28 (4–65)[b]
Lubrano [30]	63% (10/16)	50% (8/16)	NS	0% (0/16)	75% (12/16)	NS	(1–10)[k]	NS	54 (7–120)
Thelen [43]	67% (26/39)	49% (19/39)	NS	15% (6/39)	51% (20/39)	56% (22/39)	NS	33% (13/39)	NS
Adam [26]	NS	NS	NS	11% (9/85)	38% (32/85)	61% (52/85)	2.8 (1–19)	6% (5/84)	34 (0–147)
d'Annibale [34]	NS	NS	NS	NS	50% (9/18)	NS	NS	NS	NS
Okaro [45]	NS	NS	NS	17% (1/6)	33% (2/6)	NS	2.8 (1.8–4.5)	NS	70 (24–144)
Sakamoto [35]	NS	NS	NS	12% (4/34)	56% (19/34)	NS	4 (1.3–8)	26% (9/34)	11 (0–240)
Arena [46]	NS	NS	NS	0% (0/17)	NS	NS	3.7[l]	NS	44 (10–141)[b]
Gomez [72]	NS	NS	NS	0% (0/3)	33% (1/3)	NS	NS	NS	37 (24–112)
Vlastos [37]	NS	NS	NS	29% (9/31)	65% (20/31)	NS	2.9 (1–8)	0% (0/31)	22 (0–144)
Elias [27]	59% (32/54)[g, m]		NS	22% (8/54)	NS	NS	3.3 (0.4–11.1)	0% (0/54)	39 (0–186)[l]
Carlini [47]	NS	NS	NS	0% (0/17)	88% (15/17)	NS	NS	0% (0/17)	35 (5–207)
Karavias [73]	NS	NS	NS	0% (0/4)	NS	NS	NS	NS	NS
Kondo [49]	NS	NS	NS	NS	83% (5/6)	NS	5.3 (2.6–7.7)	0% (0/6)	42 (2–59)[b]
Maksan [50]	NS	NS	NS	NS	44% (4/9)	89% (8/9)	NS	0% (0/9)	NS
Pocard [53]	NS	NS	NS	NS	69% (36/52)[n]	54% (28/52)[n]	3.8 (0.4–12)[l, n]	21% (11/52)[n]	60 (0–205)[h, l, n]
Selzner [42]	NS	NS	NS	NS	71% (12/17)	NS	(1.5–5)[k]	18% (3/17)	29 (2–84)
Yoshimoto [44]	NS	NS	NS	16% (4/25)	56% (14/25)	NS	4 (1.3–7)	32% (8/25)	19 (0–120)
Seifert [51]	NS	NS	NS	13% (2/15)	53% (8/15)	53% (8/15)	4.5 (2–11)	NS	24 (0–105)
Raab [36]	NS	NS	NS	NS	59% (20/34)	NS	NS	NS	27 (9–197)[b]
Schneebaum [54]	NS	NS	NS	0% (0/6)	67% (4/6)	NS	NS	0% (0/6)	29 (22–166)
Median (range)	63% (46–67%)	50% (36–61%)	23% (17–42%)	12% (0–29%)	56% (24–88)	61% (46–100%)	3.8 (1.8–5.3)	12% (0–55%)	35 (11–71)
Percentage (n/t)	59% (82/139)	48% (61/127)	28% (32/116)	13% (123/933)	55% (503/913)	64% (263/412)		18% (151/843)	

NS = Not stated.
HER-2 = Human epidermal growth factor receptor 2.
[a] Includes 24 patients, as an additional 11 patients underwent thermal ablation.
[b] Median interval is between breast surgery and LR.
[c] Includes 50 patients, as an additional 10 patients underwent explorative laparotomy and 6 patients underwent thermal ablation.
[d] Includes 42 patients, as an additional 3 patients underwent thermal ablation.
[e] Includes 26 patients, as an additional 14 patients underwent thermal ablation.
[f] Includes 32 patients, as an additional 2 patients underwent thermal ablation.
[g] Patients have either hormone receptors.
[h] Median interval is between diagnosis of breast cancer and BCLM.
[i] Includes 38 patients, as an additional 12 patients underwent explorative laparotomy.
[j] Excludes 3 patients diagnosed with synchronous BCLM.
[k] No median.
[l] Mean.
[m] Study does not state whether the receptors are from the primary breast tumor or the BCLM.
[n] Includes 52 patients, as an additional 3 patients received a biopsy.

Table 4
Summary of surgical treatment of breast cancer liver metastases and systemic treatment.

First author	% major LR	Median number segments resected (range)	Resection margin		Chemotherapy	
			R0	R1-R2	Neoadjuvant	Adjuvant
Treska [39]	31% (4/13)	NS	NS	NS	NS	NS
Dittmar [40]	68% (23/34)	NS	62% (21/34)	32% (11/34)	38% (19/50)[a]	26% (13/50)[a]
Ehrl [32]	38% (11/29)	NS	100% (29/29)	0% (0/29)	NS	NS
Kostov [41]	77% (30/39)	4 (2–5)	85% (33/39)	15% (6/39)	NS	100% (39/39)
Mariani [22]	29% (29/100)	NS	82% (82/100)	18% (18/100)	79% (79/100)	NS
Polistina [28]	64% (7/11)[b]	3 (1–4)[b]	92% (11/12)	8% (1/12)	100% (12/12)	NS
Zegarac [55]	NS	NS	NS	NS	NS	100% (32/32)[c]
Abbott [24]	62% (53/86)	NS	90% (77/86)	10% (9/86)	76% (65/86)	35% (30/86)
Groeschl [23]	60% (68/114)	NS	86% (92/107)	14% (15/107)	88% (100/114)	65% (71/109)
van Walsum [38]	41% (13/32)	NS	91% (29/32)	9% (3/32)	41% (13/32)	44% (14/32)
Bockhorn [31]	58% (15/26)	NS	92% (24/26)	8% (2/26)	NS	NS
Hoffman [33]	54% (22/41)	NS	78% (32/41)	22% (9/41)	34% (14/41)	NS
Caralt [29]	50% (6/12)	2.5 (1–5)	92% (11/12)	8% (1/12)	55% (6/11)	80% (8/10)
Furka [48]	25% (3/12)	1 (1–4)[d]	NS	NS	NS	100% (17/17)
Lubrano [30]	56% (9/16)	3 (1–4)	100% (16/16)	0% (0/16)	100% (16/16)	100% (16/16)
Thelen [43]	51% (20/39)[e]	NS	72% (28/39)	28% (11/39)	NS	NS
Adam [26]	64% (54/85)	NS	66% (56/85)	34% (29/85)	84% (71/85)	84% (71/85)
d'Annibale [34]	28% (5/18)	1 (1–5)	NS	NS	NS	NS
Okaro [45]	100% (6/6)	4 (3–7)	100% (6/6)	0% (0/6)	NS	100% (6/6)
Sakamoto [35]	44% (15/34)	1	NS	NS	NS	65% (22/34)
Yedibela [71]	NS	NS	71% (12/17)	29% (5/17)	NS	NS
Arena [46]	80% (12/15)[f]	3 (1–5)	100% (17/17)	0% (0/17)	88% (15/17)	94% (16/17)
Gomez [72]	33% (1/3)	2 (1–3)	NS	NS	66% (2/3)	100% (3/3)
Vlastos [37]	45% (14/31)	NS	NS	NS	71% (22/31)[g]	
Elias [27]	68% (34/50)	NS	81% (44/54)	19% (10/54)	96% (52/54)	96% (52/54)
Carlini [47]	6% (1/17)	NS	NS	NS	NS	76% (13/17)
Kondo [49]	50% (3/6)	NS	83% (5/6)	17% (1/6)	NS	100% (6/6)
Maksan [50]	22% (2/9)	NS	NS	NS	NS	33% (3/9)
Pocard [53]	50% (24/48)	1 (1–5)	NS	NS	88% (46/52)[h]	54% (28/52)[h]
Selzner [42]	41% (7/17)	1	100% (17/17)	0% (0/17)	59% (10/17)	NS
Yoshimoto [44]	52% (13/25)	3 (1–5)	NS	NS	NS	96% (24/25)
Seifert [51]	60% (9/15)	4 (1–5)	73% (11/15)	27% (4/15)	20% (3/15)	NS
Raab [36]	62% (21/34)[i, j]	3 (1–5)[i]	86% (30/35)[i]	14% (5/35)[i]	NS	6% (2/34)
Median (range)	51% (6–100%)	3 (1–4)	86% (62–100%)	14% (0–34%)	78% (20–100%)	84% (6–100%)
Percentage (n/t)	53% (534/1017)		83% (683/825)	17% (140/825)	74% (523/705)	66% (486/733)

NS = Not stated.
[a] Includes 50 patients, as an additional 10 patients underwent explorative laparotomy and 6 patients underwent thermal ablation.
[b] Exclusion of a resection described as atypical.
[c] Includes 32 patients, as an additional 2 patients underwent thermal ablation.
[d] Exclusion of 5 resections described as a left lobectomy, a mesohepatectomy and 3 atypicals.
[e] Major defined as >3 segments.
[f] Exclusion of 2 resections described as left lobectomies.
[g] Timing of chemotherapy not specified as either before or after breast surgery.
[h] Includes 52 patients, as an additional 3 patients received a biopsy.
[i] A patient had 2 LRs on separate occasions.
[j] Exclusion of a resection described as ex situ resection.

the Clavien-Dindo classification [52]; 62% (58/93) were I or II (resolved spontaneously or with medication), 29% (27/93) were III (need for a surgical, endoscopic or radiological intervention), 2% (2/93) were IV (life threatening) and 6% (6/93) as V (mortality) [24,26,27,29,31–33,36,38,41,42,48,51,53].

3.5. Patient selection criteria

Twenty-one studies stated that a systematic criteria was used to select patients suitable for LR.

Performance status was evaluated in 6 studies by either the WHO [22,27,53] or the Karnofsky score [28,32,33]. Three studies selected patients (n = 203) who scored either a 1 or a 0 on the WHO score and 3 studies accepted patients (n = 82) who scored 80 or above on the Karnofsky score.

The presence of extrahepatic metastases was described as an exclusion criteria for LR in 7 studies (n = 150) [27,30,37,46,48,50,54]. Two studies included patients with bone metastases to undergo resection [22,29] and 8 studies included patients with extrahepatic metastases (bone, lymph, lung, ovary and peritoneum) that were stable [24,32,33,35,41,43,44,53].

The potential for a curative resection was considered as a criteria in 8 studies involving 207 patients [32,33,35,39,43,44,48,50].

The extent of BCLM was used as a selection criteria in 7 studies: One study included patients with only unilobar metastases [39] and 5 identified the maximum number of BCLM (≤3 metastases [27], ≤4 metastases [22], ≤5 metastases [33] and ≤7 metastases [32,41]).

Two studies including 154 patients indicated a positive response to pre-hepatectomy chemotherapy as a criteria for resection [22,27].

3.6. Prognostic factors

Twenty-two studies including 826 patients analyzed prognostic factors influencing overall survival. All studies acknowledged the need for $P < 0.05$ for statistical significance.

Age was considered irrelevant to survival in 12 of 15 studies [22,26–28,31,33,35,37,38,41,43,55]. Two studies stated an improvement in survival in patients over the age of 50 years [30,39]

Table 5
Summary of clinical outcome and survival of patients with breast cancer liver metastases undergoing resection.

First author	Median follow-up (months)	Postoperative mortality	Median hospital stay (days)	Postoperative morbidity	Recurrence rate	Median disease free survival (months)	Median overall survival (months)	Overall survival		
								1 year	3 year	5 year
Treska [39]	NS	NS	NS	NS	NS	NS	26[a]	80%	46%	11%
Dittmar [40]	NS	0% (0/34)	NS	24% (12/50)[b]	NS	NS	36[a]	NS	NS	26%
Ehrl [32]	34 (2–90)[c]	3% (1/29)	12 (4–24)	13% (4/29)	NS	NS	29[a]	NS	31%	21%
Kostov [41]	60	2% (1/42)[d]	NS	36% (15/42)[d]	NS	29	43[a]	86%	64%	38%
Mariani [22]	NS	0% (0/100)	NS	18% (18/100)	NS	NS	NS	NS	73%	50%
Polistina [28]	23 (0–81)[e]	0% (0/12)	NS	42% (5/12)	NS	22 (16–36)	29 (12–64)[a]	100%	67%[f]	34%
Zegarac [55]	37 (7–66)[g]	NS	NS	NS	NS	23[g]	37[a, g]	NS	NS	34%[g]
Abbott [24]	62 (0.3–100)	0% (0/86)	6[a, c]	21% (18/86)	NS	14[a]	57[a]	NS	NS	44%
Groeschl [23]	31	NS	NS	NS	64% (66/103)	22	52[a]	79%	52%	27%
van Walsum [38]	26 (0–188)	0% (0/32)	7 (4–58)	34% (11/32)	59% (19/32)	NS	55[a]	NS	NS	37%
Bresadola [66]	NS	NS	NS	NS	NS	NS	44 (5–93)	92%	61%	51%
Bockhorn [31]	60 (7–105)	8% (2/26)	14 (7–45)	30% (8/26)	73% (19/26)	NS	NS	88%	53%	44%
Hoffman [33]	34[a]	0% (0/41)	10[a]	22% (9/41)	NS	29[a]	58[a]	NS	68%	48%
Ercolani [67]	NS	NS	NS	NS	NS	NS	41[a]	NS	63%	36%
Caralt [29]	36 (12–113)	0% (0/12)	8 (6–24)	17% (2/12)	58% (7/12)	28 (7.8–71.7)	36 (12–113)	100%	79%	33%
Furka [48]	12 (4–48)	0% (0/17)	NS	12% (2/17)	24% (4/17)	NS	12 (4–48)	NS	NS	NS
Kollmar [68]	NS	NS	NS	NS	NS	NS	NS	NS	NS	50%
Lubrano [30]	29 (12–77)	0% (0/16)	NS	38% (6/16)	56% (9/16)	17 (12–77)	29 (12–77)	94%	61%	33%
Thelen [43]	24 (1–135)	0% (0/39)	NS	13% (5/39)	NS	NS	NS	77%	50%	42%
Lendoire [69]	NS	NS	NS	NS	NS	NS	NS	NS	NS	53%
Adam [26]	38[a]	0% (0/85)	9 (5–22)	22% (19/85)	69% (59/85)	12[a]	32[a]	NS	NS	37%
Adam [25]	NS	NS	NS	NS	NS	NS	45[a]	NS	NS	41%
d'Annibale [34]	(3–70)[h]	0% (0/18)	NS	28% (5/18)	NS	NS	NS	NS	NS	25%[i]
Okaro [45]	(2–62)[h]	0% (0/6)	9 (4–12)	0% (0/6)	50% (3/6)	NS	23 (6–70)	NS	NS	NS
Sakamoto [35]	72 (0–216)	0% (0/34)	NS	NS	76% (26/35)	NS	36 (1–240)	NS	52%	21%
Weitz [70]	NS	0% (0/29)	NS	NS	NS	NS	48[a]	NS	NS	NS
Yedibela [71]	NS	NS	NS	NS	NS	NS	40[a]	NS	70%[f]	49%
Arena [46]	NS	0% (0/17)	12 (7–24)	29% (5/17)	53% (9/17)	NS	43[a, j]	92%	52%	41%
Gomez [72]	17 (17–33)	0% (0/3)	16 (10–46)	67% (2/3)	NS	NS	17 (17–33)	NS	NS	NS
Vlastos [37]	25 (3–140)	NS	NS	NS	52% (16/31)	NS	25 (3–140)	NS	86%[f]	61%
Elias [27]	32 (3–122)	0% (0/54)	11[a, c]	13% (7/54)	56% (30/54)	NS	34[a]	NS	50%	34%
Carlini [47]	(18–130)[g]	0% (0/17)	NS	12% (2/17)	59% (10/17)	NS	53[a]	NS	NS	46%
Karavias [73]	NS	0% (0/4)	NS	NS	NS	NS	48 (10–72)	NS	NS	NS
van Ruth [74]	NS	0% (0/3)	NS	NS	NS	NS	21 (16–41)	NS	NS	NS
Kondo [49]	NS	0% (0/6)	NS	0% (0/6)	83% (5/6)	NS	28 (10–64)	NS	60%	40%
Maksan [50]	29 (10–67)	0% (0/9)	12 (9–15)	NS	56% (5/9)	NS	NS	NS	NS	51%
Pocard [53]	23 (1–72)[k]	0% (0/49)	NS	12% (6/52)[k]	NS	NS	42[a, k]	86%[k]	65%[k]	NS
Selzner [42]	17 (6–144)	6% (1/17)	7 (4–10)	0% (0/17)	71% (12/17)	6 (1–144)	24 (0–144)	NS	NS	22%
Yoshimoto [44]	NS	0% (0/25)	NS	0% (0/25)	72% (18/25)	24 (2–132)	24 (6–132)	NS	71%[f]	27%
Seifert [51]	12 (1–88)	0% (0/15)	14 (9–60)	20% (3/15)	53% (8/15)	5 (1–72)	12 (1–88)	100%	54%	NS
Raab [36]	NS	3% (1/35)[l]	NS	29% (10/35)[l]	NS	NS	27[a]	NS	NS	18%
Schneebaum [54]	NS	0% (0/6)	NS	NS	NS	21 (6–40)	42[a]	NS	NS	NS
Stehlin [75]	NS	NS	NS	NS	NS	NS	NS	NS	56%	11%
Median (range)	29 (12–72)	0% (0–8%)	11 (6–16)	21% (0–67%)	59% (24–83)	22 (5–29)	36 (12–58)	90% (77–100%)	56% (31–79%)	37% (11–61%)
Percentage (n/t)		0.7% (6/918)		20% (174/852)	62% (325/523)					

NS = Not stated.
[a] No range available.
[b] Includes 50 patients, as an additional 10 patients underwent explorative laparotomy and 6 patients underwent thermal ablation.
[c] Mean.
[d] Includes 42 patients, as an additional 3 patients underwent thermal ablation.
[e] Median follow-up of 26 patients as 14 patients underwent thermal ablation.
[f] 2 year survival.
[g] Includes 32 patients, as an additional 2 patients underwent thermal ablation.
[h] No median.
[i] Of patients who developed BCLM within 36 months after breast cancer treatment.
[j] Median overall survival of the 11 patients that are still alive.
[k] Includes 52 patients, as an additional 3 patients received a biopsy.
[l] A patient had 2 LRs on separate occasions.

whilst one study found improved survival for those under the age of 50 years [40].

The primary tumor histology, grade and the lymph node status was considered insignificant in 3, 12 and 7 studies, respectively [26,27,30,31,33,35,37–43,53,55]. The type of breast surgery did not appear to influence survival [26,31]. A positive hormone receptor status of the primary tumor was found to be a significant positive prognostic factor in 6 studies involving 341 patients [22,24,27,38,41,55], of which 3 studies included multivariate analysis [24,27,55]. One study (n = 16) identified an absence of hormone receptors as a positive predictor in overall survival [30] and 8 studies found no difference [26,28,31,35,37,39,42,43]. The expression of HER-2 improved overall survival in 1 study (n = 34) on multivariate analysis [40] and 5 studies (n = 272) could not identify a difference [24,26,43,55].

Five studies, 2 of which were multivariate analyses, including a total of 205 patients, found that the presence of extrahepatic metastases had a negative impact on overall survival [26,35,38–40,43]. Five studies involving 154 patients stated that extrahepatic metastases did not significantly affect patient survival [33,38,41,42,44].

4. Discussion

This review is currently the largest to date, describing an extensive range of disease characteristics, treatment details and outcomes extracted from 1686 patients that have undergone LR of BCLM. We have demonstrated an acceptable 5-year survival (37%) with low mortality (0.7%) and morbidity rates (20%).

Recent advances in chemotherapy have opened up the potential for BCLM patients to survive for longer. Chemotherapy can be used in conjunction with LR to produce a synergistic effect. A case-control trial described 51 patients undergoing LR and chemotherapy who were matched against 51 patients receiving chemotherapy alone based on their age, year of breast cancer diagnosis, interval between breast cancer and BCLM diagnoses, TNM stage of breast cancer, breast cancer hormone receptor status and breast cancer histology. The 3-year survival was 81% for those receiving surgical and medical treatment and 51% for patients receiving medical treatment alone ($p < 0.0001$). There was a 3.04-fold higher risk of death (CI: 1.87–4.92, $p < 0.0001$) with medical treatment alone [22]. Another similar study compared patients undergoing LR with neoadjuvant chemotherapy (n = 12) against those receiving chemotherapy (n = 38). Patients receiving chemotherapy had a median survival of 9.7 months (range, 2–15 months) compared to 29.5 months (range, 12–64 months) in those undergoing LR with neo-adjuvant chemotherapy [28].

The presence of synchronous or metachronous metastases does not seem to affect survival [29,43,55], however a prolonged interval between breast cancer treatment and diagnosis of BCLM appears to be a positive prognostic factor [24,28,29,33,39,42,53,55] with an overall survival significantly longer for patients with a disease-free interval greater than 12 months [33,42], 24 months [24,28,29,55] and 48 months [39,53]. Unlike colorectal metastasis, a solitary metastasis [26,35,37,41–44,53], unilobar tumor distribution [26,41,43], small tumor size, and the extent of resection, whether it was major or minor [26,27,33,35–38,40,42–44] were not shown to be associated with improved survival. The hormonal status and the grade of the tumor may be more important in determining the prognosis than the presence of liver metastasis. However, there is insufficient data to substantiate this hypothesis.

A number of other liver directed therapies have been proposed to treat BCLM. The use of catheter for direct chemotherapy drug administration and embolization to disrupt the vasculature supplying the tumor have been described in patients that are deemed unresectable [56]. It can be used to reduce the size of the metastasis, which may play a role in increasing the number of patients that are amenable to resection, but they are not curative treatments.

Thermal ablation by radiofrequency (RFA) or microwave (MWA) ablation has been described. It has principally been employed for the treatment of unresectable tumors or for patients who cannot undergo resection due to medical comorbidities [57]. Thermal ablation is a safe procedure with low complication rates [58,59]. A few studies had compared the efficacy of RFA over resection. Treska and Dittmar reported on 17 patients undergoing RFA, and found that the overall survival was not significantly different from patients undergoing resection [39,40]. Polistina described poorer median survival for patients receiving RFA (13.5 months) compared to resection (29.5 months) ($p < 0.05$) [28]. In a similar manner to primary liver cancer or metastatic colorectal cancer, thermal ablation is likely to have a role, but it should be considered in patients with small (<3 cm) metastases where LR is not deemed appropriate.

Current guidelines state that the assessment of distant metastases from breast cancer should only be initiated from clinical suspicion. Tests should not be routinely conducted on asymptomatic patients as it is likely to yield very little positive results and so patients will generally not benefit from a complete laboratory work-up and radiological staging [60,61]. However, there is a subset of patients who are at risk of developing asymptomatic metastatic disease which require closer surveillance and thus have a lower threshold for investigation. These are patients with positive axillary nodes, larger sized primary tumor and inflammatory breast cancer [62–64]. The detection rate for metastatic disease has improved with the application of newer modalities such as PET and PET integrated with CT (PET/CT) [64,65]. A systematic review, looking at imaging for detecting asymptomatic metastases in breast cancer, has shown that whilst conventional imaging (chest X-rays, abdominal ultrasound, bone scintigraphy, CT) detected a median prevalence of 2.1%, PET or PET/CT alone detected a median prevalence of 10.3%. Whilst these values are likely to be falsely elevated due to the selection bias within the studies, there is a clear discrepancy of detection rates of metastatic disease between the conventional method and the newer modalities [64].

This review represents a collection of non-randomized retrospective studies. The number of patients included in each of the studies is very small, with only 6 manuscripts reporting on more than 50 patients. In combining the articles with small sample sizes, there is a significant heterogeneity between the selection criteria, disease stage and treatment characteristics. Furthermore, patients in this review have undergone LR over a period of 26 years, during which time there has been a significant advancement in the medical and the surgical management, making it difficult to reflect the overall results with contemporary practice. Given that isolated resectable liver metastases are rare, it is unlikely that a prospective single center trial is feasible, and the evidence will remain constrained by potential confounders.

5. Conclusion

Liver resection is an effective treatment for liver metastases and can be performed with low morbidity and mortality. Although rarely indicated, LR for BCLM should be considered in patients with isolated liver metastases as the evidence suggests that their survival is improved compared to chemotherapy alone.

Conflicts of interest

None.

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