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# Robotic Liver Resection for Breast Cancer Metastasis: A Multicenter Case Series and Literature Review

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**Abstract**

**Background:** Breast cancer is a widespread disease and, when metastatic, has a bleak prognosis. The surgical approach for BCLM has had a limited role, but robotic surgery could find an important place. **Methods:** Data were collected from a multicenter retrospective database that includes 1070 consecutive robotic liver resections performed in nine European hospital centers from 2011 to 2023. Of the entire series, 35 were performed for BCLM in five European hospital centers. **Results:** The post-operative complication rate was 11.44%, but no severe complications occurred. The mean hospital stay was 4.65 days. One patient (2.85%) was readmitted to the hospital within 90 days after discharge and died due to heart failure, with a 90-day mortality of 2.85%. **Conclusions:** Robotic liver resection for BCLM is feasible and safe when performed in experienced centers by surgeons who have completed the learning curve.

**Keywords:** breast cancer; breast cancer liver metastasis; liver surgery; robotic liver surgery; metastatic breast cancer

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## 1. Introduction

Breast cancer (BC) is a significant issue for society worldwide, and, as recent global cancer statistics indicate, BC has overtaken lung cancer and become the most frequently diagnosed cancer worldwide [1]. Furthermore, BC is the leading cause of cancer-related mortality among women, ranking fifth in overall cancer deaths [1].

Despite screening programs, primary disseminated breast cancer is still diagnosed in 10% of patients [2] and it is the development of metastases that is the main cause of cancer deaths. In particular, patients with BC have liver metastases in 32–35% with a 5-year overall survival (OS) of 13% [3].

The management of liver metastases from breast cancer (BCLM) is an area of ongoing research, and the possibility of combining loco-regional therapies and surgical resections with systemic therapy, as is the case with metastases from colorectal cancer, is being investigated [4]. The push towards the frontier of surgery in the treatment of BCLM is also given by new robotic technologies that allow liver surgery to be performed with minimal invasiveness and very fast recovery times, while maintaining high oncological safety profiles [5].

This study aims to evaluate the feasibility in surgical and oncological terms of robotic resections for BCLM. To the best of our knowledge, this is the first published study analyzing these aspects of BCLM.

## 2. Materials and Methods

This is a retrospective multicenter study based on a database of 1070 RLRs performed in nine tertiary hepatobiliary surgery centers between 2011 and 2023, involving nine European hospitals. Of the entire series, 35 liver resections were performed for BCLM. All clinical cases were discussed in the local multidisciplinary meeting and all patients signed an informed consent form to collect clinical data. Data regarding patient characteristics and disease characteristics, referred to as preoperative data, were analyzed, as well as data regarding the surgical procedure, the post-operative period and follow-up. Liver segmentation anatomy was defined using the Couinaud classification, while the Brisbane 2000 terminology was used to define the liver resection type [6].

Demographic and anamnestic data of patients consisted of age, gender, BMI, American Society of Anesthesiologists (ASA) score, Charlson comorbidity score, and previous abdominal surgery.

Based on the findings of the preoperative CT scan performed on all patients in the cohort, we analyzed the number, size, location, and any vascular contact of the lesion. With these data, we also calculated the TAMPA difficulty index score [7]. It should be noted that all patients underwent preoperative staging with chest-abdomen-pelvis CT, while MRI was not always used.

Concerning data relating to surgery, it should be noted that all procedures were performed by experienced hepatobiliary surgeons using the Da Vinci robotic platform, but with the aid of different transection techniques and devices. Intraoperative ultrasound (IOUS) and preparation of the Pringle maneuver were performed routinely in all centers, but the use of intermittent hilar clamping varied according to the experience of each center.

Intraoperative data concern the type of liver resection performed, the conversion rate to another approach, the operating time, the number of intermittent clamps, and estimated blood loss, defined as the difference between the fluid present in the suction receptor and the lavage solution infused into the abdominal cavity.

The data on complications include both the absolute value and details of complications, as well as the rate of severe complications according to the Clavien–Dindo grading system [8] and the rate of reoperations. We also calculated the length of stay in the intensive care unit (ICU) and the total length of hospital stay. Data on histological examination, such as surgical margins and R1 resections, and 90-day data on readmission and mortality are also available. In addition, there is an analysis of disease-free survival (DFS) and patient follow-up.

## 3. Results

Patients' characteristics and perioperative data are shown in Table 1.

**Table 1.** Patients' characteristics and perioperative data.

| Variables | *n* = 35 |
|---|---|
| Age (year), mean | 61 (36–84) |
| BMI (kg/m$^2$), mean | 25 (22–40) |
| ASA score ≥ III, *n* (%) | 15 (42.5%) |
| Charlson comorbidity score, mean | 6.42 (2–17) |
| Previous open abdominal surgery, *n* (%) | 9 (25.71%) |
| Previous laparoscopic abdominal surgery, *n* (%) | 3 (8.57%) |
| Cirrhosis, *n* (%) | 1 (2.85%) |
| Number of lesions, mean | 1.26 (1–4) |
| Tumor: size of the biggest lesion (mm), mean | 29.21 (3–90) |
| Vessel contact, *n* (%) | 9 (25.7) |
| TAMPA score (group), mean | 2.11 |

BMI: body mass index; ASA: American Society of Anesthesiologists; MELD: Mayo end-stage liver disease.

The mean age was 61 years, and the mean BMI was 25 kg/m$^2$. ASA ≥ III patients were 42.85%, with a mean Charlson comorbidity score of 6.42. All the patients had previous breast surgery, but twelve (34.28%) had previous abdominal surgery, nine (25.71%) with an open approach and three (8.57%) with a laparoscopic approach. Only one of the patients (2.86%) suffered from cirrhosis of the liver, which was due to nonalcoholic steatohepatitis (NASH). In all cases, the disease was oligometastatic, and, in more than half of the patients (57.1%), the lesion was single. In 31.4%, there were two metastases, and in 11.4%, there were four.

Most of the surgeries (91.4%) had a Tampa Difficulty Score (TDS) of 2, while the remaining 8.6% had a TDS of 3.

Regarding the localization of BCLM, regardless of whether it was single or multiple, segments were affected with a frequency shown in Table 2.

**Table 2.** Localization of lesions.

| Liver Segment | Frequency of Involvement (%) |
|---|---|
| **I** | 0 |
| **II** | 17.1 |
| **III** | 17.1 |
| **IV** | 34.2 |
| **V** | 31.4 |
| **VI** | 17.1 |
| **VII** | 28.6 |
| **VIII** | 14.3 |

Intraoperative data are summarized in Table 3. According to the Brisbane 2000 terminology of liver anatomy and resections [9], major resections were performed in 5.7%, while the rate of anatomical resection was 34.3%. More specifically, 23 (65.7%) wedge resections, 4 (11.4%) segmentectomies, 6 (17.1%) bisegmentectomies, 1 (2.9%) left hepatectomy, and 1 (2.9%) right hepatectomy were performed. In particular, major liver resections were performed either because of the size of the lesion (90 mm in the right hepatectomy) or because of its proximity to vascular structures, as in the case of the left hepatectomy, where the lesion was close to both the portal pedicle and the hepatic vein. About the other resections, a parenchymal-sparing approach was used in the case of wedge resections, while segmental resections were opted for, again taking into account the size of the tumor and its proximity to the vessels. In 2 cases (5.71%), it was necessary to convert, and, in both cases, the conversions were to the open approach. The operative mean time was 210.28 min while the median was 180 min. The mean estimated blood loss was 151.17 mL with a median of 150 mL, and two times (5.7%) blood transfusion was required. In 31.4% of cases, intermittent pedicle clamping was performed.

**Table 3.** Intraoperative data.

| **Variables** | ***n* = 35** |
|---|---|
| Major resection, *n* (%) | 2 (5.71%) |
| Anatomical resection, *n* (%) | 12 (34.3%) |
| Conversion to open, *n* (%) | 2 (5.71%) |
| Conversion to laparoscopy, *n* (%) | 0 |
| Operative time (min), mean | 210.28 (90–345) |
| Estimated blood loss (mL), mean | 151.18 (25–300) |
| Blood transfusion, *n* (%) | 2 (5.71%) |
| Pedicle clamping, *n* (%) | 11 (31.4%) |

The overall post-operative complication rate was 11.4%. One patient had ascites (2.85%), two patients had pulmonary infection (5.7%), and one patient (2.85%) had other infections. None of these complications was severe (Clavien-Dindo classification $\geq 3$), and no one was reoperated. In 17 cases (48.6%), the patient spent the first post-operative night in the ICU, and every patient came back to the inpatient ward on the first post-operative day. The mean and median hospital stay were 4.65 days and 5 days, respectively. Two patients (5.7%) were readmitted to the hospital within 90 days after discharge, and seven patients (20%) had disease recurrence with a mean disease-free survival of 32 months. One patient (2.85%) died due to heart failure with a 90-day mortality of 2.85%. At a median follow-up of 24 months, there were no further deaths. All post-operative data are summarized in Table 4.

**Table 4.** Post-operative data.

| **Variables** | ***n* = 35** |
|---|---|
| Post-operative complication, *n* (%) | 4 (11.4%) |
| Ascites, *n* (%) | 1 (2.85%) |
| Pulmonary infection, *n* (%) | 2 (5.71%) |
| Other infections, *n* (%) | 1 (2.85%) |
| Severe complication (Clavien $\geq 3$), *n* (%) | 0 |
| Re-intervention, *n* (%) | 0 |
| First night in ICU, *n* (%) | 17 (48.6%) |
| Total hospital stay (days), mean | 4.65 (2–8) |
| Surgical margins (mm), mean | 9.84 (0–21) |
| R1 parenchymal, *n* (%) | 3 (8.6%) |
| Readmission at 90 days, *n* (%) | 2 (5.71%) |
| Mortality at 90 days, *n* (%) | 1 (2.85%) |

**Table 4.** *Cont.*

| Variables | $n$ = 35 |
|---|---|
| Follow-up time (months), mean–median | 26.26–24 |
| Disease recurrence, $n$ (%) | 7 (20%) |
| DFS (months), mean–median | 32–32 |

ICU: intensive care unit; DFS: disease free survival.

## 4. Discussion

In this case series, all resections were made for metachronous BCLMs in adult women with an acceptable operative risk according to the ASA score. On average, patients were not elderly, according to the World Health Organization definition [10], and were overweight, with an average 85% one-year mortality according to our data regarding the mean Charlson comorbidity index score [11]. Approximately one quarter of the patients had already undergone abdominal surgery, one third of them laparoscopic, and only one patient suffered from liver disease, specifically NASH. All cases had oligometastatic disease [12], and more than half of the patients had a single metastasis, with an average size of about three centimeters. About half of the BCLMs also involved a single hepatic segment and in about a quarter of the cases were in contact with vessels. About two-thirds of the liver resections were non-anatomical. The remaining anatomically performed liver resections were performed for reasons of lesion size or when the lesion had vascular contact, similar to what is suggested in the literature in the more frequent colorectal cancer metastases [13]. Consequently, major liver resections were performed in a small number of cases. In fact, according to our data, the average Tampa difficulty score was 2.08, indicating that most of the resections belonged to group 2 (intermediate). Of the three cases with a Tampa difficulty score of 3 (more demanding), two of them, both right posterior sectionectomies, required conversion to an open approach, both for bleeding reasons, and in both cases blood transfusions were performed. Analyzing the estimated blood loss, the mean total and the mean excluding these two cases are similar (151.18 vs. 145). Taking these data into consideration, the reasons for these similar situations appear to be multifactorial. On the one hand, we know that the type of surgery performed is very challenging in robotic surgery for anatomical reasons, and, not surprisingly, it is a more demanding surgery according to the Tampa difficulty score. It is also true that if this surgery is more demanding for the surgeon, it is also more demanding for the anesthetist. Performing a right posterior sectionectomy involves complete mobilization of the right liver, with prolonged times of increased pressure on the inferior vena cava and increased clamping times. Taking all these factors together, what probably led to the conversion of these two cases to open lies is a concomitant surgical and anesthesiological difficulty and, perhaps, a pre-operative anemic state of the patients, compatible with their female sex and previous chemotherapy [14,15]. However, the data concerning blood loss and the duration of surgery are inferior to what has been reported in other significant studies [5,16], probably due to the not very demanding resections and the better performance capability with robotic surgery. In this type of resection, therefore, we are somewhere between the times of open surgery and the times of robotic surgery. Indeed, it is well known that robotic surgery requires longer preoperative times because, in addition to the time needed to dock the robot, various procedures are also required to set up the operating theater and anesthesiological strategies [17]. However, the real gain of robotic surgery over open surgery lies in the post-operative period. Post-operative complications were 11.84%, but none of these required anything other than drug therapy. In addition, the median hospital stay was 5 days and, if we consider that in many hospitals the first night is spent in the ICU as a precaution, we can guess that robotic liver surgery has a shorter median hospital stay than open liver surgery and is similar to other open surgeries of much less difficulty. Regarding safety, only two patients had complications after hospital discharge. Of these, one was managed on an outpatient basis, while the other required hospitalization and subsequently died of cardiac arrest. All patients received post-operative chemotherapy, and, in one-fifth of the cases, there was recurrence, treated with chemotherapy.

The liver is the third most common site for BC metastasis behind bones and lungs [18] and in 10% to 25% of patients with BCLM, metastases are confined to the liver [19]. The molecular mechanisms underlying breast cancer metastasis have been reported for breast cancer dissemination to the lungs and bone [20–23], but they are not as clear for BCLMs. Ma et al., by combining the knowledge from the extant research, propose a model for BCLM consisting of 5 steps: (1) intravasation, in which the breast cancer cells come into the circulation; (2) circulation of breast cancer cells; (3) margination: CTCs arrest at the liver site by adhering to the sinusoidal endothelial cells; (4) extravasation, in which the migrated breast cancer cells pass through the endothelium and proliferate in the liver; (5) colonization of breast cancer cells [24].

For a long time, the only treatments offered for BCLM were chemotherapy and best supportive care alone, without the possibility of surgery [25,26]. However, despite constant innovations in chemotherapy and target therapies, there are few possibilities for treatment with systemic therapy alone. For this reason and because of the costs in the development and production of drugs for target therapies [27,28] other therapeutic possibilities have been explored following the route taken in other diseases involving the liver, such as hepatocellular carcinoma or liver metastases from colorectal cancer. Following the first studies showing that liver resections for BCLM can improve 5-year survival [29], international guidelines have recognized that surgical resection may be recommended in selected cases [30–33].

There are two main types of therapy for BCLM: systemic treatment and local treatment. Systemic therapy of BCLM depends on estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 status (HER2). Anthracyclines or taxanes are generally preferred chemotherapy regimens. In a retrospective study of patients who received anthracycline or anthracycline plus taxane-based chemotherapy, 66.4% of the patients achieved an objective response [34]. Radiofrequency ablation (RFA) is widely used in patients with primary liver cancer and colorectal cancer liver metastasis, but its role for BCLM remains controversial [35–37], such as for hepatic arterial embolism (TAE), transcatheter hepatic arterial chemoembolization (TACE) and hepatic arterial infusion chemotherapy (HAI) [4]. Another local non-surgical treatment is radiotherapy, but the liver parenchyma has low radiation tolerance doses. However, by delivering higher doses to small volumes, organ function can be maintained without causing functional compromise [38]. Stereotactic Body Radiation Therapy (SBRT) and Interstitial Brachytherapy (BT) are two options for radiotherapy treatment of BCLM, but patient selection criteria and optimal dose and fractionation for liver SBRT are still under investigation [39].

Regarding surgery, the principal question relative to BCLM resection remains proof of its usefulness. Because of the lack of evidence in the literature, it is difficult to draw any definitive conclusions, and it is always a topic of discussion between surgeons and oncologists at multidisciplinary meetings.

In 2013 Mariani et al. matched 51 patients who had received surgical treatment with 51 patients treated with drug therapy alone between 1988 and 2007. In 93% of cases, the patients presented with metachronous lesions, and liver resection was associated with improved survival (under multivariate analysis, a 3-year survival rate of 81% vs. 51%; $p < 0.0001$) [40].

In 2016 Sadot et al. compared sixty-nine operated patients with ninety-eight patients who had received exclusive systemic therapy. The overall survival (OS) rates did not differ between the two groups, thus questioning the utility of surgery. However, these conclusions are open to criticism because numerous biases were observed [41].

In 2019, He et al. showed 1-, 3-, and 5-year OS of 93.5%, 73.7% and 32.2%, respectively, among 67 patients with BCLM who underwent liver resection [42].

More recently, Liu Q. et al. published a paper on the variation in receptor expression in breast cancer metastases and its impact on survival. According to this paper, the positivity of estrogen receptors (ER) increases patient survival, while negativity worsens the prognosis. Similarly, Liu Q. et al. noted that patients with HER2-negative primary breast cancer develop HER2-positive tumors [43]. It can therefore be inferred that these changes in ERs and HER2 expression are a central element in the treatment of BCLM, as they may enable targeted therapy and improve the prognosis of these patients.

Also in 2025, Garzeli IU et al. [44] conducted a meta-analysis and systematic review of thirteen studies and demonstrated the efficacy of liver metastasectomy in patients with oligometastatic liver disease. According to their study, the 3-year and 5-year overall survival of patients undergoing liver metastasectomy and systemic therapy is statistically significantly higher than systemic therapy alone.

One possible explanation for the poor efficacy of systemic therapy could be the tumor microenvironment (TME). In their recent work, Godin et al. explain how BCLMs have a TME that is completely different from most solid tumors. In particular, BCLMs preserve the stromal structure of the liver and do not need angiogenesis to survive, so they have a much smaller vascular network than normal, which limits the diffusion of systemic drugs within them. On the other hand, according to Godin et al., BCLM's TME is also very rich in macrophages, and they aim to exploit the latter to deliver systemic drugs within BCLMs through nanomedicine [45].

However, all the weapons we have at our disposal against BCLMs must be used with caution. Berardi et al. recently described the case of a young woman who, following a diagnosis of unresectable BCLM, developed liver failure following multiple systemic and locoregional treatments, requiring a liver transplant (LT) [46]. LT is considered the treatment of choice for hepatocellular carcinoma in cirrhosis and end-stage liver disease, but recently there has been growing interest in studying the curative potential of LT for secondary diseases [47]. There are many ongoing trials regarding the possibility of performing LT for metastases from colorectal, neuroendocrine, and other tumors, but despite this, BCLMs are still considered an absolute contraindication to LT. Berardi et al., therefore, open the door to a new therapeutic possibility for BCLMs [47].

As mentioned above, systemic therapy for metastatic breast cancer is making great strides thanks to targeted therapy research. At the same time, liver surgery is also making great improvements, first thanks to laparoscopic surgery and now robot-assisted surgery. Thanks to the robotic system, it seems possible to overcome some of the limitations of laparoscopic surgery, which made this type of approach less safe than open surgery. In particular, robotic surgery's technologies allow useful vascular control and hemostasis. Together, the use of increasingly advanced technologies applicable to robotic surgery makes this type of approach increasingly safe from a surgical and oncological point of view [48].

## 5. Limitations

Limitations of this study include the retrospective design and potential biases of a multicenter, nonrandomized protocol. Other limitations of the study are certainly the small number of patients in the cohort and the relatively short follow-up period, as well as the lack of data on the biology of primary breast cancer.

## 6. Conclusions

Breast cancer is a terrifyingly frequent disease, and, when it is metastatic, we have few weapons at our disposal to improve prognosis despite research and economic efforts to develop increasingly targeted drugs for systemic therapy. In the wake of similar diseases such as liver metastases from colorectal cancer, encouraging data are coming from some types of loco-regional treatments for liver metastases from breast cancer. Radiotherapy has shown some satisfactory results, but studies are ongoing to identify patients who may benefit from it. Surgery, until a few years ago, was not given much consideration due to the invasiveness of liver surgery and poor outcomes. With the spread of minimally invasive liver surgery and, in particular, of robot-assisted surgery, the perioperative outcomes of liver surgery could improve, and it could play a crucial role in the treatment of liver metastases from breast cancer, as it does in liver metastases from colorectal cancer. To date, our study is the first to evaluate the safety and efficacy of robotic surgery in this setting. Locoregional treatment, including robotic liver resection, may offer a curative option for carefully selected patients with oligometastatic breast cancer confined to the liver. When combined with targeted systemic therapy and evaluated through a multidisciplinary approach, this strategy can enhance disease control and potentially prolong survival. While systemic treatment remains the backbone of metastatic breast cancer management, surgical resection or ablative techniques may improve outcomes in well-selected cases, supporting the role of locoregional therapy as a part of a comprehensive treatment plan. More in-depth and consistent studies are, however, needed to validate this suggestion and add an extra weapon in the treatment of this pathology with a poor prognosis.

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