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# Robotic liver resection for non colorectal metastases: how to deal with it. A multi-center case series

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A B S T R A C T

*Background:* The state of the art for robotic liver metastasis resection is not yet well-defined and remains a topic of debate. While hepatic resection for colorectal liver metastases (CRLM) is recognized as a valuable approach for systemic disease control, hepatectomy for non-colorectal liver metastases (NCLM) has shown varied outcomes.

*Materials and methods:* A retrospective analysis was conducted on patients who underwent robotic liver resections for NCLM from 2012 to 2023 across seven European hospital centers. Preoperative, intraoperative, and postoperative data were collected for each patient, including overall and disease-free survival.

*Results:* Distribution based on primary tumor histology revealed a prevalence of breast carcinoma (38%) and neuroendocrine tumors (NET) (17.7%) compared to other primaries. Among the hepatic resections, 58 (45.8%) were wedge resections, 8 (10%) were segmentectomies, 12 (9.5%) were bisegmentectomies, and 1 (0.8 %) was a major hepatectomy. The majority of liver resections were assessed on an intermediate level of difficulty based on Tampa Score. The mean operative time was 226 min (range 90-480). There were 3 conversions to the open approach (3.8%). Severe complications (Clavien Dindo $\geq$3) occurred in 3 patients (5.1 %). The mean hospital stay was 5.3 days. The 1,3 and 5-year overall survival (OS) was 100%, 70% and 50%, respectively. The 1,3 and 5-year disease-free survival (DFS) was 75%, 40% and 30%, respectively.

*Conclusions:* The role of robotic liver resections for non colorectal metastasis remains challenging and unclear. Our findings indicate promising oncological outcomes that surpass existing literature, suggesting potential advantages of the robotic approach. Randomized controlled trials are still missing but essential to validate the safety and feasibility of the robotic approach for NCLM treatment.

## 1. Introduction

Robotic liver resections (RLR) have become a topic of growing interest, particularly in the management of liver metastases. Robotic approach is well-established for colorectal liver metastases (CRLM), instead its role for non-colorectal, non-neuroendocrine liver metastases (NCNNLM) is less defined, partly due to the rarity and heterogeneity of these metastases, as well as the limited availability of randomized

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controlled trials (see Table 3).

The available literature mostly reports CRLM and neuroendocrine liver metastases (NELM), with studies indicating encouraging long-term outcomes for these groups. However, NCNNLM remains an area of active investigation. The complexity and diversity of NCNNLM make it difficult to develop standardized treatment protocols. Research efforts are increasingly focused on identifying the specific factors that might predict positive outcomes for NCNNLM, with the goal of guiding patient selection and refining surgical approaches.

Our study aims to contribute to this evolving field by examining the outcomes of robotic liver resections for NCLM, including NET-LM. We hypothesize that a robotic approach can provide safe and effective treatment with outcomes comparable to those achieved in CRLM. By analyzing survival rates and perioperative data, we seek to expand the current understanding of robotic liver surgery's role in NCLM management and to support the development of evidence-based protocols.

## 2. Materials and methods

Patients who underwent robotic liver resections for NCLM from 2012 to 2023 in seven European Hospital Centers were retrospectively reviewed.

Patients with histologically confirmed liver metastases, R0 resections and older than 18 years were included in the study.

Patients younger than 18 years, with American Society of Anesthesiologists (ASA) score ≥ IV, R2 resection were excluded from the robotic approach.

Preoperative, intraoperative and postoperative data were collected for each patient.

The primary endpoint of this study was to evaluate overall survival (OS) and disease free survival (DFS). Post-operative complications were analyzed at 90 days.

### 2.1. Pre-operative data

Preoperative data, in terms of patient characteristics and tumor characteristics, were recorded and analyzed. For each included patient, characteristics such as age, gender, body mass index (BMI), previous abdominal surgery, comorbidity, preoperative chemotherapy, Charlson Comorbidity Index (CCI), tumor size and primary tumor were recorded. CT scan and abdominal MRI were performed to assess the disease, systemically. The surgical risk was assessed considering the scoring system from the American Society of Anesthesiologists (ASA). The surgical indication was validated by the multidisciplinary team.

### 2.2. Intra-operative data

Liver segmentation anatomy and liver resection type were defined using the Couinaud classification and the Brisbane 2000 terminology, respectively [1,2].

Major liver resection was defined as the resection of three or more contiguous Couinaud segments [3]. Each surgical procedure included intraoperative ultrasound as an essential tool. Intraoperative data recorded included operative time, estimated blood loss, blood transfusion, use of the Pringle maneuver, conversion rate, and drain usage.

### 2.3. Post-operative data and long term outcomes

Post-operative complications including liver specific morbidity, infections, intensive care unit (ICU) stay and complication after hospital discharge, were recorded.

Adam's scoring system was used as a tool to predict recurrence free interval and overall survival [4]. The Tampa difficulty score was used to assess the intraoperative challenges and the risk of conversion [5]. Post-operative complications were graded using the Clavien-Dindo classification [6]. Long-term outcomes included overall survival and disease-free survival.

### 2.4. Literature review of minimally invasive resection of NCNNLM

A literature review was performed by searching on PubMed for articles related to liver resections for non colorectal liver metastases. The search strategy employed was: “non colorectal liver metastasis AND hepatic resections AND minimally invasive”. The exclusion criteria included: letters, editorials, congress abstract and full-text unavailability, studies not published in English. Articles were selected based on their relevance to the research question. Only the studies published after the year 2000 were included. Notably, no cohorts dedicated solely to robotic liver resections were identified.

The literature review was conducted within last 20 years.

## 3. Results

The study includes a total of 79 consecutive robotic liver resections for NCLM. Patients, tumour characteristics and peri-operative outcomes

**Table 1**
Patients, tumour characteristics and peri-operative outcomes.

| Variables | N = 79 |
|---|---|
| Age yr, mean (range) | 63 (3-84) |
| Male, n (%) | 50 (63.3%) |
| BMI (kg/m2)> 25, n (%) | 45 (56%) |
| ASA I/II/III score, n (%) | 3/40/36 (3.8/50.6/45.6 %) |
| Previous abdominal surgery, n (%) | 37 (46.8 %) |
| Preoperative chemotherapy, n (%) | 35[a, b, c] (54.7%) |
| Charlson comorbidity score, mean (range) | 7 (range) |
| Comorbidity ≥2 n, (%) | 13 (16.5 %) |
| **Number of lesions n, (%)** | |
| **1** | 43 |
| **2** | 25 |
| **3** | 5 |
| **4** | 6 |
| **Size of the biggest one mm, mean (range)** | 28 (6-70) |
| **Synchronous presentation n,(%)** | 3 (3.8 %) |
| **Contact with vessels** | |
| **Portal branch, n (%)** | 9 (11.4 %) |
| **Hepatic vein, n (%)** | 5 (4 %) |
| **Both, n (%)** | 1 (0.8 %) |
| **Type of resection** | |
| Wedge, n (%) | 58 (45.8%) |
| Segmentectomy, n (%) | 8 (10%) |
| Bisegmentectomy, n (%) | 12 (9.5%) |
| Major hepatectomy, n (%) | 1 (0.8%) |
| Operative time min, mean | 226 (90-480) |
| Conversion to open surgery, n (%) | 3(3.8 %) |
| Drain, n (%) | 50(77.2 %)[b] |
| R0, n (%) | 62/68[c] |
| Liver specific Morbidity, n (%) | 5 (6.3%) |
| Biliary Leakage, n (%) | 3 (3.8 %) |
| Hemorrhage, n (%) | 1 (1.3 %) |
| Ascitis, n (%) | 1 (1.3 %) |
| Pulmonary infections, n (%) | 4 (5.1 %) |
| Other infections, n (%) | 3 (3.8 %) |
| Prolonged pain, n (%) | 6 (7.6 %) |
| Clavien-Dindo classification (20 ND) | |
| 1, n (%) | 19 (32.2 %) |
| 2, n (%) | 7 (11.9 %) |
| 3, n (%) | 3 (5.1 %) |
| ICU stay 1/2 days, n (%) | 38/5 (48.1/6.3 %) |
| Total hospital stay days, mean (range) | 5.3 (2-14) |
| Complication after hospital discharge, n (%) | 1 (1.3 %) |
| 90-day readmission, n (%) | 2 (2.7 %) |
| OS 1,3 and 5-year | 100 %, 70 %, 50 % |
| DFS 1,3 and 5-year | 75 %, 40 %, 30 % |

[a] 15 NA.
[b] 14 NA.
[c] 11 NA.

are shown in Table 1.

### 3.1. Preoperative data

The mean age was 63 years and 50 patients (63.3%) were male patients (see Table 2). A BMI greater than 25 was observed in 45 (56%) of the patients. A total of 36 (45.6%) of patients were ASA III and 13 (16.5%) of patients had 2 or more comorbidities at the time of surgery.

The mean Charlson comorbidity score was 7. Additionally, 37 (46.8 %) of patients had undergone a previous abdominal surgery.

A total of 35 (54.7 %) of patients received neoadjuvant therapy before undergoing liver resection.

The distribution based on primary tumor histology (Fig. 1) was as follows: breast carcinoma (38%), neuroendocrine tumors (NET) (17.7%), gastric cancer (8.9%), gynecologic cancer (7.6 %), melanoma (5 %), gastrointestinal stromal tumor (GIST), lung, head and neck (ORL) and kidney cancers (3.8 %), testicular and pancreatic carcinomas (2.5%), and prostate carcinoma and retroperitoneal sarcoma (1.27%).

Surgery was performed for one metastasis in 43 patients, for 2 metastases in 25 patients, for three metastasis in 5 patients and for 4 metastasis in 6 patients.

The mean size of the largest lesion was 28 mm (range 6-70 mm). A total of 11.4 % of lesions were in contact with the portal branch and 4 % were in contact with the hepatic vein. Three patients (3.8%) underwent surgery for synchronous metastases.

### 3.2. Intra-operative data

In this series, liver resections were assessed on an intermediate level of difficulty based on Tampa Score for 59 (75%) of patients (Fig. 2).

Among the hepatic resections, 58 (45.8%) were wedge resections, 8 (10%) were segmentectomies, 12(9.5 %) were bisegmentectomies, and 1 (0.8 %) was a major hepatectomy.

The mean operative time was 226 min (range 90-480). Only one patient (1.27%) required an intraoperative blood transfusion. Pedicle clamping was performed in 24% of cases with a duration from 12 to 78 min. There were 3 conversions to the open approach (3.8%), due to posterior position of lesions and narrow contact with portal branch and hepatic vein.

In 50 patients, (77.2 %) drain was placed at the end of the procedure. R0 was achieved in 62 patients (78.5 %) and surgical margins (expressed in mm) are not described only for 11 patients of 79, while R1 was achieved in 6 patients.

**Table 3**
Post-operative outcomes of literature.

| Studies | Complications | 30-d Mortality | Hospital Stay |
|---|---|---|---|
| Adam et al., 2006 | 29 % | Not known | 14 mean (1-106) |
| Mayo SC et al., 2010 | Not known | 1.1 % | Not known |
| Takemura et al., 2013 | 17.9 % | 1.4 % | Not known |
| Schiergens et al., 2016 | 41 % | Not known | 8 mean |
| Mark Fairweather et al., 2017 | Not known | Not known | Not known |
| Dayna P. Y. Sim et al., 2017 | Not known | 1.28 % | Not known |
| Sano et al., 2018 | Not known | 1.5 % | Not known |
| Astrid Bauschke et al., 2022 | 21 % | Not known | Not known |
| Kelvin K.C. et al., 2023 | 19.5 % | 1.5 % | 8 mean |
| Yan Luk et al., 2023 | 22.5 % | 0.7 % | 8 mean |
| Our data | 15.2 % | 0 | 5.3 mean |

### 3.3. Post-operative data and long term outcomes

The total postoperative complication rate related to liver morbidity was 6.3 %, distributed as follows: biliary leakage 3.8 %, hemorrage 1.3 % and ascitis 1.3 %. Other complications included infections (pulmonary 5.1 %, others 3.8 %) and prolonged pain in 7.6 % of patients, who required a posterior resection, which is more demanding and stressful. Severe complications (Clavien Dindo ≥3) occurred in 5.1 % of patients. No patient was reoperated. The mean hospital stay was 5.3 days (range 2-14). One patient (1.3 % of 79) had complications after discharge. Only 2 patients (2.7 % of 79) were readmitted to the hospital within 90 days after discharge.

The mean follow-up period was 25 months with 7 patients lost during follow up. The mean OS was 25 months and the mean DFS was 22 months.

Death occurred in 14 (19%) patients and recurrence in 27 (37%) patients during FU.

R1 (<1 mm) resections were described in 4 cases, and in 2/4 of cases recurrence was observed; only in one case recurrence was the reason of death. In terms of incidence of death, there were not differences between patients with recurrence and without.

The 1,3 and 5-year overall survival (OS) was 100%, 70% and 50%, respectively.

The 1,3 and 5-year disease-free survival (DFS) was 75%, 40% and

**Table 2**
Review of hepatectomy for non-colorectal non-neuroendocrine liver metastases, overall survival (OS) and disease-free survival (DFS).

| Studies | Period | N. Patients | Primary tumor (GI/breast/GU/melanoma/sarcoma/o thers) | 3 year OS | 5 year OS | 3 year DFS | 5 year DFS |
|---|---|---|---|---|---|---|---|
| Adam et al., 2006 | 1983-2004 | 1452 | (314/460/332/148/0/1 98) | 49% | 36% | 27% | 21% |
| Mayo SC et al., 2010 | 1985-2009 | 339 | (269/NA/NA/NA/NA/6) | NA | 74 % | 24.2% | 5.9 % |
| Takemura et al., 2013 | 1993-2009 | 145 | (91/30/12/NA/NA/12) | 55.4% | 41 % | NR | NR |
| Schiergens et al., 2016 | 2003-2013 | 167 | (43/16/61/8/25/14) | 35% | 49% | NR | NR |
| Mark Fairweather et al., 2017 | 2003-2010 | 649 | NA | NR | 90 % | NR | NR |
| Dayna P. Y. Sim et al., 2017 | 2001-2014 | 78 | (24/6/25/NA/5/12) | NR | 66 % | NR | NR |
| Sano et al., 2018 | 2001-2010 | 1639 | NA | NR | 41 % | NR | 21 % |
| Astrid Bauschke et al., 2022 | 1995-2018 | 637 | (295/117/139/29/29/NR) | ND | 18 % | NR | NR |
| Kelvin K.C. et al., 2023 | 2009-2018 | 133 | (58/20/16/NA/5/NA) | 60 % | 48.9% | NR | NR |
| Yan Luk et al., 2023 | 1989-2019 | 151 | (62/24/4/NA/25/22) | 91.5% | 59.4% | 49.3% | 28.4% |
| Our data | 2013-2022 | 79 | (26/30/12/4/1/6) | 70 % | 50 % | 40 % | 30 % |

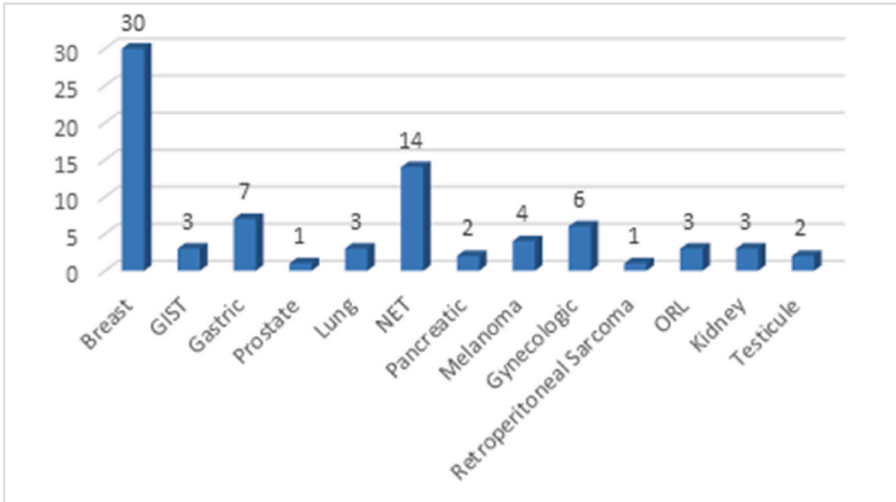


**Fig. 1.** Primary tumor histology.

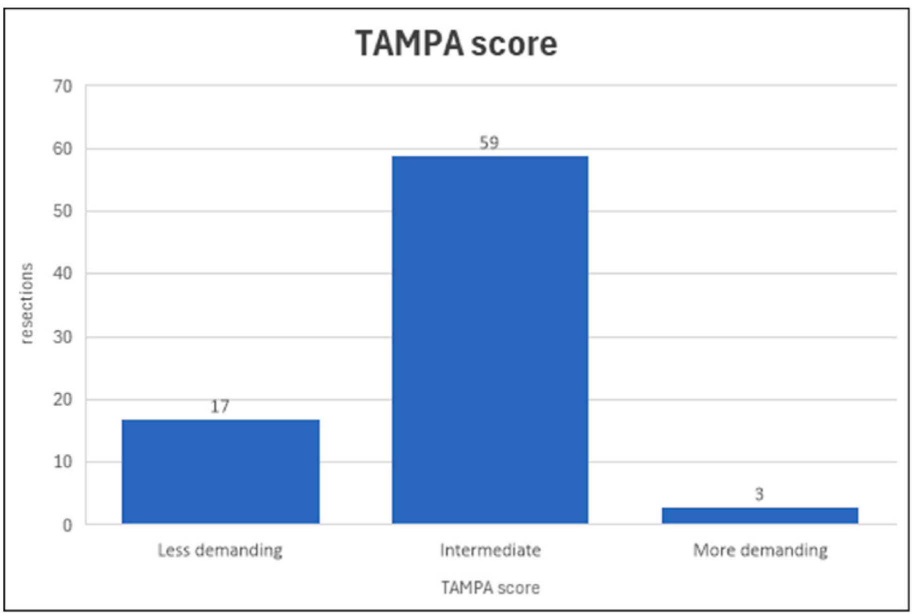


**Fig. 2.** Tampa difficulty score.

30%, respectively.

The main site of recurrence was the liver in 14 patients, followed by lung in 8 patients, bone in 4 patients, peritoneum in 3 patients, Lymph nodes in 2 patients and pancreas in 1 patient.

### *3.4. Literature review*

The literature review identified several key points addressing the safety of minimally invasive approach in terms of overall and disease free survival. The mean percentage of 3 -5 years OS was 59-52 % and 3-5 DFS was 33-19 %.

## 4. Discussion

The robotic approach for liver surgery has been expanding over the past decade. Recent retrospective analyses have demonstrated advantages, including improved surgeon ergonomics, easier access to posterior liver segment resections, and the integration of indocyanine green (ICG) imaging. Additionally, the robotic approach has been associated with a faster learning curve compared to laparoscopic methods. The centers taken into account in this series performed almost 15 robotic liver resections per year, with a shared learning curve of 10-15 procedures, before including the results above. However, perioperative outcomes such as transfusion rate, complication rate, conversion rate, R1 resection rate, and length of hospital stay showed no significant differences between robotic and laparoscopic approaches [7].

On the downside, the robotic approach involves additional operative time for docking and undocking, as well as increased costs. A modern scoring system for assessing the complexity of robotic hepatic resections, known as the Tampa Score, was introduced by Iswanto Sucandy et al. and has become a fundamental tool in standardizing robotic approaches for liver metastasis treatment [5].

Most of the outcomes reported in recent literature focus on minimally invasive surgical treatment for colorectal and neuroendocrine liver metastases. However, the role of surgical treatment for non-colorectal, non-neuroendocrine liver metastases (NCNNLM) remains uncertain due to their heterogeneity, and current efforts aim to establish the effectiveness of surgical intervention in these cases [8–10].

Most retrospective cohorts indicate better long-term outcomes for colorectal liver metastases (CRLM) compared to non-colorectal liver metastases (NCLM), specifically in terms of survival and disease-free intervals [8].

In this study, we aim to demonstrate the potential for improved oncologic outcomes with the robotic approach, focusing on overall survival (OS) and disease-free survival (DFS) as primary outcomes, and intra- and post-operative outcomes as secondary outcomes. This could establish the robotic approach as a valuable and safe alternative to open for both surgeons and patients. Our results are comparable for both short and long term outcomes to the ones reported below.

Currently, available literature on CRLM reports a promising 5-year survival rate, reaching up to 58% [8], similarly good long-term outcomes are described for neuroendocrine liver metastases [11,12], where surgical resection remains the primary means of enhancing survival. For NET liver metastases, studies report a notable difference in 5-year OS rates: from 24 to 52% for untreated cases to 43–77% for those receiving surgical resection [13].

Takemura et al. published a review of hepatectomies for non-colorectal, non-neuroendocrine liver metastases (NCNNLM), analyzing 10 case series. The reported 3- and 5-year overall survival (OS) rates were 34–57% and 19–42%, respectively, while the disease-free survival (DFS) rates at 3 and 5 years were 21–37% and 18–29% [14].

Martel et al. conducted a multi-center study demonstrating comparable 5-year OS rates between CRLM and NCNNLM groups (58% vs. 60.6%) [15].

Equally, in the NCNNLM group, the 3- and 5-year OS rates were 60% and 48.9%, compared to 57% and 39.8% in the CRLM group, with no statistically significant difference between them. Recurrence-free survival at 3 and 5 years was also similar between the NCNNLM group (32.7% and 25.1%) and the CRLM group (26.9% and 23.4%) [16].

Sano et al. provided robust evidence on the safety and efficacy of 1639 liver resections performed for NCNNLM, with a median OS time of 45 months. Overall survival rates at 5 and 10 year were 41% and 28%, respectively. Disease-free survival rates at 5 and 10 years were 21% and 15%, respectively (median of 11 months) [17].

Considering the collected data, our results demonstrated that OS rate are comparable to those previously reported in literature, while in terms of DFS are even more promising, with a 3 and 5 years DFS of 40 % and 30 %, in contrast to previous reviews that report a mean DFS of 20%.

The outcomes described reflect experience only from expert robotic centers with well established learning curves and high-volume.

Nevertheless, Dayna et al. further demonstrated the significant role of adenocarcinoma histotype in predicting 5-year recurrence and disease-free intervals [18].

Disease-free survival (DFS) may be influenced by the type of primary tumor, with more favorable outcomes reported in cases of breast cancer or neuroendocrine tumors (NET), as demonstrated by Noelia De-Armas-Conde et al. [19]. Another significant contribution to the feasibility of achieving favorable outcomes with a surgical approach for NCNNLM is highlighted in Takemura et al.'s review [8], which reports median survival times of 23–49 months at 3–5 years, with post-operative mortality and morbidity rates of 0–5% and 18–33%, respectively.

Conversely, Shiergens et al. showed poorer outcomes for NCNNLM compared to CRLM, with a lower median overall survival (35 months vs. 54 months) and a shorter recurrence-free survival (15 months vs. 29 months), respectively [9].

Then, if compared with literature examined, our results in terms of 30-day complications and mortality and hospital stay are still better.

The role of hepatic resections for NCNNLM remains a subject of debate, primarily due to the diversity and rarity of NCNNLM cases, which complicates the establishment of a standardized treatment approach. Nonetheless, a recent systematic review and meta-analysis has confirmed the efficacy and safety of hepatectomy for selected NCNNLM patients [10].

A key question is how to identify factors that could help select high-risk NCNNLM patients as surgical candidates. Adam et al. proposed a pioneering prognostic risk model based on a cohort of 1452 patients who underwent liver resection for NCNNLM. This model, widely accepted by experts, considers factors such as patient age, length of disease-free interval, extent of hepatectomy, type of primary tumor, R2 resection, and presence of extrahepatic disease [4].

To our knowledge, our case series is among the few contemporary studies focusing exclusively on robotic hepatic resections for CRLM. However, our cohort has certain limitations: the inclusion of neuroendocrine liver metastases complicates comparisons with current literature focused on NCNNLM resections. Additionally, the small sample size limits statistical significance, and the study's retrospective design introduces further constraints.

## 5. Conclusions

Our results demonstrated that OS of robotic resection for NCLM are comparable to those previously reported in literature; while in terms of DFS our results are even more promising.

We do not state that robotic approach to liver resections for NCLM is superior than open or laparoscopic approaches in terms of oncological outcomes. Our series contributes to reinforce the concept of feasibility and safety of this approach.

The current state of robotic liver resections for non-colorectal liver metastases (NCLM) remains challenging to define in terms of non-inferiority compared to other approaches, primarily due to the lack of randomized controlled trials specific to this disease category and the limited global adoption of the robotic approach.

Conclusions of this paper remain cautious regarding survival outcomes, considering bias and different tumor biology.

Nevertheless, research is increasingly focused on demonstrating the effectiveness and safety of tailored robotic liver resections.

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