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ORIGINAL ARTICLE

Current status of liver surgery for non-colorectal non-neuroendocrine liver metastases: the NON.LI.MET. Italian Society for Endoscopic Surgery and New Technologies (SICE) and Association of Italian Surgeons in Europe (ACIE) collaborative international survey

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Abstract

Despite the increasing trend in liver resections for non-colorectal non-neuroendocrine liver metastases (NCNNLM), the role of surgery for these liver malignancies is still debated. Registries are an essential, reliable tool for assessing epidemiology, diagnosis, and therapeutic approach in a single hub, especially when data are dispersive and inconclusive, as in our case. The dissemination of this preliminary survey would allow us to understand if the creation of an International Registry is a viable option, while still offering a snapshot on this issue, investigating clinical practices worldwide. The steering committee designed an online questionnaire with Google Forms, which consisted of 37 questions, and was open from October 5th, 2022, to November 30th, 2022. It was disseminated using social media and mailing lists of the Italian Society of Endoscopic Surgery and New Technologies (SICE), the Association of Italian Surgeons in Europe (ACIE), and the Spanish Chapter of the American College of Surgeons (ACS). Overall, 141 surgeons (approximately 18% of the total invitations sent) from 27 countries on four continents participated in the survey. Most respondents worked in general surgery units (62%), performing less than 50 liver resections/year (57%). A multidisciplinary discussion was currently performed to validate surgical indications for NCNNLM in 96% of respondents. The most commonly adopted selection criteria were liver resectability, RECIST criteria, and absence of extrahepatic disease. Primary tumors were generally of gastrointestinal (42%), breast (31%), and pancreaticobiliary origin (13%). The most common interventions were parenchymal-sparing resections (51% of respondents) of metachronous metastases with an open approach. Major post-operative complications (Clavien–Dindo > 2) occurred in up to 20% of the procedures, according to 44% of respondents. A subset analysis of data from high-volume centers (> 100 cases/year) showed lower post-operative complications and better survival. The present survey shows that NCNNLM patients are frequently treated by surgeons in low-volume hospitals for liver surgery. Selection criteria are usually based on common sense. Liver resections are performed mainly with an open approach, possibly carrying a high burden of major post-operative complications. International guidelines and a specific consensus on this field are desirable, as well as strategies for collaboration between high-volume and low-volume centers. The present study can guide the elaboration of a multi-institutional document on the optimal pathway in the management of patients with NCNNLM.

Keywords Non-colorectal non-neuroendocrine liver metastases · Liver resection · Liver surgery · Liver metastases

Abbreviations

NCNNLM	Non-colorectal non-neuroendocrine liver metastases
OS	Overall survival
DFS	Disease-free survival
SICE	Italian Society for Endoscopic Surgery and New Technologies
ACS	American College of Surgeons
ACIE	Association of Italian Surgeons in Europe
CRLM	Colorectal liver metastases
NELM	Neuroendocrine liver metastases

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EHD	Extrahepatic disease
CHERRIES	Checklist for Reporting Results of Internet E-Surveys RECIST: Response Evaluation Criteria In Solid Tumors

Introduction

Liver resection for colorectal liver metastases (CRLM) is a well-established procedure, with 5-year survival rates after surgery between 30 and 58%, which is superior to chemotherapy alone [1]. Surgical resection is a curative option also for neuroendocrine liver metastases (NELM), achieving long-term survival in these patients [2]. Patients with non-colorectal non-neuroendocrine liver metastases (NCNNLM) are usually excluded from surgery due to the advanced tumor stage or the presence of concomitant extrahepatic disease (EHD), which is considered a contraindication to liver resection. Indications to surgery for NCNNLM are still debated, and data reported in the literature are based primarily on small, single-institution retrospective case series. To date, no randomized clinical trial on the surgical treatment of NCNNLM has been conducted. A new data collection effort needs to be initiated, and the creation of an International Registry of liver resections for NCNNLM seems to be the ideal research tool. Yet, a Registry requires a long-term commitment in terms of funding and data analysis.

Aim of the study

The present study aimed to survey the current use of liver resections for NCNNLM in different hospitals across countries, while investigating whether the creation of an International Registry is a viable project.

Methods

This study was conducted and reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [3].

Questionnaire design

The study steering committee developed the questionnaire using a brainstorming process followed by a web-based remote discussion to identify the components and topics to include. The technical functionality of the electronic questionnaire was beta tested before the invitations were sent. Baseline information on respondents and names and locations of surgical units were stored with the questionnaire. The survey comprised 37 multiple and single-choice questions, divided into six areas (informed consent, demographics, preoperative assessment, histopathological characteristics, short- and long-term outcomes, and future perspectives) (Tables 1, 2, 3, 4, 5). Data were requested as percentages and averages. The estimated time of completion of the questionnaire was 15 min. The study was supervised and officially endorsed by the Italian Society of Endoscopic Surgery and New Technologies (SICE), the Association of Italian Surgeons in Europe (ACIE), and the American College of Surgeons (ACS) Spanish chapter.

Circulation

The survey was developed using Google Forms Survey® (Google; Mountain View, CA, USA) and disseminated through the SICE and ACIE mailing lists and social media (Twitter, Facebook, LinkedIn). It is estimated that around 800 surgeons worldwide have been reached by invitation to participate in this survey. Online access was granted from October 5th, 2022, to November 30th, 2022.

Ethics

Participation was voluntary and addressed to surgeons, regardless of their experience, position, or the center's volume. Written informed consent was obtained from each respondent. No economic benefits were granted to the participants.

Statistics

Manual search excluded duplicates from the same center from the analyses. Only the first questionnaire returned from each center was included in the final analysis. Categorical variables were reported using counts and percentages.

Results

General characteristics of the respondents

One hundred and forty-one surgeons (approximately 18% of the total invitations sent) from 27 countries in four continents (Europe 83%, Asia 6%, Africa 2%, and North and South America 9%) participated in the survey (Fig. 1). The analysis was conducted on 109 questionnaires, as 32 were excluded from duplicate centers. Of the analyzed questionnaires, 67% were from academic and 33% from non-academic hospitals, 62% were from general surgery units, and 38% were from HPB units. 57% of surgeons performed less than 50 liver resections per year, whereas 11% worked in high-volume centers, performing more than 100 liver resections annually; 78% of participants performed less than ten liver procedures for NCNNLM per year. Most respondents (57%) believed

Table 1 Data about respondents, workplace, and volume of centers

Baseline characteristics	*N* (%)
Name Surname	
Country	
Affiliation (Hospital, Town, State)	
Type of institute	
Academic	73–67%
Non-academic	36–33%
Type of service	
General surgery	68–62%
HPB surgery	41–38%
How many liver resections (all types excluding living donor hepatectomies) are performed annually at your Center (average of last 10 years)?	
< 50	62–57%
51–100	35–32%
101–150	8–7%
> 151	4–4%
How many hepatectomies for NCNNLM (non-colorectal, non-neuroendocrine, liver metastases) are performed at your center per year (average of last 10 years)?	
< 10	85–78%
11–30	20–18%
31–50	2–2%
> 51	2–2%
Has the trend of hepatectomies for NCNNLM increased over the past 3 decades at your center?	
Yes	62–57%
No	47–43%

NCNNLM non-colorectal non-neuroendocrine liver metastases

that the trend of liver resections for NCNNLM has risen in the last 3 decades, even if less than 10% of patients with NCNNLM are candidates for surgery, according to the 60% of respondents.

Preoperative evaluation

The surgical indication is validated through a multidisciplinary meeting for 96% of the respondents, followed by compliance with national guidelines for the management of the primary tumor (44%), surgeon's decision (25%), and oncologist's decision (23%) (Fig. 2). The most common selection criteria for liver resection were liver resectability (90%), followed by RECIST (Response Evaluation Criteria In Solid Tumors) criteria (69%), absence of extrahepatic disease (64%), and patient's age and comorbidities (62%) (Fig. 2). The most common primary tumors were in the gastrointestinal tract, breast, and pancreaticobiliary system (42%, 31%, and 13%, respectively) (Fig. 3). The most commonly reported patient's mean age was 60 (22.4% of respondents). Resected metastases were metachronous in over half of the cases for 34% of respondents, whereas synchronous liver metastases were reported in more than 51% of cases for only 2% of answers. Synchronous resections of primary tumors and liver metastases were rare, reported in less than 5% of cases for 54% of answers (Fig. 4). In this rare scenario, the most frequently resected primary tumor was the stomach (45%), followed by the breast (17%), kidney, skin (melanoma), and pancreas (11%) (Fig. 5). In line with CRLM and NELM, the most frequent type of liver resections were minor resections (60% of respondents); major resections and more complex procedures, such as two-stage hepatectomies and associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) were reported by 18%, 4% and 1% of surgeons, respectively (Fig. 6). The most common liver resection technique was the parenchymal sparing, followed by formal anatomical resections (51% and 31%, respectively). According to 76% of respondents, there was no cut-off in the number of possible resections. Overall, 44% of the questionnaires reported a maximum of 3 metastases removed; 60% of respondents stated that liver metastases were unilateral in 11–50% of the cases. The patients who underwent liver resection had extrahepatic disease in less than 5% of the cases for the 57% of respondents. Surgery was performed with a minimally invasive approach in less than 10% of cases for 51% of the respondents.

Table 2 Preoperative work-up and routine assessment of primary and metastatic disease

Preoperative evaluation	*N* (%)
In your experience, among patients with NCNNLM, what is the actual percentage of those who are deemed suitable for liver resection at your center?	
< 10%	65–60%
11–50%	38–35%
> 50%	6–5%
In your opinion, what the indication of liver surgery for NCNNLM relies on?	
Multidisciplinary discussion	105–96%
National guidelines	48–44%
Local guidelines	4–4%
Surgeon decision	27–25%
Oncologist decision	25–23%
Other	3–3% (patient perspectives, case reports, international trends)
What are the main selection criteria for liver surgery for NCNNLM at your center (multiple responses allowed)?	
Liver resectability	98–90%
RECIST	75–69%
Age and comorbidity	68–62%
Original TNM	20–18%
No extrahepatic disease	70–64%
Other	10–9% (patient perspective, biological behavior, time between primary tumor and metastases)
What is the mean age of the patients undergoing liver resection for NCNNLM at your center?	60 (34%)–50 (15%)–65 (14%)
In your experience, what is the most common primary tumor site of NCNNLM resected metastases?	
Breast	34–31%
GI	46–42%
Urologic	6–5%
Melanoma	4–4%
Pancreatobiliary	13–13%
Other	6–5% (lung, neuroblastoma, GIST)
Among the entire cohort of NCNNLM operated on at your center, what is the percentage of synchronous NCNNLM (within 3 months of diagnosis of primitive cancer)?	
< 10%	79–72%
11–50%	28–26%
> 51%	2–2%
Among the entire cohort of NCNNLM operated on at your center, what is the percentage of metachronous NCNNLM (beyond 3 months of diagnosis of primitive cancer)?	
< 10%	38–35%
11–50%	34–31%
> 50%	37–34%
In your experience, is there a cut-off in the number of NCNNLM that could be removed in the same procedure?	
Yes	26–24%
No	83–76%
If yes, what is the cut-off number?	3 (44%)
How often the primary tumor and the synchronous liver metastasis/metastases are resected in the same surgical procedure at your center (%)	
< 5%	59–54%
6–10%	31–28%

Table 2 (continued)

Preoperative evaluation	*N* (%)
11–20%	12–11%
> 20%	7–7%
What is the most frequent primary tumor resected in case of synchronous procedure?	
Breast	19–17%
Stomach	49–45%
Kidney	12–11%
Melanoma	5–5%
Pancreas	12–11%
Other	12–11%
What type of therapy do you advised before simultaneous procedure?	
Chemotherapy	103–95%
Biological therapy	45–41%
Hormone therapy	33–30%
Locoregional therapy	16–15%
Radiotherapy	20–18%
Other	13–8%
How many patients have extrahepatic disease at the time of surgery?	
< 5%	62–57%
5–10%	31–28%
11–20%	10–9%
> 20%	6–6%
What is the most common type of liver resection performed?	
Minor	65–60%
Major	20–18%
Parenchymal sparing	56–51%
Anatomical	34–31%
Two stage hepatectomy	4–4%
ALPPS	1–1%
In case of surgery for multiple metastases, how often liver lesions are unilateral?	
< 10%	14–13%
11–30%	32–29%
31–50%	34–31%
51–70%	16–15%
> 71%	13–12%
What is the rate of minimally invasive approach (lap/robotic)?	
< 10	56–51%
10–50	36–33%
51–70	10–9%
> 70	7–6%

NCNNLM non-colorectal non-neuroendocrine liver metastases, *RECIST* response evaluation criteria in solid tumors, *GI* gastrointestinal, *ALPPS* Associating liver partition and portal vein ligation for staged hepatectomy

Histopathology results

Ninety-two percent of the respondents reported that the mean diameter of the liver specimen was 10–50 mm, with R0 resection achieved in more than 30% of the cases for 74% of the respondents. The most common histology was adenocarcinoma (83%), followed by stromal tumors (6%).

Table 3 Histopathological characteristics

Histopathological characteristics	*N* (%)
What is the mean diameter of resected NCNNLM (measured in mm of the largest specimen removed) at your center?	
10 mm	4–4%
10–20 mm	58–53%
20–50 mm	43–39%
> 50 mm	4–4%
What is the percentage of R0 resection (neoplastic cells > 1 mm from surgical margin) achieved with surgery at your center?	
< 10%	6–6%
10–20%	13–12%
20–30%	9–8%
> 30%	81–74%
What is the most common histology of resected NCNNLM at your center?	
Adenocarcinoma	90–83%
Stromal tumor	7–6%
Sarcoma	2–2%
Melanoma	4–4%
Other	6–5% (neuroblastoma)

NCNNLM non-colorectal non-neuroendocrine liver metastases

Postoperative course

The rate of major complications (Clavien–Dindo > 2) was 20% for 44% of the respondents. 1-year overall survival and 1-year disease-free survival were > 50% for 43% and 26% of the respondents, respectively. Breast cancer was the primary tumor with the best prognosis, according to 40% of surgeons, followed by gastrointestinal tumors (28%) and urologic malignancies (24%). The most important prognostic factor was primary tumor histology (43%), absence of extrahepatic disease (25%), and R0 resections (23%).

Future perspectives

Overall, 95 surgeons (87% of respondents) agreed in joining a multicenter international study about NCNNLM.

High-volume centers subset analysis

After the global analysis, data coming from high-volume surgical units (> 100/year) were further investigated. As expected, liver resection for NCNNLM were done by minimally invasive technique in more than 50% of cases for 58% of respondents. Major complications (Clavien–Dindo > 2) occurred in less than 10% of patients according to 75% of surgeons. The mean follow-up time achieved was > 36 months for 42% of respondents. Finally, 1-year OS was > 50% according to 67% of adhering high-volume centers.

Discussion

Liver surgery for CRLM and NELM has a well-known therapeutic value, improving long-term survival and being considered the only curative option [1, 2]. However, the role of liver resections for NCNNLM still needs to be clarified, mainly due to the scarcity and the low quality of the evidence reported in the literature. The largest case series published till now dates back to 2006, when Adam and co-authors developed a prognostic model based on factors associated with poor prognosis, effectively stratifying patients into low-risk (0–3 points, 46% 5-year survival), mid-risk (4–6 points, 33% 5-year survival), and high-risk (6 points, 10% 5-year survival) groups [4]. Recent evidence [4–6] showed a progressive increase in liver procedures performed for NCNNLM, as confirmed by our survey, with encouraging post-operative results [5, 7]. However, the group of patients who would benefit more from surgery is not defined yet, and we can honestly say that we are far from designing a guideline. Furthermore, patients are not always referred to HPB units due to the wide range of primary tumors; therefore, there's a flood of data scattered across low-volume centers.

The creation of a registry is particularly useful in such situations where a comprehensive, flexible research design is needed, or when the purpose is to discover how a solution works in a wide variety of subgroups and clinical scenarios, as in our case. Nonetheless, a registry requires a large joint effort in terms of time, fundings, data management

Table 4 Postoperative course and long-term oncological outcome

Short- and long-term outcome	*N* (%)
What is the rate of Clavien–Dindo > 2 complications after liver resections for NCNNLM at your center?	
< 10%	48–44%
11–20%	48–44%
21–30%	9–8%
> 30%	4–4%
What is the mean follow-up time achieved after liver surgery for NCNNLM at your center?	
< 12 months	13–12%
12–24 months	51–47%
25–36 months	20–17%
> 36 months	25–24%
What is the 1-year survival rate for patients who underwent surgery for NCNNLM at your center?	
< 10%	4–4%
11–30%	25–23%
31–50%	33–30%
> 50%	47–43%
What is the 1-year disease-free survival rate for patients who underwent surgery for NCNNLM at your center?	
< 10%	13–12%
11–30%	30–27%
31–50%	38–35%
> 50%	28–26%
In your experience, among the group of resected patients for NCNNLM, what is the primary tumor site with better prognosis (OS and DFS)?	
Breast	43–40%
GI	31–28%
Urologic	26–24%
Melanoma	6–5%
Pancreatobiliary	1–1%
Other	2–2%
In your opinion, what is the most relevant prognostic factor of disease-free survival after liver surgery for NCNNLM?	
Age	3–3%
Primitive tumor histology	47–43%
R0 resection	25–23%
Unilateral liver involvement	7–6%
Absence of extrahepatic disease	27–25%

NCNNLM non-colorectal non-neuroendocrine liver metastases, *OS* overall survival, *DFS* disease-free survival

Table 5 Creation of an international registry

Future perspectives	*N* (%)
Would you be interested in participating in multicenter international cohort study of liver surgery for NCNNLM?	
Yes	95–87%
No	14–13%
If you are interested in participating in the European Registry of liver surgery for NCNNLM, please write down your name, surname, and email address here	

NCNNLM non-colorectal non-neuroendocrine liver metastases

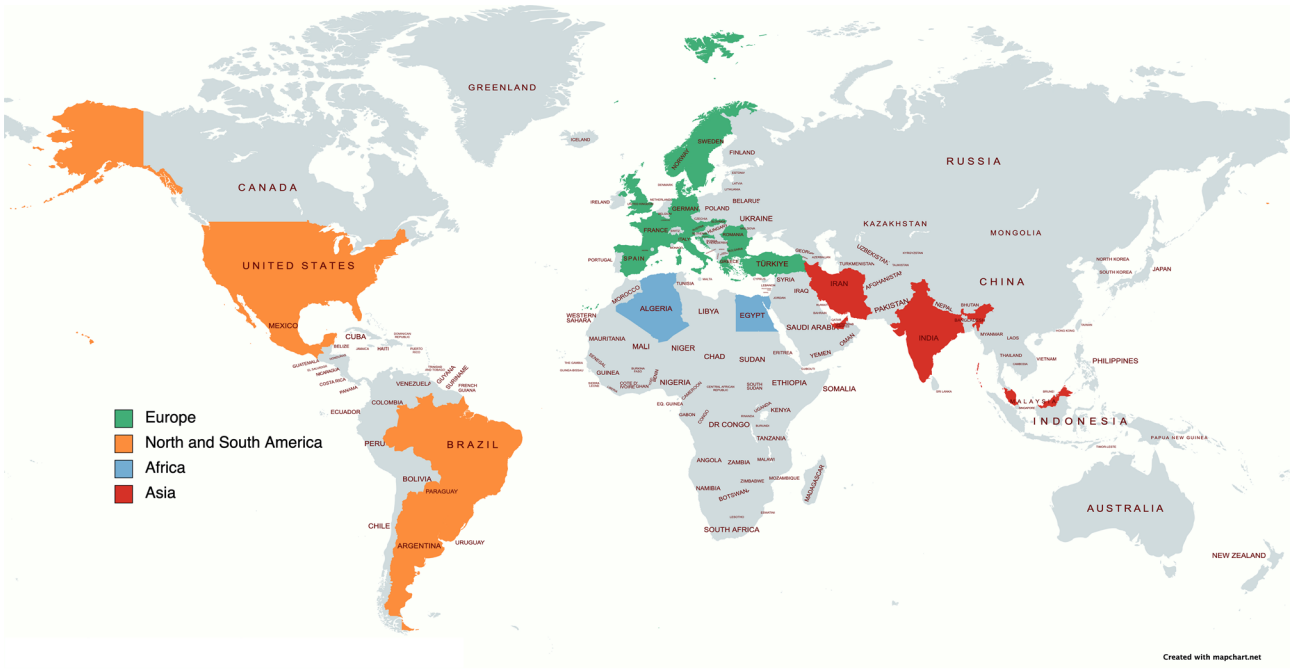


Fig. 1 Geographical distribution of the survey's respondents

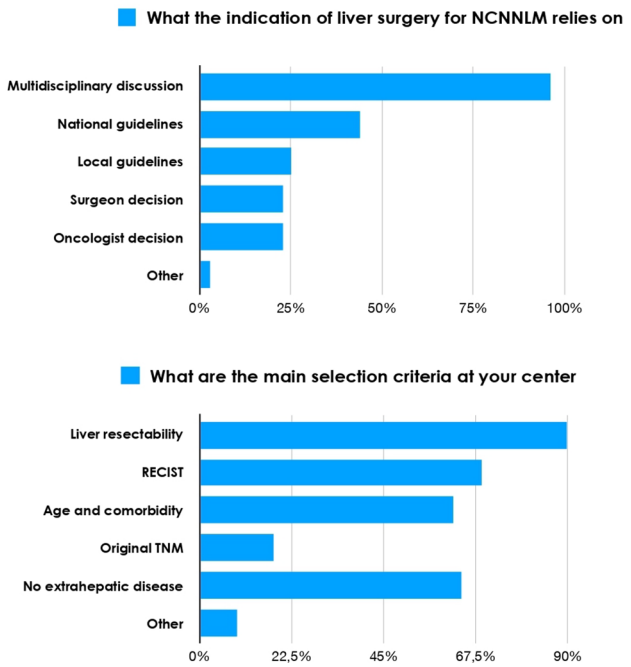


Fig. 2 Preoperative assessment

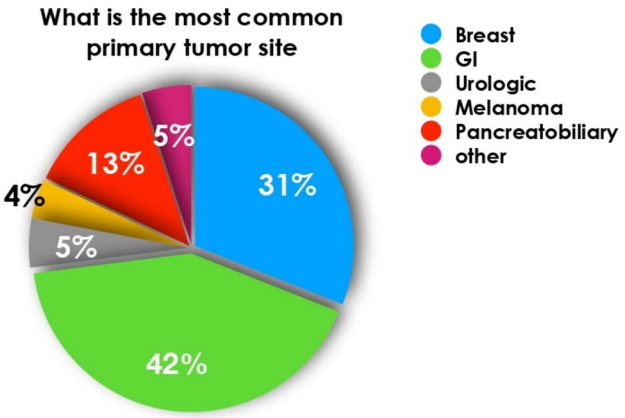


Fig. 3 Primary tumor site

and scientific commitment. This preliminary survey aimed to provide us a better idea of the current practice of liver surgery for NCNNLM across the world. Furthermore, survey's results may highlights and identify some key points on which we should focus on further studies; at last, it might allow us to investigate the surgeons opinions on the value of such a registry and their willingness to join it.

The multidisciplinary meeting was pivotal in validating the indication of surgery for 96% of respondents in our survey, in line with most of the literature [8–10]. Liver resectability and RECIST criteria were the most relevant selection criteria according to our survey (90% and 69%, respectively), followed by the absence of extrahepatic disease (EHD) (64%). More recent literature made some exceptions to these results: Aghayan et al. [8] reported that liver surgery was also considered for stable or resectable extrahepatic metastases in their study, where 16% of resected patients had

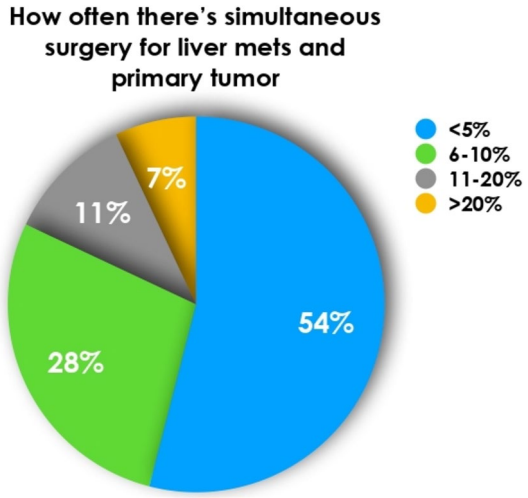


Fig. 4 Management of synchronous metastases

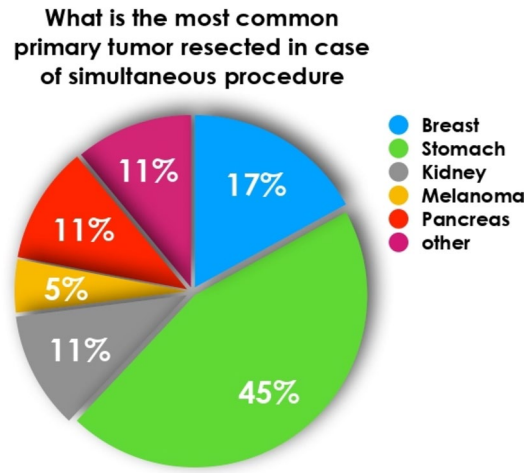
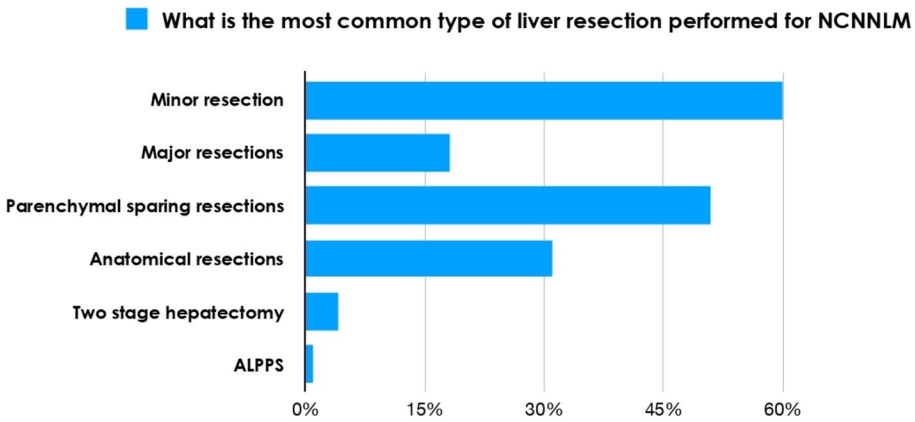


Fig. 5 Simultaneous procedures

EHD. The most common primary tumor site in our survey was the gastrointestinal tract (42% of respondents). In previous studies, the prevalence of each primary tumor varied considerably: gastrointestinal tumors and melanoma (both uveal and cutaneous) comprised 39% and 31% of a Norwegian cohort in Aghayan et al. case series [8]. In other studies, the most common primary tumor was breast [4, 8, 11, 12], genitourinary [13], or gastric cancer [14]. Metastases were most commonly metachronous in our survey. These data align with evidence from past papers and more recent studies, where the reported percentage of metachronous metastases varies from 59% [8] to 87.5% [10]. In the case of synchronous metastases, the primitive tumor was previously resected in more than 90% of patients in most Western literature, in line with survey results and geographical distribution of respondents. Asian literature made exceptions: Sano et al. [14] reported that over half of hepatectomies for synchronous lesions were simultaneous to primitive tumor surgery due to the higher prevalence of gastric cancer. The 51% of surgeons admit they perform parenchymal-sparing resections for NCNNLM treatment. Therefore, we can assume that the concept of atypical, parenchymal-sparing resections has been transferred from CRLM experience to NCNNLM because it allows multiple concomitant liver resections in the same procedure and allows safe re-resections in case of recurrence, preserving liver function without affecting oncological effectiveness. However, the oncological adequacy of wedge resections for NCNNLM has yet to be demonstrated. Surrogate endpoints of survival, such as R0 resection rates or width of resection margin, as well as post-operative outcomes (e.g., blood loss, in-hospital stay, rate of complications), are frequently analyzed in the literature but biased by the lack of information about the technique adopted for liver surgery (open vs. minimally invasive technique). Despite the well-established use of laparoscopy in liver surgery [15] and the rapid rise of robotic surgery for the treatment of primary malignancies and CRLM [16, 17], only 15% of surgeons reported using a minimally invasive approach for > 50% of resections for NCNNLM in our survey. Notably, most half

Fig. 6 Types of liver resections performed for NCNNLM



of the respondents reported a Clavien–Dindo > 2 complications rate of 11–20%. These survey data are in contrast with literature, where small series reported good results in terms of post-operative complications, conversion rates, and post-operative mortality for LLR (laparoscopic liver resections) of NCNNLM, demonstrating that surgical outcomes are comparable to/or better than open resections for NCNNLM. We can presume that the high rate of major complications reported and the wider use of laparotomic approach reflect above all the high prevalence of low-volume centers among respondents, assuming lack in HPB training or absence of dedicated devices (e.g., CUSA, robotic platform).

Even more concerning, more than a half of surgeons reported a 1-year survival rate < 50%. These results, along with the aforementioned paucity of minimally invasive approach and worse post-operative course, differ from the reported subset analysis of high-volume centers and advice in favor of centralization of patients to specialized HPB units.

According to the respondents, breast cancer was the primary tumor with a better prognosis (40%). In a review by Fitzgerald et al. [5], metastases of genitourinary origin had the most prolonged median survival (63.4 months); Harrison et al. [18] and Adam et al. [4] found similar results. However, as previously stated, the survival analysis in each study was influenced by the small number of patients examined, the different periods considered, the different duration of follow-up, and the prevalence of each tumor in the specific cohorts. Moreover, most papers do not specify the chemotherapy regimens.

Finally, the authors would like to underline that 87% of respondents was interested in joining a multicenter study on liver surgery for NCNNLM. This encouraging result demonstrate that this topic may not be a niche as suspected, and a joint effort in data collection may explain the role of liver surgery, its indications and correct timing for NCNNLM treatment, but also define clinical standards of care, thus reducing differences in practice among hospitals and countries.

Limitations

The findings of this web-based survey should be interpreted in light of some relevant limitations. First, the questionnaire had a gross definition of each tumor category due to the multiple-choice setup and the need for a short response time. The gastrointestinal group, for example, included small bowel and stomach tumors, with higher 5-year survival, and gastroesophageal junction or esophageal cancers, which conversely have a dismal prognosis. Therefore, we agree with Sano et al. [14], suggesting considering tumor-specific factors in the predictive analysis. Secondly, the overall number of respondents over the four continents was small. However, these data must be interpreted in the light of the fact that patients with NCNNLM are usually excluded from surgery due to the advanced tumor stage or the presence of concomitant extrahepatic disease, and the lack of strong evidence for surgical management of these diseases. A meta-analysis by Shih and Fan showed that e-mail surveys generally have an average response rate of 33% ± 22%; our response rate falls within those limits [19]. In that perspective, our current response rate of 18% seems to be fair and satisfactory. As a matter of fact, a high response rate minimizes the potential for bias and enhances the value of the study; however, it has been stressed that there is no scientifically established minimum acceptable response rate and it may not be associated with survey reliability or quality [20]. The non-representative nature of the population and participants' self-selection is another potential limitation. Most responding surgeons worked in academic units of Western countries and performed less than 50 liver resections per year. Therefore, the results may be biased by geographical distribution and personal experience. Lastly, closed-answer questions, especially in the context of a poorly investigated scientific field, may be exposed to limitations in terms of the possibility of limited and not-including all the possible fields of answers choices. The responses to some questions in our survey did not include some quite important factors that are considered in these still unusual scenarios, like time from diagnosis, disease stability while on chemotherapy, and the type of primary tumor.

Conclusion

The present international survey showed that surgeons believe that multimodal management should be the mainstay of treatment of NCNNLM, as established for CRLM and NELM. A judicious combination of systemic therapies, locoregional treatment, and surgical resection can adequately manage these neoplasms and improve survival. As randomized clinical trials would be difficult to project and apply due to the paucity of patients and the wide variety of tumors involved, a multi-institutional international registry may provide precious data, filling the current knowledge gap and becoming the basis for future guidelines. In the meantime, the results of the present study could guide the elaboration of a multi-society document on the optimal pathway in the management of patients affected by NCNNLM.

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