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Liver resection for metastases not of colorectal, neuroendocrine, sarcomatous, or ovarian (NCNSO) origin: A multicentric study

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ABSTRACT

Background: Liver resection is a well-established treatment for colorectal, neuroendocrine and sarcomatous metastases but remains ill-defined for metastases from other primary sites. This study aimed to analyze the outcomes of hepatic resection for metastases not of colorectal, neuroendocrine, sarcomatous, or ovarian (NCNSO) origin and to identify predictors of outcome.
Methods: Retrospective analysis of patients undergoing resection for NCNSO metastases in three western centers. Patients were analyzed according to the primary cancer. Outcomes were recurrence and survival.
Results: We analyzed 188 patients, divided in: gastrointestinal (59), breast (59) and "others" (70). Median time to recurrence was 15.3 months, while median survival was 52 months. Survival at 1, 3, and 5 years was 78%, 60.4% and 47.8%, respectively. In term of prognostic factors, metastases >35 mm from gastrointestinal tumors were associated with lower survival ($p = 0.029$) and age>60 years was associated with better survival in breast metastases ($p = 0.018$).
Conclusions: Liver resection for NCNSO metastases is feasible and results in long-term survival are similar to colorectal metastases. In gastrointestinal metastases, size (<35 mm) could be used to select patients.

1. Introduction

The liver is a common site of metastasis for many primary tumor types. Liver resection for metastatic disease has significantly increased over recent decades,[1,2] most commonly for tumors of colorectal origin; as a result of improvements in imaging and operative technique[3] and more effective chemotherapy, resection of colorectal metastases yields five-year survival of 50% or more and has become the standard of care for patients with resectable disease.[4–9] Resection of neuroendocrine[10,11] and sarcomatous[12,13] liver metastases is also widely-reported. While hepatic resection is often performed to treat ovarian and appendiceal cancer, these tumors are typically surface implants that result from peritoneal rather than hematogenous spread, and are therefore excluded from this analysis. The role of resection of liver metastases from sites other than colorectal, neuroendocrine, sarcoma, and ovarian origin (NCNSO) remains ill-defined, although a number of single-center studies have suggested that it is feasible and safe [14,15]; most of these reports included cases with sarcoma and/or ovarian cancer.

The objective of this study is to comprehensively analyze the outcomes of liver resection for NCNSO metastases and to identify predictors of recurrence and survival.

2. Materials and methods

Two hundred and three patients who underwent liver resection

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Table 1
Patients, tumors and surgical characteristics.

			GI (n = 59) N (%)	Breast (n = 59) N (%)	Others (n = 70) N (%)
Patients	Age	Median (years)	62.4	57.8	57.2
		<60 years	26 (44)	35 (60)	39 (57)
		≥60 years	33 (56)	23 (40)	30 (44)
	Gender	Male	40 (68)	0 (0)	36 (51)
		Female	19 (32)	59 (100)	34 (49)
Tumors	Presentation	Synchronous	23 (39)	6 (11)	15 (23)
		Metachronous	36 (61)	49 (89)	51 (77)
	Extrahepatic disease	No	38 (64)	35 (59)	45 (68)
		Yes	21 (36)	24 (41)	21 (32)
	Distribution	Unilobar	45 (76)	41 (75)	56 (84)
		Bilobar	14 (24)	14 (26)	11 (16)
	Number of metastases	Single	26 (51)	31 (62)	33 (56)
		Multiple	25 (49)	19 (38)	26 (44)
	Size	Median size (mm)	30	40	40
		<35 mm	31 (59)	22 (43)	24 (40)
		≥35 mm	22 (42)	29 (57)	36 (60)
	Histology	Adenocarcinoma	46 (78)	59 (100)	36 (51)
		Squamous	13 (22)	0	7 (10)
		Melanoma	0	0	17 (24)
		Other	0	0	10 (14)
Surgery	Extent of resection	Minor (<3 segments)	45 (78)	25 (42)	37 (54)
		Major (≥3 segments)	13 (22)	34 (58)	31 (46)
	Additional procedure	No	45 (76)	56 (95)	55 (79)
		Yes	14 (24)	3 (5)	15 (21)
	Margins	R0	44 (75)	36 (71)	44 (76)
		R1	7 (12)	13 (26)	10 (17)
		R2	3 (5)	2 (4)	4 (7)

for NCNSO metastases between 1990 and 2013 were identified from prospective databases at three western centers (Icahn School of Medicine at Mount Sinai in New York, University Hospital of Geneva, and University Hospital of Zürich). Preoperative evaluation was performed to assess resectability. Only patients with intraparenchymal metastases were included; those with surface implants or direct invasion of the liver by the primary tumor were excluded (n = 5). Ten other patients were also excluded, including 8 with no evidence of remaining tumor and 2 with unknown primary tumor, leaving a final study cohort of 188 patients. Data analyzed included age, gender, type and histology of primary tumor, number and size of metastases, time of occurrence (synchronous vs. metachronous), delay between resection of the primary tumor and diagnosis of liver metastasis, distribution of the metastases (unilobar vs. bilobar), whether extrahepatic disease was present (in lymph nodes or in a distant organ), margins (R0: negative microscopic margin, R1: positive microscopic margin, R2: positive macroscopic margin), the extent of the resection (number of removed segments according to Couinaud classification: minor resection is < 3 segments; major resection is ≥ 3 segments), additional procedures performed at the time of liver resection (cholecystectomy was not considered as an additional procedure), postoperative complications, tumor recurrence, and mortality.

Patients were classified according to site of the primary tumor into the following categories: gastrointestinal (pancreatic, gastric, ampullary, anal, small bowel, esophageal), breast, urogenital (endometrial, cervical, testicular, bladder, renal), pulmonary, melanoma, endocrine (adrenal, thyroid) and "various" (salivary glands, central nervous system, pharyngeal). In order to minimize the influence of heterogeneity, we performed 3 series of analyzes, based on the categories of primary tumor, previously described: (I) gastrointestinal, (II) breast and (III) "others", which included urogenital, pulmonary, melanoma, endocrine and "various".

Outcomes included recurrence and overall survival, determined from the time of liver resection. The Kaplan-Meier method was used to estimate survival, and the log-rank test was used to compare survival curves between groups. A p value of < 0.05 was considered significant; variables with significance < 0.1 were included in multivariate analyses. Statistics were performed using SPSS v22 statistical software, Chicago, IL.

The study received the approval from the ethics committees of the involved centers.

3. Results

3.1. Patient demographics, tumor characteristics, and type of surgery

The median age was around the sixth decade in the 3 groups. The GI group showed a majority of men (67.8%), while the gender ratio was more balanced in the group "others" with 51.4% of men. Regardless of the group, most patients presented with metachronous metastasis, no extrahepatic disease, and a single unilobar lesion. Tumors had a median diameter of 30 mm in the GI group and 40 mm in the 2 remaining groups (Table 1).

In terms of surgery, a minority of patients in the GI group underwent major resection (22.4%), compared to 57.6% and 45.6% of the patients in the groups breast and "others", respectively. Free margins status R0 was most often obtained, regardless of the group (Table 1).

3.2. Outcomes

The overall median follow-up was 26 months: GI 16 months, breast 35 months, and "others" 26 months. Outcomes are detailed in Table 2. Postoperative complications were observed in 45 cases (23.9%), including: 16 cases in GI (27.1%), 18 cases in breast (30.5%) and 11 cases in "others" (15.7%). Overall postoperative mortality was reported in 3 cases (1.6%).

Tumor recurrence was noted in 38 GI patients (64.4%) with a

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