Research Square

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Hepatic Resection for Metastases of pelvic squamous cell malignancies: a retrospective cohort study

Marc. A. Reschke

marc.reschke@uk-essen.de

University Hospital Essen

Nithiban Manoharan

University Hospital Essen

Phil Meister

University Hospital Essen

Jan Neuhaus

University Hospital Essen

Tom Florian Ulmer

University Hospital Essen

Ulf Neumann

University Hospital Essen

Andreas D. Rink

University Hospital Essen

Sophia M. Schmitz

University Hospital Essen

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Abstract

Background

Liver metastases originating from squamous cell carcinomas (SCCs) occur less frequently than those arising from adenocarcinomas. Data regarding the outcome of resected liver metastases are limited, with only a few cohort studies published. This study aims to determine the patient outcome following surgical therapy for liver metastases originating from pelvic SCC in our tertiary referral center.

Methods

We performed a retrospective, exploratory single-center cohort analysis of all patients who underwent liver resection between 2008 and 2025 at our institution. Retrospective data were extracted from the hospital information system for patients with liver resections and diagnoses of pelvic SCC. Patient courses were followed up and long-term survival was determined.

Results

A total of 15 patients received 20 liver resections in total. Primary tumor sites included anal carcinoma (n = 12) and cervical carcinoma (n = 3). Procedures performed comprised 10 major and 10 minor resections. Two patients with AC metastases underwent repeat resections due to recurrence. One successful two-stage hepatectomy with portal vein ligation was performed. A complete (R0) resection was achieved in 16 procedures (80%). Major complications (Clavien-Dindo ≥IIIb) occurred in 2 patients (13.3%), with no perioperative mortality. Median overall survival was 70 months, and the 5-year overall survival was 57.7%.

Conclusions

This cohort represents one of the largest single-center experiences published in the literature on liver metastases from pelvic SCCs. The surgical management of liver metastases from pelvic SCC, particularly anal carcinoma, is feasible and safe and provides long-term survival in selected cases.

Background

The concept of oligometastatic disease – a limited burden of metastatic spread potentially amenable to curative-intent local therapy – has become established across a wide range of solid tumors. In a systematic review and meta-analysis of 173 studies comprising more than 100,000 patients, Petrelli et al. demonstrated a consistent survival benefit for patients with oligometastatic compared with polymetastatic disease [1]. For colorectal cancer, liver resection for metastatic disease is now a well-established, potentially curative treatment option; a comparable level of evidence is lacking for

squamous cell carcinomas, where liver-directed surgery has traditionally been regarded with skepticism owing to the presumed systemic, hematogenous nature of metastatic spread.

The available data on liver-directed surgery for SCC nonetheless suggest that long-term survival is achievable in selected patients. In the largest published series to date – a European multicenter cohort of 102 patients from 24 centers, 56 of whom had anal SCC – Engstrand et al. reported a median OS of 50 months and a 5-year OS of 45% for patients with anal SCC liver metastases, compared with 21 months and 25% for non-anal primaries [2]. Lo et al., in a multicenter series of 21 patients, reported a median OS of 32.2 months and a 5-year OS of 50% [3]. A National Cancer Database analysis by Goldner et al. found that metastasectomy was associated with a survival benefit that was confined to patients with liver-only metastases (median OS 34 vs. 16 months without local therapy) [4].

For cervical carcinoma, the evidence base is even sparser: the largest published series comprises only 15 patients (median OS 18 months after liver resection) [5], and the remaining literature consists almost entirely of individual case reports, the first of which dates back to 1963 [6]. To date, no prospective or randomized study of liver resection for SCC metastases of the pelvis has been conducted for either entity, and, although several series included mixed SCC primaries, none has analyzed liver metastases from pelvic SCC as a distinct disease group.

Against this background, we report our single-center experience with liver resection for metastases from pelvic squamous cell malignancies, aiming to contribute to patient selection and the definition of prognostic factors in this rare disease.

Methods

This retrospective single-center cohort study included all patients who underwent liver resection between January 2008 and December 2025 at our institution. Data were extracted from the hospital information system for patients with an underlying diagnosis of anal carcinoma (AC), anal margin carcinoma, penile carcinoma, vaginal carcinoma, or cervical carcinoma; in the final cohort, only anal and cervical carcinoma primaries were represented.

A total of 18 patients were identified based on these diagnostic and procedural criteria.

Of these, three patients were excluded due to final histopathological diagnosis of cholangiocarcinoma, leaving a final study cohort of 15 patients. No formal a priori sample size calculation was performed; this retrospective, exploratory study included all eligible patients treated at our institution during the inclusion period.

These 15 patients underwent a total of 20 liver resections, including repeat resections performed in two patients for recurrent disease.

All patients received liver resection for metastases from a pelvic squamous cell carcinoma primary. Treatment of the primary tumor was performed either at our institution or, in a subset of patients, at an

external facility prior to referral for liver surgery. Every case was discussed in an interdisciplinary tumor board both prior to and following liver resection. Local control of the primary tumor was established before hepatectomy in all patients except one, who was treated with a liver-first approach; extrahepatic disease was excluded preoperatively, with the exception of one patient in whom strictly localized peritoneal nodules were resected concomitantly. To limit selection and information bias, all liver metastasis diagnoses were confirmed histopathologically and all resection decisions were made by the same interdisciplinary tumor board throughout the inclusion period, although without a prespecified, standardized selection protocol; nevertheless, referral bias cannot be excluded, as patients referred from external institutions may represent a more favorably selected subgroup than those treated entirely in-house.

The primary endpoint was overall survival, defined as death from any cause, calculated from the date of the first liver resection to the date of death or last follow-up.

Secondary endpoints included:

- Tumor recurrence
- Postoperative complications, graded according to the Clavien-Dindo classification
- Length of hospital stay
- Length of intensive care unit (ICU) stay

The study was approved by the ethics committee of the University of Duisburg-Essen (approval no. 25-12783-BO) and was conducted in accordance with the Declaration of Helsinki.

Statistical analysis was performed using IBM SPSS Statistics (version 29.0). Overall survival and recurrence-free survival were estimated using the Kaplan-Meier method. Individual disease courses were visualized using a swimmer plot generated in R studio (version 2026.07.1 + 147).

Continuous variables are presented as median with interquartile range (IQR), and categorical variables as absolute and relative frequency (n, %). A complete-case approach was used for all analyses; variables with missing values (e.g., HPV testing, not performed in all procedures) are reported with the denominator of available data rather than imputed. This study is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for cohort studies [7].

A large language model (Claude, Anthropic) was used to assist with language editing and the drafting of individual text passages. All content was reviewed, revised and verified by the authors, who take full responsibility for the content of this article.

Results

The final cohort comprised 15 patients (11 male, 73.3%; 4 female, 26.7%) with a median age of 57 years (IQR 54–65) and a median BMI of 20 kg/m² (IQR 18–22). Most patients were classified as ASA III (10, 66.7%). Cardiovascular and hepatic comorbidities were each present in 2 patients (13.3%); no patient had a pulmonary comorbidity or diabetes. The primary tumor was anal carcinoma in 12 patients (80.0%) and cervical carcinoma in 3 patients (20.0%). Primary tumor grading was predominantly G3 (11, 73.3%), and 9 patients (60.0%) had received prior radiotherapy and 12 (80.0%) prior chemotherapy. Liver metastases were diagnosed synchronously in 5 patients (33.3%) and metachronously in 10 patients (66.7%). Further information on the study cohort is summarized in Table 1.

Table 1

Baseline characteristics and primary tumor at initial diagnosis. IQR: interquartile range; BMI: body mass index; ASA: American Society of Anesthesiologists; CRT: chemoradiotherapy. Surgical therapy refers to the treatment of the primary tumor (not the liver resection): local resection, local excision of the primary tumor with organ preservation; APR, abdominoperineal rectal extirpation (anal carcinoma); radical hysterectomy (cervical carcinoma). Type of liver resection (anatomical vs. atypical, major vs. minor) is given in Table 2.

Sex	**n (%) / median (IQR)**
Male	11 (73.3)
Female	4 (26.7)
Age (years)	57 (54–65)
BMI (kg/m2)	20 (18–22)
ASA	
II	5 (33.3)
III	10 (66.7)
Comorbidities	
Cardiovascular	2 (13.3)
Pulmonary	0 (0)
Diabetes	0 (0)
Liver	2 (13.3)
T status	
T1	8 (53.3)
T2	1 (6.7)
T3	5 (33.3)
T4	0 (0)
Unknown	1 (6.7)
N status	
N0	4 (26.7)
N1	5 (33.3)
N2	1 (6.7)

Sex	n (%) / median (IQR)
Unknown	5 (33.3)
Grading	
G1	0 (0)
G2	4 (26.7)
G3	11 (73.3)
RTX	9 (60.0)
CTX	12 (80.0)
Surgical therapy of primary tumor	
Local resection	5 (33.3)
Abdominoperineal rectal extirpation (APR)	4 (26.7)
Radical hysterectomy	2 (13.3)
Definitive CRT (no primary tumor resection)	4 (26.7)
Timing of liver metastases	
Synchronous	5 (33.3)
Metachronous	10 (66.7)

In total, 20 liver resections were performed in the 15 patients, at a median time of 7 months (IQR 1–24) after diagnosis of the primary tumor. HPV testing was documented in only 3 of the 20 procedures (15%), all of which were HPV-positive. A median of 1 metastasis (IQR 1–2) with a median size of 3.3 cm (IQR 1.8–3.3) was resected per procedure. Resections were evenly split between major (10, 50%) and minor (10, 50%) hepatectomies, and between anatomical (12, 60%) and atypical (8, 40%) resections. Surgical access was laparoscopic in 10 procedures (50%), open in 8 (40%), and robotic assisted in 2 (10%). Median operative time was 170 minutes (IQR 162–194). Nineteen procedures (95%) were performed as single-stage hepatectomies; one patient (5%) underwent a successful two-stage hepatectomy with portal vein ligation. A complete (R0) resection was achieved in 16 procedures (80%), while 4 (20%) had microscopically positive margins (R1).

Table 2
Surgical procedures for liver metastases. IQR: interquartile range

Total procedures	**n (%) / median (IQR)**
	20
Time to surgery (months)	7 (1–24)
HPV testing performed	3 (15)
Number of metastases	1 (1–2)
Metastasis size (cm)	3.3 (1.8–3.3)
Liver resection	
Major	10 (50)
Minor	10 (50)
Atypical	8 (40)
Anatomical	12 (60)
Open surgery	8 (40)
Laparoscopic	10 (50)
Robotic	2 (10)
Single-stage hepatectomy	19 (95)
Two-stage hepatectomy	1 (5)
Surgery duration (min)	170 (162–194)
Resection margin	
R0	16 (80)
R1	4 (20)

Endpoints

The Kaplan-Meier estimates of overall survival and recurrence-free survival after liver resection are shown in Fig. 1. During follow-up of 6 years, 5 patients (33.3%) died and death or tumor recurrence was observed in 10 patients (66.7%), involving both hepatic and extrahepatic sites. Median overall survival was 70 months (95% CI 0.0–167.5), with a 1-, 3-, and 5-year overall survival of 80.8%, 57.7%, and 57.7%, respectively. Median recurrence-free survival was 65 months (95% CI 4.7–125.3), with a 1-, 3-, and 5-year recurrence-free survival of 70.7%, 50.5%, and 50.5%, respectively. Median ICU stay was 1 day (IQR 0–1) and median hospital stay was 9 days (IQR 6–11). Postoperative complications graded Clavien-Dindo

≥IIIa occurred in 3 patients (20.0%), ≥IIIb in 2 patients (13.3%), and ≥ IVa in 1 patient (6.7%); no perioperative mortality occurred.

Months after surgery	**0**	**12**	**24**	**36**	**48**	**60**
OS, at risk	15	8	7	5	5	5
RFS, at risk	15	7	7	5	5	5

Figure 1. Kaplan-Meier estimates of (A) overall survival and (B) recurrence-free survival after liver resection for pelvic squamous cell carcinoma metastases. OS: overall survival; RFS: recurrence-free survival

Table 3
Postoperative outcomes and endpoints. IQR: interquartile range; LOS: length of hospital stay

Survival	
Median OS, months (95% CI)	70 (0.0–167.5)
1-/3-/5-year OS, %	80.8 / 57.7 / 57.7
Median RFS, months (95% CI)	65 (4.7–125.3)
1-/3-/5-year RFS, %	70.7 / 50.5 / 50.5
Secondary endpoints	**n (%) / median (IQR)**
ICU LOS (days)	1 (0–1)
Hospital LOS (days)	9 (6–11)
Clavien-Dindo	
≥ IIIa	3 (20.0)
≥ IIIb	2 (13.3)
≥ IVa	1 (6.7)

The swimmer plot (Fig. 2) illustrates the individual disease courses of all 15 patients over a follow-up of up to 120 months after initial diagnosis, displaying the timing of primary tumor resection, (radio-)chemotherapy, diagnosis and resection of liver metastases, disease progression, and complete response, together with each patient's vital status at last follow-up. Two patients (patient 14 and patient 11) with anal carcinoma metastases underwent repeat liver resections following recurrent disease. Patient 2 underwent a two-stage hepatectomy with portal vein ligation in the sense of a liver first treatment concept. Overall, patient 14 underwent 5 liver resections. The final three procedures combined liver resection with local peritoneal resection for strictly localized peritoneal nodules.

Discussion

This cohort represents one of the largest single-center experiences on liver resection for metastases from pelvic squamous cell malignancies. The 5-year overall survival was 57.7% at a maximum follow-up of six years after liver resection – a favorable result for a population with oligometastatic disease.

Comparing our results with the three most relevant reference cohorts on liver resection for anal and cervical SCC metastases, Engstrand et al. reported a 5-year OS of 45% for anal SCC in a European multicenter cohort [2]. Lo et al. reported a 5-year OS of 50% and a median OS of 32.2 months in a multicenter series [3]. Omichi et al. reported 3- and 5-year OS rates of 52% and 47%, respectively, for mixed SCC liver metastases [8]. In contrast, Pawlik et al. reported a markedly worse 5-year OS of 20.5% [9]; this is plausibly attributable to the earlier treatment period of that cohort (1988–2006), less effective systemic pretherapy available at the time, and a heterogeneous primary tumor population in which almost half of patients had non-anal primaries, predominantly head-and-neck, lung, and esophageal SCC. In our cohort, median OS was not reached within the reported ranges of these series and was estimated at 70 months (95% CI 0.0–167.5), reflecting the relatively low number of events and wide confidence interval inherent to a small single-center sample.

Compared with these benchmark series, the survival observed in our cohort might be superior. Several factors likely contributed to this finding. Although most patients were classified as ASA III, few had relevant organ-specific comorbidities (cardiovascular and hepatic comorbidities in 13.3% each, no pulmonary disease or diabetes), reflecting careful patient selection for surgery. The primary tumor was mainly anal carcinoma (80%), a subtype consistently associated with better outcomes than other SCC primaries after liver resection [2, 8]. Furthermore, R0 resection was achieved in the majority of procedures (80%), consistent with the prognostic importance of a negative resection margin [2].

Recurrence-free survival in our cohort also compares favorably with the available literature. Median RFS was 65 months (95% CI 4.7–125.3), with a 1-, 3-, and 5-year RFS of 70.7%, 50.5%, and 50.5%, respectively. This considerably exceeds the RFS reported by Engstrand et al. (median 16 months for anal cancer and 9 months for non-anal cancer) [2], by Lo et al. (median 7.7 months, 5-year RFS 30%) [3], and by Omichi et al. (1- and 3-year RFS of 50% and 25%) [8]. Several factors likely contribute to this difference beyond patient selection: our institutional surveillance protocol with close cross-sectional imaging follow-up may detect and enable treatment of oligometastatic recurrences earlier than in some reference cohorts, and the predominance of anal carcinoma and high rate of R0 resection in our cohort are the same favorable characteristics that were associated with better OS. The very wide confidence intervals around our RFS estimates, a direct consequence of the small sample size and limited number of events, mean that the point estimates should be interpreted with caution rather than as a robust effect size, and the difference from the literature should not be over-interpreted.

Beyond overall survival, several prognostic factors have been consistently identified across the available series. A negative resection margin is the most consistent predictor of outcome: Engstrand et al. reported a hazard ratio of 6.82 for recurrence-free survival with R1 resection [2], and Pawlik et al.

reported a hazard ratio of 1.83 for overall survival [9]; in our cohort, R0 resection was achieved in 80% of procedures, in line with this principle. Synchronous versus metachronous presentation is a second recurring factor: synchronous metastasis was the strongest adverse predictor in the Pawlik cohort (HR 4.09) [9], and Bacalbasa et al. similarly reported better outcomes with metachronous disease in cervical carcinoma [5]; two-thirds of our patients (66.7%) presented metachronously. Metastasis size and number have also been implicated – Pawlik et al. found that metastases > 5 cm were associated with worse overall survival [9] – and control of the primary tumor appears relevant, as the need for salvage abdominoperineal resection was negatively associated with recurrence-free survival in the series by Lo et al. [3]. Finally, Bacalbasa et al. identified tumor differentiation grade as the only independent prognostic factor on multivariable analysis in cervical carcinoma [5]. Given the limited size of our cohort, we were not able to perform a similarly powered multivariable analysis.

A further selection factor concerns the oncological status of the primary tumor and the presence of extrahepatic disease at the time of liver resection. This principle is well established in the broader metastasectomy literature: in colorectal liver metastases, where selection criteria for hepatectomy are most extensively studied, uncontrolled extrahepatic disease has traditionally been regarded as a relative contraindication to resection. For anal SCC specifically, a recent single-center series from the Mayo Clinic restricted eligibility to patients with liver-only metastatic disease, explicitly excluding those with extrahepatic involvement at diagnosis, and found that neither synchronous nor metachronous timing significantly influenced survival once this selection was applied [10]. In our cohort, every case was evaluated within a multidisciplinary tumor board both before and after liver resection, and local control of the primary tumor was established for all patients as part of this workup – before hepatectomy in all but one patient, who was treated with a liver-first approach (patient 2, Fig. 2). The large majority of patients had no evidence of extrahepatic disease at the time of hepatectomy; the only exception was one patient (patient 14, Fig. 2) in whom strictly localized peritoneal nodules were resected concomitantly with liver metastases. This confirmed primary tumor control and near-absence of extrahepatic disease likely contributed to the favorable survival observed in our cohort, analogous to the explicit liver-only selection applied by Takacs et al. [10] and the liver-only subgroup benefit reported by Goldner et al. [4], and represent a favorable selection characteristic of our series relative to less strictly characterized reference cohorts.

The safety of liver resection in this indication is supported by the available data: Omichi et al. reported no liver failure and no 90-day mortality among 28 patients, 14% of whom underwent major hepatectomy [8], while Bacalbasa et al. observed a single early postoperative death that was not attributable to the hepatic procedure [5]. In our cohort, no perioperative mortality occurred, and major complications (Clavien-Dindo ≥IIIb) were observed in 2 patients (13.3%), consistent with liver resection being feasible in this setting at a specialized center.

The choice between surgical resection and local ablative alternatives remains largely undefined by evidence, particularly for cervical carcinoma, where stereotactic body radiotherapy (SBRT) is the best-documented alternative to surgery, with series such as MITO-RT2/RAD (83 patients, 125 lesions) [11] and

KROG 14 – 11 [12] reporting favorable local control. No study has directly compared surgical resection with SBRT or radiofrequency ablation in this setting; several published cohorts, including our reference series by Engstrand et al. [2] and Sclafani et al. [13], included a mixture of resection, ablation, and radiotherapy. At present, the choice of local modality is guided by institutional expertise and multidisciplinary discussion rather than by comparative evidence – a point also raised explicitly by Ali et al. for oligometastatic cervical carcinoma, for which no dedicated management guidelines currently exist [14].

The evolving landscape of systemic therapy is also relevant to the interpretation of surgical series such as ours. POD1UM-303/InterAACT-2 has established retifanlimab plus carboplatin/paclitaxel as a new first-line standard for inoperable locally recurrent or metastatic anal SCC [15], and KEYNOTE-826 has shown a median overall survival of 26.4 months with pembrolizumab-based therapy for persistent, recurrent, or metastatic cervical carcinoma [16]. This has two implications for future surgical series: first, the benchmark against which liver-directed surgery is compared will continue to shift as systemic therapy improves; second, a new selection window may emerge, in which patients with a good and durable response to immunochemotherapy become candidates for consolidative local therapy. This sequence – systemic induction therapy followed by resection of residual oligometastatic disease – remains entirely unexplored in this population and represents a promising direction for future study.

The true prevalence of HPV-associated disease in our cohort could not be reliably determined from the retrospective data, with HPV testing documented in only 3 of the 20 procedures. The actual rate is presumably considerably higher, given that anal and cervical carcinoma are HPV-driven in the large majority of cases; the low documentation rate more likely reflects that HPV testing was not routinely performed throughout much of our inclusion period, particularly in its earlier years, before the causal role of HPV in these malignancies became more established in clinical routine. Similarly, no data currently exist on the potential role of HPV status or circulating HPV DNA (ctHPV-DNA) as a selection or monitoring marker prior to liver resection – an area that may warrant future investigation.

This study has several limitations. It is a retrospective, single-center analysis without a control group. As with all surgical series in this field, a selection bias must be assumed: patients selected for liver resection are typically younger, in better general condition, and have more favorable tumor biology than the broader population of patients with metastatic disease – a caveat that also applies to registry-based analyses such as that of Goldner et al., in which metastasectomy itself may act as a surrogate marker for favorable patient selection [4]. As discussed above, primary tumor control was established in all patients (in one after a liver-first approach) and, with one exception, no extrahepatic disease was present at the time of liver resection; while this reflects a deliberate and favorable selection characteristic of our cohort, these criteria were applied through multidisciplinary tumor board judgment rather than a prespecified, standardized protocol. Complete long-term follow-up could not be retrieved for patients treated in the early 2010s. The small sample size precluded a robust multivariable analysis. The long inclusion period was associated with heterogeneous systemic pretherapies and imaging standards.

Although our cohort is comparatively large for a single-center series, it remains too small to support further detailed statistical subgroup analysis.

Goldner et al. explicitly called for randomized evaluation of metastasectomy in this setting [4]. Given the rarity of the disease, such a trial is realistically feasible only as an international registry study or as a prospective cohort with predefined selection criteria. Until such data become available, we believe liver resection for metastases from pelvic squamous cell carcinoma should continue to be offered, within a multidisciplinary tumor board setting, to selected patients with a controlled primary tumor, limited and technically R0-resectable liver disease, and favorable tumor biology.

Conclusions

This cohort represents one of the largest single-center experiences published in the literature on liver metastases from pelvic squamous cell malignancies. The surgical management of metastases from pelvic squamous cell carcinoma, particularly anal carcinoma, is feasible and safe and provides long-term survival in selected cases.

Abbreviations

AC
anal carcinoma
APR
abdominoperineal rectal extirpation
ASA
American Society of Anesthesiologists
BMI
body mass index
CI
confidence interval
CRT
chemoradiotherapy
CTX
chemotherapy
HPV
human papillomavirus
ICU
intensive care unit
IQR
interquartile range
LOS
length of stay

OS
overall survival
R0/R1
complete/microscopically incomplete resection
RFS
recurrence-free survival
RTX
radiotherapy
SCC
squamous cell carcinoma
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the University of Duisburg-Essen (approval no. 25-12783-BO) and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee owing to the retrospective design of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

MAR, ADR and SMS conceived and designed the study; MAR, NM, SMS collected the data; MAR, NM performed the statistical analysis; MAR, NM, PMN drafted the manuscript; TFU, UN, ADR and SMS critically revised the manuscript. All authors read and approved the final manuscript.

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Not applicable.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to data protection regulations (EU General Data Protection Regulation) and the conditions of the ethics approval, as the data contain sensitive clinical information and the small size of this rare-disease cohort carries a risk of patient re-identification even after anonymization. De-identified data are available from the corresponding author on reasonable request, subject to approval by the local data protection officer and the conclusion of a data use agreement.

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Figures

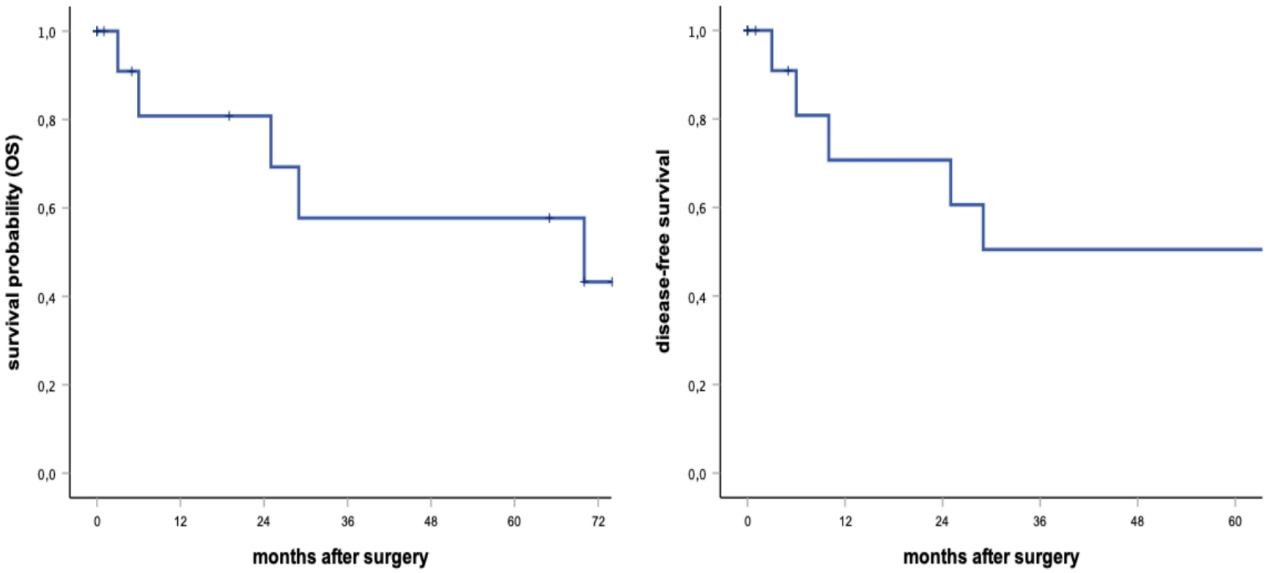


Figure 1

Kaplan-Meier estimates of (A) overall survival and (B) recurrence-free survival after liver resection for pelvic squamous cell carcinoma metastases. OS: overall survival; RFS: recurrence-free survival

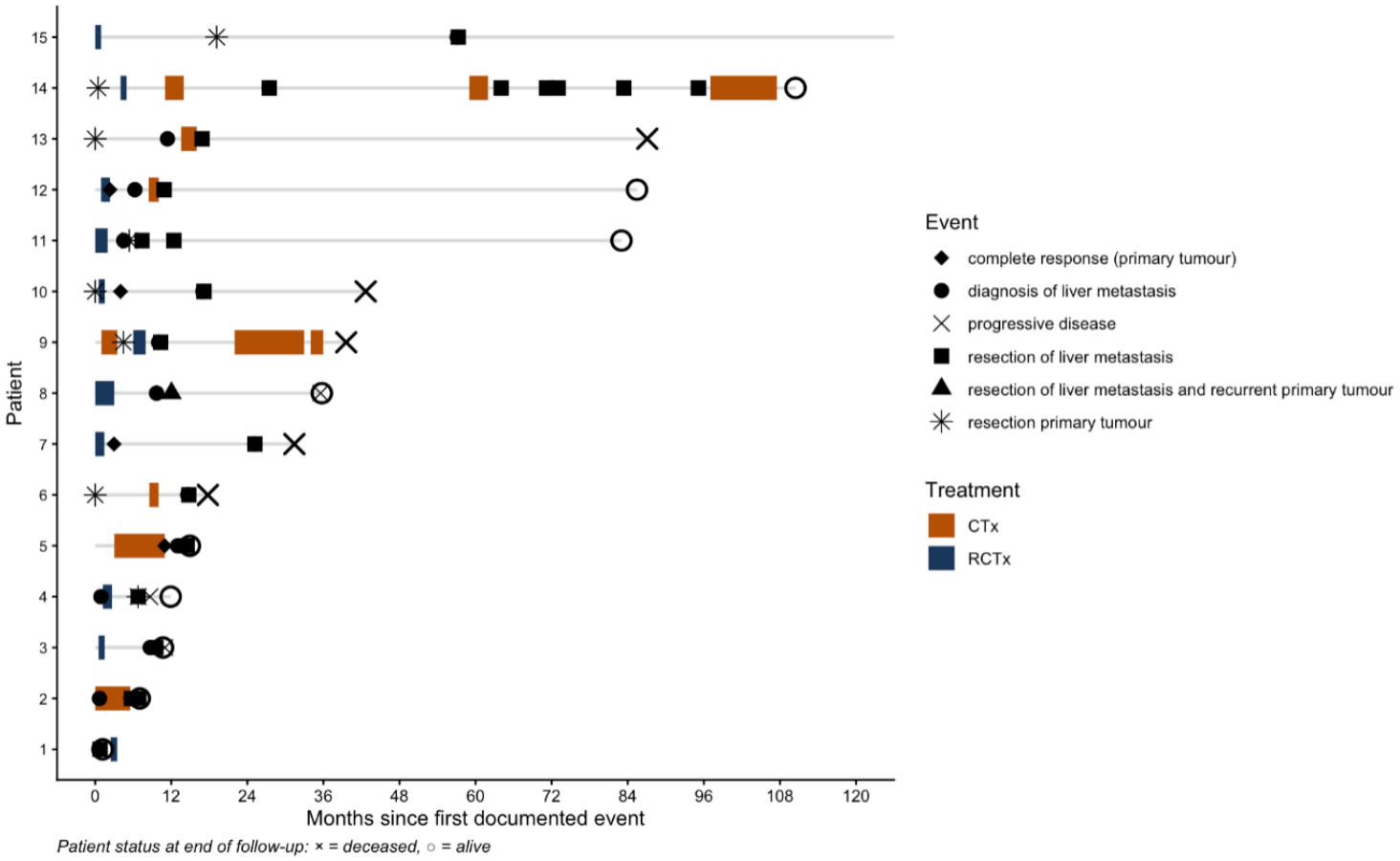


Figure 2

Swimmer plot of individual disease courses for all 15 patients, showing resection of the primary tumor, (radio-)chemotherapy, diagnosis and resection of liver metastases, disease progression, complete response, and vital status at last follow-up.