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Stepwise implementation of robotics and a certified enhanced recovery program significantly improves multiple outcome metrics in a liver surgery unit ☆

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ABSTRACT

Introduction: Minimally-invasive surgery (MIS – including laparoscopy and robotics) and enhanced recovery after surgery (ERAS®) programs reduce complications and improve functional outcome for cancer patients. Their combined impact on liver surgery cohorts remains unclear.

Materials and methods: This Austrian single centre cohort study assesses the stepwise implementation of laparoscopy, robotic-assisted-surgery (RAS), and an audited ERAS® certification. Three periods (17 months each; January 2020 to 06/2024) were compared: P1 (pre-RAS/pre-ERAS®), P2 (RAS/ERAS®-like), and P3 (RAS/ERAS®). Outcomes included intensive-care and overall length-of-stay ((ICU-)LOS), 90-day-morbidity, mortality, post-hepatectomy liver failure, haemorrhage (PHLF/PHH), and bile leakage (BL). Textbook outcome after liver surgery (TOLS) was evaluated in cancer patients (definition: no blood loss >1000 ml, MIS-conversion, PHLF/BL, severe morbidity/mortality, readmission, and R1-margin).

Results: Over the three periods $n = 225$ patients showed comparable demographics, underlying liver disease, preoperative chemotherapy, and major resection rates. MIS (RAS) increased from 31.1 % (0 %), to 71.1 % (52.6 %), and 77.3 % (45.6 %; $p < 0.001$), with less conversions (21.1 %, to 3.7 %, and 5.9 %; $p = 0.030$). Decreasing median blood-loss (400 ml–200 ml in P3; $p = 0.002$) led to low transfusion rates (P3: 5.7 %). Median LOS/ICU-LOS decreased from 9/3 days, to 6/2, and 5/1 days ($p < 0.001$), overall (severe) 90-day-morbidity from 54.1 %

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(29.5 %), to 39.5 % (14.5 %), and 35.2 % (14.8 %) (p = 0.022/p = 0.011). PHLF reduced from 13.1 %, to 1.3 %, and 5.7 % (p = 0.009). TOLS rates enhanced from 37.9 %, to 68.2 %, and 70.8 % (p = 0.002). MIS was an independent predictor of lower (severe) morbidity and LOS.

Conclusions: Implementing MIS/RAS and ERAS® in an established hepatobiliary unit significantly improves blood-loss, (ICU-)LOS, morbidity, and PHLF. This ultimately leads to substantially increased TOLS rates in common oncological indications.

1. Introduction

Outcomes after hepatectomy are determined by various patient, tumour and liver parenchyma characteristics. A direct correlation between the surgical complexity, expertise and case volume of specialized teams, and the incidence of postoperative complications has been demonstrated [1–5]. In surgical oncology a potential impact of standardized perioperative management pathways on oncological long-term outcomes has been proposed [6,7].

International guidelines such as the Enhanced Recovery After Surgery (ERAS®) society recommendations summarize evidence through standardized auditable clinical care items [8,9]. Validation studies reported varying adherence to these items, depending on patient performance status, surgical indication and access [10–12]. Safe implementation of ERAS® pathways has been documented for colorectal cancer liver metastases (CRLM) and hepatocellular carcinoma (HCC) patients, reducing hospital stay and complications without increased readmission or reoperation risk [1,13–15].

Representing a key ERAS® item, minimally-invasive liver surgery (MILS) is increasingly adopted in specialized centres. Randomized-controlled trials showed at least non-inferior oncological long-term outcomes compared to open surgery, with improved postoperative complications, quality of life, and access to adjuvant treatments [16–23]. However, broad implementation is hampered due to the slow learning curve especially for complex laparoscopy [16,24–27]. RAS more closely mimics the classical open surgical approach through wristed instruments, enhanced precision and ergonomics, integrated 3D computer augmentation, and fluorescence. This may reduce the learning curve for advanced liver procedures whilst ensuring adequate oncological outcomes [25,28–32], expediting broader acceptance and implementation of MILS within the surgical community [33–40].

Reports of a combined integration of systematic ERAS® management and hepatobiliary MILS including RAS are limited [41,42]. Therefore, the aim of this paper is to demonstrate potential synergistic effects of a stepwise integration of RAS followed by audited certification as the first ERAS®-centre in Austria in an all-comer liver surgery patient cohort.

2. Methods

2.1. Study characteristics

This single centre study utilizes prospectively acquired data of all liver surgery patients from an Austrian teaching hospital assessing three periods of 17 months each between January 2020 and June 2024 (Fig. 1, complete 90-day follow-up until September 30, 2024). The general surgical oncology department was declared a hepatobiliary centre within a regional network of 11 hospitals, with two HPB consultant surgeons (S.S. and F.P.) allocated as department chair and unit lead early 2020. Stepwise, a hepatobiliary outpatient clinic, multidisciplinary tumour board, and standard-operating procedures (SOPs) were implemented, followed by the first robotic hepatobiliary resection in 07/2021, prospective documentation in the EIAS liver protocol (ERAS® Interactive Audit System; Encare, Stockholm, Sweden) starting in January 2023 and successful ERAS® certification in September 2023 (Fig. 1A) [8,43].

Exclusion criteria were non-elective liver surgery for trauma, or unplanned re-operations of previous HPB resections, where only the index operation was counted. Operations with simultaneous extrahepatic multiorgan resections (pancreas, stomach, etc.) were included. However, for the ERAS® compliance rate calculation in EIAS only pure

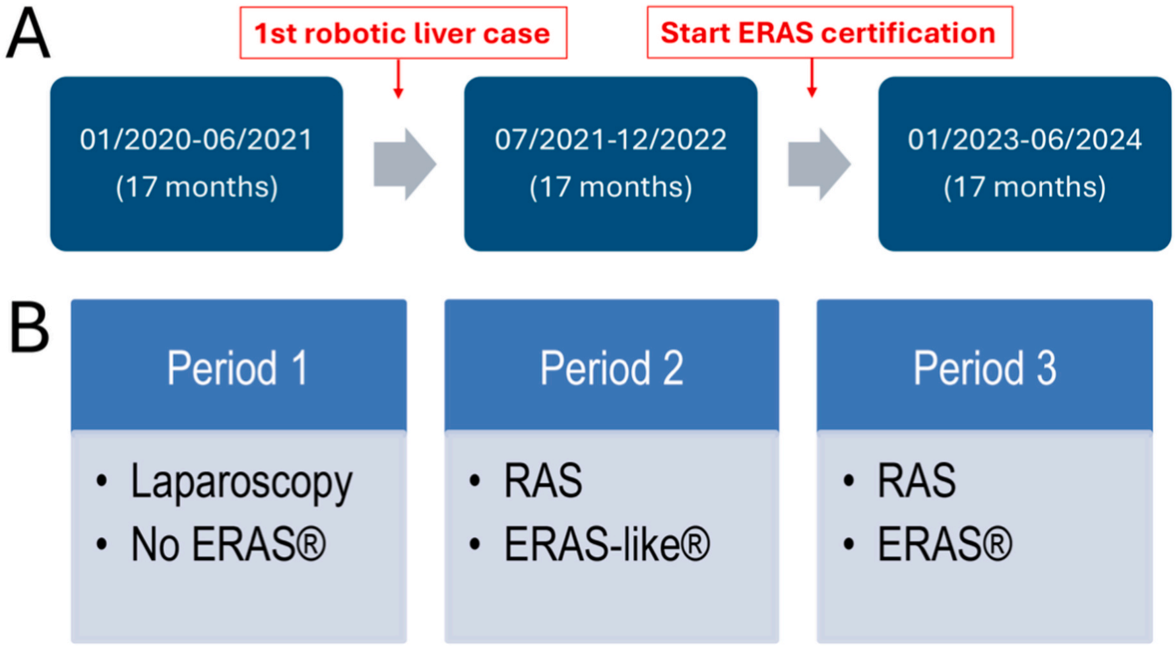

Fig. 1. A) Timeline of clinical milestones including stepwise introduction of robotic-assisted-surgery (RAS) and a certified ERAS® program within an established liver surgery unit. B) Study outline comparing the resulting three time-periods (each 17 months). ERAS® = Enhanced Recovery After Surgery.

liver cases were counted. The study was approved by the ethics committee (JKU Linz, Austria, EC-number 1140/20224) waiving individual patient consent due to the retrospective analysis.

2.2. *Study endpoints and definitions*

The aim of the study was to assess the benefit of a stepwise implementation of RAS and ERAS for consecutive liver surgery patients over the three different time-periods. The primary study endpoints comprised overall postoperative 90-days complication rate as well as postoperative intensive-care-unit and hospital length of stay ((ICU-)LOS) for the index admission. Secondary endpoints included severity grading of postoperative complications according the Clavien-Dindo Classification (severe if $\geq$ 3a), unplanned readmissions, and reoperations within 90-days after surgery [44], as well as liver-surgery-specific 90-day complications: post hepatectomy liver failure (PHLF), haemorrhage (PHH), and bile leakage (BL) classified according the International Study Group for Liver Surgery (ISGLS) [45–47]. Textbook outcome after liver surgery (TOLS) was assessed in CRLM, HCC and CCC (cholangiocellular carcinoma) patients as previously defined [48].

Detailed patient, tumour and surgical characteristics were documented individually over the three periods to assess comparability between cohorts. Liver parenchymal disease was evaluated histologically; preoperative chemotherapy was recorded in the context of the current surgery. Anatomical resections were reported according the Brisbane 2000 and Tokyo 2020 terminology. Major liver surgery was defined as resection of 4 or more segments as previously suggested, whereby left hemihepatectomy was considered a major resection even when performed without segment 1 [49–51]. Non-anatomical resections or intraoperative ablations were counted as half segments and summed up for this definition. The study is presented according the STROCCS guidelines (strengthening the reporting of cohort, cross-sectional and case-control studies in surgery) [52].

2.3. *Surgical technique*

Open resections were performed through midline incision with optional transverse extension. Parenchymal transection in open surgery was done with Kelly-clamp crush technique combined with a sealing device (Ligasure Maryland, Medtronic, Minneapolis, MN, USA or THUNDERBEAT, Olympus, Tokio, Japan) with occasional use of a cavitron ultrasonic surgical aspirator device (HEPACCS, Söring GmbH, Quickborn, Germany), laparoscopically THUNDERBEAT was used. Robotically the Intuitive DaVinci XI System (Intuitive Surgical Inc., Sunnyvale, CA, USA) was utilized, using four transverse (supra)umbilical 8 mm trocars and a 12 mm laparoscopic sub-umbilical midline assist-trocar [53]. Robotic parenchymal transection was done with microfracture-coagulation technique using the robotic fenestrated or Maryland bipolar forceps and scissors [54,55], with occasional use of the SynchroSeal device (Intuitive Surgical Inc., Sunnyvale, CA, USA) [53].

Inflow occlusion (Pringle manoeuvre) was applied at the surgeon's preference, with maximum 15–20 min clamping alternating with at least 5-min breaks. Inflow pedicle and hepatic vein branches were mostly transected with the use of stapling devices (EndoGIA, Medtronic, Minneapolis, MN, USA), metal or polymer surgical clips, or suture ligations.

2.4. *Anaesthesiologic management*

Details of stepwise introduction of individual management items can be found in the supplementary material. As part of the ERAS®-implementation process, patients were assessed according a preoperative “traffic light” risk stratification [5]. Accordingly, the perioperative management was adjusted, e.g. regarding intraoperative monitoring or planned ICU observation. A patient blood management plan was established [56]. A multimodal analgesic concept was applied in all patients, commonly utilizing epidural catheters or single spinal opioid injections in open surgery. Alternatively continuous wound infiltration catheters were applied, similar to MILS cases necessitating specimen retrieval midline incision of $\geq$7 cm, with additional single injection local anaesthesia at trocar incisions. A combination of CVP measurements and advanced minimally-invasive hemodynamic monitoring was used for intraoperative volume management.

2.5. *ERAS management and MILS integration*

For a detailed description of our ERAS® program refer to Supplementary Table S1, which gives an overview of introduced care items.

Shortly, in period 1 (Fig. 1A) no structured ERAS® program was present. However, individual ERAS® items were already routinely applied, such as abdominal drain avoidance and routine thrombosis prophylaxis. MILS in this period was performed laparoscopically, mainly for minor resections in the anterior segments.

In period 2, MILS indications were advanced introducing RAS. Through appointment of a dedicated ERAS®-expert nurse (D.R), a multidisciplinary ERAS®-care team was assembled including nurses, surgeons, anaesthetists, physiotherapists and physical medicine doctors, dietitians and psychologists [57]. After subscribing the ERAS® implementation program (EIP® Liver Protocol), standardized auditable clinical care items were added through systematic perioperative SOPs. Preoperative assessment routines for patient-fitness, anaemia, malnutrition, mental health and substance abuse were introduced [56,58–62]. To assess liver function, the LiMAx-CT volumetry algorithm (maximum liver function capacity; Humedics GmbH, Berlin, Germany) was utilized for major or technically complex resections [63,64].

Prehabilitation including physical training, home exercises, nutritional and psychological support was offered to high-risk patients. A diary was created for patient-reported outcome and experience measures (PROM/PREM) as described [65], with daily goals for mobilisation and nutrition. Standards for postoperative nutrition, mobilisation, pain management and an early post-discharge nurse-led consultation program were defined [8,66].

In period 3, ERAS® was systematically implemented, and RAS was advanced to major anatomical liver resections including hemihepatectomies and posterosuperior segmentectomies. Resections necessitating biliary or vascular reconstructions were still performed through open surgical access. Official certification as the first Austrian ERAS® centre concluded on September 25, 2023.

2.6. *Statistical analysis*

Continuous variables were reported as median with interquartile range (IQR), categorical variables as absolute numbers and percentages. Between-group comparisons were performed with the Mann-Whitney *U* test, the chi-square test, or Fisher's exact test. The association of MILS, ERAS®, and other factors on outcomes was assessed using logistic regression models. After (multi-)collinearity assessment, all variables from univariable analysis were included in the multivariable model via enter method or backwards method (likelihood ratio). The final model was selected depending on fit and explanatory strength. Factors associated with LOS were assessed through a generalized linear model (GLM). Adjusted odds ratios (OR) are displayed with 95 % confidence intervals (CI). Statistical significance was set at $p < 0.05$ (two-sided). Data analysis was performed using SPSS statistics 29 (IBM, Armonk, NY, USA). Illustrations were created in the EIAS software (Encare, Stockholm, Sweden) and with Microsoft Powerpoint (Microsoft, Redmond, Washington, USA).

Table 1
Patient, disease, and surgical characteristics (n = 225).

	Period 1 (pre-RAS/pre-ERAS®) n = 61	Period 2 (RAS/ERAS®-like) n = 76	Period 3 (RAS/ERAS®) n = 88	Period 2&3 combined n = 164	*p-value (P1 vs P2&3)*
Patient characteristics					
Age (years)	65 (58.5; 74.5)	63.5 (56.3; 72)	64.5 (56; 71)	64 (56; 72)	0.541
Male sex	33 (54.1 %)	35 (46.1 %)	44 (50.0 %)	79 (48.2 %)	0.429
BMI (kg/m^2)	26.2 (23.5; 28.4)	24.5 (22.3; 27.9)	24.7 (22.2; 29.4)	24.6 (22.3; 29.0)	0.145
ASA Classification					
1	7 (11.5 %)	7 (9.2 %)	12 (13.6 %)	19 (11.6 %)	0.825
2	43 (70.5 %)	59 (77.6 %)	63 (71.6 %)	122 (74.4 %)	
3 or 4	11 (18.0)	10 (13.2 %)	13 (14.8 %)	23 (14 %)	
Disease characteristics					
Liver parenchymal disease					
Steatosis	15 (24.6 %)	16 (21.1 %)	27 (30.7 %)	43 (26.2 %)	0.804
Fibrosis	10 (16.4 %)	16 (21.1 %)	13 (14.8 %)	29 (17.7 %)	0.820
Cirrhosis	2 (3.3 %)	7 (9.2 %)	8 (9.1 %)	15 (9.1 %)	0.166
Preoperative chemotherapy	15 (24.6 %)	19 (25 %)	21 (23.9 %)	40 (24.4 %)	0.975
Previous liver surgery	7 (11.5 %)	14 (18.4 %)	17 (19.3 %)	31 (18.9 %)	0.186
Indication for surgery					**0.015**
CRLM	11 (18 %)	25 (32.9 %)	27 (30.7 %)	52 (31.7 %)	
CCC	11 (18 %)	9 (11.8 %)	6 (6.8 %)	15 (9.1 %)	
HCC	7 (11.5 %)	10 (13.2 %)	15 (17.0 %)	25 (15.2 %)	
Non-CRLM (NET, etc.)	12 (19.7 %)	10 (13.2 %)	20 (22.7 %)	30 (18.3 %)	
Other primary liver/GBC	4 (6.6 %)	4 (5.3 %)	1 (1.1 %)	5 (3.0 %)	
Benign/pre-malignant	8 (13.1 %)	15 (19.7 %)	17 (19.3 %)	32 (19.5 %)	
Other (chronic infection, etc.)	8 (13.1 %)	3 (4.2 %)	2 (2.3 %)	5 (3.0 %)	
Surgical characteristics					
Minimally-invasive surgery	19 (31.1 %)	54 (71.1 %)	68 (77.3 %)	122 (74.4 %)	**<0.001**
RAS	0 (0 %)	40 (52.6 %)	40 (45.6 %)	80 (48.8 %)	**<0.001**
Conversion (% of MIS)	4 (21.1 %)	2 (3.7 %)	4 (5.9 %)	6 (4.9 %)	**0.030**
Major resection (>3 segments)	18 (29.5 %)	26 (34.2 %)	23 (26.1 %)	49 (29.9 %)	0.975
Multiple liver resections	14 (23 %)	15 (19.7 %)	32 (36.4 %)	47 (28.7 %)	0.392
Other substantial procedures	10 (16.4 %)	10 (13.2 %)	9 (9.1 %)	19 (11.0 %)	0.071
Colon	5 (8.2 %)	4 (5.3 %)	4 (4.5 %)	8 (4.9 %)	
Pancreas (± spleen)	0 (0 %)	4 (5.3 %)	2 (2.3 %)	6 (3.7 %)	
Stomach	5 (8.2 %)	2 (2.6 %)	2 (2.3 %)	4 (2.4 %)	
Intraoperative metrics					
Inflow occlusion/Pringle manoeuvre applied	36 (59 %)	47 (61.8 %)	51 (58 %)	98 (59.8 %)	1.000
Pringle time *(minutes)*	38 (16; 52)	42 (25; 60)	47.5 (27.3; 64.5)	45 (26; 62)	0.156
Operative time (minutes)	255 (147; 380)	294 (176; 413)	237 (132; 345)	263 (152; 380)	**0.908**
Blood loss (milliliters)	400 (200; 850)	300 (150; 600)	200 (50; 600)	300 (80; 600)	**0.002**
Blood transfusion: none	52 (85.3 %)	67 (88.2 %)	83 (94.3 %)	150 (91.5 %)	0.171
1 unit	1 (1.6 %)	1 (1.3 %)	1 (1.1 %)	2 (1.2 %)	
>1 units	8 (13.1 %)	8 (10.5 %)	4 (4.5 %)	12 (7.3 %)	

Data are presented as absolute numbers (%) or median with interquartile range (IQR).

Abbreviations: ASA = American Society of Anaesthesiologists; BMI = Body mass index; CCC = cholangiocellular carcinoma; CRLM = colorectal cancer liver metastases ERAS® = enhanced recovery after surgery; GBC = gall bladder cancer; HCC = hepatocellular carcinoma; MIS = minimally-invasive surgery; Non-CRLM = Non-colorectal liver metastases; NET = neuroendocrine tumour; RAS = robotic-assisted-surgery.

3. Results

3.1. Study cohort

The final analysis comprised 225 liver resections (Table 1). Comparing period 1 (pre-RAS/pre-ERAS®) vs. period 2&3 (RAS/ERAS® (-like)) combined, no significant differences in patient characteristics, preoperative chemotherapy rate and underlying liver disease were noted, except minor differences in the indications for surgery ($p = 0.015$). The rate of major resections, multiple hepatectomies, and additional organ resections was stable over time. However, the rate of MIS increased from 31.1 % (period 1) to 74.4 % (periods 2 and 3 combined; $p < 0.001$), mainly attributed to RAS (0 % vs. 48.8 %; $p < 0.001$), accompanied by a declining conversion rate (21.1 %–4.9 %; $p = 0.030$; Fig. 2A) and a temporary increase in operative time in period 2. Increased MIS utilization significantly decreased median blood loss from 400 ml (IQR 200 to 850) to 200 ml (IQR 50 to 600) in the most recent period ($p = 0.002$), with only 5.7 % of patients receiving intraoperative transfusions.

3.2. ERAS® program integration and compliance adherence

Fig. 2B shows ERAS®-item compliance rates comparing the pre-certification ERAS®-like period 2 audit cases (45 % overall compliance) and the official ERAS®-certification period 3 (81 %). Substantial improvements were mainly achieved in preadmission, preoperative and postoperative compliance, with only minor improvement in the already well-established intraoperative items. Supplementary Fig. S1 depicts a detailed radar chart of each single compliance-relevant item.

3.3. Postoperative outcomes

Table 2 and Fig. 3 show postoperative outcomes stratified by three periods. A significant reduction in median hospital LOS (from 9 days to 5 days; $p < 0.001$) and median ICU LOS (from 3 days to 1 day; $p = 0.002$) was achieved, without increased rates of unplanned readmissions or reoperations. Decreasing rates of overall 90-day-morbidity (54.1 %–37.2 %; $p = 0.022$) and severe complications (29.5 %–14.6 %; $p = 0.011$) were documented. More specifically, the rate of PHLF (13.1 %–3.7 %; $p = 0.009$) and clinically-relevant PHLF (ISGLS grade B/C) significantly declined (8.2 %–1.8 %; $p = 0.036$). However, no significant

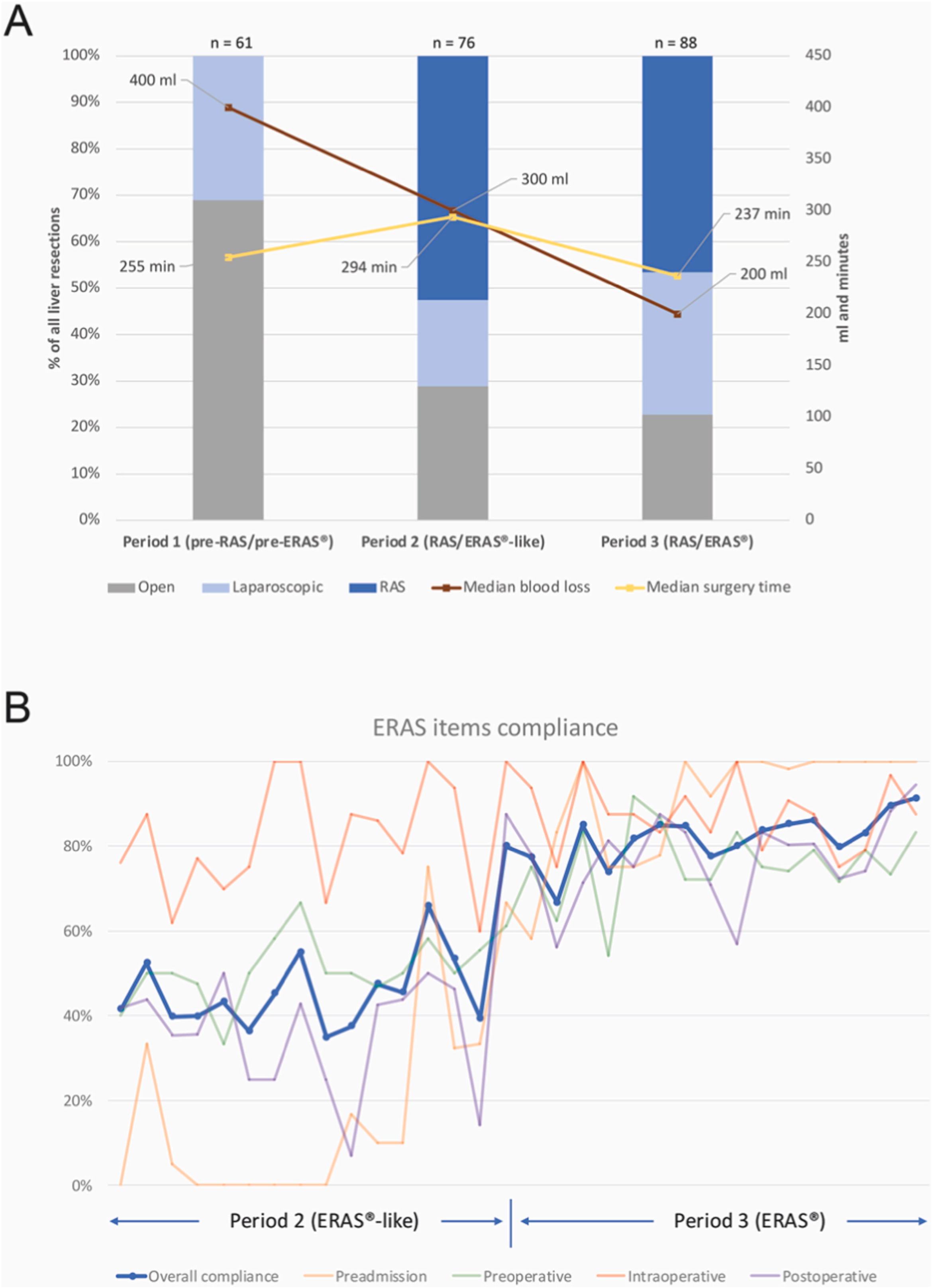

Fig. 2. A) Comparison of the three time-periods regarding surgical approach (open, laparoscopic, robotic-assisted-surgery (RAS)), median operative time and blood loss. B) Comparison of ERAS® item compliance rates (overall complicance, preadmission, prepoerative, intraoperative, and postoperative) between period 2 (ERAS®-like management and pathway.

Table 2
Postoperative outcomes after liver resection (n = 225).

	Period 1 (pre-RAS/pre-ERAS®) n = 61	Period 2 (RASERAS®-like) n = 76	Period 3 (RAS/ERAS) n = 88	Period 2&3 combined n = 164	*p-value (P1 vs P2&3)*
General outcomes					
LOS hospital, days, *median (IQR)*	9 (6; 17)	6 (4; 10)	5 (3; 8)	5.5 (3; 9)	**<0.001**
LOS ICU, days, *median (IQR)*	3 (1; 5.5)	2 (0; 3)	1 (0; 2.8)	1 (0; 3)	**0.002**
Overall 90-day morbidity	33 (54.1 %)	30 (39.5 %)	31 (35.2 %)	61 (37.2 %)	**0.022**
Severe 90-day morbidity (CD > 2)	18 (29.5 %)	11 (14.5 %)	13 (14.8 %)	24 (14.6 %)	**0.011**
90-day mortality	2 (3.3 %)	1 (1.3 %)	1 (1.1 %)	2 (1.2 %)	0.297
Unplanned readmission (30 days)	8 (13.1 %)	8 (10.5 %)	7 (8.0 %)	15 (9.1 %)	0.184
Unplanned reoperation (30 days)	8 (13.1 %)	4 (5.3 %)	7 (8.0 %)	11 (6.7 %)	0.124
Specific outcomes					
PHLF (ISGLS)	8 (13.1 %)	1 (1.3 %)	5 (5.7 %)	6 (3.7 %)	**0.009**
CR-PHLF (ISGLS Grade B/C)	5 (8.2 %)	1 (1.3 %)	2 (2.3 %)	3 (1.8 %)	**0.036**
Haemorrhage	3 (4.9 %)	1 (1.3 %)	5 (5.7 %)	6 (3.7 %)	0.459
Bile leakage	6 (9.8 %)	3 (3.9 %)	9 (10.2 %)	12 (7.3 %)	0.536
Textbook outcome after liver surgery (TOLS) variables *(CRLM/HCC/CCC patients only)*	n = 29	n = 44	n = 48	n = 82	
Unfavourable intraoperative event	11 (37.9 %)	7 (15.9 %)	7 (14.6 %)	14 (15.2 %)	**0.008**
Blood loss ≥1000 mL	10 (34.5 %)	7 (15.9 %)	5 (10.4 %)	12 (13.0 %)	**0.009**
Conversion to open (%MIS)	3 of 7 (42.9 %)	2 of 31 (6.5 %)	3 of 35 (8.6 %)	5 of 66 (7.6 %)	**0.025**
Bile leakage (ISGLS B or C)	4 (13.8 %)	1 (2.3 %)	3 (6.3 %)	4 (4.3 %)	0.093
PHLF (ISGLS B or C)	4 (13.8 %)	1 (2.3 %)	2 (4.2 %)	3 (3.3 %)	0.056
Severe 90 d-morbidity (CD > 2)	9 (31 %)	8 (18.2 %)	8 (16.7 %)	16 (17.4)	0.114
90-day mortality	2 (6.9 %)	1 (2.3 %)	1 (2.1 %)	2 (2.2 %)	0.242
Readmission for severe morbidity	2 (6.9 %)	4 (9.1 %)	2 (4.2 %)	6 (6.5 %)	1.000
R1 resection-rate	2 (6.9 %)	4 (9.1 %)	7 (14.6 %)	11 (12.0 %)	0.732
TOLS achieved (none of the above factors occurred)	11 (37.9 %)	30 (68.2 %)	34 (70.8 %)	64 (69.6 %)	**0.002**

All data are presented as absolute numbers (%) or median with interquartile range (IQR).

Abbreviations: CCC = cholangiocellular carcinoma; CD = Clavien-Dindo classification; CRLM = colorectal cancer liver metastases; CR-PHLF = Clinically relevant post-hepatectomy liver failure; ERAS® = Enhanced recovery after surgery; HCC = hepatocellular carcinoma; ICU = intensive care unit; ISGLS = International Study Group of Liver Surgery; MIS = minimally-invasive surgery; LOS = length of stay; PHLF = post-hepatectomy liver failure; RAS = robotic-assisted-surgery; TOLS = Textbook outcome after liver surgery.

difference regarding postoperative PHH or BL was noted. TOLS was assessed in a subgroup analysis of CRLM, HCC, and CCC patients combined. Over time, the TOLS-rate accomplished increased from 37.9 % (period 1) to 69.6 % (periods 2 and 3; p = 0.002).

Uni- and multivariable analysis of factors associated with postoperative (severe) complications are displayed Table 3 and Supplementary Table S2. MILS (combining laparoscopic and RAS) was a strong and independent factor for improved overall morbidity (OR 0.127; 95 % CI 0.054–0.299; $p < 0.001$) as well as severe morbidity (OR 0.159; 95 % CI 0.054–0.462; $p < 0.001$). While presence of an ERAS®-like or ERAS®-certified program (P2/P3) was a protective factor for overall and severe morbidity in univariable analysis, this no longer remained significant after multivariable correcting for confounders. Further independent factors for severe or overall morbidity were patient age, preexisting liver parenchyma damage and major resections. Supplementary Table S3 and Fig. S2 shows factors associated with hospital LOS. Again, MILS was a strong predictor of reduced LOS (OR 0.500; 95 %CI 0.347–0.720; $p < 0.001$), while major resections and concomitant resection of other organs were independent factors of prolonged LOS (OR 1.506 (95 %CI 1.046–2.168; p = 0.027 and OR 1.737 (95 %CI 1.085–2.780; p = 0.021, respectively). An ERAS®-like or ERAS®-certified program (P2/P3) was associated with reduced LOS in univariable analysis (OR 0.577; 95 %CI 0.424–0.785; $p < 0.001$) but did not remain significant in multivariable analysis (OR 0.768; 95 %CI 0.538–1.096; p = 0.146).

Granular data on patient, disease and surgical characteristics, and perioperative outcomes stratified by surgical access and time-period are presented in Supplementary Table S4. While most general patient and disease characteristics were comparable across the three time-periods and surgical approaches, open surgery over time was increasingly utilized for complex, major hepatectomies and concomitant extrahepatic resections, with consistently higher postoperative morbidity and prolonged LOS. In contrast, laparoscopic surgery recently almost exclusively was applied for minor liver resections, with decreasing operative duration, blood loss and postoperative LOS or reoperations. RAS was consistently associated with a low LOS despite a relevant rate of major resections.

4. Discussion

Stepwise implementation of MILS including RAS, in parallel to an audited ERAS® program led to profound improvements in perioperative outcomes in our hepatobiliary centre in an all-comer real-life setting. Our results demonstrate a significant and clinically meaningful reduction in blood loss, transfusion requirements, ICU and hospital LOS, (CR-) PHLF, overall and severe morbidity. Strikingly, this was accompanied by almost doubled TOLS rates in common oncological indications (from 37.9 % to 70.8 %), surpassing previous reports from international HPB centres [48,67,68]. These marked changes within a short time underline the potential of MILS and structured, specialist nurse-led, externally audited patient pathways, in a country with national average LOS after liver surgery of 10 days and MILS-rates below <20 % [12,57,69,70].

The study demonstrates, how high-level evidence can be implemented through a dedicated multiprofessional team even in non-academic general surgery units. As we have previously shown this also leads to faster restoration of patient quality-of-life (QOL) levels within 4 weeks of surgery, improved patient satisfaction and cooperation between health-care professionals [65]. Previous studies by others have underlined the importance of improved postoperative functional outcome, especially in older patients, to avoid delay of further oncological therapies [71,72]. While economic analysis was not the aim of

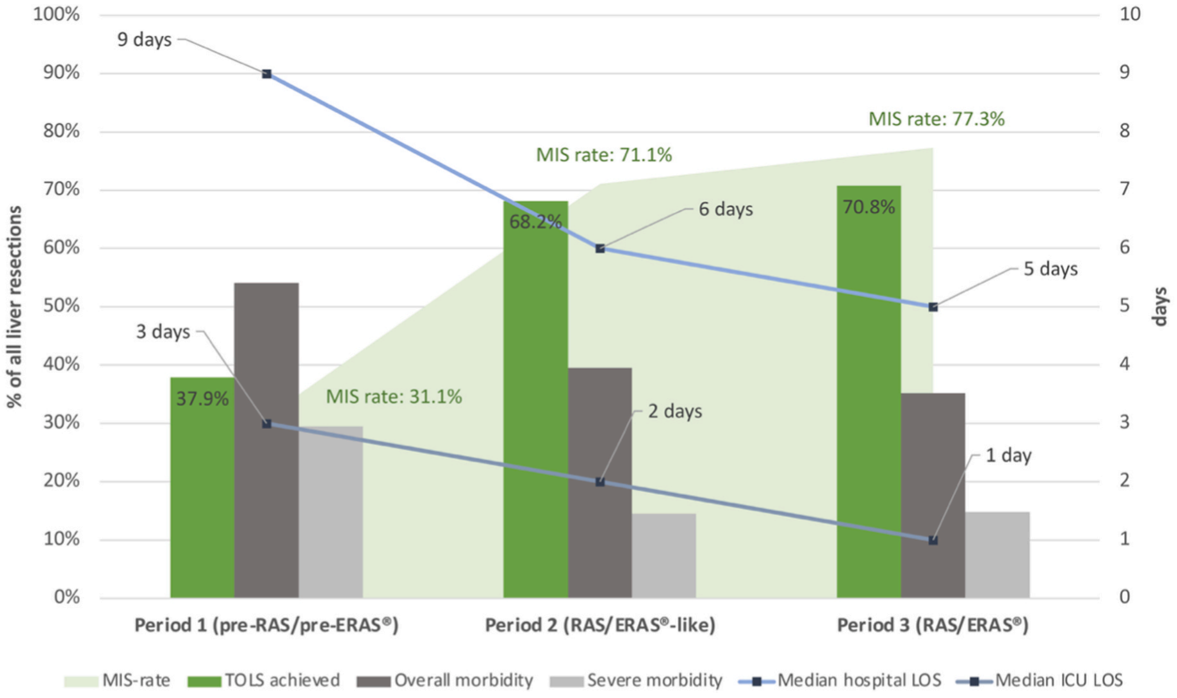

Fig. 3. Comparison of the three time-periods regarding rate of minimally-invasive surgery (MIS) and postoperative outcomes. *ERAS® = Enhanced Recovery After Surgery; ICU = intensive care unit; LOS = length of stay; RAS = robotic-assisted-surgery TOLS achieved = textbook outcome in liver surgery achieved.*

our study, others suggested these measures can ultimately also reduce costs [1,5,41].

Previously identified key factors for high compliance rates and improved outcomes include perioperative patient education, multidisciplinary nutritional and fitness optimization, stringent mobilisation and strong focus on reduction of major complications [12,73,74]. Similarly, analysis of individual ERAS® clinical item compliance rates in our centre suggests, that major improvements can mainly be achieved in the interdisciplinary preoperative and postoperative phase rather than through isolated intraoperative components. However, our findings align with existing literature supporting the significant individual benefit of increased MIS utilization within enhanced recovery pathways [41,75]. Xie et al. have demonstrated that the combination of RAS and ERAS® significantly reduces complications even in complex procedures performed in established hepatobiliary centres [42], comparable to studies in pancreatic and colorectal surgery [76,77]. Previously, the randomized controlled ORANGE II PLUS and ORANGE Segments trials demonstrated a significant reduction in time to functional recovery for laparoscopic versus open hemihepatectomy and parenchymal-preserving posterosuperior resections [18,78]. With improved patient QOL, MILS resulted in shortened time to adjuvant therapy initiation after hemihepatectomy (46.5 versus 62.8 days; $p = 0.009$). However, both studies failed to demonstrate superiority in secondary endpoints such as overall morbidity or mortality.

Most recently, the randomized, controlled German “ROC’N’ROLL” trial evaluated RAS versus laparoscopic liver surgery [79]. The endpoints were QOL, operating time, blood loss, conversion rates and complications. These endpoints together with underlying power calculations have been debated heavily [80–82]. Despite a rather low rate of anatomical major resections (20 %) it included a relevant number of technically difficult surgeries. Interestingly, the results showed no significant difference between the surgical approaches regarding QOL or the comprehensive complications index. Overall, the study did not assess which technique would be suitable to facilitate implementation of MILS within established open liver surgery units. Previous large multicentre propensity score-matched registry studies suggested RAS to be superior regarding blood loss, conversion and TOLS-rates compared to laparoscopy especially in technically challenging resections [25,75,83,84].

The potential of complex RAS compared to open surgery was demonstrated in a RCT on simultaneous rectal cancer and liver metastasectomy resulting in reduced LOS (8 vs. 11 days), morbidity (31 % vs. 58 %) and better bowel, bladder and sexual function [34]. An interesting next step would be to perform a trial comparing advanced RAS, laparoscopic, and open procedures in patients managed within dedicated ERAS® programs. While this comparison of all three techniques in a traditional RCT might be challenging due to the lack of equipoise within the liver surgery community, a cluster randomized study design could be considered.

We could confirm, that despite initial longer operative times RAS allows effective and safe MILS implementation even for advanced indications compared to conventional laparoscopy necessitating less conversions [24,85,86]. Intriguingly, as previously suggested by Xie et al., our analyses indicate that the MILS rate (almost 80 % recently) itself may have a stronger independent effect on postoperative morbidity and hospital LOS than the (additional) implementation of ERAS® programs [42]. However, interpretation is limited by overlap in the concurrent implementation of ERAS®, MILS (an ERAS-item in itself), and RAS in the later time-periods of our study.

We further noticed marked reduction in CR-PHLF, commonly a major contributor to severe morbidity and (delayed) mortality among cancer patients undergoing substantial liver resections [87,88]. While previous reports highlighted the role of ERAS® in reducing general postoperative complications, our study underlines the additional impact of minimally-invasive versus open access on liver failure [41,89]. Of note, we have implemented the LiMAx algorithm in period 2, potentially additionally influencing PHLF rates through patient selection and perioperative strategy adjustments [63,64].

Implementation of complex hepatobiliary surgery, ERAS and RAS initially encountered some resistance among team members and hospital staff, mainly due to concerns regarding patient safety, increased workload, and disruption of established routines. These barriers were addressed through early multidisciplinary engagement, structured education, and transparent communication of supporting evidence. Our

Table 3
Univariable and multivariable analysis of factors associated with overall post-operative morbidity (n = 225).

	Univariable: Any morbidity OR (95 % CI)	*P*	Multivariable: Any morbidity OR (95 % CI)§	*P*
Patient and disease characteristics				
Age (per 1 year)	1.026 (1.004–1.049)	**0.022**	1.036 (1.005–1.067)	**0.023**
Male sex	0.944 (0.556–1.603)	0.831	0.728 (0.365–1.450)	0.366
BMI (kg/m^2, per 1 point)	1.025 (0.971–1.082)	0.379	1.074 (0.996–1.160)	0.065
ASA Classification				
1 or 2	Ref			
3 or 4	1.288 (0.619–2.679)	0.499	1.060 (0.433–2.596)	0.898
Preexisting liver parenchyma disease	1.831 (1.065–3.149)	**0.029**	2.670 (1.213–5.875)	**0.015**
Preoperative chemotherapy	0.675 (0.366–1.244)	0.207	1.206 (0.512–2.839)	0.669
Previous liver surgery	1.282 (0.624–2.633)	0.499	0.777 (0.304–1.982)	0.597
Indication for surgery				
Benign or secondar liver tumour	Ref			
Primary hepatobiliary malignancy	1.835 (1.030–3.270)	**0.039**	1.004 (0.432–2.331)	0.993
Surgical & perioperative variables				
ERAS® program status (time period)				
Pre-ERAS®(P1)	Ref		Ref	
ERAS®-like or certified (P2/P3)	0.503 (0.277–0.911)	**0.023**	1.217 (0.432–2.331)	0.993
Surgical approach				
Open or converted to open	Ref		Ref	
Laparoscopic or RAS	0.139 (0.077–0.252)	**<0.001**	0.127 (0.054–0.299)	**<0.001**
Major resection	3.759 (2.062–6.853)	**<0.001**	3.220 (1.413–7.338)	**0.005**
Concomitant organ resection	2.409 (1.071–5.417)	**0.034**	2.167 (0.747–6.286)	0.155
Pringle applied	1.717 (0.990–2.978)	0.054	0.725 (0.332–1.584)	0.420
Intraoperative blood transfusion given	3.634 (1.430–9.230)	**0.007**	1.324 (0.428–4.093)	0.626

All data are given as odds ratios (OR) with 95 % confidence intervals (95 % CI).
§ = Multivariable logistic regression using Enter method (Nagelkerke R Square = 0.395; Hosmer-Lemeshow-Test p = 0.357).
Abbreviations: ASA = American Society of Anesthesiologists; BMI = Body mass index; ERAS® = Enhanced recovery after surgery; P1/2/3 = time period 1–3; RAS = robotic-assisted-surgery.

dedicated ERAS nurse played a pivotal role by coordinating pathways, educating staff and patients, monitoring compliance, and providing continuous feedback. Involvement of key stakeholders in protocol development fostered ownership and acceptance. Regular outcome audits and demonstration of early clinical benefits further facilitated integration of ERAS principles and RAS into routine hepatobiliary practice.

Limitations of this study include the non-randomized, observational design, which is prone to selection bias and restricts analysis of the individual, independent impact of different MILS techniques and the ERAS® program implementation. Access to the robotic system was limited for hepatobiliary-pancreatic cases in our hospital (one day/week), which influences the individual choice of the surgical approach. Furthermore, the surgical and multidisciplinary teams achieve more efficient and effective management over time, with a possible compound effect in outcomes. Also, the ERAS® concept focuses on active patient empowerment, representing an additional factor. These and other unobserved confounders are by definition not adjusted for in multivariable analyses. Therefore, further prospective investigations into the (non-) surgical learning curve for RAS and ERAS®, particularly in relation to patient selection, compliance, complication management, and oncological outcomes including multicentre validation are warranted [40,90].

5. Conclusion

In this European single centre study, the structured and stepwise integration of a MILS program including RAS in conjunction with an audited ERAS® pathway has led to substantial improvements in perioperative outcomes in an all-comer hepatobiliary surgery cohort including oncological patients. These findings underscore the strong compound effect of integrating high-level evidence-based strategies into daily clinical routine through a multidisciplinary care approach.

CReDiT author statement

Contribution Author(s) Study concepts: F Primavesi, I Urban, D Rappold, S Stättner, Study design: F Primavesi, I Urban, D Rappold, S Stättner, Data acquisition: F Primavesi, I Urban, D Rappold, M Tiefenthaler, J Simharl, D Baumgartner, S Petritsch, M Schausberger, D Luger, K Bogner, C Bartsch, K Kreuzhuber, J Stadler, T Königswieser, C Dopler, S Stättner, Quality control of data and algorithms: F Primavesi, D Rappold, J Simharl, R Diaz-Nieto, H Malik, F Ponholzer, S Stättner Data analysis and interpretation: F Primavesi, D Rappold, F Ponholzer, S Stättner, Statistical analysis: F Primavesi, D Rappold, F Ponholzer, S Stättner, Manuscript preparation: F Primavesi, I Urban, D Rappold, J Simharl, S Petritsch, D Luger, J Stadler, F Ponholzer, S Stättner, Manuscript editing: F Primavesi, I Urban, D Rappold, M Tiefenthaler, J Simharl, D Baumgartner, S Petritsch, M Schausberger, D Luger, K Bogner, C Bartsch, K Kreuzhuber, J Stadler, R Diaz-Nieto, H Malik, F Ponholzer, T Königswieser, C Dopler, S Stättner, Manuscript review: F Primavesi, I Urban, D Rappold, M Tiefenthaler, J Simharl, D Baumgartner, S Petritsch, M Schausberger, D Luger, K Bogner, C Bartsch, K Kreuzhuber, J Stadler, R Diaz-Nieto, H Malik, F Ponholzer, T Königswieser, C Dopler, S Stättne.

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Declaration of competing interest

All authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Non-financial support was received for the conduct of this research.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2026.111385.

Data availability

Parts of the results have been presented as a poster at the 2024 ESSO (European Society of Surgical Oncology) Congress in Antwerp, Belgium (Published abstract: European Journal of Surgical Oncology; Volume 50, Supplement 2, 109124; December 2024. DOI: 10.1016/j.ejso.2024.109124). The data underlying this study is available by request through the corresponding author.

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