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outcomes of laparoscopic and robotic major liver resections for colorectal liver metastases: A propensity-score and coarsened exact-matched controlled study

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Abstract

Background: Minimal invasive liver resections are a safe alternative to open surgery. Different scoring systems considering different risks factors have been developed to predict the risks associated with these procedures, especially challenging major liver resections (MLR). However, the impact of neoadjuvant chemotherapy (NAT) on the difficulty of minimally invasive MLRs remains poorly investigated.

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Data access

Data will be available from the corresponding author on reasonable request. It is not available publically due to ethical and privacy concerns.

Declarations

We confirm all the authors are accountable for all aspects of the work

i) Dr Goh BK has received travel grants and honorarium from Johnson and Johnson, Olympus and Transmedic the local distributor for the Da Vinci Robot.

ii) Dr Marino MV is a consultant for CAVA robotics LLC.

iii) Johann Pratschke reports a research grant from Intuitive Surgical Deutschland GmbH and personal fees or non-financial support from Johnson & Johnson, Medtronic, AFS Medical, Astellas, CHG Meridian, Chiesi, Falk Foundation, La Fource Group, Merck, Neovii, NOGGO, pharma-consult Peterson, and Promedicis.

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vi) Fernando Rotellar reports speaker fees and support outside the submitted work from Integra, Medtronic, Olympus, Corza, Sirtex and Johnson & Johnson.

Methods: Patients who underwent laparoscopic and robotic MLRs for colorectal liver metastases (CRLM) performed across 57 centers between January 2005 to December 2021 were included in this analysis. Patients who did or did not receive NAT were matched based on 1:1 coarsened exact and 1:2 propensity-score matching. Pre- and post-matching comparisons were performed.

Results: In total, the data of 5189 patients were reviewed. Of these, 1411 procedures were performed for CRLM, and 1061 cases met the inclusion criteria. After excluding 27 cases with missing data on NAT, 1034 patients (NAT: n=641; non-NAT: n=393) were included. Before matching, baseline characteristics were vastly different. Before matching, the morbidity rate was significantly higher in the NAT-group (33.2% vs. 27.2%, p-value=0.043). No significant differences were seen in perioperative outcomes after the coarsened exact matching. After the propensity-score matching, statistically significant higher blood loss (mean, 300 (SD 128–596) vs. 250 (SD 100–400) ml, p-value=0.047) but shorter hospital stay (mean, 6 (4–8) vs. 6 (5–9) days, p-value=0.043) were found in the NAT-group.

Conclusion: The current study demonstrated that NAT had minimal impact on the difficulty and outcomes of minimally-invasive MLR for CRLM.

Abbreviated abstract

The impact of neoadjuvant chemotherapy (NAT) on the difficulty of minimally invasive major liver resections (MLRs) remains poorly investigated. NAT had minimal impact on the difficulty and outcomes of minimally-invasive MLR for colorectal liver metastases.

Keywords

Major resections; Laparoscopic liver resections; Robotic liver resections; neoadjuvant chemotherapy

Introduction

Minimally invasive liver resection (MILR) is a safe alternative to open surgery, and studies have demonstrated its advantages, such as reduced blood loss, shorter hospital stay, and lower morbidity rates.(1–8) These advantages have resulted in the widespread use of MILRs worldwide, and different difficulty scoring systems (DSS) have been developed to predict the risks associated with MILR to guide surgeons when considering a minimally invasive approach. (9–13). Accurate DSS for classifying MILR are also important when auditing and benchmarking MILR to ensure a fair comparison.

The Iwate 4-level DSS, a widely used scoring system, was devised from a previous system developed in 2014 by Ban et al.(10) This scoring system considers tumor location and size, proximity to major vessels, the extent of liver resection, liver cirrhosis, and hand-assisted/ hybrid liver resections.(14) It has been shown to correlate well with the risk of intraoperative complications in MILR.(9, 15) However, unlike the Southampton scoring system (11), it does not consider the use of neoadjuvant chemotherapy (NAT) as a parameter.

The impact of NAT on the outcomes of MILR remains poorly investigated and its influence on the outcomesof MILR remain debatable. In a recent study which validated 4 commonly

used DSS including the Southampton DSS, it was demonstrating that all 4 systems significantly correlated with intraoperative technical difficulty and postoperative outcomes.(16) Notably, only the Southampton DSS included the use of NAT out of these four major DSS.(11). However, it is important to note that in a recent survey of expert MILR surgeons, 79 % surgeons were of the opinion that the use of NAT was an important factor determining the difficulty of MILR.(17).

Major liver resections (MLR) performed by minimally invasive approach are challenging and score high on difficulty scoring systems. Proper selection of patients for minimally invasive MLR is of utmost importance, and all possible risk factors have to be considered prior to surgery.(18)

As the impact of NAT on the MILR remains poorly studied and debatable, we performed this study with the primary objective of investigating the impact of NAT on the difficulty and outcomes of minimally invasive MLR for CRLM. We chose to focus on MLR as it is likely that if NAT were to influence the outcomes of MILR, this would be most significant in this cohort of patients compared to patients undergoing minor liver resections.

Methods

This is a retrospective analysis of an international multicenter database of minimally invasive liver resections performed across 57 centers. Patients who underwent laparoscopic and robotic MLR for colorectal cancer liver metastases between January 2005 to December 2021 were identified and included in this analysis. All institutions obtained their respective approvals according to their local requirements. All anonymized data were collated and analyzed centrally at the Singapore General Hospital. The Singapore General Hospital Institution Review Board provided a waiver for this study due to its retrospective nature and the use of anonymized data.

Inclusion and exclusion criteria

To reduce confounding factors, patients who underwent a concomitant major surgical procedure such as colectomy, reversal of stoma, lymph node dissection, or bilioenteric anastomoses were excluded. Patients who underwent concomitant minor procedures such as ablation, cholecystectomy, or hernia repair were included. Patients who had more than two separate concomitant liver resections and who had any history of previous liver resections were also excluded as these patients were more likely to have neoadjuvant chemotherapy and potentially for a prolonged duration.

Definitions

Postoperative complications were classified according to the Clavien-Dindo grading system (19) and were recorded up to 30-days or during the same hospital stay, including any readmissions. The types of liver resections were classified according to the Brisbane terminology.(20) Major resections included conventional major resections (left/extended left hepatectomies, right/extended right hepatectomies, central hepatectomies) and technically major resections (right anterior and right posterior sectionectomy). These resections have wide parenchymal transection surface areas at least of similar extent to conventional major

resections. The diameter of the largest lesion was used in the cases of multiple tumors. Thirty-day and 90-day mortalities were recorded.

Difficulty score

Based on the Iwate system,(9) LH were divided into 4 difficulty groups based on a 12-point scale: low (1–3), intermediate (4–6), high (7–9), and expert (10–12). The IMM system(12) divided the patients into 3 difficulty levels according to the procedure performed: Group I, wedge resection of anterior/ posterior tumors and left lateral sectionectomy; Group II, anterior segmentectomy and left hepatectomy; Group III, posterosuperior segmentectomy, right posterior sectionectomy, right hepatectomy, right anterior sectionectomy, central hepatectomy, and extended right/left hepatectomy.

Statistical analysis

To reduce confounding and selection biases and ensure the robustness of our conclusions, we employed two methodologies in the causal inference toolbox-coarsened exact matching and propensity-score matching to serve as sensitivity analyses to one another. One-to-one coarsened exact matching(21–24) was used to identify approximately-exact matches between patients who received or did not receive NAT and took into account all baseline variables shown in Table 1. Propensity-score (25–32) were likewise developed using mixed-effects logistic regression modelling of all variables shown in Table 1, with a random-effects parameter to account for between-center variation. This model exhibited good discrimination (AUC=0.752, bias-corrected 95% CI: 0.721–0.782) and calibration (P=0.983 from the Hosmer-Lemeshow test with ten deciles) (Supplementary Figures S1–S2). Propensity scores were matched using a 1:2 nearest-neighbor algorithm without replacement and a caliper of 0.20*standard deviations (SD) of the linear predictor (i.e., log odds of the propensity score). After matching, both groups were well-balanced for all variables, as shown in Table 1 and Supplementary Figures S3–4.

In the unmatched cohort, comparisons of patient characteristics and perioperative outcomes were assessed using the Mann-Whitney U test and Pearson's χ^2 test for continuous and categorical variables, respectively. Comparisons in the propensity-score and coarsened-exact matched cohorts took into account the paired nature of the data; hence, mixed-effects quantile regression (with a random-effects term to denote the matched samples) and conditional logistic regression were used for continuous and binary variables. Statistical analyses were done in Stata version 16.1 (StataCorp), and nominal $P<0.05$ indicated statistical significance.

Results

The data of 5189 patients who underwent laparoscopic and robotic major liver resections were reviewed. Of these, 1411 procedures were performed for CRLM, and 1061 cases met the inclusion criteria. Of these, 27 cases with missing data on NAT were excluded. Finally, 1034 patients (NAT: n=641; non-NAT: n=393) were included in the analyses. No significant historical bias was detected (Supplementary Figure S5).

Before matching, both cohorts were different with respect to baseline characteristics. After the matching, both 1:1 coarsened exact and 1:2 propensity-score matching, no difference in baseline characteristics was seen (Table 1).

Of the 1034 patients included, 156 (15.1%) were assigned to robotic and 878 (84.9%) to laparoscopic liver resection, and 320 (30.9%) patients developed postoperative complications. The morbidity rate (33.2% vs. 27.2%, p-value=0.043), and the rate of pringle maneuver (61.2% vs. 54.8%, p-value=0.044), were significantly higher in the NAT group. However, after the matching, these two variables were balanced between the groups (Table 2).

The Iwate-score did not differ between the groups, but a higher rate of complex resections based on the IMM-score was found in the group that received NAT (80.7 % vs. 72.0 %, p-value=0.003). This difference evened out in the matched groups.

After 1:1 coarsened exact matching, no significant differences were seen in perioperative outcomes, whereas after 1:2 propensity-score matching, statistically significantly higher blood loss (median 300 (IQR 128–596) vs. 250 (IQR 100–400) ml, p-value = 0.047) and shorter hospital stay (median 6 [IQR, 4–8] vs. 6 [IQR, 5–9] days, p-value = 0.043) were found in the NAT group. Other perioperative outcomes were similar between the groups.

Discussion

In the current analysis of an international multicenter dataset of CRLM, after 1:2 propensity-score matching, statistically significant higher blood loss and longer hospital stay were observed in patients who received NAT prior to their MLR. However, the minor difference in outcomes observed was unlikely to be clinically-significant. No significant difference was found in other intra- and postoperative outcomes. To our knowledge, this is the first study to date to specifically determine the impact of NAT on the difficulty of MLR by performing a matched controlled study and by controlling for the IMM and Iwate difficulty scores.

Many well-known factors affect the difficulty of MILR and these have been included in several difficulty scoring systems which have been recently formulated (33). The extent and type of liver resections such as MLR (hemihepatectomies and extended hemihepatectomies) and resections in the right lateral and posterosuperior segments (segments 1, 4a, 7, and 8) are well-recognized as complex, requiring substantial technical skills and extensive experience (33,34). Hence, the development of these resections by the minimally invasive approach has been slow and the learning curve long and steep, while resections in the anterolateral segments (segments 2, 3, 4b, 5, and 6) are widely accepted as a standard for the minimally invasive approach.(34–36) Additionally, the presence of cirrhosis has been well-recognized as an important parameter affecting the difficulty and outcomes of MILR .(33, 37, 38). However, the influence of NAT on the difficulty and outcomes of MILR remains debatable. Of the existing DSS, only the Southampton system considered the use of NAT in its system (33).

The effects that chemotherapy has on the liver regarding resection surgery has been well-documented. It is believed that chemotherapy changes the characteristics of the

liver parenchyma, causing fibrosis and increasing sinusoidal pressure, thus making it less amenable to transection techniques and less responsive to hemostatic equipment. Steatohepatitis has been reported to occur after treatment with 5-fluorouracil and irinotecan and is shown to be more prevalent in obese patients and with increased length of therapy.(39, 40) Oxaliplatin-containing regimens are known to cause porto-sinusoidal vascular disease and sinusoidal obstruction,(41, 42) but reports are conflicting regarding its implications on post-resection morbidity.(43, 44) In a study by Vigano et al., the authors looked at different pathological changes in the liver post-chemotherapy in patients who had received oxaliplatin and/or irinotecan-based regimens for CRLM. 60.1% of the specimens showed signs of structural change and damage, and the most common were sinusoidal obstruction, steatosis, and nodular regenerative hyperplasia, occurring in 68.5%, 24.4%, and 19.3% of the cases, respectively. Only nodular hyperplasia was associated with postoperative liver failure (OR 2.729, p-value=0.035). About 6% of the resections were performed over 270 days after chemotherapy, and significantly less pathological changes were seen in this group. Specifically, fewer cases of sinusoidal obstruction were found (p-value=0.022), a change that occurred in patients receiving oxaliplatin-containing regimens and ≥7 cycles. Interestingly, adding bevacizumab to the regimen seemed to protect against sinusoidal obstruction (OR 0.530, p-value=0.003).(45) Other reports similarly indicate a protective trait in bevacizumab when combined with oxaliplatin.(46, 47) Jara et al. found a decrease in the maximum liver function volume (LiMAx) to 73.2 % (p-value=0.001) and indocyanine green plasma disappearance (ICG-PDR) to 78.2 % (p-value=0.001) in patients that had received oxaliplatin-based chemotherapy, and an almost complete regeneration in function eight weeks post-chemotherapy.(48) These findings indicate that the parenchymal damages inflicted on the liver by chemotherapy do recede, but they persist well beyond the time at which most patients undergo surgery. Whether or not such damage is correlated with increased morbidity and difficulty of MILR is a matter of further evaluation. Unfortunately, detailed information on histopathological changes and duration and type of chemotherapy was not available and could not be studied in this analyses.

In the present study, contrary to in the Southampton DSS by Halls et al.(11) and the opinion of the majority of experienced MILR surgeons, (17) we did not find a significant correlation between NAT and the risk of perioperative morbidity after coarsened exact and 1:2 propensity score matchings of the two groups that were compared. In the propensity-score matched analysis, while a statistically significant higher blood loss in the NAT-group was observed, this result was marginal and was unlikely to be clinically significant. Notably, there was no significant difference in the transfusion rate between both groups. There was also no significant difference in other surrogates of intraoperative difficulty, including operation time, blood transfusion rate and Pringle maneuver applied.

Although, there was a statistically significant difference in postoperative hospital stay, this was also marginal and probably clinically not relevant. It should also be highlighted that length of stay as a parameter has to be interpreted with caution, as our dataset includes patients treated at centers across Asia, Europe, and Northern America, and it is well-known that cultural and social differences are important confounding factors.

At present, the Southampton DSS is the only major DSS for MILR that considers NAT as a risk factor (33). However, it is important to note that the other major DSS were developed in Asia, whereby the number of patients with CRLM undergoing MILR were small and the impact of NAT on outcomes was not studied (33). The Southampton DSS was formulated based on a retrospective study of 2856 patients from seven European referral centers (33). Of note, the findings in the Southampton study might be limited by several confounding factors, possibly accounting for the poorer outcomes observed after NAT. Firstly, the subset of patients that received NAT are more likely to have had more difficult resections, multiple resections, concomitant other operations or previous liver resections which were not corrected. This was evident in our study whereby before matching the two groups, patients that had received NAT had multiple tumors, multiple liver resections, and major liver resections significantly more often than in the NAT-naive group. They also scored higher on the IMM DSS (Table 1), indicating that NAT were more often administered to patients with tumor characteristics associated with a higher risk burden requiring more extensive resections. Notably, 24.7 % of the patients in Southampton study had benign diseases, and these were found to have lower complication rates (p-value<0.001). The patients with benign disease constituted a proportion of the group that did not receive NAT and would be a confounding factor in their non-NAT cohort having lower complications rates.

In this study, we applied stringent inclusion and exclusion criteria to minimize and mitigate the impact of several confounding factors which limited the Southampton study. Firstly, the analysis was only limited to patients with CRLM. Secondly, patients with previous liver surgery, any concomitant major surgery, and those with more than two concomitant liver resections were also excluded. The exclusion of these patients may reduce the external validity of our results somewhat, but it also reduced the risk of confounding factors. Another strength of this study is the matched groups, further reducing the risk of unforeseen confounding factors.

A major limitation of this study is that the analysis did not include the type and duration of chemotherapy administered. As mentioned, different chemotherapy regimens affect the liver differently, and more extended regimens increase the rate at which structural damage to the liver occurs. Furthermore, pathological information on liver damage such as steatohepatitis or veno-occlusive disease was not available. This could be a topic for more detailed future studies.

Conclusion

The current study demonstrated that NAT had minimal impact on the difficulty and outcomes of minimally-invasive MLR. It was associated with statistically significant increase in blood loss, but this did not correspond with an increased transfusion rate or a higher complication rate.

Supplementary Material

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Table 1.

Comparison between baseline characteristics of patients undergoing MIMH with neoadjuvant versus no-neoadjuvant chemotherapy for colorectal liver metastases

		Entire unmatched cohort			1:1 coarsened exact matching			1:2 propensity-score matching		
	All N = 1034	**NAT (N = 641)**	**Non-NAT (N = 393)**	**P-value**	**NAT (N = 93)**	**Non-NAT (N = 93)**	**P-value**	**Neoadjuvant (N = 334)**	**Non-NAT (N = 167)**	**P-value**
Mean age (SD), years	65 (56–73)	64 (55–72)	65 (58–74)	**0.019**	66 (58–73)	67 (58–77)	0.584	64 (55–71)	66 (52–74)	0.349
Male sex, n (%)	595 (57.5%)	351 (54.8%)	244 (62.1%)	**0.021**	51 (54.8%)	51 (54.8%)	1.000	184 (55.1%)	85 (50.9%)	0.376
Robotic, n (%) Laparoscopic, n (%)	156 (15.1%) 878 (84.9%)	74 (11.5%) 567 (88.5%)	82 (20.9%) 311 (79.1%)	**<0.001**	3 (3.2%) 90 (96.8%)	3 (3.2%) 90 (96.8%)	1.000	38 (11.4%) 296 (88.6%)	18 (10.8%) 149 (89.2%)	0.840
Year of surgery, n (%) 2005–2010 2011–2015 2016–2021	 83 (8.0%) 313 (30.3%) 638 (61.7%)	 53 (8.3%) 211 (32.9%) 377 (58.8%)	 30 (7.6%) 102 (26.0%) 261 (66.4%)	**0.043**	 3 (3.2%) 27 (29.0%) 63 (67.7%)	 3 (3.2%) 27 (29.0%) 63 (67.7%)	1.000	 30 (9.0%) 115 (34.4%) 189 (56.6%)	 16 (9.6%) 57 (34.1%) 94 (56.3%)	0.976
Previous abdominal surgery, n (%)	420 (65.5%)	277 (70.5%)	277 (70.5%)	0.099	68 (73.1%)	68 (73.1%)	1.000	237 (71.0%)	106 (63.5)	0.164
ASA score, n (%) 1–2 3–4	 725 (70.1%) 309 (29.9%)	 441 (68.8%) 200 (31.2%)	 284 (72.3%) 109 (27.7%)	0.237	 8 (83.9%) 15 (16.1%)	 8 (83.9%) 15 (16.1%)	1.000	 233 (69.8%) 101 (30.2%)	 118 (70.7%) 49 (29.3%)	0.836
Median tumor size, mm (IQR)	36 (24–55)	34 (20–53)	40 (28–58)	**<0.001**	40 (28–60)	40 (30–58)	0.869	33 (20–54)	32 (20–54)	0.939
Multiple tumors, n (%)	557 (53.9%)	394 (61.5%)	163 (41.5%)	**<0.001**	41 (44.1%)	41 (44.1%)	1.000	209 (62.6%)	100 (59.9%)	0.558
Concomitant minor surgery, n (%)	83 (8.0%)	62 (9.7%)	21 (5.3%)	**0.013**	3 (3.2%)	3 (3.2%)	1.000	29 (8.7%)	11 (6.6%)	0.411
Traditional major (>3 segments), n (%)	774 (74.9%)	510 (79.6%)	264 (67.2%)	**<0.001**	58 (62.4%)	58 (62.4%)	1.000	271 (81.1%)	129 (77.2%)	0.306
Technical major (RAS/RPS), n (%)	260 (25.1%)	131 (20.4%)	129 (32.8%)	**<0.001**	35 (37.6%)	35 (37.6%)	1.000	63 (18.9%)	38 (22.8%)	0.306
Difficult segments (I, IVa, VII, VIII), n (%)	825 (79.8%)	537 (83.8%)	288 (73.3%)	**<0.001**	77 (82.8%)	77 (82.8%)	1.000	278 (83.2%)	142 (85.0%)	0.607
Multiple liver resections (up to 2), n (%)	148 (14.3%)	118 (18.4%)	30 (7.6%)	**<0.001**	8 (8.6%)	8 (8.6%)	1.000	62 (18.6%)	31 (18.6%)	1.000
Median Iwate difficulty score, (range)	10 (9–11)	10 (9–11)	10 (9–11)	0.142	10 (9–11)	10 (9–11)	0.587	10 (9–11)	10 (9–11)	0.924
Iwate difficulty, n (%) Intermediate High Expert	 22 (2.1%) 387 (37.5%) 623 (60.4%)	 11 (1.7%) 230 (35.9%) 399 (62.3%)	 11 (2.8%) 157 (40.1%) 224 (57.1%)	0.171	 1 (1.1%) 23 (24.7%) 69 (74.2%)	 1 (1.1%) 23 (24.7%) 69 (74.2%)	1.000	 9 (2.7%) 123 (36.8%) 202 (60.5%)	 1 (0.6%) 68 (40.7%) 98 (58.7%)	0.229

		Entire unmatched cohort			1:1 coarsened exact matching			1:2 propensity-score matching		
	All N = 1034	**NAT (N = 641)**	**Non-NAT (N = 393)**	**P-value**	**NAT (N = 93)**	**Non-NAT (N = 93)**	**P-value**	**Neoadjuvant (N = 334)**	**Non-NAT (N = 167)**	**P-value**
IMM difficulty, n (%)				**0.003**			1.000			0.485
II	234 (22.6%)	124 (19.3%)	110 (28.0%)		16 (17.2%)	16 (17.2%)		67 (20.1%)	38 (22.8%)	
III	800 (77.4%)	517 (80.7%)	283 (72.0%)		93 (82.8%)	93 (82.8%)		267 (79.9%)	129 (77.2%)	

*NAT-Neoadjuvant chemotherapy; SD - Standard Deviation; ASA - American Society of Anesthesiologists; IQR - interquartile range; RAS - right anterior sectionectomy; RPS - right posterior sectionectomy; IMM - Institut Mutualiste Montsouris.

Table 2.

Comparison between perioperative outcomes of patients undergoing MIMH with neoadjuvant versus no-neoadjuvant chemotherapy for colorectal liver metastases

		Entire unmatched cohort			1:1 coarsened exact matching			1:2 propensity-score matching		
	All N = 1034	**NAT (N = 641)**	**Non-NAT (N = 393)**	**P-value**	**NAT (N = 93)**	**Non-NAT (N = 93)**	**P-value**	**NAT (N = 334)**	**Non-NAT (N = 167)**	**P-value**
Open conversion, n (%)	104 (10.1%)	71 (11.1%)	33 (8.4%)	0.164	9 (9.7%)	10 (10.8%)	0.819	39 (11.7%)	23 (13.8%)	0.502
Mean operating time (SD), min	315 (250–390)	312 (250–390)	318 (254–405)	0.575	305 (240–374)	322 (267–406)	0.319	306 (250–360)	311 (260–409)	0.222
Mean blood loss (SD), ml	300 (150–600)	300 (150–644)	300 (150–500)	0.135	300 (150–600)	250 (150–600)	0.136	300 (128–596)	250 (100–400)	**0.047**
Intraoperative blood transfusion, n (%)	155 (15.0%)	97 (15.1%)	58 (14.8%)	0.870	18 (19.4%)	11 (11.8%)	0.194	51 (15.3%)	28 (16.8%)	0.665
Pringle maneuver applied, n (%)	597/1015 (58.8%)	387/632 (61.2%)	210/383 (54.8%)	**0.044**	55 (59.1%)	54 (58.1%)	0.924	209/331 (63.1%)	99/164 (60.4%)	0.550
Mean postoperative stay, days (SD)	6 (4–8)	6 (4–8)	6 (5–9)	0.520	6 (4–8)	6 (4–9)	0.280	6 (4–8)	6 (5–9)	**0.043**
Postoperative morbidity, n (%)	320 (30.9%)	213 (33.2%)	107 (27.2%)	**0.043**	23 (24.7%)	28 (30.1%)	0.484	115 (34.4%)	54 (32.3%)	0.640
Major morbidity (Clavien-Dindo grade> 2)	129 (12.5%)	83 (12.9%)	46 (11.7%)	0.557	9 (9.7%)	12 (12.9%)	0.487	43 (12.9%)	24 (14.4%)	0.646
30-day mortality, n (%)	9 (0.9%)	6 (0.9%)	3 (0.8%)	0.772	0 (0.0%)	1 (1.1%)	0.317	6 (1.8%)	2 (1.2%)	0.620
90-day mortality, n (%)	17 (1,6%)	11 (1.7%)	6 (1.5%)	0.816	2 (2.2%)	2 (2.2%)	1.000	9 (2.7%)	4 (2.4%)	0.845

*NAT-Neoadjuvant chemotherapy; SD - Standard Deviation;

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