First 100 minimally invasive liver resections in a new tertiary referral centre for liver surgery

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Original Article

Background: In the last decades, there has been an exponential diffusion of minimally invasive liver surgery (MILS) worldwide. The aim of this study was to evaluate our initial experience of 100 patients undergoing MILS resection comparing their outcomes with the standard open procedures.

Materials and Methods: One hundred consecutive MILS from 2016 to 2019 were included. Clinicopathological data were reviewed to evaluate outcomes. Standard open resections were used as the control group and compared exploiting propensity score matching.

Results: In total, 290 patients were included. The rate of MILS has been constantly increasing throughout years, representing the 48% in 2019. Of 100 (34.5%) MILS patients, 85 could be matched. After matching, the MILS conversion rate was 5.8% (n = 5). The post-operative complication rates were higher in the open group (45.9% vs. 31.8%, P = 0.004). Post-operative blood transfusions were less common in the MILS group (4.7% vs. 16.5%, P = 0.021). Biliary leak occurred in 2 (2.4) MILS versus 13 (15.3) open. The median comprehensive complication index was higher in the open group (8.7 [0–28.6] vs. 0 [0–10.4], P = 0.0009). The post-operative length of hospital stay was shorter after MILS (median 6 [5–8] vs 8 [7–13] days, P < 0.0001).

Conclusions: The rate of MILS has been significantly increasing throughout the years. The benefits of MILS over the traditional open approach were confirmed. The main advantages include lower rates of post-operative complications, blood transfusions, bile leaks and a significantly decreased hospital stay.

Keywords: Laparoscopic liver resection, minimally invasive surgery, tertiary centre

INTRODUCTION

Minimally invasive liver surgery (MILS) has grown exponentially worldwide in the last decades.[1,2] The laparoscopic approach in liver surgery has been one of the major advances in surgery in recent years.[3]

Recently, several systematic reviews on laparoscopic liver resection (LLR) demonstrated fewer complications rate, decreased blood loss and transfusion rate, and a shorter hospital stay in the LLR group when compared to open liver resections and with comparable oncological outcomes.[2,4–7]
However, the increase of laparoscopic approach for liver surgery is not homogeneous worldwide.

At the same time, the relationship between outcome and hospital volume in digestive cancer surgery has been investigated.\[8,9\] El Amrani et al. have recently determined the minimal number of procedures required to define a high-volume hospital. Based on these results, the authors noted that post-operative mortality in digestive cancer surgery was lower in high-volume hospitals. In addition, they showed that the benefits of high volumes were transferable across procedures. They proposed a new minimal cut-off for several surgical procedures, setting in 76 resections per year to perform liver surgery.\[8\] In liver surgery, the association between the hospital volume and the operative outcome has been largely explored.\[10,11\] These data prompted that these procedures should be centralised in high-volume hospitals to reduce post-operative mortality and improve survival outcomes.

Recent literature aimed to define a minimum number of annual resections to be carried out to identify those centres that should perform this type of surgery. These are defined as reference centres.\[8\]

In 2016, a regional re-organisation of our health system identified our centre as the HPB hub of our catchment area. In particular, four trusts representing 1,300,000 inhabitants/72 municipalities, were united in the ‘Romagna health trust’.

After the first 4 years of activity, we performed an audit on our results to continue a path of improvement. The aim of this study was to evaluate the clinical outcomes of our first 100 MILS performed in a new referral centre for Hepato-Pancreatico-Biliary (HPB) surgery in Italy. In doing so, we exploited our database on liver resections, using the standard open resections as a control group to verify the outcomes.

**MATERIALS AND METHODS**

This study was performed according to the Strengthening the Reporting of Cohort Studies in Surgery.\[12\]

Data were extracted by an Institutional Review Board-approved retrospective database.

**Design and patients**

All consecutive patients who underwent hepatic resection (minimally invasive or open) between January 1, 2016, and January 1, 2020, were screened for inclusion. Patients were excluded if they had a biliary reconstruction and if no resections were performed. Patients were grouped as per the method of surgery: MILS or open. All patients were evaluated preoperatively for the laparoscopic approach. Performance status, tumour size and location were evaluated in the process of selecting those patients eligible for laparoscopy.

**Variables and definitions**

Collected outcomes were procedure type (open, MILS), conversion to open surgery, operative time (minutes), intra-operative blood transfusions, synchronous colo-rectal resection, overall complications, and major complications, length of hospital stay (days), in-hospital mortality. Complications, readmissions and mortality were all collected up to patient’s discharge.

Post-operative complications were graded with the classification proposed by Dindo et al.\[13\] Liver failure was defined, according to the International Study Group of Liver Surgery classification, as any alteration of international normalised ratio and bilirubin values after post-operative day 5.\[14\]

The comprehensive complication index (CCI) was used to calculate the grade of severity and number of post-operative complications.\[15,16\]

**Matching**

To minimise the impact of treatment allocation bias, laparoscopic resections were matched to open resections exploiting propensity scores. Multivariable logistic regression was performed to estimate the propensity to undergo laparoscopic resection for all patients, regardless of the actual treatment received. Propensity scores were based on predictors of treatment or on those baseline variables which differed with a \( P = 0.05 \). In this analysis, the calculation of the propensity scores was based on the type of tumour (malignant versus benign) and the number of nodules (\( \geq 3 \) vs. \(< 3 \)). Nearest neighbour matching was performed in a 1:1 ratio without replacement and with a caliper width of 0.2 standard deviation.

**Statistical analyses**

Data were analysed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA) and R Statistical Software version i386 3.3.3 (Foundation for Statistical Computing, Vienna, Austria). Analyses were performed according to the intention-to-treat principle. Before matching continuous variables were presented as median and interquartile range and were compared using the Mann–Whitney U-test. Categorical data were
presented as frequencies with percentages and were compared using the Chi-square or Fisher’s exact test, as appropriate. In the post-match analyses, the Wilcoxon signed-rank test was used to compare continuous variables while McNemar’s test was used for categorical data. In the matched cohort logistic regression was used to calculate the odds ratio (OR) for post-operative complications of perioperative variables (age, American Statistical Association (ASA) score, nodule size, number of nodules, malignant tumour, laparoscopic approach, synchronous resections and intra-operative transfusions). All variables showing \( P < 0.05 \) were included in a multivariate analysis performed in stepwise manner.

**RESULTS**

**Total cohort**

In total, 356 patients were screened, of whom 66 were excluded for reasons [Figure 1], leaving 290 patients for analysis.

The rate of MILS has been constantly increasing throughout the years, representing the 48% in 2019 [Figure 2]. The MILS procedures, which included 12 robotic liver resections, were grouped according to Kawaguchi’s difficulty score \(^{17} \) in Table 1. There was no differences with regards to the complexity of the procedure (Group 1 \( n = 19, 76\% \) Group 2 3, 12\% Group 3 3, 12\% vs. 55, 73\%; 14, 19\%; 6, 8\%; \( P = 0.656 \) and the complications rates (overall \( n = 4, 16\% \) vs. 8, 11\%; \( P = 0.444 – \text{Clavien-Dindo} >2.2, 8\% \) vs. 6, 8\%; \( P = 0.488 \)) between the MILS procedure performed during the first (2016–2017) and the second interval (2018–2019) of the study period.

Patients' characteristics grouped according to the approach are shown in Table 2. Liver status at operation was available only for 220 patients: there were 19 (14.1\%) cases of liver cirrhosis in the MILS group versus 15 (21.4\%) in the open group (\( P = 0.356 \)). The diagnosis of malignancy was less common in the laparoscopic group (72.0 vs. 86.8\%, \( P < 0.002 \)). Three or more nodules were more commonly seen in the open group (7.0 vs. 32.6\%, \( P = 0.00001 \)). Intra-operative outcomes are shown in Table 3. Conversion from MILS to open occurred in five patients (5.0\%). Major resections were more common in the open group (13.8, vs. 8.0\%; \( P < 0.00001 \)). The post-operative outcomes are shown in Table 4. Overall mortality was 0.7\% (two patients in the open group). The overall complication rate was significantly higher after open liver resection (47.8\% vs. 12.0\%, \( P = 0.026 \)). Bile leak was less often seen after MILS (2.0 vs. 10.0\%, \( P = 0.444 – \text{Clavien-Dindo} >2.2, 8\% \) vs. 6, 8\%; \( P = 0.488 \)).

**Matched cohort**

Of all MILS, 94.4\% could be matched successfully to an open control. Differences (\( P < 0.05 \)) in baseline characteristics were no longer present after matching. Intra-operative outcomes are presented in Table 2. Conversion from to open liver resection occurred in five patients (5.8\%). Post-operative outcomes are shown in Table 3. The post-operative complication rates were higher in the open group (45.9\% vs. 31.8\%, \( P = 0.004 \)). Post-operative blood transfusions were less common in
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The multivariable analysis showed that synchronous resections (8.21, 1.73–38.0; \( P = 0.008 \)) and MILS (0.49, 0.25–0.95; \( P = 0.036 \)) were factors influencing the post-operative complications rate.

**DISCUSSION**

The advances in techniques and technology have allowed the spreading of the laparoscopic approach over the last three decades and its employ even in complex surgical procedures.
Considering its complexity, the centralisation of patients who need liver surgery deemed necessary. There is a strong evidence that complex surgical procedures performed in high-volume tertiary centres for digestive cancer surgery as a part of multidisciplinary teams are associated with lower mortality risk.\[8,11,18\]

In this context, our early experience has shown that MILS in a 'young' HPB center could be associated with adequate safety parameters while maintaining the benefits of minimally invasive surgery. This was also associated with a rate of complex procedure which was in line with that of large multicentre series.\[19\]

To validate our results we performed a propensity score match comparison with the standard open resections performed in the same study period confirming that MILS was associated with improved post-operative outcomes. These included mortality and overall post-operative complications, the rate of biliary fistula and the need of blood transfusions after surgery. Similar findings were shown by a recent meta-analysis by Jin et al.;\[5\] those authors, analysing eight randomised controlled trials with a total of 554 patients, found that laparoscopy was associated with lower complication rates than open surgery.

This was also confirmed by logistic regression analysis in which the open approach and synchronous resections were found to be risk factors for complications. This is a recurrent finding in liver surgery literature. As such, a recent analysis by Wang et al.\[20\] found that the incidence of severe complications was doubled after synchronous resection (26.7%) when compared with the delayed liver resections (11.2%).

In our series, complication rates were higher than those set by Rössler 2016 et al. in their benchmark analysis.\[21\] This could be explained by the fact that our series represent a population of patients in which more than 40% were ASA >2 and this is in contrast with that reported by Rossler including only healthy living donors.

As reported above, the biliary leak occurred less commonly after LLRs (2.4 vs. 15.3%) and this is consistent with what has been reported in literature. A recent study by Smith et al.\[23\] showed a bile leak rate of 2.8% after 1388 consecutive liver resections: the authors found that the minimally invasive approach significantly reduced the odd of bile leak with an OR of 0.48 (95% confidence interval 0.23–0.99).

The conversions rate was 5.6% in the current series and this is in line with those reported in literature. In all

### Table 4: Post-operative outcomes

| Variables                  | Total cohort | Matched cohort |
|----------------------------|--------------|----------------|
|                            | MILS (n=100), n (%) | Open (n=190), n (%) | P    |
|                            | MILS (n=85), n (%) | Open (n=85), n (%) | P    |
| Post-operative complications|              |                |      |
| Yes                        | 12 (12.0)    | 91 (47.8)      | 0.026 |
| No                         | 88 (88.0)    | 99 (52.2)      |      |
| Clavien dindo Grade≥3      |              |                |      |
| Yes                        | 8 (8.0)      | 25 (13.1)      | 0.319 |
| No                         | 92 (92.0)    | 165 (86.9)     |      |
| Mortality                  |              |                |      |
| Yes                        | 0            | 2 (1.1)        | 0.546 |
| No                         | 100 (100)    | 188 (98.9)     |      |
| Post-operative blood transfusion |          |                |      |
| Yes                        | 5 (5.0)      | 23 (12.1)      | 0.060 |
| No                         | 95 (95.0)    | 167 (87.9)     |      |
| Ascites                    |              |                |      |
| Yes                        | 2 (2.0)      | 11 (5.7)       | 0.231 |
| No                         | 98 (98.0)    | 179 (94.3)     |      |
| Liver failure              |              |                |      |
| Yes                        | 0            | 2 (1.0)        | 0.545 |
| No                         | 100 (100)    | 187 (98.4)     |      |
| Subphrenic abscess         |              |                |      |
| Yes                        | 5 (5.0)      | 15 (7.8)       | 0.621 |
| No                         | 85 (85.0)    | 174 (92.2)     |      |
| Biliary fistula            |              |                |      |
| Yes                        | 2 (2.0)      | 19 (10)        | 0.015 |
| No                         | 98 (98.0)    | 170 (90)       |      |
| CCI                        |              |                |      |
| Median (IQR)               | 0 (0-8.7)    | 8.7 (0-26.2)   | 0.0002 |
| Length of hospital stay    |              |                | 0.0009 |
| Median (IQR)               | 6 (4-8)      | 8 (7-13)       | <0.0001 |

MILS: Minimally invasive liver surgery, IQR: Interquartile range, CCI: Comprehensive complication index
5 cases conversions were due to bulky tumours which is a well-established risk factor for conversion to open surgery.\cite{23-25}

As expected, the length of hospital stay was significantly shorter after the laparoscopic approach. This may reflect the improved post-operative functional outcomes which have a major impact on the decision to discharge a patient. In addition, a shorter hospital stay significantly decrease total post-operative costs as suggested by Medbery \textit{et al}.\cite{26} who reported a $7000 savings in the laparoscopic group in their comparative analysis of right hepatectomies. Similar findings were found by Polignano \textit{et al}.\cite{27} who analysed the overall hospital costs after segmentectomies and found that it was significantly lower in the laparoscopic group by an average of 2,571 pounds sterling.

In light of our results and of those reported by the most recent meta-analyses, we can support the use of the laparoscopic approach whenever technically feasible and oncologically appropriate.

This study presents a few limitations. First, some of the included laparoscopic procedures may have been part of the learning curve of one of the surgeons performing these procedures as he was trained after our centre became an HPB hub. However, the impact of the learning curve may have been limited in the outcomes of the MILS group. This could be supported by the fact that the complication rate and the level of complexity of the laparoscopic procedures were similar between the first and the second period of the study interval.

Second, this was a retrospective study and it could be affected by biases linked to its nature. In particular, patients' pre-operative clinical status was represented mostly by ASA score in this study and this might have been underestimated some characteristics which could have influenced the morbidity rate in the open group.

The strengths of this study are linked to the short study interval which minimise the time-related differences in perioperative care and operative factors. In addition, the propensity score matching mitigated the impact of the treatment allocation bias which significantly affects the outcomes in retrospective studies.

CONCLUSIONS

Our analysis confirmed the benefits of laparoscopic liver surgery over the traditional open approach in expert centres. The main advantages include lower rates of post-operative complications, blood transfusions, bile leaks and a significantly decreased hospital stay. Synchronous resections remain the procedures with the greater risk of complications and should be performed with caution even in the laparoscopic approach.

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Conflicts of interest
There are no conflicts of interest.

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