Open and laparoscopic surgeries are associated with comparable 90 day morbidities and mortalities following ERAS protocols- A prospective Study.

Keywords: Enhanced recovery after surgery (ERAS); laparoscopic surgeries; morbidity; mortality; gastrointestinal surgery.

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Ethical clearance: obtained from hospital ethical committee.

Conflict of interest: none
ABSTRACT:

Introduction:
Aim of study to evaluate 90 days mortality and morbidity after ERAS protocol and also weather there is any difference in morbidity and mortality between Open and Laparoscopic surgeries.

Material and Methods:

All the gastrointestinal surgeries performed between April 2016 to march 2019 in our institution have been analysed for morbidity and mortality after ERAS protocols and data was collected prospectively.

Results:

We performed 245 gastrointestinal and hepato-biliary surgeries between April 2016 to march 2019. Mean age of patients was 50.96 years. 135 were open surgeries and 110 were laparoscopic surgeries. Mean ASA score was 2.40, mean operative time was 111 minutes, mean CDC grade of surgery was 2.56. 40 were emergency surgeries and 205 were elective surgeries. Overall 90 days mortality rate was 8.5% and over all morbidity rate was around 9.79% . On univariate analysis morbidity was associated
significantly with higher CDC grade of surgeries, higher ASA grade, more operative
time, more blood products use, more hospital stay, open surgeries, HPB surgeries and
luminal surgeries (non HPB gastrointestinal surgeries) were associated with higher 90
days morbidity. On multivariate analysis no factors independently predicted
morbidity. On univariate analysis 90 days mortality was predicted by grade of
surgeries, higher ASA grade, more operative time, more blood products use, open
surgeries and emergency surgeries. However on multivariate analysis only more
blood products used was independently associated with mortality

Conclusion:

There is no difference between 90 day mortality and morbidity rates between open
and laparoscopic surgeries.

Introduction:

Early recovery after surgery (ERAS) protocol is becoming gold standard in peri
operative care with excellent results in colorectal, gastric and HPB surgeries.1
ERAS is a evidence based peri-operative protocol which has shown significant
improvements in perioperative outcomes.2 Despite these overwhelming evidences
implementation of these protocols has been very slow and lack wide spread approval.\textsuperscript{3}

ERAS has initially developed for colorectal surgeries \textsuperscript{4}, However its implementation is being tested in all the other fields.\textsuperscript{4} It is difficult to have a common ERAS protocol across all subspecialties of GI surgery, hence there are not many papers

We evaluated perioperative outcomes after ERAS protocols in our data which includes Upper gastrointestinal, HPB, colorectal and laparoscopic as well as open surgeries.

Laparoscopic gastrointestinal surgeries have significantly reduced peri-operative morbidity and mortalities.\textsuperscript{5} However many of these studies were done before ERAS era. Very few studies have compared laparoscopic vs open gastrointestinal surgeries after ERAS protocols.

Aims of study were to evaluate morbidity and mortality rates following ERAS protocol and if there is any difference in perioperative outcomes in morbidity and mortality between Open and Laparoscopic surgeries.

Materials and Methods:

All the gastrointestinal and HPB surgeries performed between April 2016 to march 2019 in our institution have been analysed prospectively for morbidity and mortality after ERAS protocols. Morbidity was defined as any grade of complications according to clavien-dindo classification.\textsuperscript{6} We also evaluated factors responsible for
morbidity and mortalities and studies weather there is any difference in 90 days morbidity and mortality between open or laparoscopic group following ERAS protocol. We perform laparoscopic surgery unless need for conversion in all benign and elective cases while we perform open surgeries in malignant conditions (as we have doubts about oncological outcomes of laparoscopic surgeries after recently published trials) and emergency surgeries or sometimes due to cost issues. Ethical approval for our clinical study was obtained by human research (COA number SBI-5243)

ERAS protocols:

We follow perioperative guidelines for ERAS protocol described for colorectal surgeries in all our gastrointestinal and HPB surgeries. Our ERAS protocols has been mentioned in table 1.

Statistical analysis:

Statistical analysis done using SPSS version 23. p value less than 0.05 was considered as statistical significant. Categorial values was evaluated using chi square test, numerical values were evaluated using Mann-Whitney U test. Multivariate analysis was done using logistic regression method. Cox multivariate regression analysis done to evaluate factors affecting 90 days overall and morbidity free survivals. All the factors with p value less than 0.05 were included in multivariate analysis.
Results:

We performed 245 gastrointestinal and hepatobiliary surgeries between April 2016 to March 2019. Mean age of patients was 50.96 years. 144 patients were males and 101 were females. 135 were open surgeries and 110 were laparoscopic surgeries. 11 were upper gastrointestinal surgeries (stomach and oesophagus), 27 were small intestinal surgeries, 143 were HPB surgeries, 38 colorectal and 26 hernia surgeries. Mean ASA score was 2.40, mean operative time was 111 minutes, mean CDC grade of surgery was 2.56. 40 were emergency surgeries and 205 were elective surgeries.

Overall 90 days mortality rate was 8.5% and over all morbidity rate was around 9.79%. 90 days mortality and morbidity in elective surgeries was 4.08% and 8.16% respectively.

On univariate analysis 90 days morbidity was significantly with higher CDC grade of surgeries, higher ASA grade, more operative time, more blood products use, more hospital stay and HPB and luminal surgeries were associated with higher 90 days morbidity. [Table 2]. On multivariate analysis no factor independently predicted morbidity.

On univariate analysis 90 days mortality was predicted by grade of surgeries, higher ASA grade, more operative time, more blood products use, open surgeries and emergency surgeries. [Table 3] However on multivariate analysis number of blood product used independently predicted mortality. (p= 0.046, odds ratio 1.52, 95 percent C.I. 1.008-2.317).
We also did univariate and multivariate analysis of different factors between open and laparoscopic groups.

In univariate analysis open surgeries were associated with increased morbidity and mortality, however on multivariate analysis open surgery did not independently predict morbidity.

However, multivariate analysis showed there is significantly increased operative time and hospital stay in open surgeries. [Table 4]

To confirm our findings apart from logistic regression we also did multivariate cox regression analysis of 90 day survivals which showed, only less operative time, less hospital stay and less blood products independently predicted 90 days survival.

We also did same thing for 90 days morbidity free survival, which showed no factor independently predicted morbidity free survival after cox regression multivariate analysis.

We also prepared 90 days morbidity free and overall survival curves for open and laparoscopic surgeries. [figure1,2], Which did not show statistical significance on cox multivariate analysis.

Discussion:

Enhanced recovery after surgery though initially described for colorectal surgery is now becoming standard protocol for all surgeries and it has significantly reduced hospital stay and cost without affecting morbidity and mortality.1-5
However, there are very few studies available for studying effect of ERAS protocols on morbidity and mortality in entire cohort including HPB and Gastrointestinal surgeries.

We follow ERAS protocols for every gastrointestinal and HPB surgeries as shown in table 1 so we evaluated 90 days morbidity and mortality in our series after implementing ERAS protocols and also studied various factor affecting 90 days morbidity and mortality.

We also evaluated difference in morbidity and mortality in laparoscopic vs open surgery group after implementing ERAS protocol.

In our series Overall 90 days mortality rate was 8.5% and over all morbidity rate was around 9.79%. 90 days mortality and morbidity in elective surgery was around 4.08 and 8.16 percent respectively. Mortality is defined as any death within 90 days post operative period and morbidity included clavien-dindo grade 3 and grade 4 complications, which is similar to published data. 9,10

In our study in univariate analysis morbidity was associated significantly with higher CDC grade of surgeries, higher ASA grade, more operative time, more blood products use, more hospital stay, open surgeries, HPB surgeries and luminal surgeries (non hpb gastrointestinal surgeries) were associated with higher 90 days morbidity. However on multivariate analysis no factors independently predicted morbidity.

Similarly in mortality analysis univariate analysis 90 days mortality was predicted by grade of surgeries, higher ASA grade, more operative time, more blood products use, open surgeries and emergency surgeries and on multivariate analysis only more blood products used was independently associated with mortality. These data shows
laparoscopic or open surgeries did not predicted 90 days morbidity and mortalities independently.

Thus, 90 days morbidity and mortality analysis in our series shows patient and disease related factors. Which is also shown in various published studies. \(^{11,12,13}\)

One of the main aims of our study was to evaluate 90 morbidity and mortality difference between open and laparoscopic surgeries after implementing ERAS protocol.

Various study published showed that morbidity after colorectal surgeries were less with similar mortalities after colorectal surgeries.\(^{14,15}\) In case of cholecystectomy it is now concluded that laparoscopic surgery reduces morbidity. \(^{16}\) However, all these were before wide spread use of ERAS protocol.

In our study we analysed laparoscopic and open surgery though univariate and multivariate logistic regression [figure 1] analysis. 90 days morbidity and mortality were associated with open surgery in univariate analysis but multivariate logistic regression showed open or laparoscopic surgeries did not independently predicted 90 days morbidity and mortality after following ERAS protocol across gastrointestinal and HPB surgeries.

Open surgeries were more complex in terms of more operative time, higher blood products used, high CDC grade of surgeries, emergency surgeries and high ASA grades as we do open surgeries in emergency surgeries and oncologic surgeries explaining their association with morbidity and mortality in univariate analysis.
multivariate analysis open surgeries did not predict 90 days morbidity and mortality independently confirming that patient related factors and not open or laparoscopic way of performing surgeries predict mortality and morbidity following our ERAS protocol.

To, further confirm our findings we did 90 days survival analysis on multivariate cox regression analysis which also confirmed our findings. However, hospital stay was significantly more in open group. [figure 2,3]

Spanjersberg et al 17 showed that even after implementing ERAS laparoscopic surgeries was associated with reduced morbidity and hospital stay which is contrary to our results of data including all kinds of gastrointestinal and HPB surgeries. Zhuang et al18 showed benefit of laparoscopic surgery in optimal ERAS settings is yet to be proved. Damania et al showed ERAS protocol reduced hospital stay in HPB surgeries, however they did not compare open vs laparoscopic surgeries.

However majority of such evidences are available in colorectal surgery only, ours is to our knowledge one of the first studies to show that in mixed population of hpb and gastrointestinal surgeries there is no difference in 90 days morbidity and mortality between open and laparoscopic surgeries, however hospital stay was still significantly higher in open surgery.

Our study being a retrospective study has inherent biases of retrospective study, and further randomised control trials are needed to confirm our findings. Also although primary aim of study to evaluate effect of ERAS protocol in heterogenous
populations, more data in each specific subgroups are needed and we are in process of evaluating the same.

In conclusion there is no difference in 90 days morbidity and mortality between open and laparoscopic surgeries after implementing ERAS protocols and morbidity and mortality is associated with patient and disease related factors.

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1. Preoperative course | Nill by mouth not more than 4 hours  
|-----------------|--------------------------------------------------|
|                 | Single dose antibiotics at the time of induction|

**Intra Operative and Post operative Course**

|                         | No ryle’s tube post operatively  
|------------------------|----------------------------------|
| No post Operative antibiotics except ongoing sepsis |

Early Ambulation within 6 hours

**Post Operative**

|                                             | Liquid orally within 6 hourse, soft diet in post operative day1 and normal diet according to patient,s wish from post operative day 2 |
|---------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
|                                             | No intraoperative drains                                                                                                         |

Day 1 foley,s catheter removal.

**TABLE : 1** Our ERAS protocol.
Table 2: univariate and multivariate analysis of morbidity.

| Factors                                | Morbidity Present (n=24) | Morbidity Absent (n=221) | Univariate analysis (P value) | Multivariate analysis (P value) |
|----------------------------------------|--------------------------|--------------------------|-------------------------------|-------------------------------|
| Open surgery vs Laparoscopic           | Lap:1, Open:2            | Lap:109, Open:112        | <0.0001                       | 0.091                         |
| Emergency surgery (N) = 40             | 4                        | 36                       | 1.0                           |                               |
| Luminal Surgery (non HPB gastrointestinal surgery) | 16                       | 59                       | <0.0001                       | 0.377                         |
| HPB surgery                            | 6                        | 133                      | 0.003                         | 0.573                         |
| Age (mean)                             | 51.17                    | 50.94                    | 0.850                         |                               |
| Hospital stay (mean)                   | 4.5                      | 2.95                     | <0.0001                       | 0.421                         |
| CDC grade of surgery (mean)            | 3.04                     | 2.51                     | <0.0001                       | 0.962                         |
| Blood product (mean)                   | 1.42                     | 0.51                     | <0.0001                       | 0.981                         |
| ASA grade (mean)                       | 2.83                     | 2.35                     | <0.0001                       | 0.691                         |
| Operative time (mean)                  | 168.7                    | 104.7                    | <0.0001                       | 0.142                         |
| Factors                                      | Mortality (n=21) | No mortality (n=224) | Univariate analysis (P value) | Multivariate analysis (P value) |
|---------------------------------------------|------------------|----------------------|-------------------------------|-------------------------------|
| Emmergency surgery                          | 11               | 10                   | <0.0001                       | 0.116                         |
| Open surgery (135) vs laparoscopic surgery (110) | Open surgery 21/laparoscopic surgery 0 | 114 opensurgery/110 laparoscopic surgery | <0.0001                       | 0.996                         |
| Luminal (non HPB) surgeries                 | 11               | 159                  | 0.087                         |                               |
| Morbidity (90days)                          | 5                | 19                   | 0.041                         | 0.716                         |
| Hospital stay (mean)                        | 3.42             | 3.08                 | 0.173                         |                               |
| Age (mean)                                  | 51.76            | 50.89                | 0.956                         |                               |
| Blood products (mean)                       | 2.24             | 0.44                 | <0.0001                       | 0.046, odds ratio 1.52(95 percent C.I. 1.008-2.317) |
| CDC grade of surgery (mean)                 | 3.29             | 2.5                  | <0.0001                       | 0.818                         |
| Operative time                              | 177.14           | 104.79               | <0.0001                       | 0.263                         |
|               |       |       |       |
|---------------|-------|-------|-------|
| ASA (Mean)    | 3.1   | 2.33  | <0.001| 0.656 |

Table 3: Univariate and multivariate analysis of 90 day mortality.
Table 4: multivariate analysis between open and laparoscopic surgeries

|                     | B      | S.E.   | Wald  | df | Sig.  | ODDS RATIO | 95% C.I for EXP(B) |
|---------------------|--------|--------|-------|----|-------|------------|-------------------|
| **Step 1**          |        |        |       |    |       |            | Lower            |
| morbidity_all       | -1.063 | 1.319  | .650  | 1  | .420  | .345       | .026             |
| mortality_A_1       | -21.629| 6941.449| .000  | 1  | .998  | .000       | .000             |
| LUMINAL1            | .737   | .618   | 1.425 | 1  | .233  | 2.090      | .623             |
| EMERGENCY(1)        | 2.244  | 1.118  | 4.030 | 1  | .045  | 9.433      | 1.055            |
| operative time      | -.016  | .005   | 8.739 | 1  | .003  | .984       | .973             |
| ASA                 | 1.330  | .624   | 4.546 | 1  | .033  | 3.780      | 1.113            |
| hospital stay       | 2.232  | .415   | 28.990| 1  | .000  | 9.318      | 4.135            |
| grade of surgery    | .941   | .544   | 2.986 | 1  | .084  | 2.562      | .881             |
| Constant            | 10.725 | 6941.450| .000  | 1  | .999  | 45479.336  |                  |

a. Variable(s) entered on step 1: morbidity_all, mortality_A, LUMINAL, EMERGENCY, operative time, ASA, hospital stay, grade of surgery.
Figure 2: Kaplan meier 90 days survival curve between open and laparoscopic surgery, which did not show significant difference in multivariate analysis. (p= 0.920)
Figure 3: 90 days morbidity free survival between open and laparoscopic surgeries, which did not, shows statistical significance on multivariate analysis. (p= 0.059, hazard ratio 0.127 95% C.I (0.015-1.079)