TITLE

Suture cruroplasty versus prosthetic hiatal herniorrhaphy for large hiatal hernia: A meta-analysis and systematic review of randomized controlled trials

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SHORT RUNNING HEAD

Suture vs mesh repair for hiatal hernia

MINI ABSTRACT:

We conducted a meta-analysis and systematic review of randomized controlled trials, comparing suture cruroplasty versus prosthetic hiatal herniorrhpahy for large hiatus hernia, to determine the clinical outcomes, safety and effectiveness of these two methods. Four RCT between 1991 and 2014 totaling 406 patients (Suture=186, Prosthesis=220) were analyzed and results presented.

STRUCTURED ABSTRACT:

Aims and objective: The aim was to conduct a meta-analysis of RCTs comparing two methods of hiatal closure for large hiatal hernia and to evaluate their strengths and flaws.

Material and Methods: Prospective RCTs comparing suture cruroplasty versus prosthetic hiatal herniorrhaphy for large hiatal hernia were selected by searching PubMed, Medline, Embase, Science Citation Index, Current Contents, and the Cochrane Central Register of Controlled Trials published between January 1991 and October 2014.The outcome variables analyzed included operating time, complications, recurrence of hiatal hernia or wrap migration and reoperation. These outcomes were unanimously decided to be important since they influence the practical approach towards patient management. Random effects model was used to calculate the effect size of both dichotomous and continuous data. Heterogeneity amongst the outcome variables of these trials was determined by the Cochran's *Q* statistic and I^2 index. The meta-analysis was prepared in accordance with PRISMA guidelines.

Results: Four RCTs were analyzed totaling 406 patients (Suture=186, Prosthesis=220). For only one of the four outcomes i.e. reoperation rate (OR 3.73, 95% CI 1.18, 11.82, p=0.03) the pooled effect size favored prosthetic hiatal herniorrhaphy over suture cruroplasty. For other outcomes, comparable effect sizes were noted for both groups which included recurrence of hiatal hernia or wrap migration (OR 2.01, 95% CI 0.92, 4.39, p=0.07), operating time (SMD -0.46, 95% CI -1.16, -0.24, p=0.19) and complication rates (OR 1.06, 95% CI 0.45, 2.50, p=0.90).

Conclusions: On the basis of our meta-analysis and its limitations, we believe that the prosthetic hiatal herniorrhaphy and suture cruroplasty produces comparable results for repair of large hiatal hernias. In the future a number of issues need to be addressed to determine the clinical outcomes, safety and effectiveness of these two methods for elective surgical treatment of large hiatal hernias. Presently the use of prosthetic hiatal herniorrhaphy for large hiatal hernia cannot be endorsed

routinely and the decision for the placement of mesh needs to be individualized based on the operative findings and the surgeon's recommendation.

INTRODUCTION:

Since the introduction of laparoscopic antireflux surgery in 1991[1], the repair of very large hiatal hernias, now encountered in approximately 50% of laparoscopic antireflux surgical practice[2], seems to pose a challenging predicament for surgeons. In the chronic setting there is debate about indication for surgery and what is the best operative approach. The issue of which technique i.e. laparoscopic, transthoracic or transabdominal produces better surgical outcomes for these large hiatal hernia remains contentious. This is because all these three techniques seem to produce more or less equivalent results[3]. Furthermore there also remains a debate regarding the best way to close the crural pillars of these large hiatal hernias. This is because their repair is technically demanding and the traditional suture cruroplasty which is utilized to close hiatal defects is believed to yield a high recurrence rate. The dehiscence of crural repair therefore may lead to intrathoracic migration of the wrap. This may result in either acute hiatal hernia requiring emergent surgery or recurrence of reflux and/or dysphagia over a period of time requiring difficult revisional surgery. A number of studies analyzing laparoscopic repair of very large paraesophageal hiatal hernias by x-ray or endoscopy reveal between 12% to 42% failure rate due to disruption of the hiatal hernia repair suggesting significant room for improvement[4,5]. Furthermore there remains the debate regarding indications for surgery.

As the diaphragm is under repetitive stress during respiratory (breathing, sneezing and coughing) and non-respiratory functions (expulsion of vomit, feces, and urine, laughing and preventing acid reflux), mesh repair (tensionless repair) as opposed to suture cruroplasty (tension repair) for large hiatal hernia has been cited as an alternative method for reinforcement of crural pillars thereby decreasing the hiatal disruption and preventing wrap migration. However mesh repair itself can be associated with early or late complications such as mesh infection, migration, shrinkage and mesh erosion into the esophagus or stomach[6]. Furthermore the fibrotic reaction produced by mesh can make further surgery at the esophageal hiatus extremely challenging and hazardous.

In order to improve upon the recurrence rate of suture cruroplasty, Carlson et al, in 1999[7], reported the very first randomized controlled trial of laparoscopic prosthetic reinforcement of large hiatal hernia with an excellent early outcome. Since then, a number of randomized controlled trials (RCTs)[8-14] comparing suture cruroplasty versus mesh repair of large hiatal hernias have been published, analyzing various aspects of these two approaches with conflicting results. The objective of this meta-analysis was to determine the clinical outcomes, safety and effectiveness of these two methods for elective surgical treatment of large hiatal hernias.

MATERIALS AND METHODS:

Literature Search Strategy, Study Selection and Data Collection

RCTs were identified by conducting a comprehensive search of electronic databases, PubMed, Medline, Embase, Science Citation Index, Current Contents and the Cochrane Central Register of Controlled Trials published between January 1991 and October 2014 using medical subject headings (MESH); "hernia," "hiatal," "hiatus," "paraoesophageal/paraesophageal hernia," "laparoscopic repair," "comparative study," "prospective studies," "randomized/randomised controlled trial," "random allocation," 'clinical trial," and "Human". No language restriction was applied. We further searched the bibliographies of all the included primary studies and existing reviews by hand for additional citations. Data extraction, critical appraisal and quality assessment of the identified studies were carried out by two authors (BM, MAM), who also contacted via email the original authors of some of the trials for clarification of data and to obtain unpublished, missing or additional information on various outcome measures. Only two authors (Carlson MA, , Frantzides CT- personal communication**)** responded to our request and provided further clarification regarding their three published RCTs[7-9]. The authors were not blinded to the source of the document or authorship(s) for the purpose of data extraction. Standardized data extraction forms[15] were used by authors to independently and blindly summarize all the data available in the RCTs. The data that was obtained was entered directly into MS Word tables. Double data entry method was used in order to avoid errors in data extraction. The data was compared and discrepancies were addressed with discussion until consensus was achieved. The analysis was prepared in accordance with the Preferred Reporting of

Systematic Reviews and Meta-Analyses (PRISMA) statement[16]. Random effects model was used for analysis of all the outcome variables.

Eligibility Criteria

Two reviewers (BM and MAM) individually considered the abstracts of the identified articles for eligibility. Appropriateness was determined by these independent reviewers and by discussion in case of inconsistency. The RCTs must have reported on at least one clinically relevant outcome pertaining to the intraoperative and postoperative period. Outcomes assessed were those considered to exert influence over practical aspects of surgical practice and patient management. All studies reporting on outcomes of this nature were considered and final analyses were run on outcome variables where numbers were sufficient to allow statistical analysis.

Inclusion Criteria

(i) **Type of Study:** Only randomized controlled trials published both in full peer-reviewed journals and abstract forms between January 1991 and October 2014, were included for analysis.

(ii) **Language:** No language restriction was applied

(iii) **Type of Intervention:** Two different elective laparoscopic approaches for the management of large hiatal hernia, namely suture versus prosthetic (non-absorbable and absorbable mesh) repair were being assessed for the differences in short and long term surgical outcomes.

(iv) **Type of participants:** Adult (>18 years) patients were the target population for this meta-analysis.

Exclusion Criteria

(i) Non-randomized controlled trials, duplicated RCTs, unpublished studies and abstracts presented at national and international meetings presenting the preliminary data were excluded from our analysis.

(ii) Emergency hiatal hernia surgery

Types of Outcome Measures Analyzed

The four outcome variables analyzed included (a) operative time; (b) complication rate; (c) recurrence of hiatal hernia or wrap migration; and (d) reoperation. Other outcome variables such as hospital stay could not be analyzed due to inadequate reporting methodology.

Methodological Quality

The methodological quality of the identified RCTs was assessed using Jadad Scoring system[17]. Each study was allocated a score from zero to five, zero being the lowest quality and five being the highest quality based on reporting of randomization, blinding, and withdrawals reported during the study period.

Statistical Analysis and Risk of bias across Studies

Meta-analyses were performed using odds ratios (ORs) for dichotomous outcome and standardized mean differences (SMDs) for continuous outcome measures. Data was pooled using the Mantel-Haenszel and the inverse variance method for dichotomous and continuous outcomes respectively. The slightly amended estimator of OR was used to avoid the computation of reciprocal of zeros among observed counts in the calculation of the original OR[18]. DerSimonian and Laird random effects model was used to combine the summary data[19]. This is because in clinical practice, differences in patient demographics, health care practitioner skills etc render the assumptions of the fixed effects model void when evaluating therapeutic or clinical interventions. Heterogeneity among studies was calculated using the Q statistic proposed by Cochran and I^2 index introduced by Higgins and Thompson[19-23]. If the observed value of Q was greater than the associated x^2 critical value at a given significant level, in this case 0.05, we conclude the presence of statistical significance between-studies variation. In order to pool continuous data, mean and standard deviation of each study is required. However, some of the published clinical trials did not report the mean and standard deviation, but rather reported the size of the trial, the median and interquartile range. Using these available statistics, estimates of the mean and standard deviation were obtained using formulas proposed by Hozo et al[24]. Funnel plots were produced in order to determine the presence of publication bias in the present meta-

analysis. Both total sample size and precision (reciprocal of standard error) were plotted against the treatment effects (OR for dichotomous variables and SMD for continuous variables)[19,25-27]. All estimates were obtained using a computer program written in R[28]. All plots were obtained using the metafor-package[29]. In the case of tests of hypotheses, the paper reports p-values for different statistical tests on the study variables. In general, the effect is considered to be statistically significant if the p-value is small. If one uses a 5% significance level then the effect is significant only if the associated p-value is $\leq$5%.

RESULTS:

Included Studies

Cross searching of electronic databases yielded a total of 101 abstracts and hand searches of reference lists provided a further 6 citations. After exclusion of non-relevant citations, 39 unique citations of potential relevance were retrieved for review. The process by which these citations were excluded is described in Figure 1. There was almost perfect agreement (κ=0.99) between two authors (BM and MAM) regarding inclusion of these RCTs. No further potentially relevant unpublished studies were identified through a citation search of previous published reviews on this subject. ~~*It is to be noted that no previous meta-analysis on this subject has been published to date.*~~ Eight RCTs met the inclusion criteria[7-14]. Of these, several involved the presentation of data derived from the same cohort of patients at different follow-up times[7-13]. This was particularly relevant to longer-term outcome measures such as treatment failure and re-operation rates. For the purpose of accurate statistical analysis and consistency of data compiling, in the aforementioned instances we considered all the data derived from a particular cohort of patients as being a single trial event. This reduced the apparent number of included trials to four (Figure 1, Table 1). As no language restriction was applied, no RCT published on this subject was excluded from our meta-analysis.

Methodological Quality

In general, the quality of RCTs demonstrated poor methodological quality based on Jadad score with an average score of 1.7 (out of five), with a range of 1 to 3 (Table 1). Only one study reported on

withdrawals and drop-outs[14], two described an appropriate method of randomization[10,14], whereas only one of the trials reported on the single blinding of the patients[14] (Table 1).

Heterogeneity

The *Q* test and I^2 Index are commonly used methods in meta-analysis for detecting heterogeneity. Significant heterogeneity i.e. I^2 index of 50% or more[22,30] was only present for operating time (*Q*=14.83, p= <0.0006, I^2= 88.53, CI=55.44, 99.72) (Table 2).

Publication Bias

Only one of the funnel plots belonging to operating time demonstrate asymmetry and thus suggest the presence of publication bias. Other funnel plots belonging to recurrence of hiatal hernia/wrap migration, reoperation rate and complication failed to show publication bias. However the number of studies included for all these variables were too few to sensitively detect publication bias ~~(Fig 2)~~.

Clinical Outcomes

Four RCTs (USA = 3, Australia = 1) were analyzed. For only one of the four outcomes i.e. reoperation rate (OR 3.73, 95% CI 1.18, 11.82, p=0.02) (Fig 2) the effect size estimate favored prosthetic hiatal herniorrhaphy over suture cruroplasty. For other outcomes, comparable effects were noted for both groups which included recurrence of hiatal hernia or wrap migration (OR 2.01, 95% CI 0.92, 4.39, p=0.07) (Fig 3), operating time (SMD -0.46, 95% CI -1.16, -0.24, p=0.19) (Fig 4) and complication rates (OR 1.06, 95% CI 0.45, 2.50, p=0.90) (Fig 5) (Table 2).

Description of various RCTs

Salient features of various RCTs comparing suture cruroplast versus mesh repair are detailed in Table 1. The four included studies were published between 2002 and 2014 totaling 406 patients (Suture=186, Prosthesis=220). The study size in one[9] out of 4 RCTs was less than 100 patients in both arms. There were three occasions[7-13] where several trials were involved in the presentation of data derived from the same cohort of patients at different follow-up times. For the purpose of accurate

statistical analysis, we considered all the data derived from a particular cohort of patients as being a single trial event. The size of hiatal defect in 3 out of 4 trials[9,10,12] was provided in centimeters where Watson et al[14] defined a very large hiatal hernia as more than 50% of stomach in the chest. Postoperative gastroscopy and barium swallow (esophagogram) were undertaken by all the authors[7-14] to determine the hernia recurrence. Detailed evaluation of clinical symptoms such as heartburn and dysphagia were subjectively evaluated pre and postoperatively at various time points depending on the study protocol by three RCTs[10,13,14]. However all the RCTs analyzed their data at 6 months. Randomized controlled trial by Granderath et al[10] is the only trial which provided postoperative objective assessment of reflux using 24 hour pH monitoring. Except for Watson et al RCT[14] who undertook laparoscopic partial fundoplication for the vast majority of their patients (anterior partial = 107, posterior partial = 17), the rest of the RCTs undertook hiatal repair in conjunction with laparoscopic Nissen fundoplication. The definition of recurrent hernia was either missing in some trials[9,10] whereas in the others, it varied according to the authors' preference[12,14].

DISCUSSION:

Because of a substantial failure rate of between 12% to 42%[4,5] with suture cruroplasty during the early days of laparoscopic antireflux surgery, a number of authors started experimenting with the use of mesh to improve the operative results in terms of recurrent hiatal disruption and wrap migration. The very first RCT reporting excellent early outcomes for large hiatal hernia with non-absorbable prosthesis was reported by Carlson et al[7]. The longitudinal data involving a larger cohort of patients was subsequently reported by Frantzides et al[9]. The authors reported 22% rate of recurrent hiatal hernia in the suture cruroplasty group compared to 0% in non-absorbable hiatal herniorrhapy utilizing endoscopy and barium swallow study at a mean follow-up of 3.3 years. All recurrences occurred within the first 6 months. However what constituted recurrence on oesophagogram is not clear as no precise definition is provided. Five patients underwent further surgery and placement of PTFE mesh to close the hiatal defect in the suture cruroplasty group. The other three patients refused surgery and were treated medically. No complications related to mesh such as erosion, stricture or infection have been observed by these authors.

Granderath et al[10] published another RCT analyzing 100 patients undergoing laparoscopic Nissen fundoplication along with either simple suture cruroplasty or non-absorbable polypropylene mesh placement for closure of hiatal defect either ≤5 cm or > 5 cm at 12 months follow-up. A higher postoperative dysphagia rate was observed in the prosthetic group at 6 weeks and 3 months which seems to have disappeared at 1 year follow-up[10]. In both groups 24 hour ambulatory pH study showed a significant reduction in DeMeester score postoperatively at 1 year compared to preoperative score. An intrathoracic wrap migration occurred in 13 patients in the simple cruroplasty group compared to 4 in the prosthetic group. Once again the precise nature of wrap migration is missing and furthermore whether this intrathroacic migration was partial or complete is also lacking. All four patients in the prosthetic group with hernia recurrence underwent laparoscopic redo surgery. No such information is available on 13 patients in the suture cruroplasty group who had recurrent hernias.

A multicenter RCT conducted by Oelschager et al[12] evaluating the use of biologic prosthesis for repair of large paraesophageal hernia in 108 patients was reported in 2005. The definition of recurrent hiatal hernia was based on upper gastrointestinal imaging of hiatal hernia > 2 cm or need for reoperation secondary to wrap disruption, migration or herniation at any time during the study period. This trial reported a 9% rate of recurrent hiatal hernia in the biologic prosthetic group compared to 24% in the suture cruroplasty group at 6 month follow-up. However at a median follow-up of 58 months analyzing the same cohort of 72 patients[13], the recurrence rate in both groups was similar; 59% in the suture cruroplasty group and 54% in the biologic prosthetic group. No statistical significant difference was noted in terms of relevant symptoms or quality of life issues between the two groups. No mesh related complications were seen with biologic mesh. The authors of this study concluded that the benefit of biologic prosthesis in reducing hiatal hernia recurrence diminishes at long-term follow-up. These authors emphasized the validity of their results based on the following facts; (a) the objective manner of detecting postoperative recurrence by a blinded third party i.e. radiologists and (b) the participation of experienced laparoscopic surgeons from high volume esophageal surgical centers. However they conceded that strict criteria used to diagnose the recurrence may have overestimated the recurrence rate. Nonetheless, the authors of this study feel that the biologic mesh, although may

not protect against recurrent hiatal hernias, it may reduce the risk of severe hernias leading to fewer reoperations as evident in their study. They also felt that compared to non-absorbable mesh with its known complications such as erosion into adjacent structures e.g. esophagus or stomach which leads to severe dysphagia, the biologic mesh has no long-term negative consequences.

A recent randomized controlled trial[14] assessing the role of absorbable (n=41) and non-absorable mesh (n=42) versus simple suture repair (n=43) of large hiatal hernia containing 50% of stomach in the chest showed no significant difference in hernia recurrence between suture cruroplasty versus prosthetic hiatal herniorrhaphy when assessed objectively by barium swallow and endoscopy at 12 months. The definition of recurrence included any evidence of stomach above the level of the diaphragm, irrespective of the size. The recurrence rate of 23.1% was observed in suture pair, 30.8% after absorbable mesh repair and 12.8% after non-absorbable mesh repair. Clinical outcomes were more or less similar between these three groups. Three patients in the suture group required early laparoscopic reintervention for acute hiatal hernia and another patient required revision surgery at 7 months. This is in comparison to the non-absorbable mesh group in whom 1 early recurrence was observed and no recurrence was seen in the absorbable mesh group. These results may change with more extended follow-up at 24, 36 and 60 months as seen with other clinical trials[13]. The result of the above study are in total contrast to all other RCTs reporting favorable short-term outcome of hiatal hernia repair with prosthesis, both biologic and non-absorbable (Table 4).

The pooled effect size on recurrent hiatal hernia in our meta-analysis did not show any difference in the hiatal recurrence between suture cruroplasty and prosthetic hiatal herniorrhaphy (OR 2.01, 95% CI 0.92, 4.39, p=0.07) (Fig 3), although the trend was favoring the latter group. As none of the RCTs except for the one by Oelschlager et al[13] have provided long term follow-up data to date, the true recurrent rate of hiatal hernia between the two groups may diverge with passage of time especially in the non-absorbable prosthetic group. Only long term longitudinal studies will clarify this issue.

The second variable which was closely aligned with hiatal hernia recurrence or wrap migration was reoperation rate (Table 5). In Frantzides et al study[9] 5 out of 8 patients in the suture cruroplasty group underwent further surgery and placement of PTFE mesh to close the hiatal defect. In Granderath et al RCT[10] although there was statistically significant intrathoracic wrap migration in the suture cruroplasty group (13 patients) versus the prosthetic mesh repair group (4 patients), the authors have provided reoperation details of 4 patients in the latter group, two of whom had further circular hiatal mesh placement. No such information is available regarding the fate of 13 patients in the suture cruroplasty group. In Oelschlager et al[13] long term follow-up (median 58 months) study, only two patients required surgery in the suture cruroplasty group whereas none in the biologic prosthetic group. Lastly Adelaide's RCT[14] revealed 4 revisional surgeries in the suture cruroplasty group within 30 days for (a) tight hiatal repair (n=1), (b) acute hiatal hernia (n=3) and one at 7 months for recurrent hiatal hernia (n=1). In the prosthetic mesh group, no surgery was required in the absorbable mesh group whereas 3 revisional surgeries occurred within 30 days for (a) tight hiatal repair (n=2) and acute hiatal hernia and gastric perforation (n=1). One reoperation was carried out at 8 months for persistent dysphagia.

The pooled data on reoperation in our meta-analysis showed significant higher risk of revisional surgery following suture cruroplasty compared to prosthetic hiatal herniorrhaphy (OR 3.79, 95% CI 1.20, 11.99, p=0.02) (Fig 4). The peril of reoperation cannot be underestimated as it carries higher risk of morbidity and mortality due to complex subsequent procedure, longer duration of operation, lengthy postoperative stay and higher cost to patients and insurers.

The operating time was reported by all the RCTs[9,10,12,14] (Table 6). However due to lack of availability of standard deviation in Granderath et al[10], their data was excluded for analysis. Only Frantzides et al[9] showed significantly longer operating time for the prosthetic hiatal herniorrhaphy group compared to the suture cruroplasty group. The other three RCTs[10,12,14] did not show significant difference in mean operating times for the two groups (Table 6). The pooled effect size showed comparable results for

both groups (SMD -0.46, 95% CI 1.16, 0.24, p=0.1990) (Fig 5). Longer operating times in the earlier trials may in part reflect an initial learning curve for laparoscopic prosthetic hiatal herniorrhaphy .

As far as the complication rate of suture cruroplast versus prosthetic hiatal herniorrhaphy is concerned, the present analysis showed no difference in the incidence of postoperative complications between the two groups (Table 2, Fig. 5). Once again due to lack of long term data for three out of four RCTs[9,10,14], accurate assessment of this variable cannot be determined. One of the dangers of hiatal reinforcement with non-absorbable mesh, is the risk of its erosion into the adjacent structures such as esophagus or stomach which in turn can lead to severe dysphagia[6,31,32]. This had not been observed with biologic mesh as reported by Oelschlager et al[13]. Once the long term data for all these RCTs becomes available the true incidence of complications of different types of prosthesis for hiatal closure will become clearer.

LIMITATIONS:

There are a number of limitations both statistical and clinical in this paper. Firstly, the small number of studies included in this meta-analysis remains a largely unavoidable limitation of this and many other meta-analyses conducted in surgical fields[33]. Secondly, some degree of between-study heterogeneity was detected, which may undermine the quality and legitimacy of the results obtained[33]. However in this meta-analysis, the heterogeneity was only detected in one variable. Thirdly, use of different types of prosthetic meshes i.e. both absorbable and non-absorbable for repair of hiatal hernia may be a potential limitation. Fourthly, definition of what constitutes a large hiatal hernia varies between different RCTs. Fifth, there is no standardized definition of recurrent hiatal hernia between various RCTs. Lastly, as the follow-up for most of these RCTs[9,10,14] except for one[12] has been short, the true incidence of recurrence of hiatal hernia and redo surgery are not truly known and therefore the results of any short term or medium term benefits especially of prosthetic hiatal herniorrhaphy needs to be interpreted with extreme caution.

CONCLUSIONS:

On the basis of this meta-analysis and its limitations, we believe that prosthetic hiatal herniorrhaphy and suture cruroplasty produces comparable results for repair of large hiatal hernias. In the future a number of issues need to be addressed to determine the clinical outcomes, safety and effectiveness of these two methods for elective surgical treatment of large hiatal hernias. These include (i) standardized definition of large hiatal hernia; (ii) standardized techniques of suture and prosthetic repair; (iii) type of prosthesis used – biologic versus non-absorbable; (iv) standardized method of securing the mesh such as use of sutures, tacks or biologic glues; (v) standardized classification of recurrent hiatal hernia post repair; (vi) standardized method of detecting recurrence e.g. gastroscopy, barium swallow or CT; (vii) objective assessment of recurrent hiatal hernia via 24 hour ambulatory impedance pH monitoring and lastly (viii) long term postoperative data collection of at least 5 years to detect the true incidence of hiatal hernia recurrence between suture cruroplasty and prosthetic hiatal herniorrhaphy. Until all the above mentioned issues are clarified, the routine use of prosthetic hiatal herniorrhaphy for large hiatal hernia cannot be endorsed routinely and the decision for the placement of mesh needs to be individualized based on the operative findings and the surgeon's recommendation.

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AUTHORS' CONTRIBUTIONS:

1. MAM was responsible for the concept and design of this meta-analysis. Furthermore he takes full responsibility for the integrity of the work as a whole, from inception to published article.

2. BM and MAM were responsible for acquisition and interpretation of the data.

3. SK, RMY were responsible for analyzing and interpretation of the data in depth from the statistical point of view. They were responsible for producing all the statistical diagrams (Forest and Funnel plots).

4. All authors were involved in drafting the manuscript and revising it critically for important intellectual content and have given final approval of the version to be published. Furthermore all authors have participated sufficiently in the work to take public responsibility for its content

CONFLICTS OF INTERESTS:

None

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FIGURE LEGENDS:

Figure 1: PRISMA flow diagram

Figure 2: Forrest plot for reoperation

Figure 3: Forrest plot for recurrence of hiatal hernia or wrap migration

Figure 4: Forrest plot for operating time

Figure 5: Forrest plot for complications