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Routine use of Feeding Jejunostomy in Pancreaticoduodenectomuy: A Metaanalysis.

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Abbreviations: Post operative pancreatic fistula (POPF), total parentral nutrition (TPN), Surgical site infections. (SSI)

Keywords: Pancreaticoduodenectomy; feeding jejunostomy; morbidity; mortality

Abstract:

Aims and objectives:

The primary aim of our study was to evaluate morbidity and mortality following feeding jejunostomy in pancreaticoduodenectomy compared to the control group. We

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also evaluated individual complications like delayed gastric emptying, post operative pancreatic fistula, superficial and deep surgical site infection. We also looked for time to start oral nutrition and requirement of total parentral nutrition.

Material and Methods:

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and MOOSE guidelines. [9,10]. We searched pubmed, cochrane library, embase, google scholar with keywords like "feeding jejunostomy in pancreaticodudenectomy", "entral nutrition in pancreaticoduodenectomy, "total parentral nutrition in pancreaticoduodenectomy', "morbidity and mortality following pancreaticoduodenectomy". Two independent authors extracted the data (B.V and H.P).

The meta-analysis was conducted using Open meta-analysis software. Heterogeneity was measured using Q tests and I^2, and $p < 0.10$ was determined as significant , the random-effects model was used. The Odds ratio (OR) was calculated for dichotomous data, and weighted mean differences (WMD) were used for continuous variables. Both differences were presented with 95% CI.

Results:

Four studies including Total of 1639 patients were included in the analysis. Total 843 patients were included in Feeding jejunostomy group and 796 patients included in control group without feeding jejunostomy. Over all morbidity was significantly higher in feeding jejunostomy group. (odds ratio 1.39, $p = 0.001$). However, there was no significant difference between both the group. ($p=0.07$). Delayed gastric

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emptying was significantly higher in Feeding jejunostomy group. [p=0.021]. There was no significant difference in development of pancreatic fistula between the two group. (p=0.536). Deep surgical site infection were significantly higher in feeding jejunostomy group. (p=0.013). Hospital stay was significantly more in feeding jejunostommy group, weighted mean difference of 2.094 days. (p<0.0001). There was no significant difference between readmission (p=0.536) and TPN requirement between the two group. Time to start oral feed was significantly more in feeding jejunostomy group.

Conclusion:

Feeding jejunostomy seems to be associated with increased morbidity, increased complications, increased length of stay without any significant benefits.

Background:

Pancreaticoduodenectomy is the only treatment with curative chance in cancer of distal bile duct, head of pancreas , periampullary and some of the duodenal cancers.[1,2].

However, Pancreaticoduodenectomy is still associated with very high morbidity and mortality. Though morbidity and mortality is reduced in high volume centres it still remain significant problem after pancreaticoduodenectomy. [3]. Most frequent

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complications following pancreaticoduodenectomy remains delayed gastric emptying and post operative pancreatic fistula. [4].

Post operative nutrition following pancreaticoduodenectomy is still a debatable thing with some studies favour parentral nutrition. [5], However some studies suggest entral nutrition following pancreaticoduodenectomy is safe and well tolerated. [6].

For entral nutrition after pancreaticoduodenectomy various feeding routes have been utilised and it is common practice to insert feeding jejunostomy tube after pancreaticoduodenectomy. Few studies have shown early oral nutrition is also safe after pancreaticoduodenectomy. [7].

Some studies [8] have raised concerned about practice of inserting feeding jejunostomy during pancreaticoduodenectomy and suggested they may be associated with increase morbidity and mortality after pancreaticoduodenectomy. However, there are no randomised control trials or metaanalysis available to study those concerns further.

Aims and objectives:

The primary aim of our study was to evaluate morbidity and mortality following feeding jejunostomy in pancreaticoduodenectomy compared to the control group. We also evaluated individual complications like delayed gastric emptying, post operative pancreatic fistula, superficial and deep surgical site infection.

We also looked for time to start oral nutrition and requirement of total parentral nutrition.

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Materials and Methods:

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and MOOSE guidelines. [9,10]

Study Selection:

We searched pubmed, cochrane library, embase, google scholar with keywords like "feeding jejunostomy in pancreaticodudenectomy";"entral nutrition in pancreaticoduodenectomy';"total parentral nutrition in pancreaticoduodenectomy', "morbidity and mortality following pancreaticoduodenectomy". Two independent authors extracted the data (B.V and H.P). Types of studies included in metaanalysis are described in table 1.

Inclusion criteria:

- |Studies comparing feeding jejunostomy in pancreaticoduodenectomy with controls
- |Full text articles
- |Studies comparing morbidities and mortalities between the two groups.

Exclusion criteria:

- |Studies whose full texts can not be retrieved
- |Conference abstracts

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- |Studies which did not have comparative groups
- |Duplicate studies

Statistical analysis

The meta-analysis was conducted using Open meta-analysis software. Heterogeneity was measured using Q tests and I^2, and $p < 0.10$ was determined as significant , the random-effects model was used. The Odds ratio (OR) was calculated for dichotomous data, and weighted mean differences (WMD) were used for continuous variables. Both differences were presented with 95% CI. For continuous variables, if data were presented with medians and ranges, then we calculated the means and Standard deviations according to Hozo et al. (13). If the study presented the median and inter-quartile range, the median was treated as the mean, and the interquartile ranges were calculated using 1.35 SDs, as described in the Cochrane handbook.

Assessment of Bias:

Characteristics of the studies are described in table 1. Identified studies were broadly grouped into 1 of 2 types, either randomized trials or cohort studies. Cohort studies were assessed for bias using the Newcastle-Ottawa Scale (10). Randomized trials were decided to be assessed based on the Cochrane Handbook. (11). However in final analysis we could not find any randomized clinical trials fulfilling our inclusion criteria so Newcastle-Ottawa Scale was used. [Table 2].

Results:

Literature Review:

Four studies including Total of 1639 patients were included in the analysis.

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[14,15,16,17] Details of selection process is described in Figure 1. Study details is described in Table 1. Total 843 patients were included in Feeding jejunostomy group and 796 patients included in control group without feeding jejunostomy.

Morbidity and Mortality:

Morbidity is defined as grade 3,4 complications according to Clavian-Dindo classification. [18]

Total 375 patients developed 90 day morbidity in Feeding jejunostomy group , 293 patients developed morbidity in control group. Over all morbidity was significantly higher in feeding jejunostomy group. (odds ratio 1.39, p = 0.001). (Figure 2)

30 Patients died within 90 days in feeding jejunostomy groups, 16 patient died in control group. However, there was no significant difference between both the group. (p=0.07).

Delayed Gastric Emptying and Pancreatic Fistula.

117 out of 222 patients developed delayed gastric emptying and 44/175 developed delayed gastric emptying out of data available in 3 studies.[14,16,17]. Delayed gastric emptying was significantly higher in Feeding jejunostomy group. [p=0.021]

26 out of 222 patients developed postoperative pancreatic fistula (POPF) in feeding jejunostomy group, and 18 patients out of 175 patients developed post operative pancreatic fistula (POPF). [14,16,17]. There was no significant difference in development of pancreatic fistula between the two groups. (p=0.536). (Figure 4)

Surgical site Infection:

180 patients developed Surgical Site Infection in feeding jejunostomy group and 154 patients developed SSI in the control group. There was no significant difference in SSI rates between the two groups. (p=0.193).

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Two studies (15,16) evaluated deep surgical site infections. Deep surgical site infection was significantly higher in feeding jejunostomy group. (p=0.013). (Figure 5)

Hospital stay, Readmissions, total parentral nutrition requirement and time to initiate oral feeding.

Hospital stay was significantly more in feeding jejunostommy group, weighted mean difference of 2.094 days. ($p<0.0001$). There was no significant difference between readmission ($p=0.536$) between the two groups. Time to start oral feed was significantly more in feeding jejunostomy group. (Weighted mean difference of 2.4 days,$p<0.0001$.) There was no significant difference in TPN requirement between the two group.

Feeding jejunostomy tube related complications

23 patients out of total 187 patients developed. Feeding jejunostomy tube related complications like tube dislodgement, peritonitis, leakage, etc.

Discussion:

Postoperative nutrition is one of the most important intervention to reduce morbidity and mortality following pancreaticoduodenectomy.[19] Enhanced recovery after surgery protocols are also gaining popularity in pancreaticoduodenectomy [20] which recommends early entral nutrition following pancreaticoduodenectomy. However, optimal route is still debated.

Intraoperative insertion of feeding jejunostomy is routine practice all around the world to provide entral nutrition after pancreaticoduodenectomy,but recently few studies {14,15,16,17} have questioned this protocol and found that feeding jejunostomy is associated with increased morbidity and mortality following pancreaticoduodenectomy.

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We think our study is the first metaanalyis to study morbidity and mortality associated with feeding jeujostommy.

In our metaanalysis feeding jejunostomy group was associated with significantly increased morbidity than the control group. There was no significant difference in mortality between the two groups.

In secondary analysis feeding jejunostomy group was associated with increased risk of delayed gastric emptying, there was no difference in post operative pancreatic fistula rates. There was no difference in overall surgical site infection rates, however deep surgical site infection rates were significantly higher in feeding jejunostomy group.

Hospital stay was significantly more in feeding jejunostomy group. There was no difference in readmission rates.

One of the key beliefs to insert feeding jejunostomy is that it decreases need for parentral nutrition but in our metaanalysis there was no difference in feeding jejunostomy group vs the control group. Time to start oral feed was also significantly more than the control group.

Specific complications are also associated with feeding jejunostomy like tube dislodgement, peritonitis, leaks. [21] Around 12% patients developed complications specific to feeding jejunostomy tube.

One of the key limitations of this metaanalysis is very few studies available and lack of any randomised control trials. Positive point of our metaanalysis is heterogeneity was not significant in more of the analysis.

In conclusion, Feeding jejunostomy seems to be associated with increased morbidity, increased complications, increased length of stay without any significant benefits. Randomised control trials need to be done to conclude this issue.

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Study	Publication Year	Number of Patients in study group	Number of Patients in Control Group	Type of study
Waliye etal.	2016	153	103	Retrospective Cohort
Padusis etal.	2014	623	623	Retrospective Propensity matched cohort
LI et al.	2018	33	36	Retrospective cohort
Zhu et al.	2013	34	34	Prospective cohort

Table 1. Studies included in the metaanalysis.

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Table 2 Assessment of bias in cohort studies. + Denotes low risk of bias, – denotes high risk of bias.

STUDY	Representative of exposed cohort	Selection of non exposed cohort	Ascertainment of Exposure	Demonstration that outcome was not present at start of study	Comparability of cohorts	Assessment of outcomes	Adequate time for followup	Complete Follow up of cohort	Total score
Waliye 2016	+	+	+	+	+	-	+	+	7
Padusis 2014	+	+	+	+	+	-	+	+	7
Li 2018	+	+	+	+	+	-	+	+	7
ZHU 2013	+	+	+	+	+	-	+	+	7

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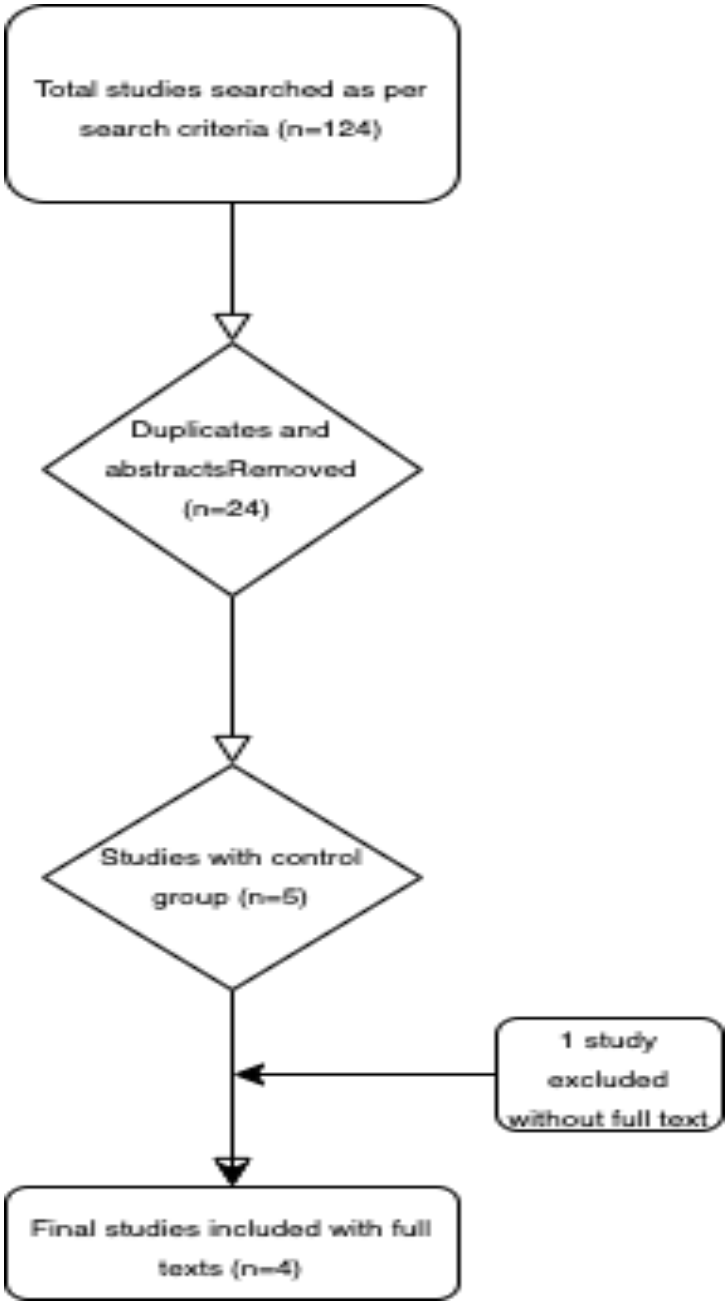

Figure: 1 Preferred Items for Reporting of Systematic Reviews and Meta-Analyses (PRISMA) 2009 flow diagram.

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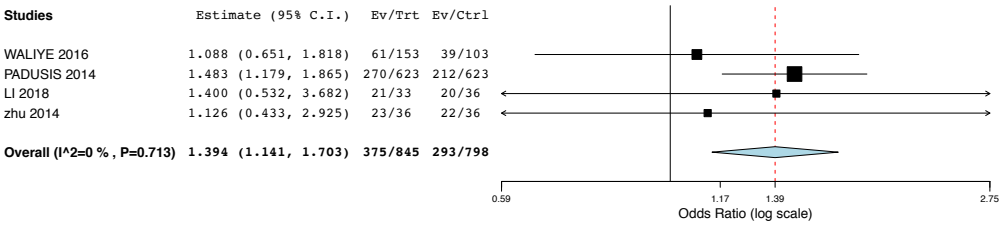

Figure 2: Feeding jejunostomy group was associated with significantly higher 90 days morbidity. (p=0.001)

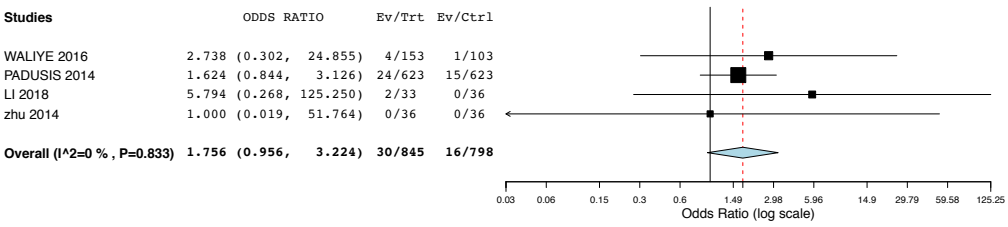

Figure 3: There was no significant difference between mortality in both the group. (p=0.07)

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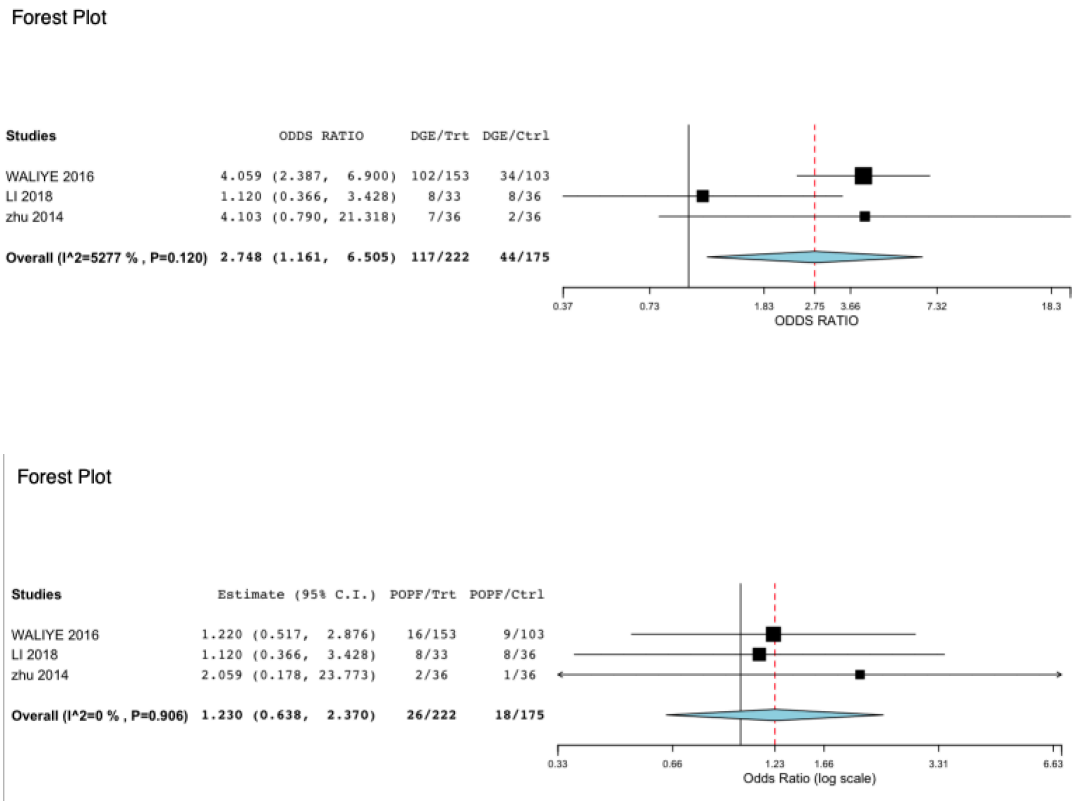

Figure 4: (a) delayed gastric emptying was significantly more in feeding jejunostomy group. (p=0.021) (b) There was no significant difference between postoperative pancreatic fistula between the two groups. (p=0.536).

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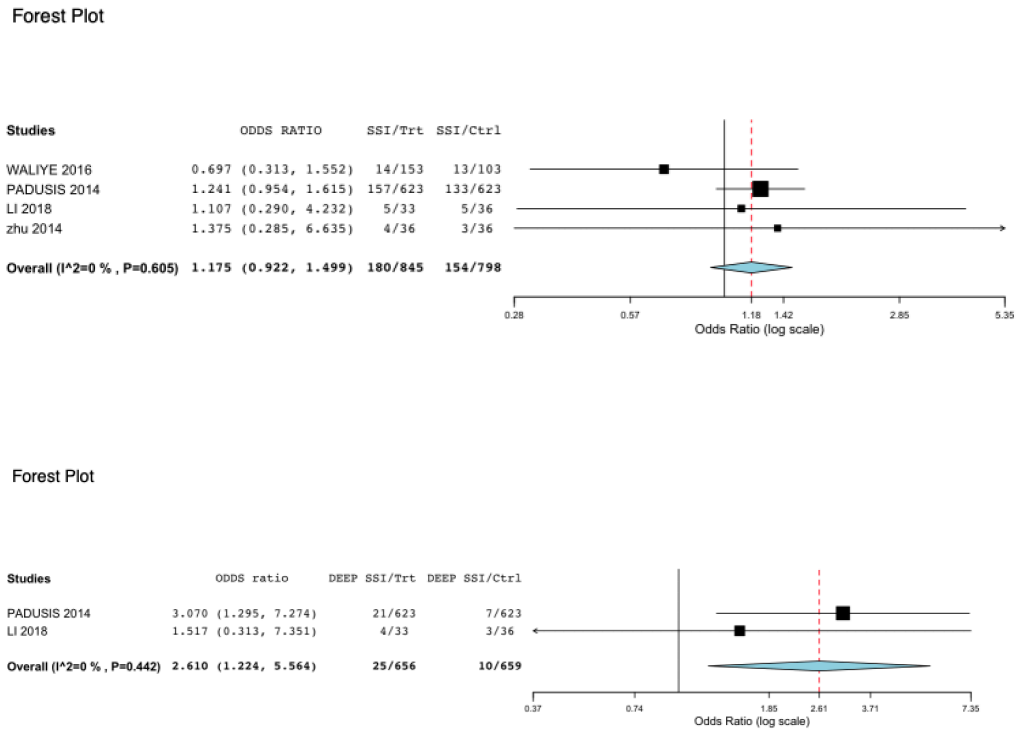

Figure 5: There was no significant difference between SSI between the two groups, However Deep SSI rates were significantly higher in feeding jejunostomy group.

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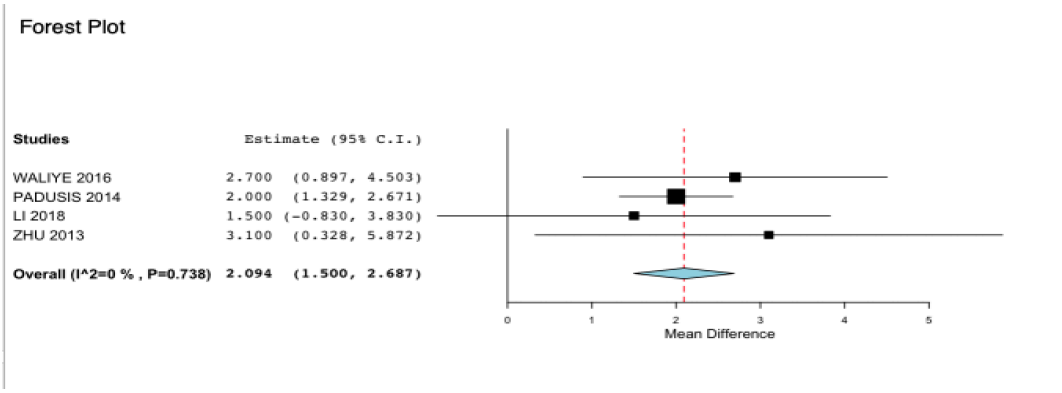

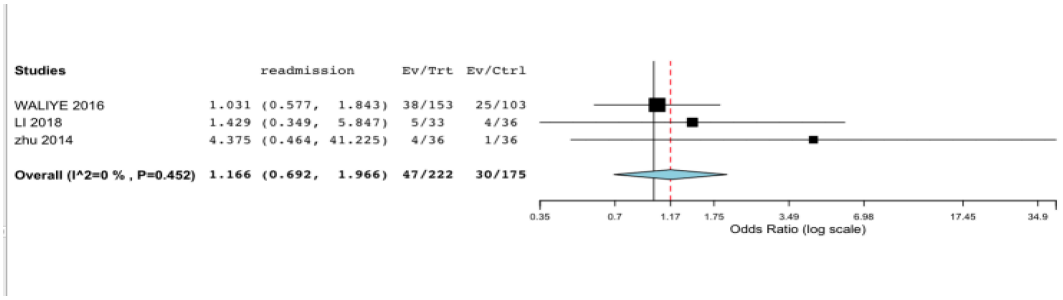

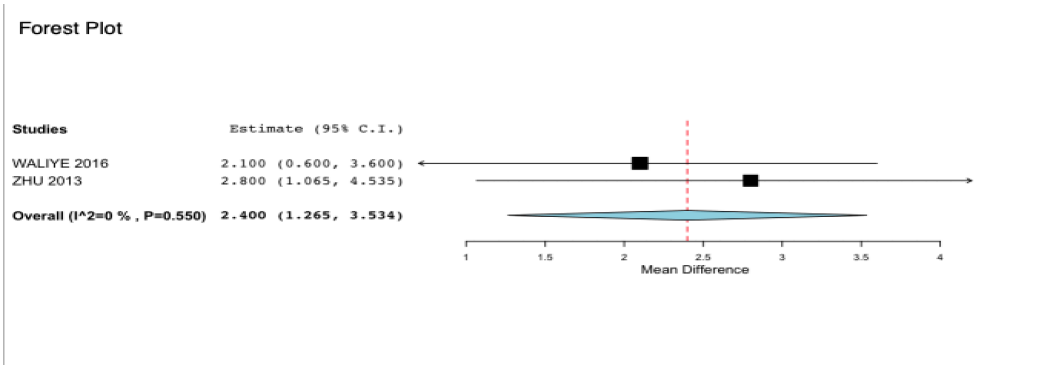

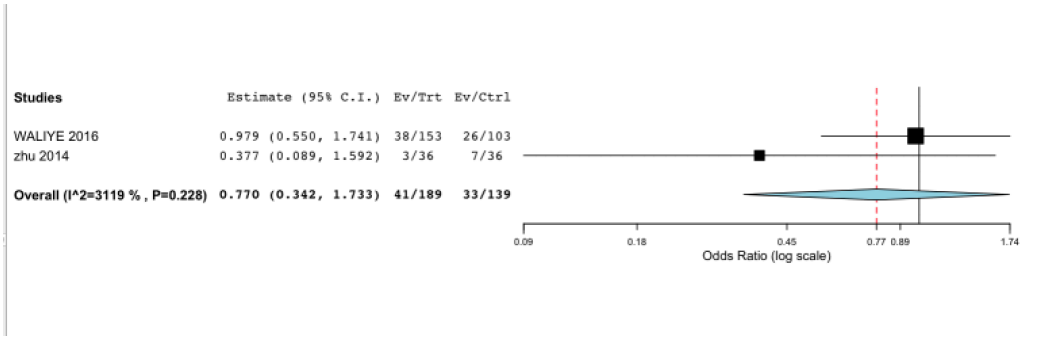

Figure 6: a) Hospital stay was more in feeding jejunostomy group. b)There was no difference in readmission. C) Time to oral feed was significantly more in feeding jejunostomy group. d) There was no difference in TPN requirement in both the group.

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