Official title:Safety and Effectiveness of Early Feeding After Bowel Anastomosis in Neonates or Infants

NCT：04464057(This study was registered on Clinical Trials. gov)

Primary Completion Date：2022-12-09

A multi-center cohort was established in August 2020,and 941 case records were uploaded to http://212.64.50.165 at discharge from hospital.

The 1st part:Safety and Effectiveness of Early Feeding After Bowel Anastomosis in upper,middle and lower intestinal events

Absract:

Purpose In order to prevent postoperative complications, delayed oral feeding(DOF) was still a common model of care following pediatric intestinal anastomosis surgery; however, early oral feeding(EOF) has been proven to be safe and effective in reducing the incidence of complications and fast recovery after some pediatric intestinal anastomosis. Unfortunately, evidence for initiating EOF after intestinal anastomosis in infants is insufficient. Hence, this study was primarily designed to evaluate the safety and efficacy of EOF in infants with intestinal anastomosis.

Methods 568 infants from the multi-center cohort were divided into three types of intestinal anastomosis: duodenal anastomosis (EOF group,n=15; DOF group,n=67), jejunal anastomosis (EOF group,n=56;DOF group,n=155), and ileal/colonic anastomosis(EOF group,n=61;DOF group,n=214). The incidence of complications and the indexes of recovery were compared between the EOF and DOF groups in the three types of anastomosis independently.

Results Parenteral nutrition(PN) time and postoperative hospital stay were significantly shorter in EOF group than that in DOF group(Duodenal anastomosis:9.00[6.00,10.00] d vs 12.00[8.00,16.00] d,p=-0.033;10.00[7.00,13.00] d vs 14.00[11.00,18.00] d,p=0.002;Jejunal anastomosis:7.00[6.00,8.00] d vs 9.00[7.00,13.00] d,p<0.001;13.00[9.00,14.00] d vs 15.00[12.00,17.00] d,p<0.001;Ileal/colonic anastomosis:6.00[5.00,7.00] d vs 8.00[6.00,10.00] d,p<0.001;7.00[6.00,10.50] d vs 10.00[8.00,13.00] d,p<0.001). There were no differences in terms of abdominal distension,vomiting,diarrhea,weight change,serum albumin change,white blood cell(WBC) count,and C reaction protein(CRP) level at discharge between the EOF and DOF groups in the three types of anastomosis (all p>0.05).No hematochezia or anastomotic leakage were found.

Statistical analysis

Data were presented as percentages, medians, or averages, and the level of statistical significance was set at 0.05. SPSS 23.0 was used for statistical analysis, and the distribution of continuous variables was examined for normality. A t-test was applied for normally distributed data, and a rank-sum test was performed for non-normally distributed data. Categorical variables were tested using the chi-squared or Fisher’s exact test.

Results :

EOF in the three types of intestinal anastomosis in neonates and infants

The types of intestinal anastomosis	EOF [n(%)]	DOF [n(%)]	Chi-square test	
			χ2	P
Duodenum(n=85)	16(18.8%)	69(81.2%)		
Jejunum(n=211)	60(28.2%)	153(71.8%)	6.657	0.036
ileum/colon(n=275)	68(19.3.2%)	284(80.7%)		
Total(n=568)	144(23.2%)	506(76.8)	-	-

Complications of EOF in the three types of intestinal anastomosis

Complications		Abdominal distension	vomit	diarrhea	**overall complication**
Duodenal anastomosis	EOF(n=15)	4(26.7%)	4(26.7%)	1(6.7%)	**7(46.7%)**
	DOF(n=67)	13(19.4%)	10(14.9%)	3(4.5%)	**22(32.8%)**
	P	0.501	0.275	0.562	**0.375**
Jejunal anastomosis	EOF(n=56)	0(0.0%)	4(7.1%)	-	**4(7.1%)**
	DOF(n=155)	8(5.2%)	3(1.9%)	-	**11(7.1%)**
	P	0.113	0.082	-	**1.000**
Ileal/Colonic anastomosis	EOF(n=61)	4(6.6%)	3(4.9%	1(1.6%	**7(11.5%)**
	DOF(n=214)	6(2.8%)	3(1.4%)	2(0.9%)	**9(4.2%)**
	p	0.236	0.125	0.530	**0.056**

There were no hematochezia and anastomotic leakage in all types of intestinal anastomosis.

Complications of EOF in the three types of intestinal anastomosis

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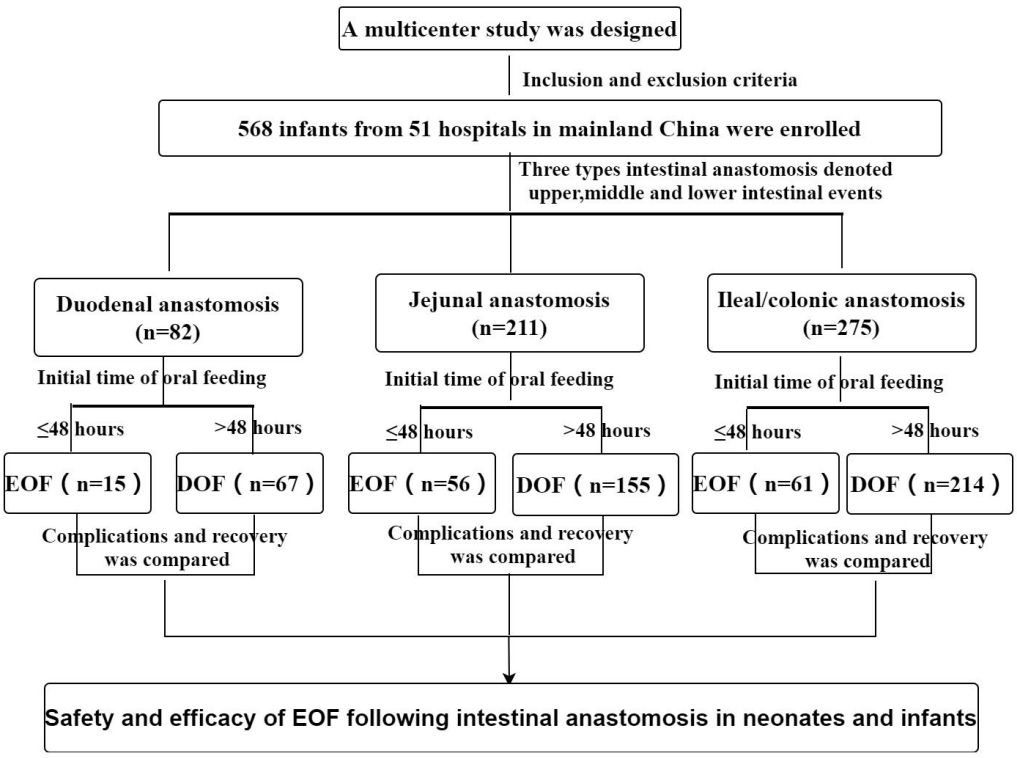
Duodenal anastomosis	EOF(n=15)	4(26.7%)	4(26.7%)	1(6.7%)	**7(46.7%)**
	DOF(n=67)	13(19.4%)	10(14.9%)	3(4.5%)	**22(32.8%)**
	P	0.501	0.275	0.562	**0.375**
Jejunal anastomosis	EOF(n=56)	0(0.0%)	4(7.1%)	-	**4(7.1%)**
	DOF(n=155)	8(5.2%)	3(1.9%)	-	**11(7.1%)**
	P	0.113	0.082	-	**1.000**

Ileal/Colonic anastomosis	EOF(n=61)	4(6.6%)	3(4.9%	1(1.6%	**7(11.5%)**
	DOF(n=214)	6(2.8%)	3(1.4%)	2(0.9%)	**9(4.2%)**
	p	0.236	0.125	0.530	**0.056**

There were no hematochezia and anastomotic leakage in all types of intestinal anastomosis.

Study Design:



2.The 2st part:Early oral feeding enhanced recovery after intestinal anastomosis in neonates and young infants less than 3 months old

Abstract:

Purpose Early oral feeding(EOF) has been proven with a low incidence of complications and fast recovery after surgery in some elective pediatric patients,however,evidence for initiating EOF after intestinal anastomosis(IA) in neonates and young infants,with immature immune system and organs, is insufficient.This tudy was primary designed to investigate the status and evaluate the feasibility of EOF in neonates and young infants with IA in mainland china. **Method** 491 neonates and young infants from 51 hospital in china mainland were divided into two groups(EOF

group,n=88;traditional oral feeding,TOF group,n=403),and the clinical characteristics were collected and analyzed for evaluation of the status of EOF in neonates and young infants.The complications and recovery were also be compared to defined the feasibility after balancing the baseline by propensity score matching(PSM).**Result** The time of TPN,PN and postoperative hospital stay were significantly shorter in the EOF group than that in the TOF group in neonates and young infants with IA(2.00[1.00,2.00]d vs. 5.00[3.00,6.00]d, p<0.001; 7.00[5.00,8.00]d vs.9.00[7.00,13.00]d, p<0.001;11.00[8.00,14.00]]d vs.14.00[11.00,17.00]d).There were significant differences in the spectrum of disorders, anastomotic sites,operative age and weight between EOF and TOF groups(p=0.002;p=0.029,p=0.045,p<0.001).The overall low rate of EOF in neonates and infants with IA was 17.9%,especially lower in intestinal atresia,stenosis,stoma closure, ileal-colonic,colonic anastomotic site,operative age less than 30 days and weight less than 2.5kg.The overall rate of and Clavien-Dindo II complications were higher in EOF than TOF group(p=0.002),however,no differences were found in severe complications(Clavien-Dindo III/ IV/V).**Conclusion** The rate of EOF in neonates and young infants with IA is low in Mainland China and the spectrum of disorders,anastomotic sites,operative age and weight maybe factors affecting the performing of EOF. Nevertheless, implementing EOF in neonates and young infants with IA maybe beneficial, enhances the recovery, and does not increase the rate of severe complications.

Keywords early oral feeding;intestinal anastomosis, neonate;young infant

Statistical analysis

Data were presented as percentages, medians, or averages, and the level of statistical significance was set at 0.05. SPSS 22.0 was used for statistical analysis, and the distribution of continuous variables was examined for normality. A t-test was applied for normally distributed data, and a rank-sum test was performed for non-normally distributed data. Categorical variables were tested using the chi-squared or Fisher's exact test.Before comparing the complications and recovery between EOF and TOF groups,a 1:2 propensity score match(PSM) with caliper 0.05 was applied to balance the baseline data between the two groups.

Results:

Baseline clinical characteristics of neonates and young infants with intestinal anastomosis in EOF and TOF groups

group		EOF（n=88,%）	TOF (n=403,%)	P
The spectrum of disorders	Intestinal atresia(n=69)	5（5.7%）	64（15.9%）	0.002
	intestinal mass(n=32)	4（6.9%）	28（4.5%）	
	intestinal necrosis(n=24)	3（5.2%）	21（3.4%）	
	intestinal stenosis(n=38)	3(3.4%)	35(8.7%)	
	biliary disease(n=178)	48(32.3%)	130(54.5%)	
	colsing the stoma(n=41)	4(4.5%)	37(9.2%)	
	patent vitelline duct(n=19)	6(n=3.2%)	13(6.8%)	
	duodenal obstruction(n=84)	15(17%)	69(17.1%)	
	adhesional obstruction(n=6)	0(0%)	6(1.5%)	
Anastomic sites	Duodenal anastomosis（n=83）	15(17.0%)	68(16.9%)	0.029
	Jejunal anastomosis(n=218)	50(56.8%)	168(41.7%)	
	Ileal anastomosis(n=123)	19(21.6%)	104(25.8%)	
	Ileal-colonic anastomosis(n=36)	2(2.3%)	34（8.4%）	
	Colonic anastomosis(n=31)	2(2.3%)	29(7.2%)	
Surgical approach	laparoscope（n=132）	19(21.6%)	113(28.0%)	0.216
	laparotomy(n=359)	69(78.4%)	290(72.0%)	
gender	male(n=259)	46(52.37%)	213(52.9%)	0.921
	female(n=232)	42(47.7%)	190(47.1%)	
Operative age（d,Median[P25%,P75%]）		40[11,65]	34[4,58]	0.045
Operateive weight（kg,Median[P25%,P75%]）		4.38[3.40,5.10]	3.58[2.8,4.5]	<0.001
Pre-operative albumin(g/L,Median[P25%,P75%]）		37.10[34.63,40.45]	36.30[33.10,39.70]	0.054
Pre-operative prealbumin(g/L,Median[P25%,P75%]）		0.15[0.10,0.17]	0.13[0.09,0.16]	0.062

Baseline clinical characteristics of young infants with intestinal anastomosis in EOF and TOF groups after PSM

group		EOF（n=86,%）	TOF (n=156,%)	P
The spectrum of disorders	Intestinal atresia(n=15)	5(5.8%)	11(7.1%)	0.963
	intestinal mass(n=15)	4(4.7%)	11(7.8%)	
	intestinal necrosis(n=9)	3(3.5%)	6(3.8%)	
	intestinal stenosis(n=11)	3(3.5%)	8(5.1%)	
	biliary disease(n=123)	46(53.5%)	77(49.4%)	
	colsing the stoma(n=13)	4(4.7%)	9(5.8%)	
	patent vitelline duct(n=13)	6(n=7.0%)	7(4.5%)	
	duodenal obstruction(n=42)	15(17.4%)	27(17.3%)	
Anastomic sites	Duodenal anastomosis（n=42）	15(17.4%)	27(17.3%)	0.927
	Jejunal anastomosis(n=130)	48(55.8%)	82(52.6%)	
	Ileal anastomosis(n=60)	19(22.1%)	41(26.3%)	
	Ileal-colonic anastomosis(n=4)	2(2.3%)	2（1.3%）	
	Colonic anastomosis(n=6)	2(2.3%)	4(2.6%)	
Surgical approach	laparoscope（n=54）	19(22.1%)	35(22.4%)	0.951
	laparotomy(n=188)	67(77.9%)	121(77.6%)	
gender	male(n=130)	44(51.2%)	86(55.1%)	0.554
	female(n=112)	42(48.8%)	70(44.9%)	
Operative age（d,Median[P25%,P75%]）		39.00[11.00,64.25]	41.50[8.25,59.00]	0.810
Operateive weight（kg,Median[P25%,P75%]）		4.33[3.38,5.03]	4.10[3.05,4.90]	0.571
Pre-operative		37.10[34.50,40.	37.20[33.93,40.0	0.725

albumin(g/L,Median[P25%,P75%]）	15]	0]	
Pre-operative prealbumin(g/L,Median[P25%,P75%]）	0.15[0.11,0.17]	0.14[0.10,0.17]	0.515

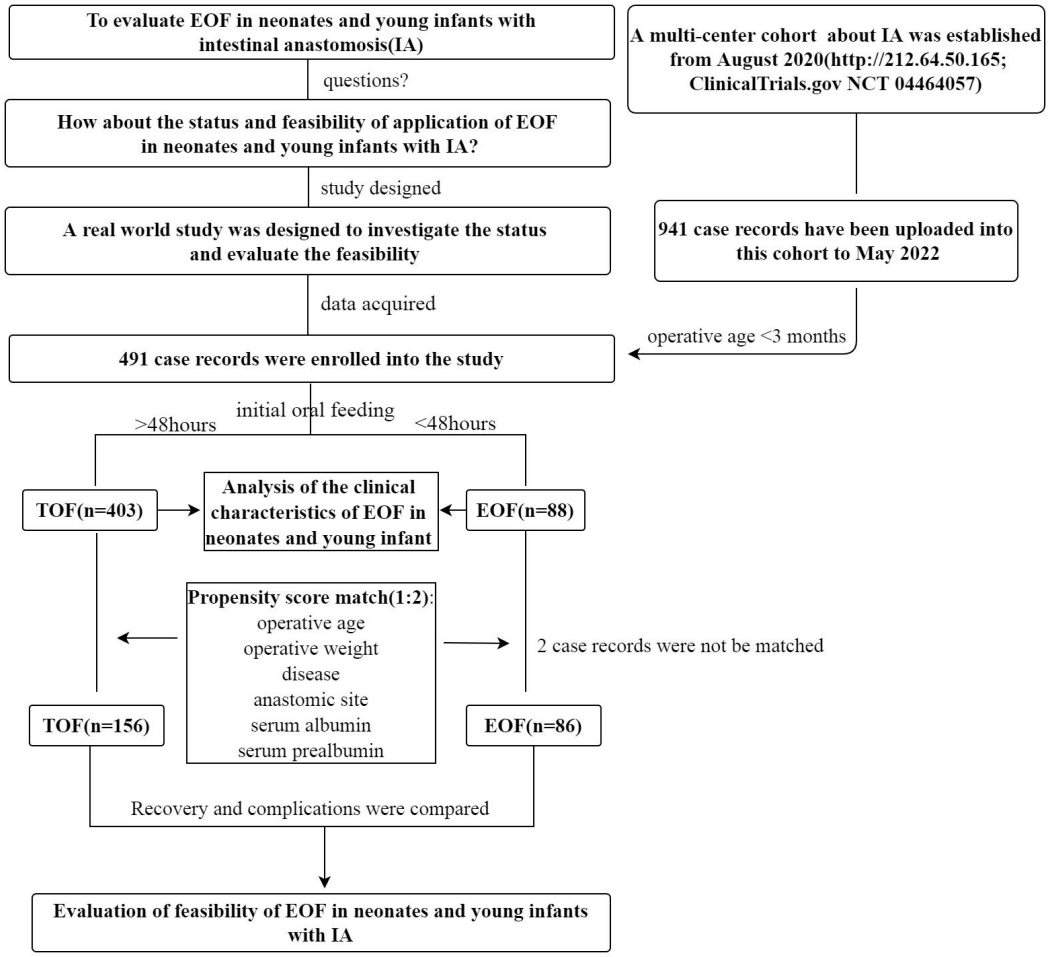
Recovery of young infants with intestinal anastomosis after EOF or TOF

gruop	EOF(n=86)	TOF(n=156)	p
weight(kg,Median[P25%,P75%])	4.45[3.40,5.00]	4.10[3.34,5.00]	0.507
albumin(g/L,Median[P25%,P75%])	36.73[34.00,41.50]	37.15[34.23,41.48]	0.510
prealbumin(g/LMedian[P25%,P75%])	0.15[0.11,0.19]	0.14[0.11,0.18]	0.255
Time of TPN(d,Median[P25%,P75%])	2.00[1.00,2.00]	5.00[3.00,6.00]	<0.001
Time of PN(d,Median[P25%,P75%])	7.00[5.00,8.00]	9.00[7.00,13.00]	<0.001
Hospital stay(d,Median[P25%,P75%])	11.00[8.00,14.00]	14.00[11.00,17.00]	<0.001

complications of young infants with intestinal anastomosis after EOF or TOF

gruop		EOF（n=86,%）	TOF(n=156,%)	p
Clavien-Dindo classifification	Grade I (n,%)	11(12.8%)	14(9.0%)	0.351
	Grade II(n,%)	6(7.0%)	0(0%)	0.002
	Grade III(n,%)	0	1(0.6%)	0.457
	Grade IV/V(n,%)	0	0	-
	overall	17（19.8%）	15（9.6%）	0.026
Abdominal distension		12(14.0%)	12(7.7%)	0.119
vomit		7(8.1%)	1(0.6%)	0.002
diarrhea		1(1.2%)	2(1.3%)	0.936
hematochezia		1(1.2%)	0(0%)	0.177
anastomotic leakage		0(0%)	1(0.6%)	0.457

Study design:


To evaluate EOF in neonates and young infants with intestinal anastomosis(IA)
questions?
How about the status and feasibility of application of EOF in neonates and young infants with IA?
study designed
A real world study was designed to investigate the status and evaluate the feasibility
data acquired
491 case records were enrolled into the study
A multi-center cohort about IA was established from August 2020(http://212.64.50.165; ClinicalTrials.gov NCT 04464057)
941 case records have been uploaded into this cohort to May 2022
operative age <3 months
initial oral feeding
>48hours
<48hours
TOF(n=403)
Analysis of the clinical characteristics of EOF in neonates and young infant
EOF(n=88)
Propensity score match(1:2):
operative age
operative weight
disease
anastomic site
serum albumin
serum prealbumin
2 case records were not be matched
TOF(n=156)
EOF(n=86)
Recovery and complications were compared
Evaluation of feasibility of EOF in neonates and young infants with IA