

Inflammatory Responses Associated with Postoperative Ileus Contribute to Anastomotic Leakage – A Post-Hoc Analysis of a Prospective Randomized Controlled Trial



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Background

Anastomotic leakage (AL) following abdominal surgery is a critical determinant of postoperative recovery. Interestingly, interventions aimed at reducing the inflammatory response and **postoperative ileus (POI)** also have a beneficial effect on AL co-occurrence.

Aim of this study: Investigate the relation of postoperative ileus with inflammation and anastomotic leakage after colorectal surgery.

Methods

A post-hoc analysis of a prospective randomized controlled trial, in which 112 patients underwent colorectal surgery, is performed. Patients were stratified for POI versus no POI

- Blood samples were taken pre- and postoperatively to determine the systemic inflammatory response and tissue damage by means of I-FABP
- Prospective registration of clinical parameters, eg. complications

Conclusion

The occurrence of POI and AL are correlated as patients with POI and an increased inflammatory response show a higher prevalence of AL.

Results

1. Complications after surgery according to the Clavien-Dindo Classification

	No POI (n = 69)	POI (n = 43)	P
No complication	45 (82)	10 (18)	<0.001
Grade I (deviation from normal postoperative course)	18 (58)	13 (42)	0.67
Grade II (requiring pharmacological treatment)	4 (40)	6 (60)	0.18
Grade IIIa (intervention not under general anesthesia)	1 (50)	1 (50)	1.00
Grade IIIb (intervention under general anesthesia)	1 (9)	10 (91)	<0.001
Grade IV (life threatening)	0	0	
Grade V (death)	0 (0)	3 (100)	0.05

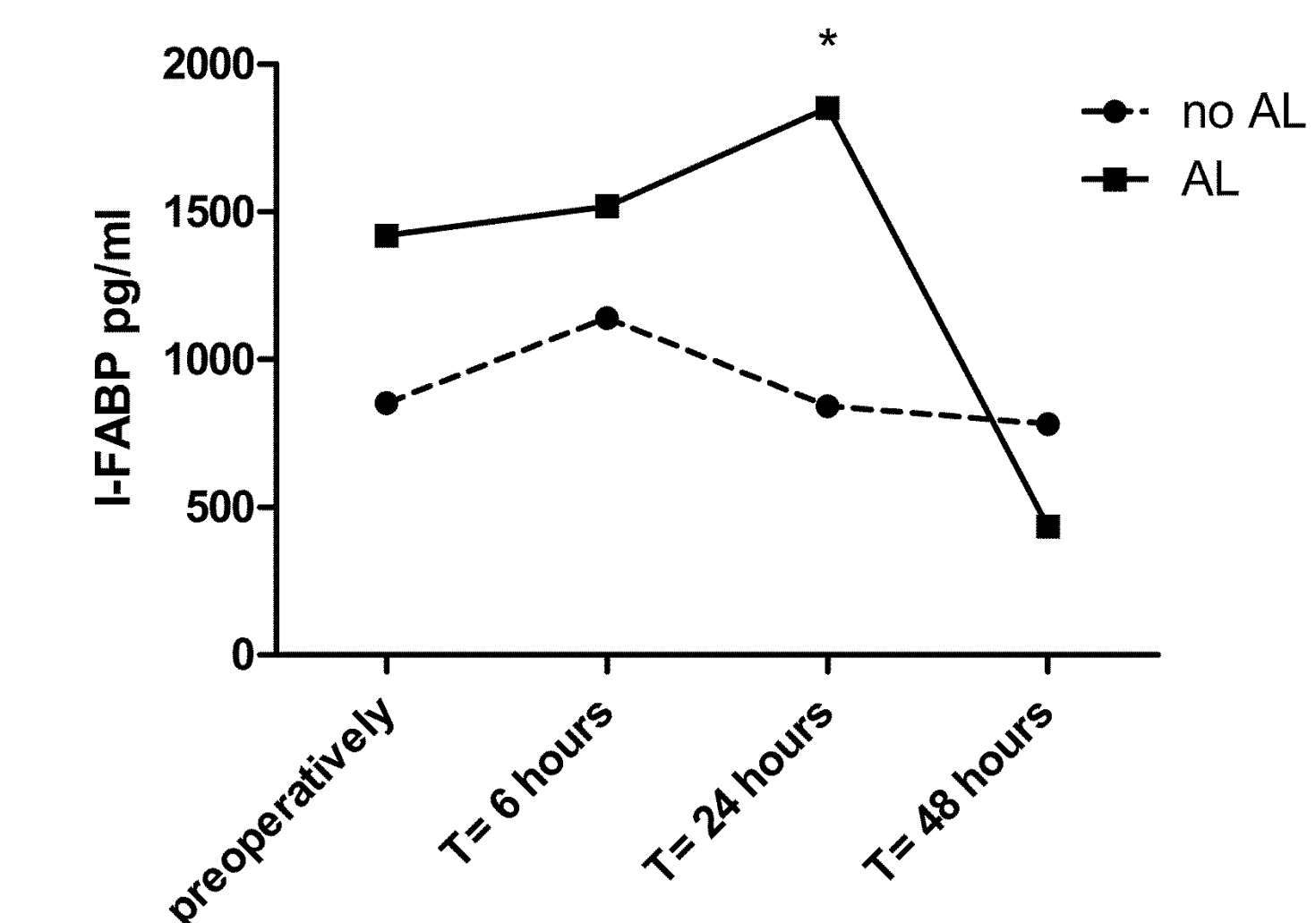
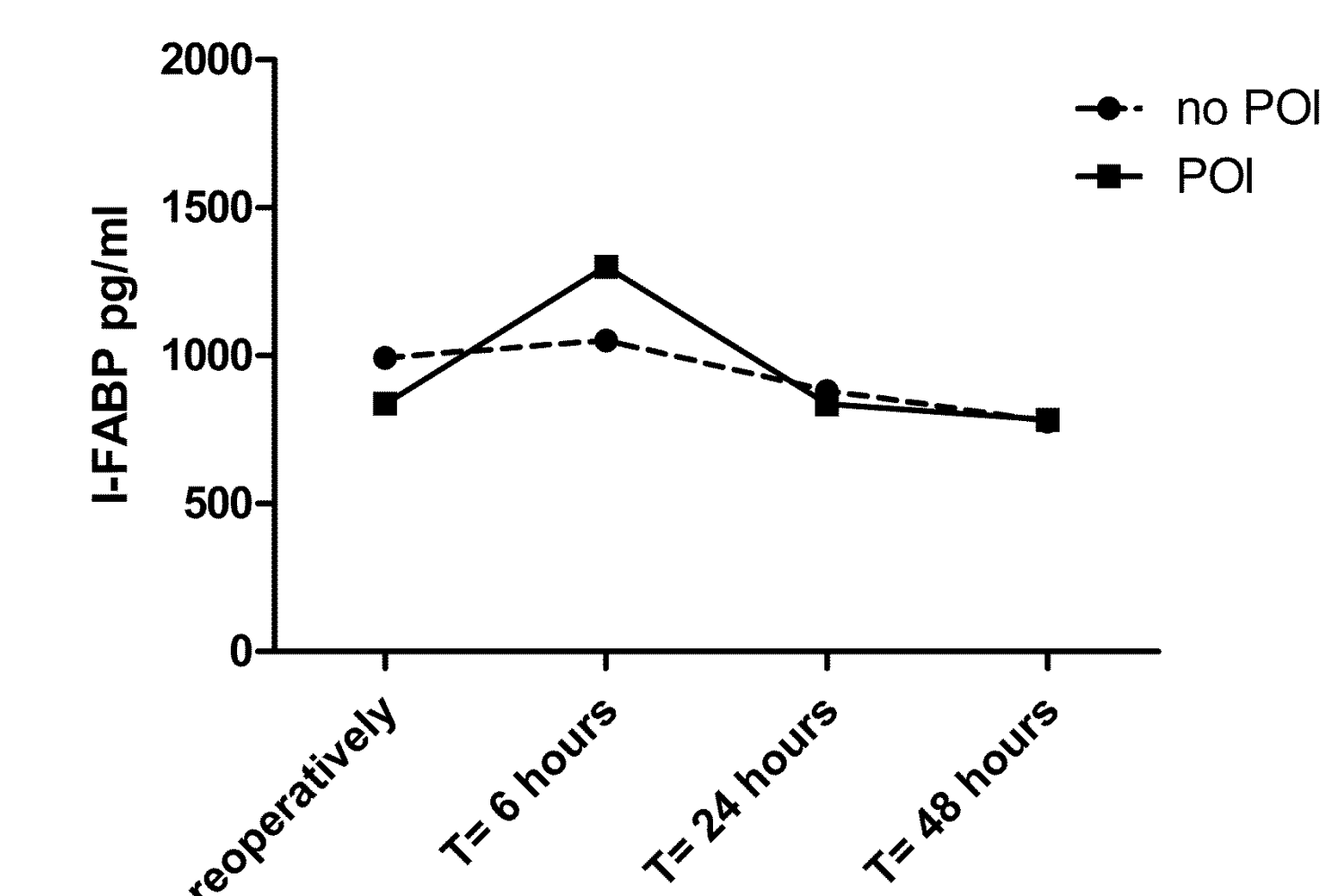
Anastomotic leakage was present in 9 of 43 patients in the POI group, and in 1 of 65 patients in the group without POI (p<0.001).

2. Univariate regression analysis of predictors of anastomotic leakage

	Odds ratio	95% CI	P
Sex	1.6	0.42-6.08	0.49
Age	1.02	0.96-1.09	0.52
BMI	0.88	0.73-1.06	0.18
ASA classification	0.88	0.24-3.25	0.85
History of abdominal surgery	0.27	0.03-2.20	0.22
Diabetes mellitus	0.44	0.05-3.72	0.45
NSAID use	0	0	1.00
Alcohol use	0.26	0.05-1.31	0.10
Neoadjuvant treatment	0.75	0.34-1.68	0.49
Surgical procedure	0.77	0.54-1.09	0.14
Colon or rectum surgery	0.16	0.02-1.3	0.09
Duration of surgery	1	0.99-1.01	0.81
Blood loss during surgery	0.79	0.22-2.8	0.71
Creation of a stoma	0.11	0.01-0.91	0.04
Days of epidural anesthesia	0.48	0.23-1	0.05
Study intervention	0.46	0.11-1.89	0.28
POI	12.57	2.73-120.65	0.0005

2. Univariate regression analysis revealed a significant association between POI and AL

3. Plasma levels of I-FABP (Intestinal Fatty Acid Binding Protein)



Patients who developed AL had significantly higher plasma levels of I-FABP compared to patients without AL at 24 hrs after onset of surgery.

4. Systemic inflammation

	No POI (n = 69)	POI (n = 43)	P
CRP POD 1, mean (SD)	107 (51)	93 (37)	0.62
CRP POD 2, mean (SD)	163 (86)	234 (77)	0.001
CRP POD 3, mean (SD)	135 (48)	157 (51)	0.38
TNF after onset of surgery, median (IQR)	0.46 (0.29)	0.51 (0.28)	0.23
TNF after four hours, median (IQR)	0.80 (0.37)	0.89 (0.56)	0.04
IL-8, after onset of surgery, mean (SD)	0.12 (0.64)	0.15 (0.95)	0.87
IL-8 after four hours, median (IQR)	166 (331)	196 (343)	0.80

4. Patients with POI had significantly higher plasma levels of TNFRSF1A (soluble tumor necrosis factor receptor 1) at 4 hrs postoperatively and higher plasma levels of CRP on the 2nd day postoperatively than patients without POI