

Late Breaking Abstracts

Topic: Nutrition and cancer

Abs n°:ESPEN2010-LB-1010

Abs Title: A RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE EFFECT OF PREOPERATIVE ENTERAL IMMUNONUTRITION ON THE SURGICAL SITE INFECTION AFTER TOTAL GASTRECTOMY

J. Fujita^{1,*}, T. Tsujinaka², T. Shimokawa³, Y. Kurokawa⁴, K. Fujitani², I. Miyashiro⁵, H. Imamura⁶, Y. Kimura⁷, K. Kobayashi⁸, H. Furukawa⁶ and Osaka Gastrointestinal Cancer Chemotherapy Study Group

¹Surgery, TOYONAKA MUNICIPAL HOSPITAL, Toyonaka, Osaka, ²Surgery, Osaka National Hospital, ³OGSG Data Center, Osaka, ⁴Surgery, Osaka University Medical School, Suita, ⁵Surgery, Osaka Medical Center for Cancer and Cardiovascular Disease, Osaka, ⁶Surgery, Sakai Municipal Hospital, Sakai, ⁷Surgery, NTT West Osaka Hospital, Osaka, ⁸Surgery, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Itami, Japan

Preferred presentation method: Poster Presentation

Rationale: A prospective randomized controlled trial was performed to investigate that preoperative enteral immunonutrition may reduce the ratio of surgical site infection (SSI) after total gastrectomy in gastric cancer patients.

Methods: Between 2004 Feb. and 2009 Dec. 240, gastric cancer patients who underwent gastric surgery were enrolled. 125 patients assigned to the immunonutrition group and 115 patients assigned to the control group. In the control group patients freely accessed to regular diet until surgery. In the immunonutrition group, patients were supplemented with 1000ml/day of immunonutrient enriched with arginine, omega-3 fatty acids and RNA (Impact®) in addition to the regular diet for 5 days before surgery. The primary endpoint was the incidence of SSI and the secondary endpoints were other infectious complications and postoperative morbidities.

Results: Age, Sex, body weight, serum albumin, general nutritional status were comparable between the two groups. 104 of 125 patients assigned to the immunonutrition group tolerated a daily intake 1000ml of Impact for 5 days. 223 patients underwent total gastrectomy, 6 patients proximal gastrectomy, 4 patients distal gastrectomy, and 7 patients simple laparotomy. In terms of tumor status, there were no significant difference between the groups in histological type, T stage, and lymph node metastasis. The incidence of SSI was 26 (20.8%) in the immunonutrition group and 24 (20.9%) in the control group (R.R: 1.00, 95% C.I: 0.61-1.63). Postoperative morbidity was 36 (28.8%) in the immunonutrition group and 30 (26.1%) in the control group. There was no difference in days of hospital stay after surgery between the groups.

Conclusion: The oral administration of immunonutrient for 5 days before surgery did not contribute to the reduction of infectious complications after total gastrectomy in gastric cancer patients.

Disclosure of Interest: None Declared

Keywords: immunonutrition, cancer, gastrectomy

LB009

A Randomized Controlled Trial to Evaluate the Effect of Preoperative Enteral Immunonutrition on the Surgical Site Infection after Total Gastrectomy

**J. Fujita ^{1,*}, T. Tsujinaka ², T. Shimokawa ³, Y. Kurokawa ⁴, K. Fujitani ², I. Miyashiro ⁵, H. Imamura ⁶, Y. Kimura ⁷, K. Kobayashi ⁸, H. Furukawa ⁶
and Osaka Gastrointestinal Cancer Chemotherapy Study Group**

¹Surgery, TOYONAKA MUNICIPAL HOSPITAL, Toyonaka, Osaka, ²Surgery, Osaka National Hospital, ³OGSG Data Center, Osaka, ⁴Surgery, Osaka University Medical School, Suita, ⁵Surgery, Osaka Medical Center for Cancer and Cardiovascular Disease, Osaka, ⁶Surgery, Sakai Municipal Hospital, Sakai, ⁷Surgery, NTT West Osaka Hospital, Osaka, ⁸Surgery, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Itami, Japan

Abstract

- **Rationale:** A prospective randomized controlled trial was performed to investigate that preoperative enteral immunonutrition may reduce the ratio of surgical site infection (SSI) after total gastrectomy in gastric cancer patients.
- **Methods:** Between 2004 Feb. and 2009 Dec. 240, gastric cancer patients who underwent gastric surgery were enrolled. 125 patients assigned to the immunonutrition group and 115 patients assigned to the control group. In the control group patients freely accessed to regular diet until surgery. In the immunonutrition group, patients were supplemented with 1000ml/day of immunonutrient enriched with arginine, omega-3 fatty acids and RNA (IMPACT®) in addition to the regular diet for 5 days before surgery. The primary endpoint was the incidence of SSI and the secondary endpoints were other infectious complications and postoperative morbidities.
- **Results:** Age, Sex, body weight, serum albumin, general nutritional status were comparable between the two groups. 104 of 125 patients assigned to the immunonutrition group tolerated a daily intake 1000ml of Impact for 5 days. 223 patients underwent total gastrectomy, 6 patients proximal gastrectomy, 4 patients distal gastrectomy, and 7 patients simple laparotomy. In terms of tumor status, there were no significant difference between the groups in histological type, T stage, and lymph node metastasis. The incidence of SSI was 26 (20.8%) in the immunonutrition group and 24 (20.9%) in the control group (R.R: 1.00, 95% C.I: 0.61 -1.63). Postoperative morbidity was 36 (28.8%) in the immunonutrition group and 30 (26.1%) in the control group. There was no difference in days of hospital stay after surgery between the groups.
- **Conclusion:** The oral administration of immunonutrient for 5days before surgery did not contributed to the reduction of infectious complications after total gastrectomy in gastric cancer patients.

Background

- Immunonutrition modulates the host immune systems and inflammatory responses. Our preliminary study demonstrated that preoperative enteral immunonutrition resulted in the changes of body composition in patients with gastrointestinal cancers.

	Before	After	p
Albumin (g/dl)	3.89 ± 0.37	3.93 ± 0.42	ns
RBP (mg/dl)	3.21 ± 1.01	3.76 ± 1.04	0.02
Arginine (mmol/ml)	91.9 ± 37.9	112.0 ± 33.4	0.01
Lipid content in WBC			
n3(µg/g)	303 ± 141	378.2 ± 139	0.02
n3/n6	0.24 ± 0.07	0.32 ± 0.08	0.001
Urinary uracil output (mmol/g CRE)	57.6 ± 63.3	88.9 ± 45.5	0.01

- Numbers of clinical studies demonstrated that perioperative immunonutrition improved the surgical outcomes in major abdominal surgery, but other studies failed to show the advantage of the treatment.
- There has been no large scaled multi-institutional phase III RCT focused on the effect of immunonutrition in a specific surgery, i.e. total gastrectomy for gastric cancer.

Objective

- **To investigate the effect of preoperative enteral immunonutrition on the incidence of surgical site infection (SSI) after total gastrectomy for gastric cancer, we conducted a prospective randomized controlled trial.**

Methods

□ Eligibility criteria

- **Histologically proven adenocarcinoma of stomach**
- **Scheduled total gastrectomy**
- **Aged less than 80 years**
- **Not malnourished**
- **Possible to ingest liquid diet**
- **Written informed consent**

□ Exclusion criteria

- **Renal dysfunction, Hepatic dysfunction**
- **Insulin dependent Diabetes Mellitus**
- **Intestinal obstruction**
- **Active infection**
- **Other sever complications**
- **Patients to whom doctors judge ineligible**

□ Treatment

- **Control group:**

Free oral ingestion of regular diet

- **Immunonutrition group:**

Oral ingestion of IMPACT[®] 1000ml/day for 5 days before surgery . NO limit for oral intake of regular diet, but priority for IMPACT.

□ **Composition of Immunonutrients**

IMPACT[®], Ajinomoto Pharma, Tokyo, Japan

Components	Per 100ml
Total energy (kcal)	101
Protein (g)	5.6
Arginine (g)	1.28
Lipids (g)	2.8
EPA (g)	0.20
DHA (g)	0.14
Carbohydrates (g)	13.4
RNA (mg)	0.13

□ **End points**

□ **Primary:**

Ratio of Surgical Site Infection (SSI)

□ **Secondary:**

Postoperative Infectious Complications

Serum CRP level on POD 3 or 4

□ **Study Design**

**Multi institutional prospective randomized controlled trial,
Phase III**

□ **Sample size**

Control group: n=120

Immunonutrition group: n=120

Results

□ Patient Characteristics

	Control (N=115)	Immunonutrition (N=125)
Age, median	66 (30-79)	63.5 (29-78)
Gender, M:F	85:32	96:30
Body weight(kg), median	60.0 (40.1-92.2)	60.9 (38.0-97.0)
Weight loss(%), median	0 (0-10.0)	0 (0-16.9)
Nutritional Status Well: Malnourished	116: 1	122: 4
Albumin (g/dL), median	4.1 (2.4-5.3)	4.2 (2.5-4.8)
TLC * (/mL), median	1792 (700-4446)	1880 (800-5952)
CRP, preop (mg/ml)	0.1 (0-10.3)	0.1 (0-7.2)
Type of surgery		
Total gastrectomy	104	119
Proximal gastrectomy	3	3
Distal gastrectomy	4	0
Simple laparotomy	4	3
Node dissection D0:D1:D2:D3	4: 20: 85: 3	4: 22: 99: 0
Tumor stage (pathologic)	(N=122)	(N=111)
pT1:T2:T3:T4	43: 36: 24: 8	43: 36: 38: 5
pN0:N1:N2:N3	62: 24: 22: 3	57: 35: 29: 1

* TLC: Total Lymphocyte Count

□ Ingestion of Immunonutrient:IMPACT[®]

	Intake (ml), mean
Day 1	917
Day 2	952
Day 3	966
Day 4	966
Day 5	923
Total (ml/day)	945

□ Postoperative Complications

	Control (N=115)	Immunonutrition (N=125)
Overall (%)	30 (26.1%)	36 (28.8%)
Abdominal abscess	7 (6.1)	11 (8.8)
Pancreatic fistula	7 (6.1)	8 (6.4)
Anastomotic leakage	3 (2.6)	3 (2.4)
Pneumonia	0 (0.0)	5 (4.0)
Wound Infection	8 (7.0)	7 (5.6)
Drain infection	1 (0.9)	3 (2.4)
IV cath. infection	1 (0.9)	2 (1.6)
Pleural effusion	1 (0.9)	1 (0.8)
Postop. Bleeding	0 (0.0)	3 (2.4)
Bowel obstruction	1 (0.9)	2 (1.6)
SSI	24 (20.9)	26 (20.8)
SIRS *	34 (29.6)	46 (36.8)

* Presence of SIRS (Systemic Inflammatory Response Syndrome) during postoperative period

End Points

	Control (N=115)	Immunonutrition (N=125)	R.R. (95% C.I.)
Surgical Site Infection (SSI)	24 (20.9%)	26 (20.8%)	1.00 (0.61-1.63) P=1.000
Superficial incisional	8 (7.0%)	7 (5.6%)	
Deep incisional	1 (0.9%)	5 (4.0%)	
Organ/space	15 (13.0%)	17 (11.2%)	
Total Morbidity	30 (26.1%)	36 (28.8%)	1.10 (0.73-1.67) P=0.667
CRP on POD 3 (or4)	9.2 (0.8-33.9)	11.0 (1.4-38.1)	P=0.114

Conclusions

- **The oral administration of immunonutrient for 5 days before surgery did not contributed to the reduction of infectious complications after total gastrectomy for gastric cancer.**

References

- **Daly JM, Weintraub FN, Shou J, et al. Enteral nutrition during multimodality therapy in upper gastrointestinal cancer patients. *Ann Surg* 1995;221:327-338.**
- **Braga M, Gianotti L, Radaelli G, et al. Perioperative immunonutrition in patients undergoing cancer surgery: results of a randomized double-blind phase 3 trial. *1999;134:428-433.***
- **Braga M, Gianotti L, Vignali A, et al. Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer. *Surgery*. 2002;132:805-814.**
- **Gianotti L, Braga M, Nespoli L, et al. A randomized controlled trial of preoperative oral supplementation with a specialized diet in patients with gastrointestinal cancer. *Gastroenterology*. 2002;122:1763-1770.**
- **Xu J, Zhong Y, Jing D, et al. Preoperative enteral immunonutrition improves postoperative outcome in patients with gastrointestinal cancer. *World J Surg*. 2006;30:1284-1289.**
- **Tsujinaka T, Hirao M, Fujitani K, et al. Effect of preoperative immunonutrition on body composition in patients undergoing abdominal cancer surgery. *Surg Today* 2007;37:118-121.**
- **Klek S, Kulig J, Sierzega M, et al. The impact of immunostimulating nutrition on infectious complications after upper gastrointestinal surgery: a prospective, randomized, clinical trial. *Ann Surg*. 2008;248:212-220.**
- **Okamoto Y, Okano K, Izuishi K, et al. Attenuation of the systemic inflammatory response and infectious complications after gastrectomy with preoperative oral arginine and omega-3 fatty acids supplemented immunonutrition. *World J Surg*. 2009;33:1815-1821.**

Participating Institutions

**OGSG: Osaka Gastrointestinal Cancer
Chemotherapy Study Group**

**National Hospital Organization Osaka Medical Center
Toyonaka Municipal Hospital
Osaka Medical Center for Cancer and Cardiovascular Disease
Sakai Municipal Hospital
NTT West Osaka Hospital
Kinki Central Hospital, Itami
Osaka Seamen's Insurance Hospital
Yao Municipal Hospital
Kansairosai Hospital
Osakakita Teishin Hospital
Hoshigaoka Kosei-Nenkin Hospital
Kitano Hospital
Himeji Central Hospital
Kansai Medical University**