L'approccio nutrizionale al paziente con neoplasia delle vie digestive superiori

In chirurgia

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Nutritional status in patients with esophageal cancer

Patients undergoing esophagectomy
median BMI at diagnosis 25 kg/m2
57% of patients obese or overweight at clinical presentation
74% losing weight
34% weight loss exceeded 10% in 6 months or 5% in 1 month
median weight loss as percentage of pre-illness weight 5.3%.

AM Ryan - Clin Nutr 2005

Dysphagia deficiencies in macronutrients (protein, fat, carbohydrate and total calories) micronutrients (vitamins and minerals) adequate fluid intake
Increased resting metabolic expenditure (23% of patients)
Increased glucose turnover and alanine-to-glucose cycle - increased peripheral glucose uptake and lactate release.
Disease stage
Genetics IL10 host genotype

Oncologic (e.g. cisplatin, 5-fluorouracil, epirubicin, irinotecan) and **radiation therapy** associated relevant gastrointestinal side effects

Nutritional intervention

At diagnosis/ staging

- Indication to laparoscopic staging
- Perioperative or neoadjuvant therapy

Perioperatively

- Preoperative nutrition
- Postoperativ morbidity

Postoperatively

- At discharge

Malnutrition in surgical patient

Clinically pertinent malnutrition (postoperative complications and medico-economic consequences)

a BMI less or equal to 18.5 or a BMI less than 21 in a patient older than 70

recent weight loss of more than 10%

a serum albumin level less than 3.0 mg/dL independent of C-reactive protein (CRP).

The presence of even one of these clinical or laboratory criteria is sufficient to define malnutrition.

French clinical guidelines on perioperative nutrition - J Visc Surg 2012

Impaired nutritional status		Severity of disease (≈ increase in requirements)	
Absent **Score 0**	Normal nutritional status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Wt loss > 5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild **Score 1**	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. *Chronic hemodialysis, diabetes, oncology*
Moderate **Score 2**	Wt loss > 5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery* Stroke* *Severe pneumonia, hematologic malignancy*
Severe **Score 3**	Wt loss > 5% in 1 mth (> 15% in 3 mths) or BMI < 18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe **Score 3**	Head injury* Bone marrow transplantation* *Intensive care patients (APACHE > 10).*
Score:	+	**Score**	**= Total score**
Age	if ≥ 70 years: add 1 to total score above		**= age-adjusted total score**
Score ≥ 3: the patient is nutritionally at-risk and a nutritional care plan is initiated **Score < 3**: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

Kondrup - Clin Nutr 2003

Access for nutritional support during multimodal therapy in esophageal cancer patients

Self-expanding esophageal stents

- Stent-related complications
- Added difficulties during esophagectomy
- Restaging?
  - Impact that shearing forces on the tumor may have on oncological outcomes,
  - Malnutrition related to depression associated anorexia and disorders of absorption and digestion secondary to cytologic toxicity

Surgical jejunostomy

- Subjecting malnourished patients to an invasive procedure
- **Laparotomic**
  - may preclude future laparoscopic gastric mobilization
- **Laparoscopic**
  - allows a complete exploration of the abdominal cavity in the same time (valuable in locally advanced esogastric junctional tumors, especially signet ring cell carcinomas)

Percutaneous radiologic gastrostomy (PRG)

- minimally invasive and cost-effective not requiring an operating room or general anesthesia

W Tessier - Surg Endosc 2013

Access for nutritional support during multimodal therapy in esophageal cancer patients

Percutaneous radiological gastrostomy

Variables		Overall $N = 269$ (%)	NS group $N = 130$ (%)	S group $N = 139$ (%)	P
Success	No	10 (3.7)	7 (5.4)	3 (2.2)	0.158
	Yes	259 (96.3)	123 (94.6)	136 (97.8)	
Complication grade[a]	IIIA	1 (0.4)	0	1 (0.7)	0.009
	IIIB	8 (3.0)	8 (6.2)	0	
	IV	0	0	0	
	V	0	0	0	

NS group patients in whom no surgical treatment was considered, *S group* patients in whom surgery was considered as a part of the multimodal treatment

[a] Dindo-Clavien classification

Personal experience 2014-2016

14 PRG

100% success

1 pt (7,1%) fever and peritonism

64,3% used during Nadj Treat

5% weight increase

Removal 1 week before surgery

No complication related to PRG

(1 conversion from MIS to open surgery)

In locally advanced EC, PRG is feasible and safe in non-selected patients and should be the procedure of choice for feeding tube placement, especially in malnourished patients with obstructive tumors

PRG does not compromise the suitability of the stomach as an esophageal substitute in patients deemed to be resectable

W Tessier - Surg Endosc 2013

ESPEN Guidelines on Enteral Nutrition: Surgery

Preoperative	Encourage patients who do not meet their energy needs from normal food to take oral nutritional supplements during the preoperative period.	C	**4.1**
	Administer preoperative enteral nutrition (EN) preferably before admission to the hospital.	C	4.1
	Patients undergoing surgery who are considered to have no specific risk for aspiration, may drink clear fluids until 2 h before anaesthesia. Solids are allowed until 6 h before anaesthesia.	A	1
	Use preoperative carbohydrate loading (the night before and 2 h before surgery) in most patients undergoing major surgery.	B	2
Type of formula	In most patients a standard whole protein formula is appropriate.	C	4.2.3
	Use EN preferably with immuno-modulating substrates (arginine, ω-3 fatty acids and nucleotides) perioperatively independent of the nutritional risk for those patients • undergoing major neck surgery for cancer (laryngectomy, pharyngectomy) • undergoing major abdominal cancer surgery (oesophagectomy, gastrectomy, and pancreatoduodenectomy) • after severe trauma.	A	4.2.3
	Whenever possible start these formulae 5–7 days before surgery and continue postoperatively for 5 to 7 days after uncomplicated surgery.	C C	4.2.3 4.2.3

In colorectal surg, hypo-osmolar 12.5% carbohydrate rich drink:
reduces postop insulin resistance
preserves skeletal muscle mass

Immune modulating formulae (arginine,o-3-fatty acids and ribonucleotides, with or without glutamine)
decrease rate of postoperative complication
decrease length of hospital stay
in undernourished and well nourished gastrointestinal cancer patients

In patients undergoing gastrectomy for gastric cancer,
early EN with immune modulating formula
less wound-healing problems
suture failure
infectious as well as global complications

A Weimann Clin Nutr 2006

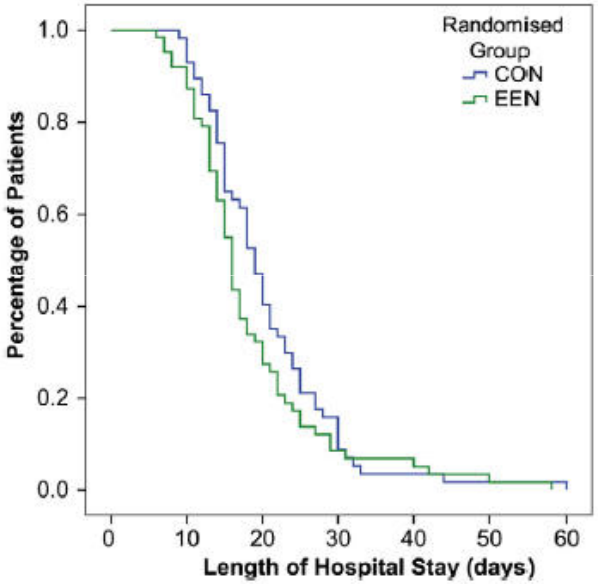
Early enteral nutrition in patients undergoing major upper gastrointestinal surgical resection

121 p submitted to UGI surg with curative resection (pancreas stomach esophagus) – jejunostomy

Group A: fasting; 10 ml/h saline jejunostomy until oral diet (POD 7-10)

Group B: EEN jejunostomy (start within 12 h postop 20 ml/h; increase 10 ml/h every 12 h, until 80 ml/h.

Primary Endpoint: LOHS
Secondary Endpoint: morbidity and mortality



Details of operative morbidity.

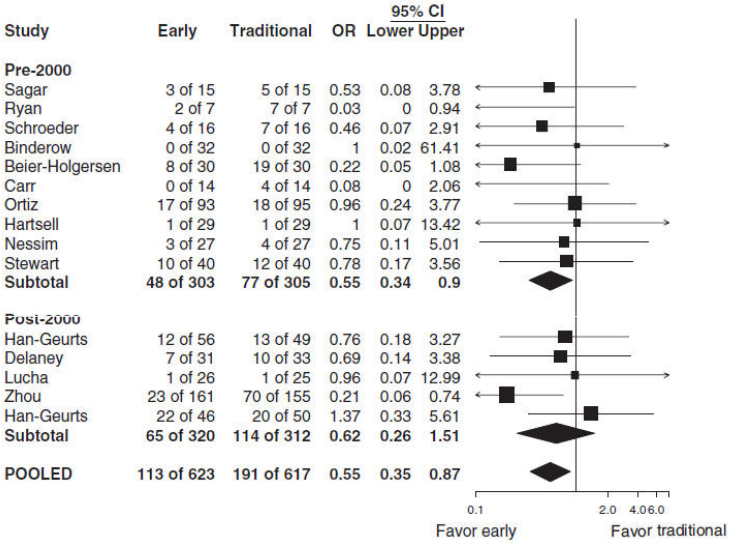
Complication	CON	EEN	Chi² (p-value)
Infective complications			
Wound infection	16 (28.1)	7 (10.9)	5.7 (0.017)
Chest infection	12 (21.1)	5 (7.8)	4.4 (0.036)
Anastomotic leak	7 (12.2)	2 (3.1)	3.67 (0.055)
Urinary tract infection	3 (5.3)	1 (1.6)	
Bacteramia	3 (5.3)	2 (3.1)	
Non-infective complications			
Pleural effusion	10 (17.5)	10 (15.6)	
Delayed gastric emptying	4 (7.0)	0	4.6 (0.031)
Myocardial infarction	1 (1.8)	0	
Major haemorrhage	2 (3.5)	0	
Chylothorax	0	1 (1.6)	
Rec. laryngeal nerve palsy	0	1 (1.6)	

Figures are numbers of patients, percentages in parentheses.

EEN feasible, safe, better clinical outcome (morbidity rate, anastomotic and septic complications, reduced LOS)

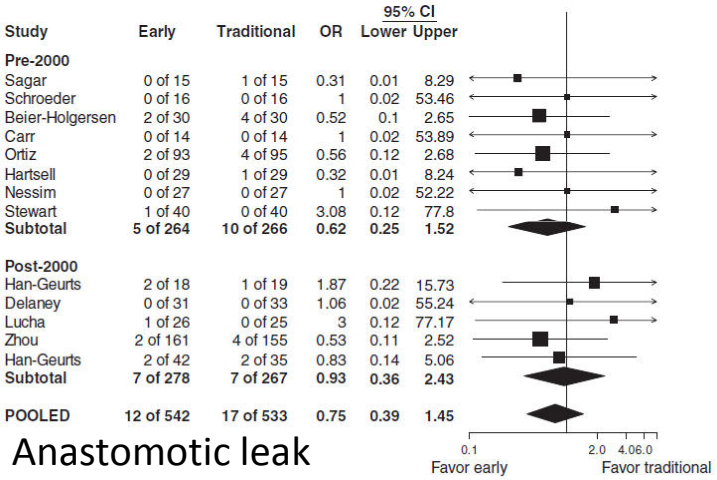
R Barlow – Clin Nutr 2011

Early feeding after resectional gastrointestinal surgery: a meta-analysis



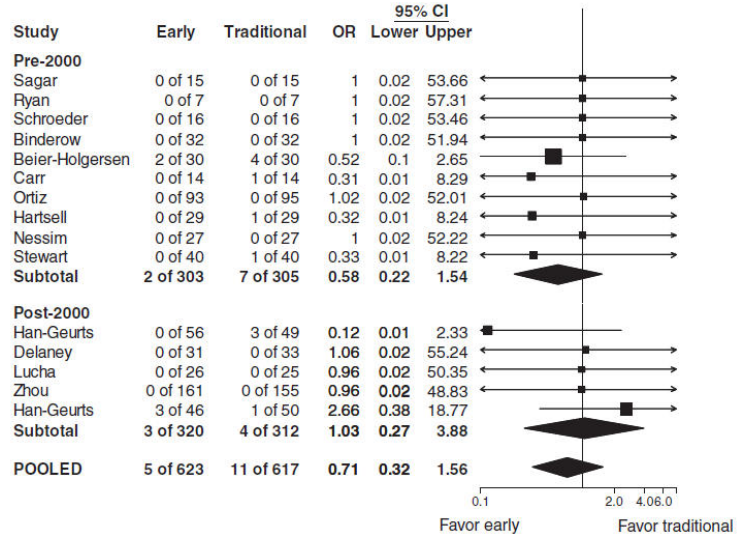
Study	Early	Traditional	OR	95% CI Lower	Upper
Pre-2000					
Sagar	3 of 15	5 of 15	0.53	0.08	3.78
Ryan	2 of 7	7 of 7	0.03	0	0.94
Schroeder	4 of 16	7 of 16	0.46	0.07	2.91
Binderow	0 of 32	0 of 32	1	0.02	61.41
Beier-Holgersen	8 of 30	19 of 30	0.22	0.05	1.08
Carr	0 of 14	4 of 14	0.08	0	2.06
Ortiz	17 of 93	18 of 95	0.96	0.24	3.77
Hartsell	1 of 29	1 of 29	1	0.07	13.42
Nessim	3 of 27	4 of 27	0.75	0.11	5.01
Stewart	10 of 40	12 of 40	0.78	0.17	3.56
Subtotal	**48 of 303**	**77 of 305**	**0.55**	**0.34**	**0.9**
Post-2000					
Han-Geurts	12 of 56	13 of 49	0.76	0.18	3.27
Delaney	7 of 31	10 of 33	0.69	0.14	3.38
Lucha	1 of 26	1 of 25	0.96	0.07	12.99
Zhou	23 of 161	70 of 155	0.21	0.06	0.74
Han-Geurts	22 of 46	20 of 50	1.37	0.33	5.61
Subtotal	**65 of 320**	**114 of 312**	**0.62**	**0.26**	**1.51**
POOLED	**113 of 623**	**191 of 617**	**0.55**	**0.35**	**0.87**

Complications



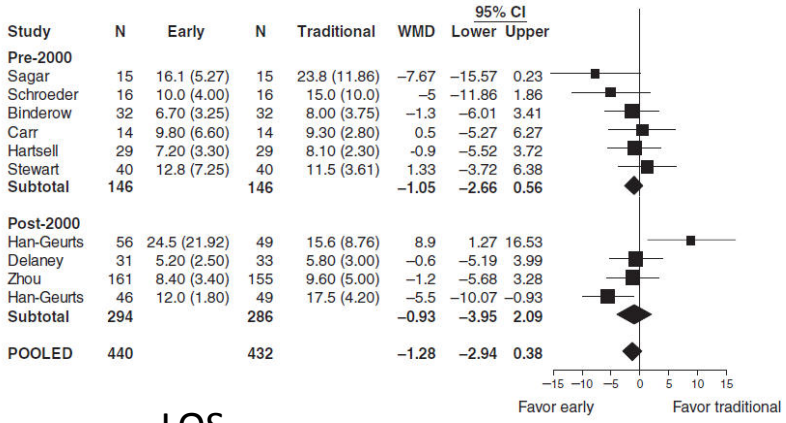
Study	Early	Traditional	OR	95% CI Lower	Upper
Pre-2000					
Sagar	0 of 15	1 of 15	0.31	0.01	8.29
Schroeder	0 of 16	0 of 16	1	0.02	53.46
Beier-Holgersen	2 of 30	4 of 30	0.52	0.1	2.65
Carr	0 of 14	0 of 14	1	0.02	53.89
Ortiz	2 of 93	4 of 95	0.56	0.12	2.68
Hartsell	0 of 29	1 of 29	0.32	0.01	8.24
Nessim	0 of 27	0 of 27	1	0.02	52.22
Stewart	1 of 40	0 of 40	3.08	0.12	77.8
Subtotal	**5 of 264**	**10 of 266**	**0.62**	**0.25**	**1.52**
Post-2000					
Han-Geurts	2 of 18	1 of 19	1.87	0.22	15.73
Delaney	0 of 31	0 of 33	1.06	0.02	55.24
Lucha	1 of 26	0 of 25	3	0.12	77.17
Zhou	2 of 161	4 of 155	0.53	0.11	2.52
Han-Geurts	2 of 42	2 of 35	0.83	0.14	5.06
Subtotal	**7 of 278**	**7 of 267**	**0.93**	**0.36**	**2.43**
POOLED	**12 of 542**	**17 of 533**	**0.75**	**0.39**	**1.45**

Anastomotic leak



Study	Early	Traditional	OR	95% CI Lower	Upper
Pre-2000					
Sagar	0 of 15	0 of 15	1	0.02	53.66
Ryan	0 of 7	0 of 7	1	0.02	57.31
Schroeder	0 of 16	0 of 16	1	0.02	53.46
Binderow	0 of 32	0 of 32	1	0.02	51.94
Beier-Holgersen	2 of 30	4 of 30	0.52	0.1	2.65
Carr	0 of 14	1 of 14	0.31	0.01	8.29
Ortiz	0 of 93	0 of 95	1.02	0.02	52.01
Hartsell	0 of 29	1 of 29	0.32	0.01	8.24
Nessim	0 of 27	0 of 27	1	0.02	52.22
Stewart	0 of 40	1 of 40	0.33	0.01	8.22
Subtotal	**2 of 303**	**7 of 305**	**0.58**	**0.22**	**1.54**
Post-2000					
Han-Geurts	0 of 56	3 of 49	**0.12**	**0.01**	2.33
Delaney	0 of 31	0 of 33	**1.06**	**0.02**	55.24
Lucha	0 of 26	0 of 25	**0.96**	**0.02**	50.35
Zhou	0 of 161	0 of 155	**0.96**	**0.02**	48.83
Han-Geurts	3 of 46	1 of 50	**2.66**	**0.38**	18.77
Subtotal	**3 of 320**	**4 of 312**	**1.03**	**0.27**	**3.88**
POOLED	**5 of 623**	**11 of 617**	**0.71**	**0.32**	**1.56**

Mortality

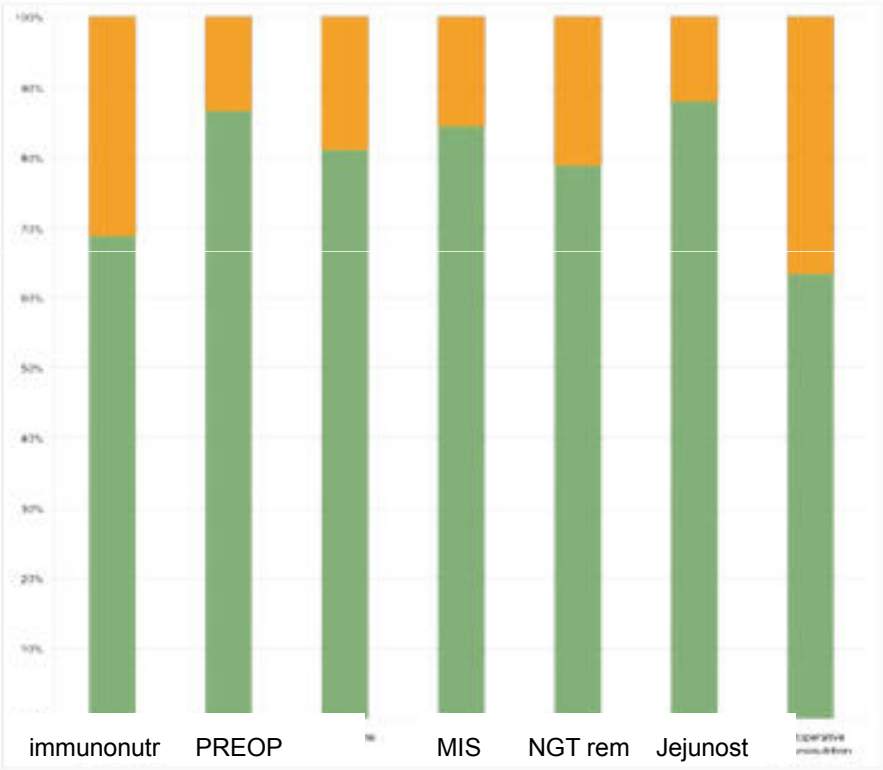


Study	N	Early	N	Traditional	WMD	95% CI Lower	Upper
Pre-2000							
Sagar	15	16.1 (5.27)	15	23.8 (11.86)	−7.67	−15.57	0.23
Schroeder	16	10.0 (4.00)	16	15.0 (10.0)	−5	−11.86	1.86
Binderow	32	6.70 (3.25)	32	8.00 (3.75)	−1.3	−6.01	3.41
Carr	14	9.80 (6.60)	14	9.30 (2.80)	0.5	−5.27	6.27
Hartsell	29	7.20 (3.30)	29	8.10 (2.30)	-0.9	−5.52	3.72
Stewart	40	12.8 (7.25)	40	11.5 (3.61)	1.33	−3.72	6.38
Subtotal	**146**		**146**		**−1.05**	**−2.66**	**0.56**
Post-2000							
Han-Geurts	56	24.5 (21.92)	49	15.6 (8.76)	8.9	1.27	16.53
Delaney	31	5.20 (2.50)	33	5.80 (3.00)	−0.6	−5.19	3.99
Zhou	161	8.40 (3.40)	155	9.60 (5.00)	−1.2	−5.68	3.28
Han-Geurts	46	12.0 (1.80)	49	17.5 (4.20)	−5.5	−10.07	−0.93
Subtotal	**294**		**286**		**−0.93**	**−3.95**	**2.09**
POOLED	**440**		**432**		**−1.28**	**−2.94**	**0.38**

LOS

E Osland – J Parent Ent Nutr 2012

Enhanced recovery program for esophagectomy



Graph. 1: Compliance to protocol in ERAS-pro Group.
Green areas represent the share of good compliance reached for each item.
*** High Carbohydrate Drinks (PREOP)**
**** Minimally Invasive Surgery: Hybrid or Total MI Esophagectomy**
***** Jejunostomies placement conforming to preoperative nutritional status (NRS)**

	ERAS-pro Group	OLD-pro Group
Operative time *	289 (171 – 529)	275 (119 – 538)
Complicated patients (major c.)	22 (24,4%)	33 (36,7%)
Hospital stay		
*All patients **	10 (6 – 70)	12 (7 – 101)
*Pts without complications **	8 (6 – 12)	10 (7 – 21)
Post-operative death	2 (2,2%)	6 (6,7%)

Tab. 2: Results of study. **** median (range)***
p = n.s.

F Puccetti, 12° ESDE Congress 2015

Postoperative setting

Patients submitted to gastrointestinal surgery

10% loss of their preoperative weight

- loss of gastric reservoir function
- lack of appetite
- altered intestinal motility
- gastro-oesophageal reflux

Feeding jejunostomies

Timing of discontinuation of jejunal feeding is variable

No studies showing clinical benefit or improvement in QOL from nutritional supplementation following hospital discharge after surgery

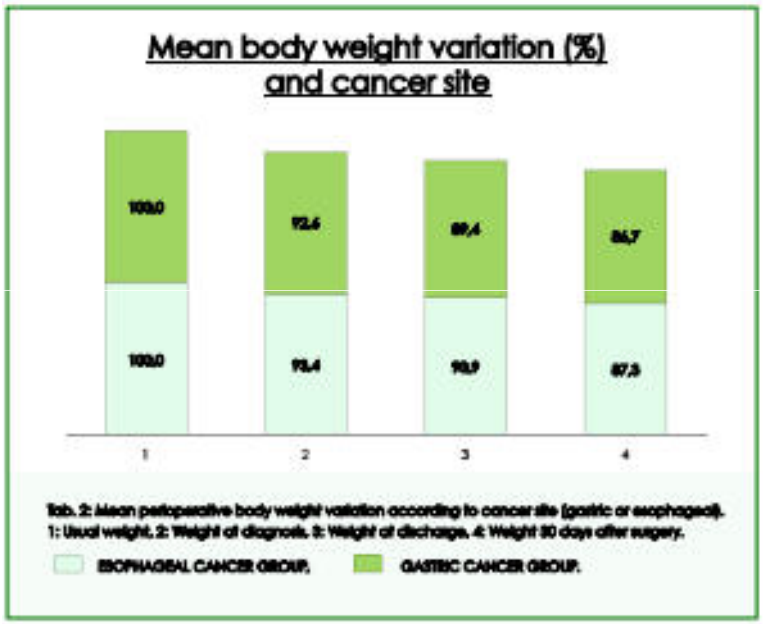
Under nutrition post hospital discharge after UGS may exacerbate the reduced QOL and fatigue

The process of enteral feeding itself may also contribute to a reduced quality of life for these patients. .

Postoperative enteral feeding after upper GI surgery

Material 41 pat. UGS (17 esoph.; 24 total (18) or subtotal (6) gastr.)

Methods Daily enteral and oral intake related to estimated energy requirements (ER).
Enteral feeding POD1. Oral feeding POD3 if uncomplicated. Oral and/or enteral energy intake of at least 60% of ER one of the discharge criterias. Weight variation and alimentary anamnesis at POD 30.



Results 1 Most patients reached their nutritional discharge criteria (NDC) on POD 6. (Oral feeding protocol not followed in 17 complicated cases (group A))

24 patients (group B) at discharge reached their feeding goal with an oral and/or enteral nutrition: oral nutrition was the only feeding route in 19,5% (87,5% of the subgroup of patients submitted to gastrectomy).

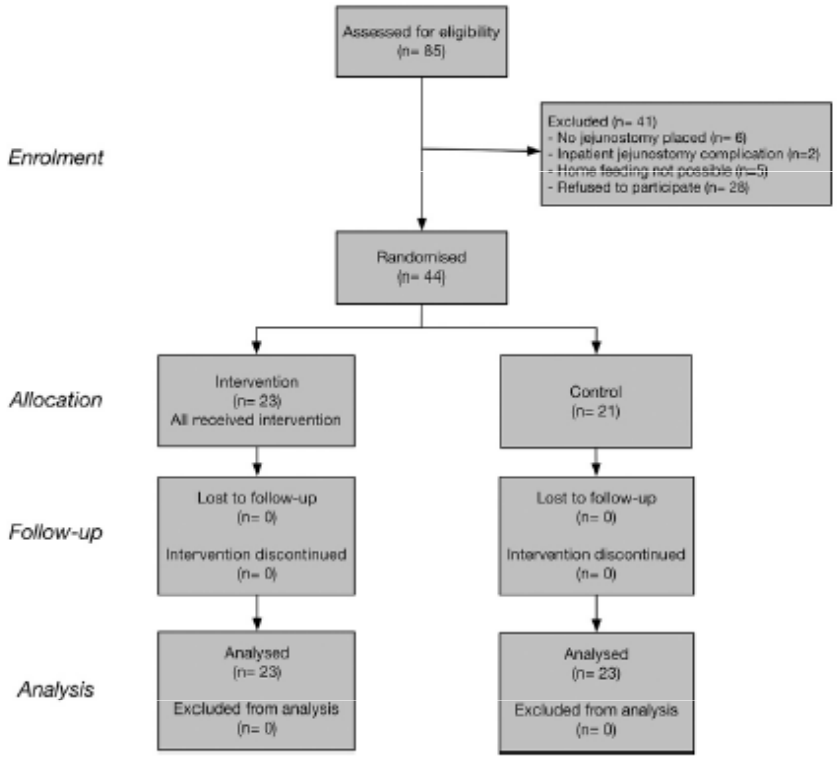
At POD 30 mean body weight variation was -7%. (-8,8% group A 6.1% group B).

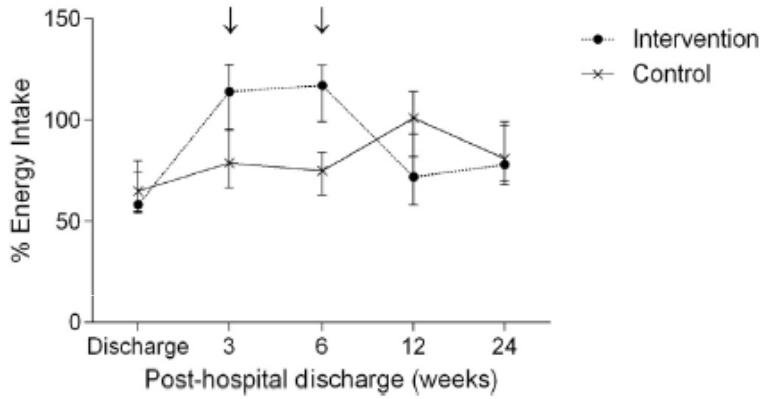
Weight loss of patients in group B submitted to gastrectomy was higher than for patients submitted to esophagectomy.

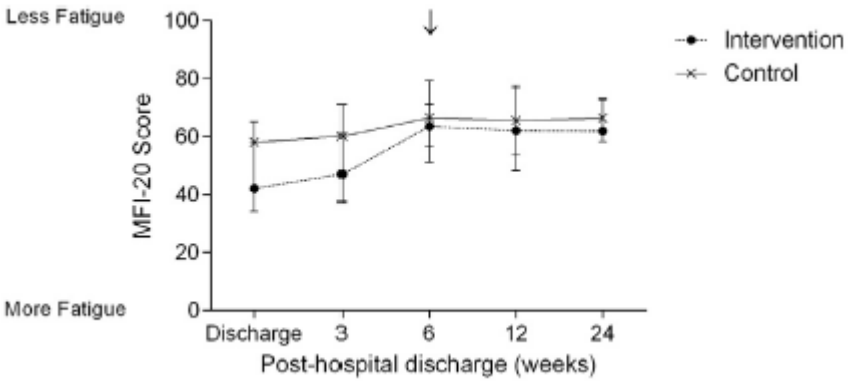
Conclusions Patients submitted to esophagectomy need an enteral feeding in order to reach early the NDC. Patients submitted to gastrectomy have a increased oral feeding but a lower total energy intake, persisting at POD 30.

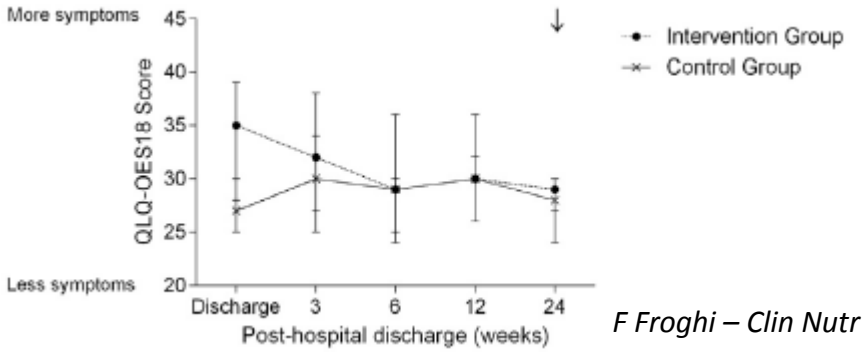
F Puccetti, II World Congress ERAS 2016

Post-discharge enteral feeding following surgical resection of an upper GI malignancy









Jejunal feeds 600 kcal/day of enteral feed via jejunostomy for 6 weeks post hospital discharge

Control group no jejunal feed post hospital discharge

F Froghi – Clin Nutr 2016

Conclusions

Perioperative nutritional support in a malnourished patients undergoing resective surgery for Upper GI cancer is effective in reducing morbidity rate (infection) and LOS

Early postoperative enteral (oral) feeding should aimed at

No data of a clear benefit of routine post discharge enteral nutritional support in patients submitted to resective upper GI cancer surgery

IMPACT Study

- ✓ Esophageal and gastric cancer patients are frequently malnourished
- ✓ Most oesophageal and gastric cancer patients will receive neoadjuvant chemo(radio)therapy that may compromise both nutritional and immune status
- ✓ Immunonutrition is efficient in the perioperative period in digestive cancer patients (ESPEN Guidelines)

2013-2015 a multicenter European randomised controlled trial was run to demonstrate that support of patients' immune function with specific nutritional intervention – immunonutrition – during the neoadjuvant treatment and prior to surgery will **improve the patients' quality of life, reduce post-surgical morbidity, and reduce haematological and mucosal toxicities.**

Design:
358 patients, 179 in each group, with oesophageal or gastric carcinoma considered suitable for curative resection at the time of staging who will receive neoadjuvant chemotherapy or chemotherapy plus irradiation neoadjuvant treatment.

Patients randomized in two groups and will receive the test product or an isocaloric control from at least one week prior to the beginning of the neoadjuvant treatment, by the oral route or via a tube until the 7th postop day

Results waited for by end 2017