

Multimodality therapy for esophageal cancer: should nutritional support be included?

Federico Bozzetti



ESMO SYMPOSIUM
Zurich 20-21 March 2009

TOPICS

- Nutritional status: obesity and weight loss (WL)
- Metabolic patterns
- Causes for the WL
- Malnutrition (obesity and WL) and prognosis
- Nutritional support:
 - Oral nutritional supplements (ONS)
 - Tube feeding (TF) and parenteral nutrition (PN)
 - Perioperative nutrition

OBESITY and W L

- Obesity/overweight are a risk factor for EC
- In > 50% BMI is high despite 74% of pts are losing weight (*Ryan 2006*)
- WL in 32 to 69% (*Martin 1999,Daly 2000,Bailey 2003*)
- Mean WL 13% (*Bozzetti 1989*)

METABOLIC PATTERNS

- Increased EE in 23% of pts (*Dempsey 2000*)
- Increased glucose turnover and alanine-to-glucose cycle (*Burt 1982*)
- Increased peripheral glucose uptake and lactate release (*Burt 1982*)

CAUSES for the WL

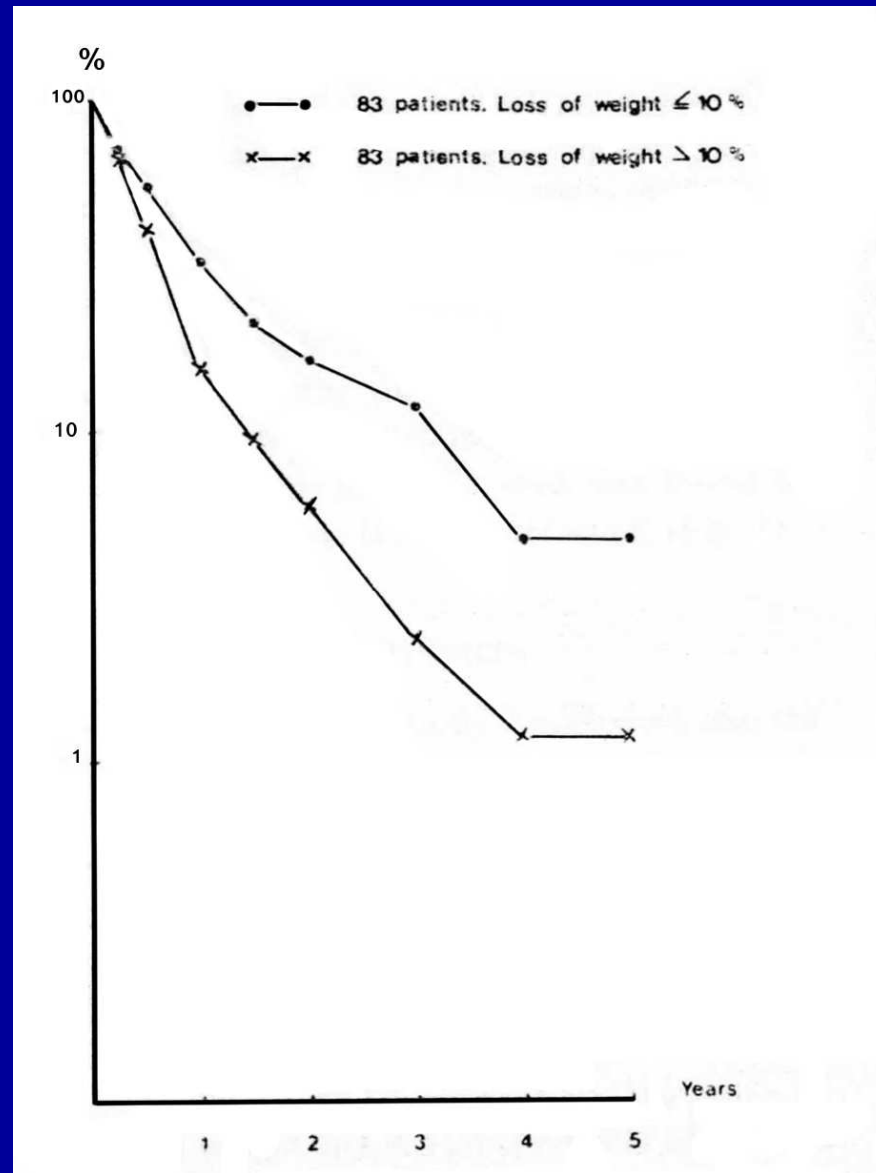
- WL is associated with reduced dietary intake, serum CRP, stage (38%,34%,28%) and IL10 genotype *(Deans 2009)*
- Cytotoxic agents and RT

OBESITY as a PROGNOSTIC FACTOR

- Injured obese pts have a block in fat metabolism and utilization, and ↑ in protein catabolism (*Jeevanandam 1991*)
- Esophagectomy in obese pts is associated with technical difficulties, longer operative times (*Blee 2002*), higher incidence of complications, longer hospital stay (*Dickerson 2002, McWhirther 1994, Fettes 2002, Healy 2007*)

WL as a PROGNOSTIC FACTOR

- WL > 15% is associated with higher postop. morbidity and mortality (62 and 38% vs 0) (*Conti 1977*)
- Malnutrition is associated with anastomotic failure (*Belghiti 1983*)
- Validity of the “Nutritional assessment index” (*Iwasa 1983, Nozoe 2002*)
- PNI is associated with long-term survival (*Nozoe 2002*)
- WL (>or<10%) should be integrated in stage-grouping (*Pedersen 1982*)



INDICATION FOR NUTRITIONAL SUPPORT

- ▶ Non dysphagic/weight-losing patients undergoing CT&RT



ONS, intensive counseling, both

- ▶ Dysphagic/weight-losing patients



TF, PN

INDICATION FOR NUTRITIONAL SUPPORT

- ▶ **Non dysphagic/weight-losing patients undergoing CT&RT**



ONS, intensive counseling, both

ONS during RT

- 3 RCT (ONS vs standard care):
 - ↑ in AA and energy intake (*Arnold 1989, Moloney 1983, Nayel 1992*)
 - ↑ in BW and TSF (*Nayel 1992*)
- 2 RCT (ONS+intensive counseling vs standard care):
 - ↑ in nutritional status and QoL, ↓ adverse effects of RT (*Isenring 2004, Ravasco 2005*)

INDICATION FOR NUTRITIONAL SUPPORT

▶ Dysphagic/weight-losing patients



TF and PN

- (I) metabolic effects**
- (II) TF during RT**
- (III) perioperative EN and PN**

(I) RCT COMPARING the METABOLIC EFFECTS of EN vs PN

(Lim 1982)

NUTRITIONAL PARAMETER	EN	PN
Weight	↑ 1% after 30 d	↑ 6% after 30 d
N balance	Pos after 7 d	Pos after 1 d
Albumin	↑ 7.4%	↑ 6.3%

(I) RCT COMPARING the METABOLIC EFFECTS of EN vs PN

(Burt 1982-83, Pearlstone 1995)

Nutritional Parameter	EN	PN	P
Weight	No change	Increase	0.05
N balance	No change	Increase	0.05
Albumin	Decrease	No change	
Transferrin, ceruloplasmin, TBK,	No change	No change	
Glucose turnover rate	↑ x 4	↑ x 4	
Gluconeogenesis from alanine	Suppressed	Suppressed	
Plasma aminoacid level	Maintained	Increase	

(I) Metabolic effects of the nutritional support *(Burt 1983,1984)*

- EN and PN lead to similar changes in substrates and hormonal environment
- EN and PN increase protein synthesis
- EN and PN decrease urinary 3Me-His

(II) TUBE FEEDING during RT

- Patients are always dysphagic, hence not suitable for RCT
- TF reduces WL, maintains QoL, prevents interruptions of therapy, decreases hospital admissions (*Campos 1990, Fietkau 1991, Tydesley 1996, Bozzetti 1998, Lee 1998, Marcy 2000, Odelli 2005*)
- Nasogastric tubes and PEG are equally effective from the nutritional point of view (*Mekhail 2001*)
- PEG does not compromise subsequent surgery (*Margolis 2001, Stockeld 2001*)

(III) R*CT COMPARING PN with EN

Author	N. pts	OUTCOME
Lim*	24	PN: better N Bal, ↑ BW
Baigrie*	97	No difference
Reynolds *	67	No difference
Page*	40	No difference in Arg-EN vs standard fluid
Gabor	88	EN: shorter ICU and hospital stay

(III) R*CT COMPARING IMMUNENUTRITION vs STANDARD NUTRITION

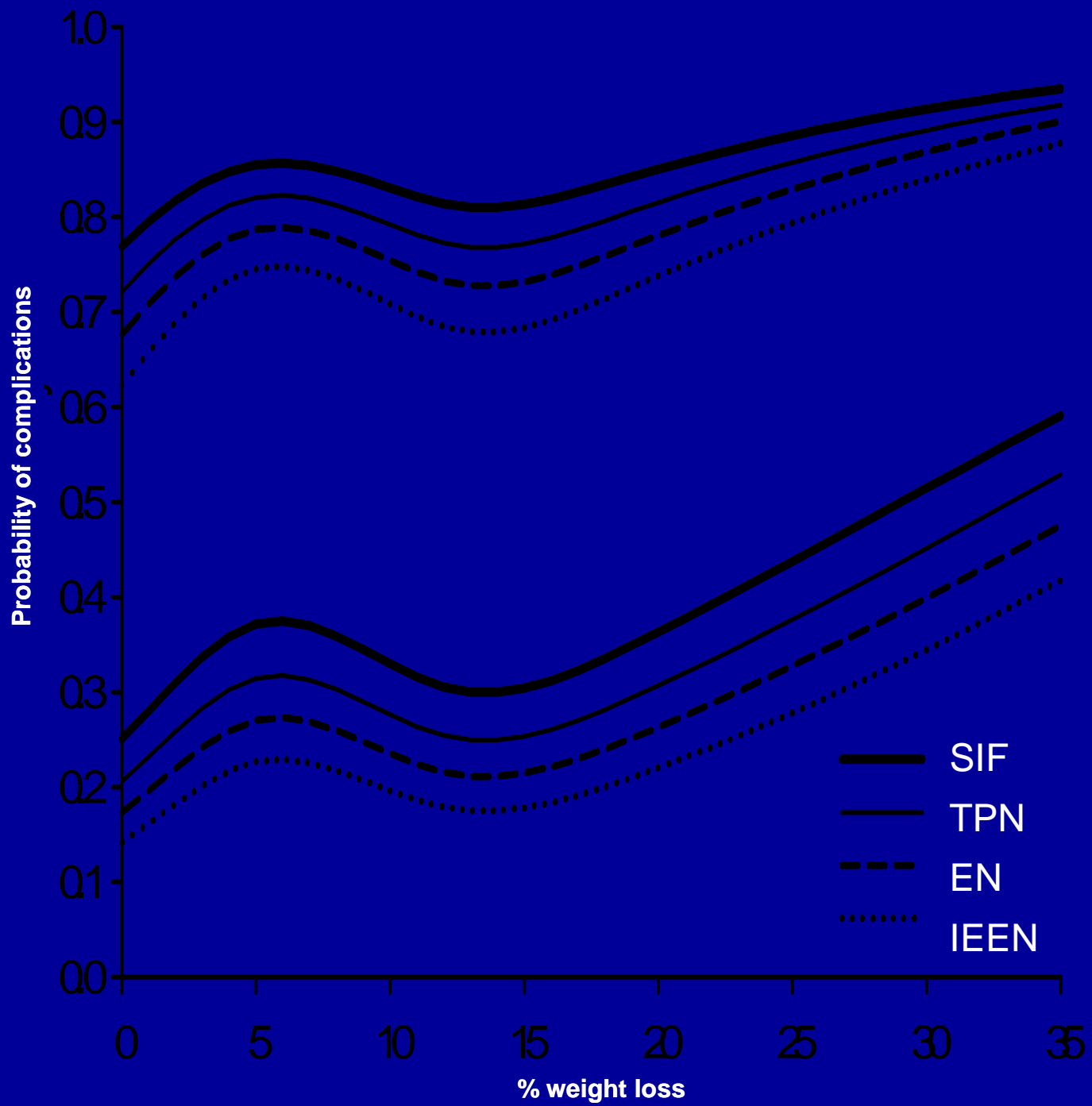
AUTHOR	N. pts	STUDY	OUTCOME
Sakurai *	30	po n-3 EN	n-3 ↑ TLC
Van Bokh*	49	Arg-EN	Arg↑ immune response
Takagi *	15	EPA- PN	EPA ↓ immune suppression
Takeuki	40	n-3 EN	n-3 ↓ infections
Aiko	29	n-3 EN	n-3 ↑ T cells

Bozzetti F, Gianotti L, Braga M, Di Carlo V, Mariani L.

Postoperative complications in gastrointestinal cancer patients: the joint role of the nutritional status and the nutritional support

CLIN NUTR 2007; 26:698-709

BACKGROUND & AIMS: This study investigated the effects of nutritional support on postoperative complications, in relation with demographic and nutritional factors, intraoperative factors, type and routes of nutritional regimens. **METHODS:** A series of 1410 subjects underwent major abdominal surgery for gastrointestinal cancer and received various types of nutritional support: standard intravenous fluids (SIF; n=149), total parenteral nutrition (TPN; n=368), enteral nutrition (EN; n=393), and immune-enhancing enteral nutrition (IEEN; n=500). Postoperative complications, considered as major (if lethal or requiring re-operation, or transfer to intensive care unit), or otherwise minor, were recorded. **RESULTS:** Major and minor complications occurred in 101 (7.2%) and 446 (31.6%) patients, respectively. Factors correlated with postoperative complications at multivariate analysis were pancreatic surgery, ($p < 0.001$), advanced age ($p = 0.002$), weight loss ($p = 0.019$), low serum albumin ($p = 0.019$) and nutritional support ($p = 0.001$). Nutritional support reduced morbidity versus SIF with an increasing protective effect of TPN, EN, and IEEN. This effect remained valid regardless the severity of risk factors identified at the multivariate analysis and it was more evident by considering infectious complications only. **CONCLUSIONS:** Pancreatic surgery, advanced age, weight loss and low serum albumin are independent risk factors for the onset of postoperative complications. Nutritional support, particularly IEEN, significantly reduced postoperative morbidity



RECOMMENDATIONS

Non dysphagic cancer pts undergoing RT

*Intensive nutritional counseling
(with/without supplements) improves
nutritional state and quality of life during
RT and decreases early and late radiation
toxicity (Grade A).*

RECOMMENDATIONS

Dysphagic patients undergoing CT&RT

In weight-losing hypophagic patients, EN (TF/PEG) may be delivered to improve or to maintain the nutritional status and to ameliorate the compliance to therapy (Grade B).

RECOMMENDATIONS

Surgical patients

The role of perioperative EN or TPN is uncertain due to the paucity of the series. However, other studies in malnourished GI cancer patients showed that nutritional support is beneficial on the occurrence of complications (**Grade B**).

RECOMMENDATIONS

Surgical patients

ESPEN GL on EN (2006) and PN (2009) recommend immune EN in all patients candidate for major surgery and (immune)EN or PN in weight-losing ones.