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# Clinical outcome of peri-operative enteral immunonutrition for oesophago-gastric cancer

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 10/03/2008 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 12/02/2009 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 31/07/2012 | Cancer | |

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**Protocol serial number**
N/A

## Study information

**Scientific Title**

The effect of peri-operative immunonutrition for oesophago-gastric cancer surgery on antioxidant status, oxidative damage and clinical outcome

## Study objectives
Our aims were to study the effect the enteral peri-operative immunonutrition in patients undergoing oesophago-gastric cancer surgery on:
1. Fatty acid plasma concentrations
2. Number of patients developing infective complications
3. Critical care and hospital length of stay
4. In-hospital mortality

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
First provided by committees of the two hospitals involved (Joint Universities and Newcastle Health Care Trust and the Multi-Research Ethics Committee):
1. Newcastle and North Tyneside Health Authority Joint Ethics Committee on the 15th November 2003 (ref: 2001/266)
2. South Tees Hospital NHS Trust on the 6th June 2002 (ref: 02/X1X)

## Study design
Randomised controlled three-armed trial

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Oesophago-gastric cancer

## Interventions
Patients were randomised to one of the following groups:

Arm 1: enteral immune enhancing diet (IED) -
This group received IED (Oxepa), seven days pre- and post-operatively. Oxepa is a complete balanced liquid feed containing omega-3 fatty acids (FAs) and antioxidants (eicosapentaenoic acid [EPA] = 0.51g per 100 ml, docosahexaneoic acid [DHA] = 0.22 g per 100 ml and Vitamin E = 21.4 mg per 100 ml). The energy density is 1.5 kcal/ml with a protein content of 6.25 g/100ml. There is no free arginine or glutamine in this feed.

Arm 2: standard enteral nutrition (SEN) -
This group received a standard nutritional formula (Ensure plus), seven days pre- and post-operatively. This is an isonitrogenous, isocaloric enteral feed without immunonutrients

Arm 3: control -
This group received no pre-operative nutritional support. Post-operatively, patients received nutritional support according to clinical requirements and consultant preference. Patients in this arm received Omolite which has no immunonutrients and lower energy and protein.

Clinical management:
All patients underwent surgical resection for upper gastrointestinal cancers. Patients with unresectable disease were withdrawn from the trial. Either nasojejunal tubes or feeding jejunostomy (Freka 9 Fr or silastic Foley 12 Fr) were inserted into the proximal jejunum at the time of the operation. Routine blood investigations (full blood count [FBC], urea and electrolytes [U+Es], liver function tests [LFTs] and C-reactive protein [CRP]) were measured seven and one days pre- and post-operatively. Fresh blood samples were transported on ice. They were then separated into plasma, red blood cells and lymphocytes into Ependorfs. Subsequently, all samples were stored in a -800°C freezer prior to analysis.

After recruitment into the study all patients underwent a standardised nutritional assessment by one of two qualified dieticians. The assessments included:
1. Weight (kg) and body mass index (BMI) (kg/m^2), seven and one days pre-, seven days post-operatively and on discharge
2. Percentage unintentional weight loss three months prior to surgery measured objectively
3. Full dietary assessment using 24 hour recall
4. Anthropometry (Jejeebhoy and Keith 2005): measurements were taken seven days pre-operatively, 7 and 14 days post-operatively:
4.1. Triceps skin fold thickness (TSF): this provides an estimate of the subcutaneous fat deposit and therefore can be used to estimate the amount of total body fat. Skinfold callipers (John Bull, British Indicators Ltd) were used in mm on the underside of the mid-point of the non-dominant upper arm, with the arm hanging loosely at the side and skin-fold parallel to the longitudinal axis of the arm.
4.2. Mid arm circumference (MMC) was measured by tape measure midway between the acromid process and the olecranon process of the non-dominant arm, with the patient's arm relaxed and hanging downwards
4.3. Mid-arm muscle circumference (Thomas and Bishop 2007): the following equation was used:

MAMC (cm) = MMC (cm) - [pi x TSF (mm)]

The fat-free mass is a combination of lean tissue (protein), water, and minerals. Since muscle is the major protein store it has been used to estimate the protein reserves of the body. MAMC and mid-arm muscle area (MAMA) provide a measure of muscle mass which is correlated with measures of total muscle mass and therefore protein status.

Pre-operative feeding:
All patients were advised to consume standard food and fluids pre-operatively and to follow their current eating plan. Pre-operative feeding was carried as outpatient therapy for seven days prior to surgery in those in the IED and SEN arms. The desired volume of enteral nutrition was 675 ml daily. The amount of artificial feed consumed was recorded in a specially designed diary. Patients were admitted to the clinical ward on the day prior to surgery.

Post-operative feeding:
A feeding jejunostomy or a fine bore nasojejunal tube was placed intra-operatively to allow post-operative enteral feeding. Patients followed the following feeding regime:
Day 1: feeding access flushed 25 ml four hourly for the first 12 hours, progressing to 25 ml/hour sterile water infusion using the quantium pump

Day 2: Commenced 25 ml/hour of feed
Day 3: Increased to 50 ml/hour of feed and to reach desired maximum rate
Days 4 - 7: Continued feed at the maximum rate
Day 8: If feed was required to continue after day seven, the feed was changed to a standard feed (Osmolite or Jevity)

Patients reached their maximum rate depending on clinical progress on an individual basis. It was not considered harmful to reach the maximum rate between three to seven days. All patients were allowed oral fluids proceeding to receive semi-solid and then normal diet as soon as this was clinically indicated and tolerated. Oesophagectomy patients were continued at a maximum rate till they were started on a soft diet (usually days 9 or 10). Patients who managed oral diet were converted to receiving overnight feeds only for two to three days. Intravenous blood and fluid replacement was continued as clinically required. Nasojejunal tubes were usually removed in total gastrectomy patients between days 8 to 10. Feeding jejunostomy were reviewed at a combined dietician/upper gastrointestinal nurse specialist clinic, two weeks following discharge, and removed generally provided that patients were meeting their nutritional requirements.

Energy requirements were calculated on an individual basis, at the start of the trial, by two experienced senior dieticians using equations for estimating basal metabolic rate. This provided guidelines on the nutritional requirements for adults requiring enteral nutrition by determining basal metabolic rate (BMR), adjusting for stress or weight loss and added a combined factor for activity and diet-induced thermogenesis (DIT). Nitrogen requirements were also calculated at the same time. Patients were considered to be in a hypermetabolic state so the nitrogen was calculated as 0.2 g/kg/day (Elia 1990).

The only violation to this protocol was in cases of chylothorax which may have been a consequence of thoracic duct injury, failure of ligation at surgery or duplicate ducts. This usually presented seven days after surgery when the patient had commenced oral intake, especially of fat-containing nutrients. Conservative management involved changing the enteral feed to one with medium-chain triglycerides to help decrease chylous loss. In the need for surgical intervention, a pre-exploratory intake of enteral fat (Peptac) was used to help locate the leaking duct.

## Intervention Type
Other

## Phase
Not Applicable

## Primary outcome(s)
Development of infective complications. Infective and non-infective complications were noted and graded daily up until discharge. Complications were defined as those published previously (Bozzetti, Braga et al. 2001). This was collected consistently by two full time research registrars designated to the trial.

## Key secondary outcome(s))
Non-infective complications, mortality, duration of hospital stay and nutritional status:
1. Jejunostomy/feeding-related complications: recorded daily till discharge
2. Antibiotic usage: the duration of both prophylactic and therapeutic antibiotic usage was noted
3. Length of hospital and critical care stay

4. Mortality: both in hospital and 30 days post-operatively was recorded
5. Concentration of fatty acids in plasma
6. Nutritional status: recorded by two dieticians such as weight, BMI, triceps skin fold thickness and mid-arm muscle circumference

### Completion date
01/01/2007

## Eligibility

### Key inclusion criteria
All patients (either sex) presenting to two tertiary centres, between April 2003 to January 2007, with histologically proven oesophageal or gastric malignancy and who were suitable for subtotal oesophagectomy or total gastrectomy with curative intent were eligible for the study.

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
All

### Key exclusion criteria
1. Less than seven days time from recruitment to operation date
2. Metastatic or unresectable disease
3. Respiratory tract dysfunction (partial pressure of oxygen in arterial blood [PaO2] less than 70 mmHg)
4. Cardiac dysfunction (New York Heart Class greater than three)
5. Hepatic dysfunction (Child-Pugh score greater than B)
6. Concurrent infection
7. Pregnancy
8. Aged less than 18 years

### Date of first enrolment
01/04/2003

### Date of final enrolment
01/01/2007

## Locations

### Countries of recruitment
United Kingdom

England

**Study participating centre**
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# Sponsor information

**Organisation**
The Northern Oesophago-Gastric Cancer Unit (NOGCU) (UK)

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
The Northern Oesophago-Gastric Cancer Unit (NOGCU) (UK) - Professor SM Griffin

**Funder Name**
The Newcastle Healthcare Charity (the Trustees) (UK) - £10,000 awarded for consumables

# Results and Publications

## Individual participant data (IPD) sharing plan

**IPD sharing plan summary**
Not provided at time of registration

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/03/2012 | | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |