ISRCTN11154654 https://doi.org/10.1186/ISRCTN11154654

Standard (D1) versus extended (D2) lymph node dissection during gastrectomy for gastric cancer in Italy: a randomised comparison of morbidity, mortality and survival

Submission date 30/03/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/04/2009	**Overall study status** Completed	
Last Edited 23/04/2021	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Italian Gastric Cancer Study Group (IGCSG) randomised clinical trial of morbidity, mortality and survival after D1 and D2 gastrectomy for gastric cancer in western patients

Acronym
IGCSG-R01

Study objectives
Nowadays D2 gastrectomy is the gold standard in most countries from the Far East. In western countries extended procedures have never gained much popularity for two main reasons. First, the evidence of survival benefit after D2 in Japan had been based solely on observational and retrospective studies. Second, although low morbidity and mortality rates have been reported also in western centres in retrospective studies, the fear of increasing post-operative complications and death rates has been confirmed by two large scale randomised controlled trials (RCTs) recently performed in Europe, which strongly concluded that D2 dissection was not recommended for western patients and made the British National Health service guidance discourage the use of D2 technique in routine clinical practice.

However, more recently the evidence of survival benefit after extended dissection in the Far East has finally come also from a RCT. Moreover, different critical appraisals of the European RCTs have concluded that the increase of morbidity and mortality observed in these trials were mostly related to spleno-pancreatectomy routinely performed in D2 total gastrectomies and to the little experience/volume of hospitals and surgeons involved, that this significant increase may have offset the long-term survival benefit of the procedure and that D2 dissection may offer cure to subset of patients with N2 disease; therefore, D2 gastrectomy may be of benefit if morbidity and mortality can be avoided.

Based on these previous reports, in 1994 the Italian Gastric Cancer Study Group (IGCSG) designed a multicentre phase II trial to test the feasibility and the safeness of the extended procedure performed in western patients with pancreas preserving splenectomy and strict quality control applied over all the centres. We found post-operative morbidity and mortality rates of 20.9% and 3.1%, comparable with those reported after the western standard D1-gastrectomy. Once documented the feasibility and safeness of D2 procedure in Italy, we have set up this new multicentre RCT to compare outcome and survival effects of D1 versus D2 (IGCSG-R01). This is the fourth RCT performed all over the world comparing these two procedures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
When our RCT was designed in 1998, there was no need for ethical approval according to regional and national regulations.

Study design
Interventional multicentre two-armed randomised controlled surgical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Gastric cancer

Interventions
The study was performed according to the rules of the JRGC as regards the extent of stomach removal and the technique of lymph-node dissection (D1 and D2 procedures) and to the Japanese Classification of Gastric Carcinoma - second English Edition by the Japanese Gastric Cancer Association, particularly as concerning the definitions of classifications and grouping of regional lymph nodes, the extent of lymph node metastasis (N) and the curative potential of gastric resection (Resection A, B or C). In this new classification the regional lymph nodes are classified into three groups (compartments or levels or tiers 1 - 3), depending upon the location of the primary tumour. The operative details of the two procedures respected the general rules for gastric cancer study, as described by the Japanese Research Society for Gastric Cancer in 1981. D1 resection entailed removal of the nodes usually defined as perigastric nodes (n1 nodes) 'en bloc' with the specimen, according to the JGCA. In D2 surgery lymph nodes of n1 tier where removed together with n2 tier nodes. In the D2 arm, during total gastrectomy, the pancreas was removed only when it was suspected to be involved by the tumour. When required (clinical T greater than 1 on the greater curvature of the proximal and middle thirds of the stomach), splenectomy was performed with the pancreas preservation technique as described by Maruyama. We have considered two different types of protocol deviation: "contamination" for D1 and "non-compliance" for D2. "Contamination" was the deviation with the pathological proof of more than 2 LN stations that were not supposed to be removed while "non-compliance" was the deviation represented by the absence of LN from more than two LN stations that were required.

Arm 1, D1 gastrectomy: the time for this procedure ranged from 3 hours to 4 hours depending on the extent of gastrectomy (3 hours for distal gastrectomy and 4 hours for total gastrectomy)
Arm 2, D2 gastrectomy: the time for this procedure ranged from 4 hours to 5 hours depending on the extent of gastrectomy (4 hours for distal gastrectomy and 5 hours for total gastrectomy)

Analysis of main outcome (survival) will be performed when at least 95% of recruited patients have accrued at least 5 years of follow up.

Intervention Type

Other

Phase
Not Applicable

Primary outcome measure
Survival: follow-up for mortality analysed with the Kaplan-Mayer risk assessment.

Secondary outcome measures
1. Complications (general and surgical) and reoperations assessed post-operatively
2. Hospital mortality, defined as death occurring within 30 days from the procedure or during patient's hospital stay

Follow-up was done at regular intervals (4 months) and follow-up data were sent every 6 months to the Reference Centre where all data were collected.

Overall study start date
01/06/1998

Completion date
13/11/2006

Eligibility

Key inclusion criteria
1. Histology proven and potentially curable gastric adenocarcinoma, not requiring emergency surgery
2. Aged younger than 80 years, either sex
3. In adequate physical condition without serious co-morbid cardio-respiratory diseases which could preclude a safe D2 procedure
4. Have not undergone previous gastric surgery
5. Does not harbor a coexisting cancer

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
320

Key exclusion criteria
1. Absence of macroscopic involvement of liver and peritoneum (HO, PO)
2. Absence of macroscopic involvement of adjacent organs (T less than 4)
3. Absence of macroscopic massive involvement of N2 nodes (enlarged nodes at coeliac area)
4. Absence of malignant cells in para-aortic nodes (16B1) at biopsy and frozen section

5. Absence of malignant cells in peritoneal washing fluid, during intra-operative fresh examination
6. Absence of macroscopic residual tumour (RO)
7. No involvement of the oesophagus, cardia or duodenum

Date of first enrolment
01/06/1998

Date of final enrolment
13/11/2006

Locations

Countries of recruitment
Italy

Study participating centre
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Sponsor information

Organisation
Health Research Aimed at the Regione Piemonte (Ricerca Sanitaria Finalizzata della Regione Piemonte) (Italy)

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Sponsor type
Government

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Funder(s)

Funder type
Government

Funder Name
Ministry of Health (Italy) - Health Research Program 2003 (ref: DEG/001 - delibera Prot. n. 1837 /27.001)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Other publications	interim analysis	01/04/2004		Yes	No
Results article	results	01/05/2010		Yes	No
Results article	results	01/01/2014		Yes	No
Results article	fifteen-year follow up results	01/06/2021	23/04/2021	Yes	No