Pancreaticoduodenectomy (classical Whipple) versus pylorus-preserving pancreaticoduodenectomy (pp Whipple) for surgical treatment of periampullary and pancreatic carcinoma (Protocol)

Diener MK, Heukaufer C, Seiler CM, Antes G, Buchler MW, Knaebel HP

This is a reprint of a Cochrane protocol, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2006, Issue 2

http://www.thecochranelibrary.com
# Table of Contents

- **Abstract** .................................................. 1
- **Background** ............................................... 1
- **Objectives** ............................................... 2
- **Criteria for Considering Studies for This Review** .................................................. 2
- **Search Methods for Identification of Studies** .................................................. 2
- **Methods of the Review** ...................................... 3
- **Potential Conflict of Interest** ................................ 4
- **Sources of Support** .......................................... 4
- **References** .................................................. 4
- **Cover Sheet** ................................................ 5
Pancreaticoduodenectomy (classical Whipple) versus pylorus-preserving pancreaticoduodenectomy (pp Whipple) for surgical treatment of periampullary and pancreatic carcinoma (Protocol)

Diener MK, Heukaufer C, Seiler CM, Antes G, Buchler MW, Knaebel HP

Status: New

This record should be cited as:

This version first published online: 19 April 2006 in Issue 2, 2006.
Date of most recent substantive amendment: 30 January 2006

ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:
Several publications pointed out both advantages and disadvantages of both techniques and the current basis of evidence remains unclear. The objective of this systematic review is to compare the effectiveness of each technique.

BACKGROUND

Pancreatic cancer is the fourth leading cause of cancer death for men and the fifth for women, accounting for 4.8% of cancer deaths in men and 5.5% in women (Edwards 2002; Jemal 2005). The aggressive biology of these tumours and the high local recurrence rate, together with the early metastatic spread, leads to disappointing five-year survival rates of between 11 and 21% after resection in large series (Sperti 1996; Yeo 1995).

The current standard therapy for pancreatic tumours situated in the head of the pancreas is the resection (Lillemoe 2000; Buchler 2003). The great improvement in pancreatic surgery has lead to mortality rates of fewer than 5% in high volume centres (Buchler 2003; Trede 1990; Yeo 1997). Moreover, mortality and morbidity rates after resection reached similar levels compared to palliative bypass operation (Gouma 1999; Koslowsky 2001; Lillemoe 1996). Nevertheless, operative morbidity remains high, occasionally approaching 30% to 40% (Bassi 2001; Gouma 2000; Richter 2003), from causes including intra-abdominal abscesses, sepsis, pancreatic fistula and delayed gastric emptying.

Two operation techniques are mainly performed in the treatment of pancreatic head cancer: the c-Whipple operation developed by Kausch (Kausch 1912) and Whipple (Whipple 1935), and the pp-Whipple operation inaugurated by Watson (Watson 1944) and popularised by Traverso and Longmire (Traverso 1980).

The c-Whipple operation consists of an en bloc removal of the pancreatic head, the duodenum, the common bile duct, the gall bladder and the distal portion of the stomach together with the adjacent lymph-nodes (Trede 1993). This operation can lead to special complications such as early and late dumping, postoperative weight loss (Seiler 2000) and postoperative reflux (Williamson 1993).

The pp-Whipple operation preserves the stomach and pylorus which is needed for the physiologically timed transport of chyme. The extent of this resection is obviously lower than the c-Whipple operation and it is therefore expected that the operation time decreases and blood loss is lower. In addition, some authors report an improved postoperative weight gain (Seiler 2000), a higher quality of life (Wenger 1999) and a better access to the biliary anastomosis for postoperative endoscopy in patients with recurrent biliary
It is unclear whether the lower extent of the resection is justified if regarded from the oncological side and if delayed gastric emptying occurs more often in the pp-Whipple operation than in the c-Whipple operation.

**OBJECTIVES**

Several publications pointed out both advantages and disadvantages of both techniques and the current basis of evidence remains unclear. The objective of this systematic review is to compare the effectiveness of each technique.

**CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW**

**Types of studies**

Randomised controlled trials (RCTs) irrespective of publication status or language.

**Types of participants**

Patients undergoing a pp-Whipple or a c-Whipple operation for periampullary or pancreatic carcinoma.

**Types of intervention**

- "pp-Whipple operation"
- "c-Whipple operation"

**Types of outcome measures**

**Primary outcome measures**

- Postoperative pancreatic associated morbidity (disease specific) such as:
  1. Leakage of pancreatic anastomosis/pancreatic fistula
  2. Intraabdominal fluid collection/abscess
  3. Delayed gastric emptying
  4. Biliary leakage
  5. Postoperative bleeding

**Secondary outcome measures**

1. Overall mortality
2. Operation time
3. Blood loss
4. Required blood replacement
5. Status of resection margins (R0/R1 resection)
6. Number and status of removed lymph nodes
7. Duration of ICU stay
8. Duration of hospital stay
9. Quality of life
10. Survival
11. General morbidity:
   - Postoperative gastrointestinal bleeding
   - Shock
   - Sepsis
   - Pulmonary insufficiency
   - Renal failure
   - Postoperative weight loss
   - Early and late dumping
   - Pancreatic exocrine and endocrine insufficiency
   - Postoperative reflux
   - Necessity for re-operation

Each of these outcome measures must be defined in the studies in order to compare the results sufficiently.

**SEARCH METHODS FOR IDENTIFICATION OF STUDIES**

See: Upper Gastrointestinal and Pancreatic Diseases Group methods used in reviews.

A search will be conducted to identify all published and unpublished randomised controlled trials.

Trials will be identified by searching the following electronic databases - The Cochrane Library, MEDLINE, EMBASE and Current Contents. Reference lists from trials selected by electronic searching will be hand-searched to identify further relevant trials.

Published abstracts from conference proceedings from the United European Gastroenterology Week (published in Gut) and Digestive Disease Week (published in Gastroenterology) will also be hand-searched.

The search strategy for this review has been constructed by using a combination of MESH subject headings and textwords relating to the use of pancreaticoduodenectomy or pylorus-preserving pancreaticoduodenectomy in the surgical treatment of pancreatic cancer.

To identify randomized controlled trials, the following search will be combined with the Cochrane highly sensitive search strategy phases one, two and three as contained in the Reviewer's Handbook (Clarke 2000)

1. exp Pancreatic Neoplasms/
2. (pancrea§ adj5 neoplas§).tw.
3. (pancrea§ adj5 cancer§).tw.
4. (pancrea§ adj5 carcin§).tw.
5. (pancrea§ adj5 tumo§).tw.
6. or/2-6
7. exp pancreatectomy/
8. (pancrea§ adj5 malig§).tw.
9. exp pancreatectom$.tw.
10. exp pancreaticoduodenectomy/
11. exp pancreaticoduodenectom$.tw.
12. exp pancreaticoduodenectomy$t.tw.
13. exp duodenopancreatectom$.tw.
14. exp pancreaticejuno$tomy/tw.
In addition members of the Cochrane UGPD Group, and experts in the field will be contacted and asked to provide details of outstanding clinical trials and any relevant unpublished materials.

**METHODS OF THE REVIEW**

The analysis will follow the published protocol corresponding to the recommendations given by the Cochrane Collaboration (Cochrane Handbook).

**Trial selection**

Two independent reviewers will scan the abstract of every trial identified by the search to determine eligibility. Identified trials will be listed and each contributor will independently evaluate whether the trials fulfil the inclusion criteria. Full articles will then be selected for further assessment if the abstract suggests the study is relevant. If these criteria are unclear from the abstract, the full article will be retrieved and reviewed for clarification. Papers not meeting inclusion criteria will be excluded and these trials will be listed with the reason for their omission. Any disagreements will be resolved by discussion with a third reviewer and, if necessary, by consultation with the review group’s editors.

**Quality assessment of trials**

Methodological quality is defined as the confidence that the study design and its report will restrict bias in the comparison of interventions (Moher 1998). According to empirical evidence (Jadad 1996; Kjaergard 2001; Moher 1998; Schulz 1995), we will assess the methodological quality by examining the generation of the allocation sequence, allocation concealment, and double blinding. The reviewers will also examine the similarity of treatment groups at baseline and follow-up. Quality assessment will be reported in the methods and results section of the review.

**Data extraction**

Data will be extracted from published and unpublished reports using standardised forms. The following data will be extracted:

1. General study information
   - title, authors, contact address
   - source
   - published/unpublished
   - year of publication
   - trial sponsors

2. Trial characteristics
   - method of randomisation
   - blinding for outcome assessor, patient and carer
   - criteria for patient inclusion and exclusion
   - sample size and sample size calculation
   - baseline characteristics and the similarities of groups at baseline
   - withdrawals and losses to follow-up

3. Study details
   - patient characteristics including mean/median age, age range, sex ratio
   - the specific pancreatic diagnosis leading to the surgical intervention
   - number of patients assigned to each treatment group
   - detail of intervention regimens
   - survival related to each intervention (hazard ratios and their 95% CI, log rank chi square values, log rank p values)
   - postoperative mortality related to each intervention
   - number of removed lymph nodes in each group
   - status of the resection margins
   - blood loss related to each intervention
   - operation time related to each intervention
   - length of hospital stay (and ICU stay) related to each intervention
   - definition of post-operative complications in the articles
   - number and frequency of post-operative complications related to each intervention
   - definition of adverse reactions and outcomes in the articles
   - adverse reactions and outcomes
   - quality of life

Statistical guidance is available from the editorial base and the reviewers’ host institutions. Accuracy of data will be secured by double data entry. Data will be combined from different trials reporting the same or similar comparisons. Dichotomous data will be summarised using, by preference, relative risks whilst continuous data summaries will be presented as weighted mean differences. Any survival or time event data will be summarised using hazard ratios. Data that are difficult to categorise or presented in different forms across trials will be dichotomised and treated as binary data. A subgroup analysis will not be performed.

Pooled estimates of effect will be calculated using the fixed effect model (DeMets 1987) and results will be investigated for statistical heterogeneity (using the I2 statistic). Where heterogeneity remains unexplained an allowance in overall estimates will be made by using random effects models (DerSimonian 1986) in addition to the fixed effect model in order to perform a sensitivity analysis. If there is an extreme level of heterogeneity, summary effect measures will be interpreted with caution. However, causes of heterogeneity will be investigated as far as the collected data allows.
POTENTIAL CONFLICT OF INTEREST

None known.

SOURCES OF SUPPORT

External sources of support

• No sources of support supplied

Internal sources of support

• No sources of support supplied

REFERENCES

Additional references

Bassi 2001

Buchler 2003

DeMets 1987

DerSimonian 1986

Edwards 2002

Gouma 1999

Gouma 2000

Jadad 1996

Jemal 2005

Kausch 1912
Kausch W. Carcinoma of the duodenal papilla and its radical excision [Das Carcinom der Papilla duodeni und seine radikale Entfernung], *Beitr Klin Chir* 1912;78:439–486.

Kjaergard 2001

Koslowsky 2001

Lillemoe 1996

Lillemoe 2000

Moher 1998

Richter 2003

Schulz 1995
Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates...

Seiler 2000

Speriti 1996

Traverso 1980

Trede 1990

Trede 1993

Watson 1944

Wenger 1999

Whipple 1935

Williamson 1993

Yeo 1995

Yeo 1997

---

**COVER SHEET**

**Title**
Pancreaticoduodenectomy (classical Whipple) versus pylorus-preserving pancreaticoduodenectomy (pp Whipple) for surgical treatment of periamplar and pancreatic carcinoma

**Authors**
Diener MK, Heukaufer C, Seiler CM, Antes G, Buchler MW, Knaebel HP

**Contribution of author(s)**
HPK:
Conceiving the review
Coordinating the review
Providing general advice on the review
MD:
Conceiving the review
Designing the review
Data collection for the review
Undertaking searches
Screening search results
Organising retrieval of papers
Screening retrieved papers against inclusion criteria
Appraising quality of papers
Extracting data from papers
Writing to authors of papers for additional information
Providing additional data about papers
Obtaining and screening data on unpublished studies
Data management for the review
Entering data into RevMan
Analysis of data
Interpretation of data
Providing a methodological perspective
Providing a clinical perspective
Providing a policy perspective
Providing a consumer perspective
Writing the review
Providing general advice on the review
Securing funding for the review
Performing previous work that was the foundation of the current study
CH:
Designing the review
Data collection for the review
Designing search strategies
Undertaking searches
Screening search results
Organising retrieval of papers
Screening retrieved papers against inclusion criteria
Appraising quality of papers
Extracting data from papers
Writing to authors of papers for additional information
Providing additional data about papers
Obtaining and screening data on unpublished studies
Data management for the review
Entering data into RevMan
Analysis of data
Interpretation of data
Providing a methodological perspective
Providing a clinical perspective
Providing a policy perspective
Providing a consumer perspective
Writing the review
Securing funding for the review

Issue protocol first published
2006/2

Date of most recent amendment
24 February 2006

Date of most recent SUBSTANTIVE amendment
30 January 2006

What’s New
Information not supplied by author

Contact address
Dr. med. Hanns-Peter Knaebel
Department of General surgery
University of Heidelberg
Im Neuenheimer Feld 110
Chirurgische Universitätsklinik Heidelberg
Heidelberg
69120
GERMANY
E-mail: Hanns-Peter.Knaebel@med.uni-heidelberg.de
Tel: 0049-6221-566986

DOI
10.1002/14651858.CD006053

Cochrane Library number
CD006053

Editorial group
Cochrane Upper Gastrointestinal and Pancreatic Diseases Group

Pancreatoduodenectomy (classical Whipple) versus pylorus-preserving pancreatoduodenectomy (pp Whipple) for surgical treatment of periampullary and pancreatic carcinoma (Protocol)
Copyright © 2006 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd