ChroPac

Duodenum-preserving head resection versus pancreatico-duodenectomy for chronic pancreatitis of the head. A randomized controlled multicentre trial

Study Protocol

(ISRCTN 38973832)

Objective

To investigate differences in

Quality of Life (QoL)

during 24 months after surgery

of duodenum-preserving pancreatic head resection (DPPHR)

versus

pancreatico-duodenectomy (PD)

Design

- **Prospective pragmatic, randomized, controlled**
- **observer and patient blinded**
- **multicentre surgical trial**
- **two parallel study groups**

Definition

- **Pragmatic trials measure effectiveness**
  - **the benefit that a treatment produces in routine clinical practice.**

- **Explanatory trials generally measure efficacy**
  - **the benefit a treatment produces under ideal conditions, often using carefully defined subjects in a research clinic.**

Roland M, Torgerson DJ. What are pragmatic trials? BMJ. 1998 Jan 24;316(7127):285.

Population

- Patients with chronic pancreatitis of the head and pain eligible for elective surgical resection
- Ability of subject to understand character and individual consequences of the clinical trial
- Written informed consent
  - Exclusion: Participation in another intervention-trial with interference of intervention and outcome of this study

Hypothesis

- The primary efficacy endpoint is the mean of the EORTC QLQ-C30 scale „physical functioning“ measured 6, 12 and 24 months after surgery. The two-sided null-hypothesis states that both surgical interventions lead to the same expected average QoL scores during 24 months after surgery:

  $H0: \mu1 - \mu2 = 0$

- The two-sided alternative-hypothesis states that the two interventions perform differently in terms of the primary efficacy endpoint:

  $HA: \mu1 - \mu2 \neq 0$.

Sample size

- The prior assumption based on the evaluation of 2 clinical trials [Makowiec F, Gastroenterology 2004 and Farkas G Lang Arch Surg 2006] is a mean intervention group difference of 10% for the EORTC QLQ-C30 scale “physical functioning” (range 0 to 100) with an estimated standard deviation of 20% 24 months after the surgical intervention.
- With a two-sided level of significance α=5% and a power of 1-β=90%, a sample size of **86 patients per intervention group** is required to detect this difference with a two-sided Student´s t- test.

Expected numbers

400 to screen

200 to randomize

172 to analyze

Baseline Data

- After screening, given informed consent and inclusion the following data are documented:

- Demographic Data:
  - Gender, Age, Height (cm), Weight (kg)
- Baseline Clinical Data:
  - Smoking, Alcohol consumption
- Duration of CP related symptoms:
  - Pain (months), Weight loss (months); Diabetes mellitus, Duration of medical treatment (months)

Baseline Data

- **Quality of Life:**
  - **EORTC QLQ-C 30 and PAN 26(CP)**
- **Results of preoperative imaging studies:**
  - **pancreatic head enlargement, enlargement of the common bile duct, compression of retropancreatic vessels**
- **Results of preoperative endoscopy:**
  - **Duodenal obstruction**
- **Frequency of ERCP (Endoscopic Retrograde Cholangio Pancreaticography):**
  - **Frequency of pancreatic stent implantation**

Randomization

- At the day of surgery
  - (centralised web based tool)
  - Block randomization

Group 1:

- Any surgical technique that removes inflamed pancreatic tissue of the head without resection of the duodenum (e.g. Beger, Frey or Berne procedure)

Group 2:

- Pylorus preserving/classic Whipple procedure

Primary efficacy endpoint

Average QoL during 24 months after surgery,

measured 6, 12 and 24 months after surgery

by the EORTC QLQ-C 30 scale
„Physical functioning“

EORTC QLQ-C30

- **Five functional scales**
  - **Physical** **primary endpoint ChroPac**
  - **Role**
  - **Cognitive**
  - **Emotional**
  - **Social**
- **Three symptom scales**
  - **Fatigue**
  - **Pain**
  - **Nausea and vomiting**

Assessment of primary endpoint

- **Investigator fills in**
  - Head line (Centre #, Screening #, Initials, Visit)
- **Patient fills in**
  - Date
  - Questions
  - No signature! No other comments!
- **Back to centre and copy of document**
- **Submission of original to Datamanagement**
- **Documentation „QoL completed y/n“ in eCRF**

Secondary endpoints

- Mortality, Morbidity, Wound Infection (CDC),
- Operation time
- Blood loss assessed by surgeons and anaesthesists
- Pulmonary infection
- Pancreatic fistula (Bassi definition)
- Delayed gastric emptying (Wente definition)
- Initial postoperative hospital stay after randomization

Secondary endpoints

- EORTC CLQ-C30 and PAN 26 (CP) subscores
- Reoperation due to recurrence of chronic pancreatitis
- Weight gain
- New onset of diabetes mellitus requiring treatment
- Development of exocrine insufficiency (continuous supplement of enzymes necessary)
- Total hospital stay after randomization
- Total hospital stay due to chronic pancreatitis within 24 months after randomization

Visits 1-6

Visit	**1** Screening	**2** Day of Surgery	**3** Day of Discharge	**4** 6 Months post OP	**5** 12 months post OP	**6** 24 months post OP
Demographics and baseline clinical data	X					
Inclusion/Exclusion	X					
Randomization		X				
Surgical intervention		X				
Assessment of secondary end-points and safety		X	X	X	X	X
Quality of Life	**X**			**X**	**X**	**X**
Tissue and blood sampling		X				

Monitoring

- **Monitoring will be performed by the KKS Heidelberg.**

- **Monitoring procedures will be adapted to the study specific risk for the patients, interpretations of ICH-GCP (E6) and standard operating procedures (SOP) of the KKS to ensure patient safety and integrity of the clinical data.**

Timetable

• Submission of grant proposal	11/2007
• Peer review	03/2008
• Full application	05/2008
• Peer review	10/2008
• Funding obtained	12/2008
• Ethical approval	04/2009
• International registration (ISRCTN)	04/2009
• Investigators Meeting	05/2009
• First patient	05/2009
• Last patient	04/2011
• Last follow up	04/2013
• Results avaliable	10/2013

Funding for Centres

- Each patient
  - Randomized
  - Treated
  - Documented
  - Follow up completed
- € 1.500
- Three Meetings!

Thank you for participating!

christoph.seiler@med.uni-heidelberg.de