

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: van der Gaag NA, Rauws EAJ, van Eijck CHJ, et al. Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010;362:129-37.

(PDF updated January 15, 2010.)

**Table 1** shows the definitions of complications related to the PBD procedure or surgical treatment.

<b>Severe PBD- and surgery-related complications.</b>	
<b>Complication</b>	<b>Criteria</b>
<b>Specific PBD (ERCP, PTC) related</b>	
Acute pancreatitis	Abdominal pain and a serum concentration of pancreatic enzymes (amylase or lipase) three or more times the upper limit of normal, that required more than one night of hospitalization
Acute cholecystitis	No suggestive clinical or radiographic signs of acute cholecystitis before the procedure and if emergency cholecystectomy is subsequently required
Perforation	Retroperitoneal or bowel-wall perforation documented by any radiographic technique or direct visual evidence
Stent Occlusion	Recurring obstructive jaundice with necessary stent replacement
<b>Specific surgery related</b>	
Pancreaticojejunostomy leakage	Drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than 3 times the serum amylase activity, graded according to clinical course (ISGPS grade A, B, C), or direct visual evidence of defect at anastomosis
Delayed gastric emptying	Gastric stasis requiring nasogastric intubation for 10 days or more, or the inability to tolerate a regular (solid) diet on or before the fourteenth postoperative day, not due to sequelae of intra-abdominal complications (i.e. abscess, anastomotic leakage)
Biliary leakage	Bilirubin in abdominal drain or dehiscence found at laparotomy
Gastro-/duodenojejunostomy leakage	Conclusive radiographic or direct visual evidence of a defect of the anastomosis
Intra-abdominal abscess formation	Intra-abdominal fluid collection with positive cultures identified by ultrasonography or computed tomography, associated with persistent fever and elevations of white blood cells
Wound infection	Requiring intervention otherwise considered as minor complication
Portal Vein Thrombosis	Conclusive radiologic evidence of thrombosis
<b>Following either procedure</b>	
Cholangitis	Elevation in temperature more than 38°C, thought to have a biliary cause, without concomitant evidence of acute cholecystitis, requiring intervention
Hemorrhage	Bleeding after the index procedure requiring transfusion of ≥4 units of packed cells within a 24-hour period, or leading to relaparotomy/intervention
(Emergency) (re)laparotomy	Any (other) reason following either preoperative biliary drainage or another surgical procedure
Pneumonia	Pulmonary infection with radiological confirmation and requiring antibiotic treatment
Mortality	In-hospital death, due to protocol complications or any cause, including progression of disease, within the study period

**Table 2** shows procedure characteristics for both groups.

<b>Procedure characteristics.*</b>				
<b>Characteristic</b>	<b>Early surgery (N=94)</b>		<b>Preoperative Biliary Drainage (N=102)</b>	
Conversion to PBD — no. (%)	5	(5)	NA	
Initial PBD attempt successful — no. (%)	4	(80) <sup>†</sup>	77	(75)
PTC as final PBD procedure	-		12	(12)
Underwent PBD — no. (%)	5	(5)	96	(94)
Time to surgery — wk				
Mean (95% CI)	1.2	(0.9-1.4)	5.2	(4.8-5.5)
Median	1.0		4.9	
IQR	0.7	- 1.1	4.1	- 6.0
Underwent surgery — no. (%)	92	(98)	95	(93)
Type of surgical treatment — no. (%)				
Resection	63	(67)	57	(56)
Palliative bypass procedure	28	(30)	33	(32)
Exploration	1	(1)	5	(5)

\* for each variable the number of patients are indicated. CI denotes confidence interval.

NA denotes not applicable, IQR interquartile range.

<sup>†</sup> percentage of total number of patients that underwent PBD

## CASE RECORD FORM

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Preoperative biliary drainage vs. (direct) operation for patients with a pancreatic/periampullary tumor

*CRF, (English version)*

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*Signature physician/researcher/data manager*

Herewith I declare I have completed this Case Record Form to my best knowledge and that the information entered is correct.

Name physician/researcher	Signature	Date							
		d	d	m	m	y	y	y	y

## PERSONALIA

---

Date registration: \_\_\_\_\_

Gender : 1 = male, 2 = female

CRF Number: \_\_\_\_\_

Date of birth: \_\_\_\_\_

Hospital File Number: \_\_\_\_\_

### INCLUSION CRITERIA

0=No, 1=Yes

1. Clinical diagnosis of jaundice due to suspected pancreatic/periampullary tumor
2. Serum bilirubin  $\leq 40 \mu\text{mol/l}$  and  $\geq 250 \mu\text{mol/l}$
3. Spiral CT-scan without signs of distant metastases or loco regional (vascular) ingrowth


***In case the answer to one of these questions is NO the patient cannot enter the trial***

### EXCLUSION CRITERIA

0=No, 1=Yes

1. Age >85 year or severe co morbidity (Karnofsky <50, see next page)
2. Current cholangitis?
3. Prior biliary drainage by means of ERCP/PTC?
4. Did the patient receive neoadjuvant or palliative chemotherapy for current malignancy?
5. Symptoms of 'gastric outlet obstruction' occur ? (Nausea/vomiting, nutritional intake < 1l/day)


***In case the answer to one of these questions is YES the patient cannot enter the trial***

**KARNOFSKY SCORE** *(please encircle the correct answer)*

100	Normal, no complaints, no evidence of disease
90	Able to carry on normal activity: minor symptoms of disease
80	Normal activity with effort: some symptoms of disease
<hr/>	
70	Cares for self: unable to carry on normal activity or active work
60	Requires occasional assistance but is able to care for Nods
50	Requires considerable assistance and frequent medical care
<hr/>	
40	Disabled: requires special care and assistance
30	Severely disabled: hospitalization is indicated, death not imminent
20	Very sick, hospitalization necessary: active treatment necessary
10	Moribund, fatal processes progressing rapidly
0	Dead

## PRIOR SURGICAL TREATMENT

Did the patient undergo earlier HPB surgery?

0= No

1= Yes (please specify)

Surgical procedure	Date							
	d	d	m	m	y	y	y	y
1.								
2.								
3.								

## RELEVANT MEDICAL HISTORY

Any other illnesses?

0= No

1= Yes (please specify)

Diagnosis	Present since (year)				cross mark	
					In the past	Actual
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						

## PERFORMANCE STATUS

ECOG-WHO Scale (shortly before randomization)

0= WHO 0: Asymptomatic

1= WHO 1: Symptomatic but completely ambulant

2= WHO 2: Symptomatic, <50% in bed during the day

3= WHO 3: Symptomatic, >50% in bed, but not bedbound

4= WHO 4: Bedbound



**PHYSICAL EXAMINATION:**

<b>Length (cm)</b>				,	
<b>Weight (kg)</b>				,	

- **Gallbladder palpable**

0= No  
1= Yes  
-7= Unknown

## BLOOD INVESTIGATIONS

- Hemoglobin \_\_\_\_\_ mmol/l
- ASAT (SGOT) \_\_\_\_\_ U/l
- ALAT (SGPT) \_\_\_\_\_ U/l
- Bilirubin (total) \_\_\_\_\_  $\mu\text{mol/l}$
- Bilirubin (direct) \_\_\_\_\_  $\mu\text{mol/l}$
- Alkalic fosfatase \_\_\_\_\_ U/l
- $\gamma$ -GT \_\_\_\_\_ U/l
- Kreatinin \_\_\_\_\_  $\mu\text{mol/l}$
- APTT \_\_\_\_\_ sec.
- PT \_\_\_\_\_ sec.
- INR \_\_\_\_\_
- Leukocytes \_\_\_\_\_  $10^9/l$
- CRP \_\_\_\_\_ mg/l
- Amylase \_\_\_\_\_ U/l
- Albumin \_\_\_\_\_ g/l

## PREOPERATIVE DIAGNOSTICS

**Modality**      **Available**      **Date**      **Tumor size in cm**      **Dilatation Pancreatic Duct**      **Dilatation CBD**  
 0=No, 1=Yes      0=No, 1=Yes      0=No, 1=Yes

		d	d	m	m	y	y	y	y			
CT-scan	<input type="checkbox"/>									_____	<input type="checkbox"/>	<input type="checkbox"/>
Ultrasound	<input type="checkbox"/>									_____	<input type="checkbox"/>	<input type="checkbox"/>
MRCP	<input type="checkbox"/>									_____	<input type="checkbox"/>	<input type="checkbox"/>

other, viz \_\_\_\_\_

## TUMOUR LOCALISATION

- 1= Pancreatic Head
- 2= Ampulla of Vater
- 3= Distal bile duct
- 4= other, viz \_\_\_\_\_

## OTHER DIAGNOSTICS / PREOPERATIVE PATHOLOGY

Modality	Available 0=No, 1=Yes	Date								Result
		d	d	m	m	y	y	y	y	
X-Thorax	<input type="checkbox"/>									_____
Biopsy	<input type="checkbox"/>									_____
Brush	<input type="checkbox"/>									_____
_____	<input type="checkbox"/>									_____
_____	<input type="checkbox"/>									_____

## MEDICATION PREOPERATIVE

**Name**

**Dosage**

- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____

**RANDOMISATION**

Only after obtaining informed consent the patient will be randomized:

- **Randomization performed?**  
If no, please specify

0= No  
1= Yes

No : \_\_\_\_\_  
\_\_\_\_\_

- **Date of randomization**

Date							
d	d	m	m	y	y	y	y

- *Result*

1= Preoperative Biliary Drainage 4-6 weeks  
2= Early Surgery (< 1 week after randomization)

**PLEASE PROCEED TO PAGE 17  
FOR EARLY SURGERY**

## PREOPERATIVE BILIARY DRAINAGE

- **Antibiotic prophylaxis**

 0= No  
 1= Yes  
 -7= Unknown
- **ERCP**

 0= No  
 1= Yes  
 -7= Unknown
- **Sphincterotomy**

 0= No  
 1= Routine  
 2= Pre-cut  
 -7= Unknown
- **Stent placement effective**  
*(unsuccessful? Please see page 14)*

 0= No  
 1= Yes  
 -7= Unknown
- **Reason of stent placement failure**
- **Length of procedure**

 \_\_\_\_\_hr    \_\_\_\_\_min
- **Number of stents placed**
- **Biliary Drainage started on:**

Date							
d	d	m	m	y	y	y	y
- **Bilirubin (after 2 weeks of drainage)**

 \_\_\_\_\_  $\mu$ mol/l
- **Successful drainage**  
*(defined as: >50% decrease of serum bilirubin after 2 weeks)*

 0= No  
 1= Yes  
 -7= Unknown
- **Stent replacement?**

 0= No  
 1= Yes  
 -7= Unknown

- **Date stent occlusion**

Date (1 <sup>st</sup> occlusion)							Date (2 <sup>nd</sup> occlusion)								
d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y

- **Date stent replacement**

Date (1 <sup>st</sup> replacement)							Date (2 <sup>nd</sup> replacement)								
d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y

## PREOPERATIVE BILIARY DRAINAGE (2nd attempt)

- **Antibiotic prophylaxis**

 0= No  
 1= Yes  
 -7= Unknown
- **ERCP**

 0= No  
 1= Yes  
 -7= Unknown
- **Sphincterotomy**

 0= No  
 1= Routine  
 2= Pre-cut  
 -7= Unknown
- **Stent placement effective**  
*(unsuccessful? Please see page 14)*

 0= No  
 1= Yes  
 -7= Unknown
- **Reason of stent placement failure**
- **Length of procedure**
\_\_\_\_\_ hr    \_\_\_\_\_ min.
- **Number of stents placed**
- **Biliary Drainage started on:**

Date							
d	d	m	m	y	y	y	y
- **Bilirubin (after 2 weeks of drainage)**
\_\_\_\_\_  $\mu$ mol/l
- **Successful drainage**  
*(defined as: >50% decrease of serum bilirubin after 2 weeks)*

 0= No  
 1= Yes  
 -7= Unknown
- **Stent replacement?**

 0= No  
 1= Yes  
 -7= Unknown

- **Date stent occlusion**

<b>Date (1<sup>st</sup> occlusion)</b>							<b>Date (2<sup>nd</sup> occlusion)</b>								
d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y

- **Date stent replacement**

<b>Date (1<sup>st</sup> replacement)</b>							<b>Date (2<sup>nd</sup> replacement)</b>								
d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y

## COMPLICATIONS OF PREOPERATIVE BILIARY DRAINAGE

Complication	Present 0= No, 1= Yes	Start Date								Stop Date								Therapy (a)	Outcome (b)
		d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y		
1. Perforation																			
2. Cholangitis																			
3. Hemorrhage																			
4. Pancreatitis																			
5.																			

- (a)
- Laparotomy with ICU admission
  - Laparotomy without ICU admission
  - Conservative treatment with ICU admission
  - Conservative treatment without ICU admission

- (b)
- cured
  - permanent damage
  - died from complication
  - other, viz \_\_\_\_\_

Number of laparotomies \_\_\_\_\_

	Date							
	d	d	m	m	y	y	y	y
Date relaparotomy 1								
Date relaparotomy 2								
Date relaparotomy 3								
Date of death								

**SURGERY DATA**

- **Date of surgery**

Date							
d	d	m	m	y	y	y	y

- **Antibiotic prophylaxis**

0= No  
1= Yes (please specify)  
-7= Unknown

Antibiotic	Dosage	Administration	Date								Duration Days
			d	d	m	m	y	y	y	y	
1.											
2.											
3.											

- **Octreotide (Sandostatin®) used**

0= No  
1= Yes  
-7= Unknown

- **Operator**

1= Surgeon  
2= Fellow  
3= Resident  
-7= Unknown

- **Tumor resectable**

0= No  
1= Yes  
-7= Unknown

- **Reason unresectability**  
(in case of unresectability)

1= Metastases  
2= Loco regional ingrowth  
3= n/a  
-7= Unknown

- **Bypass (hepaticojejunostomy)**  
(in case of unresectability)

0= No  
1= Yes  
2= Yes, + gastroenterostomy  
3= n/a  
-7= Unknown

- **Celiac plexus neurolysis**  
(in case of unresectability)

0= No  
1= Yes  
3= n/a  
-7= Unknown

- **Type of operation / Resection**

0= No  
 1= PPPD  
 2= PD  
 3= Unknown  
 4=Other, viz \_\_\_\_\_
- **Vascular resection**

0= No  
 1= Vena porta  
 2= Vena mesenterica  
 3= Confluens  
 -7= Unknown
- **Feeding jejunostomy**

0= No  
 1= Yes  
 -7= Unknown
- **Length of operation**

\_\_\_\_\_hr    \_\_\_\_\_min
- **Blood loss**

\_\_\_\_\_ml
- **Perioperative blood transfusion**

\_\_\_\_\_ packed cells
- **Postoperative stay**

1= Ward  
 2= ICU or recovery room  
 3= Other, viz \_\_\_\_\_  
 -7= Unknown



## POSTOPERATIVE COMPLICATIONS

Complication	Present 0= No, 1= Yes	Start Date								Stop Date								Therapy (a)	Outcome (b)
		d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y		
1. Wound infection																			
2. Peritonitis																			
3. Pancreatic fistula																			
4. Biliary leakage																			
5. Hemorrhage																			
5. Delayed Gastric Emptying																			
6. Intra-abdominal abscess																			
7. Wound dehiscence																			
8. Portal vein thrombosis																			
9. Deep venous thrombosis																			
10. UTI																			
11. Pneumonia																			
12. Myocardial infarction																			
13. CVA																			
14. _____																			
15. _____																			

- (a)
1. Laparotomy with ICU admission
  2. Laparotomy without ICU admission
  3. Conservative treatment with ICU admission
  4. Conservative treatment without ICU admission

- (b)
1. cured
  2. permanent damage
  3. died from complication
  4. other, viz \_\_\_\_\_

Number of relaparotomies \_\_\_\_\_

	Date							
	d	d	m	m	y	y	y	y
Date relaparotomy 1								
Date relaparotomy 2								
Date relaparotomy 3								
Date of death								

**DISCHARGE**

- Date

Date							
d	d	m	m	y	y	y	y

**READMISSION**

- Within 30 days after discharge?

0= No

1= Yes (please mention date)

- Reason of readmission \_\_\_\_\_

- Date of readmission

- Date of discharge

Date							
d	d	m	m	y	y	y	y

- Did the patient die during readmission?

0= No

1= Yes (please add date)

Date							
d	d	m	m	y	y	y	y

## MEDICATION AT DISCHARGE

Name	Dose
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____
- _____	_____

***PATHOLOGY***

***Pathology number***

--	--	--	--	--	--	--	--	--	--

- **Tumor type**

1= Adenocarcinoma

2= Adenoma

3= Neuroendocrine

4= Cystadenoma

5= Cystadenocarcinoma

6= No tumor

8= Chronic pancreatitis

7= Other, viz \_\_\_\_\_

- **Tumor size**

Centimeter (cm)

		,	
--	--	---	--

- **Differentiation**

1= Poor

2= Poor-moderate

3= Moderate

4= Moderate - well

5= Well

6= Other, viz \_\_\_\_\_

- **Lymphovascular ingrowth**

0= No

1= Yes

-7= Unknown

- **Perineural ingrowth**

0= No

1= Yes

-7= Unknown

- **Anterior surface resection margin free**

0= No

1= Yes

-7= Unknown

- <b>Pancreatic neck/body transection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Distal duodenal transection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Proximal gastric/duodenal transection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Common bile duct transection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Along SMV groove (medial, uncinate, retroperitoneal) surface resection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Posterior surface resection margin free</b>	0= No 1= Yes -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>Number of lymph nodes investigated</b>		<table border="1" style="display: inline-table; border-collapse: collapse;"><tr><td style="width: 30px; height: 20px;"></td><td style="width: 30px; height: 20px;"></td><td style="width: 30px; height: 20px;"></td></tr></table>						
- <b>Number of (tumor) positive lymph nodes</b>		<table border="1" style="display: inline-table; border-collapse: collapse;"><tr><td style="width: 30px; height: 20px;"></td><td style="width: 30px; height: 20px;"></td><td style="width: 30px; height: 20px;"></td></tr></table>						
- <b>Radicality</b>	1= R0 (micro- & macroscopic radical resection) 2= R1 (macroscopic radical, microscopic residual) 3= R2 (micro- & macroscopic residual) -7= Unknown	<input style="width: 40px; height: 20px;" type="text"/>						
- <b>TNM Classification (pathology)</b>	<table border="0" style="margin: auto;"> <tr> <td style="padding: 0 10px;"><b>pT</b></td> <td style="padding: 0 10px;"><b>pN</b></td> <td style="padding: 0 10px;"><b>pM</b></td> </tr> <tr> <td style="text-align: center;"><input style="width: 40px; height: 20px;" type="text"/></td> <td style="text-align: center;"><input style="width: 40px; height: 20px;" type="text"/></td> <td style="text-align: center;"><input style="width: 40px; height: 20px;" type="text"/></td> </tr> </table>	<b>pT</b>	<b>pN</b>	<b>pM</b>	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>	
<b>pT</b>	<b>pN</b>	<b>pM</b>						
<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>						



## STANDARDIZED FOLLOW-UP EVALUATION

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Preoperative biliary drainage vs. (direct) operation for patients with a pancreatic/periampullary tumor

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**Date follow-up**

(2 / 6 / 12 weeks after discharge)

d	d	m	m	y	y	y	y



**DIAGNOSTICS**

d	d	m	m	y	y	y	y

**Laboratory investigations** (on indication only)

- Hemoglobin .....
- Thrombocytes .....
- Leucocytes .....
- C reactive protein .....
- Bilirubin – total .....
- Bilirubin – direct .....
- ALAT (GPT) .....
- ASAT (GOT) .....
- LDH .....
- GGT .....
- AF .....
- Albumin .....
- Amylase .....
- Glucose .....
- Sodium .....
- Potassium .....
- Creatinin .....
- ..... .....
- ..... .....
- ..... .....

**RADIOLOGY**

**Modality Available Date**  
**0=No, 1=Yes**

**CT-scan**


d	d	m	m	y	y	y	y

**Ultrasound**

**MRI/MRCP**

**other, viz** \_\_\_\_\_

**READMISSION (within 120 days after randomization).**

- Reason of readmission \_\_\_\_\_

- Date of readmission

- Date of discharge

Date							
d	d	m	m	y	y	y	y

- Did the patient die during readmission?

0= No

1= Yes (please mention date)

Date							
d	d	m	m	y	y	y	y

- Intervention?

0= No

1= Yes (please specify)

Type of intervention & indication	Date							
	d	d	m	m	y	y	y	y
1.								
2.								

- Relaparotomy?

0= No

1= Yes (please specify)

Type of surgery & indication	Date							
	d	d	m	m	y	y	y	y
1.								
2.								

## PROTOCOL COMPLICATIONS

- Complications?

0= No

1= Yes (please specify)

- Describe complication(s)

1.

2.

3.

## OTHER COMPLICATIONS

- Complications?

0= No

1= Yes (please specify)

- Describe complication(s)

1.

2.

3.

## ADYUVANT THERAPY

- **Adjuvant radiotherapy?**

0= No

1= Yes (please specify)

Location for radiation therapy	Dosage				Start Date				Stop Date											
	(x cGy)				d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y
1.																				
2.																				

- **Adjuvant chemotherapy?**

0= No

1= Yes (if Yes, please specify)

Type of chemotherapy	Number of courses	Start Date				Stop Date											
		d	d	m	m	y	y	y	y	d	d	m	m	y	y	y	y
1.																	
2.																	

