Surgical Interest Group

Monash University Malaysia

Journal Club #5

Pancreas

Overview

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Get Started

PRESENTATION

Content List

01 Title of paper

02 Basic information

03 Aim of Study

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01

About This Article

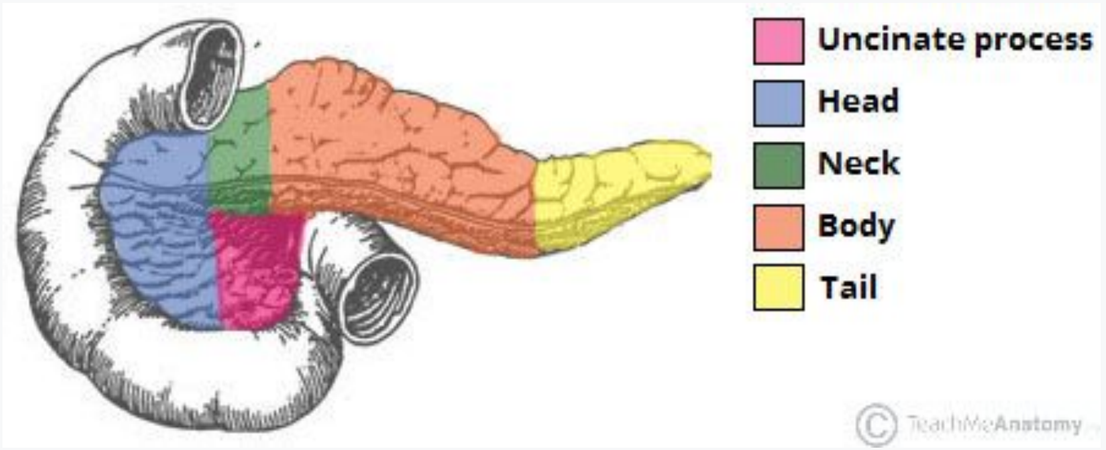
EUS-Guided Biliary Drainage Versus ERCP for the Primary Palliation of Malignant Biliary Obstruction: A Multicenter Randomised Clinical Trial

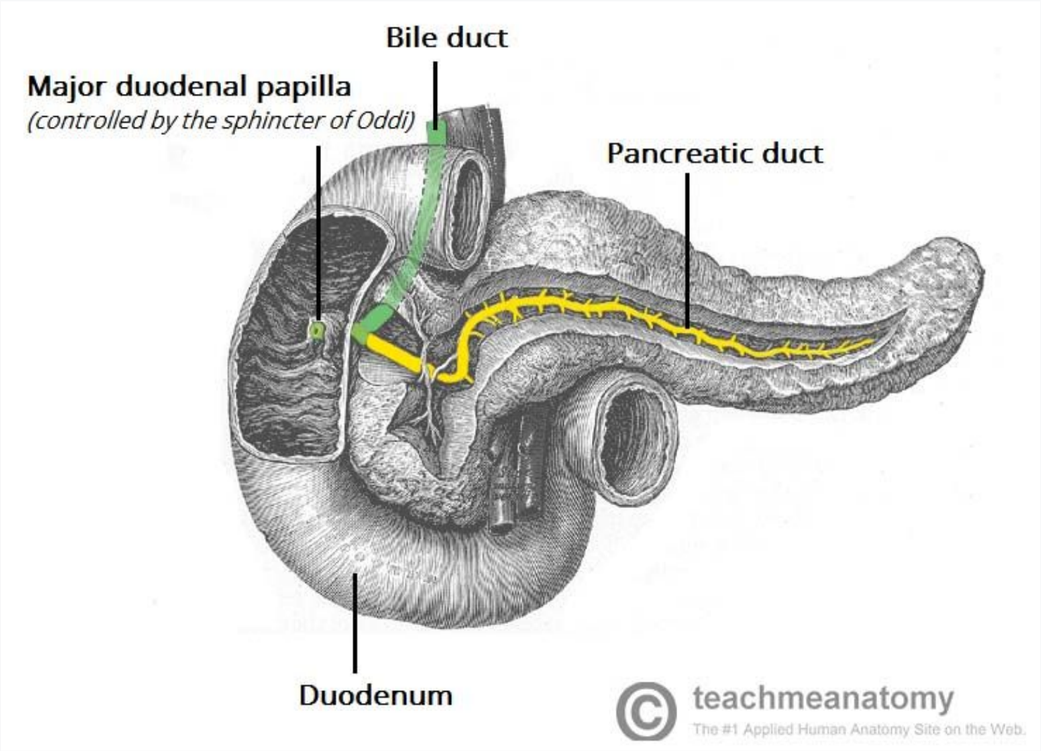
- Published: 2 July 2018
- American Journal of Gastroenterology
- Impact Factor: 10.38

02

The Pancreas

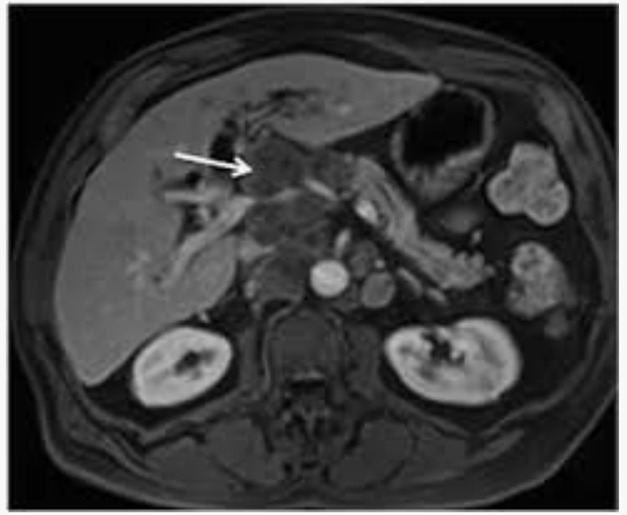
- oblong-shaped
- transpyloric plane (L1)
- Function
  - digestive (exocrine)
    - trypsin and chymotrypsin
    - amylase
    - lipase
  - hormonal (endocrine)
    - insulin
    - glucagon





Malignant biliary obstruction

- lead to jaundice, impair quality of life and hepatic function of cancer patients and result in delays in treatment
- **Symptoms**: fatigue, pruritus and nausea
- **Classification**: proximal, distal or mid
- **Causes**:
  - Primary tumour infiltration
  - compression by local extension of other tumours
  - extrinsic compression by lymph node metastases
- Poor 5-year **survival rate:** ≈ 5%



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Aim of the study

To determine whether endoscopic ultrasound (EUS)-guided biliary drainage **(EUS-BD)** is comparable to conventional transpapillary stenting with endoscopic retrograde cholangiopancreatography **(ERCP)** as a **primary palliation method in relieving malignant distal biliary obstruction.**

04

Methodology

01

RECRUITMENT

02

INCLUSION CRITERIA

03

EXCLUSION CRITERIA

RECRUITMENT

I

Randomised, controlled, non-inferiority trial

4 tertiary academic centres in South Korea

[May 2015 - Jan 2017]

II

Randomised in 1:1 ratio without risk stratification.

III

Computer-generated random numbers using **block randomization** (block size of 4)

Opaque, sealed envelopes

→ prevent **selection bias**

RECRUITMENT

IV

Patients & Statistician were **blinded**

[**DOUBLE-BLINDED**]

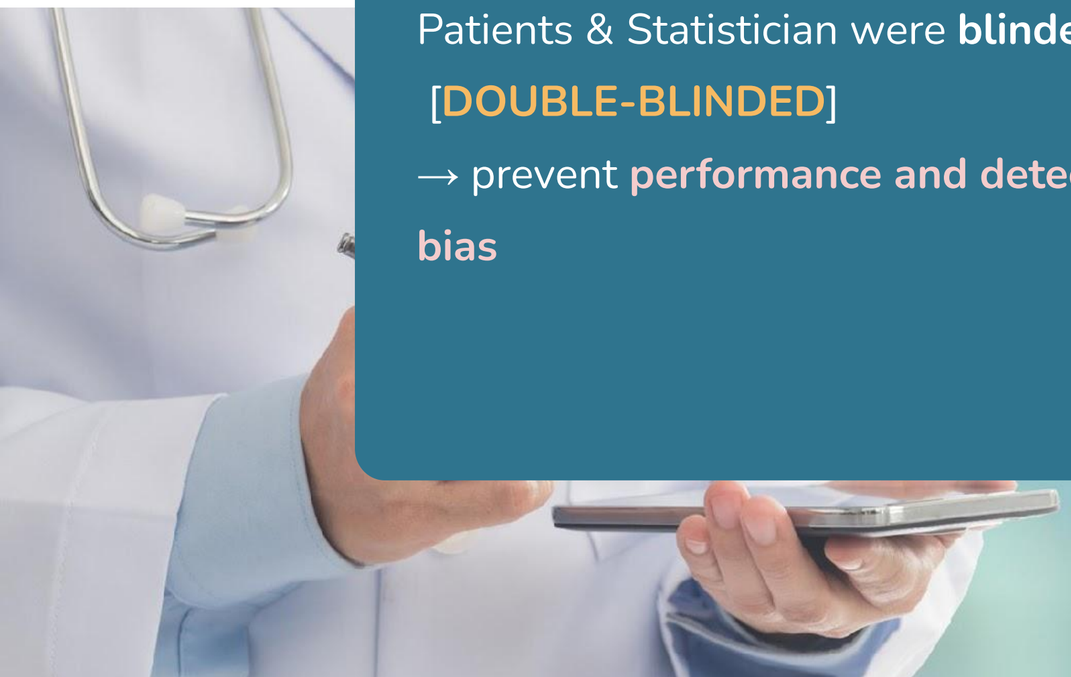
→ prevent **performance and detection bias**

V

Independent data and safety monitoring

No equipments were donated by manufacturer

→ prevent **reporting bias**



Inclusion Criteria:

- **UNRESECTABLE MALIGNANT DISTAL BILIARY OBSTRUCTION**
  - **>2 cm distal to the hilum with pathologic or radiologic diagnosis prior to endoscopic intervention**
- **>18 YEARS OLD**
- **KARNOFSKY INDEX ≥ 30%**
- **NO SERIOUS OR UNCONTROLLED COEXISTING MEDICAL ILLNESS**

KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disable; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

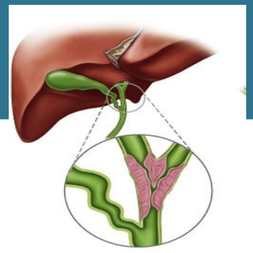
Karnofsky Performance Scale Index

- assessment tool for **functional** impairment
- compare **effectiveness** of different therapies
- assess **prognosis**
- lower score → poorer survival rate

KARNOFSKY PERFORMANCE SCALE INDEX

Exclusion Criteria:

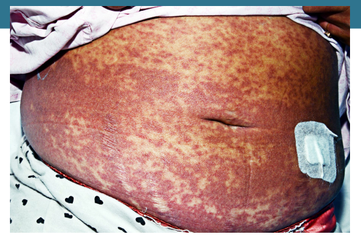
Hilar biliary obstruction



Malignant hilar biliary obstruction (MHBO)

Uncorrectable coagulopathy

History of allergy to radiocontrast agent



Refusal

05

Primary Outcome

Technical success rates

- 93.8% (60/64) in EUS-BD
- 90.2% (55/61) in ERCP

p = 0.03

Secondary outcomes

Clinical success rates:

90.0% (54/60) with EUS-BD

94.5% (52/55) with ERCP

- P=0.49, per-protocol analysis.
  - Not statistically significant

Median procedure time

EUS-BD: 5 mins

ERCP: 11 min

- P<0.001.
  - Statistically significant

Median length of hospital stay

EUS-BD group: 4 days

ERCP group: 5 days

- P=0.03
  - Statistically significant

SECONDARY OUTCOMES

Secondary outcomes

Lower rate of **early adverse events** (6.3% vs 19.7%) [p=0.03]

- procedure-related pancreatitis (0 vs 14.8%) [p=0.001]
- no serious adverse events/death

Lower rate of **late adverse events** (4.7% vs 19.4%) [p=0.01]

Higher **stent patency rate** at 6 months (85.1% vs. 48.9%) [p=0.001]

Longer mean **patency time** (208 days vs. 165 days)

Lower **reintervention rate** (15.6% vs. 42.6%) [p=0.001]

Lesser changes in **QOL scores** after 12 weeks of procedure:

- global (4.17 vs −9.03) [p=0.001]
- parts of functional
  - emotional (1.62 vs −9.72) [p=0.001]
  - cognitive (0.93 vs −11.11) [p=0.003]
- symptom scale
  - fatigue (−3.40 vs 8.02) [p=0.02]
  - pain (−17.59 vs 4.63) [p=0.01]
  - financial difficulties (2.78 vs 18.52) [p=0.01]

Table 2 Safety profile and procedure-related outcomes of ERCP and EUS-BD

	Intention-to-treat analysis			Per-protocol analysis		
Outcome measures, *n* (%)	**ERCP (*n*=61)**	**EUS-BD (*n*=64)**	***P*-value**	**ERCP (*n*=55)**	**EUS-BD (*n*=60)**	***P*-value**
Procedure time, median (IQR), min[a]	11 (7–18)	5 (3–12)	<0.001	14 (8–20)	5 (3–9)	<0.001
Follow up period, median (IQR), days	165 (99–253)	144 (101–209)	0.45	165 (99–253)	142 (90–209)	0.41
Adverse events						
Early (≤2 weeks, procedure-related)	12 (19.7)[b]	4 (6.3)[b]	0.03	12 (21.8)	2 (3.3)	0.003
Late (>2 weeks)	12 (19.4)[c]	3 (4.7)[c]	0.01	12 (21.8)	3 (5.0)	0.008
Procedure-related pancreatitis	9 (14.8)	0	0.001	8 (14.5)	0	0.002
Mild/Moderate/Severe	16 (26.2)/8 (13.1)/0	4 (6.3)/3 (4.7)/0	0.001	16 (29.1)/7 (12.7)/0	4 (6.7)/2 (3.3)/0	<0.001
Mortality						
Procedure-related	0	0		0	0	
Disease progression	51(83.6)	46 (71.9)		46 (83.6)	43 (71.7)	
Cardiopulmonary complication	0	2 (3.1)		0	2 (3.3)	
Reintervention rate	26 (42.6)[d]	10 (15.6)[d]	0.001	24 (43.6)	9 (15.0)	0.001
Reintervention method			<0.001			<0.001
ERCP	22	0		20	0	
EUS-BD	3	9[e]		3	8[e]	
PTBD	1	1		1	1	
Hospital stay, median (IQR), days	5 (4–6)	4 (3–5)	0.03	5 (4–6)	4 (3–5)	0.008

PTBD percutaneous transhepatic biliary drainage

[a]Procedure time was defined as time from biliary cannulation to stent placement in ERCP group, and time from needle puncture of the dilated bile duct to stent placement in EUS-BD group. In cases of difficult cannulation (defined as failed biliary access within 5 min of attempt), we performed early precut fistulotomy for cannulation by experts without involvement of trainees and duodenal intubation time was not included within procedure time

[b]Early adverse events included acute pancreatitis (*n*=9), acute cholecystitis (*n*=2), stent migration (*n*=1) in ERCP group and self-limited pneumoperitoneum (*n*=2), bile peritonitis (*n*=1), and acute cholangitis (*n*=1) in EUS-BD group

[c]Late adverse events included acute cholangitis (*n*=6), acute cholecystitis (*n*=3), and stent occlusion (*n*=3) in ERCP group and acute cholangitis (n=3) in EUS-BD group

[d]In ERCP group, 26 reinterventions were required due to stent clogging (*n*=14), tumor in/overgrowth (*n*=9), stent migration (*n*=1), acute cholecystitis (*n*=1), and biloma (*n*=1). In EUS-BD group, 10 reinterventions were required due to stent clogging (*n*=6), stent migration (*n*=2), and tumor in/overgrowth (*n*=2)

[e]As reintervention, these patients underwent stent reinsertion via the previous transmural fistula

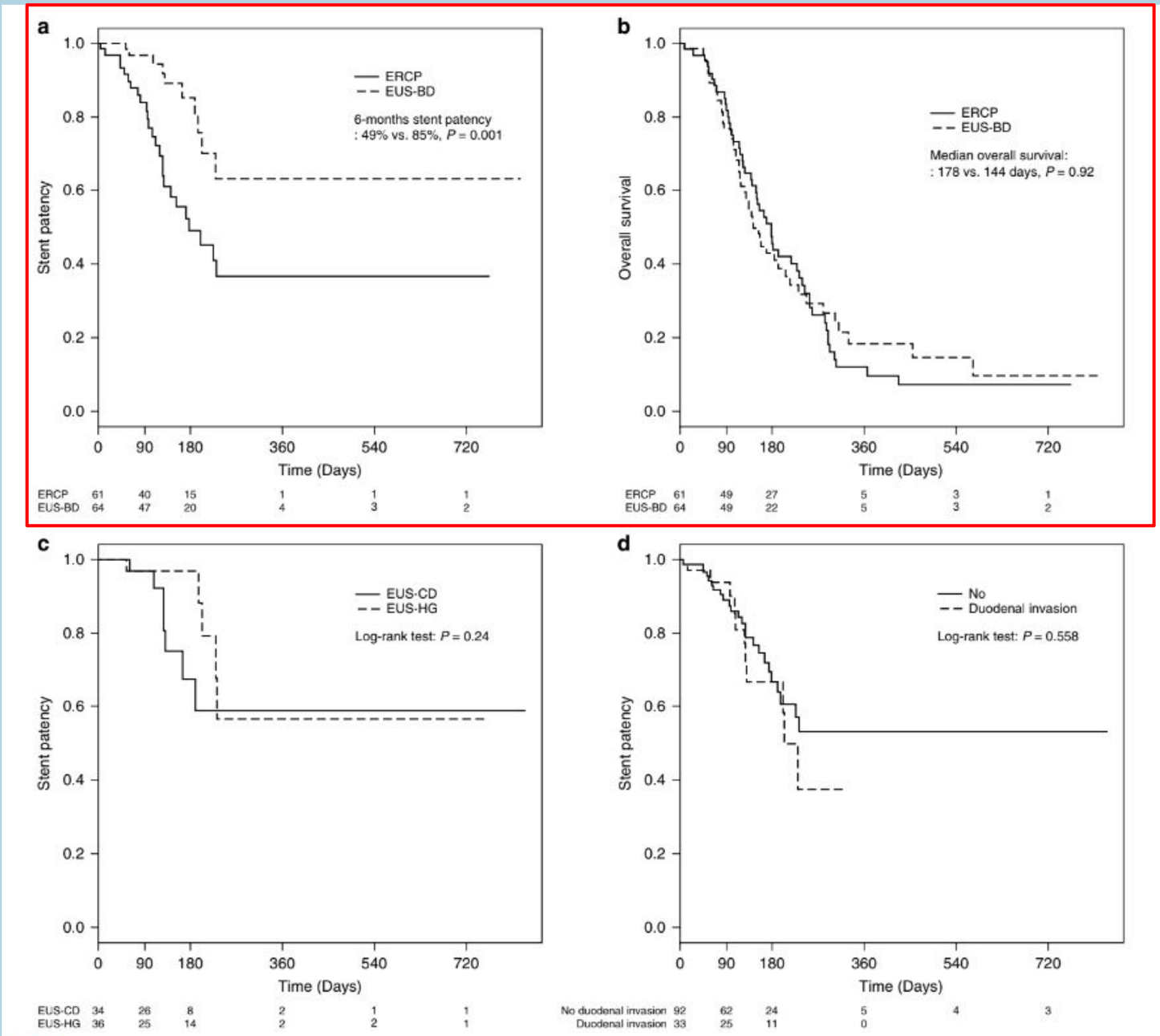


Fig. 2 Kaplan–Meier analysis with the log-rank test for stent patency (**a**) and overall survival (**b**) in ERCP and EUS-BD group, stent patency in EUS-CD and EUS-HG (**c**), and stent patency in patients with duodenal invasion and those without (**d**)

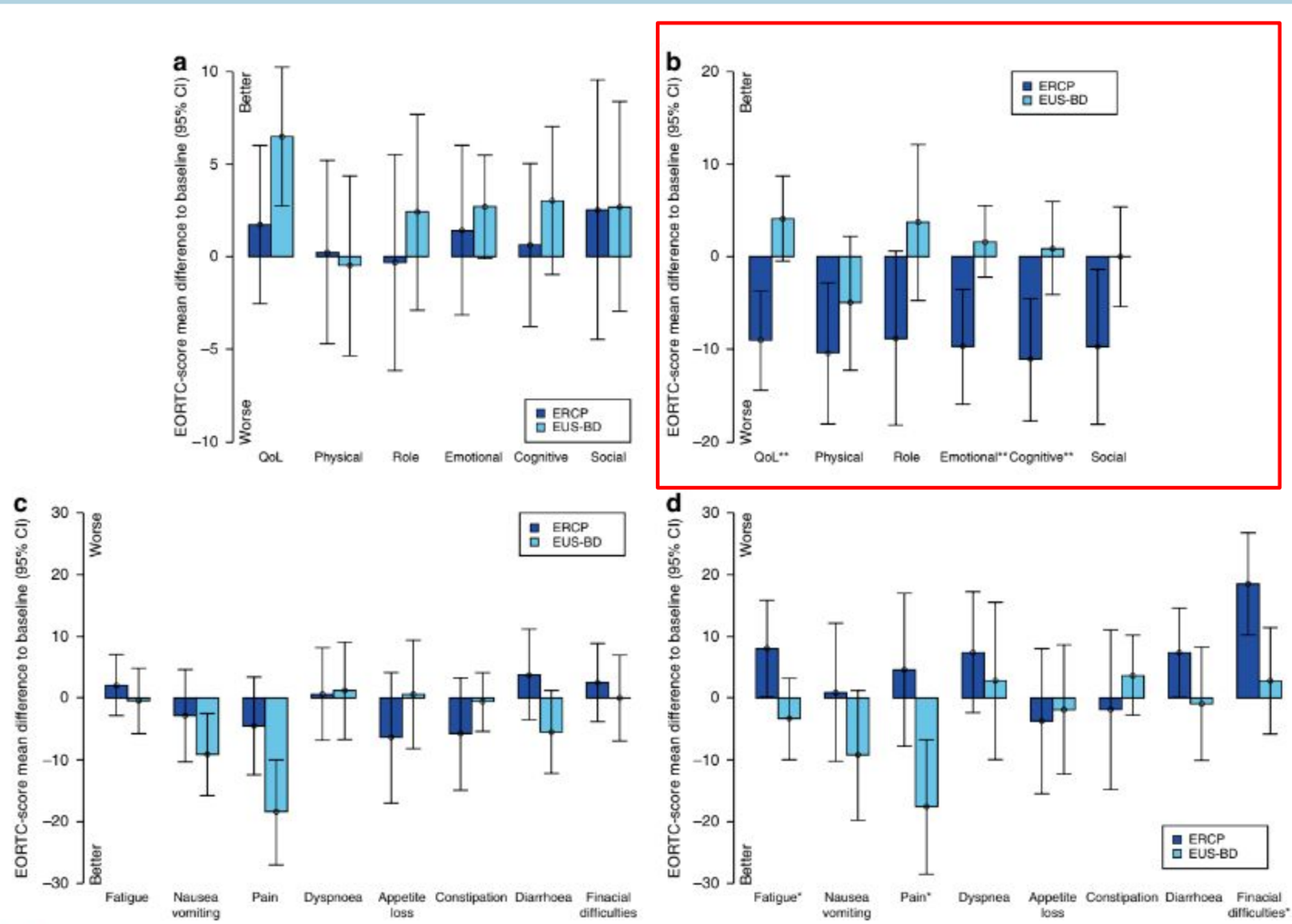
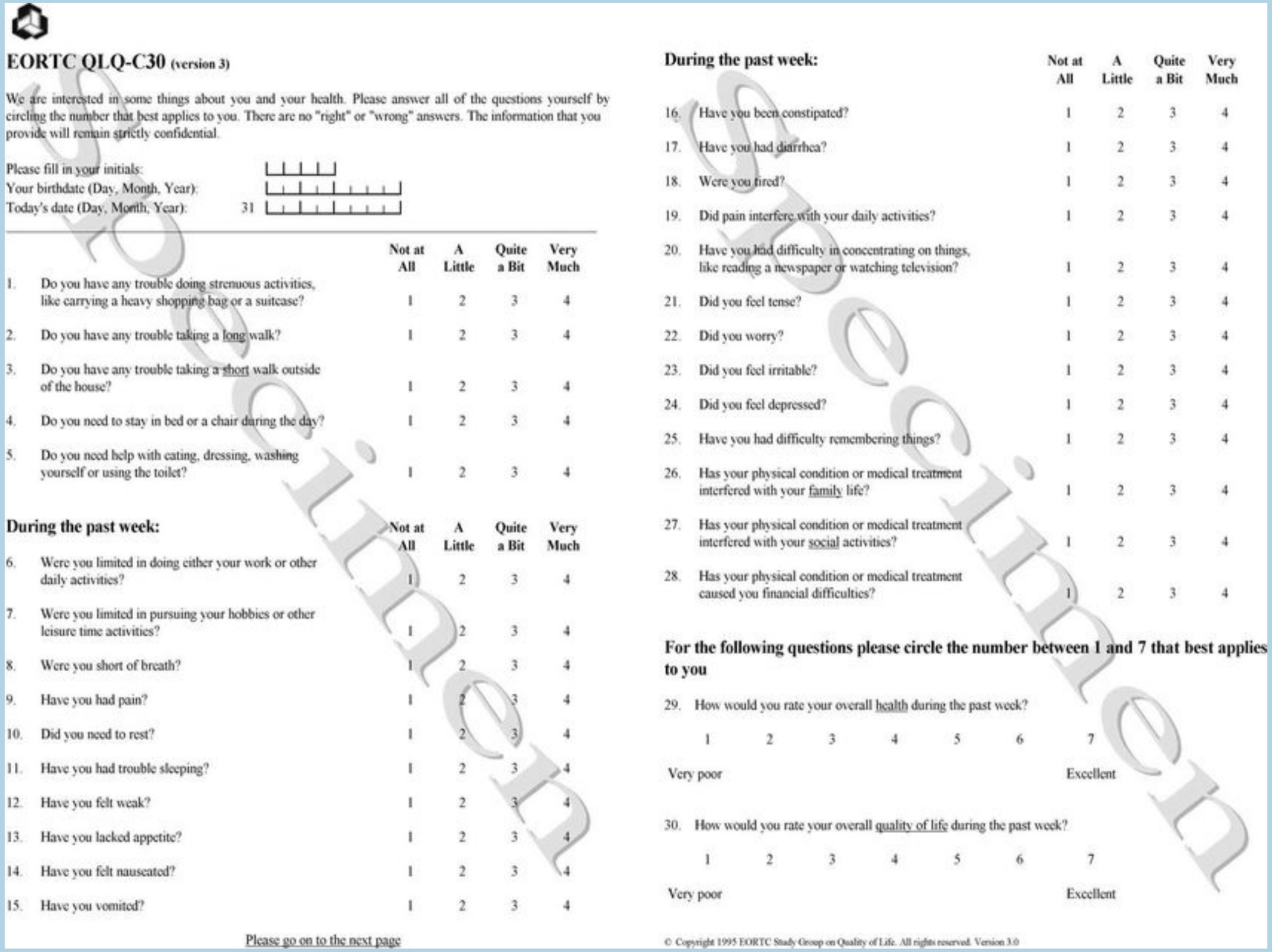


Fig. 3 Quality of life was estimated by using EORTC QLQ-C30. **a** Changes in global health status and functional scales between baseline and 4 weeks after the procedure. **b** Changes in global health status and functional scales between baseline and 12 weeks after the procedure. **c** Changes in symptom scale between baseline and 4 weeks after the procedure. **d** Changes in symptom scale between baseline and 12 weeks after the procedure. EUS-BD was associated with more preserved QOL than ERCP after 12 weeks of the procedure regrading global (4.17 vs −9.03, $P=0.001$), and parts of functional (emotional, 1.62 vs −9.72, $P=0.001$; cognitive, 0.93 vs −11.11, $P=0.003$) and symptom scale (fatigue, −3.40 vs 8.02, $P=.02$; pain, −17.59 vs 4.63, $P=0.01$; financial difficulties, 2.78 vs 18.52, $P=0.01$). $^{*}P<0.05$.$^{**}P<0.01$



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: [| | |]
Your birthdate (Day, Month, Year): [| | | | | | | |]
Today's date (Day, Month, Year): 31 [| | | | | | | |]

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4

Please go on to the next page

During the past week:		Not at All	A Little	Quite a Bit	Very Much
16.	Have you been constipated?	1	2	3	4
17.	Have you had diarrhea?	1	2	3	4
18.	Were you tired?	1	2	3	4
19.	Did pain interfere with your daily activities?	1	2	3	4
20.	Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21.	Did you feel tense?	1	2	3	4
22.	Did you worry?	1	2	3	4
23.	Did you feel irritable?	1	2	3	4
24.	Did you feel depressed?	1	2	3	4
25.	Have you had difficulty remembering things?	1	2	3	4
26.	Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27.	Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28.	Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30)

- Cancer-specific questionnaire
- 30 items organised into 15 scales
- most widely used patient-reported outcome measures
- Assess health-related quality of life, functional health, and symptoms
- Summary score was calculated as mean of combined 13 QLQ-C30 scale scores

Author discussion

- Superiority of ERCP (the standard of care) in terms of safety and efficacy has been proven by many studies
- Inherent drawbacks of ERCP:
  (a) traumatic injury of main pancreatic duct
  (b) stent occlusion by tumour growth
- Only a few retrospective studies comparing EUS-BD with conventional ERCP exists
- The first prospective, multicenter, randomised study comparing EUS-BD with ERCP as a primary modality for the palliative treatment of malignant biliary obstruction

CONCLUSION

EUS-BD and PTBD had **similar levels of efficacy** for the primary palliation of unresectable malignant distal biliary obstruction based on rates of technical and clinical success.

Robust clinical advantages (lower adverse outcomes with no risk of pancreatitis, longer stent patency with less need of reintervention, and more preserved QOL) were recognized with **EUS-BD over ERCP**, warranting further evaluation.

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THANK YOU.

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End