

Point-by-point response

Will *et al.* (Manuscript ID No.: 16940):

“Endoscopic ultrasonography-guided drainage of the pancreatic duct (EUPD) in symptomatic obstruction and enlargement of the pancreatic duct and unsuccessful ERP – indication, technical approach and therapeutic results of a unicenter long-term study”,

Dear Editor,

Many thanks for considering our manuscript as mentioned above including the constructive comments and critics as provided by the reviewer.

As follows, please, find an appropriate “point-by-point response” as indicated hopefully addressing satisfyingly all the reviewer’s remarks and recommendations.

The authors hope that you can accept our changes and responding remarks and we are looking forward to receiving your reply.

Sincerely,

Prof. U. Will, MD (on behalf of all co-authors)

The reviewer wrote:

„ ... Despite their results might be interesting there are some points which need clarification.

Major points

- *In abstract section:*

The reviewer stated:

1. “Paragraph is really long. Consult the instructions for author”

RESPONSE:

As you may have derived, the author’s primary intention was to provide the most informative “Abstract” possible including also a few detailed information, in particular, for the reader performing literature search.

As far as the authors can tell from the original “Instructions for authors” provided by the journal, there is no substantial limitation – however, according to the critic also made under point “2.” (as follows), see below how the text of the “Abstract” section was shortened.

In addition, the reviewer pointed out:

2. “Results are very detailed.”

RESPONSE:

In accordance also with point one, we shortened the “Results” paragraph of the “Abstract” section to cover both points as raised by the reviewer – the “Abstract” section is as follows:

Although ERCP is considered gold standard for symptomatic therapy in chronic pancreatitis, there are circumstances (altered anatomy of the upper GI tract after former surgery, high perioperative patient's risks, no patient's consent), in those an alternative minimally invasive approach is favorable.

The aim of this prospective unicenter observational study is to investigate technical feasibility, safety and clinical long-term outcome of the novel transluminal pancreaticography and placement of a drainage (EUPD) in a representative number of patients.

Patients and Methods: Through a defined time period, all consecutive patients who underwent EUS-guided pancreaticography and subsequent placement of a drainage with symptomatic retention of the pancreatic duct after former unsuccessful or frustrating ERCP attempt(s) were enrolled in this study to reflect daily practice and distinguishing three various approaches: i) EUS-ERP rendezvous technique, ii) EUS-guided drainage of the pancreatic duct, iii) EUS-guided, internal antegrade drainage of the pancreatic duct.

Results: From 06/2002 to 04/2014, 111 interventions in 94 patients (ERP failed in all of them) were performed aiming for EUS-guided transgastric pancreaticography and subsequent drainage (mean duration, 21 [range, 15-69] min). In all 94 patients (median age, 54 [range, 28-87] years; sex ratio, m:f = 60:34), puncture of the pancreatic duct including pancreaticography was achieved (technical success rate, 100 %). However, in 10 cases after former surgical intervention there was no need for drainage because of sufficient flow of the contrast media through the anastomosis (in one patient, histoacryl was primarily injected into the pancreatic duct because of DPTS). Primary successful placement of a drainage was achieved in 47 out of 83 patients (56.6 %) out of them, 26 subjects underwent transgastric/-bulbary positioning of a stent whereas 21 individuals were drained through the papilla using rendezvous technique. While for transgastric (retrograde) drainage, plastic prostheses were used in 11/26 patients, metal stents were inserted in further 12/26 patients. Three of 26 patients underwent placement of a ring drainage (antegrade internal drainage) because of an anastomotic stenosis after former surgical intervention. Patients with transpapillary drainage received plastic prostheses in the majority of cases ($n=20$), in 2 cases (???, $\Sigma=22$ statt 21) only metal stents (cSEM) were used. The median follow-up time period in patients who had undergone placement of a transpapillary drainage ($n=21$), was 28 (range, 1-79) months whereas that of the 26 patients with successful transgastric/transduodenal drainage was 9.5 (range, 1-82) months. Clinical success indicated by reduction of pain or no further pain by EUS-guided intervention was achieved in 68/83 patients (rate, 81.9 %) since several patients became also better with no drainage but obviously sufficient manipulation at the access site/route/channel.

Conclusions: EUPD is a safe and feasible alternative approach to ERP, which i) can only be performed by experienced interventional endoscopists/-sonographers in centers with great expertise of therapeutic EUS, and ii) deserves further attention by a continuing systematic study analysis possibly with a multicenter design and following evaluation of patients in whom it is indicated, e.g., in case of former GI surgery and the papilla cannot be reached endoscopically or catheterized due to severe changes of chronic pancreatitis to finally achieve a general validation and recommendation on this novel therapeutic approach.

The reviewer wrote:

3. Are required key-words, no key definitions

RESPONSE:

According to this critic, we changed the key words as follows:

Key words: Endoscopic ultrasonography (EUS) – EUS-guided transmural pancreaticography – EUS-guided drainage of the pancreatic duct (EUPD) –

Prospective unicenter long-term study – Technical success Clinical success – Plastic prosthesis – Metal stent

- *In the text:*

The reviewer remarked:

1. Is not clear perioperative therapy. Only antibiotic? Clarify it.

RESPONSE:

As it is written in the text off he „Patients and Methods“ section, there are some details which need to be taken into account periinterventionally such as:

- Informed consent – described
- Perioperative administration of antibiotics – described
- Intraoperative observation whether there is flow of contrast media through the stenotic anastomosis after balloon dilatation and/or stent implantation for antegrade or retrograde drainage – is described
- Postinterventional clinical observation and registration for clinical success indicated by a loss of pain as one of the main aspects of clinical success – described
- Postprocedural imaging using transabdominal ultrasound to depict air bubbles

To avoid redundant remarks and not to enlarge the manuscript unnecessarily, we did not favor to additionally list all of this aspects again in a separate Table, also to limit text, No. of Figures and Tables at all.

The authors respectfully ask for the reviewer’s understanding for this position.

The reviewer criticized:

2. Tables 2 and 3 not summarize clearly the results pragraph. Improve the tables

RESPONSE:

With all of our respect, we did not want to reflect the text of the “Results” section within the tables 2 and 3 and vice versa. Actually, we were going to provide additional information to the text – finally to avoid double depiction / description of data as it usually has to be pursued to avoid it.

The authors beg politely the editor and reviewer to accept this opinion.

The reviewer suggested:

3. It wpould be appropriate to add a table with the clinic-pathological features of patients selected for this study. Alternatively improves table 1

RESPONSE - The authors followed the reviewer’s recommendation as you can see:

Table 1. Clinicopathological characteristics of EUPD (2002-2014).

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CATEGORY	DATA	

Clinicopathological characteristics		
Patients: * <i>n</i> (%) (enrolled in total)	<i>n</i> = 94	100 %
* Age [years]	Mean, 54	Range, 28-87
* Sex ratio [<i>n</i>]	m : f	60 : 34
Interventions [<i>n</i> (%)]	<i>n</i> = 111	100 %
Duration of the procedure [min]	Mean, 21	Range, 15-69
EUS-guided pancreatography: * Indication	<i>n</i> = 94	100 %
* Success rate	<i>n</i> = 94	100 %
EUS-guided drainage: * Indication	<i>n</i> = 83	100 % (88.3 % out of <i>n</i> =94)
* Success rate	<i>n</i> = 47	56,6 %

Indication for EUPD [<i>n</i> _{Total} = 94]	Number [<i>n</i>]	Percent [%]
Chronic pancreatitis	35	37

Former surgical intervention with retention of the pancreatic duct	30	32
Pancreas divisum	15	16
Disconnected pancreatic tail syndrome	9	10
Persisting fistula postoperatively	5	5

EUS-guided drainage of the pancreatic duct	Number [<i>n</i>]	Percent [%]
Total No.	83	100
Success rate	47	56,6
Route of access [<i>n</i> =47]: * Transpapillary * Transgastrically	21 26	44.7 55.3

Minor points

The reviewer commented:

Methods and Discussion are not be read fluently . Improves it.

RESPONSE:

To improve it, all authors carefully proof-read the manuscript once again including the impraival by a native speaker providing “language service”.

You may see the substantial number of corrections made (and marked by the Word correction function).

Sincerely,

Prof. U. Will, MD (on behalf of the co-authors)