

Perforated Duodenal ulcers – surgery or endoscopic stent treatment, a randomized multicentre study

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Boras, Sweden

Summary

Perforated duodenal ulcer is a life threatening complication of peptic ulcer disease. Despite the decline in ulcer disease during the last decades, ulcer perforations remain a serious condition with high morbidity and mortality. Many patients are old and co-morbid. The standard treatment is surgical closure using open or laparoscopic techniques. We started to treat some of the old and co-morbid patients, who had high operative risks, with covered duodenal stents together with percutaneous drain placement. The results are promising [1]. We now plan to start a randomised multicentre study comparing stent placement and surgical closure for perforated duodenal ulcers.

Background

Perforated duodenal ulcer is a life threatening complication of peptic ulcer disease. The incidence of uncomplicated peptic ulcer disease has decreased during the last decades but complications such as perforations still pose a serious threat. Both morbidity and mortality rates (10-40%) are still high [2,3]. In a recently published Norwegian epidemiological study the current incidence of perforated ulcers was 6.5/100 000 inhabitants/year and 1/3 of these were duodenal perforations. This study also shows that the population suffering from ulcer perforations are old and have a high degree of co-morbidity. The 30-day mortality rate was 16% for all ulcer perforations but as high as 23% for the duodenal localisation. The older patients had worse prognosis, mortality was 50 times higher for patients above 60 years [4].

The traditional treatment of a perforated duodenal ulcer is surgical closure, performed using open or laparoscopic surgical techniques. Results vary in the literature but high morbidity rates (up to 35%) due to surgical or medical complications are reported together with mortality rates of 5-16% [5,6]. The risks increase with age, co-morbidities and technically complicated surgical procedures[7].

Conservative treatment with antibiotics and nasogastric tube has been advocated and is still in use for old and co-morbid patients. However, this method has shown poor results with high mortality rates. In a Suisse retrospective study comprising 332 patients treated for perforated ulcer 12 were treated conservatively. Eight of them died (8/12) [8]. In a recent Egyptian study percutaneous drain placement through a mini-laparotomy was added to the conservative strategy. This technique seemed to slightly decrease the mortality rate (20%) [9].

Placement of covered stents has become the treatment of choice for oesophageal perforations, iatrogenic or spontaneous. The method has shown good results together with percutaneous pleural drainage [10,11]. The same principle is used to treat anastomotic leakages after gastric-bypass-surgery where covered stents together with abdominal drains are used to treat leakages in the gastroenteroanastomosis [12,13]. Also for these patients with good results. The main advantage of stent treatment is the avoidance of surgery, which in itself carries risks of further complications.

Inspired by these results we started to treat patients with perforated duodenal ulcers with placement of a covered duodenal stent (table 1) a couple of years ago. The first two patients had leakages after surgical closure, and the other 8 patients were primarily treated with a stent due to co-morbidities or high operative risks. 8/10 of these patients had an abdominal drain placed either at an initial laparoscopy or post stent placement using radiologic

Program Director/Principal Investigator (Last, First, Middle):

techniques. The mortality in this series was 1/10. The first eight patients in our series constitute the case-series that we published in Endoscopy 2013 [1].

Early start of postoperative oral nutrition is advantageous for the all patients after major abdominal surgery as the gut flora is better preserved and the bacterial translocation from the gut is minimized [14]. Duodenal stent placement makes oral intake possible almost immediately after the placement. In our series the median time till oral intake was 3 days (0-7). The first 4 patients had nil per mouth for a few days after stents placement as we were more cautious, but the last 3 patients started oral intake immediately after the stent procedure [1].

	Age	Gender	Indication for stent treatment	Primary stenting	Abdominal drainage	Time from admission to stenting (days)	Stent removal after (days)	Hospital stay post stenting (days)
Patient 1	71 y	Female	Postoperative leakage x 3	No, after surgery	At primary surgery	36	21	21
Patient 2	66 y	Male	Postoperative leakage x 1	No, after surgery	At primary surgery	10	56	14
Patient 3	87 y	Female	Deteriorated condition, delayed diagnosis	Yes	No	7		1 (†)
Patient 4	80 y	Female	Technically difficult surgical closure	Yes	Yes, at laparoscopy	3	15	22
Patient 5	87 y	Female	Post ulcer stricture, perforation after dilatation	Yes	No	<1	44	9
Patient 6	62 y	Male	Known dense abdominal adhesions, high technical operative risk	Yes	Yes, percutaneous	<1	40	17
Patient 7	86 y	Female	Refused surgery, leaking after 5 days of conservative treatment	Yes	Yes, percutaneous	7	14	14
Patient 8	81 y	Female	Severe comorbidities, High operative risk	Yes	Yes, percutaneous	3	33	36
Patient 9	77	Female	Difficult closure, frail patient	Yes	Yes, at laparoscopy	0	12	6
Patient 10	70	Male	Severe comorbidities, difficult closure, obese	Yes	Yes, at laparoscopy	2	35	20
Mean:	77y	7 Female 3 male			Median:	3	33	17

Table 1: Results from our series, the first 10 patients

Hypothesis

Based on the results from our series together with the reported good results from stent treatment of postoperative leakages and oesophageal perforations, we believe that stent treatment of perforated duodenal ulcers can be an option even in uncomplicated cases.

We expect stent treatment together with percutaneous drain placement to result in shorter operating times, a less pronounced surgical trauma, fewer complications and quicker recovery

We also believe that old and co-morbid patients have the most to gain from this new method as they today have the poorest prognosis.

A disadvantage with stent placement is that the patients need to return for gastroscopy with stent extraction after 2-3 weeks.

Aim

To compare stent placement and surgical treatment of a perforated duodenal ulcer in a prospective randomised multicenter study.

Study design

Prospective randomised multicenter study

Method

Inclusion

Patients presenting at the ER with symptoms and signs consistent with a G-I perforation together with findings of free air on a CT-scan, will be evaluated for inclusion.

Randomisation will take place before confirmation of the diagnosis. (To give the endoscopist time to go to the hospital.)

Groups:

1. Stent placement
2. Surgical closure, open or laparoscopic technique

A diagnostic laparoscopy will be performed to establish the diagnosis. If a perforation is not evident a peroperative gastroscopy will be performed. If a perforated duodenal ulcer is not found the patient will be excluded from the study.

Stent treatment:

Laparoscopic lavage of the abdominal cavity will be performed as needed. A peroperative gastroscopy will be performed and a guide wire will be placed into the bowel distally to the duodenum. A covered duodenal stent will be introduced over the wire and placed with the oral end in the stomach and the covered part covering the perforation. The partially covered Hanaro duodenal stent from MI-tec Korea will be used.

Surgical closure:

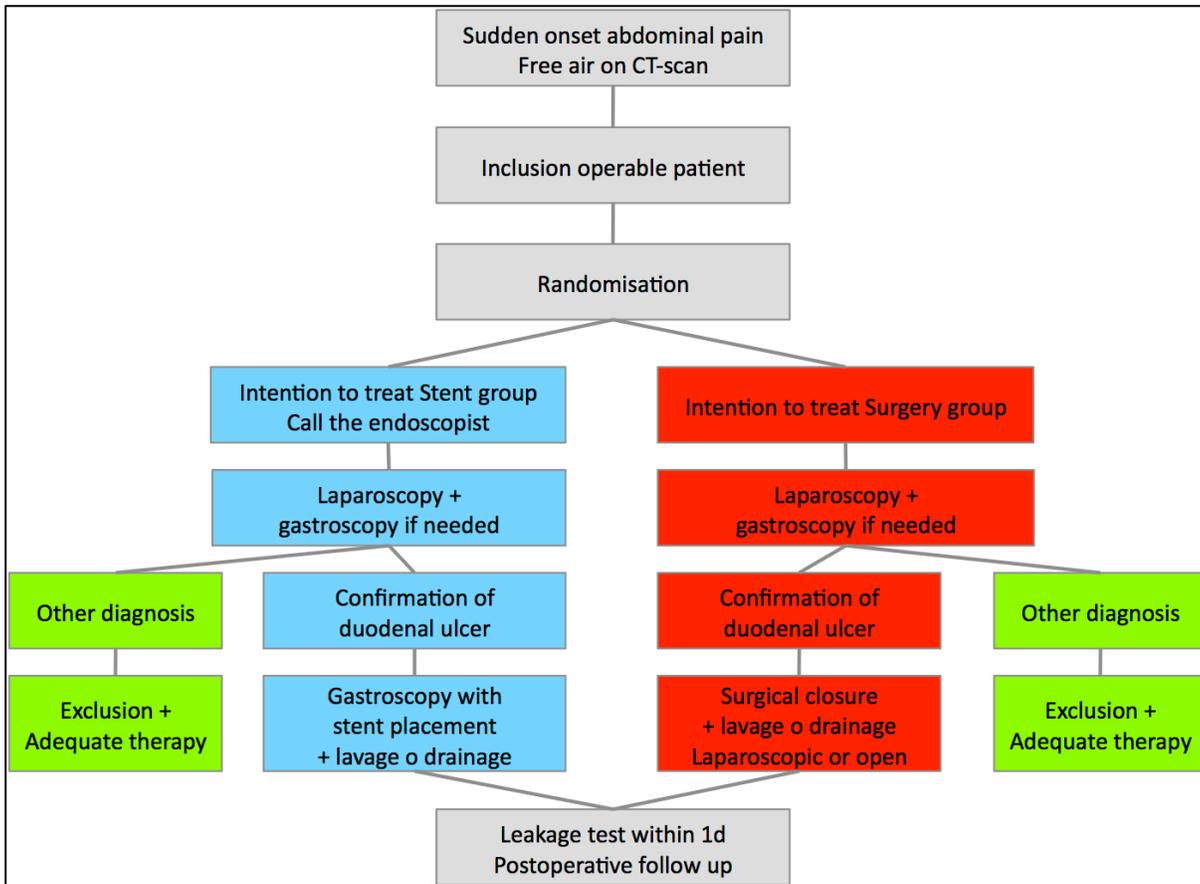
Surgical closure can be performed using open or laparoscopic surgery, according to the surgeon's preference. Lavage will be performed as above.

Postoperative follow up:

Intravenous PPI-treatment starts immediately postoperatively. Leakage test using methylene blue will be performed on the first postoperative day. If there is no leakage the patient can start oral intake of liquids at once and take oral medication the next day.

- Stented patients continue with liquid and soft food until stent-extraction.
- Operated patients start oral intake according to local guide-lines
- Ordinary mobilisation according to the patients' capacity
- Body temperature twice daily during at least three days
- Blood samples for Hb, CRP and WBC levels during at least three days and more if needed
- All medication for pain relief, including regional anaesthesia will be recorded.
- Daily self-estimation of pain and nausea using a VAS-scale.
- Further radiologic examinations can be performed if clinically indicated
- Complications will be recorded and classified according to Clavien-Dindo
- Hospital stay will be recorded
- Endoscopic stent extraction will take place two weeks post stent placement

Study design, flow chart:



Inclusion criteria:

- Age > 18 years

- Admitted with clinical suspicion of G-I perforation
- Free air on a CT-scan
- ASA score ≤ 4
- Autonomic patient
- No need for language translation

Exclusion criteria

- Age < 18 years
- ASA-score >4
- Non-autonomic patient
- Need language translation

IRB

We are currently working on the IRB application

Endpoints:

Primary endpoint:

- Complications according to Clavien-Dindo [15,16]

Secondary endpoints:

- Hospital stay
- Consumption of analgesics

Power calculation

The intention of the study is to show that stent treatment results in fewer complications than surgery. However, there are no previous results to base a power calculation on. The literature on perforated ulcer treatment is limited and mainly noncurrent.

We have performed a retrospective study at our own hospital including all patients treated for a perforated duodenal ulcer during 2009-2012. A total of 27 patients were identified, 19 were operated with surgical closure or resection and 8 received stent treatment (the last 8 in table1) [17]. 8/19 (42%) patients in the operated group and 2/8 (25%) in the stent group had complications showing a tendency towards fewer complications in the stent group but no statistically significant difference as the number of patients in this study was limited [17].

To show non-difference in outcome after stent treatment and surgery we assume that the new treatment (stent) results in 10% complications and that surgical closure results in 30%. Calculations give that 50 patients in each group will be needed to achieve 80% power with an α -level of 5%. An intermediate analysis will be performed when 50% of the inclusions are completed for correction of these calculations.

Feasibility

This will be a regional study in the region of Västra Götaland with four cooperating hospitals. We have 1.7 million inhabitants. According to the recently published Norwegian study the incidens of perforated duodenal ulcers is calculated to 2/100 000 inhabitants / year. [4]. Leading to 30 cases/year in our region. To achieve more efficient inclusion, we plan to invite more surgical centres in other Swedish regions.

Statistics

All patient data will un-identified and handled group-wise.

Group-wise comparisons will be performed using non-parametric statistic methods. Wilcoxon's sign-rank test will be used for pair-wise comparisons and the Mann-Whitney-U test for non-pair-wise comparisons. The Chi-square test will be used for nominal comparisons. A p-value of < 0.05 will be considered statistically significant. All analyses will be performed using the SPSS software 20.

Available resources

We have the resources in the clinical setting in our hospital. Both for stenting and surgical procedures. We also have an organisation with study nurses and enthusiastic co-workers.

References

1. Bergstrom M, Vazquez JA, Park PO. Self-expandable metal stents as a new treatment option for perforated duodenal ulcer. *Endoscopy* 2013;45:222-225
2. Moller MH, Shah K, Bendix J, et al. Risk factors in patients surgically treated for peptic ulcer perforation. *Scand J Gastroenterol* 2009;44:145-152, 142 p following 152
3. Bertleff MJ, Lange JF. Perforated peptic ulcer disease: a review of history and treatment. *Dig Surg* 2010;27:161-169
4. Thorsen K, Soreide JA, Kvaloy JT, Glomsaker T, Soreide K. Epidemiology of perforated peptic ulcer: age- and gender-adjusted analysis of incidence and mortality. *World J Gastroenterol* 2013;19:347-354
5. Hemmer PH, de Schipper JS, van Etten B, et al. Results of surgery for perforated gastroduodenal ulcers in a Dutch population. *Dig Surg* 2011;28:360-366
6. Lau H. Laparoscopic repair of perforated peptic ulcer: a meta-analysis. *Surg Endosc* 2004;18:1013-1021
7. Kim JM, Jeong SH, Lee YJ, et al. Analysis of risk factors for postoperative morbidity in perforated peptic ulcer. *J Gastric Cancer* 2012;12:26-35
8. Alizadeh N, Buhler L, Huber O, Morel P. [Conservative treatment of gastroduodenal peptic ulcer perforations: indications and results]. *Schweiz Med Wochenschr Suppl* 1997;89:17S-19S
9. Saber A, Gad MA, Ellabban GM. Perforated duodenal ulcer in high risk patients: is percutaneous drainage justified? *N Am J Med Sci* 2012;4:35-39
10. Johnsson E, Lundell L, Liedman B. Sealing of esophageal perforation or ruptures with expandable metallic stents: a prospective controlled study on treatment efficacy and limitations. *Dis Esophagus* 2005;18:262-266
11. van Boeckel PG, Sijbring A, Vleggaar FP, Siersema PD. Systematic review: temporary stent placement for benign rupture or anastomotic leak of the oesophagus. *Aliment Pharmacol Ther*;33:1292-1301
12. Blackmon SH, Santora R, Schwarz P, Barroso A, Dunkin BJ. Utility of removable esophageal covered self-expanding metal stents for leak and fistula management. *Ann Thorac Surg*;89:931-936; discussion 936-937
13. Eubanks S, Edwards CA, Fearing NM, et al. Use of endoscopic stents to treat anastomotic complications after bariatric surgery. *J Am Coll Surg* 2008;206:935-938; discussion 938-939
14. Shou J, Motyka LE, Daly JM. Intestinal microbial translocation: immunologic consequences and effects of interleukin-4. *Surgery* 1994;116:868-876
15. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-213
16. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187-196
17. Nsouli G, J. A-V, M. B, Park PO. Behandling av perforerat ulcus duodeni: rafi eller stent? *Svensk kirurgi* 2013;Abst SFÖAK 256

Biographical sketches

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
 Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Per-Ola Park	POSITION TITLE Associate Professor of Surgery, Senior Consultant Surgeon
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Medical Education at University of Lund, (Lund-Malmö) 1971-1977	B.S.	06/1973	Med school
Specialist General Surgery University of Uppsala, Thesis	MD	11/1978 07/1983	
Sahlgrenska University of Gothenburg	PhD Associate Professor	11/1991 12/2009	Surgery Surgery

A. Personal Statement

The goal of the proposed research is to investigate if endoscopic stent treatment is as safe and efficient as surgical closure of a perforated duodenal ulcer. It is planned as a multi-center study. I have the expertise, leadership and motivation necessary to successfully carry out and lead the proposed study. I have been both participating in as well as organizing multicenter studies. I also have a well organized working staff and co-workers to carry out the study. I and my co-workers are experienced surgeons and interventional endoscopists. I have a long experience in advanced endoscopic treatments both experimentally and clinically. My research field is “mini-invasive surgery and NOTES” and I was together with my co-worker first to publish NOTES transgastric cholecystectomy. We are well experienced in stent treatment of the esophagus, bile ducts and colon. We have published articles on experimental and clinical endoscopic stent treatments including a case series of stent treatment of perforated duodenal ulcers. The current application builds logically on my prior work, and I have chosen co-investigators (Drs. Maria Bergström and Jorge Alberto Arroyo Vázquez) who provide additional expertise. The project is also planned to be a part of Dr Jorge Alberto Arroyo Vázquez’s thesis. In order to speed up the inclusions we have invited all the hospitals in the region to participate in the study. They have accepted the invitation.

In summary, I have a demonstrated record of successful and productive research projects in the field of therapeutic endoscopy as well as surgery and my expertise and experience have prepared me to lead the proposed project.

B. Positions and Honors

Positions and Employment

Appointments after Specialist in General Surgery:

Malmö Allmänna Sjukhus 1983-1987: Junior Staff Surgeon

Värnamo Sjukhus 1987-1996: Senior Consultant

6 months appointment at Dep of Surgery, Uppsala Akademiska sjukhus 1989

3 months appointment at Dep of Surgery, Linköpings Universitetssjukhus 1993

7 months appointment at Dep of Surgery, Ryhovs Sjukhus, Jönköping 1995

Centrallasarettet, Växjö 1996-2002: Senior Consultant

Sahlgrenska University Hospital/Östra 2002-2009: Consultant at Dep of Surgery

Member of Upper Gastrointestinal team

Head of Endoscopic Unit/Östra 2002-2008

Present appointment:

South Älvsborgs Hospital, Borås 2009--: Consultant at Dep of Surgery

Member of Upper Gastrointestinal team

Head of Upper Gastrointestinal team 2012 –

Other Experience and Professional Memberships

Member of Editorial Board, Endoscopy 2006-2008, and Gastrointestinal Endoscopy

Member of the Swedish Medical Society 1978—

Member of The Swedish Surgical Society 1983—

Member of the Executive Board of the Swedish Laparoscopic Society 1992-1994

Member of the Swedish Gastroenterology Society 2007—

Member of the Executive Board of the Swedish Gastroenterology Society 2007-2009

Reviewer Gastrointestinal Endoscopy 2006-

Reviewer Endoscopy 2008-

Reviewer World journal of gastrointestinal endoscopy 2010-

Reviewer Surgical Innovation 2011-

Honors

Mentor of the Year at Växjö Central Hospital 2002

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Angenete, E., D. Asplund, M. Bergstrom, and P.O. Park, *Stenting for colorectal cancer obstruction compared to surgery - a study of consecutive patients in a single institution*. Int J Colorectal Dis. 2012 May;27(5):665-70. Epub 2011 Nov 29.
2. Bergström, M., Arroyo-Vázquez, JA., Park, PO.: *Self Expandable Metal Stents (SEMS) as a new treatment option for perforated duodenal ulcer –a case series*. Endoscopy. Endoscopy 2013;45(3):222-5. Epub 2012 Dec 3.

Additional recent publications of importance to the field (in chronological order)

1. Park, P.O., M. Bergstrom, K. Ikeda, A. Fritscher-Ravens, and P. Swain, *Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos)*. Gastrointest Endosc, 2005. **61**(4): p. 601-6.
2. Swanstrom, L.L., R. Kozarek, P.J. Pasricha, S. Gross, D. Birkett, P.O. Park, V. Saadat, R. Ewers, and P. Swain, *Development of a new access device for transgastric surgery*. J Gastrointest Surg, 2005. **9**(8): p. 1129-36; discussion 1136-7.
3. Bergstrom, M., K. Ikeda, P. Swain, and P.O. Park, *Transgastric anastomosis by using flexible endoscopy in a porcine model (with video)*. Gastrointest Endosc, 2006. **63**(2): p. 307-312.
4. Bergstrom, M., P. Swain, and P.O. Park, *Measurements of intraperitoneal pressure and the development of a feedback control valve for regulating pressure during flexible transgastric surgery (NOTES)*. Gastrointest Endosc, 2007. **66**(1): p. 174-8.
5. Park, P.O., M. Bergstrom, K. Ikeda, A. Fritscher-Ravens, S. Mosse, M. Kochman, and P. Swain, *Endoscopic pyloroplasty with full-thickness transgastric and transduodenal myotomy with sutured closure*. Gastrointest Endosc, 2007. **66**(1): p. 116-20.
6. Bergstrom, M., P. Swain, and P.O. Park, *Early clinical experience with a new flexible endoscopic suturing method for natural orifice transluminal endoscopic surgery and intraluminal endosurgery (with videos)*. Gastrointest Endosc, 2008. **67**(3): p. 528-33.
7. Raju, G.S., A. Fritscher-Ravens, R.I. Rothstein, P. Swain, A. Gelrud, I. Ahmed, G. Gomez, M. Winny, T. Sonnanstine, M. Bergstrom, and P.O. Park, *Endoscopic closure of colon perforation compared to surgery in a porcine model: a randomized controlled trial (with videos)*. Gastrointest Endosc, 2008. **68**(2): p. 324-32.
8. Park, P.O. and M. Bergstrom, *Transgastric peritoneoscopy and appendectomy: thoughts on our first experience in humans*. Endoscopy, 2010. **42**(1): p. 81-4.
9. Park, P.O., M. Bergstrom, R. Rothstein, P. Swain, I. Ahmed, G. Gomez, and G.S. Raju, *Endoscopic sutured closure of a gastric natural orifice transluminal endoscopic surgery access gastrotomy compared with open surgical closure in a porcine model. A randomized, multicenter controlled trial*. Endoscopy, 2010. **42**(4): p. 311-7.

Program Director/Principal Investigator (Last, First, Middle): Prof Per-Ola Park

10. Park, P.O., G.L. Long, M. Bergstrom, C. Cunningham, O.J. Vakharia, G.J. Bakos, K.R. Bally, R.I. Rothstein, and C.P. Swain, *A randomized comparison of a new flexible bipolar hemostasis forceps designed principally for NOTES versus a conventional surgical laparoscopic bipolar forceps for intra-abdominal vessel sealing in a porcine model*. *Gastrointest Endosc*, 2010. **71**(4): p. 835-41.
11. Azadani, A., H. Jonsson, P.O. Park, and M. Bergstrom, *A randomized trial comparing abdominal contamination and postoperative infection rates between NOTES, laparoscopic and open surgery in pigs*. *Gastrointest Endosc*. 2012 Apr;75(4):849-55. Epub 2012 Jan 28.
12. Azadani, A., M. Bergstrom, J. Dot, M. Abu-Suboh-Abadia, J.R. Armengol, and P.O. Park, *A new in-vivo method for testing closures of gastric NOTES incisions using leak of the closure or gastric yield as end-points*. *J Laparoendosc Adv Surg Tech A*. 2012 Jan-Feb;22(1):46-50. Epub 2011 Dec 6.

D. Research Support

Ongoing Research Support

Borås Forsknings- och utvecklingsfond mot cancer

Swedbank Sjuhärads stiftelse för forskning vid Södra Älvsborgs Sjukhus

Completed Research Support

Familjen Erling-Perssons Stiftelse

Greta Andersons fond för vetenskaplig forskning

Walter Andersons fond för vetenskaplig forskning

Euro-NOTES

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Maria Bergstrom		POSITION TITLE Senior Consultant Surgeon	
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Gothenburg University medical education	MD	01/89	Med. school
Värnamo Hospital, Sweden	Authorization	12/90	Internship
Östra Hospital, Gothenburg, Sweden	Specialist, general surgery	07/96	Residency, general surgery
Gothenburg University	Ph.D.	12/07	laparoscopic surgery

A. Personal Statement

The goal of the proposed research is to investigate if endoscopic stent treatment is as safe and efficient as surgical closure of a perforated duodenal ulcer. It will be a multi-center study. I will be participating faculty and co-PI. I have a broad experience from research in experimental cell-lines, animal studies and human clinical studies. I also have good organizing capacity and writing skills. My thesis work was carried out on laparoscopic surgery and peritoneal physiology including both experimental and human studies. I am both a senior surgeon and interventional endoscopist. I have together with our research team taken part in the early development and research on NOTES, publishing the first NOTES transgastric cholecystectomy and early survival studies with NOTES gastroenteroanastomoses.

Our current research projects focus on mini-invasive surgery. We are all experienced in G-I stent placement and carry out these procedures in our daily practice. As surgeons in an emergency hospital we also treat perforated ulcers on a regular basis. As we already see and treat these patients, inclusion for the study will be fairly easy. In summary I believe I have the experience, enthusiasm and capacity to launch this study and also to complete it together with my co-workers.

B. Positions and Honors

1989-1990	Internship, Värnamo, Sweden
1991-1993	Residency, Skene, Sweden
1993-1996	Residency, Östra hospital, Gothenburg, Sweden
1996-2006	Staff surgeon, Östra hospital, Gothenburg, Sweden
2006-2009	Consultant surgeon, Sahlgrenska University Hospital /Östra, Gothenburg, Sweden
2009-	Senior Consultant surgeon, South Älvsborg Hospital, Boras, Sweden

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Angenete, E., D. Asplund, M. Bergstrom, and P.O. Park, *Stenting for colorectal cancer obstruction compared to surgery--a study of consecutive patients in a single institution*. Int J Colorectal Dis, 2012. **27**(5): p. 665-70. Acc No 22124678
2. Bergstrom, M., J.A. Vazquez, and P.O. Park, *Self-expandable metal stents as a new treatment option for perforated duodenal ulcer*. Endoscopy, 2013. **45**(3): p. 222-5. Acc No 23208777

Additional recent publications of importance to the field (in chronological order)

1. Park, P.O., M. Bergstrom, K. Ikeda, A. Fritscher-Ravens, and P. Swain, *Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos)*. Gastrointest Endosc, 2005. **61**(4): p. 601-6. Acc No 15812420
2. Bergstrom, M., K. Ikeda, P. Swain, and P.O. Park, *Transgastric anastomosis by using flexible endoscopy in a porcine model (with video)*. Gastrointest Endosc, 2006. **63**(2): p. 307-312. Acc No 16427940
3. Bergstrom, M., P. Falk, and L. Holmdahl, *Effect of acidosis on expression of mesothelial cell plasminogen activator inhibitor type-1*. Surg Endosc, 2006. **20**(9): p. 1448-52.
4. Bergstrom, M., P. Swain, and P.O. Park, *Measurements of intraperitoneal pressure and the development of a feedback control valve for regulating pressure during flexible transgastric surgery (NOTES)*. Gastrointest Endosc, 2007. **66**(1): p. 174-8.

5. Park, P.O., M. Bergstrom, K. Ikeda, A. Fritscher-Ravens, S. Mosse, M. Kochman, and P. Swain, *Endoscopic pyloroplasty with full-thickness transgastric and transduodenal myotomy with sutured closure*. *Gastrointest Endosc*, 2007. **66**(1): p. 116-20.
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7. Bergstrom, M., P. Falk, P.O. Park, and L. Holmdahl, *Peritoneal and systemic pH during pneumoperitoneum with CO2 and helium in a pig model*. *Surg Endosc*, 2008. **22**(2): p. 359-64.
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13. Azadani, A., M. Bergstrom, J. Dot, M. Abu-Suboh-Abadia, J.R. Armengol-Miro, and P.O. Park, *A new in vivo method for testing closures of gastric NOTES incisions using leak of the closure or gastric yield as endpoints*. *J Laparoendosc Adv Surg Tech A*, 2012. **22**(1): p. 46-50.

D. Research Support

List both selected ongoing and completed research projects for the past three years (Federal or non-Federally-supported). *Begin with the projects that are most relevant to the research proposed in the application.* Briefly indicate the overall goals of the projects and responsibilities of the key person identified on the Biographical Sketch. Do not include number of person months or direct costs.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Jorge Alberto Arroyo Vázquez		POSITION TITLE Resident surgeon	
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EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Universidad Autónoma de Guadalajara, Mex	MD	06/01	Med. school
Hospital de la Santa Creu I Sant Pau, Barcelona, Spain	Mexican authorization	07/02	Internship
South Älvsborg Hospital, Borås, Sweden	Swedish autorization	07/09	Internship
South Älvsborg Hospital, Borås, Sweden	.		Residency, general surgery

A. Personal Statement

I will participate as junior researcher. I will work hard on this project that will be a part of my thesis.
I am a minimal invasive fellow.

B. Positions and Honors

2001-2002	Internship, Hospital de la Santa Creu I Sant Pau, Barcelona, Spain
2002-2003	General practitioner, Secretaria de Salud Jalisco, Mexico
2005-2007 Sweden	Assistant doctor, Sahlgrenska University Hospital, Gothenburg,
2008-2009	Internship, South Älvsborg Hospital, Borås, Sweden
2009-	Residency, South Älvsborg Hospital, Borås, Sweden

C. Selected Peer-reviewed Publications

- Bergstrom, M., J.A. Vázquez, and P.O. Park, *Self-expandable metal stents as a new treatment option for perforated duodenal ulcer*. Endoscopy, 2013. **45**(3): p. 222-5.

SAGES RESEARCH GRANT APPLICATION BUDGET SHEET

Detailed budget for 12 month period from _____ through _____.

Dollar amount requested (Omit cents) 30000

Total for the grant request may not exceed \$30,000.

* Salary funds should be used for staff required to execute the study, but should not be used for salary support of the principal investigator. If salary support exceeds 50% of the project budget, then specific justification is required.

**Funds requests for travel for the presentation of a SAGES funded study should be limited to \$1,000.

NAME	POSITION TITLE	TIME/EFFORT		SALARY
		%	Hrs/ Week	
1. Dr Per-Ola Park	Principal Investigator*			
2. Dr Maria Bergstrom	Co-investigator	10		
3. Dr Jorge Arroyo Vázquez	Co-investigator	20		
4. Sari Karhu, nurse	Study nurse	20		
5.				
CONSULTANT COSTS		statistician \$1500		
EQUIPMENT (List all Items & Total Equipment Cost)		Items		
SUPPLIES (List all Items & Total Supplies Cost)		Stents,		
TRAVEL**				
PATIENT CARE COSTS				
CONSORTIUM/CONTRACTUAL COSTS				

Program Director/Principal Investigator (Last, First, Middle): Prof Per-Ola Park

OTHER EXPENSES all Items & Total Cost)	(List Items
TOTAL DIRECT COSTS	