



complicanze in EUS

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Crema

Lecture plan

Background

1. Complications to non-interventional EUS
2. Complications to EUS-guided biopsy
3. Complications to EUS-guided treatments
 - Risk factors for complications
 - Specific complications: prevention and management

Background

1. EUS : accurate modality for locoregional staging of esophageal, gastric, rectal, and pancreatic cancers
2. EUS-guided interventional procedures, either diagnostic (biopsy) or therapeutic
3. Because of the nature of this procedure and the equipment required, EUS and its interventional applications would be expected to be associated with a set of complications different from those associated with standard endoscopic procedures
4. For EUS-guided sampling or puncture the GI lumen must be crossed to gain access to sterile structures
5. 1 paper in 1983, 700 papers/year from 2007: safety issues addressed consistently from 2005

Complications to non-interventional EUS

The most severe complication : **esophageal perforation**

- **prospective** study of >400 patients: perforation rate of **0.03%**
- **retrospective** in 43,852 EUS: **0.03%** rate of cervical esophageal perforation
- For comparison: **0.03%** rate of perforation, at any anatomic site, in 211,410 diagnostic upper GI endoscopic examinations in USA
- majority of perforations from EUS in the setting of esophageal stenosis, either malignant or benign, often unclear whether perforation caused by the echoendoscope itself or by esophageal dilatation prior to the EUS

Bacteremia after conventional EUS : prospectively 2% with no clinical sign of infection.

This value is within the range observed for diagnostic upper endoscopy

Rosch T, GIE 1993 , Van Dam J, Cancer 1993, Nick NJ , GIE 1996, Das A, GIE 2001, Janssen J, GIE 2004

Complications to non-interventional EUS

	Procedures	AE n (%)
Conventional EUS upper gastrointestinal tract	9,847	5 (0.05) 3 perforations 2 bleeding
Conventional EUS lower gastrointestinal tract	884	
	10,731	5 (0.046)

2 complications occurred within first 100 conventional EUS performed by 6 operators (2/600: 0.33 %)
3 complications from the remaining 10,131 procedures (0.02%, p =0.0008)

triggering factors for complications of conventional EUS were identified in 4/5 patients:
pathological wall conditions in 3 perforations; repeated vomiting at the beginning of the exam in 1 bleeding

Complications to non-interventional EUS

Recommendations

- Operator experience matters: appropriate supervised training
- Caution if luminal stenosis : DO NOT DILATE
- NO antibiotic prophylaxis in patients undergoing EUS

Complications to EUS-guided biopsy

systematic analysis of EUS-guided FNA related morbidity and mortality

**morbidity rate in 10,941 patients in 51 studies:
0.98%**

overall mortality rate 0.02%

EUS-FNA related complications	No.	%
Chest or abdominal pain	37	34.6
Acute pancreatitis	36	33.6
Mild-moderate	33	
Severe	3	
Bleeding	14	13.1
Fever	12	11.2
Infection	5	4.7
Perforation	2	1.9
Bile leakage	1	0.9
Total	107	100

Wang KX, GIE 2011

Complications to EUS-guided biopsy

	Retrospective studies	Prospective studies	P value
Pancreas	0.59%	2.64%*	.0000
Pancreatic mass	0.35%	2.44%*	.0000
Pancreatic cyst	2.33%	5.07%†	.0363

Retrospective studies underreport AEs

Liver	2.29%	2.44%	.9337
Abdominal mass	0%	0.36%	.0875
Ascites	3.33%	4.0%	.4256
Total	0.64%	1.72%*	.0000

FNA of liver: third highest morbidity rate

Risk increased by 3-10 in cystic lesions

	Total no. of patients	Pain	Pancreatitis	Fever	Bleeding	Infection	Perforation
Pancreas	8246 (1780/6466)	31 (25/6)	36 (12/24)	7 (3/4)	8 (5/3)	2 (1/1)	1 (1/0)
Pancreatic mass	7337 (1642/5695)	24 (22/2)	26 (11/15)	4 (2/2)	5 (4/1)		1 (1/0)
Pancreatic cyst	909 (138/771)	7 (3/4)	10 (1/9)	3 (1/2)	3 (1/2)	2 (1/1)	

Complications to EUS-guided biopsy-pancreatic cystic lesions

- Brush through 19G needle: abandoned for severe AEs including death
- Minibiopsy forceps through 19G: 22% of AEs in 61 pts
- NCLE through 19G needle : 3-9% AEs, acute pancreatitis, bleeding

IT Consensus GL for pancreatic cystic neoplasms , DLD 2014

ESGE guidelines, Endoscopy 2017

Crinò S, GIE 2019

Complications to EUS-guided biopsy

RISK FACTORS

- Cystic lesions : at risk for bleeding /infection
- Operator experience : most AEs among first 100 procedures
- Needle size/passes: NO differences in AEs for different calibers or number of passes

Buscarini E, DLD 2006

Thomas T, AJG 2009

Wang KY, GIE 2011

Complications to EUS-guided biopsy-specific complications

INFECTION

- Bacteremia: similar to EUS without FNA: NO ab prophylaxis
- **Antibiotic prophylaxis** (fluoroquinolones, + treatment 3-5 days after) for EUS-guided puncture of cystic lesions: **Key Performance Indicator, target 95%**
- Avoid puncturing mediastinal cysts

EFSUMB guidelines , EJU 2016

ESGE guidelines, Endoscopy 2017

ESGE guidelines, Endoscopy 2018

Complications to EUS-guided biopsy-specific complications

BLEEDING

- Patient history, and coagulations check-up :INR<1.5, platelet count >50,000
- APA and anticoagulation stopped if cystic lesion; Aspirin may be continued if solid mass
- pancreatic cyst bleeding: STOP needle passes, EUS observation, antibiotics



Complications to EUS-guided biopsy-specific complications

Recommendation 22

Cystic pancreatic masses requiring surgery should not be managed with EUS-guided biopsy alone (LoE 5, GoR D). Strong consensus.

be a clinician not only an endosonographer

Complications to EUS-guided biopsy-specific complications

ACUTE PANCREATITIS

- the site of the puncture should be as close as possible to the pancreatic lesion to reduce transversing of normal pancreas
- number of needle passes should be as low as possible: ROSE ?

Complications to EUS-guided biopsy-specific complications

PERFORATION

- GI wall perforation during EUS FNA is generally due to the endoscopic instrument itself rather than to the needle and includes esophageal or duodenal perforation
- Up to 24% of esophageal perforation after stricture dilation: DO NOT DILATE esophageal stricture for completing EUS(-FNA)
- 0.06% in a 2009 prospective trial

Complications to EUS-guided biopsy-specific complications

TUMOR SEEDING

- 2003-2016 14 cases of needle tract seeding after EUS-FNA
- 11/14 after EUS-FNA of pancreatic masses
- the transgastric needle track not resected: resectable tumors of body and tail of most concern!

Complications to EUS-guided treatments

- **EUS-guided drainage of pancreatic fluid collections**
- **EUS-guided Celiac plexus neurolysis/block**
- EUS-guided drainage of abdominal (non-peripancreatic) and pelvic collections
- EUS-guided Biliary drainage
- EUS-guided Pancreatic duct drainage
- EUS-guided tumor treatment

Complications to EUS-guided drainage of pancreatic fluid collections

- EUS guided drainage of symptomatic PFCs : transmural stents has mostly replaced surgery or percutaneous drainage
- high success rate 87%-97%
- low AEs 6%-34%, and mortality 0%-1% rates

Baron T, GIE 2002 Hookey LC, GIE 2006

Cahen D, Endoscopy 2005

Varadarajulu S, J Gastrointest Surg 2011

Complications to EUS-guided drainage of pancreatic fluid collections

Systematic review

Total	55 studies	1867 pts	Complications 17% (0%-52%)
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- **bleeding** (69 cases),
- **superinfection** (52 cases)
- **stents migration** that required endoscopic reintervention (51 cases)
- **perforation** treated with surgery (27 cases) or conservatively (18 cases)
- **5 deaths** procedure related

**With advent of LAMS
after 2014....**

	LAMS (n = 31)	Plastic (n = 29)	P values
Resolution of SIRS at 24 hours post-treatment: n (%)	4 (44.4)	9 (69.2)	0.384
Resolution of organ failure at 24 hours post-treatment: n (%)	1 (50.0)	1 (25.0)	0.999
Treatment success: n (%)	29 (93.5)	28 (96.6)	0.999
Length of hospital stay (days):			
Mean (SD)	6.2 (9.0)	12.2 (21.1)	0.129
Median	3	4	
IQR	6	13	
Range	0–38	0–103	
Adverse events: n (%)			
Overall	13 (41.9)	6 (20.7)	0.077
Stent-related	10 (32.3)	2 (6.9)	0.014
Prior protocol change	8 (25.8)	0	0.005
After protocol change	2 (6.5)	2 (6.9)	0.999
Clinical	3 (9.7)	4 (13.8)	0.702
Total no. of procedures for treatment success: n (%)			
Mean (SD)	2.8 (1.2)	3.2 (1.5)	0.192
Median	2	3	
IQR	1	2	
Range	2–7	2–7	
Total no. of readmissions: n (%) *			
0	21 (67.7)	18 (62.1)	0.645
1	8 (25.8)	9 (31.0)	
2	0	2 (6.9)	
3	2 (6.5)	0	
WON recurrence: n (%)	1 (3.2)	0	0.999
Mean costs, 2017 US\$:			
Total cost [†]	53 117	50 132	0.775
Procedure cost	12 155	6609	<0.001

**RCT:
non-superiority
of LAMS
over plastic stents
for drainage
of WON**

**higher rate of
stent- related
adverse events
if LAMS not removed
within 3 weeks**

Bang JY Gut 2018

Complications to EUS-guided drainage of pancreatic fluid collections

lumen-apposing metal stents or plastic stents?

Metanalysis of studies published since the revised Atlanta classification (2014 to current) included to estimate and compare the pooled rates of clinical success and adverse-events

pooled rate of clinical-success with LAMS 88.5% and with PS 88.1% $P = 0.93$

No difference was noted in the pooled rates of all adverse-events, **LAMS: 11.2% (6.8-17.9, $I^2 = 82.0$) vs PS: 15.9% (8.4-27.8, $I^2 = 78.8$); $P = 0.38$**

LAMS and PS demonstrate equal clinical outcomes and equal adverse-events in the drainage of pancreatic
WON

Complications to EUS-guided drainage of pancreatic fluid collections

Recommendations

- LAMS must be removed after 3 weeks
- NO LAMS if vascular lesions (pseudoaneurysms) in proximity

Complications to EUS-guided Celiac plexus neurolysis/block

Close to 2000 cases reported

- Most frequent (up to 30% of patients) AEs: diarrhea, abdominal pain and hypotension, usually mild (grade I-II) and self-limiting
- serious AEs reported: bleeding, abscess, abdominal ischemia, permanent paralysis and death
- the risk of serious morbidity and mortality should be weighed against expected benefits particularly in patients with a long life expectancy (*i.e.* patients with chronic pancreatitis)

Fabbri C, WJG 2014

Complications to EUS-guided treatments

procedure	Reported cases	AEs rate (range)	Mortality rate
EUS –guided necrosectomy	283	28% (0-46)	
EUS-guided Biliary drainage	1127	26%	0.4%
EUS-guided ancreatic duct drainage	248	20% (7-55)	
EUS-GD of abdominal (non-peripancreatic) and pelvic collections	120	13%	
EUS-guided gallbladder drainage	97	16%	

Complications to EUS-guided treatments- EUS-guided gallbladder drainage

non-inferiority RCT

to evaluate technical feasibility

EUS-guided vs percutaneous

59 patients

technical success

clinical success

adverse events

0% vs 3%, NS)

Recommendation 32

EFSUMB Guidelines, EJU 2016

In patients with acute cholecystitis unsuitable for cholecystectomy, EUS-guided gallbladder drainage may be considered equivalent to percutaneous transhepatic gallbladder drainage (LOE 1b; GoR B; strong consensus: 100%).

Complications to EUS-guided treatments of pancreatic cancer

Author, publication year	Study type	LoE	Therapeutic techniques	No. of patients	Technical success%	Response to treatment	Complications
Chang 2000	Case series	4	Cytoimplant	8	100	Partial 3	Iperbilirubinemia 3 Gastrointestinal toxicity 3
Nonogaki 2007	Case series	4	Dendritic cells and gemcitabine	5	100	Partial 1; stable disease 2	0
Irisawa 2007	Case series	4	Dendritic cells	7	100	Partial 3	0
Hirooka 2009	Case series	4	Dendritic cells and gemcitabine	5	100	Partial 1; stable disease 2	Hematologic toxicity 2
Hecht 2012	Case series	4	TNFrade/chemoradiation	50	100	Complete 1; partial 2; stable disease 2	Acute pancreatitis/cholangitis 3
Levy 2011	Case series	4	Gemcitabine	36	100	3 R0 resections	0
Hecht 2003	Case series	4	ONYX-015	21	100	Partial 4; stable disease 6	Infection 2 Duodenal perforation 2 Cystic fluid collection 1
Arcidiacono 2012	Case series	4	RFA	22	72	NA	Abdominal pain 3 Bleeding 1 Jaundice 2
Scopelliti S 2018	Case series	4	RFA	10	100	NA	0

Complications to EUS-guided injection of pancreatic cystic lesions

Author, publication year	Study type	LoE	Therapeutic techniques	No. of patients	Technical success%	Response to treatment	Complications
Gan 2005§	Case series	4	Ethanol lavage	25	100	Complete 8	0
Oh 2008	Case series	4	Ethanol lavage-paclitaxel	14	100	Complete 11	Acute pancreatitis 1
DeWitt 2009*	RCT	1b	Ethanol lavage vs saline lavage	25 vs 17	100	Complete 14	Abdominal pain 10 Intracystic bleeding 1 Acute pancreatitis 1
Oh 2009^	Case series	4	Ethanol lavage-paclitaxel	10	100	Complete 6 Partial 2	0
Oh 2011	Case series	4	Ethanol lavage-paclitaxel	52	100	Complete 29	0
Di Maio 2011+	Case series	4	Single vs double ethanol lavage	13	100	Complete 5	Abdominal pain 1
Caillol 2012°	Case series	4	Ethanol lavage	13	100	Complete 11	0
DeWitt 2014	Case series	4	Ethanol lavage-paclitaxel	22	100	Complete 10 Partial 5	Acute pancreatitis 3 Peritonitis 1
Oh 2014	Case series	4	Ethanol lavage-paclitaxel	10	100	NA	Intracystic bleeding 1 Abdominal pain 5 Vomiting 1

Complications to EUS

CONCLUSIONS

- remind absolute and relative contraindications to liver biopsies
- antibiotic prophylaxis/treatment if infection risk
- be a clinician not only an endosonographer: integrate clinical and imaging data
- know/use all different available techniques, including transcutaneous: choosing wisely = choosing safely
-KNOW EUS-RELATED ADVERSE EVENTS!

*....EUS e tanto altro al
maggior evento della
Gastroenterologia IT.....*



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