Supporting Information 1

Summary documents of detailed literature searches for ESGE QIC Pancreatobiliary Working Group performed by:

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SUCCESS RATE OF CANNULATION

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1.1 (A I) Statement: Does experience of endoscopists influence the rate of deep cannulation of the common bile duct / pancreatic duct during ERCP in patients with native papillas?

Population
Patients undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of cannulation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Catheterization"[Mesh] OR cannulation[Title/Abstract]) AND ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
(clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND (endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND ('cannulation'/exp OR cannulation:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic reviews' OR 'systematic reviews'/de OR 'systematic review'/lim OR [meta analysis]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 #2 or #1 or #5 or #3 or #4
#7 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8 ERCP:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 MeSH descriptor: [Catheterization] explode all trees
#11 cannulation:ti,ab,kw (Word variations have been searched)
#12 #10 or #11
#13 #12 and #6 and #9

Primary studies

PubMed

Embase
(clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND (endoscopic
Results of the bibliographic searches
After removing duplicates, 269 articles (10 reviews and 259 primary studies) were found. Another study was found through references included in others clinical questions and another one was suggested by experts. One potentially relevant systematic review and 10 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Five studies were excluded: two because the objective of the studies was no in the inclusion criteria: one assessed the technical proficiency needed to perform needle-knife pre-cut papillotomy (NKPP) in case of cannulation was unsuccessful within 20 minutes with standard ERCP (Fukatsu 2009); the other assessed risk factors of post ERCP pancreatitis (Nakai 2014); two because the intervention was not in the inclusion criteria: precut sphincterotomy (Akaraviputh 2008, Harewood 2002); two studies (Ekkelenkamp 2014, Verma 2007) because already included in the systematic review of Shahidi 2015.

Included studies
6 studies were finally included: one systematic review (Shahidi 2015) and 4 cohort studies (Chibbar 2014, Garrow 2009, Kapral 2008, Peng 2013) and 1 cross sectional (Oppong 2012). Data of two studies (Garrow 2009 and Chibbar 2014) were extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.
<table>
<thead>
<tr>
<th>Study</th>
<th>Number of ERCP</th>
<th>Number of endoscopist who performed ERCP</th>
<th>Intervention and control</th>
<th>Success rate of cannulation</th>
</tr>
</thead>
</table>
| Shahidi 2015 | 4477 ERCPs (4 studies) not specified whether all patients were with native papillas | 53 trainees (4 studies) | ERCP training required to achieve procedural competency | **Pancreatic duct Cannulation:** 2 studies Threshold to define competency: success rates between 80% and 85%. Competency achieved by between 70 and 160 ERCPs. On further stratification, only 1 study explicitly incorporated deep PD cannulation into their definition of competency. Competency was reached in this study by 160 ERCPs.  

**Common bile duct cannulation:** 4 studies  
Threshold to define competency success rates between 80% and 85%. Competency achieved by between 160 and 400 ERCPs for 2 studies  
Of note, when explicitly evaluating deep CBD cannulation in cases with native papillary anatomy, only 1 study was able to reach competency (≥80%), which occurred between 350 to 400 ERCPs. |
# Table 2: Results of primary studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of ERCP</th>
<th>Number of endoscopist who performed ERCP</th>
<th>Intervention and control</th>
<th>Success rate of cannulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chibbar 2014</td>
<td>465 ERCPs: not specified whether all patients were with native papillas</td>
<td>6 endoscopists (3 HVE and 3 LVE)</td>
<td>high volume ERCP (HVE) group performed at least 75 ERCPs / endoscopist / year vs low volume ERCP (LVE) group performed less than 75 ERCPs each during the year.</td>
<td>Successful cannulation LVE group =78.6% HVE group=91.0% (p=0.001, OR 2.8)</td>
</tr>
<tr>
<td></td>
<td>HVE =367 ERCPs LVE=98 ERCPs</td>
<td></td>
<td></td>
<td>Once adjusted for ERCP complexity, the OR for successful cannulation was 2.64 (p=0.002) between the HVE and LVE groups.</td>
</tr>
<tr>
<td>Garrow 2009</td>
<td>7896 ERCP cases; not specified whether all patients were with native papillas</td>
<td>59 doctors from 3 countries</td>
<td>Less experienced practitioners by &lt;150 cases in the last year More experienced practitioners by &lt;1000 total lifetime</td>
<td>Biliary cannulation Less experienced=94.0% More experienced=98.0% p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minor papilla cannulation Less experienced=82.1% More experienced=95.7% p&lt;0.0001</td>
</tr>
<tr>
<td>Kapral 2008</td>
<td>3132 ERCPs not specified whether all patients were with native papillas</td>
<td>2618 patients 89 endoscopists</td>
<td>&lt; 50 ERCP per year (68 endoscopists) vs &gt;50 ERCP per year (21 endoscopists)</td>
<td>Cannulation rates &lt; 50 ERCP per year, % (n)=84.2 (978) &gt;50 ERCP per year, % (n)=91.2 (2132) P&lt;0.001</td>
</tr>
</tbody>
</table>
| Oppong 2012 | 19848 ERCPs with cannulation attempts in patients with native papillae | 66 endoscopists from US and UK | <100 ERCP a year (19 endoscopists) vs >100 ERCP per year (47 endoscopists) | Cannulation rates ≥90%  
< 100 ERCP per year, % =63.1  
>100 ERCP per year, % =85.1  
P=0.09 |
|---|---|---|---|---|
| Peng 2013 | 13018 ERCPs in native papillae | 85 endoscopists | Categories for the endoscopist’s prior hands-on training volume: 0(no formal training)=40 (47.1%)  
1–100= 6 (7.1%)  
101–150=8 (9.4%)  
151–200=5 (5.9%)  
201–250=7 (8.2%)  
>250 procedures=19 (22.4%)  
Lifetime volume (estimated cumulative number of prior ERCPs)  
Median (range, IQR) 1200 (175–15000, 587–2500)  
Annual volume (estimated by number of ERCPs performed the preceding year)  
Median (range, IQR) 150 (10–940, 90–239) | Overall deep biliary cannulation success rate  
Annual volume p=0.01  
≤90: Reference  
91-150: 1.28 (0.72-2.29)  
151-239: 1.85 (0.95-3.60)  
>239: 2.79 (1.46-5.31) |
Quality of evidence

Study limitations (risk of bias): yes (two conference abstracts; low quality systematic review; high quality for retrospective cohort).
Inconsistency of results: no
Indirectness of evidence: yes (all but two studies did not specify whether all patients were with native papilla)
Imprecision: no (included more than 25000 ERCP)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because evidence came from observational studies with study limitation and indirectness.

Conclusions

Success rate of cannulation is influenced by experience of endoscopists: less experienced endoscopists had significantly lower success rates for biliary cannulation (VERY LOW QUALITY OF EVIDENCE).

References

Included studies
Excluded studies


PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n=0)
DARE (n=0)
CENTRAL (n=10)

Records identified through PubMed
(n=1 SR, 117 primary studies)

Records identified through Embase
(n=100 SR, 227 primary studies)

Records identified through references included in others clinical questions
(n=1)
Records suggested by experts
(n=1)

Records after duplicates removed
(n=10 SR, 260 primary studies)

Screening

Records screened
(n=271)

Records excluded
(n=259)

Eligibility

Studies awaiting classification
(n=0)

Full-text articles assessed for eligibility
(n=12)

Full-text articles excluded, with reasons
(n=6)

Included

Studies included
(n=6)
STONExTRACTION

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1.2 (All) Statement: Does experience of endoscopists influence the success rate of extraction of common bile duct (CBD)-stones of <1 cm during ERCP in patients with native papillas?

Population
Patients with bile duct stones (synonym: choleodocholithiasis) undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of stone extraction

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

**Embase**
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti AND (endoscopist:ab,ti OR endoscopists:ab,ti)))) AND (endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND (Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR ('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti ) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti))) AND (remov*:ab,ti OR extract*:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR)** and **Database of Abstracts of Reviews of Effects (DARE)**

1. MeSH descriptor: [Clinical Competence] explode all trees
2. MeSH descriptor: [Education, Medical, Graduate] explode all trees
3. MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
4. (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
5. (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
6. #2 or #1 or #5 or #3 or #4
7. MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
8. ERCP:ti,ab,kw (Word variations have been searched)
9. #8 or #7
10. CBD or bile duct:ti,ab,kw (Word variations have been searched)
11. MeSH descriptor: [Common Bile Duct] explode all trees
12. #10 or #11
13. stone or calculus:ti,ab,kw (Word variations have been searched)
14. #12 and #13
15. Choledocholithiasis:ti,ab,kw (Word variations have been searched)
16. MeSH descriptor: [Choledocholithiasis] explode all trees
17. #14 or #15 or #16
18. Any MeSH descriptor with qualifier(s): [Surgery - SU]
19. extraction or removal:ti,ab,kw (Word variations have been searched)
20. #18 or #19
21. #9 and #5 and #17 and #20 Publication Year from 2000 to 2015

**Primary studies**

**PubMed**
train*[Title/Abstract]) AND (endoscopist*[Title/Abstract] OR endoscopists*[Title/Abstract])) AND ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP*[Title/Abstract]) AND (Choledocholithiasis[Text Word] OR ("Common Bile Duct"[Mesh] OR CBD*[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi*[Text Word] OR calculus*[Text Word]))) AND ("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) NOT ("systematic review*[Title/Abstract] OR "systematic reviews*[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane*[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis*[Title/Abstract] OR metanalysis[Title/Abstract]) NOT ("animals*[MeSH Terms] NOT "humans*[MeSH Terms]) NOT Case Reports[ptyp]

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)))) AND (endoscopic retrograde cholangiopancreatography/exp OR ERCP:ab,ti) AND (Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR ("common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti ) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti)) AND (remov*:ab,ti OR extract*:ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volumet:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 #2 or #1 or #5 or #3 or #4
#7 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8 ERCP:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 CBD or bile duct:ti,ab,kw (Word variations have been searched)
#11 MeSH descriptor: [Common Bile Duct] explode all trees
#12 #10 or #11
#13 stone or calculus:ti,ab,kw (Word variations have been searched)
#14 #12 and #13
#15 Choledocholithiasis:ti,ab,kw (Word variations have been searched)
#16 MeSH descriptor: [Choledocholithiasis] explode all trees
#17 #14 or #15 or #16
#18 Any MeSH descriptor with qualifier(s): [Surgery - SU]
#19 extraction or removal:ti,ab,kw (Word variations have been searched)
#20 #18 or #19
#21 #9 and #5 and #17 and #20 Publication Year from 2000 to 2015
Results

Results of the bibliographic searches
After removing duplicates, 83 articles (1 reviews and 82 primary studies) were found. No potentially relevant systematic reviews were found; 6 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Four studies were excluded: two studies because no outcome of interest (Cote 2012, Kalaitzakis 2015: the outcome was failed index ERCP procedure when percutaneous biliary drainage and/or (open, laparoscopic, or transcystic) common bile duct exploration was performed during the same (index) hospital episode); two studies because no comparison of interest (Swan 2013, Yiassemidou 2012).

Included studies
Two studies were finally included (Enochsson 2010, Garrow 2009). Data of Garrow 2009 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided. Enochsson 2010 not specified the size of common bile duct (CBD) stones and whether all patients were with native papillas.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of ERCP</th>
<th>Intervention</th>
<th>Success rate of stone extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enochsson 2010</td>
<td>11,074 ERCPs</td>
<td>High volume &gt;1000 ERCP case/year low volume &lt; 200 ERCP case/year Intermediate volume center (200-1000 ERCP)</td>
<td>Successful Common bile duct stone extraction, %</td>
</tr>
<tr>
<td></td>
<td>8088 patients in 51 hospitals.</td>
<td></td>
<td>Low-volume centers =72.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High-volume centers =81.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High-to low P value = 0.0008</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intermediate volume center = 77.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High-to intermediate: P value = ns</td>
</tr>
<tr>
<td>Garrow 2009</td>
<td>7896 ERCP cases; not specified whether all patients were with native papillas</td>
<td>Less experienced practitioners by &lt;150 cases in the last year More experienced practitioners by &lt;1000 total lifetime</td>
<td>Bile duct stone extraction (&lt;10 mm)</td>
</tr>
<tr>
<td></td>
<td>59 doctors from 3 countries</td>
<td></td>
<td>Less experienced = 98%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>More experienced = 100% p = 0.001</td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): yes
Inconsistency of results: no
Indirectness of evidence: yes: in both studies it was not specified whether all patients were with native papillas
Imprecision: no (two studies with a total of 18970 ERCPs)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of evidence came from observational studies with study limitation and inconsistency.

Conclusions

For unspecified size of stones, high-volume canters had a slightly higher success rate of CBDS extraction than low-volume canters. Success rates for bile duct stone extraction <10 mm were higher in high volume centres
(VERY LOW QUALITY OF EVIDENCE)

References

Included studies

Excluded studies
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n = 0)
- DARE (n = 0)
- CENTRAL (n = 0)

Records identified through PubMed (n = 1 SR, 38 primary studies)

Records identified through Embase (n = 1 SR, 59 primary studies)

Records after duplicates removed (n = 1 SR, 82 primary studies)

Screening

Records screened (n = 83)

Records excluded (n = 77)

Eligibility
- Studies awaiting classification (n = 0)

Full-text articles assessed for eligibility (n = 6)

Full-text articles excluded, with reasons (n = 4)

Included
- Studies included (n = 2)
SUCCESS RATE OF STENT PLACEMENT

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1.3 (A III(a)) Statement: Does experience of endoscopists influence the success rate of stent placement for biliary obstruction during ERCP - independent of the etiology of the stricture?

Population
Patients with bilary (= bile duct) stenosis (synonym: common bile duct stricture)

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of stent placement

1.4 (A III(b)) Statement: Does experience of endoscopists influence the success rate of stent placement for biliary benign obstruction (e.g., cholangitis, pancreatitis, sclerosing papillitis, postoperative stenosis, stones) during ERCP?

Population
Patients with benign bilary stenosis

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers
Outcome
Success rate of stent placement

1.5 (A III(c)) Statement: Does experience of endoscopists influence the success rate of stent placement in patients with bile duct cancer?

Population
Patients with bile duct cancer (synonym: extrahepatic biliary cancer)

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of stent placement

1.6 (A III(d)) Statement: Does experience of endoscopists influence the success rate of stent placement in patients with pancreatic cancer?

Population
Patients with pancreatic cancer

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of stent placement

Inclusion criteria for III (a - d):
- Extrahepatic biliary stricture (= obstruction is below the bifurcation)
- Common bile duct stenosis
Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

**PubMed**


**Embase**

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND ("endoscopic retrograde cholangiopancreatography"/exp OR ERCP:ab,ti) AND (("common bile duct"/exp OR CBD:ab,ti OR bile duct:ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stenosis/exp OR stenosis:ab,ti OR cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinoma*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) AND (biliary stent/exp OR stent:ab,ti OR stents:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
Primary studies

PubMed
OR metanalysis[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) NOT Case Reports[ptyp]

**Embase**
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND (((common bile duct'/exp OR CBD:ab,ti OR 'bile duct:ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti OR cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinoma*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor/exp OR 'pancreas tumor/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) AND ('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [system analysis]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

**Cochrane Central Register of Controlled Trials (CENTRAL)**
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 #2 or #1 or #5 or #3 or #4
#7 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8 ERCP:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 MeSH descriptor: [Stents] explode all trees
#11 stent:ti,ab,kw (Word variations have been searched)
#12 #10 or #11
#13 MeSH descriptor: [Common Bile Duct] explode all trees
#14 CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#15 obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#16 cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)
#17 #13 or #14
#18 #15 or #16
#19 #17 and #18
#20 benign:ti,ab,kw (Word variations have been searched)
#21 #15 and #20
#22 cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)
#23 MeSH descriptor: [Cholangitis] explode all trees
#24 MeSH descriptor: [Pancreatitis] explode all trees
#25 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#26 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#27 #19 or #21 or #22 or #23 or #24 or #25 or #26
#28 #6 and #9 and #12and #27 Publication Year from 2000 to 2015
Results

Results of the bibliographic searches
After removing duplicates, 155 articles (3 reviews and 152 primary studies) were found. No potentially relevant systematic reviews were found; 4 primary studies were considered potentially relevant and acquired in full text. (See flow chart)

Excluded studies
Four studies were excluded: two because no outcome of interest (Chibbar 2014, Ekkelenkamp 2014); one because narrative review (Freeman 2005) and one because editorial (Freeman 2010).

Conclusions
No conclusion can be drawn because no evidence was found.

References

Excluded studies
POST-ERCP COMPLICATIONS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.7 (A IV) Statement: Does experience of endoscopists influence the prevention of complications following ERCP (% of patients suffering from post-ERCP complications)?

Population
Patients undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Complications

Post-ERCP complications (short term complications), e.g.:
- bleeding (following sphincterotomy at ERCP, often immediately after sphinterotomy, sometimes also with delay if patient under anticoagulation-drugs)
- perforation (usually happening during ERCP)
- stent dislocation (migration, late complication)
- post-ERCP pancreatitis (immediately after ERCP)
Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

**Systematic reviews and meta-analysis**

**PubMed**


**Embase**

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti))) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND (endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND (intestine perforation/exp OR perforation:ab,ti OR perforations:ab,ti OR 'gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti OR 'pancreatitis'/exp OR pancreatitis:ab,ti OR (("biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) AND (dislocation:ab,ti OR migration:ab,ti)) OR 'side effect'/exp OR side:ab,ti OR 'adverse outcome'/exp OR adverse:ab,ti OR 'complication'/exp OR complication:ab,ti OR complications:ab,ti OR negative:ab,ti OR safety:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR cochrane rev[Title/Abstract] OR cochrane rev[Title/Abstract] OR metaanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 #2 or #1 or #5 or #3 or #4
PubMed

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) AND (endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND (intestine perforation'/exp OR perforation:ab,ti OR perforations:ab,ti OR 'gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti OR 'pancreatitis'/exp OR pancreatitis:ab,ti (("biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) AND (dislocation:ab,ti OR migration:ab,ti)) OR 'side effect'/exp OR side:ab,ti OR...
Results of the bibliographic searches
After removing duplicates, 622 articles (20 reviews and 602 primary studies) were found. No potentially relevant systematic reviews were found; 22 primary studies were considered potentially relevant and acquired in full text. (See flow chart)

Excluded studies
16 studies were excluded: seven studies because outcome not in the inclusion criteria (Chennat 2010, Ekkelenkamp 2015, Garrow 2009, Kalaitzakis 2013, Kalaitzakis 2015, Nguyen 2010 (assess the association between likelihood of CCY and hospital volumes of CCY, pancreatitis, and endoscopic retrograde cholangio-pancreatography), Varadarajulu 2006); 5 studies because no comparison of interest assessed (Boudreau 2009, Nakai 2014, Rice 2010 (poster abstract of Rice 2011), Rice 2011, Swan 2009); one study because narrative review (Rabenstein 2002); one study...
because no comparison and outcome of interest (Troendle 2014); two because same studies of studies already included (Enochsson 2010 Pancreatology: same study of Enochson 2010 Gastrointest. Endosc; Kapral J. Gastroenterol. Hepatol. Erkr. 2008: same study of Kapral 2008 Endoscopy but published in German language).

**Included studies**
Six studies were finally included (Chibbar 2015, Enochson 2010, Glomsaker 2013, Harewood 2002, Kapral 2008, Testoni 2010)

Data of Chibbar 2014 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.
<table>
<thead>
<tr>
<th>Study</th>
<th>Number of ERCP</th>
<th>Number of endoscopist</th>
<th>Intervention</th>
<th>Bleeding</th>
<th>Pancreatitis</th>
<th>Perforation</th>
<th>Other complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chibbar 2014</td>
<td>465 ERCPs:</td>
<td>6 endoscopists</td>
<td>high volume</td>
<td></td>
<td></td>
<td></td>
<td>Overall complication rate</td>
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<tr>
<td></td>
<td>HVE =367 ERCPs</td>
<td>(3 HVE and 3 LVE)</td>
<td>ERCP (HVE)</td>
<td></td>
<td></td>
<td></td>
<td>HVE group= 5.2% LVE group = 7.1% (p=0.45, OR 0.71)</td>
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<tr>
<td></td>
<td>LVE= 98 ERCPs</td>
<td></td>
<td>group performed at least 75 ERCPs/ endoscopist/ year</td>
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<td></td>
<td></td>
<td>adjusted for ERCP complexity, the OR for complication 0.59 between the HVE and LVE groups</td>
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<td>low volume</td>
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<td></td>
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<td></td>
<td>ERCP (LVE)</td>
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<td></td>
<td></td>
<td></td>
<td>group performed less than 75 ERCPs each during the year.</td>
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<tr>
<td>Enochsson 2010</td>
<td>11,074 ERCPs</td>
<td>8088 patients in 51 hospitals.</td>
<td>High volume &gt;1000 ERCP case/year</td>
<td>Perioperative High-volume centers =0.5% Low-volume centers = 0.4% High-to low P =ns Intermediate volume center= 0.7% High-to intermediate P = ns</td>
<td>High-volume centers =3.7% Low-volume centers = 2.4% High-to low P =0.0123 Intermediate volume center= 2.4% High-to intermediate P = 0.0027</td>
<td>High-volume centers =0.3% Low-volume centers = 0.3% High-to low P =ns Intermediate volume center= 0.2% High-to intermediate</td>
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<td></td>
<td>Low-volume &lt; 200 ERCP case /year</td>
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<td></td>
<td>Perioperative complications High-volume centers =2.1% Low-volume centers = 3.1% High-to low P =0.0255 Intermediate volume center= 2.4% High-to intermediate</td>
</tr>
<tr>
<td>Study</td>
<td>Methodology</td>
<td>Volume centers:</td>
<td>Postoperative Complications</td>
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<tr>
<td>Glomsaker</td>
<td>2808 ERCP (but 2675 procedures included in the multivariable regression analysis)</td>
<td>48 endoscopists</td>
<td>High-volume centers = 1.1% Low-volume centers = 0.9% High-to low P = ns</td>
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<td>&gt;150 ERCPs annually vs less</td>
<td>intermediate volume center = 0.8% High-to intermediate P = ns</td>
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<td>OR: 1.70 (95% CI 1.08, 2.69)</td>
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<td></td>
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<td>Severe or fatal according to Cotton et al grade</td>
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<td>OR: 1.74 (95% CI 1.02, 2.98)</td>
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<td></td>
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<td>Severe or fatal according to Dindo–Clavien grade</td>
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<td></td>
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<td>OR: 2.45 (95% CI 1.56, 3.84)</td>
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<td></td>
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<td></td>
<td>Other complications</td>
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<td></td>
<td></td>
<td></td>
<td>OR: (OR 3.27, 2.00 to 5.43)</td>
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</tr>
<tr>
<td>Study</td>
<td>ERCPs</td>
<td>Patients</td>
<td>Endoscopists</td>
<td>First 200 ERCP procedures vs subsequent 53 ERCP</td>
<td>Initial 200=2% Subsequent 53=1% P=ns</td>
<td>Initial 200=11% Subsequent 53=11% P=ns</td>
<td>Initial 200=0% Subsequent 53=0% P=ns</td>
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<tr>
<td>Harewood</td>
<td>253</td>
<td>253</td>
<td>1</td>
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<tr>
<td>2002</td>
<td>ERCP</td>
<td>patients</td>
<td>who underwent precut biliary sphincterotomy one endoscopist</td>
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<tr>
<td></td>
<td>2618</td>
<td>89</td>
<td>89 endoscopists</td>
<td>&lt;50 ERCP per year (68 endoscopists) vs &gt;50 ERCP per year (21 endoscopists)</td>
<td>&lt;50 ERCP per year, % (n)=4.7 (982) &gt;50 ERCP per year, % (n)=3.2 (2128) P=ns</td>
<td>&lt;50 ERCP per year, % (n)=5.6 (947) &gt;50 ERCP per year, % (n)=4.9 (2098) P=ns</td>
<td>&lt;50 ERCP per year, % (n)=0.6 (974) &gt;50 ERCP per year, % (n)=0.5 (2129) P=ns</td>
</tr>
<tr>
<td>Kapral</td>
<td>3132</td>
<td>2618</td>
<td>89 endoscopists</td>
<td>&lt;50 ERCP per year (89 endoscopists) vs &gt;50 ERCP per year (21 endoscopists)</td>
<td>&lt;50 ERCP per year, % (n)=2.8 (951) &gt;50 ERCP per year, % (n)=1.6 (966) P=ns</td>
<td>&lt;50 ERCP per year, % (n)=1.5 (2102) P=0.022</td>
<td>cardiopulmonary complications &lt;50 ERCP per year, % (n)=1.6 (966) &gt;50 ERCP per year, % (n)=0.6 (2112) P=0.014</td>
</tr>
<tr>
<td>2008</td>
<td>ERCPs</td>
<td>patients</td>
<td>endoscopists</td>
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<tr>
<td>Testoni 2010</td>
<td>3,635 ERCP</td>
<td>3,331 ERCPs were carried out by expert operators and 304 by less-experienced operators</td>
<td>ERCP volume high-volume centers vs low-volume centers. ERCP experience (endoscopist) low grade if the career-long total performance was fewer than 200 procedures and/or the current number &lt; 40 per year</td>
<td>Low-ERCP volume (center) =OR 1.3 (95% CI 0.81 – 1.95) Low-ERCP experience (endoscopist) =OR 0.7 (95% CI 0.32 – 1.25)</td>
<td>Overall complications &lt; 50 ERCP per year, % (n)=13.6 (916) &gt;50 ERCP per year, % (n)=10.2 (2035) P=0.007</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): no (six studies of high quality and one conference abstract)
Inconsistency of results: no for bleeding and perforation, yes for pancreatitis and overall complications
Indirectness of evidence: no
Imprecision: no (seven studies with greater of 21000 ERCP included)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because evidence came from observational studies.

Conclusions

Overall complications

Overall complication rates were not significantly changed according to the level of experience or volume centers but one study showed that endoscopists with a case volume exceeding 50 ERCPs per year had lower overall complication rates. An increased risk of severe complications was observed in centres with an annual ERCP volume of more than 150 procedures (VERY LOW QUALITY OF EVIDENCE).

Bleeding

Bleeding was not associated with experience of endoscopist or volume centers (LOW QUALITY OF EVIDENCE).

Perforations

Perforations was not associated with experience of endoscopist or volume centers (LOW QUALITY OF EVIDENCE).

Pancreatitis

When the cut off between high and low volume of ERCP per year is 200 or less ERCP per year, post-ERCP pancreatitis was not associated with the case volume of either the single endoscopist or the center according to all but one study that found an increase in pancreatic when hospital volume was greater than 150/year. When the comparison is between very high-volume centers (>1000 ERCP case/year) and intermediate ((200-1000 ERCP)- and low-volume centers (< 200 ERCP case/year), higher frequency of pancreatitis were shown in high volume centers (VERY LOW QUALITY OF EVIDENCE).

Other complications

Endoscopists with a case volume exceeding 50 ERCPs per year had lower rates of Cholangitis and cardiopulmonary complications (LOW QUALITY OF EVIDENCE).
References

Included studies

Excluded studies
1.8 (A V(a)) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence accurate staging of esophageal cancer (e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

Population
Patients with esophageal cancer undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS performed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of esophageal cancer (according to the UICC staging system)
1.9 (A V(b)) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence accurate staging of gastric cancer (e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

**Population**
Patients with gastric cancer undergoing EUS

**Intervention**
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS performed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

**Control**
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

**Outcome**
accurate staging of gastric cancer (according to the UICC staging system)

1.10 (A V(c)) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence accurate staging of pancreatic cancer (e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

**Population**
Patients with pancreatic cancer undergoing EUS

**Intervention**
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS performed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

**Control**
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers
Outcome
accurate staging of pancreatic cancer (according to the UICC staging system)

1.11 (A V(d)) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) influences accurate staging of bile duct cancer (e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

Population
Patients with bile duct cancer (synonym: extrahepatic biliary cancer) undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS performed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of bile duct cancer (according to the UICC staging system)

1.12 (A V(e)) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) influences accurate staging of rectal cancer (e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

Population
Patients with rectal cancer (synonym: extrahepatic biliary cancer) undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS performed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers
Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of rectal cancer (according to the UICC staging system)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND (endoscopic echography'/exp OR EUS:ab,ti) AND ("cancer
staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) AND (('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR esophagus:ab,ti OR esophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti ORmalign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'meta analysis'/de OR 'systematic review' OR 'systematic reviews' OR 'meta analysis'/de OR 'systematic review'/lm OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #4 or #3 or #2 or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 EUS:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Neoplasm Staging] explode all trees
#12 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 lymph node:ti,ab,kw (Word variations have been searched)
#15 metastasis:ti,ab,kw (Word variations have been searched)
#16 #13 or #14
#17 #16 and #15
#18 staging or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#19 #17 or #18 or #11 or #12
#20 MeSH descriptor: [Common Bile Duct] explode all trees
#21 CBD or biliary or pancreatic or bile duct or rectal or gastric or oesophageal:ti,ab,kw (Word variations have been searched)
#22 cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#23 #20 or #21
#24 #23 and #22
#25 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#26 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#27 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#28 MeSH descriptor: [Rectal Neoplasms] explode all trees
#29 #24 or #28 or #27 or #25 or #26
#30 #29 and #19 and #7 and #10 Publication Year from 2000 to 2015
Primary studies

PubMed

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND (endoscopic echography/exp OR EUS:ab,ti) AND (cancer staging/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (("lymph node"/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp)) AND ((("common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) NOT (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'systemic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
Results of the bibliographic searches
After removing duplicates, 112 articles (6 reviews and 106 primary studies) were found. No potentially relevant systematic reviews were found; 5 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Included studies

Clinical question A_V. (a)

One study (van Vliet 2006) assessing accurate staging of esophageal cancer was included.
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention</th>
<th>T stage-accuracy</th>
<th>N stage-accuracy</th>
<th>M stage-accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Vliet 2006</td>
<td>244 patients underwent EUS followed by esophageal resection without neoadjuvant chemo- or radiotherapy.</td>
<td>low-volume center: EUS performed by (4 senior and 5 junior endoscopists with fewer than 50 EUS staging procedures per year</td>
<td>Overall Low-volume center (EUS probe passage)= 54% (94/173) Low-volume center (no EUS probe passage)= 69% (49/71) High-volume centers= 68%-89%</td>
<td>Low-volume center (EUS probe passage)= 64% (110/171) Low-volume center (no EUS probe passage) =51% (33/65) High-volume centers, % =70-84</td>
<td>Low-volume center (EUS probe passage)= 92% (157/171) Low-volume center (no EUS probe passage) =88% (57/65) High-volume centers, % =81-97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High volume Centers found by literature search : higher than 50 per year</td>
<td>T1 Low-volume center (EUS probe passage)= 21% (9/43) Low-volume center (no EUS probe passage) =- High-volume centers=33%-100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T2 Low-volume center (EUS probe passage)= 25% (10/40) Low-volume center (no EUS probe passage) 0% (0/6) High-volume centers 12.5%-84%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3 Low-volume center (EUS probe passage)= 85% (75/88) Low-volume center (no EUS probe passage) 79% (49/62) High-volume centers 75%-94%</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>T4</strong>&lt;br&gt;Low-volume center (EUS probe passage)&lt;br&gt;0% (0/2)&lt;br&gt;Low-volume center (no EUS probe passage)&lt;br&gt;0% (0/3)&lt;br&gt;High-volume centers&lt;br&gt;50%-100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only one study with 244 patients)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as moderate because of imprecision

Conclusions

Staging in low volume centres is less accurate than staging performed in high volume (MODERATE QUALITY OF EVIDENCE)

Clinical question A V. (b)

No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between accurate staging of gastric cancer and experience or training programs of endoscopists because no evidence was found.

Clinical question A V. (c)

One study (Harewood 2002) assessing accurate staging of pancreatic cancer was included.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harewood 2002</td>
<td>20 patients with pancreatic masses underwent EUS-FNA</td>
<td>Group A (n=9): patients examined by initial experience which included a formal training period of 2 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 endosonographers</td>
<td>Group B (n=11): patients examined by later experience subsequent to “hands-on” training</td>
<td>Accuracy based on the original pathology interpretation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Group A= 33% (3/9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Group B= 91% (10/11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p =0.004 vs. group A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>multivariate analysis : variable predictive of an accurate EUS-FNA result : endosonographer experience</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OR = 3.0 (95% CI 1.1-8.4)</td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only one study with 20 patients)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision

Conclusions

Staging at the initial endosonographer experience is less accurate than staging performed after formal training
(LOW QUALITY OF EVIDENCE)

Clinical question A V. (d)

No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between accurate staging of bile duct cancer and experience or training programs of endoscopists because no evidence was found.

Clinical question A V. (e)

Three study (Carmody 2000, Morris 2011, Marusch 2011) assessing accurate staging of rectal cancer were included.
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention</th>
<th>T stage-accuracy</th>
<th>N stage-accuracy</th>
<th>Other</th>
</tr>
</thead>
</table>
| Carmody, 2000 | 41 patients with a diagnosis of a rectal neoplasm undergoing a TRUS examination | 1-12 examinations vs 13-24 examinations vs 25-36 examinations performed by the same operator | Accuracy of Depth Invasion(T)  
1-12=58%  
13-24=92%  
25-36=83%  
Initial 12 examinations=58%  
Last 24 examinations=87%  
p= 0.048 | | Overall Accuracy of TN stage  
1-12=58%  
13-24=92%  
25-36=75% |
| Marusch 2011  | 7096 patients with rectal carcinoma who did not receive neoadjuvant radio-chemotherapy after EUS | hospital volume  
≤10EUS/year  
Vs  
11-30EUS/year  
Vs  
>30EUS/year | uT-pT correspondence by hospital volume, %  
≤10EUS/year=63.2% (95%CI 61.5%-64.9%)  
11-30 EUS/year=64.6% (95%CI 62.9%-66.2%)  
>30EUS/year =73.1% (95%CI 69.4%-76.5%)  
Under staging by hospital volume, %  
≤10EUS/year=17.3% (95%CI 16.0%-18.7%)  
11-30EUS/year=19.5% (95%CI 18.1%-20.8%)  
>30EUS/year =13.5% (95%CI 10.9%-16.5%) | |
| Morris 2011 | 272 patients with rectal adenocarcinoma assessed by ERUS 233 were assessable for T-stage and 142 for N-stage | All examinations performed by a single operator  
Time period 1: 1 year; 40 patients examined  
Time period 2: 3 years: 110 patients examined  
Time period 3: 3 years: 122 patients examined | **Over staging by hospital volume, %**  
≤10EUS/year=19.4% (95%CI 18.1%-20.9%)  
11-30EUS/year=16.0% (95%CI 14.8%-17.3%)  
>30EUS/year=13.3% (95%CI 10.8%-16.3%) | **T-stage correct**  
Time Period 1 =32/39  
Time Period 2=79/96  
Time Period 3=80/98  
Accuracy, %  
Time Period 1=82.1  
Time Period 2=82.3  
Time Period 3=81.6  
P=0.99 | **N-stage Correct**  
Time Period 1=20/24  
Time Period 2=38/56  
Time Period 3=46/62  
Accuracy, %  
Time Period 1=83.3  
Time Period 2=67.9  
Time Period 3=74.2  
P=0.31 |
Quality of evidence

Study limitations (risk of bias): yes (not all patients received the reference standard and were included in the analysis)
Inconsistency of results: no
Indirectness of evidence: yes (two studies compared accuracy of examinations performed by only one endosonographer)
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of study limitations and indirectness

Conclusions

Accuracy of staging of rectal cancer does not seem to be strongly correlated with endosonographer experience, nor by hospital volume

(LOW QUALITY OF EVIDENCE)

References

Included studies

**PRISMA 2009 Flow Diagram**

1. **Identification**
   - Records identified through CDSR (n = 0)
   - DARE (n = 0)
   - CENTRAL (n = 1)

2. **Screening**
   - Records identified through PubMed (n = 0 SR, 37 primary studies)
   - Records identified through Embase (n = 6 SR, 92 primary studies)

3. **Eligibility**
   - Records after duplicates removed (n = 6 SR, 106 primary studies)

4. **Included**
   - Records screened (n = 112)
     - Records excluded (n = 107)
     - Studies awaiting classification (n = 0)
     - Full-text articles assessed for eligibility (n = 5)
     - Full-text articles excluded, with reasons (n = 0)
     - Studies included (n = 5)
IDENTIFICATION OF DEFINED LANDMARKS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.13 (A VI) Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – „gastroenterological education-training endoscopy“ (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EF SUMB, DEGUM) influence the quality performance of EUS (% of examinations with well documented depiction of relevant structures, specific for the indication of EUS) ? (Esophageal cancer: visualization of the tumor, mediastinum (lymph nodes), gastroesophageal junction, celiac axis (lymph nodes) and left lobe of the liver (to rule out metastatic disease). Diseases of the pancreato-biliary system: Visualization of the entire pancreas (signs of chronic pancreatitis, pancreatic cyst) pancreatic duct, common bile duct (stricture, dilation, stones). Rectal cancer: visualization of the tumor: location, extension, infiltration of surrounding structures; visualization of surrounding structures: genitourinary structures, iliac vessels, sphincter apparatus, lymph nodes)

Population
Patients undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
Identification of defined landmarks
Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

**Systematic reviews and meta-analysis**

**PubMed**


**Embase**

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti)) AND (endoscopic echography'/exp OR EUS:ab,ti) AND (((common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR "lymph node'/exp OR 'lymph node':ab,ti OR 'lymph
Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw  (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw  (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw  (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 EUS:ti,ab,kw  (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Common Bile Duct] explode all trees
#12 CBD or biliary or pancreatic or bile duct or rectal or gastric or esophageal:ti,ab,kw  (Word variations have been searched)
#13 #11 or #12
#14 cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw  (Word variations have been searched)
#15 MeSH descriptor: [Lymph Nodes] explode all trees
#16 lymph node:ti,ab,kw  (Word variations have been searched)
#17 #14 or #15 or #16
#18 #13 and #17
#19 MeSH descriptor: [Esophagogastric Junction] explode all trees
#20 pancreatitis:ti,ab,kw  (Word variations have been searched)
#21 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#23 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24 MeSH descriptor: [Rectal Neoplasms] explode all trees
#25 MeSH descriptor: [Pancreatitidis] explode all trees
#26 #15 or #16
#27 mediastinum or celiac axis:ti,ab,kw  (Word variations have been searched)
#28 #26 and #27
#29 MeSH descriptor: [Pancreatic Cyst] explode all trees
#30 pancreatic cyst:ti,ab,kw  (Word variations have been searched)
#31 CBD or bile duct:ti,ab,kw  (Word variations have been searched)
Primary studies

PubMed
Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 EUS:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Common Bile Duct] explode all trees
#12 CBD or biliary or pancreatic or bile duct or rectal or gastric or esophageal:ti,ab,kw (Word variations have been searched)
#13 #11 or #12
#14 cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#15 MeSH descriptor: [Lymph Nodes] explode all trees
#16 lymph node:ti,ab,kw (Word variations have been searched)
#17 #14 or #15 or #16
#18 #13 and #17
#19 MeSH descriptor: [Esophagogastric Junction] explode all trees
#20 pancreatitis:ti,ab,kw (Word variations have been searched)
#21 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#23 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24 MeSH descriptor: [Rectal Neoplasms] explode all trees
#25 MeSH descriptor: [Pancreatitis] explode all trees
#26 #15 or #16
#27 mediastinum or celiac axis:ti,ab,kw (Word variations have been searched)
#28 #26 and #27
Results

Results of the bibliographic searches
After removing duplicates, 367 articles (11 reviews and 356 primary studies) were found. No potentially relevant systematic reviews were found; 8 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
All the eight studies were excluded: five studies because no outcome of interest (Camody 2000, Harewood 2002, Kachare 2014, Mertz 2004, Morris 2011); one because no comparison of interest (Quinton 2014); one because no intervention of interest: EUS elastography (Soares 2015); one because letter without useful data (Jadav 2013).

Included studies
No studies were retrieved fulfilling the inclusion criteria.

Conclusions
No conclusion can be drawn about the influence experience or training of endoscopists on the quality performance of EUS (% of examinations with well documented depiction of relevant structures, specific for the indication of EUS) because no evidence was found.
References

Excluded studies
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n=0)
- DARE (n=0)
- CENTRAL (n=10)

Records identified through PubMed (n=1 SR, 111 primary studies)

Records identified through Embase (n=11 SR, 318 primary studies)

Records after duplicates removed (n=11 SR, 356 primary studies)

Screening
- Records screened (n=367)

Eligibility
- Full-text articles assessed for eligibility (n=9)
- Studies awaiting classification (n=0)

Included
- Studies included (n=0)

Rejected
- Records excluded (n=358)
- Full-text articles excluded, with reasons (n=9)
ADEQUATE SAMPLING OF PATIENTS UNDERGOING EUS-FNA

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.14 (A VII (a)). Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – “gastroenterological education-training endoscopy” (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence the quality performance of EUS-FNA (adequate sampling (sampling sufficient enough for quantity and quality, diagnostic rates, sensitivity, accuracy) of solid masses (e.g., tumor, lymph node)?

Population
Patients with solid masses (esophagus, mediastinum, stomach, pancreas, bile duct system, rectum: tumor, lymph nodes) undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA performed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA performed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Adequate sampling (sampling sufficient enough for quantity and quality, diagnostic rates, sensitivity, accuracy) of solid masses (diagnosing cancer vs. benign lesion)
1.15 (A VII(b)). Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – “gastroenterological education-training endoscopy” (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence the quality performance of EUS-FNA (adequate sampling (sampling sufficient enough for quantity and quality, diagnostic rates, sensitivity, accuracy) of inflammation (e.g., autoimmune pancreatitis)?

Population
Patients with inflammation (e.g., autoimmune pancreatitis) undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA performed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA performed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Adequate sampling (sampling sufficient enough for quantity and quality, diagnostic rates, sensitivity, accuracy) of inflammation

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti))) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND ('endoscopic echography'/exp OR 'endoscopic ultrasound' Guided fine needle biopsy'/exp OR 'endoscopic ultrasound' Guided fine needle biopsy OR (EUS:ab,ti AND FNA:ab,ti)) AND (laboratory diagnosis'/exp OR sampling:ab,ti OR specimens:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11 EUS and FNA:ti,ab,kw (Word variations have been searched)
#12 #8 or #9 or #10 or #11
#13 MeSH descriptor: [Specimen Handling] explode all trees
#14 specimen or sampling:ti,ab,kw (Word variations have been searched)
#15 #13 or #14
#16 #15 and #12 and #7 Publication Year from 2000 to 2015
Primary studies

PubMed

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND ('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimen:ab,ti OR specimens:ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR meta-analysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2 or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11 EUS and FNA:ti,ab,kw (Word variations have been searched)
#12 #8 or #9 or #10 or #11
#13 MeSH descriptor: [Specimen Handling] explode all trees
#14 specimen or sampling:ti,ab,kw (Word variations have been searched)
#15 #13 or #14
Results

Results of the bibliographic searches
After removing duplicates, 226 articles (4 reviews and 222 primary studies) were found. No potentially relevant systematic reviews were found; 16 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Eleven studies were excluded: six because no outcome of interest (Eloubeidi 2005, Groth 2008, Harewood 2000, Lin 2008, Mertz 2004, Varadarajulu 2015); two because no comparison of interest (Lankarani 2011, Nteene 2012); one because patients not in the inclusion criteria (breast) (Feoli 2008); one because comparison and outcome not in the inclusion criteria (Kemp 2010); one commentary of excluded studies (Navani 2011).

Included studies
5 studies were finally included (DePew 2012, Houlton 2011, Nayar 2011, Piramanayagam 2014, Wahidi 2014).

Clinical question A VII (a)

All five studies provided data on adequate sampling of solid masses. The location of sampling is heterogeneous.

Data of Piramanayagam 2014 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention</th>
<th>Sampling</th>
<th>Sampling adequacy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DePew 2012</strong></td>
<td>1275 patients</td>
<td>procedures performed annually by each proceduralist</td>
<td>mediastinal and hilar lymph nodes</td>
<td>Average number of EBUS-TBNA procedures performed annually by each proceduralist was not associated with a difference in sampling adequacy p:0.21</td>
</tr>
<tr>
<td></td>
<td>1304 endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 proceduralists resulting in 2414 LN biopsies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Houlton 2011</strong></td>
<td>790 patients</td>
<td>Low-volume clinicians (&lt;20 FNAs performed) =125 clinicians</td>
<td>thyroid</td>
<td><strong>Non diagnostic results, %</strong></td>
</tr>
<tr>
<td></td>
<td>thyroid FNA interpreted at the 3 hospital Centers</td>
<td>high-volume clinicians (≥20 FNAs performed) =9 clinicians</td>
<td></td>
<td>High volume clinicians(mean FNAs performed=45)=16%</td>
</tr>
<tr>
<td></td>
<td>FNAs were performed by 134 physicians and interpreted by 16 pathologists</td>
<td></td>
<td>Low volume clinicians(mean FNAs performed=3.1)=15%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P=0.47</td>
<td></td>
</tr>
<tr>
<td><strong>Nayar 2011</strong></td>
<td>228 consecutive patients with solid pancreatic Lesions</td>
<td>Comparison 1</td>
<td>Pancreas</td>
<td><strong>Inadequate sampling</strong></td>
</tr>
<tr>
<td></td>
<td>EUS-FNA</td>
<td>First 80 cases of a single endoscopist (KO1) who did not receive any hands-on training (independent practice 2003/2004) vs same endoscopist (KO2) after having performed over 500</td>
<td></td>
<td>Comparison 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>KO1: 13/80 (16.25%)</td>
<td>KO2: 4/68 (6%)</td>
<td>P: 0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comparison 2</td>
<td>KO2: 4/68 (6%)</td>
<td>MN: 8/80 (10%)</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Intervention</td>
<td>Disease Types</td>
<td>Other Information</td>
</tr>
<tr>
<td>-------</td>
<td>--------------</td>
<td>--------------</td>
<td>---------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Piramanayaga m 2014</td>
<td>132 EUS FNA</td>
<td>One-week, intensive, short-term, hands-on EUS training program on tissue acquisition</td>
<td>pancreatic-biliary malignancy, metastatic cancer, luminal cancer, granulomatous/benign lymph nodes, chronic pancreatitis/benign disease</td>
<td>Overall rate of non-diagnostic specimens: First 18 months=34.2%, Second 18 months=18.2%, P=0.03</td>
</tr>
<tr>
<td>Wahidi 2014</td>
<td>13 pulmonary trainees from three training programs and were observed over a 2-year period</td>
<td>Before EBUS-TBNA, all participants had to complete 30 conventional bronchoscopies, an EBUS-specific didactic curriculum, and a simulation session with a plastic airway model.</td>
<td>Mediastinal, hilar, and peri-bronchial structures</td>
<td>% Endoscopist who complete the essential steps of EBUS-TNBA and perform the procedure successfully with adequate tissue sampling: Average of five procedures (95% CI, 2-7)=25%, After 9 procedures (95% CI, 4-13)=50%, After 13 procedures (95% CI, 7-16)=75%</td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): no (5 case series studies)
Inconsistency of results: yes (studies assessing the impact of case volume on adequacy did not find an association; studies assessing the impact of experience (n .of cases analysed) found an association )
Indirectness of evidence: no
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of inconsistency and observational data.

Conclusions

Case volume did not seem to have a significant impact on non diagnostic results and inadequate sampling.
Rate of non diagnostic samples decrease with the increase of the number of procedures performed and after a formal training programs
(VERY LOW QUALITY OF EVIDENCE).

Clinical question A VII. (b)
No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between adequate sampling of inflammation and experience or training programs of endoscopists because no evidence was found.
References
Included studies

Excluded studies
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n = 0)
- DARE (n = 0)
- CENTRAL (n = 15)

Screening

Records identified through PubMed (n = 1 SR, 173 primary studies)

Records identified through Embase (n = 4 SR, 58 primary studies)

Records after duplicates removed (n = 4 SR, 222 primary studies)

Records screened (n = 226)

Records excluded (n = 210)

Eligibility

Studies awaiting classification (n = 0)

Full-text articles assessed for eligibility (n = 16)

Full-text articles excluded, with reasons (n = 11)

Included

Studies included (n = 5)
MANAGEMENT OF PATIENTS UNDERGOING EUS-FNA

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.16 (A VIII). Does experience of endoscopists or teaching endoscopists in formal training programs (e.g., GATE – “gastroenterological education-training endoscopy” (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE), EFSUMB, DEGUM) influence the management of patients undergoing EUS-FNA (e.g., tissue sampling of both primary tumor and lesion outside of primary field)?

Population
Patients undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA performed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA performed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Percentage of examinations in which EUS-FNA would change the patient management (e.g., tissue sampling of both primary tumor and lesion outside of primary field)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:
Systematic reviews and meta-analysis

**PubMed**


**Embase**

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND ("endoscopic echography"/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ("endoscopic ultrasound":ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND ("patient care"/exp OR management:ab,ti OR impact:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2 or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11 EUS and FNA:ti,ab,kw (Word variations have been searched)
#12 #8 or #9 or #10 or #11
#13 MeSH descriptor: [Patient Care Management] explode all trees
#14 patient management or impact:ti,ab,kw (Word variations have been searched)
#15 #13 or #14
#16 #7 and #12 and #15 Publication Year from 2000 to 2015
Primary studies

PubMed

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) AND ("endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ("endoscopic ultrasound":ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND (‘patient care’/exp OR management:ab,ti OR impact:ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic reviews' OR 'systematic reviews' OR cochrane OR meta-analysis OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [case report]/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Clinical Competence] explode all trees
#2 MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3 MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4 (center or hospital or clinic) and volumeti,ab,kw (Word variations have been searched)
#5 (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6 (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7 #6 or #5 or #4 or #3 or #2or #1
#8 MeSH descriptor: [Endosonography] explode all trees
#9 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11 EUS and FNA:ti,ab,kw (Word variations have been searched)
#12 #8 or #9 or #10 or #11
#13 MeSH descriptor: [Patient Care Management] explode all trees
#14 patient management or impact:ti,ab,kw (Word variations have been searched)
#15 #13 or #14
#16 #7 and #12 and #15 Publication Year from 2000 to 2015
Results

Results of the bibliographic searches
After removing duplicates, 167 articles (5 reviews and 162 primary studies) were found. Other five studies were suggested by authors. No potentially relevant systematic reviews were found; 13 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Thirteen studies were excluded: four studies because no outcome of interest (Houlton 2011, Lankarani 2011, Pyramanayagan 2014, Varadarajulu 2015); five because no comparison of interest (Bluen 2012, Chong 2005, Del Vecchio Blanco 2015, Mortensen 2001, Shami 2004); one because no intervention of interest (Feoli 2008); one because editorial (Kahaleh 2013); one because letter without useful data (Hirdes 2011); one because narrative review without useful data (Scheiman 2008)

Conclusions
No conclusion can be drawn about the influence experience or training of endoscopists on the management of patients undergoing EUS-FNA because no evidence was found.
References

Excluded studies

**PRISMA 2009 Flow Diagram**

**Identification**
- Records identified through CDSR (n = 0)
- Records identified through PubMed (n = 1 SR, 54 primary studies)
- Records identified through Embase (n = 5 SR, 129 primary studies)
- Records suggested by authors (n = 5 primary studies)

**Screening**
- Records after duplicates removed (n = 5 SR, 167 primary studies)

**Eligibility**
- Records screened (n = 172)
- Records excluded (n = 159)
- Studies awaiting classification (n = 0)
- Full-text articles assessed for eligibility (n = 13)
- Full-text articles excluded, with reasons (n = 13)

**Included**
- Studies included (n = 0)
SUCCESS RATE OF CANNULATION

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.17. Frequency with which cannulation of biliary duct in patients with native major papillae without surgically altered anatomy undergoing ERCP for extraction of common bile duct stones is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP

Intervention
deep cannulation of biliary duct

Control
None

Outcome
achieved cannulation rate

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Cholangiopancreatography", Endoscopic Retrograde[Mesh] OR ERCP[Title/Abstract]) AND
("Catheterization"[Mesh] OR cannulation[Title/Abstract] OR "biliary cannulation"[Text Word]) AND
("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) AND
("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])
Embase
('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND ('cannulation'/exp AND 'bile duct'/exp) OR cannulation:ab,ti) AND ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2 ERCP:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Catheterization] explode all trees
#5 cannulation:ti,ab,kw (Word variations have been searched)
#6 biliary cannulation:ti,ab,kw (Word variations have been searched)
#7 #4 or #5 or #6
#8 MeSH descriptor: [Ampulla of Vater] explode all trees
#9 native papilla:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 #7 and #3 and #10 Publication Year from 2000 to 2016

Primary studies

PubMed

Embase
('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND ('cannulation'/exp AND 'bile duct'/exp) OR cannulation:ab,ti) AND ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'case report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2 ERCP:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Catheterization] explode all trees
#5 cannulation:ti,ab,kw (Word variations have been searched)
#6 biliary cannulation:ti,ab,kw (Word variations have been searched)
#7 #4 or #5 or #6
#8 MeSH descriptor: [Ampulla of Vater] explode all trees
Results

Results of the bibliographic searches
After removing duplicates, 246 articles (5 reviews and 241 primary studies) were found. 51 primary studies were considered potentially relevant and acquired in full text. (See flow chart). A sample size of 100 patients was used as a cut off for inclusion.

Excluded studies
23 articles were excluded: 1 because no population of interest (Skinner 2014); 1 because ERCP was performed by trainees (Pan 2015); 17 because conference abstracts (Alburquerque 2013 United Eur. Gastroenterol. J, Alburquerque 2013 Gastrointest. Endosc, Ansstas 2009, Cha 2011, Chiba 2013, Cote 2010, Familiar 2012, Familiar Gastrointest. Endosc 2012, Georgopoulus 2013, Holt 2015 Gastrointest. Endosc, Lee 2010, Mariani 2016, Morgado 2016, Nakai 2014, Nakai 2016, Romagnuolo 2012, Skinner 2014 Gastrointest. Endosc); 1 because conference abstract of already included study (Holt 2015); 1 because reported the results only for the subgroup of patients (n: 46) with Periampullary diverticula (Tyagi 2009); 1 (Coelho-Prabhu 2012) because reported the results only for the subgroup of patients (n: 78) who received precut sphincterotomy with a converted needle knife; 1 because reported the results only for the subgroup of patients (n: 50) with double-guide-wire method (Grönroos 2011).

Awaiting assessment
For study (Ahmad 2005) it was impossible to retrieve the full text.

Included studies
<table>
<thead>
<tr>
<th>Study</th>
<th>N and characteristic of patients undergoing ERCP</th>
<th>Years of recruitments</th>
<th>Intervention</th>
<th>Cannulation rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailey 2008 (RCT)</td>
<td>413 patients with native papilla</td>
<td>between August 2003 and April 2006 tertiary referral University hospital Australia</td>
<td>cannulation with either sphincterotome and contrast injection (n:211) or sphincterotome and guide-wire cannulation (n: 202)</td>
<td>Overall: 97.3%</td>
</tr>
<tr>
<td>Cote 2010</td>
<td>1544 patients with a native papilla that could be reached by using a duodenoscope</td>
<td>between January 2006 and April 2008 Two tertiary care, academic medical centers, USA</td>
<td>first technique: standard techniques without a pre-cut sphincterotomy or stent placement. second technique in case of failure: a 0.025- or 0.035-inch guidewire is advanced to the level of the mid pancreatic body to allow placement of a soft polyethylene stent. If cannulation is unsuccessful after several minutes, a precut sphincterotomy is performed over the PD stent</td>
<td>first techniques: 1452/1544 (94%) adding second technique: 1523/1544 (98.6%)</td>
</tr>
<tr>
<td>Fukatsu 2008</td>
<td>501 consecutive patients with an intact duodenal papilla</td>
<td>Between October 2002 and February 2006 University Hospital, Japan</td>
<td>Standard procedure: cannulation using standard manoeuvres needle-knife pre-cut papillotomy (NKPP) when Standard procedure was unsuccessful within 20 min</td>
<td>Standard procedure: 421/501 (84.03%) adding NKPP: 76/80 (95%) Overall: 497/501 (99.2%)</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Details</td>
<td>Methodology</td>
<td>Results</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
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<tr>
<td>Geraci 2013</td>
<td>500 consecutive ERCPs</td>
<td>Between January 2008 and December 2012 surgical endoscopy unit, Italy</td>
<td>Biliary cannulation was attempted by using a standard three-lumen sphincterotome after the intravenous administration of hyoscine butylbromide 20mg. When biliary cannulation was not achieved by standard sphincterotome, we used hydrophilic guidewire or needle-knife pre-cut papillotomy with or without a pancreatic stent.</td>
<td></td>
</tr>
<tr>
<td>Halttunen 2013</td>
<td>100 patients with native papilla</td>
<td>Between June 2011 and February 2012 University Central Hospital, Helsinki</td>
<td>0.025-inch guide wire and sphincterotome group (n = 50) 0.035-inch guide wire and sphincterotome group (n = 50).</td>
<td></td>
</tr>
<tr>
<td>Halttunen 2014 (RCT)</td>
<td>907 consecutive patients with native papilla</td>
<td>Between 1 January 2010 and 31 May 2011 10 Scandinavian endoscopy units</td>
<td>first technique: wire-guided cannulation (WGC) with a straight hydrophilic wire preloaded in a sphincterotome (67.6%), followed by catheter cannulation with (14.3) or without (13.3) a guide wire. second technique in case of failure: J-tip wires, needle knife (NKS) both in the precut and fistula technique, precut sphincterotomy with or without guide wire in the pancreatic duct, and pancreatic stenting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>With intra-diverticula ampulla (IA): 81/81 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without intra-diverticula ampulla (IA): 412/419 (98%)</td>
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<tr>
<td></td>
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<td></td>
<td>Overall: 493/500 (98.6%)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>0.025-inch guide wire and sphincterotome group: 40/50 (80%)</td>
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<td></td>
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<td></td>
<td>0.035-inch guide wire and sphincterotome group: 40/50 (80%)</td>
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<td></td>
<td>Overall: 80/100 (80%)</td>
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<td></td>
<td>First technique: 679/907 (74.9%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Adding second technique: 883/907 (97.4%)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Patients Description</td>
<td>Dates</td>
<td>Technique</td>
<td>Success Rates</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Holt 2016</td>
<td>524 consecutive patients with native papilla</td>
<td>Between November 1, 2013 and September 22, 2014</td>
<td>Standard cannulation technique was defined as biliary cannulation by using a sphincterotome or cannula, with or without device exchange or wire tip or contrast material guidance. Advanced cannulation techniques included cannulation beside a pancreatic wire or stent, needle-knife access papillotomy over a pancreatic stent or performed freehand, cannulation through a duodenal stent, and back-loading of the duodenoscope over a duodenal wire to pass a luminal stricture.</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>single tertiary-care center, USA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang 2015 (RCT)</td>
<td>279 patients with native papilla undergoing consecutive therapeutic ERCP</td>
<td>Between January 2013 and December 2014</td>
<td>Double-guidewire technique group DWT (n=137)</td>
<td>86.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hospital, China</td>
<td>Trans-pancreatic sphincterotomy group TPS (n=142)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Overall: 248/279 (88.9%)</td>
<td></td>
</tr>
<tr>
<td>Ito 2014</td>
<td>146 patients with difficult biliary cannulation who underwent cannulation</td>
<td>Between December 2004 and April 2012</td>
<td>Cannula/sphincterotome under guidance of injected contrast with P-GW (SGT: single-guidewire technique); SGT was done with a 0.025-inch guidewire. If biliary cannulation with SGT was unsuccessful, (double-guide-wire technique) DGT was attempted. Other techniques such as pre-cut</td>
<td>69.9%</td>
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<tr>
<td></td>
<td></td>
<td>Hospital, Japan</td>
<td>SGT: 102/146 (69.9%)</td>
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<td></td>
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<td></td>
<td>Adding DGT: 120/146 (82.2%)</td>
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<td></td>
<td></td>
<td></td>
<td>Adding pre-cut sphincterotomy: 126/146 (86.3%)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Procedure Details</td>
<td>Success Rates</td>
<td></td>
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<tr>
<td>---------------</td>
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<td>------------------------------------------------------------------------------------</td>
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<td></td>
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<tr>
<td>Katsinelos 2008 (RCT)</td>
<td>332 patients</td>
<td>Between June 2006 and December 2006, Two tertiary referral centers, Greece</td>
<td>standard ERCP catheter (n: 165) hydrophilic guide-wire (HGW) (n: 167)</td>
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<tr>
<td></td>
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<td>If cannulation had not succeeded after 10 minutes with the technique assigned at randomization, a further attempt was made for an additional 10 minutes using the alternative technique</td>
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<td></td>
<td>primary success rate of selective CBD cannulation</td>
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<td></td>
<td></td>
<td></td>
<td>standard ERCP catheter : 89/165 (53.9%)</td>
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<td></td>
<td></td>
<td></td>
<td>HGW: 136/167 (81.4%)</td>
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<td></td>
<td></td>
<td>Successful crossover cannulation</td>
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<td></td>
<td></td>
<td></td>
<td>standard ERCP catheter : 40/74 (54.0%)</td>
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<td></td>
<td></td>
<td></td>
<td>HGW: 4/31 (12.9%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Overall: 269/332 (81.0%)</td>
<td></td>
</tr>
<tr>
<td>Kawakami 2012 (RCT)</td>
<td>400 consecutive patients with naive papillae who were candidates for ERCP</td>
<td>Between September 2009 and March 2010, 15 referral endoscopy units, Japan</td>
<td>C group: 72/101 (71.3%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>C+GW group: 75/102 (73.5%)</td>
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<td></td>
<td></td>
<td>S group: 68/100 (68%)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>S+GW group: 67/97 (69.1%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Overall: 282/400 (70.5%)</td>
<td></td>
</tr>
<tr>
<td>Kubota 2013</td>
<td>134 patients who underwent needle-knife sphincterotomy (NKS)</td>
<td>Between May 2004 and July 2011, two-centers (university and Medical</td>
<td>NKPP: 31/36 (86.1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Needle-knife precut papillotomy without pancreatic stent (NKPP) (n:36 patients)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Overall: 126/134 (94.0%)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Dates</td>
<td>Procedure</td>
<td>Results</td>
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<tr>
<td>Lopes 2014</td>
<td>1087 consecutive patients with naive papilla</td>
<td>Between November 2006 and December 2010</td>
<td>Papillotomy with a small incision using a layer-by-layer method over a pancreatic stent (NKPP-SIPS) (n: 98 patients)</td>
<td>Standard methods: 883/1087 (81%) adding NKF: 1049/1087 (96%)</td>
</tr>
<tr>
<td>Miao 2015</td>
<td>1059 patients</td>
<td>Between May 2012 and April 2013</td>
<td>Standard method: A duodenoscope was inserted into the duodenal papilla. A catheter was then inserted via the papilla. In the case of failing to enter the bile duct but repeated (more than three times) insertion of the catheter into the pancreatic duct, a pancreatic guide-wire or plastic stent was placed, and bile duct cannulation was attempted again (n: 163). If the guide-wire repeatedly entered the pancreatic duct but failed to enter the bile duct, a Pre-cut papillotomy was performed (n:69).</td>
<td>Standard methods: 896/1059 (84.6%) adding the assistance of a pancreatic guide-wire or plastic stent: 990/1059 (93.5%) adding pre-cut papillotomy: 1057/1059 (99.8%)</td>
</tr>
<tr>
<td>Nakai 2015</td>
<td>800 Consecutive patients with a native papilla undergoing therapeutic ERCP</td>
<td>Between January 2008 and October 2013</td>
<td>Wire-guided cannulation (WGC) In cases of difficult cannulation, the</td>
<td>WGC: 564/800(70.5%) adding DGW: 121/800 (15.1%) or PGW: 41/800 (5.1%)</td>
</tr>
</tbody>
</table>
by using WGC Academic center, Japan method and timing of rescue techniques were determined at the discretion of the endoscopists:
- contrast material–assisted cannulation,
- a double-guide-wire (DGW) technique,
- a pancreatic duct guide-wire (PGW) technique,
- or a percutaneous trans-hepatic biliary drainage–assisted rendezvous technique. Prophylactic PD stent placement was performed at the discretion of the endoscopists.

| Panteris 2008 | 601 undergoing ERCP: 117 with Periampullary diverticula (PAD) and 484 without PAD | Between May 2001 and December 2006 General Hospital, Greece | Cannulation was attempted by using a sphincterotome after the administration of 20 mg Buscopan patients with PAD: 111/117 (94.9%) Patients without PAD: 459/484 (94.8%) Overall: 570/601 (94.8%) |
| Park 2012 | 154 patients with difficult cannulation: 33 with PAD, 121 without PAD | Between December 2005 and October 2010 Department of internal Medicine, Korea | needle-knife fistulotomy with PAD: 31/33 (93.9%) without PAD: 107/121 (88.4%) Overall: 138 / 154 (89.6%). |
| Parlak 2015 | 1201 patients with naive papilla. 222 (18.5%) had peripapillary diverticulum PPD | recruitment period not reported Reference clinic, hospital, Turkey | In the presence of PPD, a sphincterotome or ERCP catheter installed with guidewire was used for the cannulation attempt. The guidewire easily entered into the pancreatic duct, instead of the common bile duct. Without Peripapillary Diverticulum: 947/979 (97%) With PPD: 210/222 (95%) Overall: 1157/1201 (96.3%) |
then the guide-wire was left there. After that, with the help of another guide-wire-installed sphincterotome standing next to the previously placed guide-wire in the pancreatic duct, the cannulation of biliary system was tried to be completed. In the presence of deep-seated, crooked papilla without orifice observed or catheter unapproachable papilla, to reveal papillary orifice, a 5-F ERCP catheter was used to give the right position to papilla and to adjust the suitable cannulation angle. Then, the cannulation was attempted with another 5-F ERCP catheter or 5-F sphincterotome with the guide-wire passed through endoscope. In patients, who failed in the cannulation attempts with any of the 2 methods at each of the 5 trials, if a guide-wire stayed in the pancreatic duct, cannulation was achieved by precut with standard sphincterotomy over the wire previously left in the pancreatic duct with transpancreatic septotomy or with
<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Type of Papilla</th>
<th>Time Period</th>
<th>Technique</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peng 2013</td>
<td>13018 patients with native papilla</td>
<td>Between March 28, 2007 and May 18, 2011</td>
<td>Conventional deep biliary cannulation without pre-cut sphincterotomy: 10903/12142 (89.8%)</td>
<td>Conventional (without precut): 10903/12142 (89.8%)</td>
<td>Overall: 11648/13018 (95.6%)</td>
</tr>
<tr>
<td>Rajnakova 2003</td>
<td>626 patients with native papilla</td>
<td>Between January 1991 and December 1996</td>
<td>ERCP; no further information provided</td>
<td>592/626 (94.6%)</td>
<td></td>
</tr>
<tr>
<td>Ramesh 2014</td>
<td>243 patients underwent 3Fr or 5Fr pancreatic stent placement following sphincterotomy for manometry-proven sphincter of Oddi dysfunction (SOD).</td>
<td>Between 2002 and 2012</td>
<td>3Fr stent placement (n=133) 5Fr stent placement (n=110)</td>
<td>3Fr stent 133/133 (100%) 5Fr stent 110/110 (100%)</td>
<td>Overall: 243/243 (100%)</td>
</tr>
<tr>
<td>Sasahira 2015 (RCT)</td>
<td>274 patients with naive papilla who underwent ERCP and a guidewire was unintentionally inserted into the main pancreatic duct within 10 attempts and 10 minutes</td>
<td>Between April 2011 and June 2012</td>
<td>Double wire guide technique (EDG) (n:137) repeated use of single guide-wire cannulation (RSG) (n:137)</td>
<td>RSG: 133/137 (97%) EDG: 134/137 (97.8%)</td>
<td>Overall: 267/274 (97.4%)</td>
</tr>
</tbody>
</table>
| Testoni 2011 | 2003 patients who had undergone endoscopic retrograde cholangio-pancreatography | Between 2000 and 2008 tertiary referral centre, Italy | Pre-cut sphincterotomy | Without pre-cut: 1717/1834 (93.6%)  
With precutting: 161/170 (94.7)  
Overall: 1878/2003 (93.7%) |
|---|---|---|---|---|
| Tham 2004 | 344 consecutive patients undergoing ERCP: With periampullary diverticula (n=83)  
Without periampullary diverticula (n=261) | ERCP performed with standard technique | With periampullary diverticula: 78/83 (94%)  
Without periampullary diverticula: 245/261 (94%)  
Overall: 323/344 (94%) |
| Tsuchiya 2015 (RCT) | 131 patients who required selective biliary cannulation of the native papilla | Between May 2012 and February 2013  
Multicenter, hospitals, Japan | J-tip guide-wire (groups J), n=66  
angled-tip guide-wire groups (groups A), n=65  
If biliary cannulation was not achieved within 10 min, the guide-wire was changed to another type and the insertion was continued for another 10 min (cross-over method).  
Success rate of first GW  
J group: 56/66 (84.8%)  
A group: 52/65 (80%)  
Final success rate after switching to other guide-wire  
J group: 66/66 (100%)  
A group: 65/65 (100%) |
| Vihervaara 2012 | 105 consecutive patients admitted for ERCP with intended biliary cannulation and with unhindered access to a native papilla | University Hospital, Finland | conventional wire-guided method with cannula and guide-wire.  
If this conventional cannulation method failed and the guide-wire more than once passed into the pancreatic duct, the double-guidewire method was used.  
If the double-guide-wire–assisted cannulation failed in terms of biliary cannulation  
Cannula with guide-wire: 84/105 (80%)  
Adding Double-guide-wire technique: 97/105 (92.4%)  
Adding Needle-knife technique: 104/105 (99%) |
cannulation or if the guide-wire entered neither the bile duct nor the pancreatic duct, the needle-knife–assisted cannulation, which according to us means a needle-knife fistulotomy, was the last option.

| Zhang 2016 | 1130 consecutive patients with intact papilla who were established as candidates for therapeutic ERCP | Between January 2008 and March 2015 tertiary referral center, China | conventional group with repeated cannulation trials in patients with difficult bile duct cannulation; wire-guided cannulation technique with a sphincterotome preloaded with a 0.035-inch guide-. (n=532) NKPF group: NKPF in case of difficult biliary cannulation (n=598) | conventional group: 483/532 (90.8 %) NKPF group: 591/598 (98.8 %) Overall: 1074/1130 (95%) |

Conclusions

Achieved cannulation rate ranged from 70.5% and 100% (median: 96%, mean 91.4%).

References

Included studies


Awaiting assessment

Excluded studies


STONE EXTRACTION

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro
Tumori- CPO Piemonte

1.18. Frequency with which extraction of common bile duct stones of <1cm in patients with
native major papillae without surgically altered anatomy undergoing ERCP is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP for
extraction of common bile duct stones

Intervention
extraction of common bile duct stones of <1 cm

Control
none

Outcome
achieved extraction rate

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to
29/6/2016 separately for systematic reviews and primary studies using the following search
strategies:

Systematic reviews and meta-analysis

PubMed
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) AND
("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) AND
(Choledocholithiasis[Text Word] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR
"Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text
Word]))) AND ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND
(papilla[Title/Abstract] OR papillae[Title/Abstract]))) AND ("systematic review"[Title/Abstract]
OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR metanalysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])
Primary studies
Results of the bibliographic searches
After removing duplicates, 167 articles (2 reviews and 165 primary studies) were found. 18 primary studies were considered potentially relevant and acquired in full text and another one was suggested by experts (see flow chart).
Because few studies potentially relevant were found, also conference proceedings were considered. A sample size of 50 patients was used as a cut-off for inclusion.

Excluded studies
17 studies were excluded: 7 because size of stones were not reported (Baron 2004, Daradkeh 2000, Kim 2009, Schreurs 2002, Tham 2004, Vitale 2016, Xiu 2013); 5 because stones were greater than 1 cm (Garcia-Cano 2009, Draganov 2009, Kalogeropoulos 2014, Itokawa 2013, Paspatis 2013); 1 because size of stone ranged from 2 to 25 mm and no separate data for stone < 1 cm were provided (Tsujino 2008); 1 because size of stone ranged from 1 to 35 mm and no separate data for stone < 1 cm were provided (Takezawa 2004); 1 because no intervention of interest (Mattila 2014), 1 because no outcome of interest was reported (Li 2013), 1 because only for a minority of cases (n:24) ERCP was used (Chiappalone 2000).

Included studies
Two studies were finally included (Kuo 2012, Oppong 2012).
<table>
<thead>
<tr>
<th>Study</th>
<th>N and characteristic of patients undergoing ERCP for stone extraction</th>
<th>Years of recruitments Setting</th>
<th>Intervention</th>
<th>stone extraction rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuo 2012</td>
<td>222 consecutive patients with stones ≤ 1 cm from December 2004 through the end of November 2008. Department of Internal Medicine, Division of Hepato-Gastroenterology Taiwan</td>
<td>Endoscopic papillary balloon dilation</td>
<td>201/222 (94.6%)</td>
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</tr>
<tr>
<td>Oppong 2012</td>
<td>4371 ERCPs with attempts of &gt;1 cm stone extraction in patients with native papillas tertiary and secondary care units in the UK and USA, May 2011</td>
<td>UK attempts: 900 USA attempts: 3471</td>
<td>UK: 96% USA: 99% P&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**

No definite conclusions can be drawn because only two studies were retrieved addressing this question. In these studies stone extraction rate ranged between 94% and 99%.
References

Included studies

Excluded studies


SUCCESS RATE OF STENT PLACEMENT

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.19. Frequency with which stent placement in patients with native major papillae without surgically altered anatomy undergoing ERCP for stent placement in cases of biliary obstruction below the bifurcation is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP for stent placement in cases of biliary obstruction below the bifurcation

Intervention
stent placement

Control
None

Outcome
achieved stent placement rate

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

**Systematic reviews and meta-analysis**

**PubMed**
Endoscopic retrograde cholangiopancreatography/EXP OR ERCP:ti,ab,kw (Word variations have been searched)

#3 #8 or #7

#4 MeSH descriptor: [Stents] explode all trees

#5 stent:ti,ab,kw (Word variations have been searched)

#6 #4 or #5

#7 MeSH descriptor: [Ampulla of Vater] explode all trees

#8 native papilla:ti,ab,kw (Word variations have been searched)

#9 #8 or #7

#10 MeSH descriptor: [Common Bile Duct] explode all trees

#11 CBD or biliary or bile duct:ti,ab,kw (Word variations have been searched)

#12 obstruction or occlusion:ti,ab,kw (Word variations have been searched)

#13 cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)

#14 #10 or #11

#15 #12 or #13

#16 #14 and #15

#17 benign:ti,ab,kw (Word variations have been searched)

#18 #12 and #17

#19 cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)

#20 MeSH descriptor: [Cholangitis] explode all trees

#21 MeSH descriptor: [Pancreatitis] explode all trees

#22 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees

#23 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
PubMed


Embase

('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND (("common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR carcinom*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) AND ("biliary stent"/exp OR stent:ab,ti OR stents:ab,ti) AND ("Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')
Results

Results of the bibliographic searches
After removing duplicates, 178 articles (1 review and 177 primary studies) were found. 31 primary studies were considered potentially relevant and acquired in full text. (See flow chart).
A sample size of 50 patients was used as a cut off for inclusion.

Excluded studies

Included studies
Six studies were finally included (Kim 2013, Kubota 2013, Freeman 2004, Miao 2004, van Berkel 2004, Varadarajulu 2005) with a total of 632 participants.

Conclusions

Successful stent placement rate ranged from 95% and 100% (median: 99%).
<table>
<thead>
<tr>
<th>Study</th>
<th>N and characteristic of patients undergoing ERCP for stent placement</th>
<th>Years of recruitments Setting</th>
<th>Intervention</th>
<th>stent placement rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim 2013</td>
<td>72 patients with ampullary adenoma &lt; 25 mm diameter and no invasion into the bile or pancreatic duct</td>
<td>September 2005 – March 2012 Digestive and disease center and Research Institute Korea</td>
<td>endoscopic excision (en bloc resection in 3% and piecemeal in 17%) of the adenoma, followed by immediate insertion of a pancreatic stent over the guide wire that have been previously placed in the pancreatic duct, and was positioned across the pancreatic duct orifice</td>
<td>72/72 (100%)</td>
</tr>
<tr>
<td>Kubota 2013</td>
<td>98 patients who underwent needle-knife sphincterotomy (NKS)</td>
<td>between May 2004 and July 2011 two-centers (university and Medical Center), Japan</td>
<td>Needle-knife precut papillotomy with a small incision using a layer-by-layer method over a pancreatic stent that would represent a good landmark for precut (NKPP-SIPS) (n: 98 patients)</td>
<td>93/98 (95%)</td>
</tr>
<tr>
<td>Freeman 2004</td>
<td>225 patients in whom pancreatic stent placement via the major papilla was intended.</td>
<td>1998 (conventional technique) and 2000 modified technique tertiary referral center for pancreaticobiliary endoscopy USA</td>
<td>Conventional technique: deep passage to at least the genu of the pancreatic duct of a 0.018-in guide-wire or a 0.025- to 0.035-in ‘‘hybrid’’ floppy-tip guide-wire. Modified short-wire technique for small or tortuous ducts. The Roadrunner guide-wire was used. If the guide-wire could not be passed beyond the first turn in the pancreatic duct , the tip of the guide-wire was passed a short distance beyond the pancreatic sphincter (at least 1-2 cm), just enough to allow insertion of a short (2 or 3 cm) small diameter (3F, 4F, or 5F) stent. If the duct was of sufficient diameter, the soft tip of the guide wire was knuckled and curled inside the main duct below the sharp turn to provide a better anchor. If the duct was diminutive, the straight tip of the guide-wire was impacted into the first turn in the duct and a small diameter (3F or 4F) stent was inserted</td>
<td>222/225 (99%)</td>
</tr>
<tr>
<td>Source</td>
<td>Study Details</td>
<td>Procedure</td>
<td>Results</td>
<td></td>
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<tr>
<td>Miao 2004</td>
<td>80 patients with benign biliary strictures or malignant biliary strictures</td>
<td>From June 2001 to October 2002 Department of gastroenterology China plastic stent: (n:52) gold stent (n: 28) Through papilla of duodenum, contrast medium was injected and location of stricture of bile duct was revealed. A catheter was introduced into the dilated bile duct via the introducer. A guide wire was inserted through the occlusive part of biliary duct. The occlusive part of biliary duct was dilated with a balloon catheter. A stent was inserted into the occlusive bile duct under fluoroscopic control or endoscopy.</td>
<td>80/80 (100%)</td>
<td></td>
</tr>
<tr>
<td>van Berkel 2004</td>
<td>60 patients with distal malignant bile duct obstruction.</td>
<td>February 1998 and September 1998 Department of gastroenterology The Netherlands Tannenbaum design stent with a stainless steel mesh and an inner Teflon coating (TTC). (n:30) conventional polyethylene (PE) stent (n:30)</td>
<td>60/60 (100%)</td>
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</tr>
<tr>
<td>Varadarajulu 2005</td>
<td>97 consecutive patients with pancreatic duct (PD) disruption due to chronic pancreatitis (47), acute pancreatitis (44), operative injury (4), and trauma (2).</td>
<td>from 1995 to 2002 single institution; no more information provided USA Upon identification of the PD disruption as extravasation of contrast into the PFC, a 0.035-inch guide-wire was inserted into the PD and a Geenen pancreatic stent with an internal flap was inserted. When a 3F stent was placed, a small cut was made on the stent to create an internal flap. The PD was cannulated with a 0.018-inch guide-wire when there was an extremely narrow PD stricture or when a 3F stent was placed. The choice of stent was based on specific ductal anatomic features. Strictures were dilated with a 3-4-5F; a 5-7-10F, step-wise dilator; or a rigid, biliary dilating balloon.</td>
<td>92/97 (95%)</td>
<td></td>
</tr>
</tbody>
</table>
References

Included studies


Excluded studies


1.20. Frequency with which EUS-FNP would change patients' management in patients with distant metastasis, ascites, and lymphadenopathy who undergo tissue sampling of both the primary tumor and lesion outside of the primary field.

Population
patients with distant metastasis, ascites, and lymphadenopathy undergoing EUS-guided FNA who have tissue sampling of both the primary tumour and lesions outside of the primary field

Intervention
EUS fine needle biopsy

Control
none

Outcome
percentage of patients in which EUS-FNA changed patients’ management

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
OR ascites[Title/Abstract] OR ascite[Title/Abstract] OR lymphadenopaties[Title/Abstract]) AND ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

**Embase**

('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND (‘patient care'/exp OR management:ab,ti OR impact:ab,ti) AND ('ascites'/exp OR 'lymphadenopathy'/exp OR 'lymph node metastasis'/exp OR 'lymph node metastas*':ab,ti OR ascites:ab,ti OR ascite:ab,ti OR lymphadenopaties:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Endosonography] explode all trees
#2 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4 EUS and FNA:ti,ab,kw (Word variations have been searched)
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Patient Care Management] explode all trees
#7 patient management or impact:ti,ab,kw (Word variations have been searched)
#8 #6 or #7
#9 MeSH descriptor: [Ascites] explode all trees
#10 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#11 lymphadenopathy or metastasis or ascites:ti,ab,kw (Word variations have been searched)
#12 #9 or #10 or #11
#13 #5 and #8 and #12 Publication Year from 2000 to 2016

**Primary studies**

**PubMed**


**Embase**

('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND (‘patient care'/exp OR management:ab,ti OR impact:ab,ti) AND ('ascites'/exp OR
Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4 EUS and FNA:ti,ab,kw (Word variations have been searched)
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Patient Care Management] explode all trees
#7 patient management or impact:ti,ab,kw (Word variations have been searched)
#8 #6 or #7
#9 MeSH descriptor: [Ascites] explode all trees
#10 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#11 lymphadenopathy or metastasis or ascites:ti,ab,kw (Word variations have been searched)
#12 #9 or #10 or #11
#13 #5 and #8 and #12 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 246 articles (5 reviews and 241 primary studies) were found. 27 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
18 studies were excluded: 12 studies because conference abstracts (Chin 2013, Gara 2016, Kurita 2015, Levy 2014, Issa 2014, Giovannini 2012,Rao 2011, Lankarani 2011, El Hajj 2011, Majmundar 2009, Hassan 2009, Coppola 2013); 2 studies because no intervention of interest (Ferrero 2013, Mui 2014); 3 studies because no outcome of interest (Del Vecchio Blanco 2015, Gleeson 2011, Will 2010), 1 study (Hirdes 2010) because patients were not in the inclusion criteria: more than half of the samples were patients without an established diagnosis of primary cancer.

Included studies

Studies awaiting assessment
For two studies (Kliment 2013, Morris, 2009), it was impossible to retrieve the full text.
<table>
<thead>
<tr>
<th>Study</th>
<th>N and characteristic of patients</th>
<th>Years of recruitments</th>
<th>Intervention</th>
<th>Patients in which EUS-FNA changed patients’ management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annema 2005</td>
<td>242 patients with suspected (n 142) or proven (n 100) lung cancer and enlarged (&gt; 1 cm) mediastinal LNs scheduled for mediastinoscopy/tomy (94%) or exploratory thoracotomy (6%).)</td>
<td>recruitment period not reported the Netherlands</td>
<td>EUS-FNA of mediastinal mass before surgery</td>
<td>70%</td>
</tr>
<tr>
<td>Araujo 2013</td>
<td>36 patients with gastro-oesophageal junction (GEJ) adenocarcinoma suspected distant LN metastases</td>
<td>January 2009 - August 2012 France</td>
<td>EUS-FNA of distant lymphnodes</td>
<td>54.2%</td>
</tr>
<tr>
<td>Bodtger 2009</td>
<td>40 patients referred to EUS for known or suspected lung cancer with enlarged left adrenal gland</td>
<td>2000-2006 Denmark</td>
<td>EUS-FNA of an enlarged left adrenal gland (LAG)</td>
<td>48% (avoided surgery: 18% gained surgery: 30%)</td>
</tr>
<tr>
<td>Hassan 2010</td>
<td>81 consecutive patients with gastric carcinoma and suspected distant metastases (tumour, nodes, metastasis ) or suspicious lesions in distant organs</td>
<td>2001-2007 Denmark</td>
<td>EUS-FNA 81/ 234 underwent EUS-FNA because of suspected distant metastasis (35%).</td>
<td>41.9%</td>
</tr>
<tr>
<td>Singh 2007</td>
<td>93 consecutive patients with a newly detected lung mass suspicious of lung cancer or with a recent tissue diagnosis of non–small cell lung cancer (NSCLC).</td>
<td>March 2004 - July 2005 USA</td>
<td>EUS- FNA for diagnosis of lung cancer and metastasis</td>
<td>8.6%</td>
</tr>
<tr>
<td>Talebian 2010</td>
<td>152 consecutive patients with (suspected) NSCLC who were medically fit to undergo surgical resection of the lung tumour</td>
<td>August 2003 - February 2007 the Netherlands</td>
<td>EUS-FNA of mediastinal mass before surgical staging</td>
<td>39%</td>
</tr>
</tbody>
</table>
Quality of evidence

Clinical question 1: patency vs no patency
Factors that can lower quality
- Study limitations (risk of bias): yes (case series)
- Inconsistency of results: yes
- Indirectness of evidence: no
- Imprecision: no
- Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as very low for study limitation and indirectness
Factors that can higher quality
- Large magnitude of effect: no
- Opposing plausible residual bias or confounding: no
- Dose-response gradient: no

Conclusions

EUS-FNA seems to have a relevant impact on patients management, changing planned intervention in percentages of patients ranging from 8.6% to 70%. However variability is high. For lung cancer patients percentages ranged from 8.6% to 70%, for gastric cancer patients from 42% to 54.2% (VERY LOW QUALITY EVIDENCE).

References

Included studies

Excluded studies

Studies awaiting assessment
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n = 0)
- DARE (n = 0)
- CENTRAL (n = 7)
- Records identified through PubMed (n = 6 SRs, 397 primary studies)
- Records identified through Embase (n = 32 SRs, 636 primary studies)

Records after duplicates removed (n = 36 SRs, 915 primary studies)

Screening
- Records screened (n = 951)
- Records excluded (n = 929)

Eligibility
- Studies awaiting classification (n = 2)
- Full-text articles assessed for eligibility (n = 27)
- Full-text articles excluded, with reasons (n = 18)

Included
- Studies included (n = 7)
DIAGNOSTIC RATE OF ADEQUATE EUS-FNA SAMPLING

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.21. Frequency of successful diagnostic tissue sampling in patients with solid lesions undergoing EUS-FNA.

Population
patients with solid lesions undergoing EUS-FNA

Intervention
EUS fine needle biopsy

Control
none

Outcome
diagnostic rate of adequate EUS-FNA sampling

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

**Embase**
('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND ('laboratory diagnosis'/exp OR 'sampling':ab,ti OR specimen:ab,ti OR specimens:ab,ti) AND (adequate:ab,ti OR satisf*:ab,ti OR suitable:ab,ti OR sufficient:ab,ti)) AND ('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti OR stomach:ab,ti OR mediastinum:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph nodes':ab,ti OR 'lymph node':ab,ti OR 'lymphnodes':ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR 'digestive system cancer'/exp) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'systematic review' OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Endosonography] explode all trees
#1 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4 EUS and FNA:ti,ab,kw (Word variations have been searched)
#5 #1 or #2 or #3 or #4
#6 Any MeSH descriptor with qualifier(s): [Pathology - PA]
#7 MeSH descriptor: [Specimen Handling] explode all trees
#8 specimen or sampling:ti,ab,kw (Word variations have been searched)
#9 #6 or #7 or #8
#10 adequate or sufficient or suitable:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 CBD or biliary or pancreatic or bile duct or rectal or gastric or esophageal or mediastinum:ti,ab,kw (Word variations have been searched)
#13 cancer or neoplasm or malign or tumor or carcinoma or lymph nodes:ti,ab,kw (Word variations have been searched)
#14 MeSH descriptor: [Lymph Nodes] explode all trees
#15 #13 or #14
#16 #12 and #15
#17 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#18 MeSH descriptor: [Rectal Neoplasms] explode all trees
Primary studies

PubMed

Embase
("endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND ('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimens:ab,ti OR specimen:ab,ti) AND (adequate:ab,ti OR satisf*:ab,ti OR suitable:ab,ti OR sufficient:ab,ti)) AND ((("common bile duct'/exp OR 'bile duct'/exp OR 'bile duct':ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti OR stomach:ab,ti OR mediastinum:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumours:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph nodes':ab,ti OR 'lymph node':ab,ti OR 'lymph node':ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR 'digestive system cancer'/exp) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic review'/de OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metaanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR "case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
Results

Results of the bibliographic searches
After removing duplicates, 612 articles (20 reviews and 592 primary studies) were found. 36 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Overall 11 studies were excluded.

Pancreas
8 studies were excluded: 3 because no outcome of interest (Chen 2012, Park 2016, Siddiqui 2011); 3 because EUS–FNA was performed only in a subgroup of patients smaller than 100 (Aso 2014, Imaoka 2009, Matsuyama 2013); 2 (Lee 2003, Rocca 2007) because 26% and 30% respectively of patients had cystic lesions and no separate results were reported for solid lesions.

Mediastinal Lymph Nodes
1 study was excluded patients were not in the inclusion criteria: clinical diagnosis of mediastinal granulomatous lymphadenitis (Manucha 2013).

Gastric lesions
1 study was excluded because no outcome of interest (Hoda 2009).

All sites
1 study was excluded because no outcome of interest (Sodikoff 2013).

Studies awaiting assessment
4 studies were classified as awaiting assessment because written in German, Japanese, Chinese and we were not able to get the translations (Bohle 2013, Furuhat 2012, Gao 2016, Sudhof 2004).
Included studies
Overall 21 studies were included.
Pancreas: 12 studies (Alatawi 2015, Ardengh 2008, Baek 2015, Cleveland 2010, Eloubeidi 2003,
Mediastinal Lymph Nodes: 1 study (Fritscher-Ravens 2000).
Gastric lesions: 1 study (Mekky 2010).
2004, Carrara 2016)
<table>
<thead>
<tr>
<th>Study</th>
<th>N and characteristic of patients</th>
<th>Setting</th>
<th>Intervention</th>
<th>Diagnostic rate of adequate EUS-FNA sampling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alatawi 2015 (RCT)</td>
<td>100 consecutive patients with solid pancreatic tumours of at least 2 cm in size showed on CT scanner or MRI</td>
<td>Between 1 April 2012 and 30 March 2013 tertiary referral academic center for biliary-pancreatic pathology France</td>
<td>EUS-FNA with standard 22G Echo-ultra TM needle (n=50)</td>
<td>EUS FNA: 45/50 (90%) EUS-FNB 50/50 (100%) Overall 95/100 (95%)</td>
</tr>
<tr>
<td>Ardengh 2008 (data extracted from abstract because full text not available)</td>
<td>611 patients with pancreatic tumors</td>
<td>From January 1997 to December 2006 setting not reported</td>
<td>cytological smears (n=282) only cell blocks (n=329)</td>
<td>cytological smears + cell blocks: 595/611 (97.4%)</td>
</tr>
<tr>
<td>Baek 2015</td>
<td>191 cases of solid pancreatic lesions</td>
<td>Between January 2010 and December 2012 Department of Pathology, Seoul National University Hospital - Korea</td>
<td>Endoscopic ultrasound guided fine needle aspiration cytology (EUS-FNAC); details on needle not provided</td>
<td>171/191 (89.5%)</td>
</tr>
<tr>
<td>Cleveland 2010</td>
<td>247 solid pancreatic masses 276 lymph nodes</td>
<td>Between 1997 and 2007 tertiary care center USA</td>
<td>EUS-FNA for cytodiagnosis; default needle gauge was 22. Exceptions were noted in the clinical record</td>
<td>pancreatic tumours 240/247 (97%) lymph nodes 252/276 (91%)</td>
</tr>
<tr>
<td>Eloubeidi 2003</td>
<td>101 consecutive patients with suspected pancreatic carcinoma based on clinical results and/or other imaging studies</td>
<td>Between July 2000 and August 2001 University of Alabama at Birmingham USA</td>
<td>Endoscopic ultrasound-guided fine-needle aspiration biopsy with a 22-gauge needle (EUS-FNAB)</td>
<td>99/101 (98%)</td>
</tr>
<tr>
<td>Fritscher-Ravens 2001</td>
<td>114 patients with focal solid pancreatic masses</td>
<td>recruitment period not reported Department of Interdisciplinary</td>
<td>EUS-FNA with 22-gauge needle for cytodiagnosis</td>
<td>112/114 (98.2%)</td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Study Details</td>
<td>Procedure Details</td>
<td>Results</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
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</tr>
<tr>
<td>Hucl 2013 (RCT)</td>
<td>144 Consecutive patients with a pancreatic mass lesion or peri-intestinal lymphadenopathy</td>
<td>Between March 2011 and July 2012</td>
<td>fine needle biopsy with both a newly developed 22G core needle (the FNB needle) (n=145) standard 22G fine needle aspiration (FNA) needle (n=145)</td>
<td>FNB: 125 (86.2 %) FNA: 127 (87.6 %)</td>
</tr>
<tr>
<td>Iglesias-Garcia 2011</td>
<td>182 patients with solid pancreatic masses</td>
<td>a 2-year study period (dates not reported)</td>
<td>EUS-FNA with standard 22-gauge needle with on-site cytopathologist (n: 95) cases without on-site cytopathologist (n: 87) cases</td>
<td>on-site cytopathologist 94/95(98.9%) without on-site cytopathologist:76/87 (87.4%)</td>
</tr>
<tr>
<td>Kamata 2016 (RCT)</td>
<td>214 consecutive patients with solid pancreatic masses who presented to eight referral centers, Japan</td>
<td>April - September 2013</td>
<td>standard 25-gauge needle (n=108) for core biopsy a 25-gauge needle with a core trap (ProCore) for core biopsy (n=106)</td>
<td>standard 25-gauge needle: 81.1 % a 25-gauge needle with a core trap (ProCore): 69.4 %;</td>
</tr>
<tr>
<td>Mitsuhashi 2006</td>
<td>267 patients with solid pancreatic masses</td>
<td>Between February 1996 and October 2000 California Irvine Medical Center USA</td>
<td>EUS-FNA for cytodiagnosis with 22-gauge, 10-cm needle</td>
<td>253/267 (95.9%)</td>
</tr>
<tr>
<td>Möller 2009</td>
<td>192 patients with solid pancreatic masses</td>
<td>6-year period until the end of 2006 three centers, no more details provided</td>
<td>EUS-FNA with 22-gauge needles for cytological and histological diagnosis</td>
<td>histology: 86.5% cytology: 92.7% cytology + histology: 190/192 (98.9%)</td>
</tr>
<tr>
<td>Study</td>
<td>N and characteristic of patients</td>
<td>Setting</td>
<td>Intervention</td>
<td>Diagnostic rate of adequate EUS-FNA sampling</td>
</tr>
<tr>
<td>---------------</td>
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</tr>
<tr>
<td>Will 2010</td>
<td>153 consecutive patients with pancreatic tumor lesions revealed by any imaging procedure</td>
<td>From January 2000 to March 2003</td>
<td>EUS-FNA with 19 or 22-gauge needles for cytological and patho-histological diagnosis</td>
<td>cytology: 152/153 (99.3%) patho-histology: 96/153 (62.7%)</td>
</tr>
<tr>
<td><strong>Mediastinal Lymph Nodes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fritscher-Ravens 2000</td>
<td>153 patients with Mediastinal lymphadenopathy</td>
<td>Between November 1997 and November 1999</td>
<td>EUS-FNA with 22-gauge Vilmann-Hancke needle or a 22-gauge Wilson-Cook echo tip for cytodiagnosis</td>
<td>150/153 (98%)</td>
</tr>
<tr>
<td><strong>Gastric tumours</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mekky 2010</td>
<td>141 consecutive patients with submucosal tumours of the stomach</td>
<td>Between January 2000 and December 2008</td>
<td>EUS-FNA with 22-gauge needles for cytodiagnosis</td>
<td>117/141 (83%)</td>
</tr>
<tr>
<td><strong>All sites</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aithal 2007</td>
<td>167 patient with mural and extramural solid masses suitable for both FNA and tru-cut biopsy that could be approached via trans-oesophageal (n:57) or trans-gastric approach (n: 86); patients that can</td>
<td>period of recruitment not reported three centers UK</td>
<td>dual sampling with both FNA for cytology and tru-cut biopsy for histology (n: 95) sequential sampling( FNA only when tru-</td>
<td>adequacy of samples reported only for tru-cut biopsy dual sampling: tru-cut biopsy 85/95 (89%) sequential sampling: 64/75 (89%)</td>
</tr>
</tbody>
</table>
be approached via with trans-duodenal (n:24) only when the lesion can be approached with the scope in a relatively straight position.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Procedures</th>
<th>Diagnoses</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrara 2016</td>
<td>144 consecutives patients with solid masses: pancreas (n:102), adenopathies (n:21), parietal masses of the GI tract (n:17) other locations (n: 4).</td>
<td>EUS-FNA for cytological diagnosis with 25-G needles (n:72)</td>
<td>Between August 2013 and October 2014 Endoscopy Unit of the Humanitas Research Hospital Italy</td>
<td>25-G group :58/72 (81%) 22-G group 49/72 (68%); Overall: 107/144 (74.3%)</td>
</tr>
<tr>
<td>Jhala 2004</td>
<td>209 consecutive samples from 151 patients: pancreas (n:84; solid 76, cystic 8), lymph nodes and spleen (n: 91; lymph nodes :89, spleen 2), gastrointestinal tract (n: 15; esophagus 5, stomach 3, duodenum 7), liver and biliary tract (n:11; liver 7, biliary tract 4), adrenal glands (n: 4), and others (n:4; mediastinum 3, retro-peritoneum 1)</td>
<td>EUS-FNAB EUS-guided fine-needle aspiration biopsy with 22-gauge needle for cytological diagnosis</td>
<td>The University of Alabama at Birmingham, USA</td>
<td>96% (201 of 209).</td>
</tr>
<tr>
<td>Larghi 2011</td>
<td>120 consecutive patients: Enlarged lymph nodes (n:37), Abdominal mass (n:26), Sub-epithelial lesion (n:17), Pancreatic body or tail mass (n:13), Thickened oesophago-gastric wall (n:11), Mediastinal mass (n:6), Liver mass (n:5), Spleen mass (n:2), Left adrenal mass (n:2), Perirectal mass (n:1)</td>
<td>EUS-guided fine-needle tissue acquisition (EUS-FNTA) with a 19-gauge needle.</td>
<td>Between January 2007 and December 2008 Tertiary care academic medical center Italy</td>
<td>116 of the 119 patients (97.5%)</td>
</tr>
<tr>
<td>Mehmood 2015</td>
<td>393 patients: mediastinal</td>
<td>EUS-FNA with 22-gauge</td>
<td>Between August 2008 and</td>
<td>369 / 393 (93.9%)</td>
</tr>
<tr>
<td>Study</td>
<td>Patients and Lesions</td>
<td>Procedures and Equipment</td>
<td>Success Rate</td>
<td></td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Paik 2015</td>
<td>33 procedures in 125 patients: pancreas (n: 58), Lymph node (n=48), retroperitoneal mass (n=8), Ampulla of Vater (n=2), Gallbladder (n=8), Common bile duct (n=2), Duodenum (n=2), Liver (n=5)</td>
<td>Between October 2011 and March 2013. Department of gastroenterology, Korea</td>
<td>EUS-guided fine needle biopsy with 22G ProCore needle using capillary sampling (EUS-FNB)</td>
<td>122/133 (94%)</td>
</tr>
<tr>
<td>Wittmann 2006</td>
<td>159 patients: pancreas (n: 83), mediastinum (n:55), oesophagus (n: 9), stomach (n:7), rectum (n: 2), hepatic hilum (n: 1), hypopharynx (n: 1) third part of duodenum (n:1).</td>
<td>Between May 2002 and April 2005 University College London Hospitals UK</td>
<td>EUS-FNA with 22-gauge needle for cytology (159) EUS-TNB true-cut needle biopsy with 19-gauge outer cutting needle for histology (n:96) EUS-FNA/TNB (n: 96)</td>
<td>EUS-FNA: 91% EUS-TNB: 88% EUS-FNA/TNB: 97%</td>
</tr>
</tbody>
</table>
Conclusions

Overall adequate samples ranged from 62.7% to 100% (mean 90.8%, median: 94%).

Pancreatic lesions: adequate samples ranged from 62.7% to 100% (mean 90.4%, median: 95.9%): in the eight studies were EUS-FNA was performed for cytodiagnosis adequate samples ranged from 87.4% to 99.3% (mean 94%, median 94.3%); in the six studies were FNB were performed for histological diagnosis adequate samples ranged from 62.7% to 100% (mean 83.4%, median 86.2%).

Mediastinal Lymph Nodes: adequate sample was obtained in 98% of patients were EUS-FNA was performed for cytological diagnosis (one study).

Gastric lesion: adequate sample was obtained in 83% of patients were EUS-FNA was performed for cytological diagnosis (one study).

All sites: in the studies that included patients with lesions at various sites and reported only overall results adequate samples ranged from 74.3% to 97.5% (median 94%, mean 91.7%): in the four studies were EUS_FNA was performed for cytodiagnosis adequate samples ranged from 74.3% to 96% (mean 88.8%, median 92.4%); in the four studies were FNB were performed for histological diagnosis adequate samples ranged from 88% to 97.5% (mean 92.1%, median 91.5%)

References

Included studies


Excluded studies


Awaiting assessment


B VISUALIZATION OF DEFINED LANDMARKS IN EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.1 (B I(a)). Does the visualization of defined landmarks improve the quality of EUS in patients suffering from esophageal cancer?

Population
Patients suffering from oesophageal cancer undergoing EUS

Intervention
Visualization of the tumour, mediastinum (lymph nodes), gastro-oesophageal junction, celiac axis (lymph nodes) and left lobe of the liver (to rule out metastatic disease)

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients’ management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

Embase
(endoscopic echography/exp OR EUS:ab,ti) AND (cancer staging/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'esophagus cancer'/exp) AND (lymph node/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'lower esophagus sphincter'/exp OR ("liver'/exp OR liver:ab,ti) AND ("left lobe":ab,ti OR 'right lobe':ab,ti))) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metaanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Esophageal Neoplasms] explode all trees
#9 esophageal:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 MeSH descriptor: [Esophagogastric Junction] explode all trees
#15 lymph nodes:ti,ab,kw (Word variations have been searched)
#16 mediastinum:ti,ab,kw (Word variations have been searched)
#17 celiac axis:ti,ab,kw (Word variations have been searched)
#18 MeSH descriptor: [Liver] explode all trees
#19 liver:ti,ab,kw (Word variations have been searched)
#20 "right lobe" or "left lobe":ti,ab,kw (Word variations have been searched)
#21 #18 or #19
#22 #21 and #20
#23 #22 or #13 or #14 or #15 or #16 or #17
#24 #6 and #7 and #12 and #23 Publication Year from 2000 to 2015
Primary studies

PubMed

Embase
(endoscopic echography/exp OR EUS:ab,ti) AND ("cancer staging"/exp OR stag*:ab,ti OR TNM:ab,ti OR "patient management":ab,ti OR "clinical management":ab,ti OR impact:ab,ti) AND (("esophageal":ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR "oesophagus cancer"/exp) AND ("lymph node":exp OR "lymph node":ab,ti OR "lymph nodes":ab,ti OR "lymphnodes":ab,ti OR "mediastinum lymph node":exp OR "celiac axis":ab,ti OR "lower esophagus sphincter":exp OR (("liver":exp OR liver:ab,ti) AND ("left lobe":ab,ti OR "right lobe":ab,ti)) NOT (cochrane OR "systematic review"/de OR "systematic review" OR "systematic reviews"/de OR "systematic reviews" OR "meta analysis"/de OR "meta analysis" OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR "case report":exp OR "case report" OR "report of case")

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Esophageal Neoplasms] explode all trees
#9 esophageal:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 MeSH descriptor: [Esophagogastric Junction] explode all trees
Results of the bibliographic searches
After removing duplicates, 500 articles (33 reviews and 467 primary studies) were found. 7 systematic reviews and 29 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 2 further potentially relevant articles were retrieved in the references of the retrieved studies. (See flow chart).
In first instance systematic reviews were considered. All assessed only the accurate staging outcome and the most updated review included primary studies published up to June 2010. So we selected primary studies which assessed accurate staging only if published since July 2010 and primary studies which assessed the impact on patients management published within 2000 and August 2015.

Excluded studies

Included studies

Accurate staging
None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging.
We found 5 systematic reviews (Kelly 2001, Puli 2008, Sgourakis 2011, Thosani 2012, Van Vliet 2008) and 4 primary studies (Bergeron 2014, Dhupar 2015, Lee 2014, Meister 2013) assessing the diagnostic accuracy of EUS. All the studies used histopathology as reference standard. Because the overlapping of primary studies included in the systematic reviews was low (less than 50%) we extracted data from all the SRs.
Two SRs (Kelly 2001, Thosani 2012) assessed the accuracy of EUS for T staging, the other three reviews assessed the accuracy of EUS for N staging (Puli 2008, Sgourakis 2011, Van Vliet 2008). Three primary studies assessed accuracy of EUS both for T and N stage for esophageal cancer (Lee 2014, Bergeron 2014, Meister 2013), one study (Dhupar 2015) assessed the accuracy of EUS for T stage of the gastro-esophageal junction cancer. For T stage the studies used different cut off to measure sensitivity, specificity and overall accuracy. N stage was measured for regional and celiac lymph nodes.

Overall accuracy for T stage ranged from 48% to 86.7%. Accuracy for T1 stage ranged from 83% to 86.7%; for T2 ranged from 75% to 86.7%; for T3 ranged from 79% to 93.3%; for T4 it was of 95% in one study. One SR assessed the sensitivity and specificity of EUS in distinguishing T1,T2 vs T3,T4 and they ranged from 71-100 and 66.7-100 respectively. Sensitivity and specificity of EUS in staging T1a ranged from 41.6% to 85% and from 81.3% to 87% respectively. Sensitivity and specificity of EUS in staging T1b ranged from 58% to 86% and from 49% to 86% respectively.

Sensitivity and specificity of EUS for N1 stage of regional lymph nodes ranged from 76% to 80% and 70% to 72% respectively. Sensitivity and specificity of EUS for N1 stage of celiac lymph nodes ranged from 67% to 85% and 95% to 98% respectively.

**Impact on patients’ management**

None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the impact on patient management.

We found eight studies (Shah 2004, Bulsiewicz 2014, Walker 2011, Subasinghe 2010, Gheorghe 2006, Preston 2003, Pouw 2011, Shumaker 2002) that assessed the impact of EUS results on management plans. The studies differed substantially for the measures used to assess the impact on patients’ management. Outcomes, results and authors conclusions are reported in the table below.

**Overlapping of primary studies between systematic reviews**

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(the overlapping of the studies included in Sgourakis 2011 could not be assessed because the review did not provide the references of the included studies)
Accurate staging

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<td>Sensitivity (95% CI): 0.85 (0.82-0.88)</td>
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<td>Specificity (95% CI): 0.87 (0.84-0.90)</td>
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<td>PLR (95% CI): 6.62 (3.61-12.12)</td>
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<td>1963 patients with oesophageal cancer who performing EUS 31 studies on EUS for regional lymph node metastases with 1841 participants 5 studies on EUS for celiac lymph node metastases with 339 participants</td>
<td>Sensitivity (95% CI) = 0.80 (0.75–0.84) Specificity (95% CI) = 0.70 (0.65–0.75)</td>
<td>Sensitivity (95% CI) = 0.85 (0.72–0.99) Specificity (95% CI) = 0.96 (0.92–1.00)</td>
<td>Sensitivity (95% CI) = 0.67 (0.62–0.71) Specificity (95% CI) = 0.98 (0.97–0.99) PLR (95% CI) = 14.96 (11.17–20.03) NLR (95% CI) = 0.34 (0.30–0.39)</td>
<td>PLR = 14.56 (10.97–19.33) NLR = 0.34 (0.30–0.39)</td>
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<td>Ranges of specificity to correctly stage T3/T4 and not under stage cancers as T1/T2 66.7–100</td>
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<td></td>
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<td>8 on EUS for celiac lymph node metastases</td>
<td>Sensitivity = 0.76 (0.74-0.79)</td>
<td>Sensitivity = 0.76 (0.74-0.79)</td>
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<td></td>
<td></td>
<td></td>
<td>Specificity = 0.72 (0.69-0.75)</td>
<td>Specificity = 0.72 (0.69-0.75)</td>
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<td>Celiac lymph node metastases</td>
<td>Celiac lymph node metastases</td>
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<td></td>
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<td></td>
<td>Sensitivity = 0.81 (0.72-0.88)</td>
<td>Sensitivity = 0.81 (0.72-0.88)</td>
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<td></td>
<td></td>
<td></td>
<td>Specificity = 0.95 (0.92-0.98)</td>
<td>Specificity = 0.95 (0.92-0.98)</td>
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<tr>
<td>Study</td>
<td>Patients Details</td>
<td>T0 (Sensitivity)</td>
<td>T1a (Sensitivity)</td>
<td>T1b (Sensitivity)</td>
<td>T2 (Sensitivity)</td>
<td>T3 (Sensitivity)</td>
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<tr>
<td>Dhupar 2015</td>
<td>181 patients (median age 66 years) with GE junction oesophageal cancer</td>
<td>6% (1/18)</td>
<td>56% (23/41)</td>
<td>58% (41/71)</td>
<td>10% (2 / 21)</td>
<td>70% (21 / 30)</td>
</tr>
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<td></td>
<td>Overall accuracy T stage: 48/181(48%)</td>
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<tr>
<td>Lee 2014</td>
<td>15 patients (mean age=68.1 ± 7 y) newly diagnosed with oesophageal cancer</td>
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<td></td>
<td>Accuracy for distinguishing T1 lesions= 86.7%</td>
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<tr>
<td></td>
<td>Accuracy for distinguishing T2 lesions= 86.7%</td>
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<tr>
<td></td>
<td>Accuracy for distinguishing T3 lesions= 93.3%</td>
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<td></td>
<td>Overall accuracy: 86.7%</td>
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<td>Bergeron 2014</td>
<td>107 patients (mean age :66 years, range, 39-91 years with oesophageal high-grade dysplasia, carcinoma in situ, or T1 oesophageal cancer</td>
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<td></td>
<td>cT1a lamina propria tumour invasion</td>
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<td></td>
<td>Sensitivity: 41.6%</td>
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<tr>
<td></td>
<td>Specificity : 81.35%</td>
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<td></td>
<td>Invasion superficial to the submucosa (&lt;cT1b)</td>
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<tr>
<td></td>
<td>Sensitivity = 72%</td>
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<tr>
<td></td>
<td>Specificity= 48.7%</td>
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<tr>
<td></td>
<td>Sensitivity 0% none of the patients with EUS predicted to have lymph node involvement actually had pathologically positive lymph nodes. Specificity: 90% (likely due to the large number of patients (89/107) with pN0)</td>
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</tbody>
</table>
| Meister 2013 | 143 patients (mean age 63.8 ± 10.7) with oesophageal cancer | T1 | Sensitivity (95 % CI) = 0.68 (0.58–0.79)  
Specificity (95 % CI) = 0.97 (0.96–1)  
Accuracy (95 % CI)= 0.83 (0.77–0.89) | T2 | Sensitivity (95 % CI) = 0.39 (0.23–0.56)  
Specificity (95 % CI) = 0.84 (0.75–0.89)  
Accuracy (95 % CI)= 0.75 (0.65–0.79) | T3 | Sensitivity (95 % CI) = 0.72 (0.56–0.89)  
Specificity (95 % CI) = 0.81 (0.7–0.86)  
Accuracy (95 % CI)= 0.79 (0.70–0.84) | T4 | Sensitivity (95 % CI) = 0.13 (0–0.35) | | N1 | Sensitivity (95 % CI) = 0.76 (0.65–0.89)  
Specificity (95 % CI) = 0.71 (0.56–0.84)  
Accuracy (95 % CI)= 0.74 (0.65–0.83) | | | | | | | | 11% | 11% |
Specificity (95 % CI) = 0.97 (0.95–1.0)
Accuracy (95 % CI)= 0.93 (0.89–0.97)
Overall accuracy T stage: 60%

Considering only tumours of the GE junction (n = 38)

<table>
<thead>
<tr>
<th>T stage</th>
<th>Sensitivity (95 % CI)</th>
<th>Specificity (95 % CI)</th>
<th>Accuracy (95 % CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>0.7 (0.42–0.98)</td>
<td>0.1 (0–1)</td>
<td>0.92 (0.84–1)</td>
</tr>
<tr>
<td>T2</td>
<td>0.27 (0.04–0.49)</td>
<td>0.82 (0.67–0.98)</td>
<td>0.61 (0.45–0.76)</td>
</tr>
<tr>
<td>T3</td>
<td>0.83 (0.62–1)</td>
<td></td>
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</tr>
</tbody>
</table>
Specificity (95 % CI) = 0.58 (0.39–0.77)
Accuracy (95 % CI)= 0.66 (0.51–0.81)

T4
Sensitivity (95 % CI) = Not calculable due to only one case
Specificity (95 % CI) = 0.97 (0.92–1)
Accuracy (95 % CI)= 0.94 (0.88–1)

Q*: the value of TPR where TPR=(1−FPR) with 95% CI
This value was obtained from the intercept of the SROC curve and a line plotting sensitivity equals specificity. Due to the dichotomy chosen for cancer staging, T1 or T2 is analogous to a positive diagnosis in a conventional 2´2 table, and therefore T3 or T4 is analogous to a negative diagnosis. This implies that sensitivity is a measure of the ability of EUS to correctly stage T1/T2 and not over-stage cancers as T3/T4, and conversely specificity is a measure of the ability of EUS to correctly stage T3/T4 and not understage cancers as T1/T2. Neither understaging nor overstaging can be assumed to have more or less impact than the other: understaging cancer will result in surgical operations which are unnecessary and overstaging will result in palliative or non-surgical treatments when resection may have been possible. The most appropriate threshold is one which minimises both understaging and overstaging
**Impact on patients’ management**

<table>
<thead>
<tr>
<th>Study</th>
<th>N patients</th>
<th>Outcome</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah 2004</td>
<td>22 patients with known or suspected esophageal cancer</td>
<td>Change in management plan on the basis of EUS results</td>
<td>Management plan changes post-EUS: 12/22 (56%)</td>
<td>Based on EUS examination findings, clinicians requesting EUS alter patient management in one half of cases, and more often pursue a less-complicated approach. EUS substantially impacts clinical care.</td>
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<td>Toward more complex : 5/12 (42%)</td>
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<td>Toward less complex: 7/12 (58%)</td>
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<tr>
<td>Bulsiewicz</td>
<td>135 patients (median age 65 years) with Barrett's oesophagus (BE) and HGD</td>
<td>Frequency of patients excluded from endoscopic therapy based on EUS</td>
<td>Non nodular disease=0/79; none underwent EMR, all received EMR</td>
<td>EUS did not alter management in patients with non-nodular HGD or IMC. Because the diagnostic utility of EUS in subjects with non-nodular BE is low, the value of performing EUS in this setting is questionable. For patients with nodular neoplasia, resection of the nodule with histologic examination had greater utility than staging by EUS.</td>
</tr>
<tr>
<td>2014</td>
<td>(n=106, 79%) or IMC (n=29, 21%) had staging by EUS (79 non-nodular, 56</td>
<td>findings</td>
<td>Nodular disease:</td>
<td></td>
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<tr>
<td></td>
<td>nodular).</td>
<td></td>
<td>At EUS, 8 had endosonographic evidence of submucosal invasion (14%).</td>
<td>EUS improved the ability to provide loco-regional disease.</td>
</tr>
<tr>
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<td>EMR provided more useful information than did EUS. In six cases, if</td>
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<td>EMR had not been performed, EUS would have understaged the disease.</td>
<td>EUS and integrated PET/CT appear to independently affect treatment decisions, indicating complimentary and necessary roles in the staging of ECA.</td>
</tr>
<tr>
<td>Walker 2011</td>
<td>81 patients (mean age=63.5 (±11.6) years) with biopsy proven oesophageal</td>
<td>Change in management plan following EUS results</td>
<td>EUS re-directed patient care to neo-adjuvant therapy prior to surgical</td>
<td>EUS and integrated PET/CT appear to independently affect treatment decisions, indicating complimentary and necessary roles in the staging of ECA.</td>
</tr>
<tr>
<td></td>
<td>cancer diagnosed from May 2004 to December 2007</td>
<td></td>
<td>resection= 26/69 (37.7%)</td>
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<td>Among these 26 patients = 6 had nodal involvement or loco-regional</td>
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<td>disease on PET/CT. Thus EUS improved the ability to provide loco-</td>
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<td></td>
<td></td>
<td>regional disease</td>
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<tr>
<td>Study</td>
<td>Patients/Details</td>
<td>Change in Management Plan</td>
<td>EUS Findings</td>
<td>Impact/Conclusion</td>
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<td>----------------</td>
<td>---------------------------------------------------------------------------------</td>
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<td>----------------------------------------------------------------------------</td>
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<tr>
<td>Subasinghe 2010</td>
<td>30 patients (mean age= 58.2 years, range, 45–84 years) with histologically proven carcinoma of the oesophagus</td>
<td>Change in management plan previously stated on the basis of CT findings, after EUS results</td>
<td>EUS staging revealed a more advanced stage of cancer in the majority of patients. It appears to be far more superior in detecting lymph node involvement compared with CT. Therefore, EUS may have a significant impact on deciding the treatment modality of a patient with oesophageal carcinoma.</td>
<td></td>
</tr>
<tr>
<td>Gheorghe 2006</td>
<td>41 patients with oesophageal cancer</td>
<td>Preoperative EUS staging changed the decision for surgery in 18 of 41 patients (44%) (p&lt;0.0001)</td>
<td>esophageal EUS offers useful information to clinicians who treat patients with esophageal cancer, impacts clinical decision making, and should be used in appropriate settings to plan therapeutic strategy</td>
<td></td>
</tr>
<tr>
<td>Preston 2003</td>
<td>100 patients (median age 68, range 33–88)</td>
<td>EUS deemed useful by surgeons in making management</td>
<td>The addition of EUS data did not significantly affect the mean number</td>
<td></td>
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</tbody>
</table>
years), with carcinoma of the oesophagus or oesophagogastric junction

between surgeons with and without EUS results
Usefulness of EUS according to surgeons

decisions:
in 87.0% 65% and 63.0% of patients by the 3 surgeons
Number of concordant management plans,
without EUS :56%
with EUS=62%
of concordant results for management by radical surgery alone, non-surgical therapy with curative intent and neoadjuvant therapy plus surgery There was, however, an increase in the mean number of patients for whom non-surgical palliation was planned, from 18.5 to 24.

Pouw 2011
131 patients (mean age 66± 12.6 years) with early oesophageal or cardia neoplasia who were considered for endoscopic treatment

Number of patients excluded from diagnostic ER and directly referring the patient for surgery based on EUS results only. To investigate the relative contribution of EUS over the preceding endoscopic examination, cases were separated into 2 groups: abnormal EUS and normal endoscopy and abnormal EUS and abnormal endoscopy.

Patients referred for diagnostic ER:
Normal EUS: 105/131(80%)
Abnormal EUS. 26/ 131 (20%)
abnormal EUS and normal endoscopy= 14/26 (54%)
in 7 of these 14 patients (50%) no sub-mucosal invasion or other risk factors for lymph node metastasis were found on diagnostic ER
abnormal EUS and abnormal endoscopy :12/26 (46%)
the additional value of EUS during the workup including ER and follow-up was very limited. In none of the patients did EUS alone change the treatment policy. In addition, the results of this study strengthen the role of diagnostic ER as a final step in the workup for endoscopic treatment

Shumaker 2002
180 patients (mean age 66.5 ears) referred for preoperative staging of esophageal cancer by EUS

Proportions of EUS stage I and 4 tumours that would not be treated with combined modality therapy:
Stage I esophageal cancer are not offered neoadjuvant Chemoradiotherapy
Stage IV: unresectable

Stage I: 23/180 (14%)
Stage IV: 19/180 (12%)
Preoperative staging of esophageal cancer with EUS identifies a significant proportion of patients (26% in this series) with stage I and IV tumors who may be spared combined modality therapy
Quality of evidence

**Accurate staging**

*Study limitations (risk of bias):* no.

*Inconsistency of results:* yes

*Indirectness of evidence:* yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)

*Imprecision:* no,

*Publication bias:* not assessed

**Overall quality of evidence**

The overall quality of evidence was judges as low because of indirectness and inconsistency

**Impact on patients management**

*Study limitations (risk of bias):* no

*Inconsistency of results:* yes

*Indirectness of evidence:* yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS impact patients management)

*Imprecision:* no

*Publication bias:* not assessed

**Overall quality of evidence**

The overall quality of evidence was judges as low because of inconsistency and indirectness.

**Conclusions**

Overall accuracy for T stage ranged from 48% to 86.7%. Sensitivity and specificity of EUS in distinguishing T1,T2 vs T3,T4 and they ranged from 71-100 and 66.7-100 respectively. Sensitivity and specificity of EUS for N1 stage of regional lymph nodes ranged from 76% to 80% and 70% to 72% respectively. Sensitivity and specificity of EUS for N1 stage of celiac lymph nodes ranged from 67% to 85% and 95% to 98% respectively *(LOW QUALITY OF EVIDENCE).*

No conclusion can be drawn on the impact of EUS results on changes in patients managements, three studies concluding that EUS was not useful or did not have a significant impact and five concluding that EUS significant impacted on patients management *(LOW QUALITY OF EVIDENCE).*
References

Included studies


Excluded studies
17. Shami V.M.; Villaverde A.; Stearns L.; Chi K.D.; Kinney T.P.; Rogers G.B.; Dye C.E., and Waxman I. Clinical impact of conventional endosonography and endoscopic ultrasound-guided fine-needle aspiration in the assessment of patients with barrett's esophagus and high-grade dysplasia or intramucosal carcinoma who have been referred for endoscopic ablation therapy. Endoscopy. 2006; 38(2):157-161;
20. Thosani N.; Lunagariya A.; Guha S., and Bhutani M. Under staging and over staging rates of EUS between squamous cell carcinoma and adenocarcinoma while evaluating for submucosal invasion (T1B) of superficial esophageal cancers: A systematic review and meta-analysis. Am. J. Gastroenterol. 2011; 106S19-S20;
PRISMA 2009 Flow Diagram

Identification

Records identified through
- CDSR (n=0)
- DARE (n=0)
- CENTRAL (n=8)

Records identified through PubMed
(n=7 SR, 144 primary studies)

Records identified through Embase
(n=33 SR, 445 primary studies)

Screening

Records after duplicates removed
(n=33 SR, 467 primary studies)

Records screened
(n=502)

Records excluded
(n=464)

Eligibility

Studies awaiting classification
(n=0)

Full-text articles assessed for eligibility
(n=7 SRs, 31 primary studies)

Full-text articles excluded, with reasons
(n=21)

Included

Studies included
(n=5 SRs, 12 primary studies)
B VISUALIZATION OF DEFINED LANDMARKS IN EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.2 (B I(b)). Does the visualization of defined landmarks improve the quality of EUS in patients suffering from pancreatic cancer?

Population
Patients suffering from pancreatic cancer undergoing EUS

Intervention
Visualization of the entire pancreas, pancreatic mass (tumour, cancer), local lymph nodes (peri-pancreatic), celiac axis (lymph nodes) and left lobe of the liver and visible parts of the right lobe (to rule out metastatic disease), vascular infiltration: mesenteric artery, mesenteric vein, portal vein; infiltration of other peri-pancreatic organs.

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients’ management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

**Embase**
('endoscopic echography'/exp OR EUS:ab,ti) AND (cancer staging/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((pancreatic:ab,ti AND cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti )) OR 'pancreas tumor'/exp) AND (lymph node'/exp OR 'lymph node':ab,ti OR 'lymphnodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'mesenteric artery'/exp OR 'mesenteric vein'/exp OR (mesenteric:ab,ti AND (veins:ab,ti OR vein:ab,ti OR artery:ab,ti OR arteries:ab,ti)) OR 'vascular infiltration':ab,ti OR (infiltration:ab,ti AND ('peripancreatic organ':ab,ti OR 'peripancreatic organs':ab,ti))) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#9 pancreatic:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 lymph nodes:ti,ab,kw (Word variations have been searched)
#15 celiac axis:ti,ab,kw (Word variations have been searched)
#16 MeSH descriptor: [Mesenteric Arteries] explode all trees
#17 MeSH descriptor: [Mesenteric Veins] explode all trees
#18 mesenteric and (artery or vein):ti,ab,kw (Word variations have been searched)
#19 vascular infiltration:ti,ab,kw (Word variations have been searched)
#20 peripancreatic organ and infiltration:ti,ab,kw (Word variations have been searched)
Primary studies

PubMed

Embase
(‘endoscopic echography’/exp OR EUS:ab,ti) AND (‘cancer staging’/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((pancreatic:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'pancreas tumor'/exp) AND (‘lymph node’/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'mesenteric artery'/exp OR 'mesenteric vein'/exp OR (mesenteric:ab,ti AND (veins:ab,ti OR vein:ab,ti OR artery:ab,ti OR arteries:ab,ti)) OR 'vascular infiltration':ab,ti OR (infiltration:ab,ti AND ("peripancreatic organ":ab,ti OR "peripancreatic organs":ab,ti))) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
Results

Results of the bibliographic searches
After removing duplicates, 282 articles (9 reviews and 273 primary studies) were found. 2 systematic reviews and 6 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 1 further potentially relevant article was retrieved in the references of the retrieved studies. (See flow chart).

Excluded studies
Five studies were excluded: one because did not assess no outcome of interest (Vukobrat-Bijedic 2014), one because written in Chinese language (Tian 2008) and three because they were conference abstract (Iglesias-Garcia 2010, Nawaz 2010, Wong 2010).

Included studies
4 studies were finally included (Kala 2007, Li 2014, Shah 2004, Soriano 2004).
None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging or impact on patients’ management.

Accurate staging
We found one systematic review (Li 2014) assessing the diagnostic accuracy of EUS in TN staging and evaluation of vascular invasion in Pancreatic Cancer. The review included 20 studies including 726 patients.
For the T1–2 staging, the overall sensitivity, specificity, PLR, NLR, were 0.72 (95% CI, 0.65–0.79), 0.90 (95% CI, 0.87–0.93), 6.27 (95% CI, 3.23–12.14), 0.28 (95% CI, 0.12–0.64), respectively.
For the T3–4 staging, the overall sensitivity, specificity, PLR, NLR were 0.90 (95% CI, 0.87–0.93), 0.72 (95% CI, 0.65–0.79), 3.58 (95% CI, 1.57–8.19), 0.16 (95% CI, 0.08–0.31), respectively.
For N staging the overall sensitivity, specificity, PLR, NLR were 0.62 (0.56–0.68), 0.74 (0.68–0.80), 2.54 (1.73–3.75), 0.51(0.38–0.68), and 6.67 (3.29–13.51), respectively.
For vascular invasion the overall sensitivity, specificity, PLR, NLR were 0.87 (0.80–0.92), 0.92 (0.86–0.96), 7.16 (3.61–14.19), 0.20 (0.14–0.30), and 56.19 (24.46–129.08), respectively.
**Impact on patients’ management**

We found two primary studies (Kala 2007, Soriano 2004) that assessed the ability of EUS in predicting tumor resectability, that we considered as a proxy of impact on patient management. In Kala 2007, 41 patients with pancreatic cancer underwent EUS and laparotomy. In 53% of patients cancer was judged non-resectable at EUS and at laparotomy 51% were found actually non-resectables. In 34% of patients cancer was judged resectable at EUS and at laparotomy 32% were found actually resectables. In 17% of patients EUS did not allow even judge about resectability before surgery. In conclusion in 83% of patients resectability and non-resectability were well predicted by EUS.

In Soriano 2004, 52 patients received EUS followed by surgical procedure. EUS has a sensitivity, specificity and overall accuracy in predicting resectability of 23%, 100% and 67% respectively. Finally we found a study that assessed the impact of EUS results on management of known or suspected malignancies (Shah 2004). In this study the physicians requesting EUS were contacted before the EUS examination and were asked: “How would you manage this patient if EUS were not available?” After the examination the referring clinicians were recontacted within 1 week of the procedure, informed of the EUS findings, and asked: (1) “What management plan will you recommend to this patient given the EUS findings?” and if the management strategy differed compared with the pre-EUS response, (2) “Is the recommended change in the management plan directly the result of the EUS findings?” 43 patients were included for which EUS was requested to evaluate solid pancreatic masses (n 19), cystic lesions (n 6), and suspected pancreatic masses (n 8). Requesting physicians changed management strategies in 49% of patients after pancreatic EUS procedures. This most often involved a less-complex approach (71%), and included 32% of patients in whom surgery was no longer recommended.

**Quality of evidence**

**Accurate staging**

*Study limitations (risk of bias):* no.

*Inconsistency of results:* no

*Indirectness of evidence:* yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)

*Imprecision:* no

*Publication bias:* not assessed

**Overall quality of evidence**

The overall quality of evidence was judges as moderate because of indirectness for accurate staging.

**Impact on patients’ management**

*Study limitations (risk of bias):* no.

*Inconsistency of results:* no

*Indirectness of evidence:* yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the patients' management)

*Imprecision:* yes (only 3 studies with 133 patients)

*Publication bias:* not assessed

**Overall quality of evidence**

The overall quality of evidence was judges as low because of imprecision and indirectness.
Conclusions

No direct conclusions can be drawn about the impact of quality of EUS on accurate staging or impact on patient management.

For the T1–2 staging, the overall sensitivity and specificity were 0.72 and 0.90. For the T3–4 staging, the overall sensitivity and specificity were 0.90 and 0.72.

For N staging the overall sensitivity and specificity were 0.62 and 0.74

For vascular invasion the overall sensitivity and specificity were 0.87 and 0.92

(MODERATE QUALITY OF EVIDENCE)

Tumour resectability was correctly predicted by EUS in 67%-83% of patients

Treatment plan was altered in 49% of patients after pancreatic EUS results.

(LOW QUALITY OF EVIDENCE).

References

Included studies

Excluded studies

B VISUALIZATION OF DEFINED LANDMARKS IN EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.3 (B I(c)). Does the visualization of defined landmarks improve the quality of EUS in patients suffering from rectal cancer?

Population
Patients suffering from rectal cancer undergoing EUS

Intervention
Visualization of the tumor (location, extent, infiltration of surrounding structures). Visualization of surrounding structures: genitourinary structures, iliac vessels, sphincter apparatus, lymph nodes.

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients’ management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
"lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR extention[Title/Abstract] OR location[Title/Abstract] OR (sphincter[Title/Abstract] AND apparatus[Title/Abstract]) OR (iliac[Title/Abstract] AND (vessel [Title/Abstract] OR vessels[Title/Abstract])) OR (genitourinary[Title/Abstract] AND (structures[Title/Abstract] OR structure[Title/Abstract]))) AND ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract])

Embase

("endoscopic echography"/exp OR EUS:ab,ti) AND (cancer staging/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((rectal:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti )) OR 'rectum cancer'/exp) AND ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnodes':ab,ti OR extention:ab,ti OR location:ab,ti OR (sphincter:ab,ti AND apparatus:ab,ti) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti))) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)

#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Rectal Neoplasms] explode all trees
#9 rectal:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 lymph nodes:ti,ab,kw (Word variations have been searched)
#15 extention:ti,ab,kw (Word variations have been searched)
#16 location:ti,ab,kw (Word variations have been searched)
#17 sphincter and apparatus:ti,ab,kw (Word variations have been searched)
#18 iliac vessel:ti,ab,kw (Word variations have been searched)
#19 genitourinary structures:ti,ab,kw (Word variations have been searched)
#20 #13 or #15 or #14 or #16 or #17 or #18 or #19
#21 #6 and #7 and #12 and #20 Publication Year from 2000 to 2015
Primary studies

PubMed

Embase
(endoscopic echography/exp OR EUS:ab,ti) AND ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((rectal:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumours:ab,ti OR masses:ab,ti)) OR 'rectum cancer'/exp) AND (lymph node/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR extention:ab,ti OR location:ab,ti OR (sphincter:ab,ti AND apparatus:ab,ti)) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti))) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Rectal Neoplasms] explode all trees
#9 rectal:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
Results of the bibliographic searches

After removing duplicates, 229 articles (10 reviews and 219 primary studies) were found. 1 systematic reviews and 42 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 1 further potentially relevant article was found in the references of the retrieved studies. (See flow chart).

Excluded studies
25 studies were excluded: 1 because no comparison of interest: comparison of frontal probe with radial probe (Beer-Gabel 2009); 4 because written in Chinese language (Guo 2014, Ju 2006, Zhang 2009, Zhu 2013); 1 because written in Hungarian language (Bor 2013); 1 because written in Serbian language (Radovanovic 2008); 1 because written in Greek (Kalantzis 2004); 7 because conference abstracts (Azzam 2010, Cote 2010, Gleeson 2015, Kim 2014, Kim 2013, Silon 2014, Senturk 2013); 5 because patients not in the inclusion criteria (Fuchsjaeger 2003, Hunerbein Surg Endosc 2000, Hunerbein Ann Surg 2000, Kim 2006, Santoro 2007); 3 because a narrative reviews (Frascio 2001, Frascio 2001b, Pessaux, 2001); one because study design not in the inclusion criteria: accuracy measured in case control design including patients with known rectal cancer and patients with known other diseases (Joksimovic 2005); one (Bianchi 2006) because the 18% of the sample underwent preoperative chemoradiotherapy).

Included studies

Accurate staging
We didn’t find studies exactly matching the review question, i.e. whether the quality of EUS influenced the accurate staging.
We found one systematic review and 16 primary studies assessing the diagnostic accuracy of EUS. Because we found one systematic review assessing the accuracy of N staging updated up to January 2008, primary studies assessing diagnostic accuracy for N staging were considered only since 2008. For T staging all the studies published since 2000 were considered. All the studies used histopathology as reference standard.
N staging
The systematic review included 35 studies with 2732 participants with rectal cancer and reported the following values of diagnostic accuracy of EUS for nodal invasion of rectal cancer:
Sensitivity = 73.2% (95% CI 70.6–75.6), Specificity = 75.8% (95% CI 73.5–78.0), Positive likelihood ratio = 2.84 (95% CI 2.16–3.72) and Negative likelihood ratio = 0.42 (95% CI 0.33–0.52). Overall accuracy ranged from 63.2% to 84.3% in the six primary studies which reported this value. In the seven primary studies which reported the values, sensitivity and specificity of EUS ranged from 45.4% to 95.5% and from 71.1% to 95.5% respectively.

T staging
Overall accuracy reported in 10 primary studies ranged from 73.7% to 91.3%. In the five primary studies which reported the values, sensitivity and specificity of EUS ranged from 70.59% to 93.8% and from 80% to 99.2% respectively. Over-staging ranged from 2.75% to 17.6%. Downstage ranged from 2.5% to 20%.
<table>
<thead>
<tr>
<th>Study</th>
<th>N patients</th>
<th>T staging</th>
<th>N staging</th>
<th>Cases overstaged by EUS</th>
<th>Cases understaged by EUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puli 2009</td>
<td>35 studies with 2732 participants with rectal cancer</td>
<td></td>
<td><strong>Sensitivity</strong> = 73.2% (95% CI 70.6–75.6)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Specificity</strong> = 75.8% (95% CI 73.5–78.0)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Positive likelihood ratio</strong> = 2.84 (95% CI 2.16–3.72)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Negative likelihood ratio</strong> = 0.42 (95% CI 0.33–0.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ahuja 2015</td>
<td>86 patients with rectal cancer initially staged as T2N0 by EUS</td>
<td><strong>NPV</strong> for tumor depth amenable to primary resection = 83.7% (95% CI, 74.2–90.8).</td>
<td><strong>NPV</strong> = 87.2% (95% CI, 78.3–93.4).</td>
<td><strong>T</strong>: 16.3% (T2 instead of T1)</td>
<td><strong>T</strong>: 16.3% (T3 instead of T2) <strong>N</strong>: 12.8% <strong>TN</strong>: 23.3%</td>
</tr>
</tbody>
</table>
| Bali 2004           | 31 patients with biopsy-proven rectal cancer underwent evaluation of the invasion of the rectal wall, the mesorectal lymph nodes status and the pelvic organs using EUS | **T staged correctly**
T2 =50%
T3=84%
**Overall accuracy** = 79% | **T**: 10.3% | **T**: 10.3% |
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients Description</th>
<th>Rectal Wall Invasion</th>
<th>Overall Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can 2000</td>
<td>27 patients in whom rectal carcinoma was pathologically pre-diagnosed. Median age=56.3 years (range 32-84 years).</td>
<td>Rectal wall invasion Accuracy= 81% Specificity=80% Sensitivity=85.7%</td>
<td></td>
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</tr>
<tr>
<td>Halefoglu 2008</td>
<td>34 consecutive patients who had biopsy proven rectal carcinoma underwent both MRI and ERUS examinations before surgery. Mean age= 58.7 (range 29- 75 years).</td>
<td>Accuracy= 85.29% (24 / 34). Sensitivity = 70.59% Specificity = 90.20%. Discriminating between pT1-pT2 and pT3-pT4 tumors Accuracy = 76.47% Sensitivity=87.5% Specificity= 50%. PPV=80.77% NPV =62.50%</td>
<td>T =17.6%</td>
<td>T =11.7%</td>
<td></td>
</tr>
<tr>
<td>Genna 2000</td>
<td>42 patients with a preoperative histological diagnosis of adenocarcinoma localised in the rectal segment, extending up to 10cm from the dentate line, undergoing radical surgical</td>
<td>Overall accuracy =81% Sensitivity T1=67% T2=60% T3=92% T4=67% Specificity T1=100% T2=94% T3=67% T4=100%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Description</td>
<td>PPV</td>
<td>NPV</td>
<td>Accuracy</td>
<td>Sensitivity</td>
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<td>-----------------------------------------------------------------------------</td>
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<td>-------------</td>
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<tr>
<td>Ju 2009</td>
<td>78 patients with rectal Carcinoma, mean age of 61 years (range 32 - 78).</td>
<td>T1=100%</td>
<td>T1=98%</td>
<td>T1=100%</td>
<td>54.5%</td>
</tr>
<tr>
<td>Kalantzis 2002</td>
<td>80 patients with histologically proven colorectal cancer. Prior to surgery all patients underwent colonoscopy and biopsy, double-contrast barium enema, ultrasound and lower and upper abdomen computed tomography. Mean age=69.8±11 years</td>
<td>T1=100%</td>
<td>T1=100%</td>
<td>T1=100%</td>
<td>92.5%</td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Rectal Carcinoma</td>
<td>Specificity:</td>
<td>Sensitivity:</td>
<td>PPV, %</td>
</tr>
<tr>
<td>---------------</td>
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</tr>
<tr>
<td>Kocaman 2014</td>
<td>50</td>
<td>60±12 years</td>
<td>T2=73%</td>
<td>T2=100%</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T3=100%</td>
<td>T3=82%</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T4=100%</td>
<td>T4=100%</td>
<td></td>
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<tr>
<td>Kolev 2014</td>
<td>71</td>
<td></td>
<td>T1=97.1%</td>
<td>T1=92.8%</td>
<td>97.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T2=94.3%</td>
<td>T2=93.1%</td>
<td>94.3</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>T3=95.7%</td>
<td>T3=91.6%</td>
<td>95.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T4=98.5%</td>
<td>T4=100%</td>
<td>98.5</td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Description</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Accuracy</td>
</tr>
<tr>
<td>-------------</td>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
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<td>-------------</td>
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</tr>
<tr>
<td>Kuran 2014</td>
<td>38</td>
<td>38 patients diagnosed with rectal cancer, mean age = 57.6 ± 11.3 years</td>
<td>98.5%</td>
<td>98.2%</td>
<td>98.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stenotic lesions: 13, Non-stenotic lesions: 25</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><em>Accuracy</em> 73.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>By stenotic lesion: 68%, Non-stenotic lesion: 84.6%</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Assessment of internal sphincter involvement</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td><strong>Sensitivity</strong> = 100%</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Specificity</strong> = 100%</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Accuracy</strong> = 100%</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Assessment of external sphincter involvement</td>
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<tr>
<td></td>
<td></td>
<td><strong>Sensitivity</strong> = 100%</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Specificity</strong> = 96.3%</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Accuracy</strong> = 96.8%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mukae 2015</td>
<td>705</td>
<td>705 patients (714 lesions) with early CRC undergoing EUS to estimate depth of tumor invasion.</td>
<td>90%</td>
<td>81.0%</td>
<td>86.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sensitivity for pTis or pT1a (endoscopic resection indicated) = 90%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Patients Details</td>
<td>Specificity for pT1b (colectomy indicated)</td>
<td>Overall accuracy</td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>---------------------------------------------</td>
<td>------------------</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Palacios Fanlo 2000</td>
<td>120 patients with rectal cancer&lt;br&gt;Mean age=70 years (range 39-85 years)</td>
<td>87%</td>
<td>89%</td>
<td>100%</td>
<td>96.4%</td>
</tr>
<tr>
<td>Ravizza 2011</td>
<td>92 patients with rectal neoplasia (adenomas and primary adenocarcinomas located within 15 cm from the anal verge)&lt;br&gt;Median age= 64.5 years (range 40–85)</td>
<td>91.3%</td>
<td>83%</td>
<td>100%</td>
<td>95.9%</td>
</tr>
<tr>
<td>Shami 2004</td>
<td>60 consecutive patients diagnosed with rectal carcinoma referred for endoscopic ultrasound staging&lt;br&gt;Mean age=not reported</td>
<td>82%</td>
<td>95%</td>
<td>86%</td>
<td>95.9%</td>
</tr>
<tr>
<td>Surace 2014</td>
<td>77 reports ultrasound with the final diagnosis of rectal cancer&lt;br&gt;Mean age=not reported</td>
<td>95.8% [69.9-99.6]&lt;br&gt;pT is=90% [46.3-98.9]&lt;br&gt;pT1=77.8% [45.3-93.7]</td>
<td>90% [46.3-98.9]&lt;br&gt;pT is= 42.11% [23.06-63.95]</td>
<td>77.8% [45.3-93.7]</td>
<td>91.4%</td>
</tr>
</tbody>
</table>

T: 5.8%<br>T: 4.2%<br>6.5% (from T2 to T1 in 5 cases from T3 to pT0–1)
<table>
<thead>
<tr>
<th>pT</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>100%</td>
<td>96%</td>
<td>80%</td>
<td></td>
<td>96%</td>
</tr>
<tr>
<td>T2</td>
<td>73%</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td>70%</td>
</tr>
<tr>
<td>T3</td>
<td>99.3%</td>
<td>99.3%</td>
<td></td>
<td></td>
<td>99.3%</td>
</tr>
</tbody>
</table>

Presence of lymph nodes
Sensitivity=70%
Specificity=86%
PPV=80%
NPV=100%
Accuracy=83%

characteristics lymph nodes (malignant)
Sensitivity=100%
Specificity=22%
PPV=74%
NPV=100%
Accuracy=76%

Unsal 2012
31 consecutive patients with resectable rectal carcinoma
Mean age= 3.7 ± 11.5 years
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity=100%</th>
<th>Specificity=88%</th>
<th>PPV=66%</th>
<th>NPV=100%</th>
<th>Accuracy=84%</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>Sensitivity=100%</td>
<td>Specificity=96%</td>
<td>PPV=66%</td>
<td>NPV=100%</td>
<td>Accuracy=96%</td>
</tr>
<tr>
<td>Overall T:</td>
<td>Sensitivity: 93.4%</td>
<td>Specificity: 96.5%</td>
<td>Accuracy: 80.6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Impact on patients’ management

We didn’t find studies that directly assess the review question (i.e. whether the quality of US impact patient management). We found 3 primary studies (Kim 2014, Shah 2004, Shami 2004) assessing the impact of EUS results on patients’ management. One study (Kim 2014) assessed the utility of EUS for assessing the risk of invasion or metastasis of NETs less than 10mm in diameter and found that its necessity is questionable because rectal NETs smaller than 10 mm have a very low possibility of invasion to the proper muscle layer and a low risk of adjacent lymph node metastasis. The two other studies the impact of EUS results on changes of patients’ management and found that in 38%- to 50% of cases clinicians changed management plans.

<table>
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<tr>
<th>Study</th>
<th>N patients</th>
<th>Outcomes</th>
<th>Results</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td>Kim 2014</td>
<td>76 patients with rectal neuroendocrine tumors (NETs) less than 10 mm in diameter</td>
<td>Utility of EUS for assessing the risk of invasion or metastasis of NETs less than 10mm in diameter</td>
<td>7 lesions were located in the mucosa and 69 lesions were located in the submucosa. This finding was consistent with histologic results</td>
<td>Although EUS is a useful method for evaluating the depth of invasion, its necessity is questionable in cases of rectal NETs ≤10 mm in size. As shown in this study, rectal NETs smaller than 10 mm have a very low possibility of invasion to the proper muscle layer and a low risk of adjacent lymph node metastasis. The number of rectal NETs included in this study is too small to conclude that rectal NETs less than 10 mm in diameter have an extremely low possibility of invasion to the proper muscle or risk of metastasis and further studies including a larger number of rectal NETs less than 10 mm in size are needed to verify our findings.</td>
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<td>Shah 2004</td>
<td>10 patients with known or suspected rectal malignancies</td>
<td>Changes in management plan</td>
<td>Management plan changes post-EUS= 4/10 (40%) More complex= 2/4 (50%)</td>
<td>Based on EUS examination findings, clinicians requesting EUS alter patient management in one half of cases, and more</td>
</tr>
</tbody>
</table>
Surgery alone to neoadjuvant therapy and surgery = 2
Less complex = 2/4 (50%)
Surgery to chemotherapy = 1
Neoadjuvant therapy and surgery to surgery alone = 1

often pursue a less-complicated approach. EUS substantially impacts clinical care, and should be used in appropriate settings to guide patient management.

<table>
<thead>
<tr>
<th>Study</th>
<th>Changes in management plan</th>
<th>Impact on patients’ management</th>
<th>Preoperative staging with endoscopic ultrasound resulted in a change of management in 38 percent of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shami 2004</td>
<td>60 consecutive patients diagnosed with rectal carcinoma referred for endoscopic ultrasound staging</td>
<td>The additional staging information provided by EUS (more than CT alone) effected a change in management in 18 of 48 (38 percent) patients. All of these cases involved identification of lymph nodes by EUS not detected by CT, therefore, upstaging the cancer and identifying a group of patients who would undergo preoperative neoadjuvant therapy</td>
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</table>

**Quality of evidence**

**Accurate staging**
- **Study limitations (risk of bias):** no
- **Inconsistency of results:** yes
- **Indirectness of evidence:** yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)
- **Imprecision:** no
- **Publication bias:** not assessed

**Overall quality of evidence**
The overall quality of evidence was judged as low because of indirectness and inconsistency for accurate staging.
Impact on patient management

Study limitations (risk of bias): yes
Inconsistency of results: no
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the patients’ management)
Imprecision: yes (only 3 studies with a total of 146 participants)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of study limitation, imprecision and indirectness.

Conclusions

Accurate staging
No direct conclusions can be drawn about the impact of quality of EUS on accurate staging or impact on patient management.
For N staging the systematic review reported a pooled sensitivity of 73.2% (95% CI 70.6–75.6), and a pooled specificity = 75.8% (95% CI 73.5–78.0). Overall accuracy ranged from 63.2% to 84.3.% in the six primary studies which reported this value. In the seven primary studies which reported these values, sensitivity and specificity of EUS ranged from 45.4% to 95.5% and from 71.1% to 95.5% respectively.
For T staging the overall accuracy reported in 10 primary studies ranged from 73.7% to 91.3%. In the five primary studies which reported these values, sensitivity and specificity of EUS ranged from 70.59% to 93.8% and from 80% to 99.2% respectively. Overstage ranged from 2.75% to 17.6%. Downstage ranged from 2.5% to 20%
(LOW QUALITY EVIDENCE)

Impact on patient management
In 38%- to 50% of cases clinicians changed management plans on the basis of EUS results
(VERY LOW QUALITY EVIDENCE).
References

Included studies


Excluded studies
PRISMA 2009 Flow Diagram

**Records identified through**
- CDSR (n = 0)
- DARE (n = 1)
- CENTRAL (n = 1)

**Records identified through PubMed**
- (n = 4 SR, 105 primary studies)

**Records identified through Embase**
- (n = 8 SR, 175 primary studies)

**Records after duplicates removed**
- (n = 10 SR, 219 primary studies)

**Records screened**
- (n = 230)

**Records excluded**
- (n = 186)

**Studies awaiting classification**
- (n = 0)

**Full-text articles assessed for eligibility**
- (n = 44)

**Full-text articles excluded, with reasons**
- (n = 25)

**Studies included**
- (n = 19)
**B VISUALIZATION OF DEFINED LANDMARKS IN EUS**

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.4 (B I(d)). Does the visualization of defined landmarks improve the quality of EUS in patients with subepithelial gastric masses (synonym: submucosaltumor)?

**Population**
Patients with subepithelial gastric masses (synonym: submucosaltumor)

**Intervention**
Visualization of the mass (tumor) including the exact location within the gastric wall layer, differentiation of the wall layers, signs of infiltration, lymph nodes.

**Control**
Not to visualize the above mentioned landmarks

**Outcome**
Accurate Staging, impact on patients’ management
Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

**Systematic reviews and meta-analysis**

**PubMed**


**Embase**

('endoscopic echography'/exp OR EUS:ab,ti) AND ('cancer staging'/exp OR stag*::ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((gastric:ab,ti OR stomach:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'stomach cancer'/exp) AND ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'vascular infiltration':ab,ti OR location:ab,ti OR 'wall layer':ab,ti OR 'wall layers':ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'systematic review' OR 'systematic reviews' OR 'meta analysis' OR 'meta analysis' OR metanalysis OR cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Stomach Neoplasms] explode all trees
#9 gastric or stomach:ti,ab,kw (Word variations have been searched)
#10 Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11 #9 and #10
#12 #11 or #8
#13 MeSH descriptor: [Lymph Nodes] explode all trees
#14 lymph nodes:ti,ab,kw (Word variations have been searched)
#15 location:ti,ab,kw (Word variations have been searched)
#16 vascular infiltration:ti,ab,kw (Word variations have been searched)
#17 wall layer:ti,ab,kw (Word variations have been searched)
#18 #13 or #15 or #14 or #15 or #16
#19 #6 and #7 and #12 and #18Publication Year from 2000 to 2015

Primary studies

PubMed

Embase
('endoscopic echography'/exp OR EUS:ab,ti) AND ('cancer staging'/exp OR stag*.:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) AND ((gastric:ab,ti OR stomach:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti )) OR 'stomach cancer'/exp) AND ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'vascular infiltration':ab,ti OR location:ab,ti OR 'wall layer':ab,ti OR 'wall layers':ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 MeSH descriptor: [Patient Care Management] explode all trees
#5 staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Stomach Neoplasms] explode all trees
#9 gastric or stomach:ti,ab,kw (Word variations have been searched)
Results of the bibliographic searches
After removing duplicates, 309 articles (10 reviews and 299 primary studies) were found.
4 systematic reviews were considered potentially relevant and acquired in full text (See flow chart). In first instance systematic reviews were considered. All assessed only the accurate staging outcome and the most updated review included primary studies published up to January 2015. So we selected primary studies which assessed accurate staging only if published between January and August 2015 and primary studies which assessed the impact on patients management published within 2000 and August 2015. Seven primary studies were acquired in full text as potentially relevant. 1 further potentially relevant article was retrieved in the references of the retrieved studies.

Excluded studies
Three studies were excluded: one because it was conference abstract (Antonini 2013) and one because it did not assess our outcomes of interest (Vukobrat-Bijedic 2013), one because did not assess intervention of interest (Hassan 2010).

Included studies
4 reviews (Kelly 2001, Kwee 2009, Mocellin 2015, Mocellin 2011) and 5 primary studies (Ganpathi 2006, Kutup 2012, Shah 2004, Willis 2000, Yamamoto 2012) were finally included. The overlapping of primary studies included in the four systematic reviews was near total, i.e. all but two of the studies included in the other SRs were also included in Mocellin 2015, which was also of high methodological quality, the most updated and included the largest number of studies; we therefore extracted data only from Mocellin 2015.
Overlapping of primary studies between systematic reviews

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Accurate staging

Only one (Yamamoto 2012) of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging. The study included 75 patients suspected of having early gastric cancer who received EUS. EUS examination were evaluated for quality according to the following criteria: quality of the EUS images: according to: (1) repeatability of detection (presence [1] or absence [0]), (2) appropriate placement of the probe (ensuring the proper spacing between the probe and the lesion [1]) or impingement of the probe (probe was positioned too close to the lesion; [0]), and (3) clarity of the five layers of the gastric wall including the lesion (clear [1] or unclear [0]). The scores were summed (total ranged from 0 to 3) to calculate the quality of the EUS image of each lesion. The study found that the quality of the EUS influence the accuracy of diagnosis (N (%) of correct diagnosis by EUS image quality

Low (score 0,1) quality EUS allowed only 35.7% of correct diagnosis, whereas High (score 2, 3 allowed 93.4% of correct diagnosis

We found one systematic review (Mocellin 2015) assessing the diagnostic accuracy of EUS in TN staging of gastric carcinoma. The review included 66 studies including 7747 patients. For T1 - T2 versus T3 - T4 staging, the overall sensitivity and specificity were 0.86(95% CI: 0.81-0.90) and 0.90 (95% CI: 0.87 to 0.93), respectively. 

For N staging the overall sensitivity and specificity were: 0.83 (95% CI: 0.79 to 0.87) and 0.67 (95% CI: 0.61 to 0.72), respectively.
Impact on patient management
We didn’t find studies that directly assess the review question. We found four primary studies assessing the impact of EUS results on patients’ management. We found three primary studies (Ganpathi 2006, Kutup 2012, Willis 2000) that assessed the ability of EUS in predicting tumor resectability, that we considered as a proxy of impact on patient’s management.
In Ganpathi 2006, 109 patients with gastric cancer underwent EUS and surgical exploration. 89% of the patients actually underwent the proposed treatment on the basis of EUS. 7% were down staged by EUS, i.e. proposed for gastrectomy and found inoperable (n:3), received palliative gastrectomy (n:3) received bypass (n:2). 3.7% were over staged by EUS: deemed as inoperable received radical gastrectomy (n:1) and extended resection (n:1); proposed for bypass and received extended resection (1).
In Willis 2000 116 patients received EUS followed by surgical procedure. EUS has a sensitivity in correctly predicting curative surgery by standardized gastrectomy with radical lymphadenectomy of 94% and a specificity in correctly excluding this therapy of 83%. Overall accuracy was of 91.4%.
In Kutup 2012, 123 patients received EUS in order to assess whether they should receive surgery (if T1/2N0) or neoadjuvant or perioperative chemotherapy (if T3/4, or any N+).
Cases correctly classified by EUS were 51.3% of cases with histopathological T1/2N0 and 91.8% of cases with histopathological T3/4, or any N+. Overall EUS correctly predicted further management in 79.7% of patients.
A fourth study assessed the impact of EUS results on management of known or suspected malignancies (Shah 2004). In these studies the physicians requesting EUS were contacted before the EUS examination and were asked: “How would you manage this patient if EUS were not available?” After the examination the referring clinicians were recontacted within 1 week of the procedure, informed of the EUS findings, and asked: (1) “What management plan will you recommend to this patient given the EUS findings?” and if the management strategy differed compared with the pre-EUS response, (2) “Is the recommended change in the management plan directly the result of the EUS findings?” 15 patients were included for which EUS was requested to evaluate known or suspected cancers (n=5) and submucosal masses (n=10).
Requesting physicians altered patient management in 60% of patients after gastric EUS. A less-complex management strategy was involved in the majority (78%), and included 2 of 5 patients in whom surgery was no longer considered.

Quality of evidence

Accurate staging
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes only one study with 75 patients
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision
Impact on patient management

Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: yes
Imprecision: yes  only three studies with 240 patients
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision  and indirectness.

Conclusions

High-quality EUS images increased the diagnostic accuracy of EGC invasion depth. Lower-quality EUS images may lead to an inaccurate diagnosis (LOW QUALITY OF EVIDENCE)

No direct conclusions can be drawn about the impact of quality of EUS on impact on patient management. Tumor resectability /unresectability was correctly predicted by EUS in 79.7% - 91% of patients Treatment plan was altered in 60% of patients after pancreatic EUS results (LOW QUALITY OF EVIDENCE).
References

Included studies
5. Mocellin S. and Pasquali S. Diagnostic accuracy of endoscopic ultrasonography (EUS) for the preoperative locoregional staging of primary gastric cancer. Cochrane Database Syst Rev. 2015; 2CD009944;

Excluded studies
1. Antonini F.; Siquini W.; Piergallini S.; Belfiori V.; Marraccini B.; Lo Cascio M.; Manfredi C., and Macarri G. Diagnostic value of eus in the selection of patients with gastric cancer eligible for a neoadjuvant chemotherapy. Dig. Liver Dis. 2013; 45S198
ADMINISTRATION OF ANTIBIOTICS IN PATIENTS UNDERGOING ERCP

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

3.1 (C I(a)). Administration of antibiotics in patients undergoing ERCP

Population
Patients undergoing ERCP suffering from either
- cholangitis
- primary sclerosing cholangitis
- biliary obstruction without cholangitis, successful placement of drainage/stent
- biliary obstruction without cholangitis, unsuccessful placement of drainage/stent
- pancreatic cyst / pseudocyst communicating with pancreatic duct

Intervention
Administration of antibiotics

Control
No administration of antibiotics

Outcome
Preventing an inflammation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and randomized controlled trials using the following search strategies:
**Systematic reviews and meta-analysis**

**PubMed**

("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) AND 
("Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR 
CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR 
pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR 
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) AND 
("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR 
cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] 
OR metanalysis[Title/Abstract])

**Embase**

('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND 
(('common bile duct'/exp OR 
CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR 
occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti 
OR 'cholangitis'/exp) AND ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) 
AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 
'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane 
review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of 
Effects (DARE)**

#1 MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2 antibiotic:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Common Bile Duct] explode all trees  4
#5 CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8 stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 #6 and #9
#11 MeSH descriptor: [Cholangitis] explode all trees
#12 Cholangitis:ti,ab,kw (Word variations have been searched)
#13 #10 or #11 or #12
#14 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15 ERCP:ti,ab,kw (Word variations have been searched)
#16 #14 or #15
#17 #16 and #13 and #3 Publication Year from 2000 to 2015
Randomized controlled trials

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) AND 
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) AND 
(Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT
("animals"[MeSH Terms] NOT "humans"[MeSH Terms])

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND
(('common bile duct'/exp OR CBD:ab,ti OR bile duct:ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti) OR Cholangitis:ab,ti OR 'cholangitis'/exp) OR Cholangiopancreatography, Endoscopic Retrograde/exp OR ERCP:ab,ti) AND
('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2 antibiotic:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Common Bile Duct] explode all trees
#5 CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8 stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 #6 and #9
#11 MeSH descriptor: [Cholangitis] explode all trees
#12 Cholangitis:ti,ab,kw (Word variations have been searched)
#13 #10 or #11 or #12
#14 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15 ERCP:ti,ab,kw (Word variations have been searched)
#16 #14 or #15
#17 #16 and #13 and #3 Publication Year from 2000 to 2015
Results
Results of the bibliographic searches

After removing duplicates, 177 articles (26 reviews and 151 primary studies) were found. Three potentially relevant systematic reviews were found and acquired in full text. All of these were pertinent and so we screened only RCTs published after March 2010 (data of search update of the latest systematic reviews included available in full text). One potentially relevant primary study was acquired in full text for more evaluation (Minami 2014) (See flow chart).

Excluded studies

The primary study published after March 2010 was excluded because it was not an RCT and did not assess the outcome of interest (Minami 2014)

Included studies

Three studies were finally included: all were systematic reviews (Bai 2009, Brand 2010); for one only conference abstract was available (Romana 2015).

Overlapping of primary studies included in the systematic reviews.

<table>
<thead>
<tr>
<th>Studies included</th>
<th>SR</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Brand 2010</td>
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<tr>
<td>Brandes 1981</td>
<td>X</td>
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<tr>
<td>Byl 1995</td>
<td>X</td>
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<tr>
<td>Finkelstein 1996</td>
<td>X</td>
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<tr>
<td>Llach 2006</td>
<td>X</td>
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<tr>
<td>Lorenz 1996</td>
<td>X</td>
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<tr>
<td>Niederau 1994</td>
<td>X</td>
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<tr>
<td>Räty 2001</td>
<td>X</td>
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<tr>
<td>Sauter 1990</td>
<td>X</td>
</tr>
<tr>
<td>Spicak 2001</td>
<td>X</td>
</tr>
<tr>
<td>Van Den Hazel 1996</td>
<td>X</td>
</tr>
<tr>
<td>Study</td>
<td>N studies included</td>
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<tr>
<td>---------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Romana 2015</td>
<td>10 RCTs</td>
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<td></td>
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<tr>
<td>Brand 2010</td>
<td>9 RCTS</td>
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<tr>
<td>Bai 2009</td>
<td>7 RCTs</td>
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</tr>
</tbody>
</table>
at patients with suspicious biliary obstruction:

Antibiotics=2.8% (12/425)
Control= 5.4%(24/441)
RR=0.33; 95% CI:0.03-3.32

Quality of evidence

Study limitations (risk of bias): no (for Romana 2015 methodological quality could not be fully assessed because only a conference abstract was available)
Inconsistency of results: yes for cholangitis
Indirectness of evidence: no (all but one study did not specify whether all patients were with native papilla
Imprecision: no (included more than 1700 ERCP)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as high for pancreatitis, moderate for cholangitis because of inconsistency

Conclusions

Prophylactic antibiotics seem to reduce cholangitis (MODERATE QUALITY OF EVIDENCE), septicemia, and pancreatitis. in patients undergoing elective ERCP (HIGH QUALITY OF EVIDENCE).
References

Included studies

Excluded studies
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n=2)
- DARE (n=1)
- CENTRAL (n=15)
- Records identified through PubMed (n=3 SR, 55 RCTs)
- Records identified through Embase (n=25 SR, 110 RCTs)

Records after duplicates removed (n=26 SR, 151 RCTs)

Screening
- Records screened (n=177)
- Records excluded (n=173)

Eligibility
- Studies awaiting classification (n=0)
- Full-text articles assessed for eligibility (n=4)
- Full-text articles excluded, with reasons (n=1)

Included
- Studies included (n=3)
ADMINISTRATION OF ANTIBIOTICS IN PATIENTS UNDERGOING EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

3.2 (C I(b)). Administration of antibiotics in patients undergoing EUS

Population
Patients undergoing EUS including EUS-FNA suffering from either
- EUS-FNA of solid masses in the upper GI-tract
- EUS-FNA of solid masses in the lower GI-tract
- EUS-FNA of cystic lesions

Intervention
Administration of antibiotics

Control
No administration of antibiotics

Outcome
Preventing an inflammation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and randomized controlled trials using the following search strategies:
**Systematic reviews and meta-analysis**

**PubMed**


**Embase**

('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti)) OR (EUS:ab,ti AND FNA:ab,ti)) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2 antibiotic:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Endosonography] explode all trees
#5 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#6 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#7 EUS and FNA:ti,ab,kw (Word variations have been searched)
#8 #4 or #5 or #6 or #7
#9 #3 and #8 Publication Year from 2000 to 2015

**Randomized controlled trials**

**PubMed**


**Embase**

('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND ("endoscopic echography'/exp OR endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti)) OR (EUS:ab,ti AND FNA:ab,ti)) AND (randomized controlled trial/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))
Results of the bibliographic searches

After removing duplicates, 421 articles (45 reviews and 376 primary studies) were found. No potentially relevant systematic reviews were found; 6 RCTs studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

All the studies were excluded: three studies because the comparison was not in the inclusion criteria: two regimens of antibiotics were compared (Kehinde 2013, Kwok 2015, Luong 2015); two because they were not RCT (Guarner-Argente 2011, Rivera 2010).

Awaiting assessment

One study was awaiting assessment because it written in Chinese (Yang 2001).

Included studies

No studies fulfilled our inclusion criteria

Conclusion

No conclusion can be drawn because no studies fulfilling our inclusion criteria were found.
References

Excluded studies

Awaiting assessment
PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n=0)
- DARE (n=0)
- CENTRAL (n=8)

Records identified through PubMed (n=1 SR, 204 RCTs)

Records identified through Embase (n=44 SR, 176 RCTs)

Records after duplicates removed (n=45 SR, 376 RCTs)

Screening
- Records screened (n=421)

Eligibility
- Studies awaiting classification (n=1)
- Full-text articles assessed for eligibility (n=6)
  - Full-text articles excluded, with reasons (n=5)

Included
- Studies included (n=0)
ANTIBIOTICS TO CONTRAST MEDIA FOR PREVENTION OF CHOLANGITIS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte  
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte  
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

3.3 (C I(c)). Adding antibiotics to contrast media for prevention of cholangitis

**Population**
Patients undergoing ERCP suffering from either
- cholangitis
- primary sclerosing cholangitis
- biliary obstruction without cholangitis, successful placement of drainage/stent
- biliary obstruction without cholangitis, unsuccessful placement of drainage/stent
- pancreatic cyst / pseudocyst communicating with pancreatic duct
- Independent of the indication for ERCP

**Intervention**
Adding antibiotics to contrast media

**Control**
No administration of antibiotics to contrast media

**Outcome**
Preventing an inflammation

**Bibliographic searches**

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:
Systematic reviews and meta-analysis

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) AND
("Contrast Media"[Mesh] OR "contrast medium"[Title/Abstract] OR "contrast medium"[Title/Abstract]) AND

Embase
("antibiotic agent"/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND ("contrast medium"/exp OR 'contrast media':ab,ti OR 'contrast medium':ab,ti) AND (("common bile duct"/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti OR 'cholangitis'/exp) AND ("endoscopic retrograde cholangiopancreatography"/exp OR ERCP:ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2 antibiotic:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Common Bile Duct] explode all trees
#5 CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8 stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 #6 and #9
#11 MeSH descriptor: [Cholangitis] explode all trees
#12 Cholangitis:ti,ab,kw (Word variations have been searched)
#13 #10 or #11 or #12
#14 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15 ERCP:ti,ab,kw (Word variations have been searched)
#16 #14 or #15
#17 MeSH descriptor: [Contrast Media] explode all trees
#18 contrast media:ti,ab,kw (Word variations have been searched)
#19 #113 or #114
#20 #16 and #13 and #3 and #19 Publication Year from 2000 to 2015
Primary studies

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) AND
("Contrast Media"[Mesh] OR "contrast media"[Title/Abstract] OR "contrast medium"[Title/Abstract]) AND
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) AND ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) AND ('contrast medium'/exp OR 'contrast media':ab,ti OR 'contrast medium':ab,ti) AND ("common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti) OR Cholangitis:ab,ti OR 'cholangitis'/exp) AND ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) AND ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2 antibiotic:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Common Bile Duct] explode all trees
#5 CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8 stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 #6 and #9
#11 MeSH descriptor: [Cholangitis] explode all trees
#12 Cholangitis:ti,ab,kw (Word variations have been searched)
#13 #10 or #11 or #12
#14 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15 ERCP:ti,ab,kw (Word variations have been searched)
#16 #14 or #15
#17 MeSH descriptor: [Contrast Media] explode all trees
#18 contrast media:ti,ab,kw (Word variations have been searched)
#19 #113 or #114
#20 #16 and #13 and #3 and #19 Publication Year from 2000 to 2015
Results

Results of the bibliographic searches
After removing duplicates, 33 articles (1 review and 32 primary studies) were found. No potentially relevant systematic reviews were found; 1 randomized controlled trials was considered potentially relevant and acquired in full text; moreover 4 primary studies were suggested by authors. (See flow chart)

Excluded studies
Two studies were excluded because they were laboratory studies without the outcome of interest (Jendrzejewski 1980, Ramirez 2010).

Included studies
Three studies were finally included (Collen 1980, Norouzi 2013, Pugliese 1986). All assessed the effectiveness of adding gentamicin to contrast media
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention</th>
<th>Control</th>
<th>Post-ERCP complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collen 1980</td>
<td>61 Patients undergoing ERCP for standard diagnostic indications</td>
<td>80 mg of gentamicin added to each 60 cc of contrast media (n=29)</td>
<td>placebo (n=32)</td>
<td>post-ERCP septic complication</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Placebo group: 1/32 (3%) one patient developed a febrile episode with subsequent blood cultures growing Escherichia coli. Gentamicin group: 1/29 (3%) one patient developed a febrile episode with subsequent blood cultures growing Escherichia coli.</td>
</tr>
<tr>
<td>Norouzi 2013</td>
<td>114 patients with non-calculous obstructive jaundice who underwent endoscopic biliary stenting</td>
<td>10 mg (2 mL) gentamicin (n=57) 2 g ceftriaxone intravenously 30 min before ERCP and daily for 3 days.</td>
<td>distilled water (n=57) 2 g ceftriaxone intravenously 30 min before ERCP and daily for 3 days.</td>
<td>post-ERCP cholangitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intervention group: 5/57 Placebo group: 5/57</td>
</tr>
<tr>
<td>Pugliese 1986</td>
<td>330 consecutive patients undergoing ERCP (with absence of fever, normal white blood cell count and no rises in serum and urine amylase levels)</td>
<td>Gentamicin 1,6mg/ml (n=168)</td>
<td>without gentamicin (n=162)</td>
<td>Increase of white blood cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>gentamicin: 13/168 (7.74%) no gentamicin: 5/162 (3.09%) RR: 2.51 [95%CI 0.91, 6.87] with a trend in favor of no gentamicin</td>
</tr>
<tr>
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<td>Fever +/- white blood cells</td>
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<td></td>
<td></td>
<td>gentamicin: 16/168 (9.52%) no gentamicin: 6/162 (3.70%) RR: 2.57 [95%CI 1.03, 6.41] in favor of no gentamicin</td>
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<tr>
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<td></td>
<td>Acute Pancreatitis</td>
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<td>gentamicin: 1/168 (0.59%) no gentamicin: 0/162 (0%) Acute cholangitis</td>
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<tr>
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<td></td>
<td></td>
<td>gentamicin: 0/168 (0%) no gentamicin: 0/162 (0%) Acute cholangitis</td>
</tr>
</tbody>
</table>
Quality of evidence

Study limitations (risk of bias): no (RCTs; two studies at unclear risk of bias for all items but attrition bias, for which they were at low risk).
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no (three studies with 505 patients overall)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as high

Conclusions

The incidence of post-ERCP complications is not modified by the addition of gentamicin to the contrast media.

References

Included studies

Excluded studies
PRISMA 2009 Flow Diagram

**Identification**
- Records identified through CDSR (n=0)
- DARE (n=0)
- CENTRAL (n=1)

**Screening**
- Records identified through PubMed (n=0 SR, 1 RCTs)
- Records identified through Embase (n=1 SR, 6 RCTs)
- Records suggested by authors (n=4)

**Records after duplicates removed**
(n=1 SR, 10 primary)

**Eligibility**
- Records screened (n=11)
- Records excluded (n=31)
- Studies awaiting classification (n=0)
- Full-text articles assessed for eligibility (n=5)
- Full-text articles excluded, with reasons (n=2)

**Included**
- Studies included (n=3)
EUS-FNA IN PATIENTS WITH SUSPECTED PANCREATIC CANCER

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

4 (D). Risks of performing EUS-FNA in patients with suspected pancreatic cancer
4.1 (D I). Due to the potential risk of seeding metastases EUS-FNA is often not performed in patients with unclear pancreatic masses

Population
Patients with unclear pancreatic mass / suspected pancreatic cancer undergoing EUS-FNA

Intervention
Performing EUS-FNA to clarify the diagnosis

Control
No EUS-FNA

Outcome
Tumor spread, seeding metastases

Suggested statement. The risks of performing EUS-FNA in patients with undiagnosed pancreatic masses include tumour spread and seeding of metastases.

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

(((Suspect*[Title/Abstract] OR unclear*[Title/Abstract]) AND (mass*[Title/Abstract] OR masses*[Title/Abstract] OR malign*[Title/Abstract] OR cancer*[Title/Abstract] OR tumor*[Title/Abstract] OR tumour*[Title/Abstract]) AND (pancrea*[Title/Abstract])) OR
("Pancreatic Neoplasms"[Mesh] AND (Suspect*[Title/Abstract] OR unclear[Title/Abstract]))
AND ("systematic reviews"[Title/Abstract] OR "systematic review"[Title/Abstract] OR "meta analysis"[Publication Type] OR "meta analysis"[Title/Abstract] OR "meta analysis"[Publication Type] OR "systematic review" OR "systematic review")
AND "systematic reviews" OR "systematic review" OR "meta analysis" OR "meta analysis"

Embase
(((suspect*:ab,ti OR unclear:ab,ti) AND (mass:ab,ti OR masses:ab,ti OR malign:ab,ti OR cancer:ab,ti OR tumor:ab,ti OR tumour:ab,ti) AND pancreas*:ab,ti) OR (pancreas cancer'/exp AND (suspect*:ab,ti OR unclear:ab,ti))) AND ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti))
AND ('tumor volume'/exp OR 'lymph node metastasis'/exp OR 'metastasis'/exp OR infiltration:ab,ti OR metastasis:ab,ti OR metastases:ab,ti OR 'cancer spread':ab,ti OR 'tumor spread':ab,ti) AND (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1 MeSH descriptor: [Endosonography] explode all trees
#2 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4 EUS and FNA:ti,ab,kw (Word variations have been searched)
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Tumor Burden] explode all trees
#7 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#8 MeSH descriptor: [Neoplasm Metastasis] explode all trees
#9 infiltration or metastasis or tumor spread or cancer spread:ti,ab,kw (Word variations have been searched)
#10 #6 or #7 or #8 or #9
#11 suspected or unclear:ti,ab,kw (Word variations have been searched)
#12 mass or malign* or cancer or tumor:ti,ab,kw (Word variations have been searched)
#13 pancreas or pancreatic:ti,ab,kw (Word variations have been searched)
#14 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#15 #12 and #13 and #11
#16 #11 and #14
#17 #16 or #15
#18 #17 and #10 and #5 Publication Year from 2000 to 2015

Primary studies

PubMed
(((Suspect*[Title/Abstract] OR unclear[Title/Abstract]) AND (mass[Title/Abstract] OR masses[Title/Abstract] OR malign*[Title/Abstract] OR cancer[Title/Abstract] OR...

**Embase**
(((suspect*:ab,ti OR unclear:ab,ti) AND (mass:ab,ti OR masses:ab,ti OR malign:ab,ti OR cancer:ab,ti OR tumor:ab,ti OR tumour:ab,ti) AND pancreas*:ab,ti) OR (pancreas cancer/exp AND (suspect*:ab,ti OR unclear:ab,ti))) AND (endoscopic echography/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR (endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) AND (tumor volume/exp OR 'lymph node metastasis'/exp OR 'metastasis'/exp OR infiltration:ab,ti OR metastasis:ab,ti OR metastases:ab,ti OR 'cancer spread':ab,ti OR 'tumor spread':ab,ti OR 'tumour spread':ab,ti) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

**Cochrane Central Register of Controlled Trials (CENTRAL)**
#1 MeSH descriptor: [Endosonography] explode all trees
#2 MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3 endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4 EUS and FNA:ti,ab,kw (Word variations have been searched)
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Tumor Burden] explode all trees
#7 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#8 MeSH descriptor: [Neoplasm Metastasis] explode all trees
#9 infiltration or metastasis or tumor spread or cancer spread:ti,ab,kw (Word variations have been searched)
#10 #6 or #7 or #8 or #9
#11 suspected or unclear:ti,ab,kw (Word variations have been searched)
#12 mass or malign* or cancer or tumor:ti,ab,kw (Word variations have been searched)
#13 pancreas or pancreatic:ti,ab,kw (Word variations have been searched)
#14 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#15 #12 and #13 and #11
#16 #11 and #14
#17 #16 or #15
#18 #17 and #10 and #5 Publication Year from 2000 to 2015
Results

Results of the bibliographic searches
After removing duplicates, 154 articles (3 reviews and 151 primary studies) were found. No relevant studies were found addressing this question.

Conclusions

No conclusion can be drawn about tumor spread and seeding metastases performing EUS-FNA in patients with unclear pancreatic masses because no evidence was found.
Clinical question 4

Population
patients undergoing EUS for staging of GI-cancer, (e.g. - esophageal cancer, - pancreatic cancer, - biliary cancer, - rectal cancer )

Intervention
endoscopic ultrasound

Control
None

Outcome
successful staging (TNM)

Clinical question 5

Population
Patients with pancreatic cancer undergoing EUS

Intervention
Documentation of pancreatic masses along with vascular involvement, lymphadenopathy and distant metastases

Control
none

Outcome
documentation rate
Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/9/2016 separately for systematic reviews and primary studies using the following search strategies:

**Systematic reviews and meta-analysis**

**PubMed**


**Embase**

('endoscopic echography'/exp OR EUS:ab,ti) AND ('cancer staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) AND ("common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR oesophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumours:ab,ti OR cancers:ab,ti OR carcinoma*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'oesophagus cancer/exp OR 'digestive system cancer'/exp) AND (cochrane OR 'systematic review'/de OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

**Cochrane Database of Systematic Reviews (CDSR)** and **Database of Abstracts of Reviews of Effects (DARE)**

#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 stage or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#5 MeSH descriptor: [Lymph Nodes] explode all trees
#6 lymphnode:ti,ab,kw (Word variations have been searched)
#7 #5 or #6
metastasis:ti,ab,kw (Word variations have been searched)
MeSH descriptor: [Lymphatic Metastasis] explode all trees
#7 and #8
#3 or #4 or #9 or #10
#1 or #2
cancer or malign or mass or neoplasm or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
rectal:ti,ab,kw (Word variations have been searched)
gastric:ti,ab,kw (Word variations have been searched)
pancreatic:ti,ab,kw (Word variations have been searched)
biliary or CBD or bile duct:ti,ab,kw (Word variations have been searched)
MeSH descriptor: [Common Bile Duct] explode all trees
esophageal:ti,ab,kw (Word variations have been searched)
#14 or #15 or #16 or #17 or #18 or #19
#20 and #13
MeSH descriptor: [Rectal Neoplasms] explode all trees
MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
MeSH descriptor: [Pancreatic Neoplasms] explode all trees
MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#27 or #22 or #23 or #24 or #25 or #26
#21 or #20 and #13
#18 #11 and #12 and #27 Publication Year from 2000 to 2016

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS>Title/Abstract)) AND ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR infiltration>Title/Abstract) OR TNM>Title/Abstract) OR ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (metastasis>Title/Abstract) OR metastases>Title/Abstract)) OR "Lymphatic Metastasis"[Mesh]) AND ("Common Bile Duct"[Mesh] OR CBD>Title/Abstract) OR "Bile Duct"[Title/Abstract] OR biliary>Title/Abstract) OR pancreatic>Title/Abstract) OR rectal>Title/Abstract) OR gastric>Title/Abstract) OR esophageal>Title/Abstract) OR oesophageal>Title/Abstract) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract]) OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract]) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh]) NOT ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract]) OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) NOT Case Reports[ptyp]

Embase
(endoscopic echography/exp OR EUS:ab,ti) AND (cancer staging/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR ("lymph node/exp OR "lymph node":ab,ti OR "lymph nodes":ab,ti OR "lymphnode":ab,ti OR "lymphnodes":ab,ti)) AND (metastasis:ab,ti OR metastases:ab,ti) OR "lymph node metastasis/exp) AND ("common bile duct/exp OR CBD:ab,ti OR "bile duct":ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR
esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) NOT (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

**Cochrane Central Register of Controlled Trials (CENTRAL)**

#1 MeSH descriptor: [Endosonography] explode all trees
#2 EUS:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Neoplasm Staging] explode all trees
#4 stage or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#5 MeSH descriptor: [Lymph Nodes] explode all trees
#6 lymphnode:ti,ab,kw (Word variations have been searched)
#7 #5 or #6
#8 metastasis:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#10 #7 and #8
#11 #3 or #4 or #9 or #10
#12 #1 or #2
#13 cancer or malign or mass or neoplasm or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#14 rectal:ti,ab,kw (Word variations have been searched)
#15 gastric:ti,ab,kw (Word variations have been searched)
#16 pancreatic:ti,ab,kw (Word variations have been searched)
#17 biliary or CBD or bile duct:ti,ab,kw (Word variations have been searched)
#18 MeSH descriptor: [Common Bile Duct] explode all trees
#19 esophageal:ti,ab,kw (Word variations have been searched)
#20 #14 or #15 or #16 or #17 or #18 or #19
#21 #20 and #13
#22 MeSH descriptor: [Rectal Neoplasms] explode all trees
#23 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#25 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#26 MeSH descriptor: [Esophageal Neoplasms] explode all trees
#27 #21 or #22 or #23 or #24 or #25 or #26
#28 #18 #11 and #12 and #27 Publication Year from 2000 to 2016

**Results**

**Results of the bibliographic searches**

After removing duplicates, 4627 articles (197 reviews and 4430 primary studies) were found. 34 potentially relevant systematic reviews were considered potentially relevant and acquired in full text. In first instance, given the high number of updated systematic reviews, only systematic reviews were considered.
Excluded studies
12 articles were excluded: 5 because conference abstracts (Gentry 2009, Puli 2009 A498, Puli 2009 AB341, Thosani 2011, Vetro 2011); 1 because did not report the outcomes of interest (De Witt 2006); 1 because assessed the diagnostic accuracy of EUS only as an add on test after CT for periampullary and pancreatic cancer (Tamburrino 2016); 1 because assessed the diagnostic accuracy of EUS-FNA (Treadwell 2016); 1 because pooled together studies assessing patients with colon and rectal cancer (Li 2015 Asian Pac J Cancer Prev); 1 because it was a narrative review without useful data (Skandarajah 2006); 1 because did not report TNM staging (Qumseya 2015) and 1 because in Chinese language (Zhou 2014).

Included studies
We finally included 22 systematic reviews (one for gastric cancer and esophageal cancer): 2 on biliary cancers, 3 on pancreatic cancer, 7 on gastric cancer, 4 on rectal cancer, 7 on esophageal cancer.
All the reviews assessed the diagnostic accuracy of EUS for TNM staging, but none reported data about the successful staging, defined as the percentage of patients for whom the TNM staging were successful (irrespective to its accuracy) over the total number of patients for whom TNM staging was attempted.
Table 1. Successful Staging and Documentation Rate for biliary cancer

<table>
<thead>
<tr>
<th>Authors, publication date</th>
<th>n. of studies included, n. of participants</th>
<th>Reference standard</th>
<th>Successful staging/documentation rate</th>
<th>Accuracy of EUS to diagnose T stage tumor</th>
<th>Accuracy of EUS to diagnose N stage tumor</th>
<th>Accuracy of EUS to detect vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Taan 2015</td>
<td>22 articles included with 1003 patients</td>
<td>EUS for the staging of periampullary cancers</td>
<td>Sensitivity: 97% (474/488) Specificity: / PV: 93% (213/240) NPV: 83% (10/12)</td>
<td>Sensitivity: 56% (75/133) Specificity: 76% (78/103) PV: 62% (40/65) NPV: /</td>
<td>Sensitivity: 83.9% (47/56) Specificity: 97% (101/104) PV: 91% (41/45) NPV: 91% (89/98)</td>
<td></td>
</tr>
<tr>
<td>Trikudanathan 2014</td>
<td>14 studies included with 422 patients</td>
<td>T1, 11 studies 327 patients</td>
<td>N stage, 12 studies 332 patients</td>
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<tr>
<td>EUS staging for ampullary cancers</td>
<td>Reference standard: histopathology</td>
<td>Sensitivity (95% CI): 0.77 (0.69–0.83) Specificity (95% CI): 0.78 (0.72–0.84)</td>
<td>Sensitivity (95% CI): 0.70 (95% CI: 0.62–0.77), Specificity (95% CI): 0.74 (0.67–0.80),</td>
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<tr>
<td></td>
<td></td>
<td>T2, 12 studies 351 patients</td>
<td>Positive LR: (95% CI): 2.49 (1.91–3.24)</td>
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<tr>
<td></td>
<td></td>
<td>Sensitivity (95% CI): 0.73 (0.65–0.80) Specificity (95% CI): 0.76 (0.70–0.82)</td>
<td>Negative LR (95% CI): 0.46 (0.36–0.59)</td>
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<tr>
<td></td>
<td></td>
<td>T3, 11 studies 327 patients</td>
<td>DOR: (95% CI): 6.53 (3.81–11.19)</td>
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<tr>
<td></td>
<td></td>
<td>Sensitivity (95% CI): 0.79 (0.71–0.85) Specificity (95% CI): 0.76 (0.71–0.83)</td>
<td>The EUS definition of N-stage disease varied across studies, with some studies relying exclusively on lymph node size (&gt;10 mm) and others on characteristic malignant lymph node morphology (e.g. uniformly hypoechoic, rounded contour, sharply demarcated borders, close proximity to ampullary tumour).</td>
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<td></td>
<td>T4, 4 studies 148 pz</td>
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<tr>
<td></td>
<td></td>
<td>Sensitivity (95% CI): 0.84 (0.73–0.92) Specificity (95% CI) 0.74 (0.63–0.83)</td>
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</tr>
</tbody>
</table>
Table 2. Successful Staging and Documentation Rate for gastric cancer

<table>
<thead>
<tr>
<th>Authors, publication date</th>
<th>n. of studies included, n. of participants</th>
<th>Successful staging/ documentation rate</th>
<th>Accuracy of EUS to diagnose T stage tumour</th>
<th>Accuracy of EUS to diagnose N stage tumour</th>
<th>Depth of invasion (mucosal (M), sub-mucosal (SM) invasion, serosal involvement)</th>
<th>Distant metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardoso 2013</td>
<td>22 articles included with 2445 patients</td>
<td></td>
<td>T2 staging pooled accuracy: 65% (95% CI: 57–73%)</td>
<td>Pooled accuracy for N staging: 64% (95% CI: 43–84%)</td>
<td>Serosal involvement Sensitivity: varied between 77.8% and 100% Specificity: varied between 67.9% and 100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reference standard: histopathology</td>
<td></td>
<td>T1 staging, pooled accuracy: 77% (95% CI: 70–84%)</td>
<td>Pooled sensitivity: 74% (95% CI: 66–81%)</td>
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<td></td>
<td>T3 staging, pooled accuracy: 85% (95% CI: 82–88%)</td>
<td>Pooled specificity: 80% (95% CI: 74–87%)</td>
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<td>T4 staging, pooled accuracy: 79% (95% CI: 68–90%)</td>
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<tr>
<td>Kwee 2007</td>
<td>23 studies included with 2012 patients</td>
<td></td>
<td>Diagnostic accuracy of EUS for overall T staging varied between 65% and 92.1%</td>
<td></td>
<td>Serosal involvement Sensitivity: varied between 77.8% and 100% Specificity: varied between 67.9% and 100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reference standard: histopathology</td>
<td></td>
<td></td>
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<tr>
<td>Study</td>
<td>No of studies</td>
<td>No of patients</td>
<td>Reference standard: histopathology</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Accuracy in discriminating T1 and T2 versus T3 and T4 (50 studies, 4397 patients)</td>
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<tr>
<td>Kelly 2001</td>
<td>13</td>
<td>not reported</td>
<td>histopathology</td>
<td>range: 67% -100%</td>
<td>range: 87.5% - 100%</td>
<td></td>
</tr>
<tr>
<td>Mocellin 2015</td>
<td>66</td>
<td>7747 patients</td>
<td>histopathology</td>
<td></td>
<td></td>
<td>Accuracy: 0.86 (95%CI 0.81-0.90) Specificity: 0.90 (95%CI 0.87-0.93)</td>
</tr>
<tr>
<td>Mocellin 2011</td>
<td>54</td>
<td>5601 patients</td>
<td>histopathology</td>
<td></td>
<td></td>
<td>Accuracy in discriminating T1/ T2 versus T3 and T4 (41 studies, 3510 patients)</td>
</tr>
<tr>
<td>Pei 2015</td>
<td>16</td>
<td>Mucosal invasion</td>
<td></td>
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</tr>
</tbody>
</table>
3931 patients Reference standard: final histopathologic evaluation of endoscopically or surgically resected specimen

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Studies</th>
<th>No. of Patients</th>
<th>T1 Sensitivity (%)</th>
<th>T1 Specificity (%)</th>
<th>T2 Sensitivity (%)</th>
<th>T2 Specificity (%)</th>
<th>T3 Sensitivity (%)</th>
<th>T3 Specificity (%)</th>
<th>T4 Sensitivity (%)</th>
<th>T4 Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puli 2008</td>
<td>22</td>
<td>1896</td>
<td>88.1% (84.5-91.1)</td>
<td>100.0% (99.7-100.0)</td>
<td>82.3% (78.2-86.0)</td>
<td>95.6% (94.4-96.6)</td>
<td>89.7% (87.1-92.0)</td>
<td>94.7% (93.3-95.9)</td>
<td>99.2% (97.1-99.9)</td>
<td>96.7% (95.7-97.6)</td>
</tr>
</tbody>
</table>

Sensitivity (T1) = 76 (74–78)  
Specificity (T1) = 72 (69–75)  
Sub-mucosal invasion  
Sensitivity (T2) = 62 (59–66)  
Specificity (T2) = 78 (76–80)  
Sensitivity (N1) = 73.2% (95% CI: 63.2-81.7).  
Specificity (N1) = 88.6% (84.8-91.7).
## Table 2. Successful Staging and Documentation Rate for pancreatic cancer

<table>
<thead>
<tr>
<th>Authors, publication date</th>
<th>n. of studies included, n. of participants</th>
<th>Successful staging/documentation rate</th>
<th>Accuracy of EUS to diagnose T stage tumor</th>
<th>Accuracy of EUS to diagnose N stage tumor</th>
<th>Vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Li 2014</strong></td>
<td>20 studies, with 726 patients</td>
<td></td>
<td>Accuracy in discriminating T1 and T2 versus T3 and T4 (16 studies, 588 patients)</td>
<td>14 studies, 506 patients</td>
<td>8 studies, 294 patients</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Sensitivity: 0.72 (95% CI, 0.65–0.79)</td>
<td>Sensitivity (95% CI) 0.62 (0.56–0.68)</td>
<td>Sensitivity (95% CI) 0.87 (0.80–0.92)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Specificity: 0.90 (95% CI, 0.87–0.93)</td>
<td>Specificity (95% CI) 0.74 (0.68–0.80)</td>
<td>Specificity (95% CI) 0.92 (0.86–0.96)</td>
</tr>
<tr>
<td><strong>Nawaz 2013</strong></td>
<td>29 studies, with 1330 patients</td>
<td></td>
<td>69% (95% CI: 51–82%)</td>
<td>25 studies with 886 patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Specificity 81% (95% CI: 70–89%)</td>
<td>sensitivity 85% (95% CI: 76–91%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>specificity 91% (95% CI: 85–94%)</td>
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</tr>
<tr>
<td><strong>Li 2013</strong></td>
<td>8 studies, number of patients not reported</td>
<td></td>
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<td></td>
<td>Sensitivity: 0.66 (95% CI 0.56 -0.75)</td>
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<td></td>
<td>Specificity: 0.94 (95% CI 0.85 - 0.97)</td>
</tr>
</tbody>
</table>
Table 3. Successful Staging and Documentation Rate for rectal cancer

<table>
<thead>
<tr>
<th>Authors, publication date</th>
<th>n. of studies included, n. of participants</th>
<th>Successful staging/documentation rate</th>
<th>Accuracy of EUS to diagnose T stage tumour</th>
<th>Accuracy of EUS to diagnose N stage tumour</th>
<th>Accuracy of EUS to diagnose M stage tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li 2015</td>
<td>71 studies with 5152 patients</td>
<td>Reference standard: histopathology or follow-up data</td>
<td>Sensitivity: 0.63 (0.58, 0.68) Specificity: 0.80 (0.77, 0.83)</td>
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</tr>
<tr>
<td>Puli 2010</td>
<td>11 studies, 1791 participants</td>
<td>Reference standard: surgery</td>
<td>accuracy of T0 staging</td>
<td>Sensitivity: 97.3% (95% CI: 93.7–99.1) Specificity: 96.3% (95% CI: 95.3–97.2)</td>
<td></td>
</tr>
<tr>
<td>Puli 2009a</td>
<td>42 studies, with 5039 participants</td>
<td>T1</td>
<td>Sensitivity 87.8% (95%CI 85.3–90.0%) Specificity 98.3% (95% CI 97.8–98.7%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Reference standard: surgery | T2  | Sensitivity 80.5% (95% CI 77.9–82.9%) Specificity 95.6% (95% CI 94.9–96.3%),  
   |  |  
   | T3  | Sensitivity 96.4% (95% CI 95.4–97.2%) Specificity 90.6% (95% CI 89.5–91.7%)  
   |  |  
   | T4  | Sensitivity 95.4% (95% CI 92.4–97.5%) Specificity 98.3% (95% CI 97.8–98.7%).  
   |  |  
| **Puli 2009b**  | 35 studies, 2732 participants  
   | Reference standard: surgery |  
   |  |  
   |  | Sensitivity 73.2% (95% CI 70.6–75.6) Specificity: 75.8% (95% CI 73.5–78.0).  
   |  |  

## Table 4. Successful Staging and Documentation Rate for oesophageal cancer

<table>
<thead>
<tr>
<th>Authors, publication date</th>
<th>n. of studies included, n. of participants</th>
<th>Reference standard</th>
<th>Successful staging/documentation rate</th>
<th>Accuracy of EUS to diagnose T stage tumour</th>
<th>Accuracy of EUS to diagnose N stage tumour</th>
<th>Accuracy of EUS to diagnose M stage tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kelly 2001</strong></td>
<td>13 studies, n of patients not reported</td>
<td>Reference standard: histopathology</td>
<td></td>
<td>sensitivity: range: 71% - 100% specificity: range: 66.7% - 100%</td>
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<tr>
<td><strong>Luo 2016</strong></td>
<td>44 studies, 2880 patients</td>
<td>Reference standard: histopathology</td>
<td>42 studies T1</td>
<td>Sensitivity: 77% (95%CI: 73 to 80) Specificity: 95% (95%CI: 94 to 96)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>T2</td>
<td>Sensitivity: 66% (95%CI: 61,70 Specificity 88% (95%CI: 86,89)</td>
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<td></td>
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<td></td>
<td>T3</td>
<td>Sensitivity: 87% (95%CI: 95.89 Specificity 87% (95%CI: 84,89)</td>
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<td>T4:</td>
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<td>34 studies</td>
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<td></td>
<td></td>
<td></td>
<td>Sensitivity: 81% (95%CI: 79,82)</td>
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<td>Specificity 76% (95%CI: 73,78)</td>
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<tr>
<td>Reference Standard</td>
<td>Sensitivity</td>
<td>Specificity</td>
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<tr>
<td>Surgery or appropriate follow-up</td>
<td>84% (95% CI: 79.89)</td>
<td>96% (95% CI: 95.97)</td>
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<tr>
<td><strong>Puli 2008a</strong></td>
<td>49 studies with 2558 patients</td>
<td>43 studies</td>
<td>44 studies</td>
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<tr>
<td>T1</td>
<td>Sensitivity: 81.6% (95% CI: 77.8-84.9)</td>
<td>Specificity 99.4% (95% CI: 99.0-99.7)</td>
<td>Sensitivity: 84.7% (95% CI: 82.9-86.4)</td>
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<tr>
<td>T2</td>
<td>Sensitivity: 81.4% (95% CI: 77.5-84.8)</td>
<td>Specificity 96.3% (95% CI: 95.4-97.1)</td>
<td>Specificity: 84.6% (95% CI: 83.2-85.9)</td>
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<tr>
<td>T3</td>
<td>Sensitivity: 91.4% (95% CI: 89.5-93.0)</td>
<td>Specificity 94.4% (95% CI: 93.1-95.5),</td>
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<tr>
<td>T4:</td>
<td>Sensitivity: 92.4% (95% CI: 89.2-95.0)</td>
<td>Specificity 97.4% (95% CI: 96.6-98.0)</td>
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<tr>
<td><strong>Puli 2008b</strong></td>
<td>25 studies with 2029 patients</td>
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<td>Distant metastases</td>
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<tr>
<td></td>
<td>Sensitivity: 67.2% (95% CI: 62.6–71.6).</td>
<td>Specificity 97.9% (95% CI: 97.1–98.6)</td>
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<tr>
<td>Study</td>
<td>Number of Studies</td>
<td>Patients</td>
<td>Reference Standard</td>
<td>T1a</td>
<td>Sensitivity (95% CI)</td>
<td>Specificity (95% CI)</td>
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<tr>
<td>Thosani 2012</td>
<td>19 studies</td>
<td>1019</td>
<td>Final pathologic staging per histologic evaluation of EMR or surgically resected specimen.</td>
<td>T1a</td>
<td>0.85 (95% CI 0.82-0.88)</td>
<td>0.87 (95% CI 0.84-0.90)</td>
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<tr>
<td>Van Vliet 2008</td>
<td>31 studies</td>
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<td>Regional lymph nodes (N stage)</td>
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<tr>
<td>Young 2010</td>
<td>8 studies</td>
<td>132</td>
<td>Surgical or EMR pathology</td>
<td></td>
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</tbody>
</table>
References

Included studies


Excluded studies


9. Thosani, N.; Lunagariya, A.; Guha, S., and Bhutani, M. Under staging and over staging rates of EUS between squamous cell carcinoma and adenocarcinoma while evaluating for submucosal invasion (T1B) of superficial esophageal cancers: A systematic review and meta-analysis. Am. J. Gastroenterol. 2011;


PRISMA 2009 Flow Diagram

Identification
- Records identified through CDSR (n=3)
- DARE (n=14)
- CENTRAL (n=48)

Records identified through PubMed (n=57 SR, 1732 primary studies)

Records identified through Embase (n=184 SR, 3832 primary studies)

Records after duplicates removed (n=197 SRs, 4430 primary studies)

Screening
- Records screened (n=197)

Eligibility
- Studies awaiting classification (n=0)
- Full-text articles assessed for eligibility (n=34)

Included
- Full-text articles excluded, with reasons (n=12)
- Studies included (n=22)