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Systematic review of the impact of endoscopic ultrasound on the management of patients with esophageal cancer

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Objectives: Although endoscopic ultrasound (EUS) staging of esophageal cancer is established in clinical practice, high-quality evidence about its impact on patient outcomes is not available. This study aims to determine the impact of EUS for esophageal cancer staging on patient management and survival.
Methods: A systematic review was conducted using Medline, PreMedline, Embase, and The Cochrane Library. Included studies were (i) comparative studies reporting survival following EUS esophageal cancer staging, (ii) therapeutic impact studies reporting change in patient management following EUS. The quality of included studies was critically appraised.
Results: One systematic review, five studies reporting therapeutic impact, and two studies reporting patient survival were identified. The design and quality of the therapeutic impact studies varied widely. Management changed in 24–29 percent of patients following EUS staging of esophageal cancer (two studies). No studies provided data on the avoidance of surgery for this indication. One retrospective cohort study with historical control found EUS staging of esophageal cancer improved patient survival; a second study with similar

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design limitations did not find a survival benefit for EUS staging in patients undergoing resection. These studies had a high potential for bias, limiting the value of these findings. **Conclusions:** Two studies provided evidence of a change in patient management following EUS for staging esophageal cancer, a higher level of evidence for a clinical benefit than can be obtained from accuracy studies alone. This evidence contributed to a recommendation for public funding of EUS in staging esophageal cancer in Australia.

Keywords: Endosonography, Esophageal neoplasms, Evidence-based medicine, Biomedical technology assessment, Patient outcomes assessment

Over the past two decades, endoscopic ultrasound (EUS) has become standard practice for staging gastrointestinal cancers, based on the diagnostic accuracy of the test (11;12;16;21). EUS staging (in particular celiac lymph node staging) has been demonstrated to be predictive of survival and the ability to achieve complete surgical resection (2;5;14;15). However, studies of patient prognosis following the use of EUS are not designed to compare patient survival or disease progression for patients staged with versus without EUS and, therefore, conclusions about the impact of adopting EUS cannot be made based on this type of evidence. Clinical guidelines recommend the use of EUS for presurgical staging of esophageal cancer where it may potentially improve treatment selection, in particular, selection for surgical resection (1). The widespread clinical acceptance of the use of EUS, however, has preceded the current era of more rigorous evidence-based assessment of diagnostic tests.

The clinical value of a diagnostic test depends on how much it improves patient outcomes compared with existing tests (6). In general, this depends on the accuracy of the test to detect or exclude disease, the impact of this information on treatment decisions, and the effectiveness of treatment. This can be assessed by randomized controlled trials of the new test versus standard practice. Frequently, trial evidence of test effectiveness is not available. Sometimes, studies of test accuracy may suffice when the effect of treatment is already known (7;13). In other situations, for example with EUS where the test results are interpreted in a cascade of clinical and diagnostic information (4), this may not be the case. In a hierarchical framework of evidence for diagnostic tests, accuracy studies provide level 2 evidence, whereas studies of the impact of the test on choice of therapy or management ("therapeutic impact studies," level 4), or patient outcomes (level 5), provide evidence of greater clinical relevance (Supplementary Table 1, available online at http://www.journals.cambridge.org/jid_thc) (6).

An important potential benefit of EUS for staging is in avoiding unnecessary surgery in patients with advanced disease. In these patients, EUS may lead to avoidance of surgical morbidity and mortality and improvements in quality of life. In addition, increased accuracy of staging with EUS may increase appropriate selection of patients for neoadjuvant therapies. This potentially may have a positive impact on chances of cure in those individuals diagnosed at an appropriate stage. A UK trial of the impact of EUS for staging gastroesophageal cancer on patient outcomes is expected to report in 2009 (17). This trial will capture all the downstream effects of EUS staging on patient outcomes. In the interim, studies investigating whether EUS changes patient management may provide preliminary evidence about the clinical impact of the test (7). This systematic review was conducted as part of a broader Australian Medical Services Advisory Committee review of EUS (16) to determine the impact of EUS for esophageal cancer staging on patient management and survival.

METHODS

Literature Search

The electronic databases MEDLINE (1966 to May, week 1, 2005), PreMEDLINE (13 May 2005), EMBASE (1980 to 2005, week 20), The Cochrane Library (Issue 3, 2005), and health technology assessment Web sites were searched to identify relevant studies. Systematic search strategies were designed by a consultant health sciences librarian using a combination of indexing and text words covering many terms, including (but not limited to) endoscopic ultrasound, endosonography, gastrointestinal neoplasms (exploded), esophagus tumor, management, decision making, and survival. Reference lists of included articles were screened for relevant papers, and clinical experts were consulted. A single reviewer assessed studies for eligibility. Included studies were checked for eligibility by a second reviewer.

Study Selection

Included studies were controlled studies of EUS for staging esophageal neoplasms reporting therapeutic impact or patient survival. Therapeutic impact studies included were randomized controlled trials or interventional studies recording a pretest management plan and reporting the changes in the management plans. These study designs provide stronger evidence for demonstrating test impact on patient management than retrospective studies (7). Exclusion criteria were less than 10 patients, catheter-probe or intraoperative EUS, or studies reporting patient prognosis following the use of EUS without a control group. No language restrictions were applied.

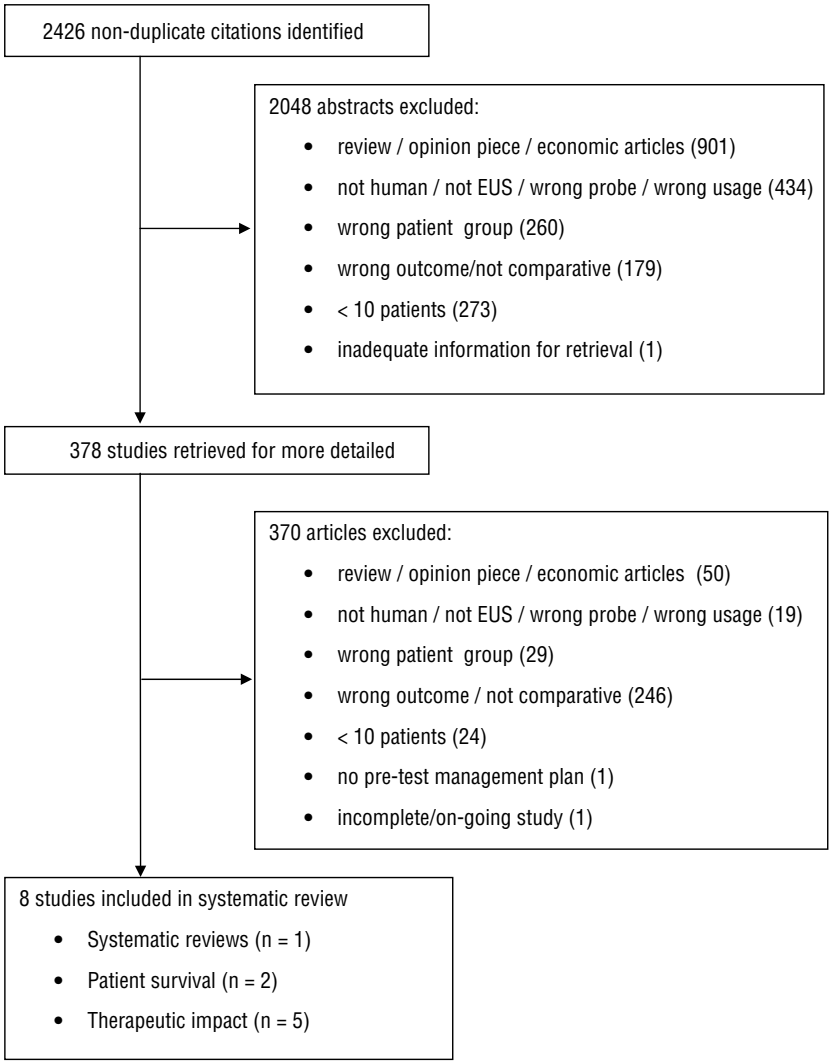

Figure 1. QUORUM flowchart of study selection.

A total of 2,426 nonduplicate citations were screened and 8 eligible studies were identified (Figure 1). These studies included one systematic review, two studies reporting patient outcomes, and five studies reporting therapeutic impact.

Data Extraction

The study characteristics and outcomes of eligible studies were extracted by one reviewer and checked by a second reviewer. Systematic reviews and studies reporting survival outcomes were assessed using quality assessment criteria for systematic reviews and case series described by the Centre for Reviews and Dissemination (18). No formal guidelines for quality assessment of management studies were identified. These studies were assessed by criteria based on the elements described by Guyatt et al. (7).

Due to dissimilarities in the characteristics and outcomes of the identified studies, no meta-analysis was performed. Too few included studies were identified to undertake an assessment of publication bias.

RESULTS

Systematic Review

One systematic review of EUS in gastroesophageal cancer published in 1998 was identified (9). This high-quality review concluded that endoscopic ultrasound was highly accurate in staging tumors of the esophagus and stomach. The review did not identify any evidence of the impact of EUS on health outcomes. The two before–after studies of therapeutic impact identified are included in the current review (10;19).

Therapeutic Impact

Study Characteristics. Five studies reported on the impact of EUS on pretest management plans. The design and quality of these studies varied (Table 1). No studies enrolled

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Table 1. Characteristics of Included Studies Reporting the Effect of EUS on Patient Management Plans

Author (reference) country, no. of centers	Study design EUS characteristics	Patients (*N* or %)	Physicians completing EUS & management plan Accuracy	Outcomes	Quality characteristic[a]
Chong et al., 2005 (3) Australia, single center	Prospective pre-test, post-test case series EUS radial scanners, cytopathologist on-site	Included 70% (231) of consecutive patients receiving EUS. Indications: • Esophageal staging (22%), diagnosis (10%) • pancreaticobiliary (31%) • mediastinal/lung (19%) • gastric (15%) • duodenal (2%) EUS + FNA in 30% Exclusions: • Inadequate questionnaire completion (99, 30%)	EUS: • Single experienced gastroenterologist Management plan: • referring physicians (62%), surgeons (38%) Accuracy: in patients with surgery or histology ($n = 68$) Overall = 84% EUS-FNA ($n = 32$) = 88% EUS: NR Management plan: • referring physicians Accuracy: NR	• Change in management • Altered diagnosis • Investigations avoided • Usefulness (four-point scale) • Whether clinicians would order EUS again Outcomes reported by: • Disease site: Y • Staging/diagnosis: Y • EUS ± FNA: Y	Consecutive: N Accuracy reported: Y Management plan by referring clinician: Y Outcomes reported by specific indication/use: Y
Jafri et al., 1996 (10) USA, single center	Prospective pre-test, post-test case series EUS radial scanner	Included 94% (63) of consecutive patients undergoing EUS, indications unclear. Diagnostic findings: • Esophageal (21%) • Normal (17%) • Gastric (21%) • Pancreatic (6%) • Miscellaneous (35%)		• Change in management • Change in management directly attributable to EUS • Usefulness • Change in certainty of diagnosis • Change to more/less invasive management Outcomes reported by: • Disease site: N • Staging/diagnosis: N • EUS±FNA: Y	Consecutive: N Accuracy reported: N Management plan by referring clinician: Y Outcomes reported by specific indication/use: N

Nickl et al., 1996 (19) USA, multicenter American Endosonography Club Study	Prospective pre-test, post-test case series EUS NR	Included 92% (393) of consecutive patients undergoing EUS. Indications: • Esophageal staging (11%), other (10%) • Stomach, duodenal (19%) • Mediastinum (3%) • Pancreaticobiliary & hepatic (51%) • Colorectal (16%) Exclusions: • Procedures conducted for research purposes (35, 8%).	EUS: • 15 senior endosonographers from 10 centers, experienced in 100–2,000 procedures over 1–14 years Management plan: • Endosonographer • Completed within 6 hours of EUS Accuracy: NR EUS: NR Management plan: • Consultant esophagogastric surgeons $n = 3$ • Blinded to outcomes • One of four options • Pre-test plan mean of two assessments, second determined 1 month after post-test plan	• Change in management • Breakdown of management changes • Surgery avoided • Change in further diagnostic testing, with detail • Major changes (between surgical & nonsurgical, invasive & noninvasive or further follow-up & discharge) • Change to more/less invasive, risky or expensive management Outcomes reported by: • disease site: Y • Staging/Diagnosis: Y • EUS±FNA: unclear	Consecutive: N Accuracy reported: N Management plan by referring clinician: N Outcomes reported by specific indication/use: Y
Preston et al., 2003 (22) UK, single center	Reassessment of randomized, de-identified cases with pre-test post-test plan EUS radial scanner, no dilatation	100 consecutive patients undergoing EUS. Indication: • Staging biopsy-proven esophageal or esophagogastric junction carcinoma (100%).	Accuracy: In patients undergoing resection (29) T staging: Se: 76.4% Sp: 75.0% Ac: 75.9% N staging: Se: 83.3% Sp: 87.5% Ac: 85.7%	• Change in number of concordant management plans • Usefulness • Agreement of concordant results with actual management decisions Outcomes reported by: • Disease site: Y • Staging/diagnosis: Y • EUS±FNA: Y	Consecutive: N Accuracy reported: Y Management plans not determined in normal setting. Outcomes reported are change in proportion of concordant plans between clinicians.

Table 1 Continued.

Author (reference) country, no. of centers	Study design EUS characteristics	Patients (*N* or %)	Physicians completing EUS & management plan Accuracy	Outcomes	Quality characteristic[a]
Shah et al., 2004 (23) USA, single center	Prospective pre-test, post-test case series EUS-FNA radial scanners, EUS+FNA linear	Included 18.4% (90) of consecutive patients undergoing EUS for known or suspected malignancies. Indications: • Esophageal staging (13%), establishing diagnosis (11%) • Gastric (17%) • Pancreatic (48%) • Rectal (11%) Exclusions: • Referral by study authors or endosonographers • Pre-test communication with endosonographers regarding management • Inability to contact referring clinicians before EUS	EUS: • One of three experienced endosonographers • Operator blinded to pre-test management plan Management plan: • Referring surgeons (33%), gastroenterologists (58%), oncologists (3%), internists (4%), pulmonologist (1%) Accuracy: NR	• Change in management • Breakdown of management changes • Surgery avoided • Investigations avoided • Change to less/more complex management Outcomes reported by: • Disease site: Y • Staging/diagnosis: N • EUS±FNA: Y	Consecutive: N Accuracy reported: N Management plan by referring clinician: Y Outcomes reported by specific indication/use: N

[a] Consecutive refers to a consecutive series of patients presenting with a defined clinical indication.
Ac, accuracy; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; N, no, NR, not reported; Se, sensitivity; Sp, specificity, Y, yes.

a consecutive series of patients based on a specific clinical presentation, rather than on referral for testing. No studies incorporated independent review of adequacy of pretest workup, diagnosis, or contribution of the test to the management decision. In one study, three separate clinicians determined the management plans before and after EUS, and change in the number of concordant management plans, rather than the proportion of patients in whom management changed, was reported (22). The generalizability of the change in management data was limited in different studies by endosonographers determining the management plan (19), by determining the management plan out of a standard clinical setting (22), or by blinding the EUS operator to the pretest management plan (23). Only two of five studies provided concomitantly determined accuracy data (3;22), and no studies discussed evidence of the effectiveness of the treatments provided.

The type of outcomes reported and the adequacy of the breakdown of results also varied greatly between studies (Table 1). Three studies investigated patient management plans following esophageal cancer staging by EUS (3;19;22). One other study reported outcomes for mixed esophageal indications, including both staging and diagnosis (23). The fifth study only reported change in patient management data for a total population, which included patients with nonesophageal indications (10).

Data Summary. Preston et al. (22) reported that the number of concordant management plans for radical surgery alone in esophageal cancer patients did not change with the addition of EUS information (20 percent with and without EUS). EUS staging information increased the number of patients for whom there were concordant plans for nonsurgical palliation (from 18.5 percent to 24.0 percent, $p = .34$, t-test). The level of agreement between the three surgeons was low, with a mean level of agreement of 56 percent without EUS data, and 62 percent with EUS data (average of two assessments, $p = .39$, t-test).

In two studies, EUS for staging esophageal cancer changed patient management in 24 percent and 29 percent of patients (Table 2) (3;19). EUS (without fine-needle aspiration [EUS-FNA]) changed patient management in a greater percentage of patients when all indications were considered (40 percent and 74 percent). Management also changed in a greater proportion of patients when data on the use of EUS for esophageal staging and/or diagnosis is combined (32 percent to 55 percent in two studies) (3;23). Further investigations were avoided in 14 percent to 33 percent of these patients (3;23), and surgery was avoided in 18 percent in a single study (23). Data on the proportion of patients in whom surgery was avoided was not reported separately for patients receiving EUS for staging esophageal cancer in any of the identified studies. Surgery was avoided in 10 percent to 16 percent of patients in populations with mixed indications (Table 2).

Patient Survival

Study Characteristics. Two retrospective cohort studies, reporting survival in patients with esophageal cancer staged with versus without EUS using a historical control group, were identified (8;24). These studies provide low-quality evidence of comparative survival as the potential for selection bias and differences in concomitant therapies is high (Table 3). Neither study reported the inclusion of all consecutive patients eligible for EUS staging.

Data Summary. Harewood and Kumar (8) stated that there was no significant change in stage-dependent treatment practices during the time period of the study. EUS staging increased the selection of patients for preoperative neoadjuvant chemotherapy, from 15 percent in the historical control group to 33 percent ($p = .01$; Table 3). EUS also increased survival (adjusted hazard ratio 0.66; 95 percent confidence interval, 0.47 to 0.90; $p < .01$) and decreased the tumor recurrence rate (adjusted hazard ratio 0.63, 95 percent confidence interval, 0.43 to 0.87; $p < .01$; Table 3).

The survival outcomes reported in a different study by van Westreenen et al. (24) were only for patients undergoing surgical resection, rather than for all patients tested or presurgically staged as resectable. The median survival time of patients staged with and without EUS was similar (25.6 versus 28.0 months, respectively; Table 3). The proportion of patients who underwent unnecessary laparotomy was not significantly different for staging with versus without EUS (50 percent versus 44 percent, $p = .66$, χ^2 test).

DISCUSSION

This systematic review identified five studies reporting the therapeutic impact of EUS, and two studies reporting the effect of EUS for staging esophageal cancer on patient survival. In one of the latter studies, EUS increased selection of patients for preoperative neoadjuvant chemotherapy, increased survival, and reduced the recurrence rate (8). The other study found no survival benefit for patients staged with EUS, but only reported data for patients undergoing resection rather than for all patients staged (24). Neither study was designed to assess potential improvements in quality of life following EUS staging to avoid unnecessary surgery in patients with advanced disease. Both studies were retrospective cohort studies with historical control groups and thus do not provide reliable evidence of the effect of EUS on patient survival due to the high potential for bias. Nevertheless, EUS has become accepted in clinical practice as a standard of care.

There is currently an ongoing randomized controlled trial investigating patient outcomes (including survival, treatment selection, complete resection rate, and quality of life, plus health resource utilization) following the addition of EUS to standard testing in the staging of patients with gastric and esophageal cancer (UK COGNATE) (17). Results of this trial are not expected until January 2009. In the absence of

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Table 2. Effect of EUS on Patient Management Plans in Patient Populations Including Those Undergoing Staging for Esophageal Cancer

Author	EUS	*N*	Change in management		Surgery avoided		Investigations avoided	
			n	(%)	*n*	(%)	*n*	(%)
Esophageal indications								
Chong et al., 2005 (3)	EUS for staging and/or diagnosis (FNA in 3)	75	24	(32.0)	—	—	25 investigations	(33.3)
	EUS for staging	51	15	(29.4)	—	—	—	—
Nickl et al., 1996 (19)	Esophageal cancer staging, major change	41[a]	10[a]	(24.0)	—	—	—	—
Shah et al., (2004) (23)	EUS staging and/or diagnosis	22	12	(54.5)	4	(18.2)	3 imaging and/ or endoscopy	(13.6)
Mixed indications								
Chong et al., 2005 (3)	EUS – FNA	162	64	(39.5)	—	—	70	(43.2)
	EUS + FNA	69	47	(68.1)			45 investigations	65.2
Jafri et al., 1996 (10)	EUS–FNA	63	30	(47.6)	8	(12.7)	16 endoscopy + biopsy	(25.4)
Nickl et al., 1996 (19)	EUS (proportion with FNA not reported)	393	291	(74.0)	41	(10.4)	87/386 testing	(22.5)
		Major:	120	(30.5)				
Shah et al., 2004 (23)	EUS ± FNA (FNA in 20)	90	46	(51.1)	14	(15.6)	—	—

[a] *n*/*N* estimated from figure and reported % change.
EUS, endoscopic ultrasound; FNA, fine-needle aspiration.

trial evidence, studies reporting on the impact of EUS on patient management may provide preliminary evidence of clinical impact (7).

Five such studies of therapeutic impact reporting the use of a pretest management plan were identified. These studies indicated that EUS changed management in 40 percent to 74 percent of patient populations with mixed indications. Surgery was avoided in 10 percent to 16 percent of all patients. Two studies reported data specifically for patients undergoing EUS for staging of esophageal cancer. In these studies, EUS changed patient management in 24 percent to 29 percent of patients. However, the impact of EUS in avoiding surgery, an important potential benefit, was not reported separately for patients undergoing EUS for esophageal cancer staging.

Accuracy studies of EUS in staging esophageal carcinoma have estimated the impact of EUS on patient management (20;25). In one of these studies, surgery was avoided in 78 percent of patients undergoing EUS-FNA, or 45 percent of the total receiving EUS (20). In the other study, contraindication to surgical resection based on detection of advanced or metastatic disease in 77 percent of patients undergoing preoperative nodal staging of esophageal carcinoma was reported (25). These estimates are greater than suggested by the identified therapeutic impact studies. The absence of a pretest recorded management plan in the accuracy studies is likely to result in the inclusion of patients in whom surgery was not planned before EUS. The study by Vazquez-Sequeiros et al. (25) includes all patients with esophageal carcinoma, including those in whom unresectable disease was detected with other prior imaging (computed tomography). Patients in whom surgery was not planned due to other factors, for example, health status or patient age, are also likely to be included in these studies. Similarly, Parmar et al. (20) reported that EUS-FNA directed management in all patients biopsied. However, the pretest management plan for these patients was not reported and there may have been no *change* in the management plan. These discrepancies in the estimates of the effect of EUS on patient management emphasize the role of therapeutic impact studies in providing evidence for the value of EUS.

The EUS management studies varied widely in both study design and the quality of reporting. Twenty years ago, Guyatt et al. suggested factors that should be incorporated into the study design of diagnostic before–after studies to optimize the validity of the results (Table 4) (7). Many of these factors have not been addressed in the studies identified in this review.

One study attempted to ensure the validity of the patient management plans by requiring three separate clinicians to determine the plans (22). The authors then reported the change in the number of concordant plans with the addition of EUS data. However, this approach did not provide information on the proportion of patients who had a change in management. The study did demonstrate that management plans varied between different clinicians (agreement of 56 percent and 62 percent before and after EUS, respectively).

The generalizability of the findings of the studies was also limited for a variety of other reasons. One of the most common problems encountered was authors reporting study results with an inadequate degree of separation by clinical

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Table 3. Studies Reporting on Survival of Patients with Esophageal Cancer Staged with Versus without EUS

Author (country)	Study design Test characteristics	Patient characteristics *N*	Results	Comments
Harewood and Kumar, 2004 (8) USA	Retrospective cohort with historical control EUS radial scanner ± FNA, dilatation in $n = 7$, cytotechnologist on site	Esophageal squamous cell carcinoma or adenocarcinoma, no distant metastases on chest or abdominal CT EUS $n = 107$; control $n = 60$	*Mortality*: Adjusted HR (95% CI) = 0.66 (0.47 – 0.90); $p = .008$. *Recurrence rate*: Adjusted HR (95% CI) = 0.63 (0.43 – 0.87); $p = .004$. HRs adjusted for age, sex, tumor stage & location *Preoperative neoadjuvant therapy*: EUS = 32.7%, 35/107 control = 15.0%, 9/60; $p = .01$ *Survival*: (EUS + CT $n = 18$; CT $n = 59$) CT alone median = 28.0 months CT+EUS median = 25.6 months *Unnecessary surgical exploration*: EUS+CT = 50%, 18/36; CT alone = 44%, 47/106; $p = .66$[a]	EUS $n = 13$ from late 1998, $n = 94$ from 2000; control patients from 1998 before routine use of EUS. Consecutive: No Follow-up ≥ 24 months for those without recurrence. Cox proportional hazards
van Westreenen et al., 2005 (24) The Netherlands	Retrospective cohort with historical control. EUS radial scanner±FNA, or miniprobe if not traversable Single slice spiral CT	Esophageal or gastroesophageal junction cancer (biopsy proven), fit for curative surgery. Preoperatively staged resectable. Exclusion: preoperative chemotherapy or radiography EUS+CT $n = 36$; CT $n = 106$		EUS+CT staging 1997, CT staging 1992–1996. Consecutive: No Survival data only for those undergoing resection, not total eligible patient population. Follow-up: NR, graphically appears longer for CT group.

[a] Pearson's χ^2 determined post-hoc by reviewers
EUS, endoscopic ultrasound; CI, confidence interval; FNA, fine-needle aspiration; CT, computed tomography; HR, hazard ratio; NR, not reported.

Table 4. Before–after Studies of Therapeutic Impact: Optimizing Study Design

Problem	Solution
Uncertainties of retrospective review	Prospective study
Unclear study question	Choose specific presentation or clinical problem
Possibility of deleterious therapeutic impact	Concomitant documentation of accuracy
Inaccurate reporting	Chart review applying consistent criteria
Inadequate pre-test workup	Independent review
Uncertain relation between test result and change in therapy	Independent review
Uncertain relation between change in therapy and outcome	Detailed description of changes in therapy and subsequent outcome
Generalizability to different physicians	Description of training of participating physicians
Pre-test plans elicited after test available	Strict adherence to study protocol

Note. Reproduced from Guyatt et al. (1986) (7).

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indication, or by nature of management change. This greatly limited the usefulness of the available data for assessing the benefit of EUS in avoiding unnecessary surgery in patients with esophageal cancer, despite identification of five relevant studies. The apparent difference in outcomes when the data are considered for esophageal staging only, rather than for all indications, also highlights the importance of collecting and reporting data by specific clinical indication. Thus, high-quality studies of the impact of EUS on avoiding surgery in patients with esophageal cancer are still required.

A multitude of studies assessing the diagnostic accuracy of EUS have been published (9;12;16). However, evidence of accuracy only provides level 2 evidence in a six-level hierarchical framework of evidence for the efficacy of diagnostic tests (Supplementary Table 1) (6). The current review, therefore, focused on level 4 and 5 evidence of efficacy, studies of therapeutic impact and patient survival, respectively. Although the studies identified have methodological limitations, they provide a higher level of support for a clinical benefit of EUS than accuracy studies alone (6). A broader Australian Medical Services Advisory Committee review incorporating these studies determined that the body of evidence was sufficient for a recommendation for public funding in Australia (16).

Therapeutic impact studies can provide important evidence-based information on the clinical utility of diagnostic tests. They can be conducted in routine practice settings and may be simpler and less costly to conduct than a randomized controlled trial. Ideally such studies should be designed to replicate clinical practice, include a pretest management plan and report outcomes separated by indication and the intended purpose of the diagnostic test (e.g., diagnosis or staging) in a consecutive series of presenting patients (7).

Recommendations for when these studies are required or where they may replace the need for randomized trials do not currently exist. In some situations, accuracy studies alone may be sufficient for test assessment, and neither trials nor patient management studies are required (13). It has also been stated that where evidence of change in management from an accurate test leads to institution of a treatment proven to be effective, or avoidance of a procedure associated with considerable risk, the benefit of the diagnostic test is established (7). Other scenarios where these studies are likely to have an important role include where therapeutic decisions are strongly influenced by factors other than test accuracy, such as individual patient characteristics, prior test results, or patient preference, and also where the new test is used to differentiate between several differential diagnoses.

The lack of comprehensive practical guidelines for the design, reporting, and appraisal of therapeutic impact studies may be the reason for the inconsistent and limited quality of existing data identified in the current review. The development of clear guidelines including recommendations for the role of these studies in providing evidence for diagnostic test effectiveness is essential.

In conclusion, although EUS is established in clinical practice, high-quality evidence about its impact on patient outcomes is not available at this time. In particular, further studies investigating the impact of EUS on patient survival are required. Two therapeutic impact studies have reported that EUS changes management in approximately one quarter of patients undergoing esophageal cancer staging. These studies provide a higher level of evidence of a clinical benefit of EUS than can be obtained from accuracy studies alone and contributed to a recommendation to provide public funding for EUS in staging of esophageal cancer in Australia.

POLICY IMPLICATIONS

Inclusion of therapeutic impact studies in health technology assessments can provide important additional evidence for test effectiveness. This review established that EUS has an impact on the management of patients with esophageal cancer, a necessary condition for the test to lead to improved patient outcomes. This finding provided higher evidence for test effectiveness than existed from accuracy studies alone. A recommendation for public funding of EUS staging in esophageal cancer patients was approved by the Australian Minister for Health and Ageing on February 5, 2007.

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