



GOBIERNO
DE ESPAÑA

MINISTERIO
DE CIENCIA
E INNOVACIÓN



Ministerio de Ciencia e Innovación

Instituto
de Salud
Carlos III

A|e Agencia de Evaluación
I|S de Tecnologías Sanitarias

Transient Elastography for the Diagnosis of Liver Fibrosis: A Systematic Review and Meta-Analysis

*Polo de Santos MM
Asensio del Barrio C
Luengo Matos S
Sánchez Gómez L
Alcázar Alcázar R
Sarría Santamera A*

Project funded by Health Research Fund (FIS), reference PI 07/90061

INTRODUCTION (1/2)

- Liver fibrosis is a common pathway for a multitude of liver pathologies, and it is associated with a high morbidity and mortality.
- The diagnosis of liver fibrosis is relevant for estimation of prognosis, surveillance, and treatment decisions in patients with chronic liver disease.
- Liver biopsy is the gold standard method of diagnosis of liver fibrosis. However, biopsy is an invasive and painful procedure, not exempt of complications.

INTRODUCTION (2/2)

- Transient elastography (TE) (FibroScan®) (Echosens, Paris, France) is a new non-invasive diagnostic technology that uses low-frequency vibration and ultrasound to measure liver fibrosis. The shear wave propagation velocity (measured in kPa) is directly related to tissue stiffness.
- TE is a simple and rapid procedure which can be performed in the outpatient setting with immediate results.
- Results of TE are more representative of the entire liver than results of liver biopsy (volume > 100 times greater than biopsy).
- TE seems to be an effective and safe method for the diagnosis of liver fibrosis and could be an alternative to liver biopsy.



OBJECTIVE

To assess the scientific evidence available on the effectiveness and safety of the transient elastography for the diagnosis of liver fibrosis in relation to the hepatic biopsy.

METHODOLOGY (1/4)

- Systematic review of scientific literature and meta-analysis.
- Studies published until March of 2008 were included without sample size or language restrictions.
- MEDLINE (PubMed), EMBASE, the Cochrane Library, DARE, NHS EED, HTA of CRD, IME, HSR proj, Web of Science, SciSearch, databases accessible through DATASTAR, and conference abstract databases were retrieved.
- Websites of scientific societies, publications related to the subject, and bibliographies of relevant articles were checked.

METHODOLOGY (2/4)

➤ Inclusion criteria:

- Any study design assessing diagnostic effectiveness and safety of TE.
- Patients diagnosed with any hepatic pathology who received TE and liver biopsy to confirm the diagnosis.

➤ Exclusion criteria:

- Duplicate publications.
- Studies with insufficient data on diagnostic effectiveness.
- Case reports.

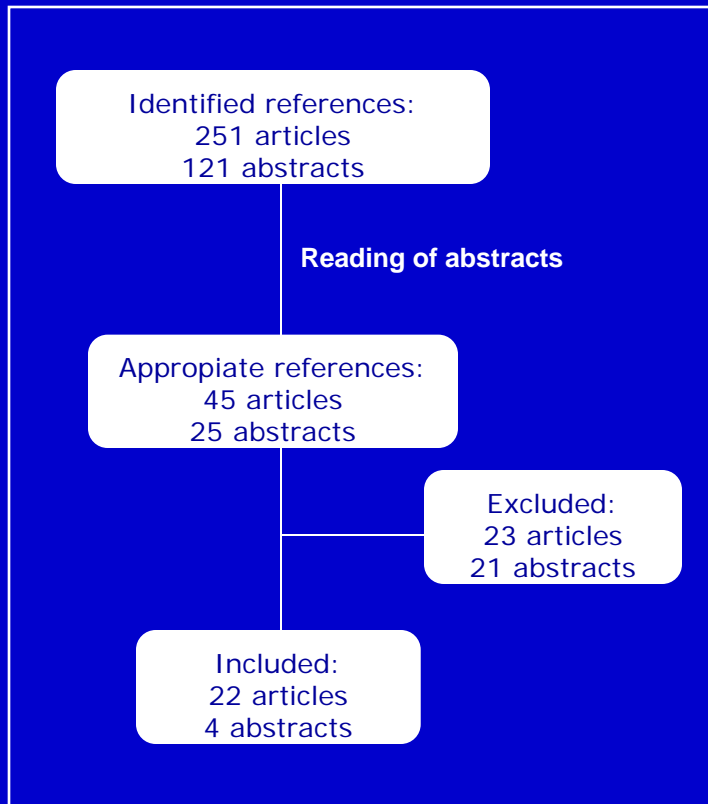
METHODOLOGY (3/4)

- The identification and selection of studies was done thoroughly and independently by two experienced reviewers.
- Quality of the scientific evidence was assessed using the QUADAS questionnaire.
- Liver fibrosis was established according to the METAVIR scale:
F \geq 1: mild fibrosis; F \geq 2: moderate fibrosis; F \geq 3: severe fibrosis; F=4: cirrhosis.
- The F \geq 2 stage was chosen for the analyses, as F \geq 2 is considered to be a hallmark of progressive liver disease.
- Qualitative and quantitative analyses (meta-analysis) were done.

METHODOLOGY (4/4)

- Diagnostic parameters (Sp, Se, LR's, DOR), with their corresponding 95% CI, were extracted.
- 2x2 contingency tables were estimated.
- Threshold effect was examined by plotting Se and (1-Sp) of each study in the ROC plane and calculating the Spearman correlation coefficient.
- Heterogeneity was assessed using forest plots and the Cochrane-Q test and I^2 index.

RESULTS (1/5)



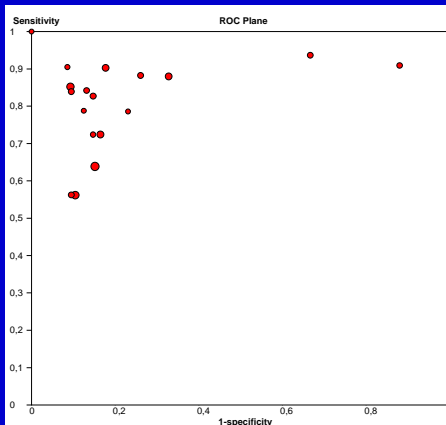
- Included publications: 26 case series (22 articles, 4 abstracts).
- Age: 16-86 years (1 study in children).
- Chronic HCV with or without HIV or HBV infection: 22 studies.
- High quality of studies.
- Correlation between TE and biopsy ($p < 0.05$).
- Agreement inter/intraobserver: only 4 studies reported an intraclass correlation coefficient > 0.90 .

RESULTS (2/5)

Meta-analysis using random effects model:

18 studies with data for fibrosis stage $F \geq 2$; $n=2,288$ patients.

- Cut-off range: 4-9 kPa; Median: 7.6.
- There was no threshold effect (correlation coefficient: 0.161).
- There was great heterogeneity for all parameters ($p < 0.001$; $I^2 = 57\%$ for DOR; and $I^2 > 80\%$ for Se, Sp, and LR's).

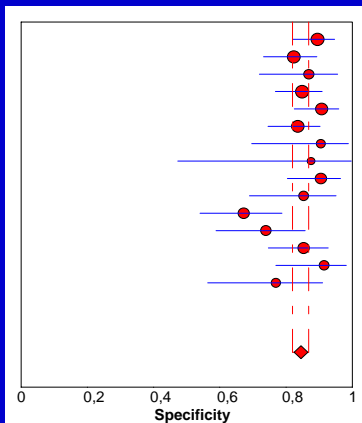


2 outliers identified and 1 study with perfect results (Sp and Se = 100%).

RESULTS (3/5)

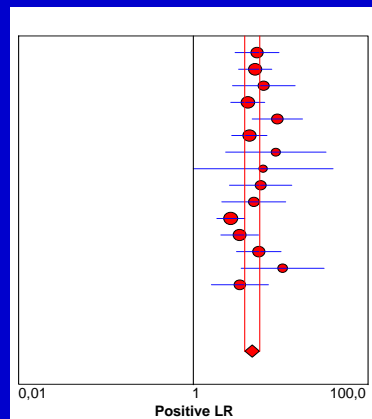
- Excluding the 3 studies: n=2,082 patients.
 - There was no threshold effect (correlation coefficient: 0.098).
 - There was heterogeneity in the Se ($X^2=93.59$, $p<0.001$; $I^2=85.0\%$) and LR- (Cochrane-Q=80.8, $p<0.001$; $I^2=82.7\%$).
 - There was no heterogeneity in the Sp, LR+, and DOR.

Specificity



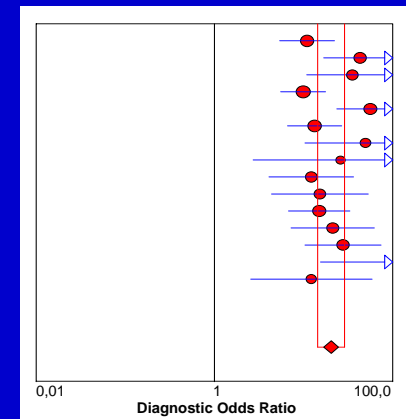
Pooled Sp: 0.84 (0.82-0.87)
 $X^2=25.5$ $df=14$ ($p=0.0299$)
 $I^2 = 45\%$

Likelihood ratio +



Pooled LR+: 4.72 (3.87-5.76)
Cochran-Q = 20.9 $df=14$ ($p=0.1049$)
 $I^2 = 32.9\%$

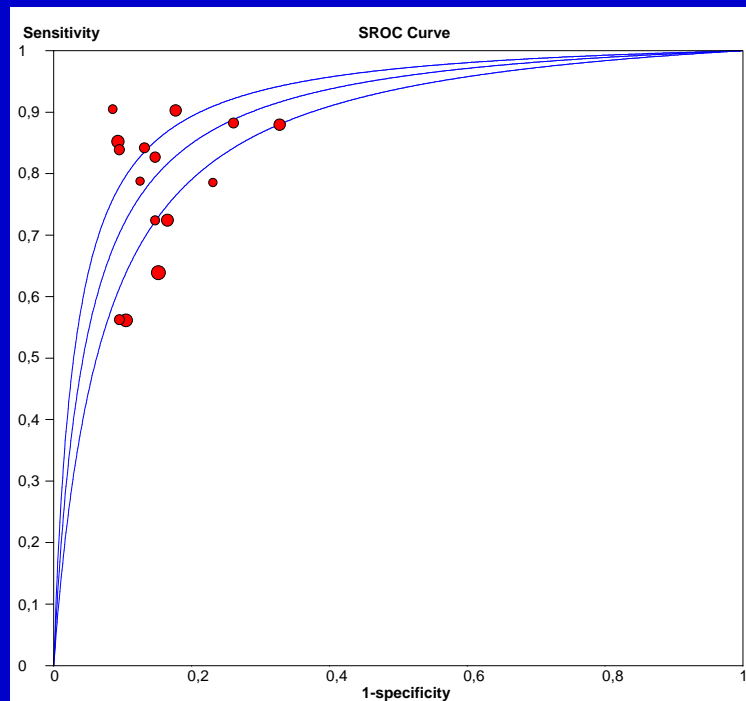
Diagnostic odds ratio



Pooled DOR: 20.36(14.37-28.84)
Cochran-Q=24.8 $df=14$ ($p=0.0369$)
 $I^2 = 43.5\%$

RESULTS (4/5)

➤ SROC curve for the 15 studies:



AUC = 0.89

SE (AUC) = 0.0126

$Q^* = 0.8258$

SE (Q^*) = 0.0133

RESULTS (5/5)

- **No publications reported adverse effects of TE.**
- **Limitations of use of TE:**
 - Obese patients.
 - Narrow intercostal spaces.
 - Presence of ascites.

CONCLUSIONS

- Significant heterogeneity was found among the single studies.
- Transient elastography seems to be a good diagnostic tool for $F \geq 2$, but for the high heterogeneity found, caution must be taken when interpreting the results.
- Transient elastography is a safe and clinically useful procedure, but it seems that for $F \geq 2$ it may not be able to substitute a liver biopsy.
- We are studying reasons to explain heterogeneity and the performance of transient elastography in others levels of liver fibrosis.

Thank you very much

mpolo@isciii.es