101學年度第11次實證醫學月會

影像醫學部

Reporter: R1趙敏芳

Tutor: VS 郭禹廷醫師

臨床情境分析 (Clinical Scenario)

- Asking: 形成一個可以回答的問題（PICO）
- Acquire: 搜尋過程
- Appraisal: 文獻評讀方式
- Apply: 證據之外推
- Audit: 自我評估

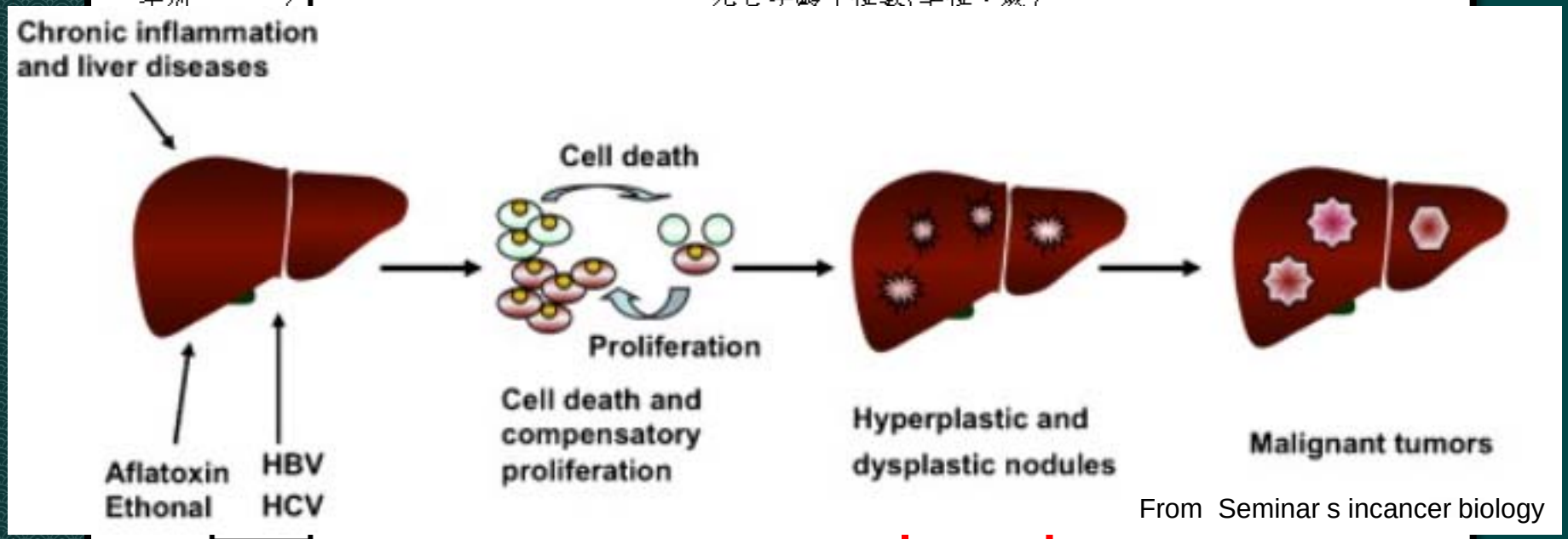
衛生署統計2011/12/31

死因概況(續)

標準化死亡率單位：每十萬人

年別	肺炎		慢性肝病及肝硬化		腎炎、腎徵候群及腎性病變		自殺		高血壓性疾病		結核病	孕產婦死亡率	嬰兒死亡率
	死因順位	標準化死亡率	死因順位	標準化死亡率	死因順位	標準化死亡率	死因順位	標準化死亡率	死因順位	標準化死亡率	標準化死亡率	0/0000	0/00
80 年	7	19	6	21	8	17	12	8	9	17	12	8	5
84 年	8	18	6	23	7	20	11	8	9	15	9	8	6
85 年	8	19	6	23	7	19	11	9	9	15	9	8	7
90 年	8	17	6	22	7	18	9	12	10	8	6	7	6
95 年	6	19	7	19	8	17	9	17	10	6	3	7	5
99 年	4	26	8	16	10	12	11	14	9	12	2	4	4
增減率 99 vs.95		36.8		-15.8		-29.4		-17.6		100.0	-33.3	-42.9	-20.0
增減率 99 vs.90		52.9		-27.3		-33.3		16.7		50.0	-66.7	-42.9	-33.3
增減率 99 vs.85		36.8		-30.4		-36.8		55.6		-20.0	-77.8	-50.0	-42.9

衛生署統計2011/12/31



From Seminar s incancer biology

主要死因死亡年齡中位數(續)

年別		死亡年齡中位數(單位：歲)								
	女	80.0	81.0	78.0	62.0	84.0	72.0	79.0	49.0	82.0
10年		5.4	4.0	5.6	20.0	3.8	0.0	4.0	2.1	2.6
增減數	男	4.1	1.4	2.8	15.9	5.2	3.8	2.7	2.1	4.0
	女	3.9	2.5	5.4	26.5	2.4	4.3	3.9	2.1	1.2

Patient's Concern

- 在慢性B型肝炎下，是否一定要用切片才可診斷肝纖維化情形?是否可以用超音波追蹤?

Metavir scoring system

0 =

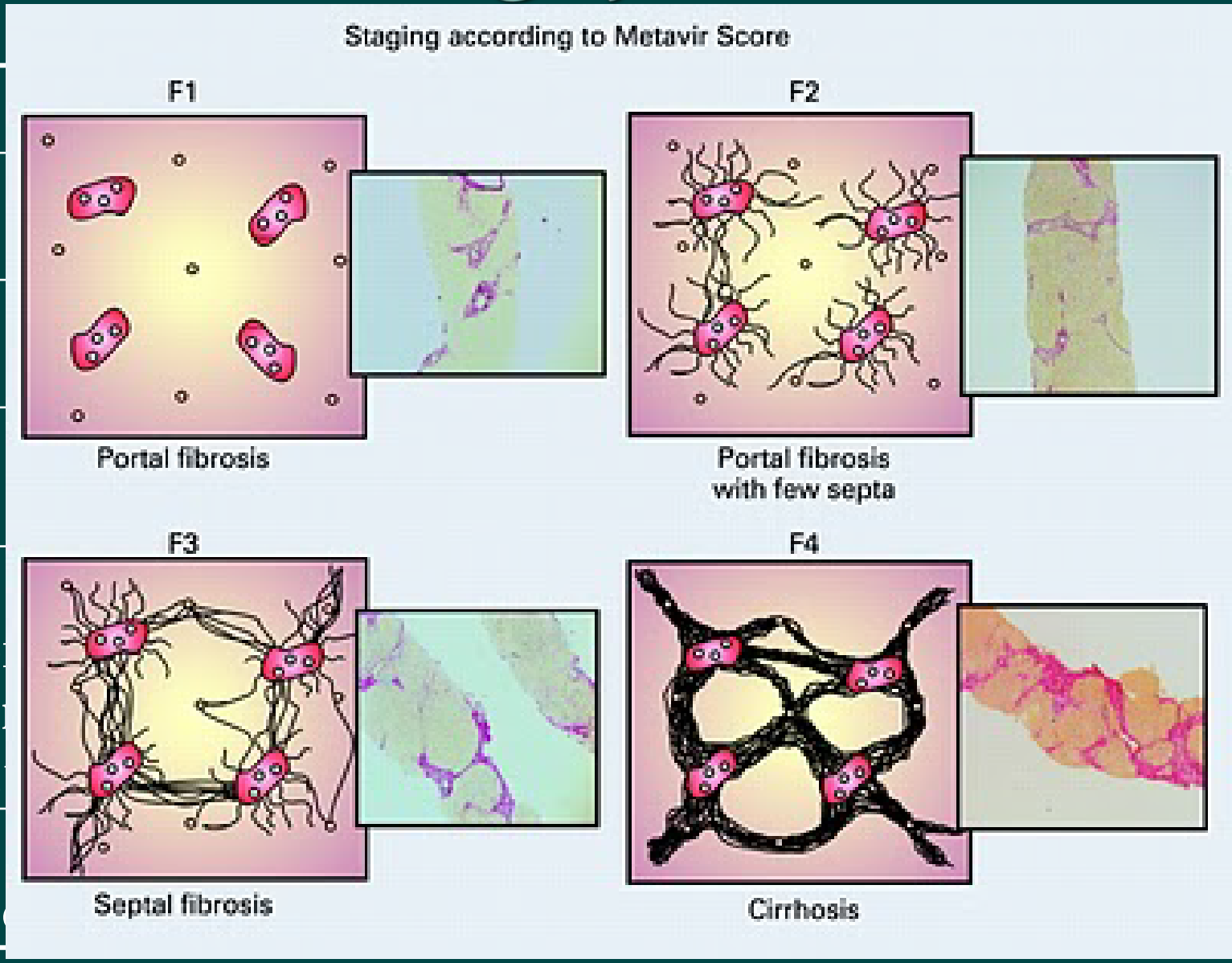
1 =

2 =

3 =
fib
con
con

4 =
sev

ty



Types of sonography for detecting liver stiffness

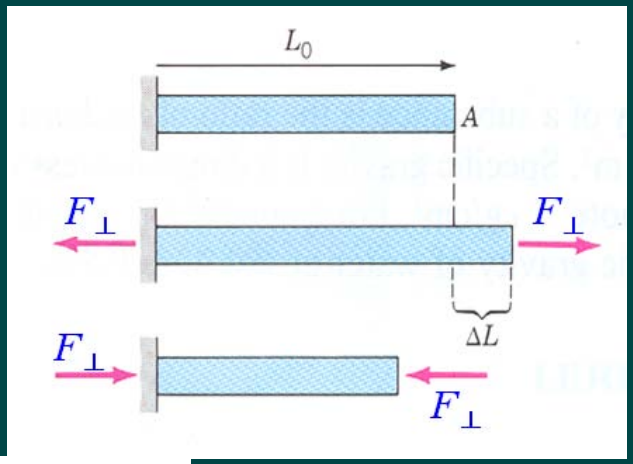
- Elastography
- Fibroscan
- ARFI (Acoustic Radiation Force Impulse)

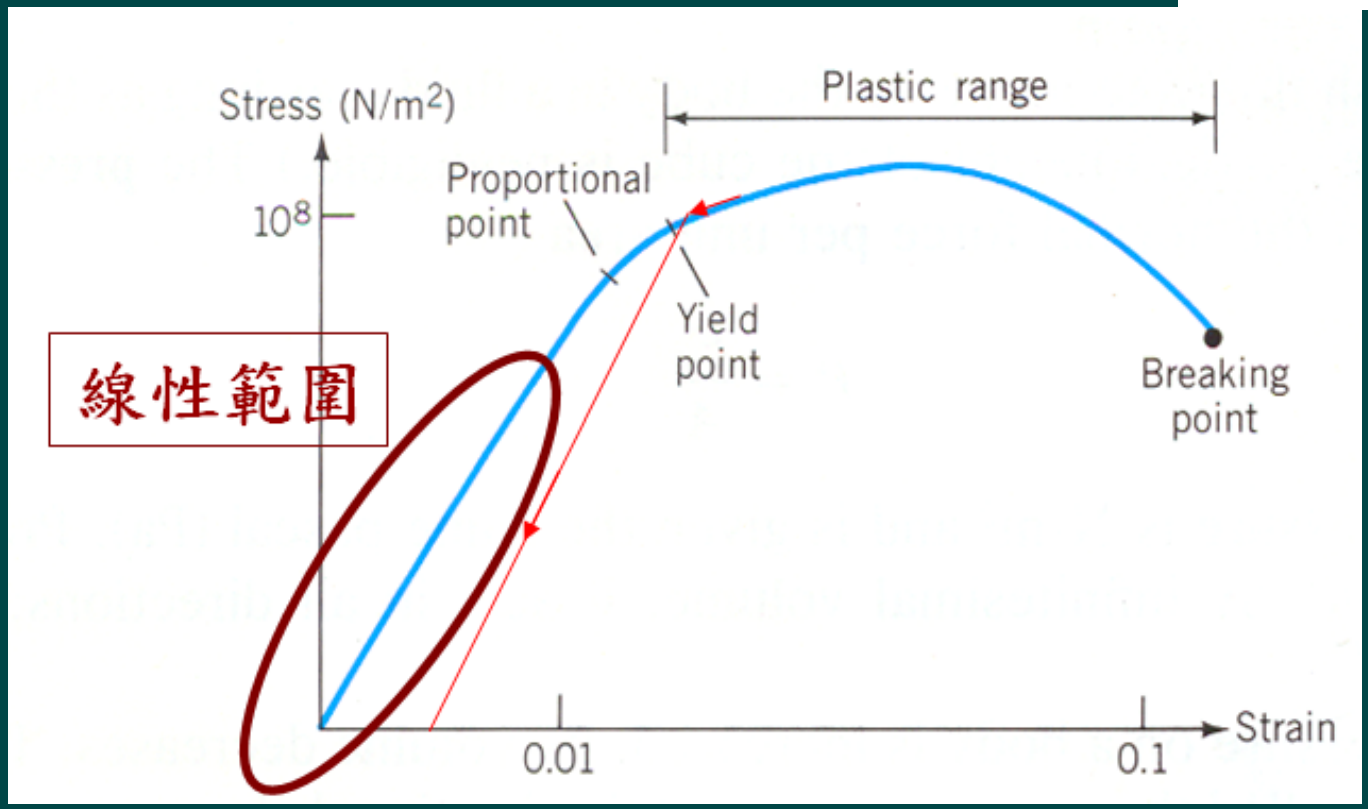
Background-Principle

- Solid V.S. Water
- Stress in the solid to give deformation
  - Tension stress, tension strain, Young's modulus
  - Shear stress, shear strain, shear modulus.
  - Volume stress, volume strain, Bulk modulus

Background

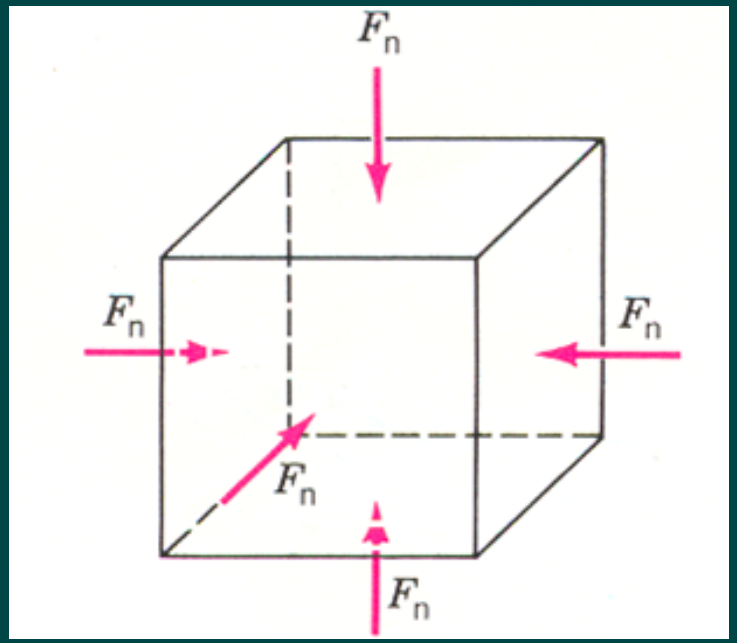
Young’ s modulus



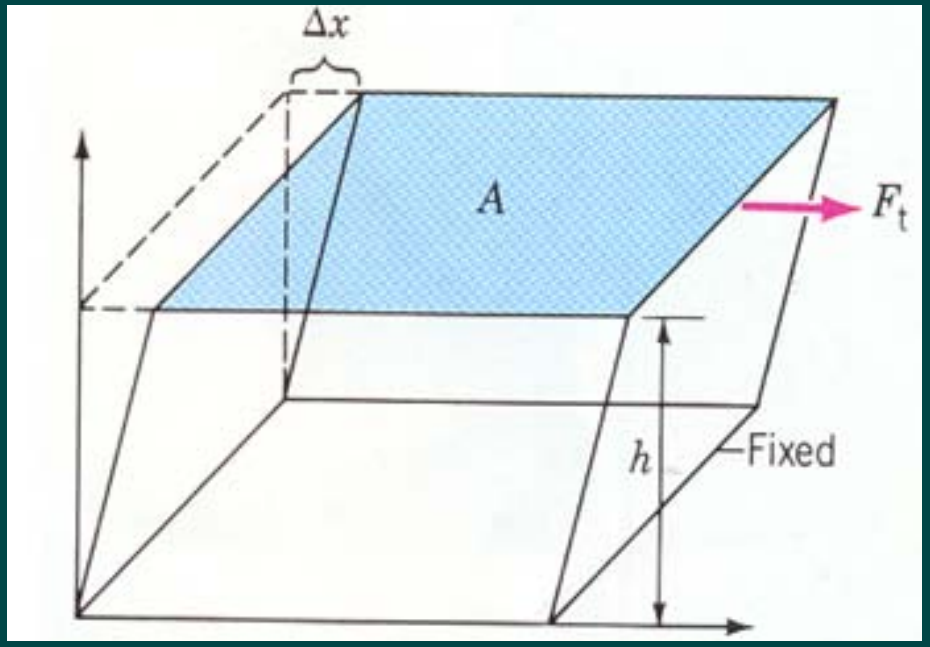


Background

Bulky modulus



Shear modulus



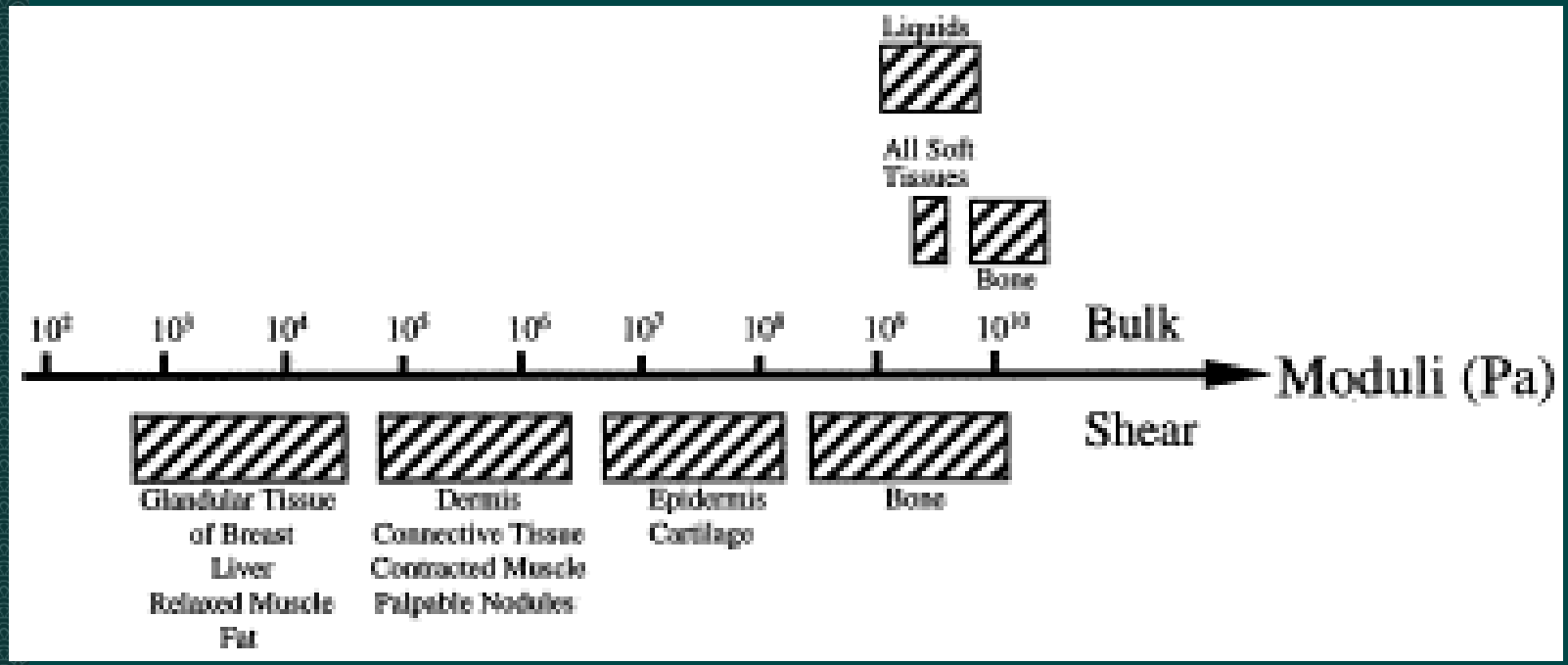
Background

TABLE 14.2 ELASTIC MODULI ($\times 10^9$ N/m^2)

	Y	S	B
Cast iron	100	40	90
Steel	200	80	140
Aluminum	70	25	70
Concrete	20		
Pine	7.6		
Water			2.1
Mercury			2.6

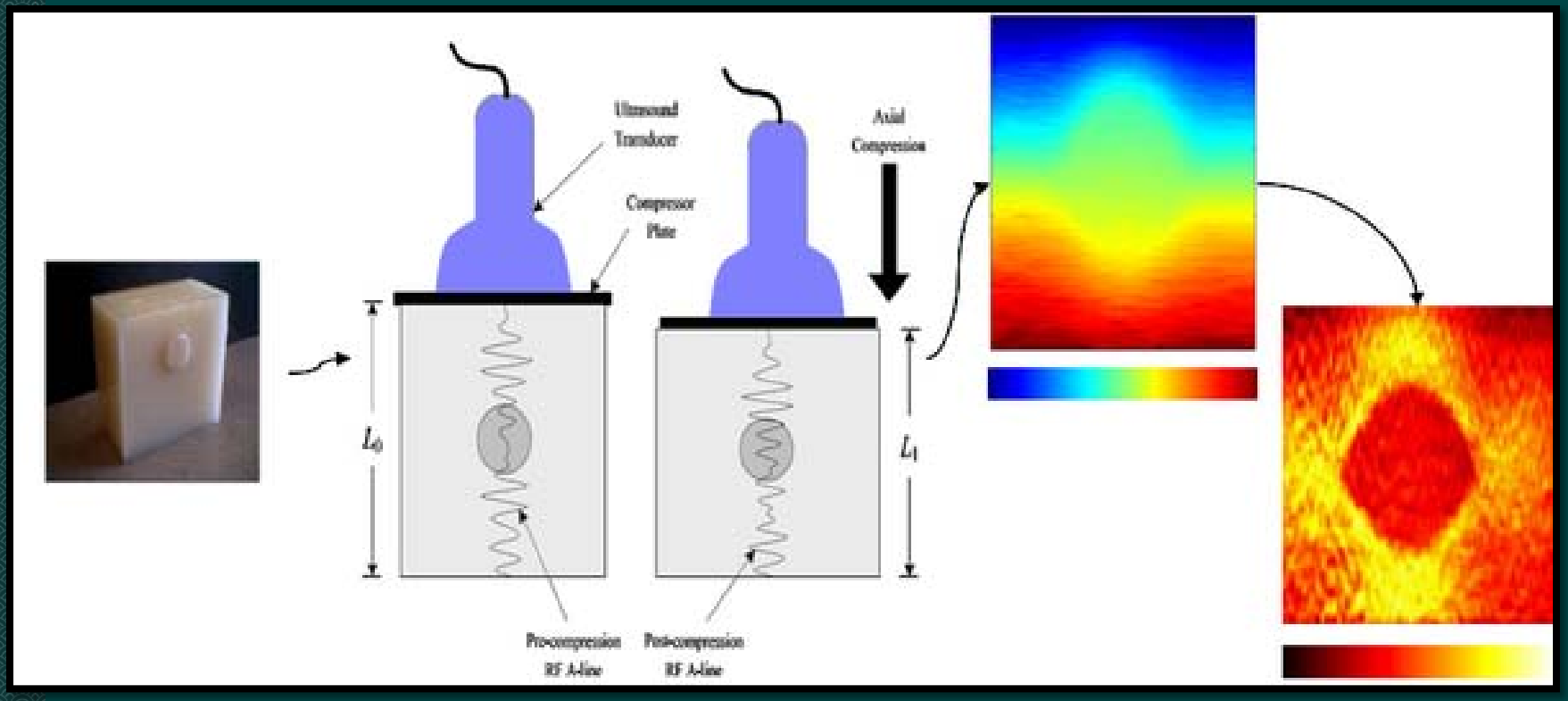
Fluid can not support tension stress and shear stress.

Background



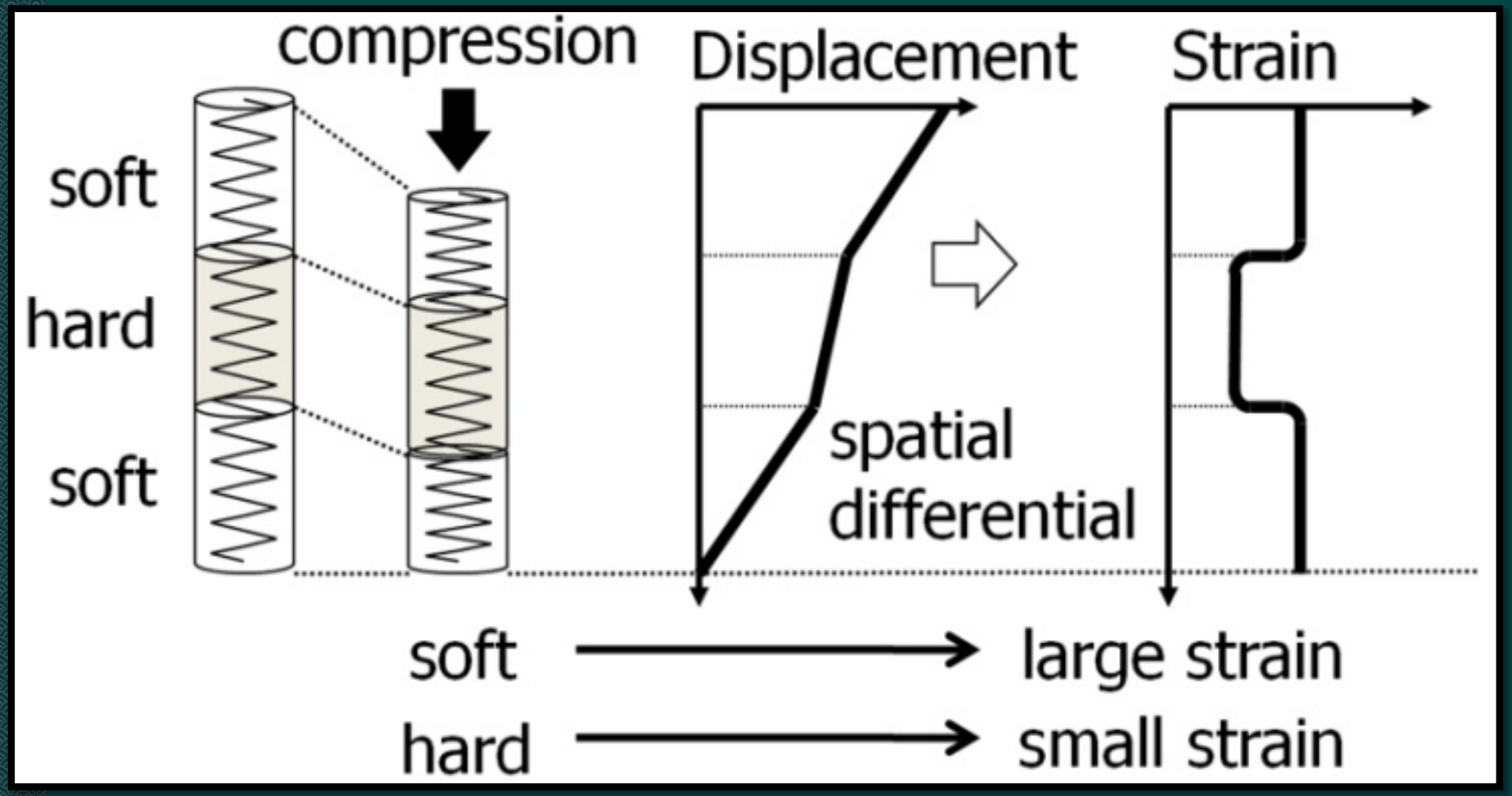
Shear modulus has wider range.

Background~Elastography



Tension stress, tension strain, Young's modulus

Background


compression
Displacement
Strain
soft
hard
soft
spatial
differential
soft
large strain
hard
small strain

Background

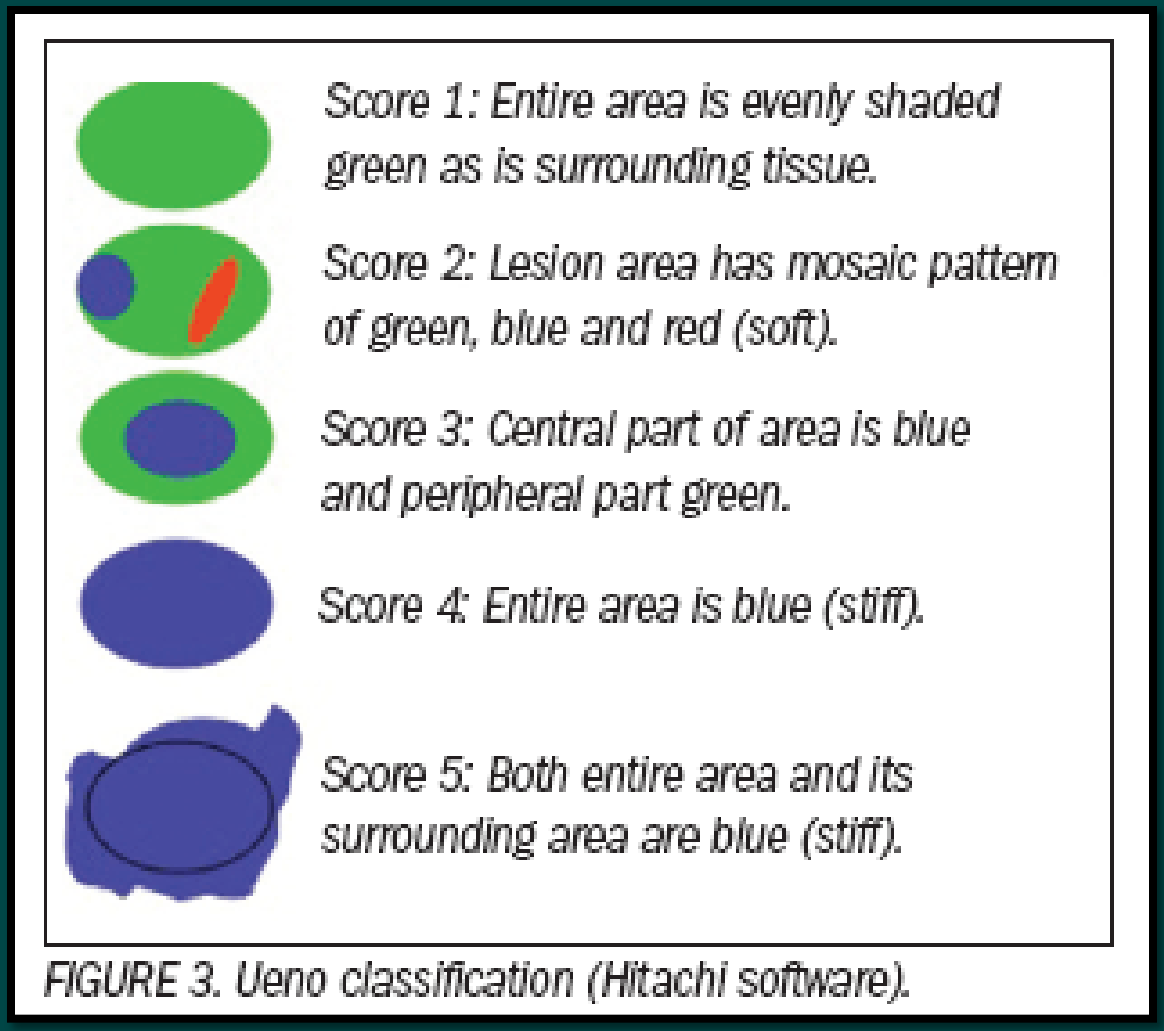
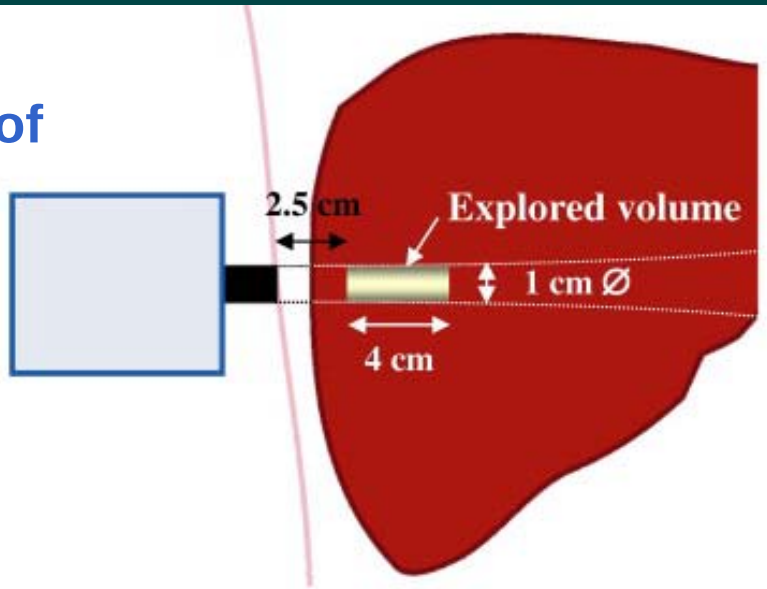


FIGURE 3. Ueno classification (Hitachi software).

Background

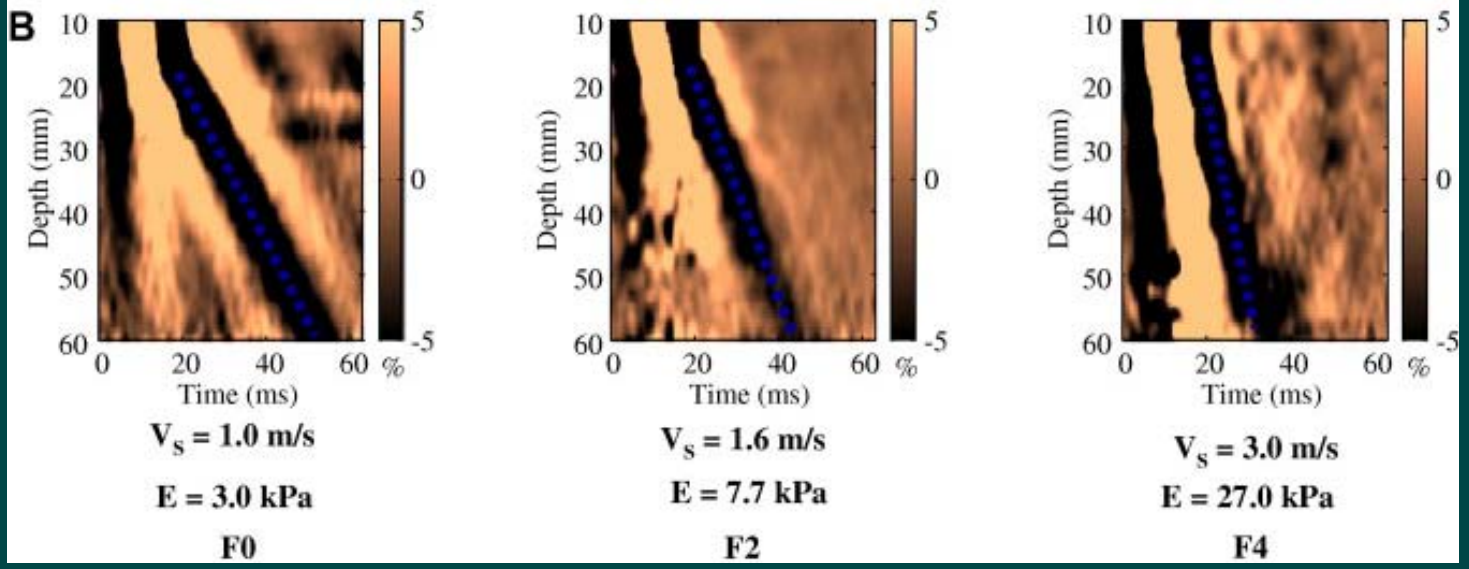
Vibration of

50 MHz

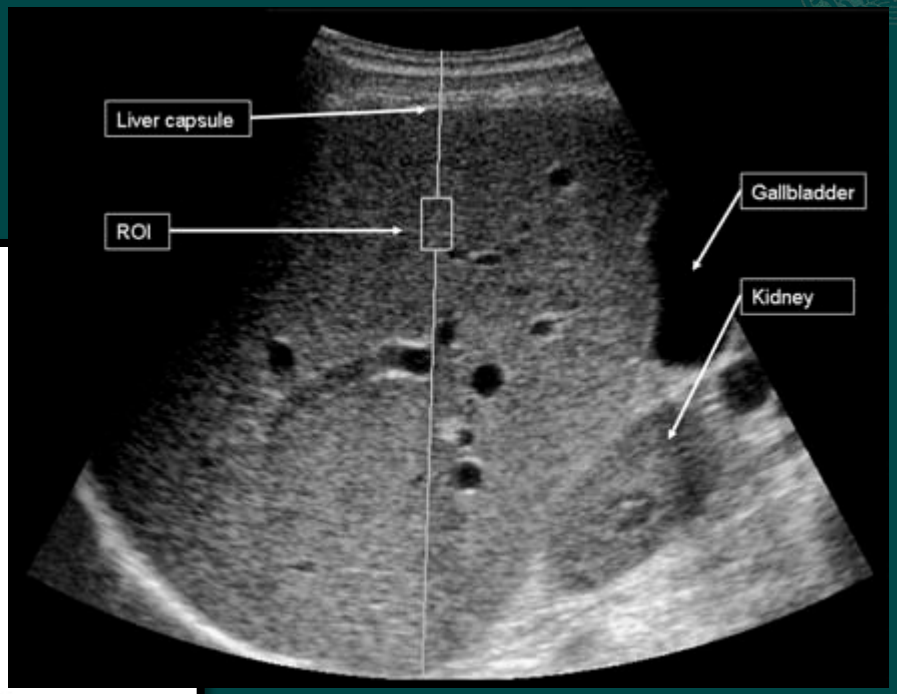


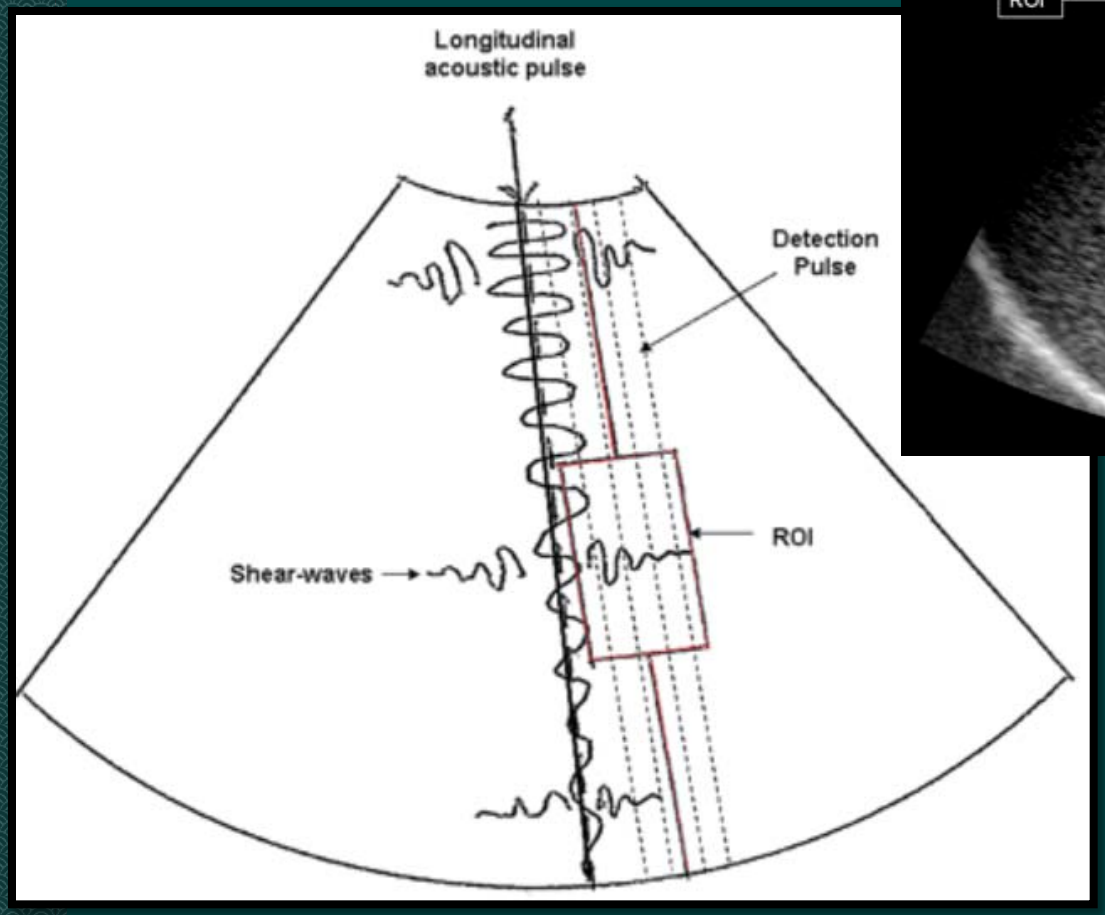
1) Hard tissue: faster shear wave

2) Soft tissue: slower shear wave



Acoustic Radiation Force Impulse (ARFI)

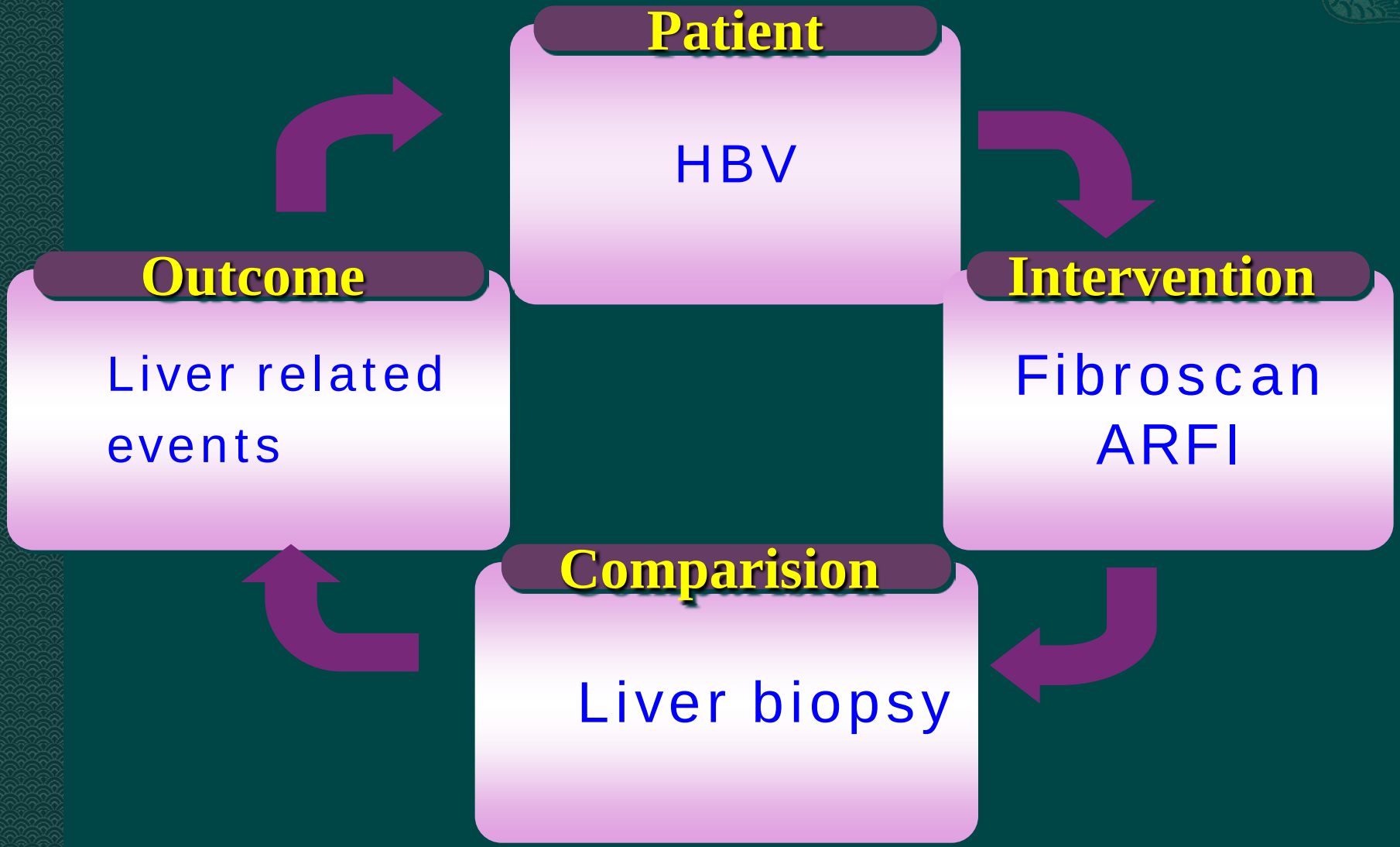




臨床情境分析 (Clinical Scenario)

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上
- Audit
  - 自我評估

Clinical Question



臨床情境分析 (Clinical Scenario)

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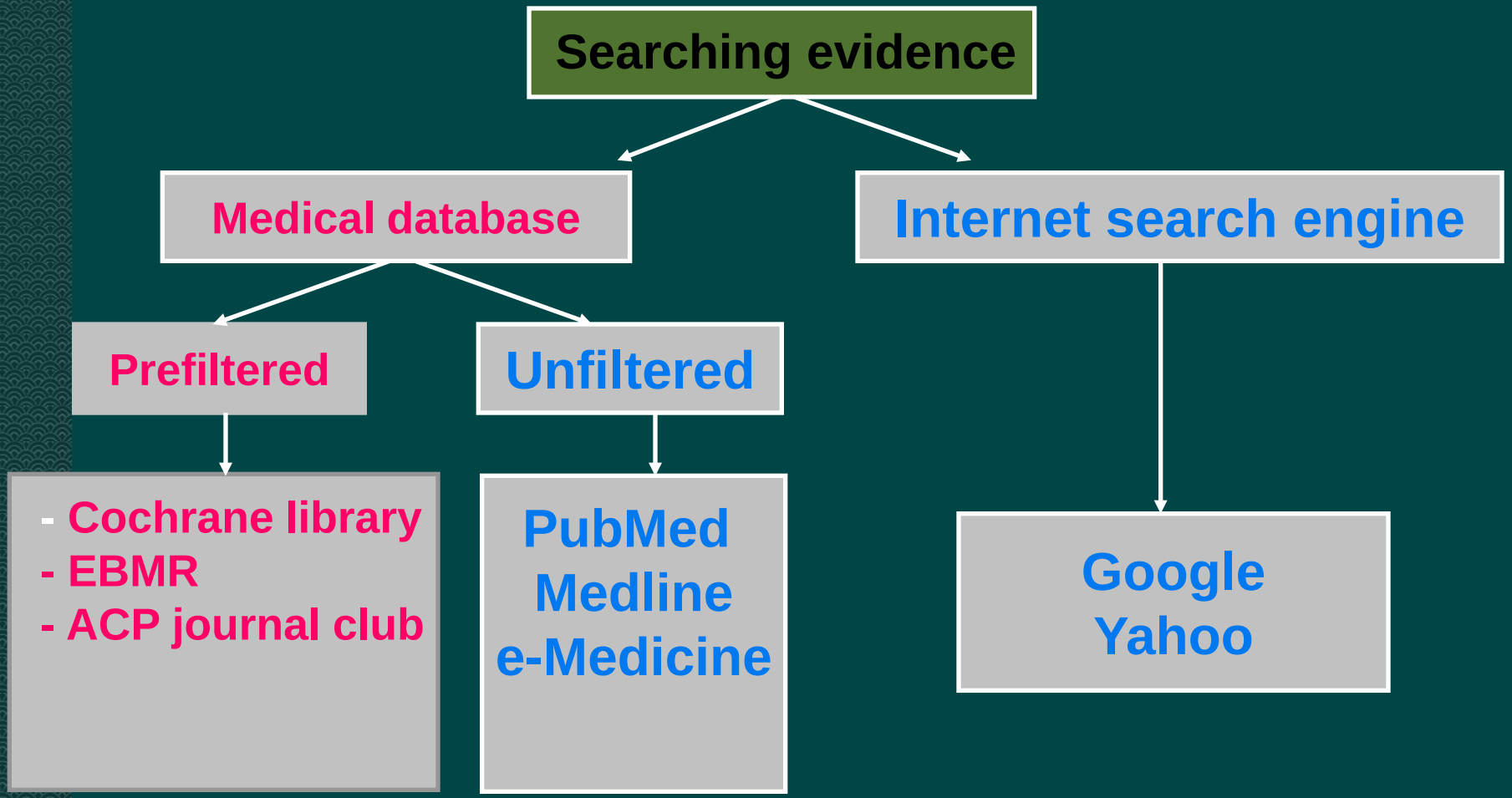
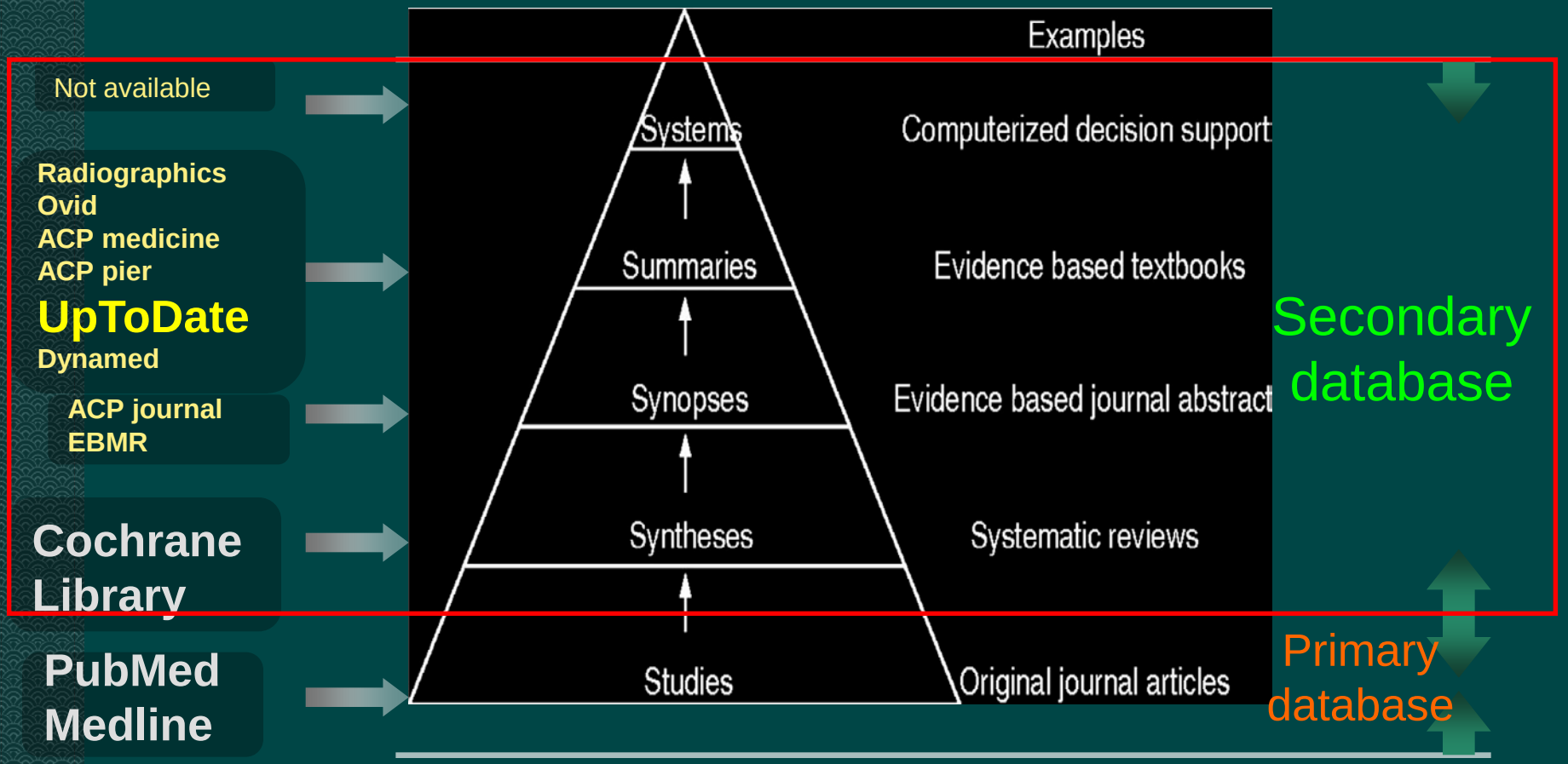
Database


Searching evidence
Medical database
Internet search engine
Prefiltered
Unfiltered
- Cochrane library
- EBMR
- ACP journal club
PubMed
Medline
e-Medicine
Google
Yahoo

The "5S" levels



Key Word

HBV, Cirrohosis, elastography

Cochrane library	0/0
Up to date	1/1
Medline	3/44

Noninvasive assessment of hepatic fibrosis

- Result
  - Cirrhosis: Sensitivity:87%, Specificity:91%
  - Stages II-IV fibrosis: Sensitivity:70%, Specificity:84%

(Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis; Clin Gastroenterol Hepatol. 2007;5(10):1214.)

  - Limitation: ascites, elevated central venous pressure (such as heart failure), BMI > 28-30

Noninvasive assessment of hepatic fibrosis

- Controversial point
  - Hepatic inflammation & steatosis → ↓ accuracy rate.
  - Serum AST <100 U/L → ↑ accuracy rate.
  - Alcoholic cirrhosis: ↑ accuracy by using nonstandard cutoff values

(F3 fibrosis:17 kPa; F4 fibrosis: 21.1 kPa)

PubMed.gov

Prediction of Liver-Related Events Using Fibroscan in Chronic Hepatitis B Patients Showing Advanced Liver Fibrosis

Seung Up Kim[1,2,5☯], Ji Hoon Lee[1☯], Do Young Kim[1,2,5], Sang Hoon Ahn[1,2,5,6], Kyu Sik Jung[1], Eun Hee Choi[3], Young Nyun Park[4,6], Kwang-Hyub Han[1,2,5,6], Chae Yoon Chon[1,2,5], Jun Yong Park[1,2,5*]

1 Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, **2** Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea, **3** Department of Biostatistics, Yonsei University College of Medicine, Seoul, Korea, **4** Department of Pathology, Yonsei University College of Medicine, Seoul, Korea, **5** Liver Cirrhosis Clinical Research Center, Seoul, Korea, **6** Brain Korea 21 Project of Medical Science, Seoul, Korea

- Liver stiffness measurement as a useful predictor of liver related events development in CHB patients with advanced liver fibrosis.

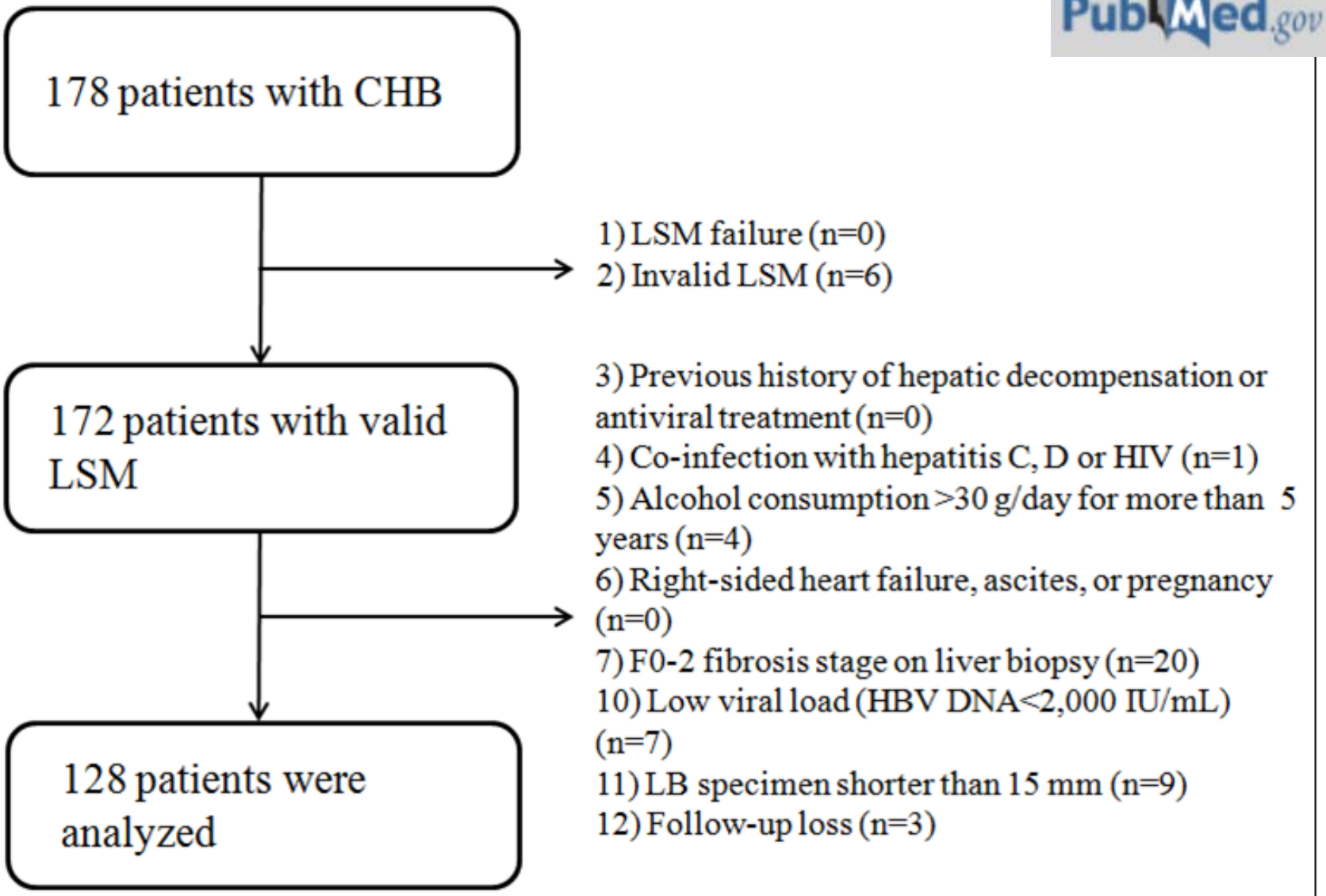
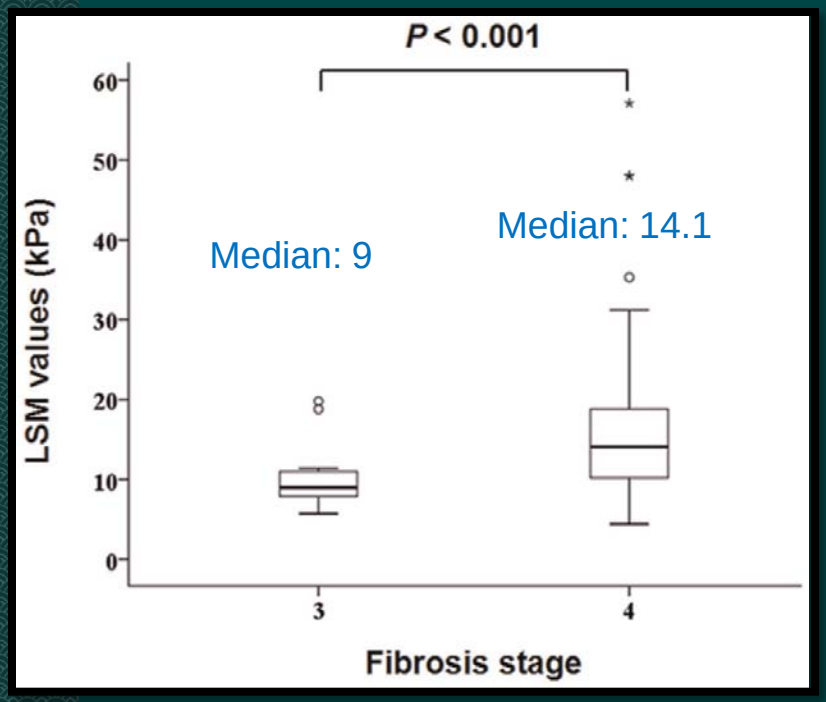
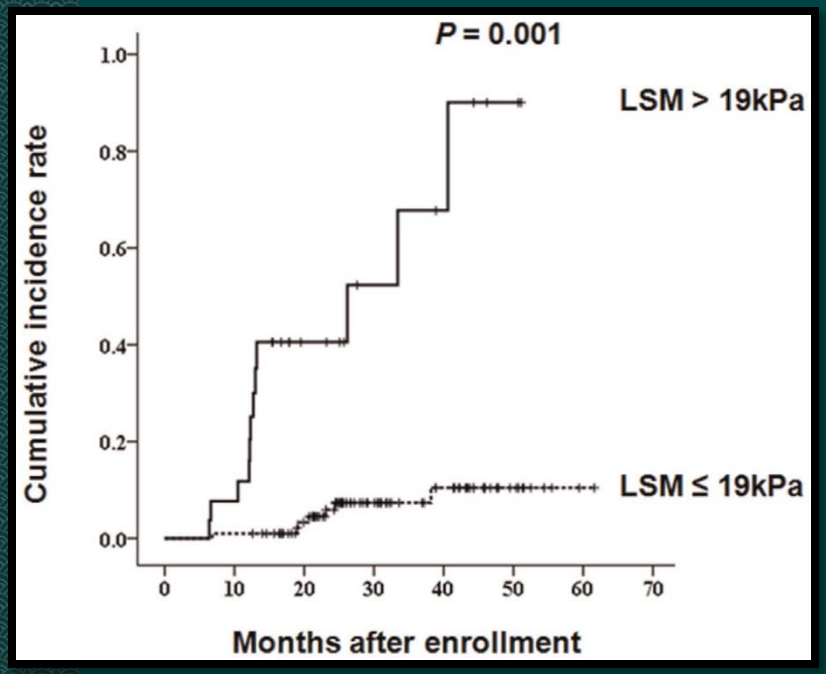

178 patients with CHB
1) LSM failure (n=0)
2) Invalid LSM (n=6)
172 patients with valid LSM
3) Previous history of hepatic decompensation or antiviral treatment (n=0)
4) Co-infection with hepatitis C, D or HIV (n=1)
5) Alcohol consumption >30 g/day for more than 5 years (n=4)
6) Right-sided heart failure, ascites, or pregnancy (n=0)
7) F0-2 fibrosis stage on liver biopsy (n=20)
10) Low viral load (HBV DNA<2,000 IU/mL) (n=7)
11) LB specimen shorter than 15 mm (n=9)
12) Follow-up loss (n=3)
128 patients were analyzed

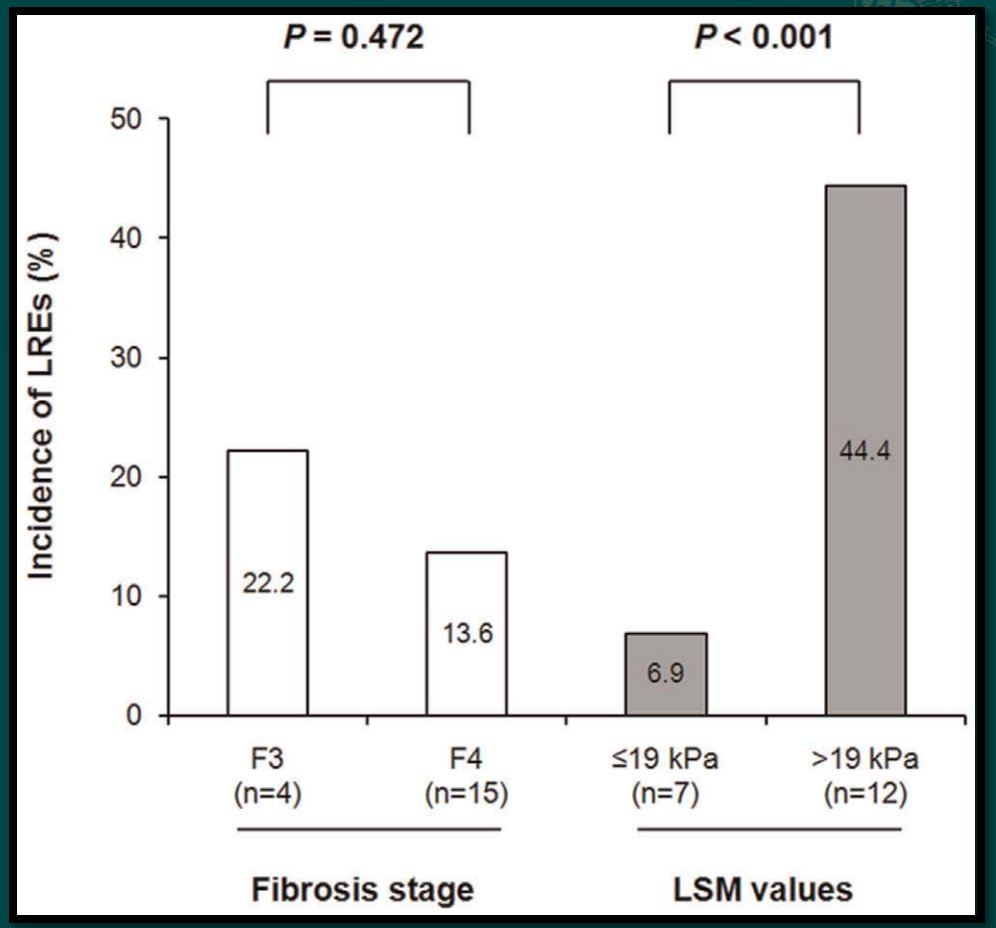
Table 1. Baseline Characteristics (n = 128).

Variables	Values
Demographic data	
Age (years)	52.2±9.3
Male	72 (56.3)
Diabetes mellitus	11 (8.6)
Body mass index (kg/m^2)	24.0±2.9
Laboratory data	
Serum albumin (g/dL)	4.2±0.5
Total bilirubin (mg/dL)	0.8±0.3
Alanine aminotransferase (IU/L)	44.4±21.6
Prothrombin time (%)	90.9±9.8
Platelet count (10^9/L)	148.5±48.4
Alpha-fetoprotein (ng/mL)	4.7 (0.8–50.6)
Histological data	
Fibrosis stage, 3/4	18 (14.1)/110 (85.9)
Activity grade, 1–2/3–4	97 (75.8)/31 (24.2)
Liver stiffness measurement	
LSM values (kPa)	12.9 (4.4–57.1)
Success rate (%)	100 (63–100)
Interquartile range/median value (kPa)	0.15 (0.01–0.30)
Antiviral agent	
Lamivudine	49 (38.3)
Entecavir	79 (61.7)

Variables are expressed as mean ± SD, median (range), or n (%).
HBeAg, hepatitis B e antigen; LSM, liver stiffness measurement; kPa, kilopascal.


P < 0.001
LSM values (kPa)
Median: 9
Median: 14.1
Fibrosis stage


P = 0.001
LSM > 19kPa
LSM ≤ 19kPa
Cumulative incidence rate
Months after enrollment


P = 0.472
P < 0.001
Incidence of LREs (%)
22.2
13.6
6.9
44.4
F3 (n=4)
F4 (n=15)
≤19 kPa (n=7)
>19 kPa (n=12)
Fibrosis stage
LSM values

World Journal of Gastroenterology

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doi:10.3748/wjg.v18.i10.1077

World J Gastroenterol 2012 March 14; 18(10): 1077-1084
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

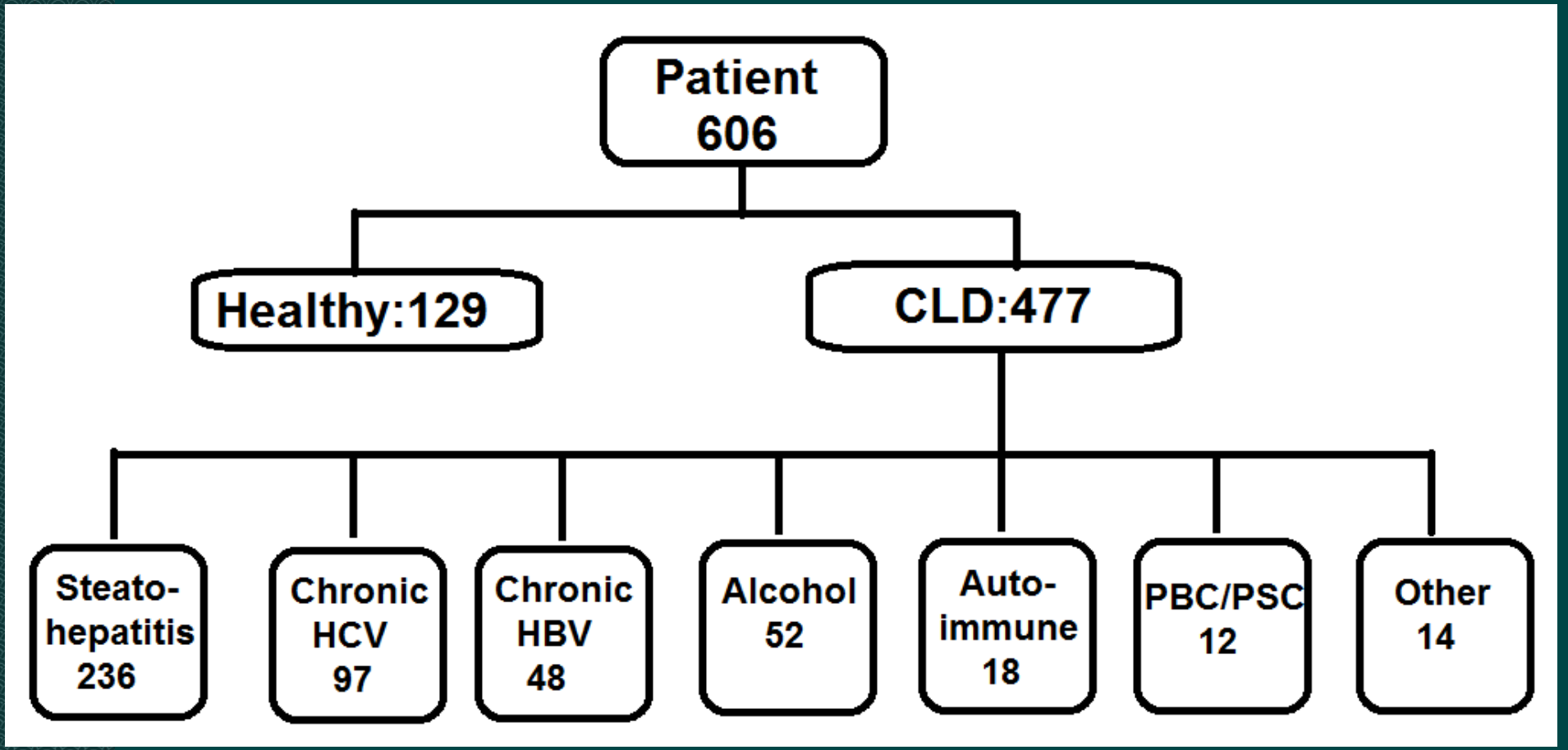
BRIEF ARTICLE

Evaluation of acoustic radiation force impulse imaging for determination of liver stiffness using transient elastography as a reference

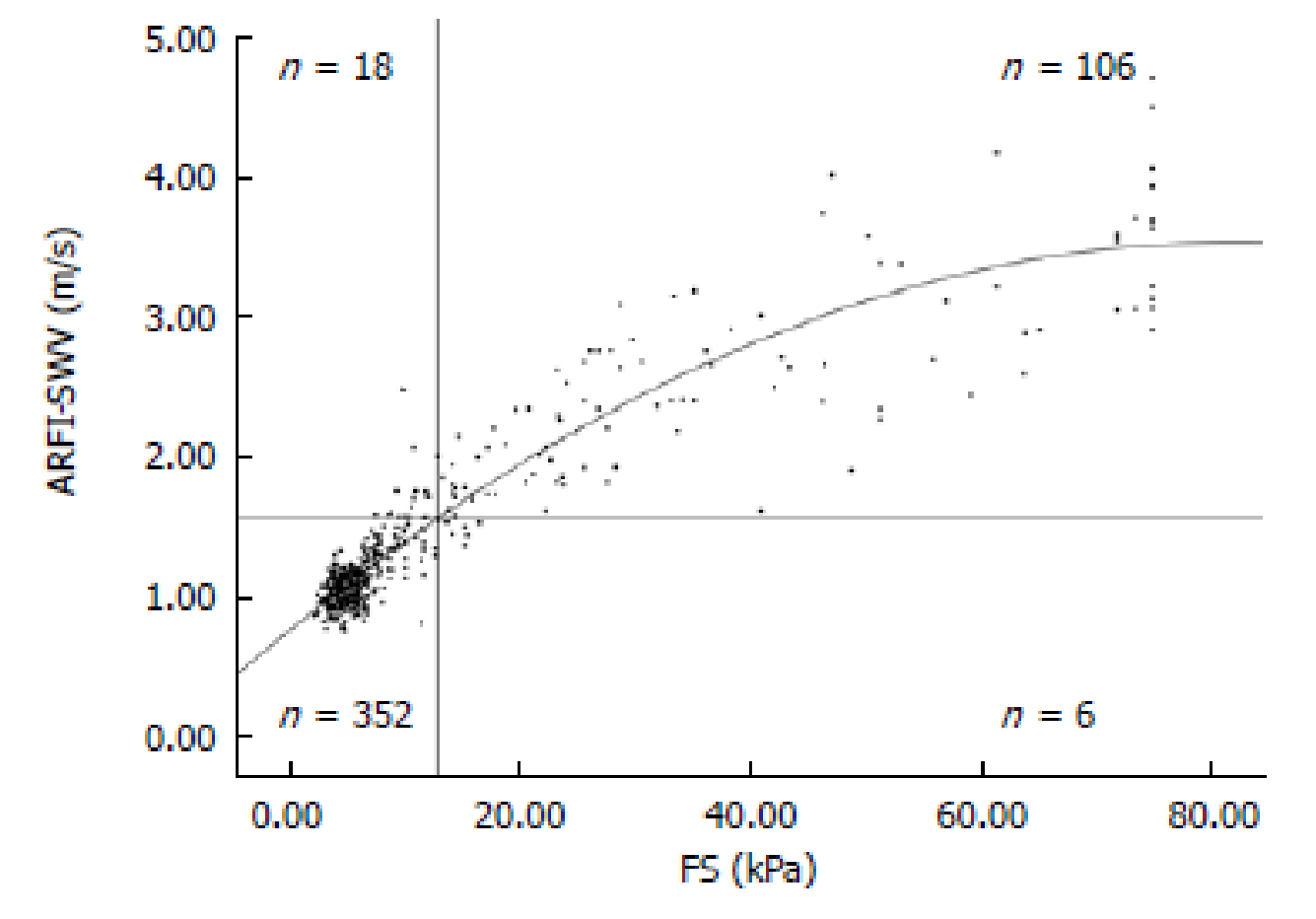
Gerald Kircheis, Abdurrahman Sagir, Christoph Vogt, Stephan vom Dahl, Ralf Kubitz, Dieter Häussinger

- ARFI-SWV correlated significantly with FS-LS.
- ARFI is the visual control by B-mode sonography and the variable depth of the measurement.

Basic data

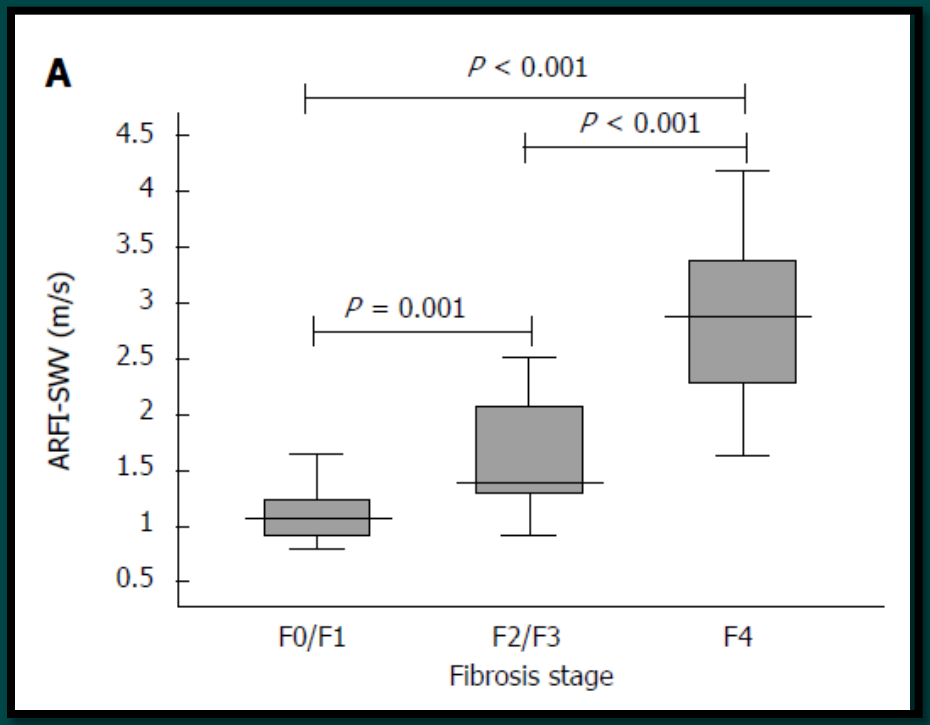

Patient
606
Healthy:129
CLD:477
Steato-hepatitis 236
Chronic HCV 97
Chronic HBV 48
Alcohol 52
Auto-immune 18
PBC/PSC 12
Other 14

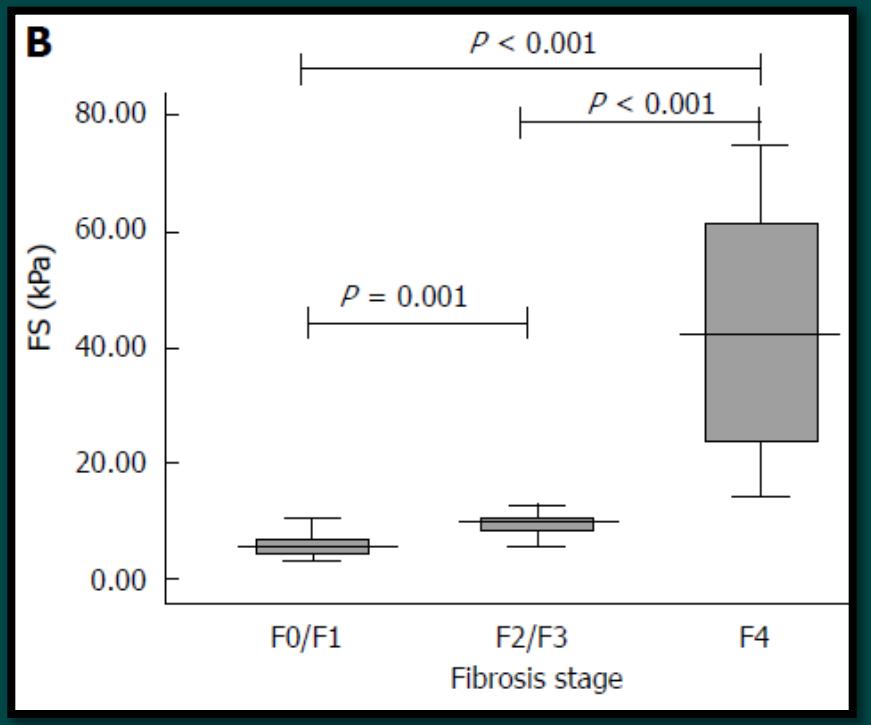
Result



ARFI significantly correlated with FibroScan

Result


A
P < 0.001
P < 0.001
P = 0.001
ARFI-SWV (m/s)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
F0/F1
F2/F3
F4
Fibrosis stage


B
P < 0.001
P < 0.001
P = 0.001
FS (kPa)
80.00
60.00
40.00
20.00
0.00
F0/F1
F2/F3
F4
Fibrosis stage

Result

Table 2 Diagnostic accuracy of acoustic radiation force impulse imaging shear wave velocity and liver stiffness measured by transient elastography

	AUROC	Cut-off	PPV	NPV	Sensitivity (%)	Specificity (%)
Comparison to all patients [ARFI-SWV (n = 482)]						
FS < 7.6 kPa	0.969	1.29 m/s	0.93	0.90	91.4	92.6
FS > 13.0 kPa	0.991	1.60 m/s	0.85	0.98	92.3	96.5
Comparison with liver biopsy [ARFI-SWV (n = 68) and FS-LS (n = 59)]						
Non significant liver fibrosis						
ARFI-SWV (n = 23)	0.929	1.32 m/s	0.83	0.91	87.0	80.0
FS-LS (n = 20)	0.920	7.6 kPa	0.85	0.95	94.9	85.0
Liver cirrhosis						
ARFI-SWV (n = 28)	0.934	1.62 m/s	1.0	0.85	100	85.7
FS-LS (n = 24)	0.958	13.0 kPa	1.0	0.91	100	91.4

AUROC: Area under the receiver operating characteristic curves; CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value; ARFI-SWV: Acoustic radiation force impulse imaging shear wave velocity; FS-LS: Liver stiffness measured by transient elastography.

PubMed.gov

Research Article

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

ARFI, FibroScan®, ELF, and their combinations in the assessment of liver fibrosis: A prospective study

Gonzalo Crespo[1], Guillermo Fernández-Varo[2], Zoe Mariño[1], Gregori Casals[2], Rosa Miquel[3], Stella M. Martínez[1], Rosa Gilabert[4], Xavier Forns[1], Wladimiro Jiménez[2,5], Miquel Navasa[1,*]

[1]*Liver Unit, Hospital Clínic, CIBERehd, IDIBAPS, Barcelona, Spain;* [2]*Department of Biochemistry and Molecular Genetics, Hospital Clínic, CIBERehd, IDIBAPS, Barcelona, Spain;* [3]*Department of Pathology, Hospital Clínic, CIBERehd, IDIBAPS, Barcelona, Spain;* [4]*Department of Radiology, Hospital Clínic, CIBERehd, IDIBAPS, Barcelona, Spain;* [5]*Department of Physiology, University of Barcelona, CIBERehd, IDIBAPS, Barcelona, Spain*

ARFI is as effective as either FibroScan or ELF in the non-invasive assessment of liver fibrosis

Table 1. Baseline characteristics of the patients included in the study. Qualitative variables are shown in n (%) and quantitative variables in median (range).

	Non-transplant (n = 59)	Transplant (n = 87)	*p* value
Age (yr)	48 (20-73)	60 (35-76)	0.001
Gender (male)	30 (51)	60 (69)	0.027
Etiology			0.001
HCV	24 (41)	63 (72)	
NASH	8 (14)	2 (2)	
OH	4 (7)	11 (13)	
Cholestatic disease	7 (12)	2 (2)	
HBV	2 (3)	8 (9)	
Others	14 (23)	1 (1)	
BMI (kg/m^2)	25.1 (18.5-44.4)	25.8 (19.3-39.4)	0.32
Abdominal perimeter, cm	90 (65-125)	94 (67-130)	0.1
Transjugular biopsies, number	15 (27)	27 (31)	0.46
Biopsy length, mm	19 (15-40)	20 (15-32)	0.66
Portal tracts, number	9 (6-20)	9 (6-16)	0.89
Time from transplant, mo	n.a.	43 (6-250)	
ALT (IU/ml)	65 (10-768)	62 (9-501)	
Fibrosis stage			
F ≥2	33 (56)	37 (42)	0.1
F4	15 (25)	9 (10)	0.016

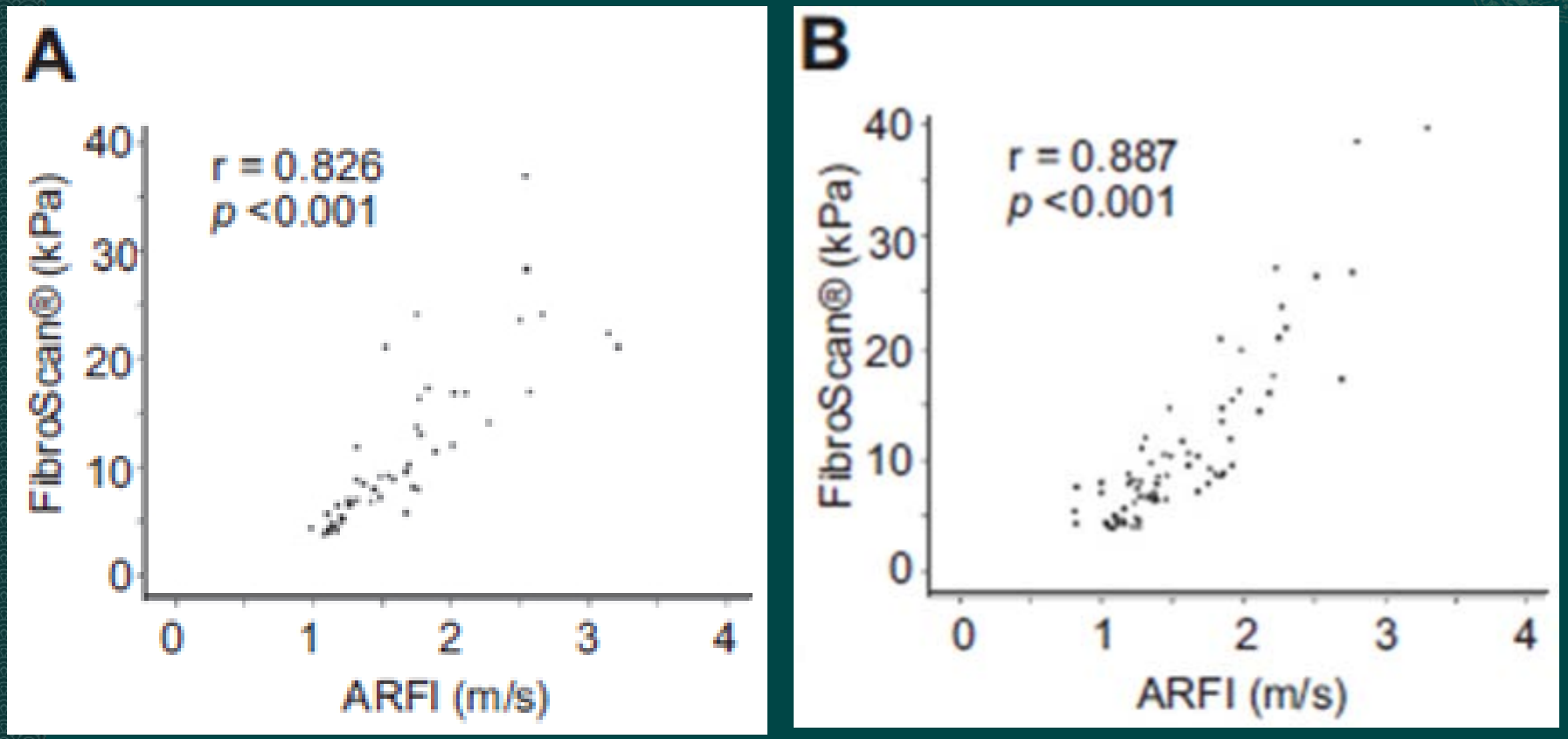
HCV, hepatitis C virus; NASH, non-alcoholic steatohepatitits; OH, alcoholic liver disease; HBV, hepatitis B virus; BMI, body mass index; ALT, alanine aminotransferase.

Exclusion Criteria(29/146)

- Ascites
- Chronic kidney failure
- Acute or chronic graft rejection
- Biopsies < 15 mm ;< six portal tracts.

Non-transplant

Transplant



ARFI significantly correlated with FibroScan in non-transplant patients as well as in transplant recipients

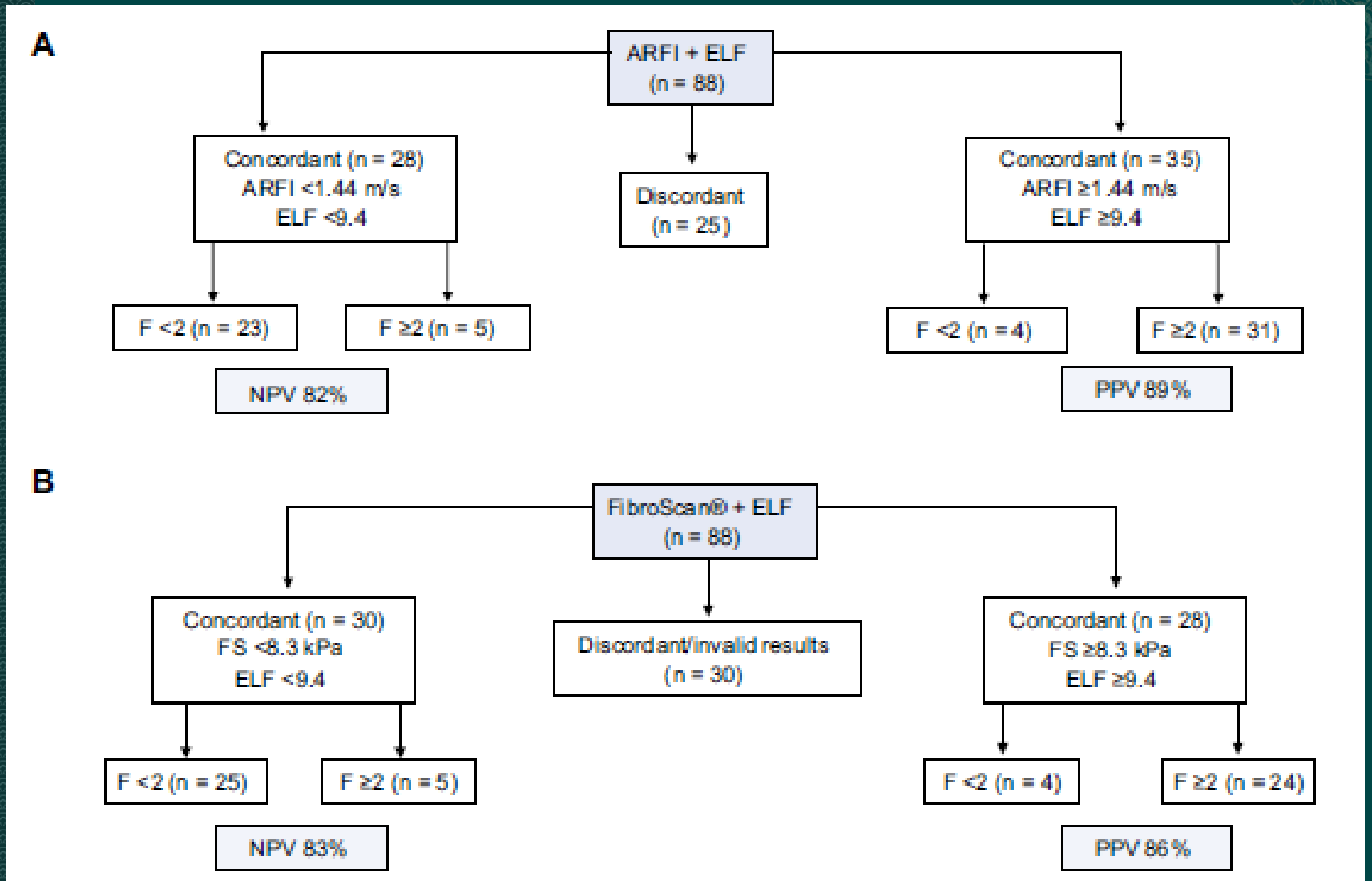

A
ARFI + ELF
(n = 88)
Concordant (n = 28)
ARFI <1.44 m/s
ELF <9.4
Discordant
(n = 25)
Concordant (n = 35)
ARFI ≥1.44 m/s
ELF ≥9.4
F <2 (n = 23)
F ≥2 (n = 5)
F <2 (n = 4)
F ≥2 (n = 31)
NPV 82%
PPV 89%
B
FibroScan® + ELF
(n = 88)
Concordant (n = 30)
FS <8.3 kPa
ELF <9.4
Discordant/invalid results
(n = 30)
Concordant (n = 28)
FS ≥8.3 kPa
ELF ≥9.4
F <2 (n = 25)
F ≥2 (n = 5)
F <2 (n = 4)
F ≥2 (n = 24)
NPV 83%
PPV 86%

Table 2. Diagnostic performance of ARFI, FibroScan® and ELF for the diagnosis of F ⩾2 and cirrhosis.

Non-transplant, (n = 59)	Cut-off for F ≥2	Se (%)	Sp (%	PPV (%)	NPV (%)	LR+	LR-	DOR
ARFI	1.43 m/s	88	73	81	83	3.26	0.16	20.4
FibroScan®	8.25 kPa	85	81	81	84	4.47	0.19	23.5
ELF	9.3	79	77	81	74	3.43	0.27	12.7
	Cut-off for F4							
ARFI	2.05 m/s	93	95	87	98	18.6	0.07	265.7
FibroScan®	16.5 kPa	87	89	59	97	7.91	0.15	54.7
ELF	10.4	93	79	61	97	4.43	0.09	49.2
Transplant, (n = 87)	Cut-off for F ≥2	Se (%)	Sp (%	PPV (%)	NPV (%)	LR+	LR-	DOR
ARFI	1.39 m/s	89	80	77	91	4.45	0.14	31.8
FibroScan®	8.4 kPa	82	80	76	86	4.1	0.22	18.6
ELF	9.4	86	56	59	85	1.95	0.25	7.8
	Cut-off for F4							
ARFI	1.92 m/s	89	90	50	99	8.9	0.12	74.1
FibroScan®	15.1 kPa	87	89	47	99	7.91	0.15	52.7
ELF	10.3	78	72	24	96	2.78	0.3	9.3

Se, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; LR+, likelihood ratio positive; LR−, likelihood ratio negative; DOR, diagnostic odds ratio.

EBM的步驟

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- **Appraisal**
  - **嚴格評讀文獻**
- Apply
  - 是否可應用到病人身上
- Audit
  - 自我評估

Appraisal--VIP

- Validity
  - 可信度(效度)
- Impact (Importance)
  - 影響程度
- Practice
  - 臨床可使用性

Validity

- Same site(intercostal), the skin to liver capsule <2cm, same days

Limit:

- 1. Success rate>60%
- 2. Different standard values in different liver disease, species. (Selection bias)

(Ex: non-alcohol steatohepatitis: lower cutoff value)

Conclusion

- Liver stiffness measurement as a useful predictor of liver related events development in CHB patients with advanced liver fibrosis.
- ARFI-SWV correlated significantly with FS-LS.
- ARFI-SWV has higher success rate compared to fibroscan

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這個檢查在我們的診療環境是否合理？

■是	□否	□ 不清楚
評論： • 是否有這個自費項目 → NO(高長) • 是否容易取得 → No(未來) • 是否符合經濟效益(花費不會太高) → ？ => 自費		

我們的病人從檢查中得到什麼好處或壞處？

評論：

- **Benefit:**
  - **Physical: 避免biopsy的併發症**
  - **Psychological: 減輕病人心中焦慮**
  - **Economical: 降低感染率、併發症、入院率**
- **Harms:**
  - **Radiation dose: Nil**

可以給病人的建議為何？

評論：

對於B型肝炎患者，可以在第一次做肝切片前，先做**fibroscan** 或 **ARFI** 當作基準值，之後可用此基準值來做追蹤。

EBM的步驟

- Asking
  - 將病人的問題寫成PICO
- Acquire
  - 找資料來回答問題
- Appraisal
  - 嚴格評讀文獻
- Apply
  - 是否可應用到病人身上
- Audit
  - 自我評估

自我評估：結論

Step 1: Asking 1. 我有提出任何臨床問題嗎？ 2. 我提出的是結構完整的問題？	 有 是
Step 2: Acquire 1. 我知道在我的臨床領域中現有的最佳證據來源？ 2. 在搜尋方面我變得更有效率？	 是 是

Step 3: Appraisal 1.對我而言，應用此研究證據之評讀指引變得更簡單？ 2.我是否盡全力做評讀了？	 是 是
Step 4: Apply 1.我盡力將審慎評估之結果融入診療中？ 2.我是否將搜尋到的最佳證據應用到我的臨床工作中？	 是 是

Thank you for your attention