Ultralyd elastografi av lever

Grunnkurs i gastroenterologisk ultralyd 23.11.2021

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Hvorfor gjør vi elastografi av leveren?

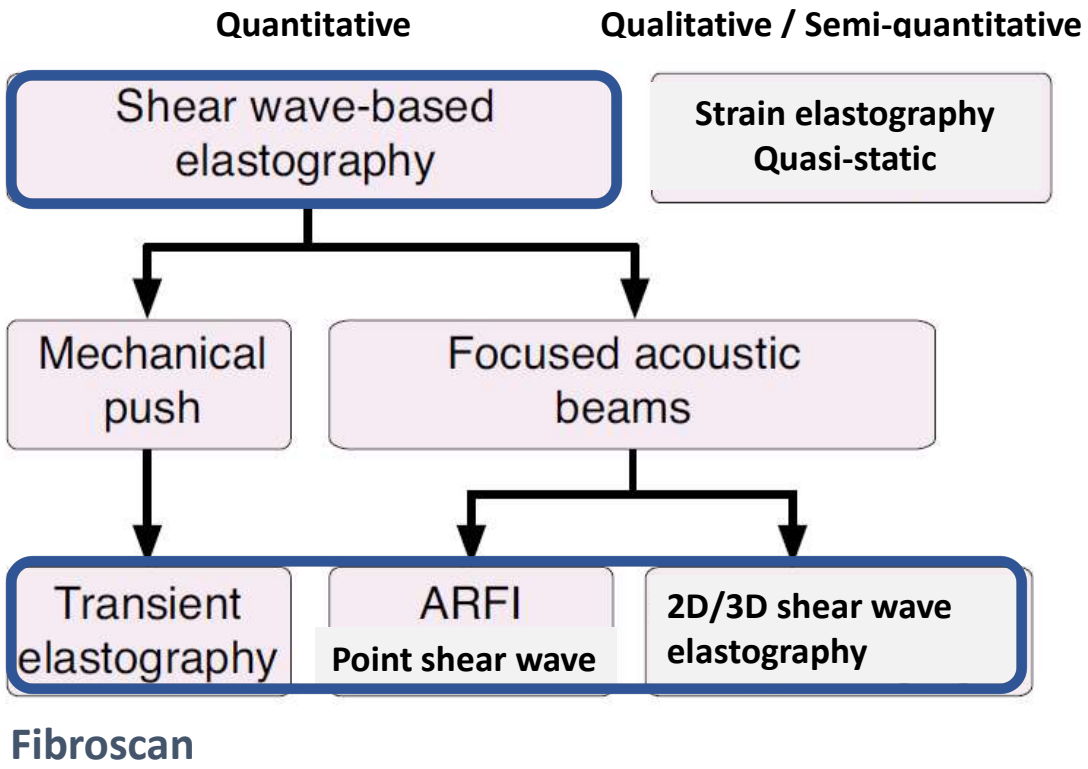
- Karakterisere lesjon i lever/andre organer
  - Harde tumores ofte maligne, myke ofte benigne
  - Lesjoner i bryst, thyroidea, pankreas, prostata

- **Elastografi av lever – «leverstivhetsmåling»**
  - Evaluere grad av fibrose / cirrhose
  - Endring i inflammasjon under behandling?

Agenda

- Ulike metoder
- Elastografi i praksis
- Cut-off-verdier
- Indikasjoner

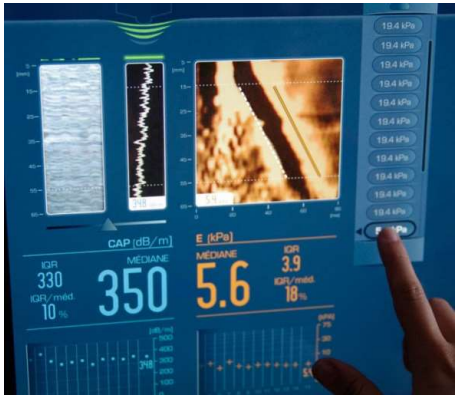
Ultralyd elastografi: Ulike metoder



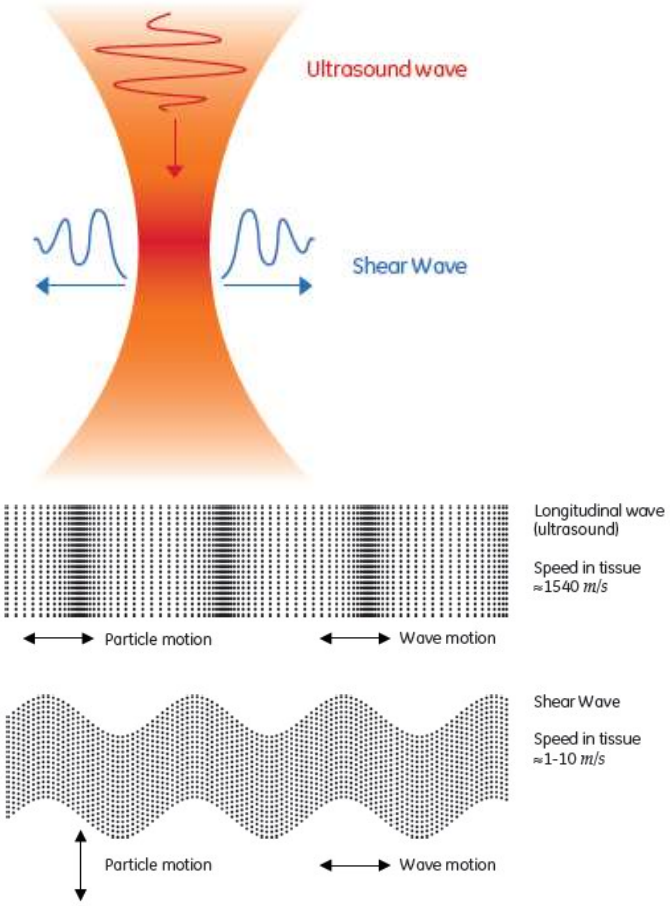
Transient elastografi (TE) – Fibroscan®

- Emitterer en **vibrasjonspuls**
- Måler skjærebølgehastighet
- Resultat oppgis i kPa (kalkulert)

- **Fordeler:**
  - Enkelt
  - Kvalitetssikring
  - **10 valide målinger**
  - **SR > 60 %** (success rate)
  - **IQR/M < 30 %** (v/median>7kPa)



Point/2D shear wave elastografi



En akustisk “push pulse” genererer lokalisert vevsforskyvning, såkalte skjærebølger

→ **shear waves**

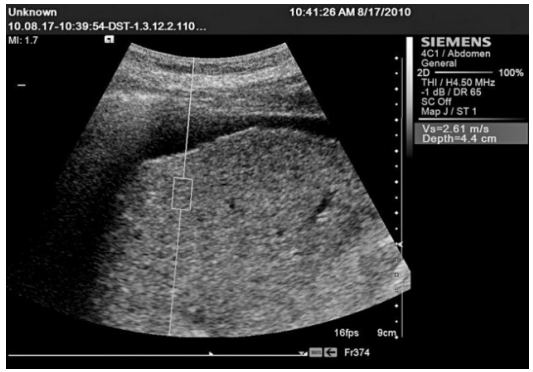
Måler skjærebølgehastigheten i **m/s**

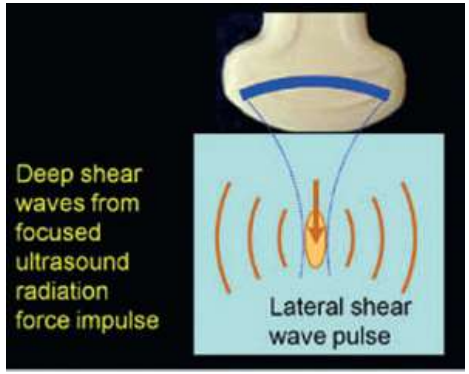
Resultat gis som m/s eller (kalkulert) **kPa**

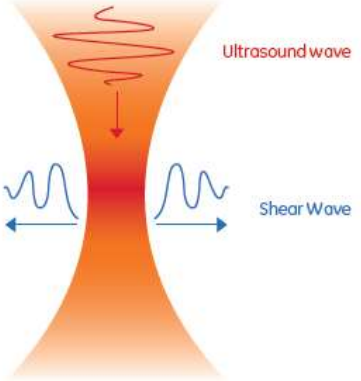
Stiv lever -> høy skjærebølgehastighet

Point/2D shear wave elastografi

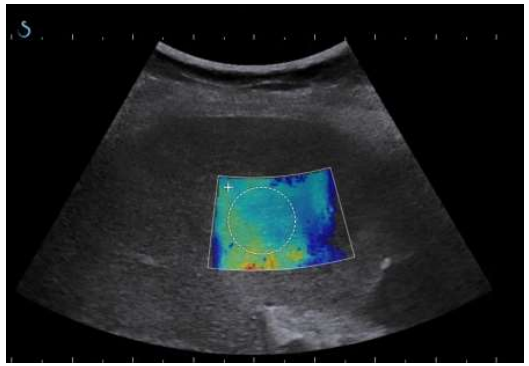
pSWE

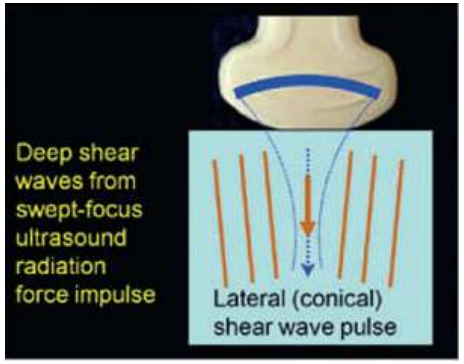


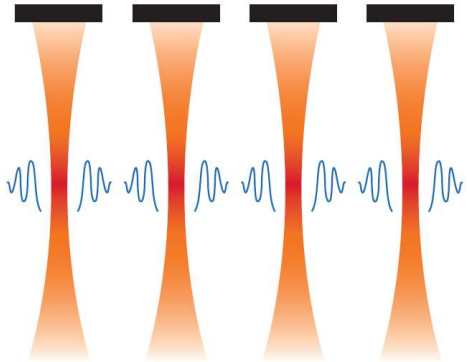




2D-SWE







Kvalitetsindikatorer

Adekvat B-mode-bilde
ROI ≥10 mm under kapsel, best ved 4-5 cm dybde

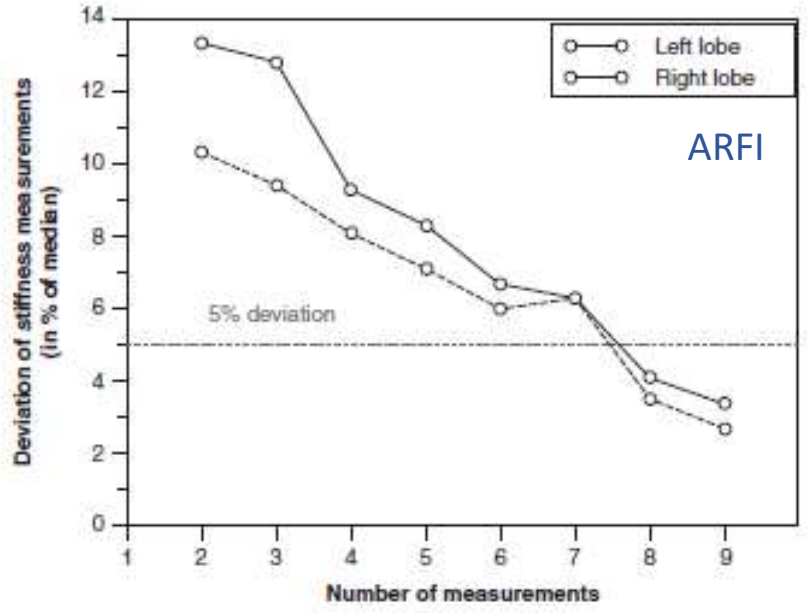
Median av 10 målinger
IQR/median ≤ 30%

Adekvat B-mode-bilde
Stabilt elastogram
ROI ≥10 mm under kapsel
Analyseboks ≥15 (10) mm

Median av 3-5 målinger (?)
Oppgi IQR

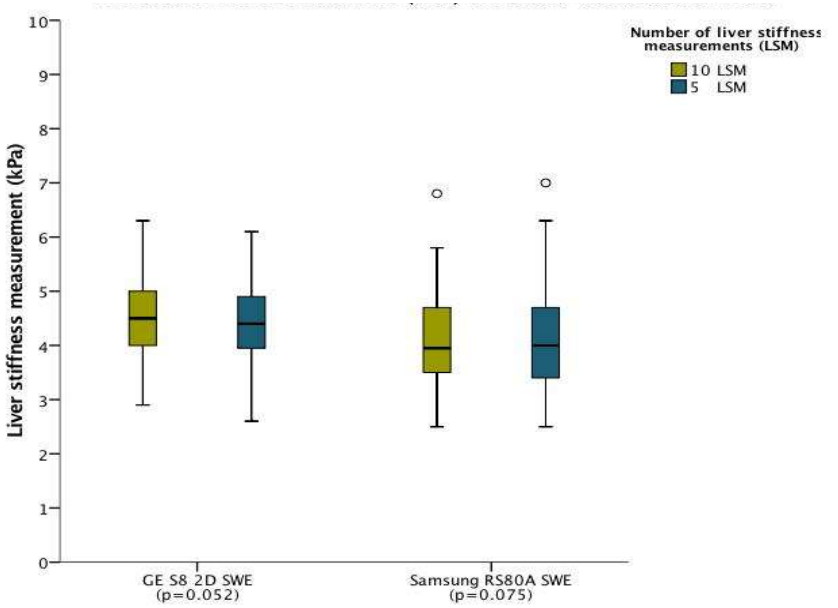
Kvalitetsindikatorer: Antall målinger

Medianverdi av 5 malinger: >8% avvik
Median av 8 malinger: <5% avvik



Karlas et al., Scand J Gastroenterol. 2011

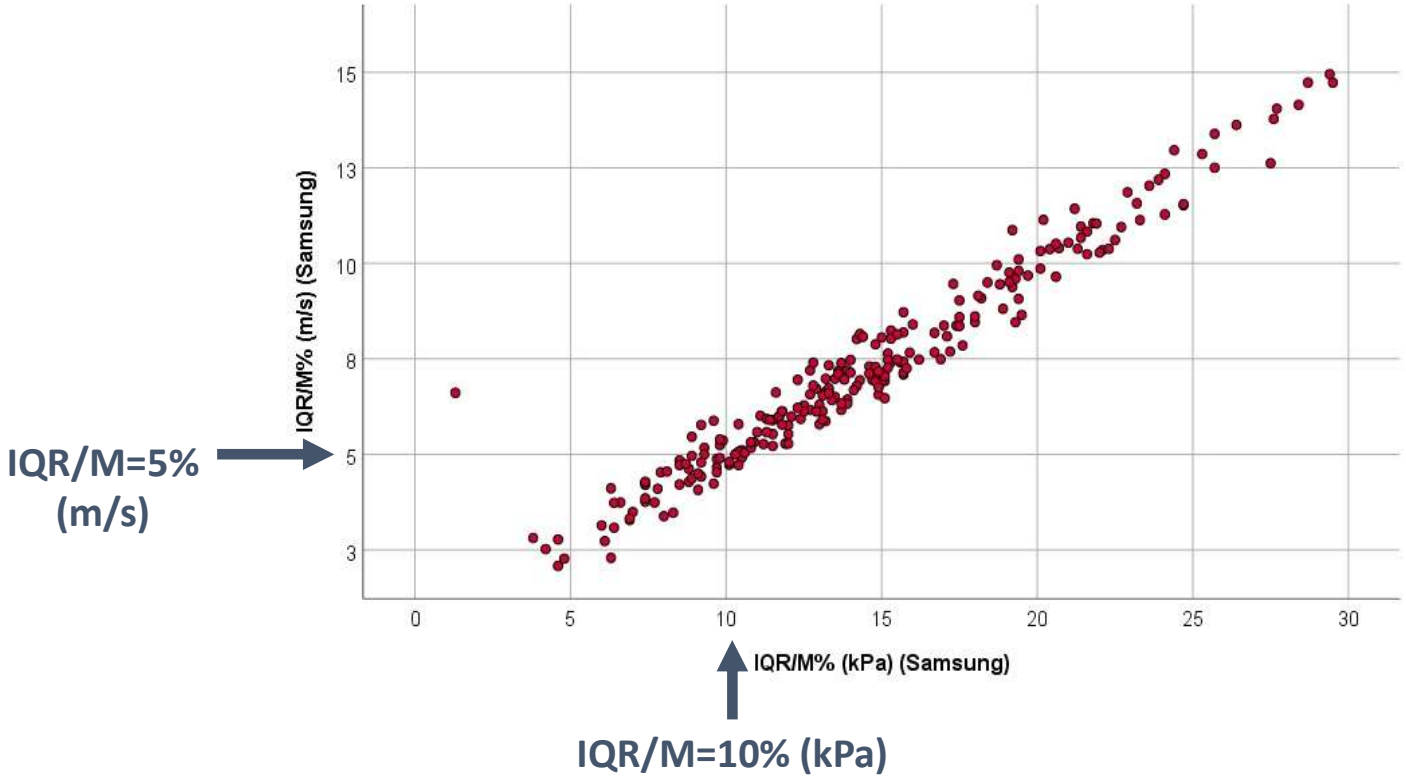
Ingen signifikant forskjell mellom 5 og 10 målinger for 2D- eller pSWE hos friske voksne



Mulabecirovic et al., PLOS one 2018

Spredningsmålet IQR/M (%)

IQR/M ≥ 30% gjelder for måleverdier i kPa – tilsv. måling i m/s gir halve IQR/M%



Shear wave velocity (SWV) is related to tissue elastic modulus (E) through:

$E = 3\rho(c)^2$

c = SWV

ρ = density (1000kg/m^3)

Mjelle et al.,

Agenda

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- Elastografi i praksis
- Cut-off-verdier
- Indikasjoner

Faktorer som påvirker leverstivhetsmålinger

- **Inflammasjon** (ALAT/ASAT > 5 x ULN)
- **Cholestase** ekstra-/ intrahepatisk, bilirubin
- **Høyre hjertesvikt**
- **Matinntak**

- Etiologi av leversykdommen (?)
- Kjønn – menn > kvinner (?)
- Rase – europeere > asiater
- BMI > 30 (usikre målinger?)

Utstyr (metode, plattform, probe)

Elastografi i praksis

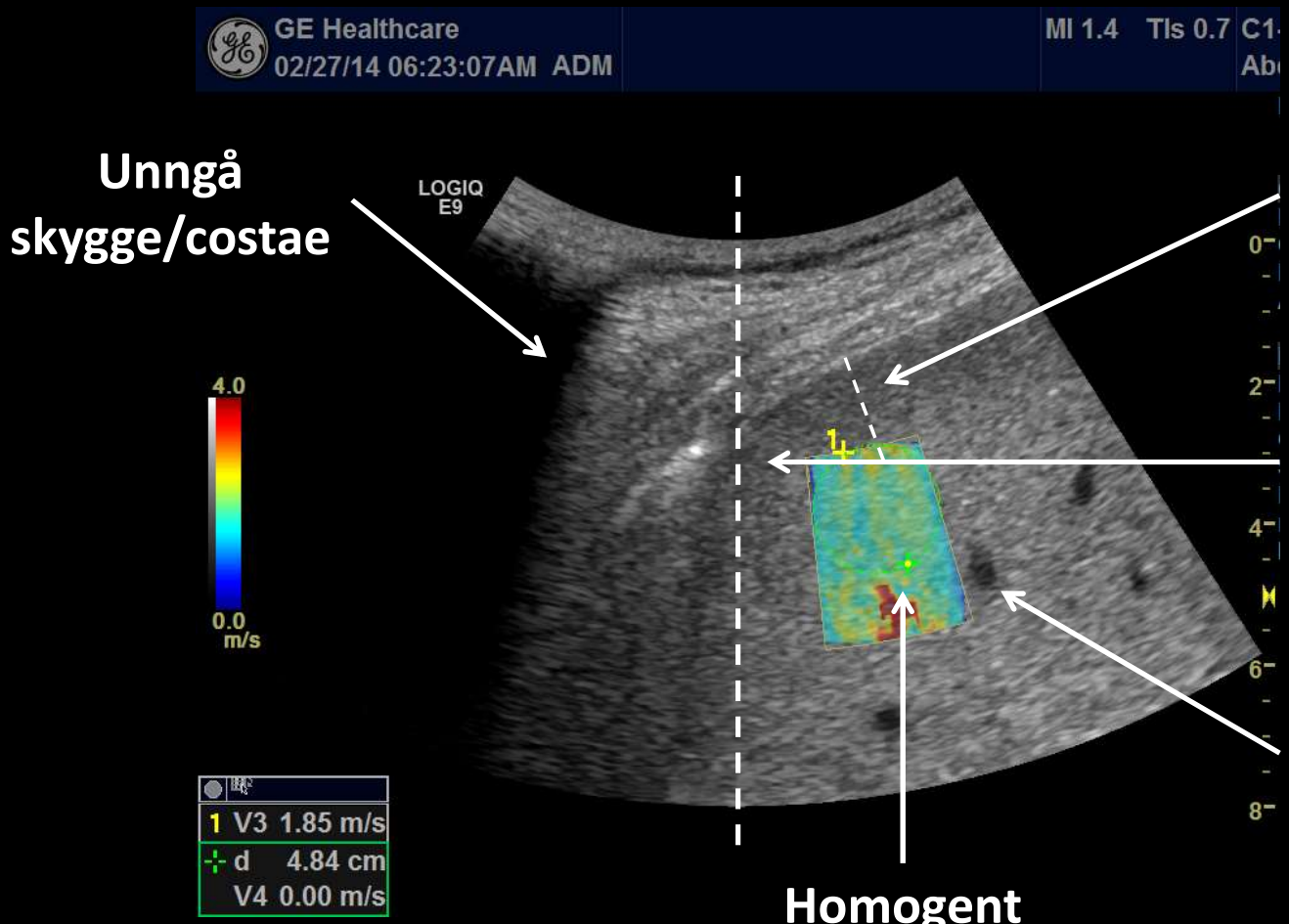
Kontrollere før undersøkelsen

- Fastende > 3 timer
- Cholestase/ikterus?
- Aktivt alkoholmisbruk/aktiv hepatitt?
- Høyresidig hjertesvikt (leverstuvning)?

Undersøkelsen

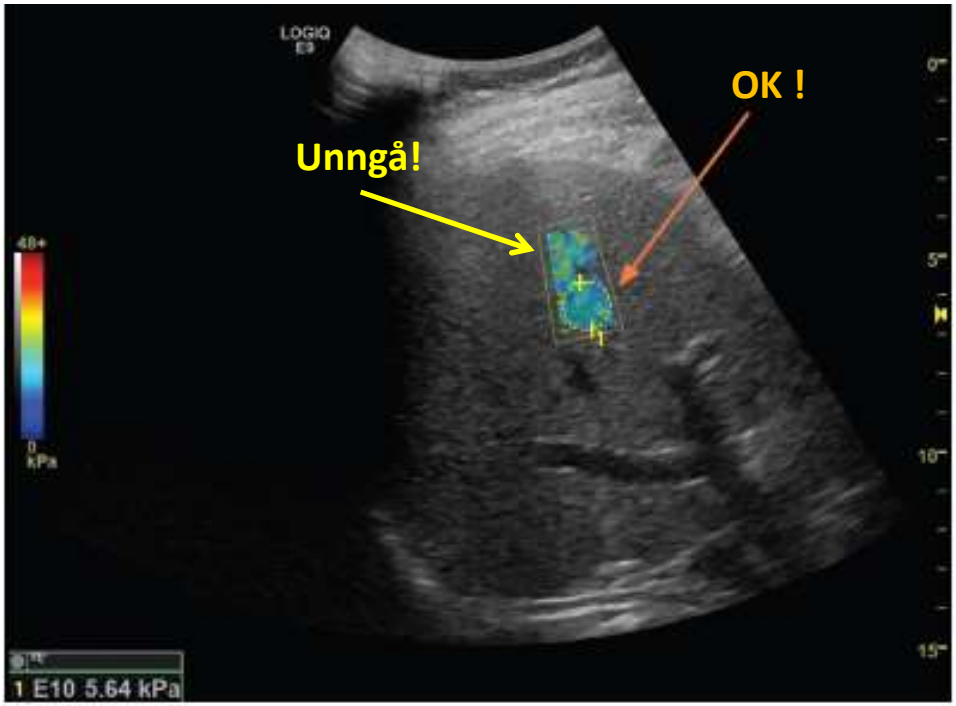
- Stabilt, lett trykk på proben
- Avslappet puste-stopp
- Intercostalt høyre flanke, flatt ryggleie
- Dybde > 1-2 cm fra leverkapsel
- Godt B-mode-bilde/elastogram

2D-SWE: Plasser ROI / elastogram riktig

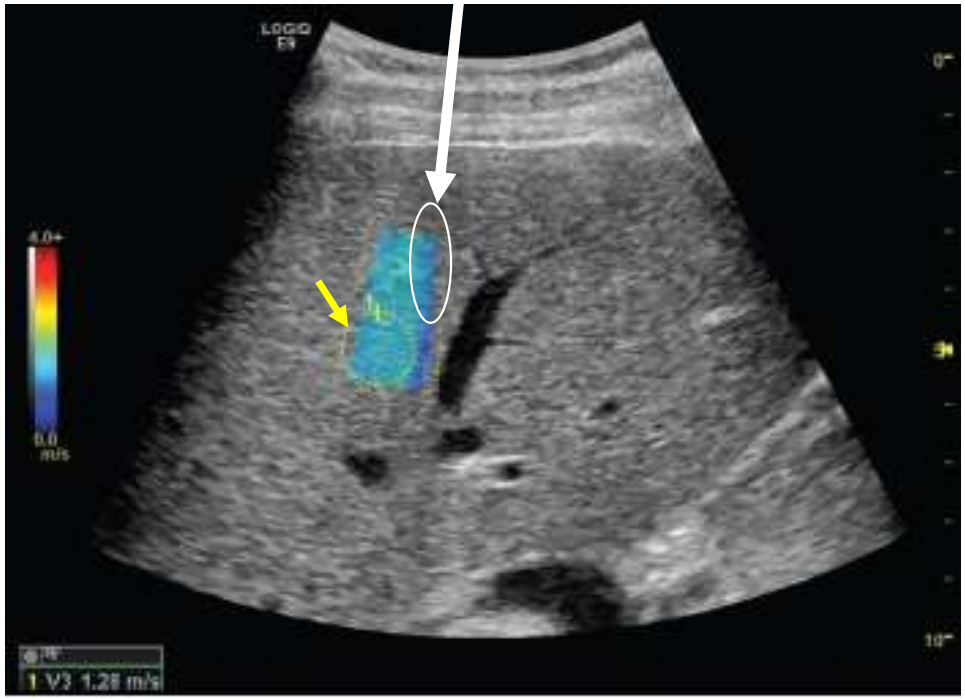


Plassering av ROI v/ 2D-shear wave elastografi

Plasser ROI i område med homogen farge – heterogen: dårlig kontakt??

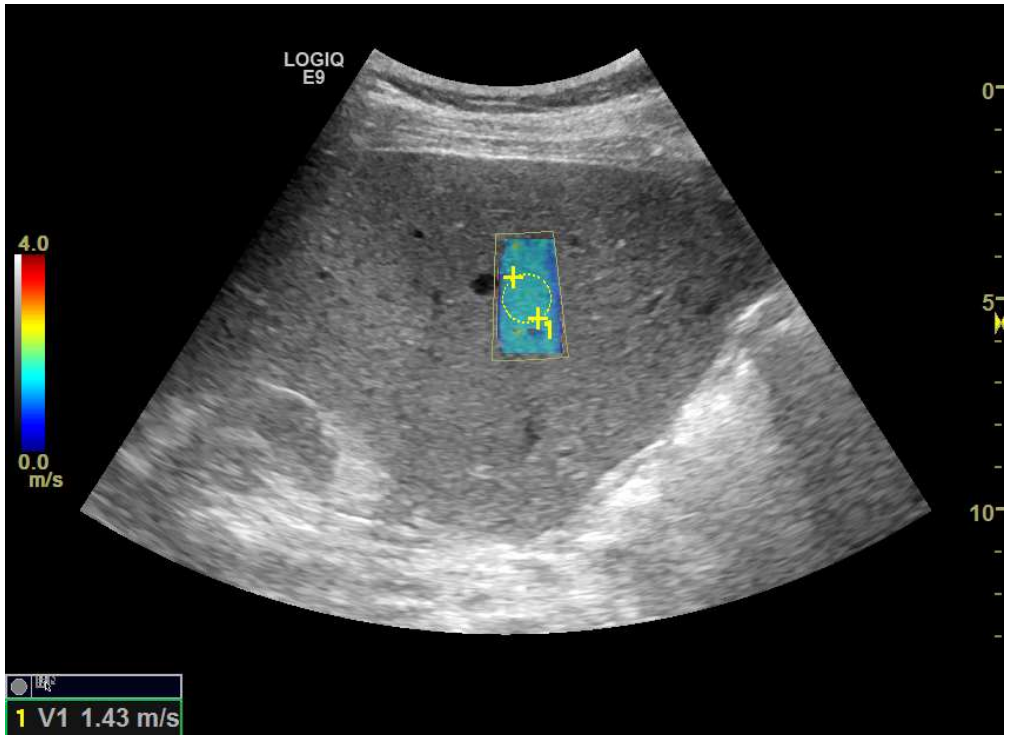


Unngå områder med vertikale linjer (bevegelsesartefakt)

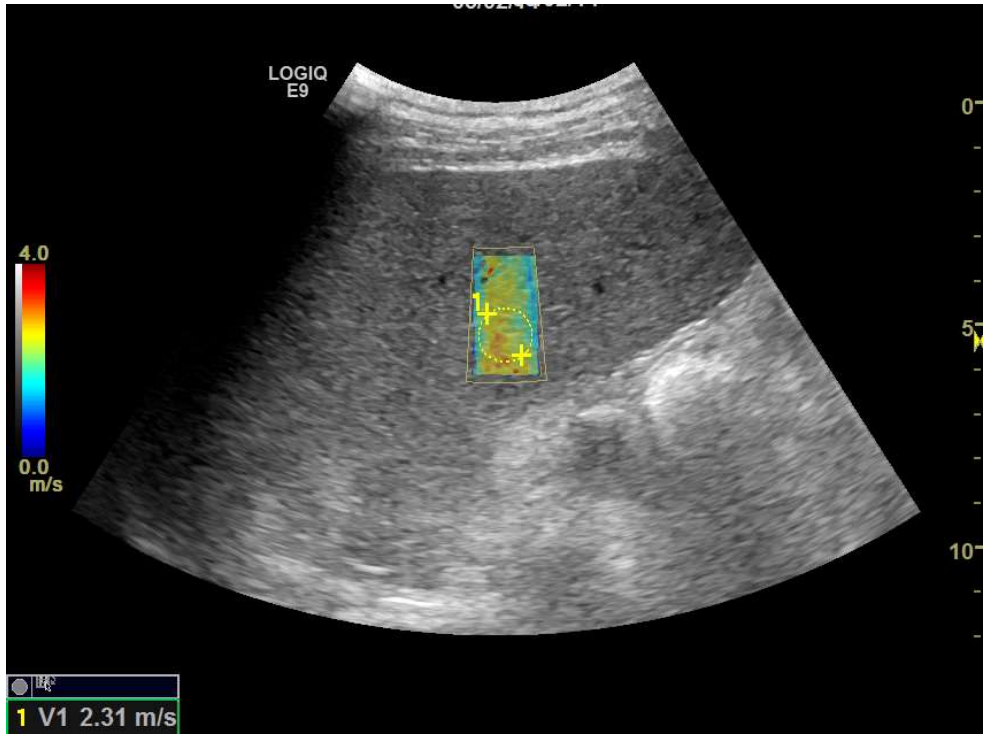


Elastogrammet gir en idé om fibrosegrad

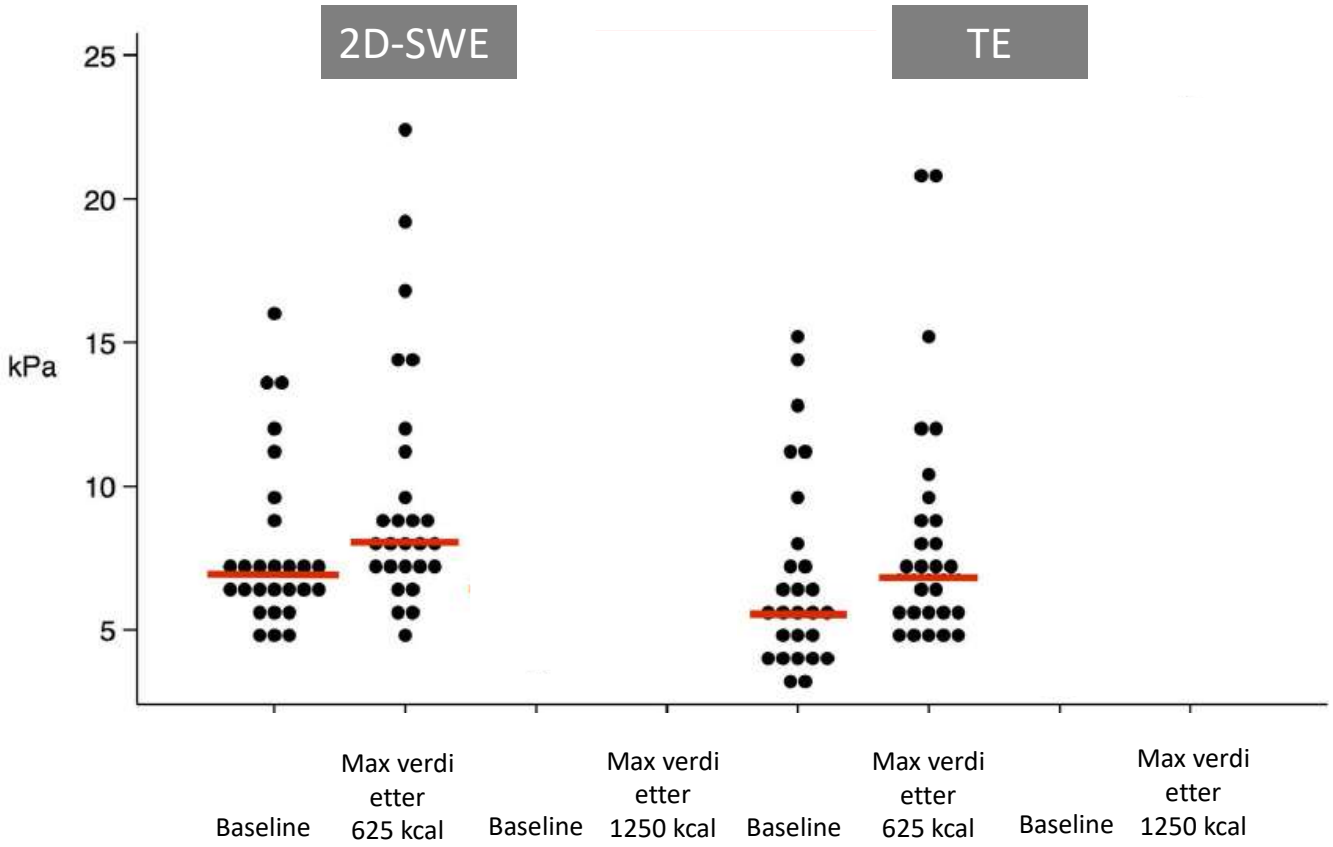
HCV uten signifikant fibrose



HCV og cirrhose

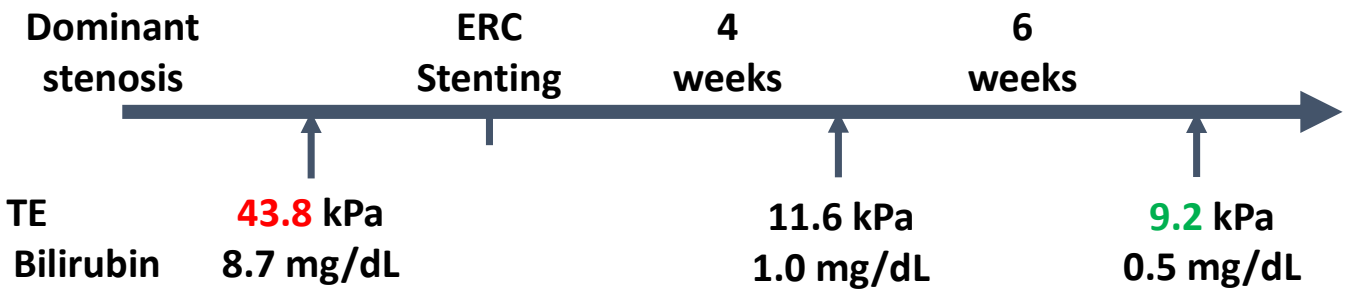


Betydningen av faste



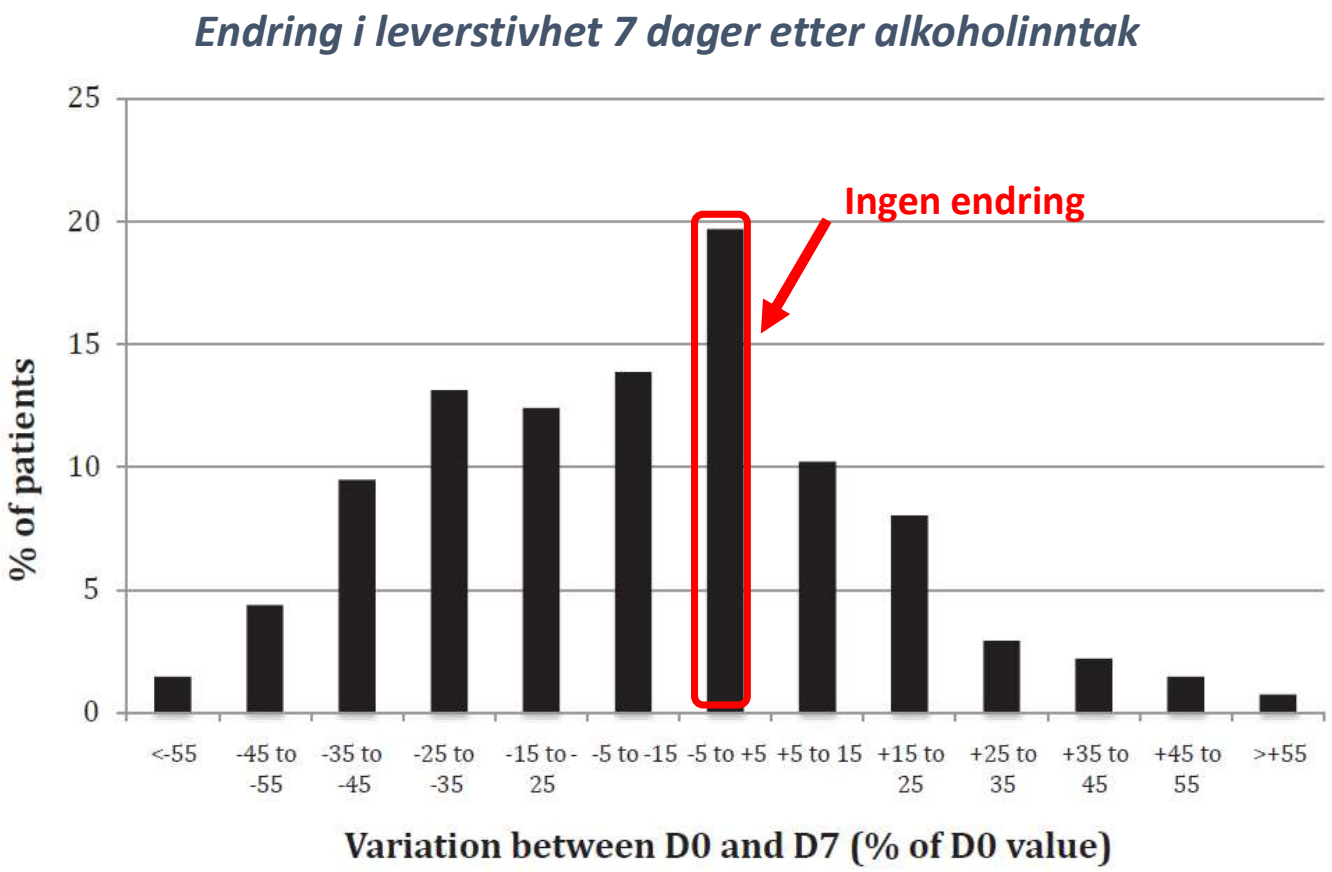
Thiele. PLOS one . 2017

Betydningen av cholestase



Ehlken et al., Gastroenterology 2014

Leverelastografi ved alkoholisk leversykdom



- In patients with ALD, LSM by TE <8 kPa is recommended to rule-out advanced fibrosis in clinical practice, with the following NITs as alternatives, if TE is not available (**LoE 3; strong recommendation**).
  - Patented tests: ELF™ <9.8 or FibroMeter™ <0.45 or FibroTest® <0.48
  - Non-patented tests: FIB-4 <1.3
- Upon referral of patients at risk of ALD, LSM by TE ≥12-15 kPa is recommended to rule-in advanced fibrosis, after considering causes of false positives (**LoE 2; strong recommendation**).
- In patients with elevated liver stiffness and biochemical evidence of hepatic inflammation (AST or GGT >2xULN), LSM by TE should be repeated after at least 1 week of alcohol abstinence or reduced drinking (**LoE 3; strong recommendation**).

Clinical Practice Guidelines
ËASL, JHEP 2021

Agenda

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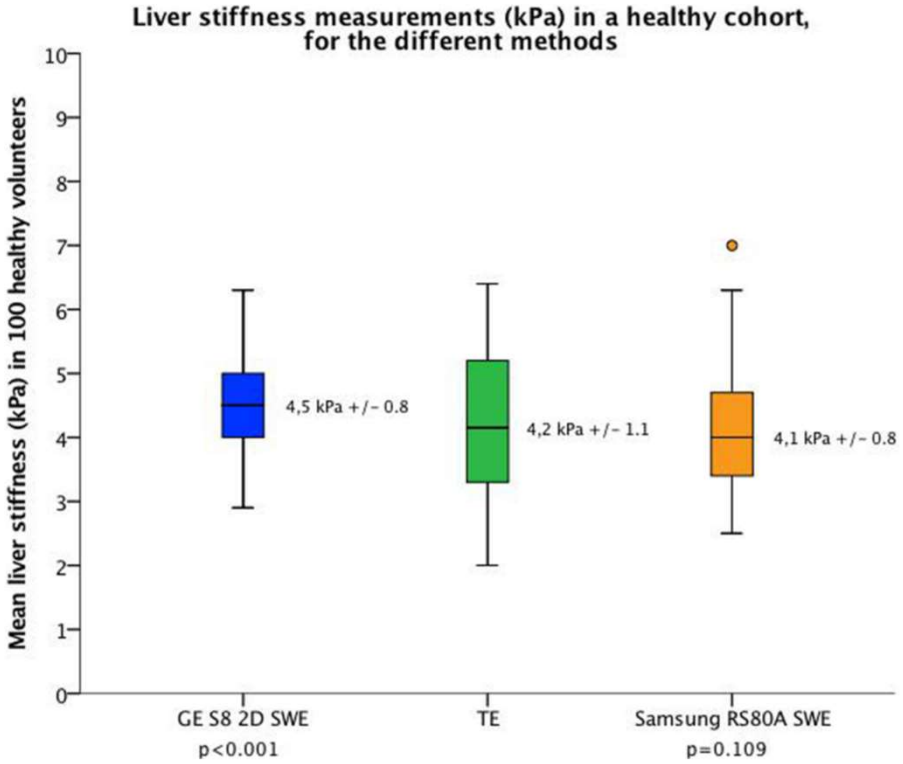
- Cut-off-verdier
- Indikasjoner

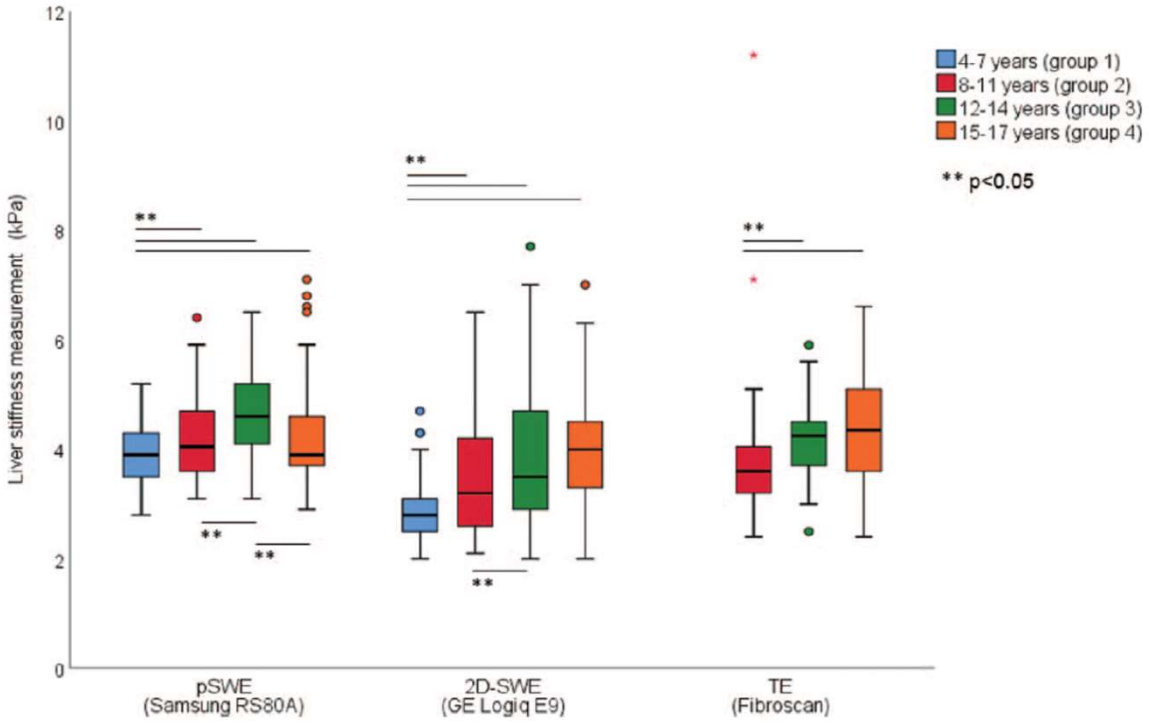
Norske normalverdier for flere plattformer

VOKSNE



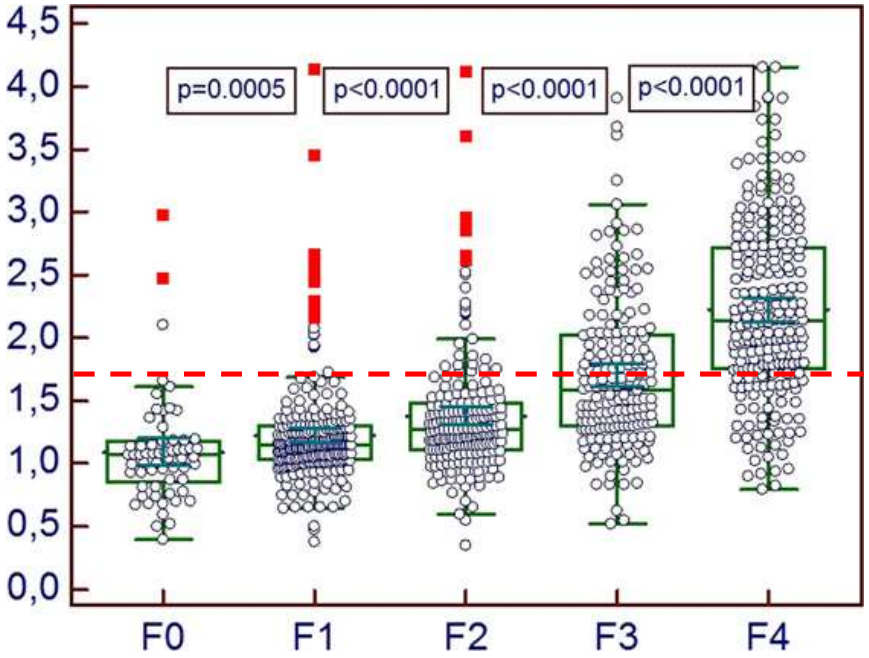
Mulabecirovic et al., PLOS one 2018

BARN



Mjelle et al., Jped Gastro Nutr 2019

Elastografi kan utelukke cirrhose (og sign.fibrose)



N= 914 HCV (10 sentra, 5 land)
ca 50:50 europeere/asiater

- Typisk «excellent» AUROC og NPV for F4 - utelukker cirrhose
- Kan ha rimelig god AUROC og NPV for F2 signifikant fibrose
- Skiller dårlig mellom intemediære stadier av fibrose
- Cut-off-verdier avhenger av utstyr og etiologi

Elastografi kan utelukke cirrhose (og sign.fibrose)

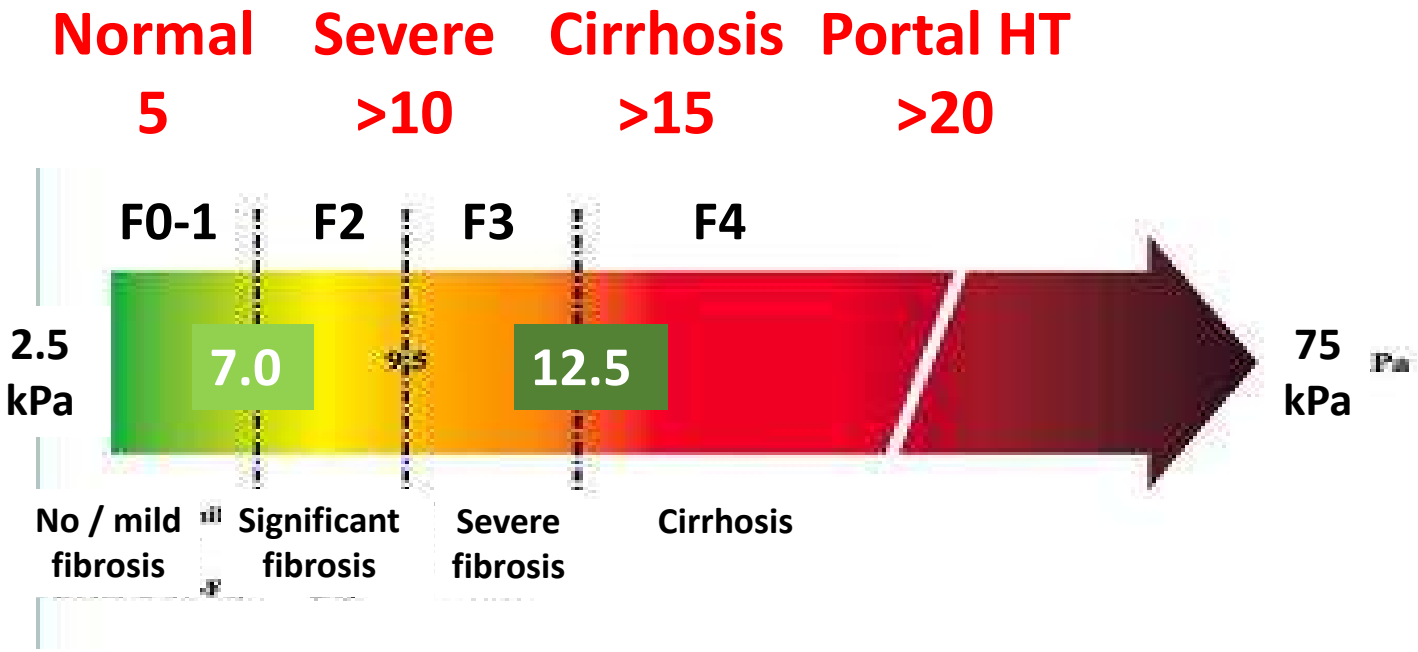
Table 4 Comparison of ARFI for different underlying liver diseases using a random effect meta-analysis

AUROC for	Fibrosis stage $F \geq 2$	Fibrosis stage $F \geq 3$	Fibrosis stage $F = 4$
All patients ($n = 518$)	0.87 (0.83, 0.92)	0.91 (0.86, 0.96)*	0.93 (0.89, 0.97)
HCV only ($n = 380$)	0.88 (0.83, 0.93)	0.90 (0.84, 0.97)*	0.92 (0.87, 0.98)*
HBV only ($n = 51$)	0.79 (0.63, 0.96)*	0.83 (0.70, 0.96)*	0.90 (0.79, 1.00)*
NASH only ($n = 77$)	0.86 (0.75, 0.96)*	0.86 (0.58, 1.00)*	0.94 (0.81, 1.00)

ARFI, Acoustic Radiation Force Impulse; AUROC, area under the ROC curve; HCV, chronic hepatitis C; HBV, chronic hepatitis B; NASH, nonalcoholic steatohepatitis. *For these classifications, hetereogeneity between the studies was significant.

Meta-analysis
Friedrich-Rust *et al.*, J Viral Hepatitis 2012

Cut-off-verdier ved TE



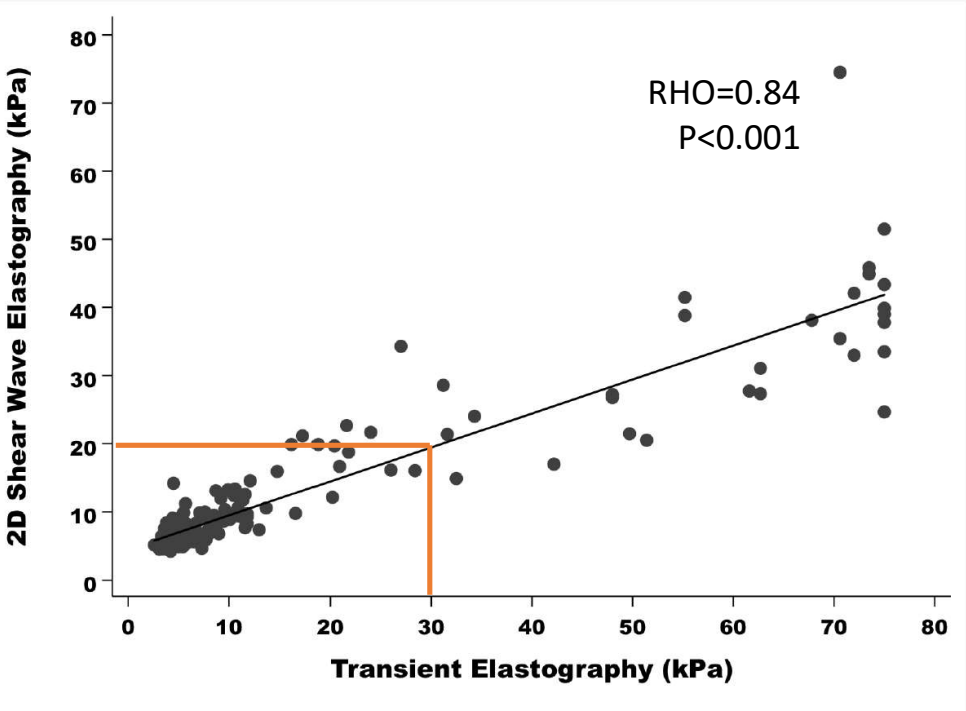
Cut-off-verdier er systemspesifikke

Table 2 Performance of point shear wave elastography (n = 98) and transient elastography (n = 101) in patients with chronic hepatitis C

Parameter	Method	$F \geq 2$	$F \geq 3$	$F = 4$
Cut-off in kPa	PSWE	5.7	5.8	7.2
	TE	6.9	7.3	9.3
AUC	PSWE	0.80 (0.71-0.87)	0.88 (0.80-0.94)	0.95 (0.89-0.99)
	TE	0.82 (0.73-0.89)	0.95 (0.88-0.98)	0.92 (0.85-0.97)
Sensitivity %	PSWE	62.0 (47.2-75.3)	85.2 (66.3-95.8)	90.0 (55.5-99.7)
	TE	62.7 (48.1-75.9)	89.9 (70.8-97.6)	90.0 (55.5-99.7)
Specificity %	PSWE	91.7 (80.0-97.7)	84.5 (74.0-92.0)	88.6 (80.1-94.4)
	TE	83.7 (70.3-92.7)	80.8 (69.9-89.1)	87.8 (79.2-93.7)
PPV %	PSWE	88.6 (73.3-96.8)	67.6 (49.5-82.6)	47.4 (24.4-71.1)
	TE	80.0 (64.1-91.1)	63.2 (45.7-78.4)	45.0 (23.1-78.5)
NPV %	PSWE	69.8 (57.0-80.8)	93.7 (84.7-98.3)	98.7 (93.1-100)
	TE	68.3 (55.0-79.7)	95.2 (86.5-99.0)	98.7 (93.2-100)

Ferraioli, WJG 2014

TE vs 2D-SWE



Thiele, Gastroenterology 2016

Agenda

- Ulike metoder
- Elastografi i praksis
- Cut-off-verdier
- Indikasjoner – «alle» kroniske leversykdommer

EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2021 update☆

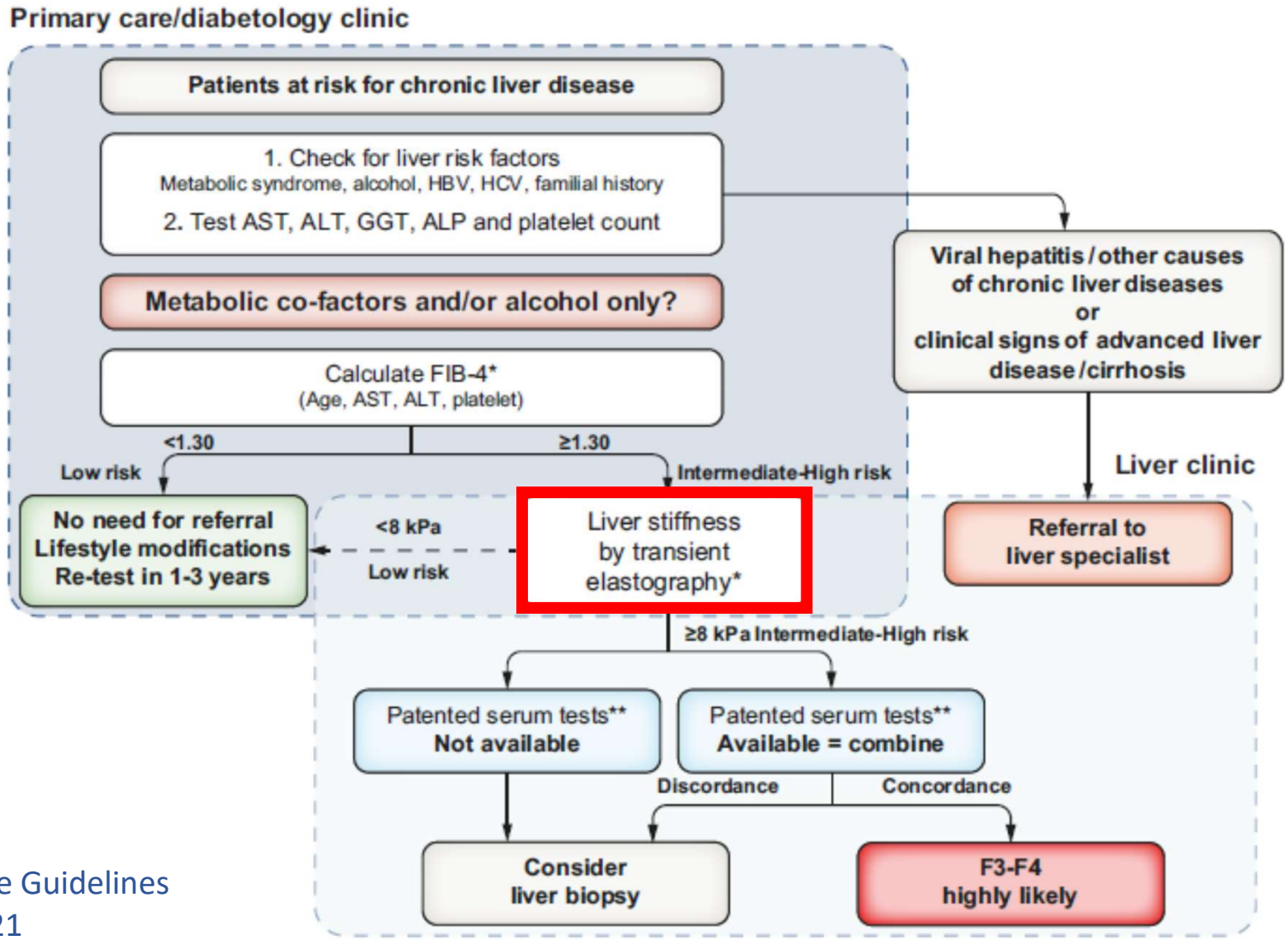
European Association for the Study of the Liver*

Table 2. Advantages and disadvantages of the main non-invasive tests used to diagnose and stage liver fibrosis.

	Serum markers		Transient elastography	pSWE	2D-SWE
Advantages	Non-patented • Good reproducibility • High applicability (95%) • No cost and wide availability • Well validated • Can be performed in the outpatient clinic • Prognostic value of some has been validated for some aetiologies of chronic liver disease on population level	Patented Good reproducibility • High applicability (95%) • Well validated • Can be performed in the outpatient clinic • Prognostic value of some has been validated for some aetiologies of chronic liver disease	• Most widely used and validated technique • Point-of-care (bedside; rapid, easy to learn) • Qual • Good • High (AUROC >0.9) • Prognostic value in compensated cirrhosis well validated	• Can be performed in combination with regular ultrasound if the device is provided with adequate software (ascites and obesity) • Performance equivalent to that of TE for advancedfibrosis and cirrhosis • Prognostic value in cirrhosis • High applicability for spleen stiffness measurement	• Can be performed in combination with regular ultrasound if the device is provided with adequate software • Measures liver stiffness in real time • Good applicability • High performance for the diagnosis of significant fibrosis and cirrhosis • Prognostic value in compensated cirrhosis
Disadvantages	• Non-liver-specific • Performance not as good as TE and patented serum markers • False positive results with FIB-4 and NFS in case of age>65 yrs	• Cost • Non-liver-specific • Performance not as good as TE for cirrhosis • False positive results in case of extrahepatic inflammatory conditions, profibrotic, extrahepatic disease and other (*e.g.* haemolysis, Gilbert syndrome)	• Requires a dedicated device • ROI cannot be chosen • Applicability (>95%) lower than serum biomarker: (obesity, ascites, operator experience) • False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake	• False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake	• False positive in case of acute hepatitis, extrahepatic cholestasis, liver congestion, food intake and excessive alcohol intake

Høy prognostisk verdi for cirrhose

2D-SWE, bidimensional shear wave elastography; FIB-4, fibrosis-4; MRE, magnetic resonance elastography; MRI, magnetic resonance imaging; NFS, NAFLD fibrosis score; pSWE, point-shear wave elastography; TE, transient elastography.



Clinical Practice Guidelines
ËASL, JHEP 2021

Hepatitt C: Hva med leverstivhet post-SVR?

Statement

- Non-invasive scores and LSM by TE and other elastography methods are not accurate in detecting fibrosis regression after SVR in HCV patients diagnosed with cACLD prior to antiviral therapy (**LoE 3**).

Recommendations

- The routine use of non-invasive scores and LSM by TE and other elastography methods is currently not recommended to detect fibrosis regression after SVR in HCV patients (**LoE 3; strong recommendation**).
- Cut-offs of LSM by TE used in patients with untreated HCV should not be used to stage liver fibrosis after SVR (**LoE 4; strong recommendation**).

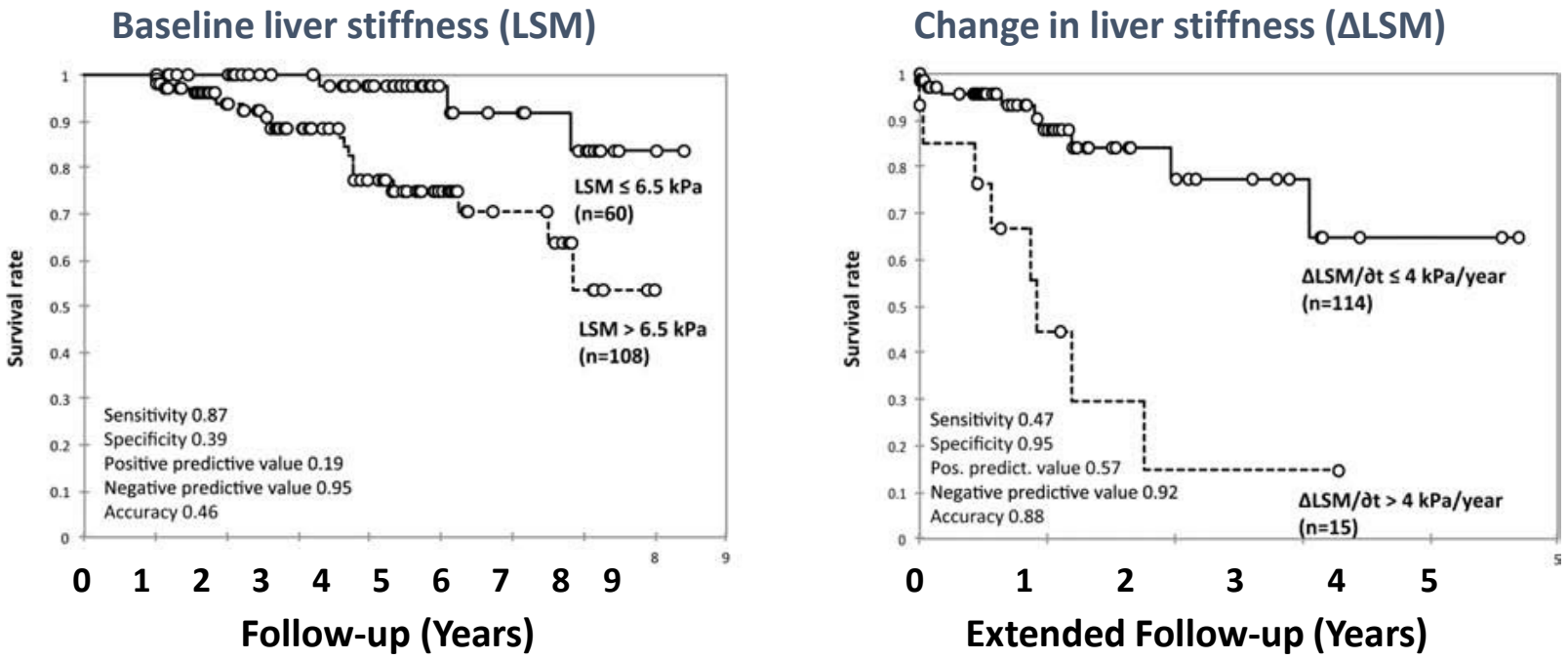
Statement

- In patients with cACLD previous to antiviral therapy for HCV, LSM post-SVR could be helpful to refine the stratification of residual risk of liver-related complications; yearly repetition of LSM can be carried out while we await confirmatory data (**LoE 3**).

Recommendations

- Patients with cACLD previous to antiviral therapy for HCV should continue to be monitored for HCC and portal hypertension irrespective of the results of NITs post-SVR (**LoE 3; strong recommendation**).

Baseline leverstivhet og endring er prognostisk ved PSC (figuren) og PBC



LSM…should be used for risk stratification in PSC…and PBC
EASL CPG Nonivasive, JHEP 2021

PSC: Corpechot et al., Gastroenterology 2014
PBC: Corpechot et al., Hepatology 2012

Elastografi ved portal HT: Sparer gastroskopier

TE <10 kPa: Rule out cACLD (compensated advanced chronic liver disease)

TE >15 kPa: Probable cACLD

TE <20 kPa+ tpk ua: Variceal screen by endoscopy not needed

- Baveno VI: consensus in portal hypertension (position paper)

Franchis et al., J Hepatol 2015

- Independent validation - *Maurice et al., J Hepatol 2016*

Oppsummering

- Elastografi bruker ultralyd til å måle leverstivhet som **uttrykk for fibrose**; resultat som m/s eller kPa
- **OBS feilkilder**, andre årsaker til økt leverstivhet
- **Sjekk kvalitet** på B-mode, elastogram, IQR/M
- **Oppgi system!** Cut-offverdier er systemspesifikke

- «Elastografi (Logic E10), hø: Median 6,2 kPa, IQR/M 15%. Normal. God kvalitet.»

- **Elastografi står sentralt i evaluering og oppfølging av alle pasienter med kroniske leversykdommer**