

Kronik Hepatit Yönetimi Kursu

Fibroscan Etkin Bir Tanısal Yaklaşım mıdır?

Prof. Dr. Mustafa Kemal ÇELEN

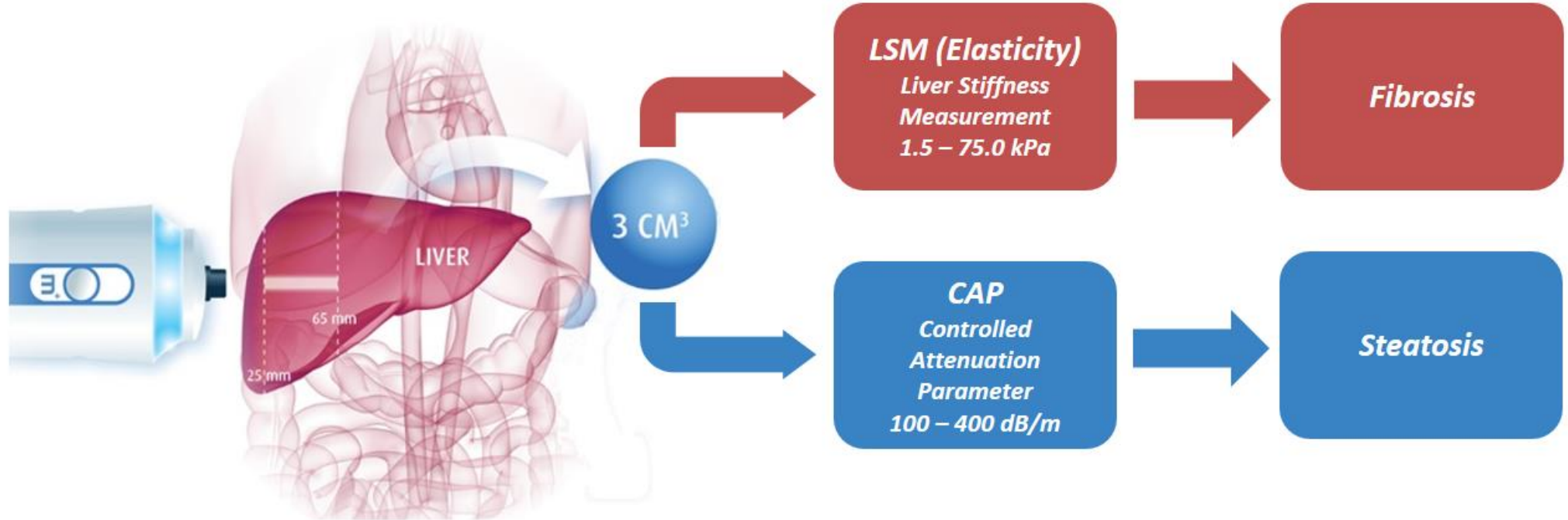
Dicle Üniversitesi

Enfeksiyon Hastalıkları



@mkc_celen

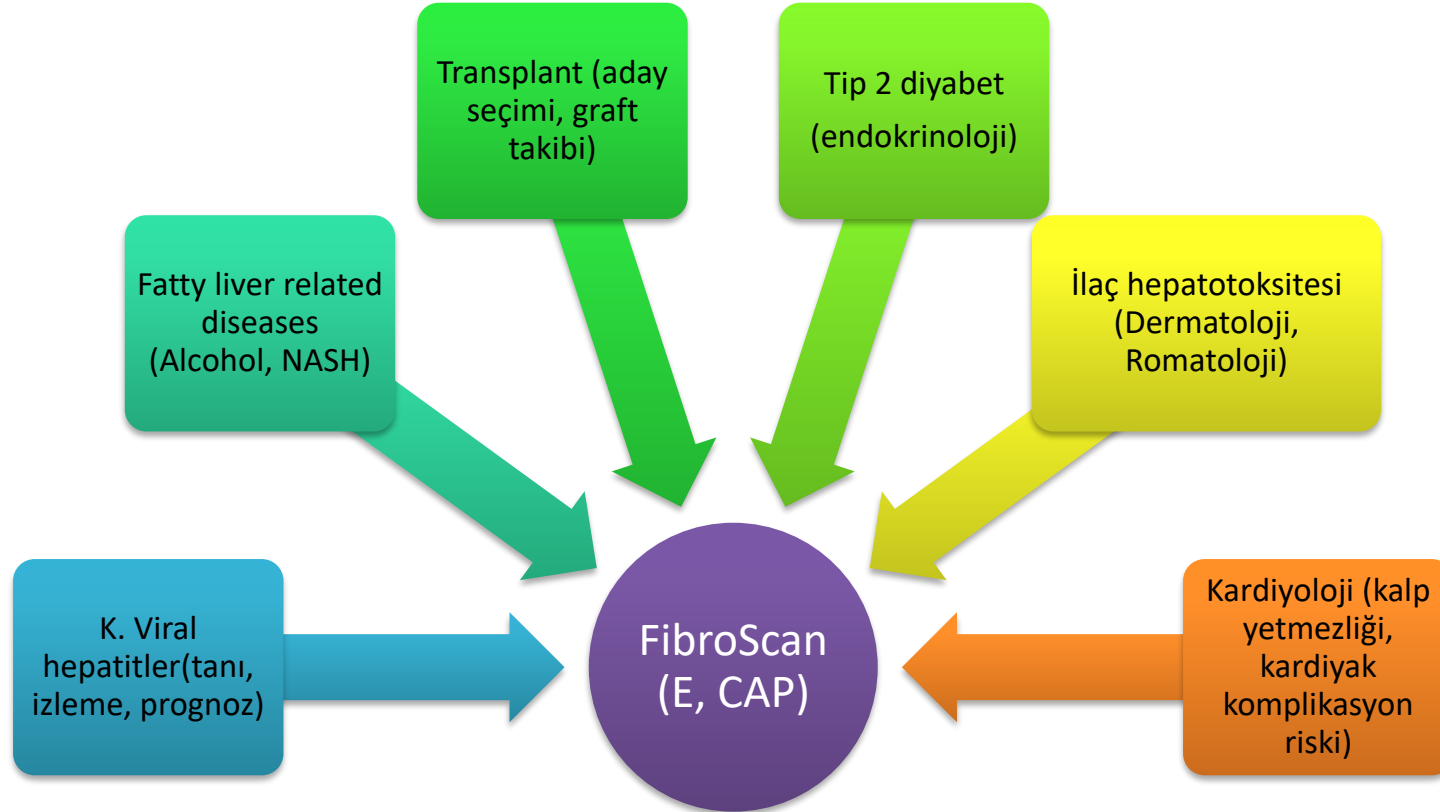
FibroScan: Aynı bölgeden (ROI) iki parametre simültane olarak ölçülür

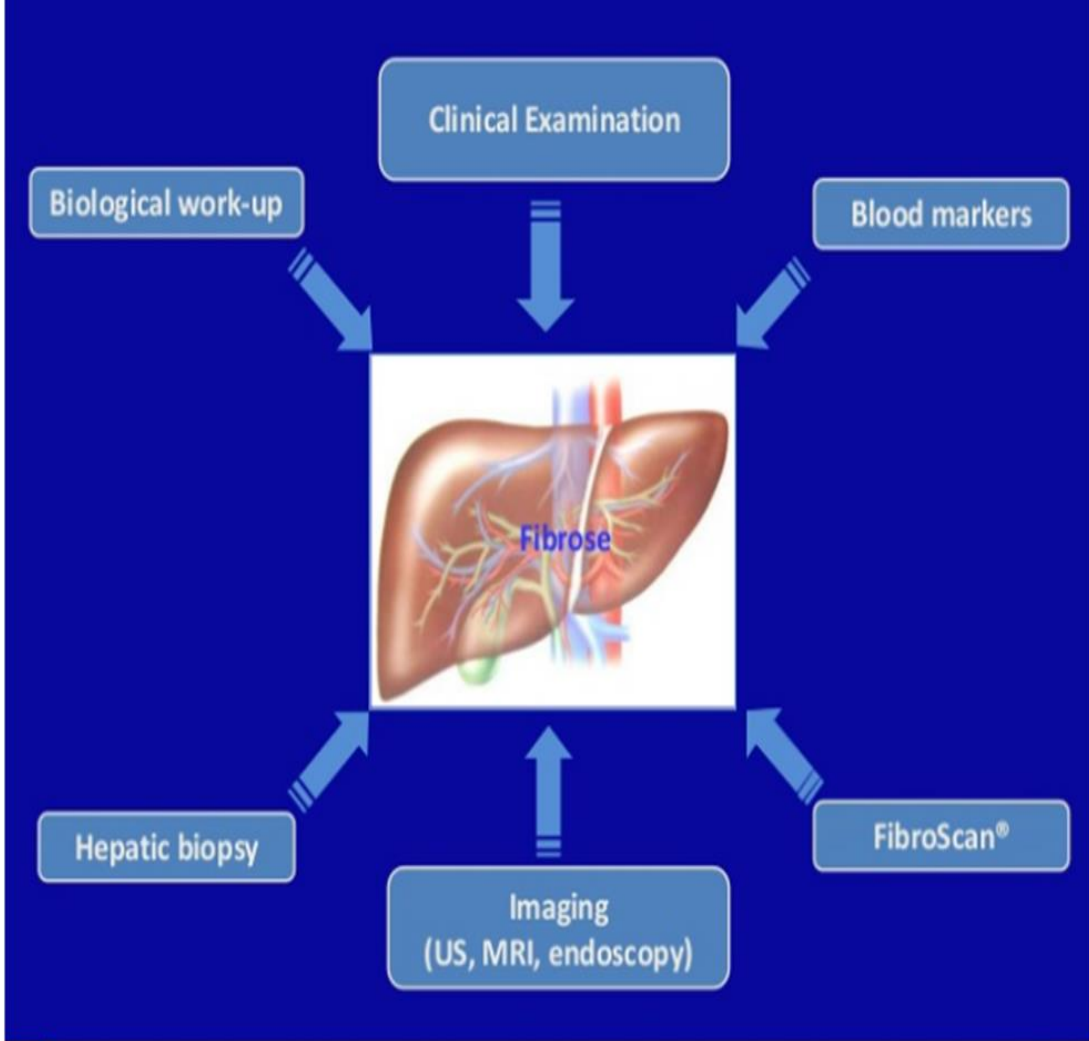


FibroScan (VCTE)

- Çok geniş klinik uygulama alanları

- Tüm kronik karaciğer hastalıkları (Viral hepatitler, NAFLD, Alkol, Otoimmün, PBC, PSK, Wilson, Hemokromatoz, ...)
- Hepatoloji dışında yeni ilginç klinik uygulama alanları (Endokrinoloji, Kardiyoloji, Dermatoloji, AIDS)

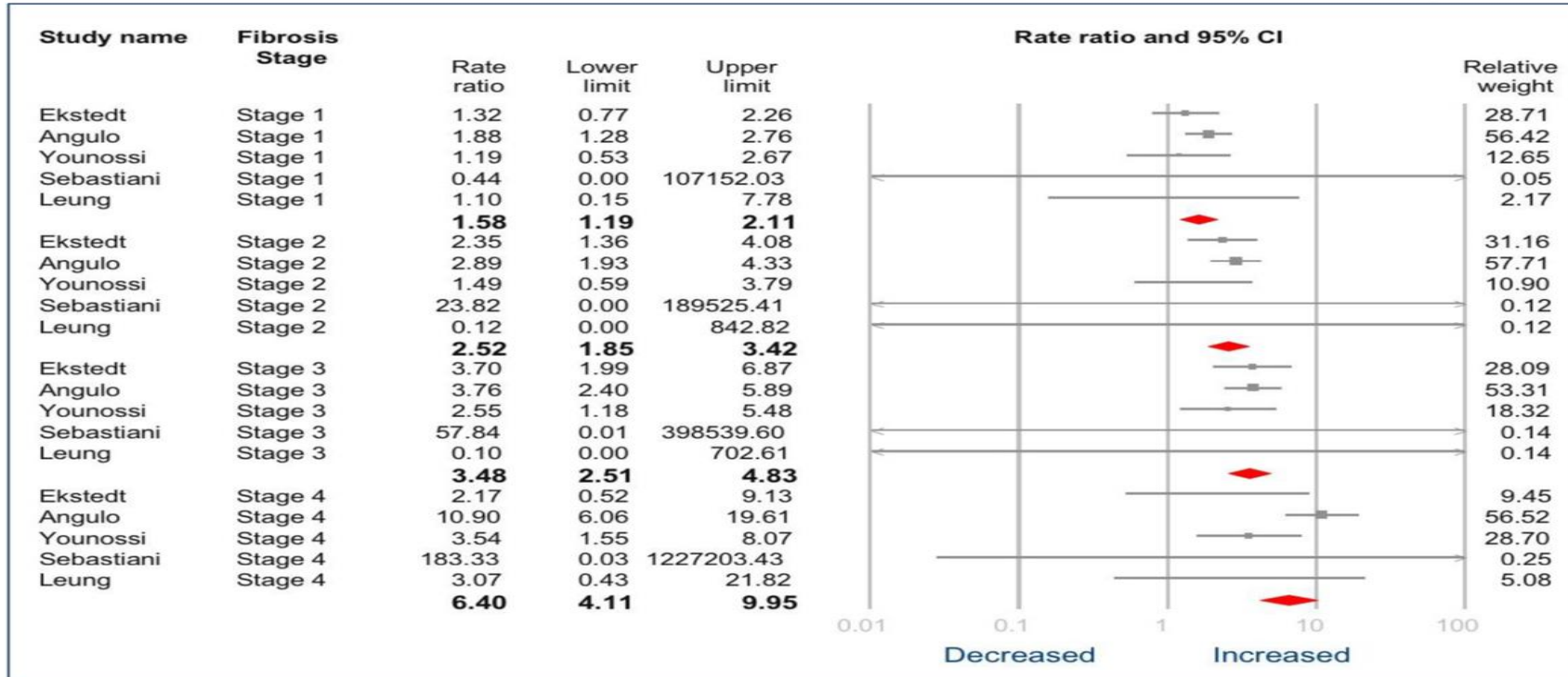




Karaciğer stiffness değerlerinin (LSM) yorumlanması konunun uzmanları tarafından hastaya ait tüm bilgiler dikkate alınarak (öykü, muayene, laboratuvar, radyoloji) yapılmalıdır, sonuç buna göre raporlanmalıdır.

Metaanaliz: NAFLD'da Mortalite Fibrozis ile Birlikte Artar

All-Cause Mortality Rate Ratio by Fibrosis Stage



*All-cause mortality: No heterogeneity for Fibrosis stages 1-3 vs. 0 ($I^2=0$); for stage 4 vs. stage 0 = 52%; P-value for difference between groups=0.001

1495 hasta, 17452 hasta-yılı

Liver biopsy size AASLD guidelines¹

- Biopsy of at least **2 – 3 cm in length** is recommended
Needle of **16-gauge in caliber** is recommended
- Presence of fewer than **11 complete portal tracts**
may be incorrect in recognition of grading & staging

**Even a 25mm long liver biopsy
has 25% rate of discordance for fibrosis staging²**

AASLD guidelines. Hepatology 2009 ; 49 : 1017 – 1044.

² Bedossa P et al. Hepatology 2003 ; 38 : 1449 – 57.

Karaciğer biyopsisi-uyumsuzluk

- Laparoskopik gözlemlerle, hatta **otopsi ile siroz tanısı konulan hastaların %10 ila %30'unda karaciğer biyopsisi ile aynı tanıya varılamadığı** gösterilmiştir

-

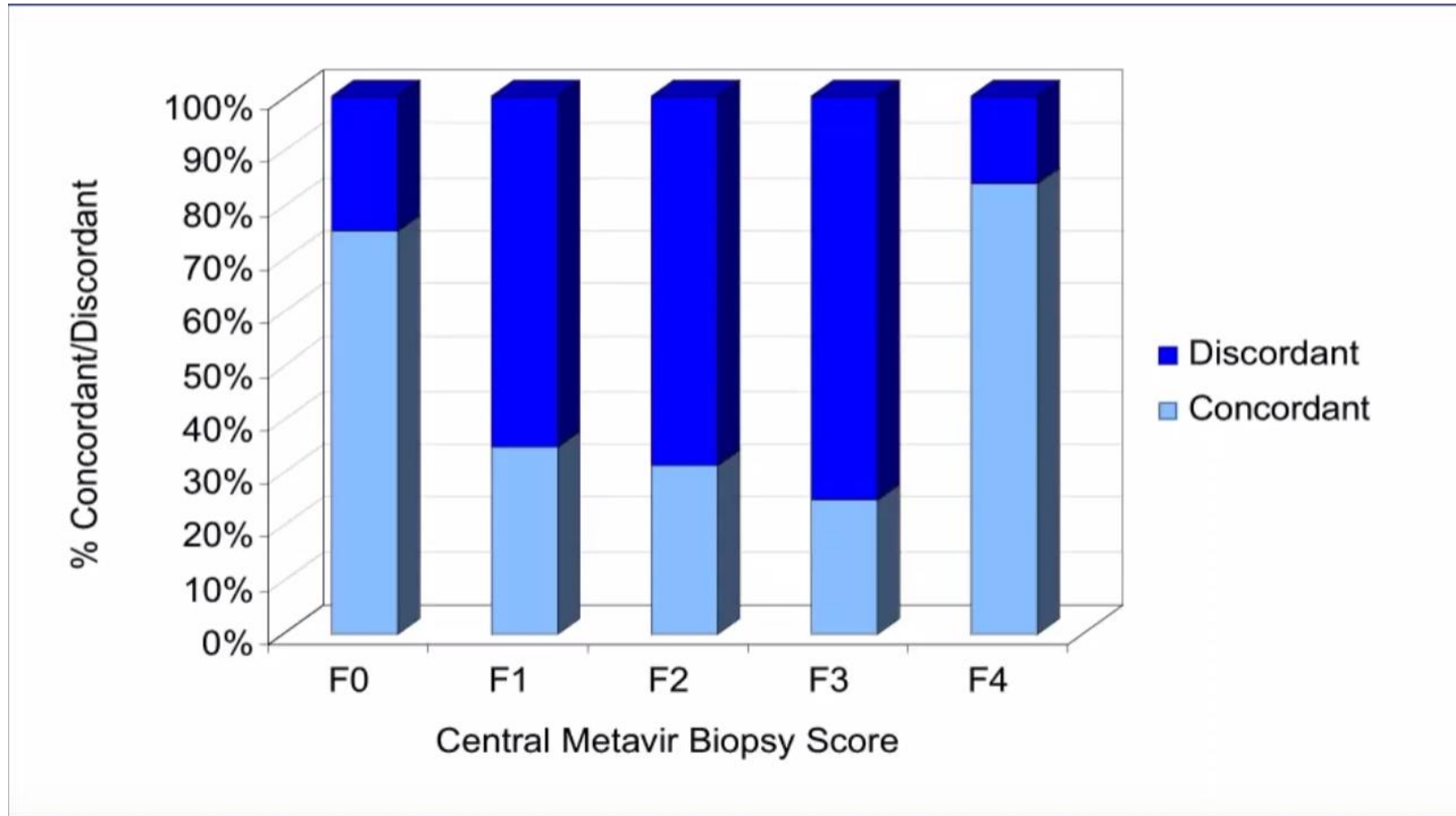
%30'unda önemli ağrı

<%1 inde ciddi kanama

%2-3 ünde hastane yatış ihtiyacı

%0.33 ünde mortalite gibi sonuçlara yol açar.

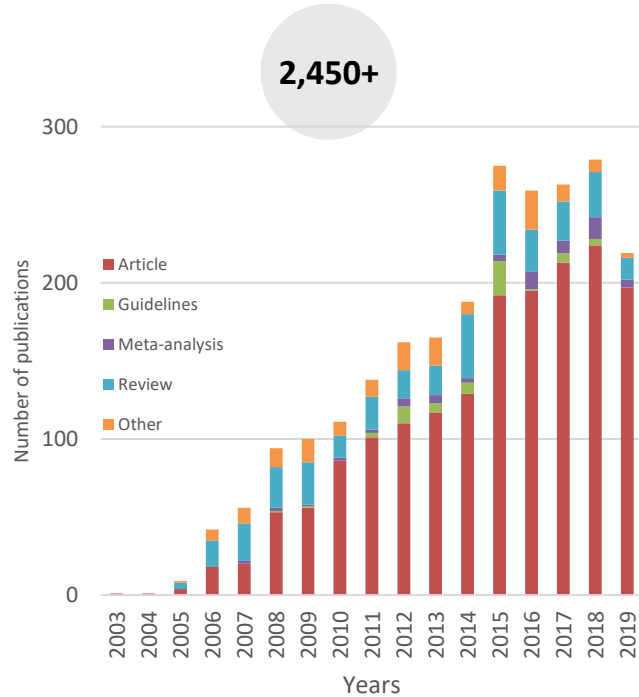
3 patolog arasındaki uyum/uyumsuzluk oranı(n=234)



FibroScan Klinik Yayınları:

Farklı etyolojilere bağlı karaciğer hastalıklarda yaygın kullanımı klinisyenlere ekta güven kazandırır

2450'den fazla, metaanalizleri de içeren klinik yayınlar



→ **FibroScan is useful in the entire range of chronic liver diseases¹**

– HBV, HCV, NAFLD, Alkolik Kc, PBC, Otoimmün hepatit, Mtx...

→ **FibroScan is useful at different steps of liver patient care continuum**

→ Toplum taraması²

→ Tedavi başlama kararı verilmesinde³

→ Tedavi monitorizyonunda⁴

→ Komplikasyon riski ve prognoz değerlendirilmesinde⁵

→ Karaciğer trasplantasyonu sonrası takipte⁶

→ **FibroScan is useful in different clinical settings**

– Hastaneler, 1. basamak, araştırma, tıp merkezi, hapishaneler, muayenehane

→ **When used in clinical practice FibroScan**

• **avoids most existing biopsies**, 60% to 85% in clinical publications⁷ and probably above in real clinical practice

• **is used in much broader circonstances** where biopsies could not be envisaged due to costs, risks and patient reluctance

→ **FibroScan is a cost-effective alternative to biopsy**

– Total cost of a biopsy between 1,000-1,500€ vs. 100-150€ for a FibroScan exam⁸

¹Steadman et al. 2013 : "Evaluation of the efficacy of VCTE in patients with chronic liver disease" (57 pooled clinical studies); Chon et al. 2012: "Evaluation of the efficacy of VCTE in patients with chronic hepatitis B" (18 pooled clinical studies); Adebajo et al. 2012: "Use of VCTE to assess fibrosis for patients with hepatitis C recurrence after liver transplantation" (6 pooled studies); Wang et al. 2015: "Performances of CAP for steatosis evaluation" (11 pooled studies); - ² Roulot, D., et al.: Tansient elastography as a screening tool for liver fibrosis and cirrhosis in a community-based population over 45 years, Gut, 2010 - ³ Zioli, m., et al., Non-invasive assessment of liver fibrosis by stiffness measurement: a prospective multicentre study in patients with chronic hepatitis C. Hepatology, 2005 - ⁴ Arima, Y., et al., Reduction of liver stiffness by interferon treatment in the patients with chronic hepatitis C. Hepatology Research, 2010 - ⁵ Meta-analysis: Singh et al. 2013 "Prognostic value of VCTE for clinical outcomes" (17 studies pooled) - ⁶ Rigamonti, C., m.F. Donato, and m. Colombo, Transient elastography in the early prediction of progressive recurrent hepatitis C following liver transplantation. Hepatology, 2010 - ⁷ Wong et al. Hepatology 2010 (NAFLD), Chan et al. Journal of Viral Hepatitis 2008 (HBV), Boursier et al. Hepatology 2012 (HCV) - ⁸ K THAVORN, D COYLE (Nov 2015) Transient Elastography and Controlled Attenuation Parameter for Diagnosing Liver Fibrosis

Klinik Rehberlerde Fibroscan Tavsiyeleri

Recommended in guidelines of prominent health and clinical organization globally

“TE can be considered the non-invasive standard for the measurement of liver stiffness.”

“All HCV patients should be screened to exclude cirrhosis by TE if available.”

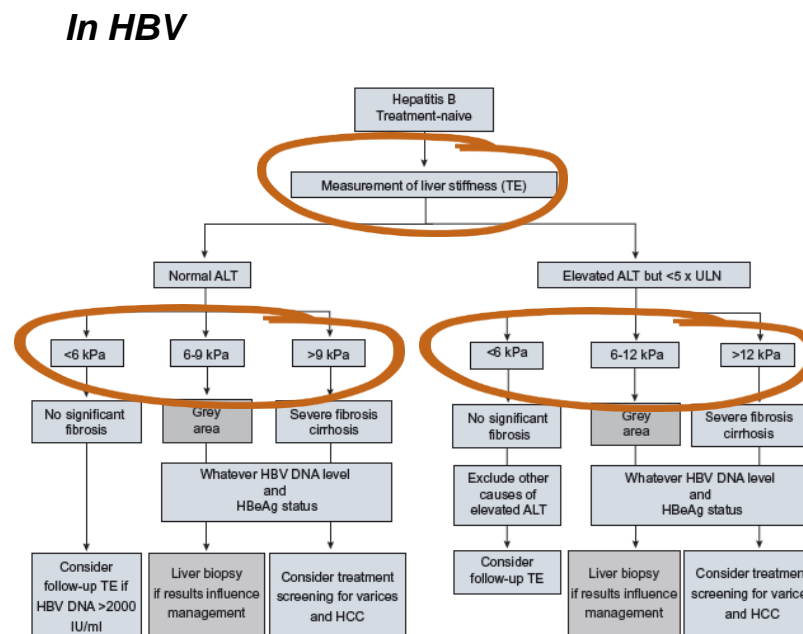
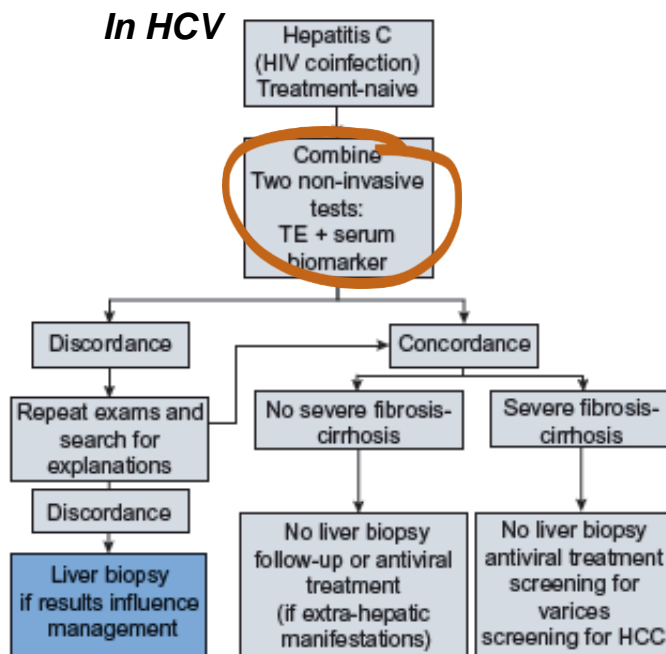
“in HBV, liver biopsy should only be considered in doubtful cases after TE.”

“in NAFLD (...) TE can be used as first line procedure (...) and follow-up assessment (...) should be performed.”

EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis, 2015, Journal of Hepatology
TE = “Transient Elastography” = VCTE



+ Also recommended in 60 guidelines on Echosens online clinical library, including:



FibroScan: Uluslararası Rehberler*

- **EASL/ALEH 2015 Clinical Practice Guidelines (*Non-invasive tests for evaluation of liver disease severity and prognosis*)**
 - “Transient Elastography [FibroScan] can be considered the non-invasive standard for the measurement of liver stiffness”
- **Europe:**
 - EASL guidelines recommend the use of FibroScan® for fibrosis assessment in both HCV infected and HIV-HCV coinfecting patients.
- **United States:**
 - AASLD guidelines (2014) recommend the use of FibroScan® VCTE in combination with blood markers for fibrosis assessment in HCV infected patients.
- **France:**
 - French Health Authority recommends use of FibroScan® since 2008.
 - ➔ As a first tool for cirrhosis diagnosis in HCV patients without comorbidities
 - ➔ As a first tool for cirrhosis diagnosis in HIV-HCV coinfecting patients
- **Spain:**
 - Recommendation by the AEEH and Spanish Health Minister:
 - ➔ Use for fibrosis assessment and decision of antiviral treatment in HCV infection and HIV/HCV coinfection (2012)
 - ➔ Use for fibrosis follow up after HCV related liver transplantation (November 2011)
 - ➔ For evaluation of portal hypertension (May 2012)
- **United Kingdom (UK):**
 - Recommendation by the National Institute for Health and Care Excellence (NICE) for HBV management (biopsy and treatment decision) and follow up (2013).
 - NICE recommendations for use of FibroScan in Primary Care (2020)
- **Canada**
 - Recommendation of the Canadian Association for the Study of the Liver

* *Non-exhaustive list* ➔ FibroScan® is recommended for fibrosis assessment in HCV patients

AGA SECTION

American Gastroenterological Association Institute Guideline on the Role of Elastography in the Evaluation of Liver Fibrosis



Joseph K. Lim,¹ Steven L. Flamm,² Siddharth Singh,³ Yngve T. Falck-Ytter,⁴ and the Clinical Guidelines Committee of the American Gastroenterological Association

¹Section of Digestive Diseases and Yale Liver Center, Yale University School of Medicine, New Haven, Connecticut;

²Departments of Medicine and Surgery, Feinberg School of Medicine, Northwestern University, Chicago, Illinois; ³Division of Gastroenterology, University of California-San Diego, La Jolla, California; and ⁴Division of Gastroenterology and Hepatology, Cleveland VA Medical Center and University Hospitals, Case Western Reserve University, Cleveland, Ohio

AGA Review Cutoff Value Reference

Significant Fibrosis

Disease	Advanced Fibrosis Cutoff kPa	Sensitivity %	Specificity %	PPV		NPV	
				Low Prevalence	High Prevalence	Low Prevalence	High Prevalence
HCV	≥ 9.5	78	86	23	70	99	90

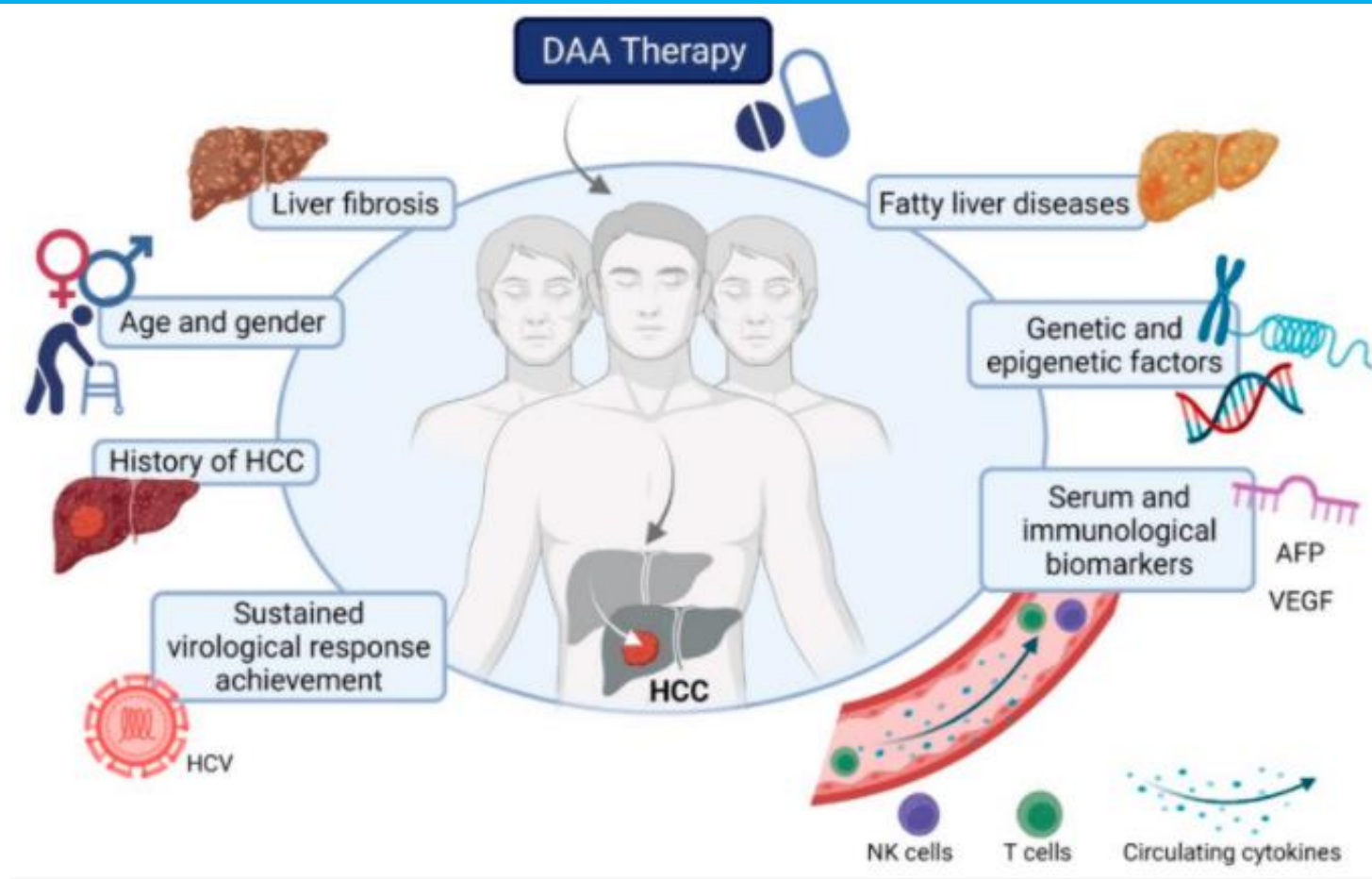
Post SVR LS < 9.5kPa AGA suggests patients can leave specialty care

AGA Review Cutoff Value Reference

Cirrhosis

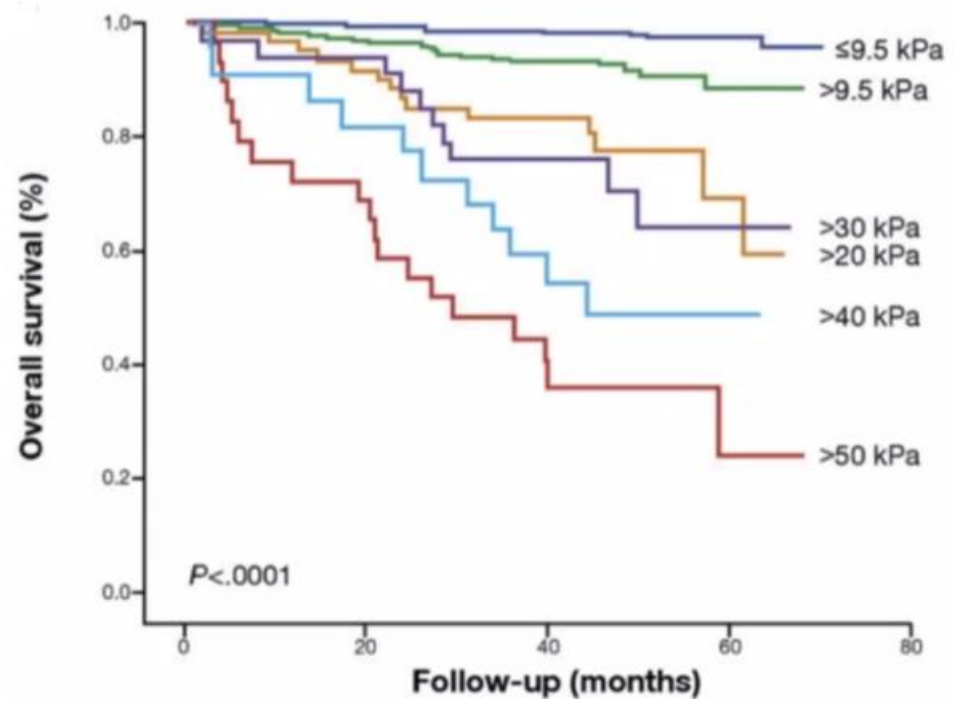
Disease	Cirrhosis Cutoff kPa	Sensitivity %	Specificity %	PPV		NPV	
				Low Prevalence	High Prevalence	Low Prevalence	High Prevalence
HCV	≥ 12.5	86	91	33	80	99	94
HBV	≥ 11.0	81	83	20	67	99	91
Alcoholic Liver Disease	≥ 12.5	95	71	15	100	58	97
Chronic Liver Disease High-Risk Esophageal Varices	≥ 19.5	89	56	10	34	99	95

Direk etkili antiviral tedaviden sonra HCC gelişimini predikte eden faktörler



Fibroscan kronik hepatit C'de 5 yıllık outcome'ı tahmin eder

1457 Kronik Hepatit C'li hasta
Outcomes: Ölüm veya karaciğer transplantasyonu ihtiyacı



AGA Elastografi Rehberi

Fibroscan, kalıcı viral yanıt(SVR) elde edilmiş kronik HCV'li yetişkinlerde, hangi hastalar poliklinik takibinden çıkarılabilir?

- **Antiviral tedaviden sonra SVR elde etmiş siroz olmayan HCV hastalarında, karaciğer fibrozunu dışlamak için 9.5 kPa'lık Fibroscan eşik değerinin kullanılmasını önermektedir.**

AGA Elastografi Rehberi

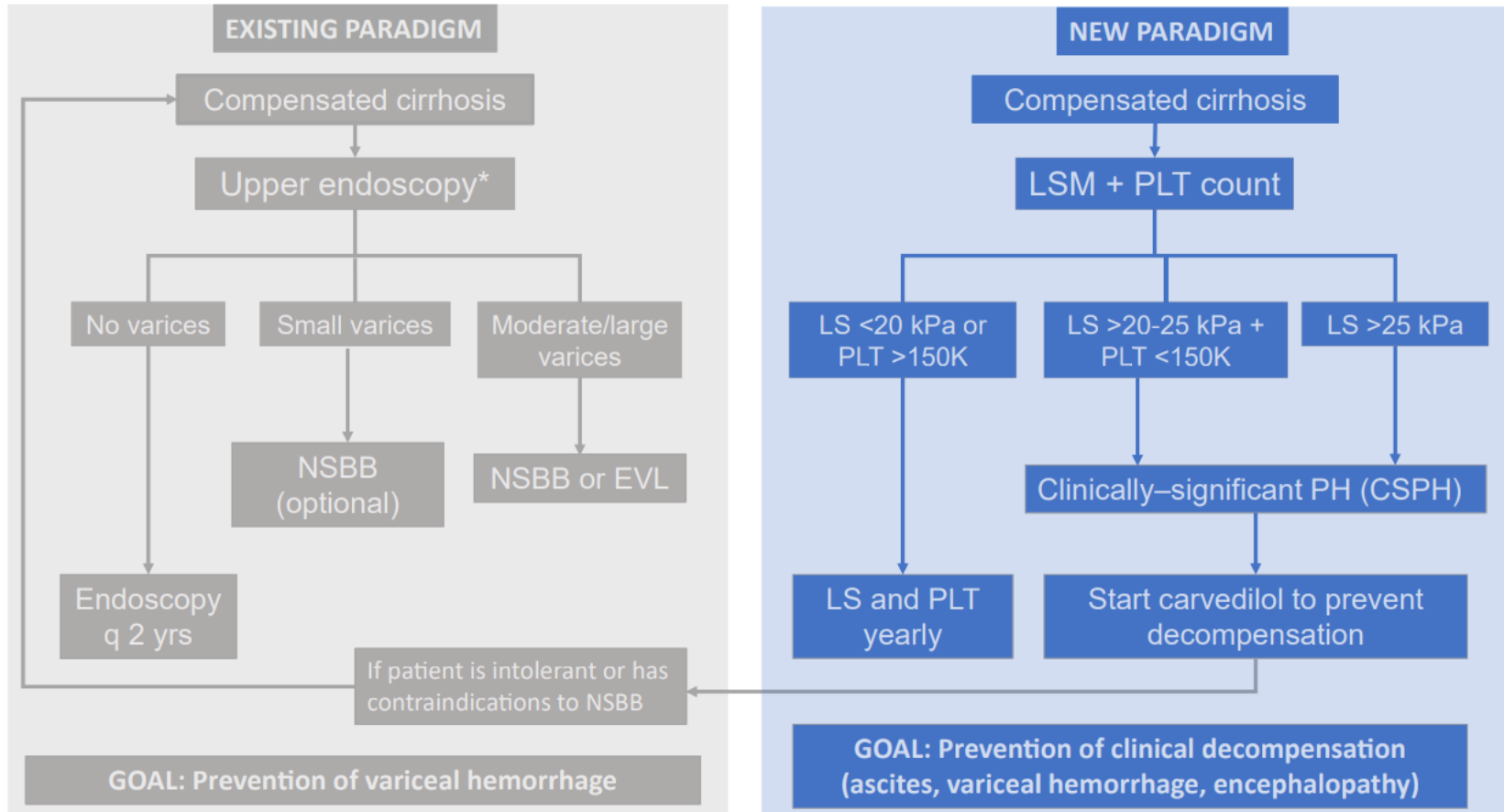
*Sirozdan şüphelenilip Fibroscan yapılan erişkinlerde, Fibroscan'de hangi eşik değeri yüksek riskli **özofagus varisleri ekarte** edilip rutin endoskopik tarama ihtiyacını ortadan kaldırabilir?*

- *Sirozdan şüphelenilen hastalarda AGA, yüksek riskli özofageal varisleri açısından özofagogastroduodenoskopi ihtiyacını değerlendirmek için*

19.5 kPa'lık (karaciğer stiffness'ı)

eşik değerinin kullanılmasını önermektedir.

Kompanse sirozun yönetiminde Fibroscan









Vaka-1

- 42 yaşında,
- HBeAg negatif kronik hepatit B enfeksiyonu
- AST:32 U/L, ALT:36 U/L, PLT:265.000 HBVDNA:65.000 IU/ml,
- Ultrason normal

Vaka-1 devam

- Karaciğer biyopsisi: HAI:4, F0
- 2 yıl sonra ALT: 33 U/l,
HBVDNA:57.000 IU/ml
- Şuan öneriniz ne olur?
- Fibroscan: LSM:3.5 kPa (F0 fibrozis)

Very low probability of significant liver inflammation in chronic hepatitis B patients with low ALT levels in the absence of liver fibrosis

Milan J. Sonneveld¹  | Willem P. Brouwer¹  | Bettina E. Hansen² | Henry L.-Y. Chan³  |
Teerha Piratvisuth⁴ | Ji-Dong Jia⁵  | Stefan Zeuzem⁶ | Rong-Nan Chien⁷ | Hannah Choi² |
Robert J. de Knegt¹  | Cynthia Wat⁸ | Vedran Pavlovic⁸ | Anuj Gaggar⁹ | Qing Xie¹⁰ |
Maria Buti¹¹  | Robert A. de Man¹ | Harry L.A. Janssen^{1,2} | for the SONIC-B Study Group

- Karaciğer inflamasyonu sadece karaciğer biyopsisi ile değerlendirilebildiğinden serum ALT, risk stratifikasyonu için kullanılır ancak ALT ve inflamasyon arasında kısıtlı bir ilişki var.

- AASLD rehberine göre normal/hafif yüksek ALT düzeyi olan ve significant fibrozis saptanmayan (noninvazif) hastalarda biyopsinin amacı karaciğer inflamasyonunu dışlamaktır.

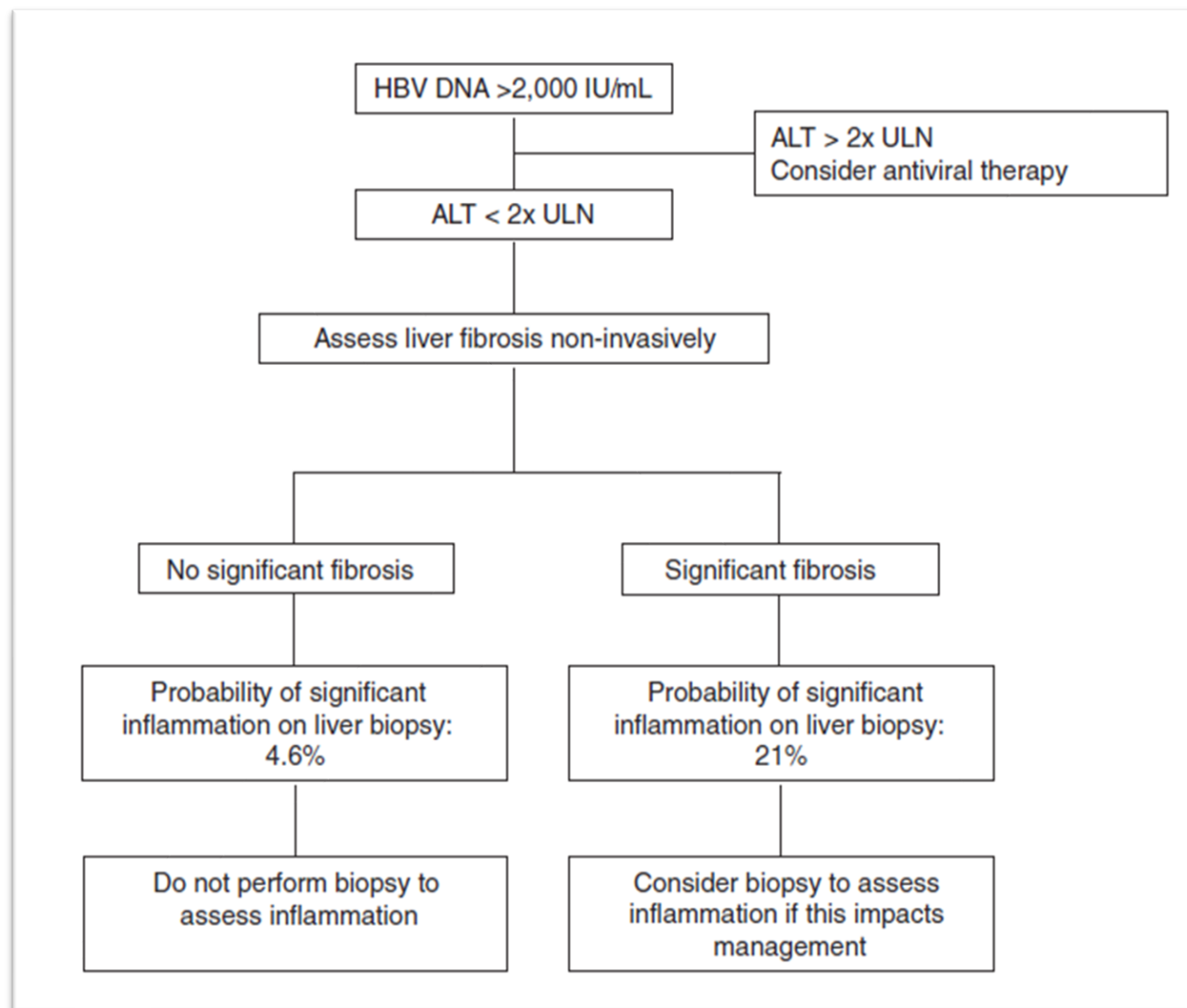
TABLE 3 Factors associated with the presence of significant inflammatory activity on liver biopsy

Variable	OR (95% CI)	P
Age	1.019 (1.008-1.029)	<0.001
Sex (male)	1.070 (0.825-1.387)	0.611
HBeAg-positive	0.829 (0.634-1.084)	0.171
Race		
Caucasian	Ref	<0.001
Asian	1.907 (1.489-2.444)	
Other	1.164 (0.740-1.831)	
ALT		
<ULN	Ref	<0.001
1-2 × ULN	1.560 (0.788-3.088)	
>2 × ULN	3.555 (1.847-6.841)	
HBV DNA (log c/mL)	1.038 (0.971-1.110)	0.273
AST (×ULN)	1.131 (1.073-1.192)	<0.001
Presence of fibrosis ^a	5.321 (4.109-6.892)	<0.001

ULN, times the upper limit of normal. For ALT the ULN is 35 for men and 25 for women.

The local ULN was used for AST.

^aIshak ≥ 3 or METAVIR ≥ F2.



Sonuç

- Bu çalışmaya göre, non-invaziv yöntemle significant fibrozis(Metavir F2) saptanmayan ve ALT düzeyi $<2 \times \text{ULN}$ olan hastalarda anlamlı karaciğer inflamasyonu çok düşük oranda ($<5\%$) saptanmıştır.



Yorum

- ALT < 2kat olan hastalarda Fibroscan ile fibrozis dışlanıyorsa bu hastalarda inflamatuvar aktiviteyi (HAI) deęerlendirmek için karacięer biyopsisi yapılmamalıdır.



Vaka 2

- 52 yaşında
- HBeAg (-) kronik hepatit B enfeksiyonu
- Trombosit:134.000, PT:12 sn INR:1.1
- AST: 35 U/L ALT:32 U/L
- Ultrasonografi: Karaciğer parankimi kaba ve splenomegali mevcut.
- HBVDNA: 1400 IU/ml, Delta (-)

Öneriniz nedir?

- Karaciğer biyopsisi: HAl:4 F1 fibrozis

- Peki bu durumda ne yapmalıyız?

- Fibroscan: 24 kPa (Siroz)

Şimdi Öneriniz nedir?



- Yeniden biyopsi: HAI:5, Ishak fibrosis:5/6

Kronik Hepatit B Tanı ve Takibi...

- Karaciğer Biyopsisi
- FibroMeter®
- FibroScan®
- FibroMeterVCTE®

**Kronik hepatit B takibinde
MASLD ve MASH ne kadar önemli?**

Table 2

Characteristics of the Non-Invasive Tests used in the clinical practice for staging fibrosis in chronic hepatitis B.

Non-Invasive Test	Easy to Perform	Cost-Effective	Readily Available	High Diagnostic Accuracy for Advanced Fibrosis/Cirrhosis	Influenced By Biological Variation (Age, BMI)	Avoids Further Invasive or Other Complex Diagnostic Testing	False Positive Result
APRI	x	x	x		x **		
FIB-4	x	x	x		x **		
Fibrotest [®]		x			x **	x	x *
VCTE	x	x		x	x ††	x	
p-SWE				x	x †	x	
2D-SWE				x	x †	x	

Karaciğer biyopsisi-uyumsuzluk

- Laparoskopik gözlemlerle, hatta **otopsi ile siroz tanısı konulan hastaların %10 ila %30'unda karaciğer biyopsisi ile aynı tanıya varılamadığı** gösterilmiştir

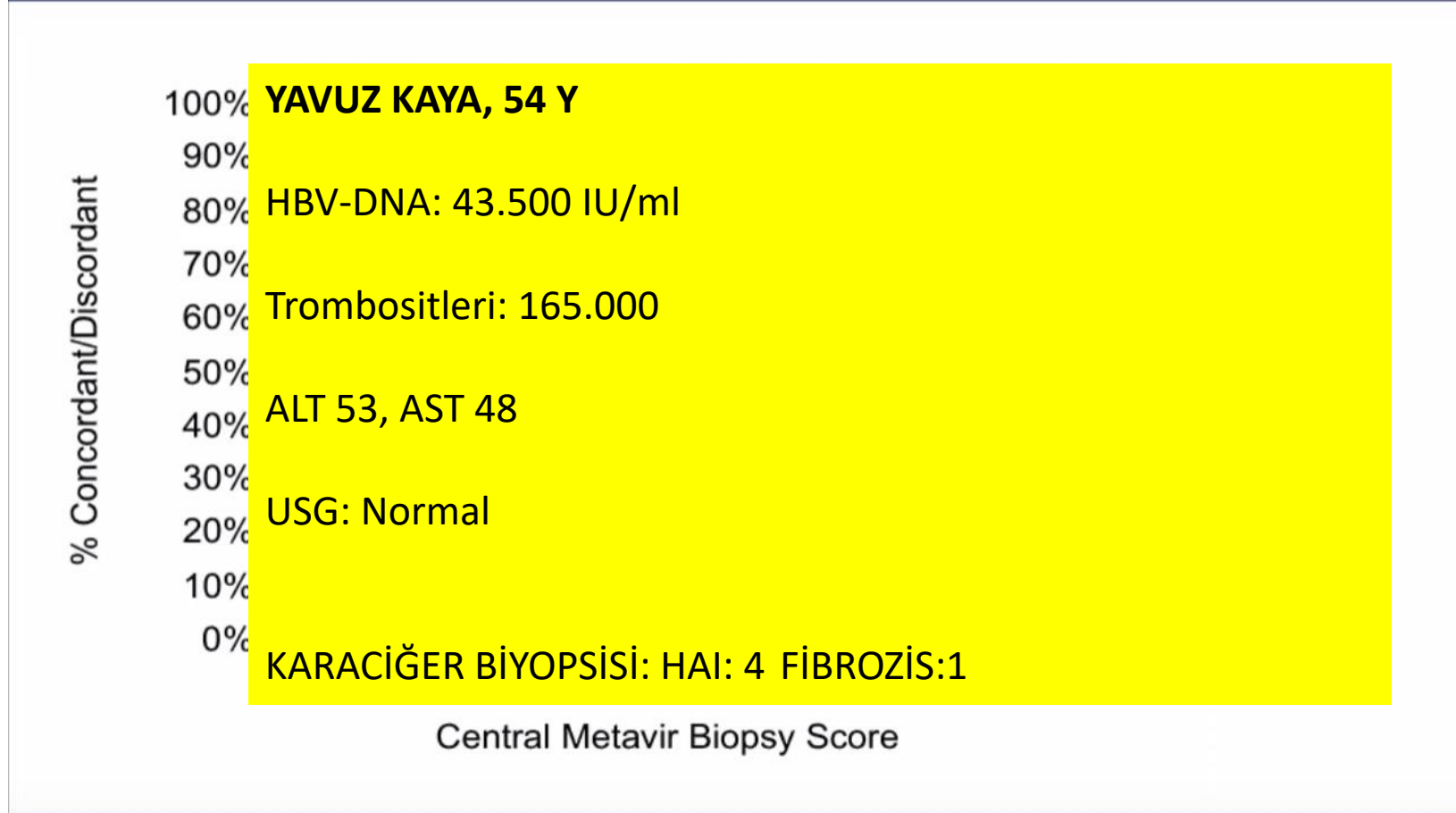
%30'unda önemli ağrı

<%1 inde ciddi kanama

%2-3 ünde hastane yatış ihtiyacı

%0.33 ünde mortalite gibi sonuçlara yol açar.

3 patolog arasındaki uyum/uyumsuzluk oranı(n=234)





FM Ref Number: 6625-15e6-82bd7

DOKTOR

ÇELEN MUSTAFA KEMAL
DICLE UNİVERSİTESİ HASTANESİ ENFEKSİYON HASTALIKLARI AD
21280 Diyarbakir - Türkiye

LABORATUVAR

DICLE UNIVERSITY
HOSPITAL
21280 DIYARBAKIR - Türkiye

HASTA

Soyadı KAYA
Adı YAVUZ
Doğum tarihi 9.11.1969
Cinsiyet Erkek

BIYOBELİRTEÇLER

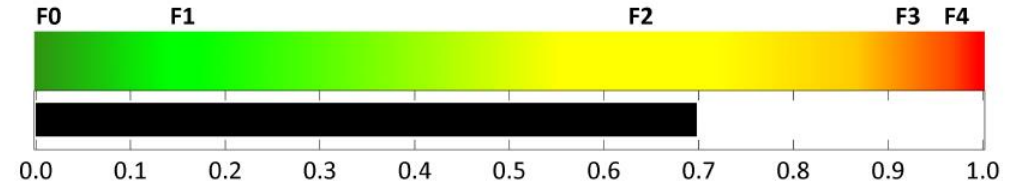
Kan tahlili tarihi : 9.10.2023			
Protrombin oranı	94.0 %	AST	48.0 UI/L
GGT	32.0 UI/L	ALT	53.0 UI/L
Trombosit	165.0 G/L	Üre	4.6 mmol/L
A2M	2.77 g/L	Yaş	53.9 y
Cinsiyet	Erkek		

SONUÇLAR

FibroMeter

Fibrozis skoru

Skor Sınıflandırma¹
0.70 F2[F1-F3]
F2 üstünlüğü ama F1 ve F3 mümkünlerdir



CirrhoMètre

Siroz skoru

0.10

CirrhoMeter grafiği ve sınıflandırılması görüntülenmemiştir çünkü bu hasta için en uygun test FibroMeter testidir.

FibroScan®

FIBROSCAN® READINGS

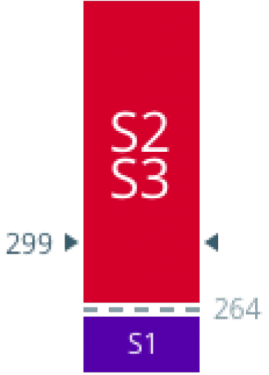
VCTE liver examination date: 10/18/2023

CAP = 299 dB/m

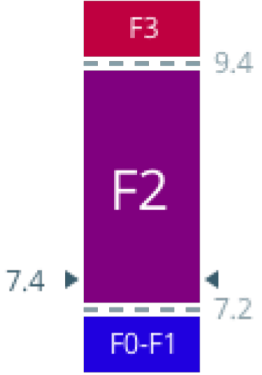
E = 7.4 kPa

RESULTS

STEATOSIS GRADE



FIBROSIS STAGE





FibroScan Detection of Fatty Liver/Liver Fibrosis in 2266 Cases of Chronic Hepatitis B

Tingchen He¹, Jing Li¹, Yanling Qiu¹, Guotao Lu¹, Xiaofeng Cao², Zhibiao Zhang^{1*}

FibroScan karaciğerin eş zamanlı hem sertliği hem de CAP ölçümü non-invazif olarak değerlendirilebilir

2266 kronik hepatit B hastası; fibrozis, siroz ve MASLD açısından değerlendirilmiş

Fibroscan, KHB takip ve yönetiminde güvenilir bir yöntem olarak değerlendirilmiş

between FibroScan liver stiffness measurement/CAP values and liver function, blood fat, uric acid metabolite, fibrosis, and hepatitis B virus load. **Results:** A total of 2266 CHB patients were enrolled in the study and divided into three groups: non-significant and significant fibrosis; non-cirrhotic

the weight of liver fat accounts for more than 5% of the total liver weight, or where the histological appearance of fat accounts for 30% or more of liver volume.² Fatty liver includes alcoholic fatty liver disease (ALD) and non-alcoholic



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DICLE ÜNİVERSİTESİ HASTANESİ ENFEKSİYON HASTALIKLARI AD
21280 Diyarbakir - Türkiye

LABORATUVAR

DICLE UNIVERSITY
HOSPITAL
21280 DIYARBAKIR - Türkiye

HASTA

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BIYOBELİRTEÇLER

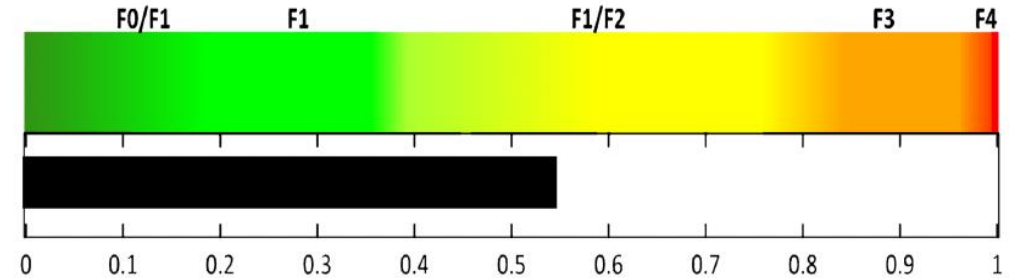
Kan tahlili tarihi : 9.10.2023 - FibroScan muayene tarihi : 18.10.2023

Protrombin oranı	94.0 %	AST	48.0 U/L
Trombosit	165.0 G/L	A2M	2.77 g/L
GGT	32.0 U/L	Karaciğer elastikiyeti	7.4 kPa
Yaş	53.9 y	Cinsiyet	Erkek

SONUÇLAR

FibroMeter^{VCTE}
Fibrosis skoru

Skor 0.55 Sınıflandırma¹ F1/F2
F1 ve F2 arasında olasılık



Diagnostic usefulness of FibroMeter VCTE for hepatic fibrosis in patients with nonalcoholic fatty liver disease

Dincses, Elif^a; Yilmaz, Yusuf^{b,c}

[Author Information](#) 

European Journal of Gastroenterology & Hepatology 27(10):p 1149-1153, October 2015. | DOI: 10.1097/MEG.0000000000000409

BUY

 Metrics

Abstract

Background

Liver fibrosis is an important prognostic determinant in patients with nonalcoholic fatty liver disease (NAFLD). The FibroMeter VCTE is a diagnostic tool comprising both biochemical markers and transient elastography (TE) originally developed for the diagnosis of fibrosis in patients with chronic viral hepatitis. In this pilot study, we investigated the diagnostic performance of the FibroMeter VCTE tool for determining fibrosis in patients with biopsy-proven NAFLD. Its diagnostic accuracy was also compared with those of the NAFLD fibrosis score (NFS) and TE alone.

Patients and methods

FibroMeter VCTE, NFS, and TE were determined in 52 patients with NAFLD. The results of liver biopsies were considered the gold standard. Areas under the receiver operating characteristic curve were used to express the diagnostic accuracy of each test.

Çalışmada toplam 52 hasta dahil edilmiş

KC biyopsisi, TE ve FibroMeterVCTE

Duyarlılık %90 %90 %100

Özgüllük %78 %76 %93

İleri Fibroziste FibroMeterVCTE (p<0,05)

YAVUZ KAYA, 54 Y

HBV-DNA: 43.500 IU/ml

Trombositleri: 165.000

ALT 53, AST 48

USG: Normal

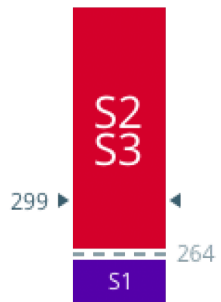
KARACİĞER BİYOPSİSİ: HAI: 4 FİBROZİS:1
FIBROSCAN® READINGS

VCTE liver examination date: 10/18/2023

CAP = 299 dB/m

RESULTS

STEATOSIS GRADE



FI



FibroMeter



22320

TEÇLER

2023

Karaciğer Biyopsisi: HAI 4 Fibrozis 1
FibroMeter: skor 0.70 F2 (F1-F3)
FibroScan: 7.4 kPa F2
FibroMeterVCTE: skor 0.50 F1/F2

Adı YAVUZ
Doğum tarihi 9.11.1969
Cinsiyet Erkek

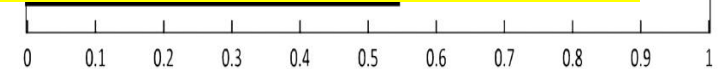
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Trombosit	165.0 G/L	A2M	2.77 g/L
GGT	32.0 U/L	Karaciğer elastikiyeti	7.4 kPa
Yaş	53.9 y	Cinsiyet	Erkek

SONUÇLAR

Skor Sınıflandırma1

TİTCK, endikasyon dışı başvurusu yapıldı...

12 ay süre ile Entecavir 0.5 mg tb tedavisi onaylandı





TEŞEKKÜRLER SORULAR?

