





# Non-invasive Tests in NAFLD

### **Creating Pathways between Primary Care and Liver Clinics**

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☑ I have the following potential conflicts of interest to report:

Speaker's bureau: Allergan, Gilead, Intercept, Merck, Novo Nordisk, Pfizer, Servier

Honoraria : Abbvie, echosens, intercept, Gilead

# The challenge is to identify patients with NASH and advanced fibrosis



The challenge is to identify patients most at risk of complications, especially those with advanced fibrosis, and link them to care

### Liver biopsy is impractical and has many limitations



# Outline

• Critical issues when using non-invasive tests

• Evidence in NAFLD

• Referral pathways

# Available non-invasive tests: two different but complementary approaches

#### « Biological » approach



#### « Physical » approach



EASL-ALEH Clinical Practice Guidelines. J Hepatol 2015; 63: 237–64

## Critical issues when using non-invasive tests

1. Availability

2. Cost

3. Applicability

4. Context of use

# Available non-invasive tests: Availability and cost



EASL-ALEH Clinical Practice Guidelines. J Hepatol 2015; 63: 237–64

# **Applicability of non-invasive tests**



Poynard et al. BMC Gastroenterol 2011

Castera et al. Hepatology 2010

#### **Applicability of elastography techniques**



Castera L, Friedrich-Rust M, Loomba R. Gastroenterology 2019; 156: 1264-81

# Available non-invasive tests: Context of use



EASL-ALEH Clinical Practice Guidelines. J Hepatol 2015; 63: 237–64

# Importance of context of use



# Prevalence of advanced fibrosis according to the target population

	NAFLD (%)	F3–F4 (%)
Liver clinic	100	20–25
Diabetes clinic	73	17
General population	25	2.5

Kwok R et al. Gut 2016;65:1359–68; Younossi ZM et al. Hepatology 2016;64:73–84

# Importance of context of use



## Outline

#### Critical issues when using non-invasive tests

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Referral pathways

### FIB-4 and NFS are the most validated serum scores

	Number of studies (number of patients)	AUC value (mean)
APRI Advanced fibrosis	29 (6,746)	0.75
FIB-4 Advanced fibrosis	34 (8,245)	0.80
NFS Advanced fibrosis	38 (9,245)	0.78
BARD score Advanced fibrosis	30 (7,791)	0.73

Meta-analysis of 64 studies; N=13,046 patients

Xiao G et al. Hepatology 2017;66:1486-501

# Head-to-head comparison: FIB-4, NFS and ELF<sup>™</sup>

	Number of patients	AUC value (mean)
FIB-4		
Advanced fibrosis	3,123	0.78
NFS		
Advanced fibrosis	2,417	0.74
ELF™		
Advanced fibrosis	3,173	0.80

ELF<sup>™</sup> performance is similar to that of FIB-4, but widespread application is limited by cost and availability

Anstee QM et al. Hepatology 2019.

## FIB-4 vs. NFS



Sterling RK et al. Hepatology 2006;43:1317–25; Angulo P et al. Hepatology 2007;45:846–54

## Elastography techniques in NAFLD Summary

Technique	Evidence in NAFLD	Fat Detection & quantification	Failure rate	Point- of- Care	Availability	Cost
VCTE	N=25 3862	Yes CAP	<7% XL probe	Yes	+++	€
pSWE/ARFI	N=8 834	No	2%	No	++	€€
2D-SWE	N=2 447	No	13%	No	+	€€
MRE	N=6 676	Yes PDFF	0-2%	No	+	€€€

#### Castera L, Friedrich-Rust M, Loomba R. Gastroenterology 2019; 156: 1264-81

## VCTE has high diagnostic accuracy



Meta-analysis; 17 studies; N=2,642 NAFLD patients with F3-F4

Xiao G et al. Hepatology 2017;66:1486–501

#### VCTE has high NPV but suboptimal PPV for F3-F4 in NAFLD



 Tapper et al. Am J Gastroenterol 2016; 111: 677-84
 Petta et al. APT 2017; 46 : 617-27

 Siddiqui et al. CGH 2019;17:156–163
 Eddowes PJ et al. Gastroenterology 2019; 156: 1717-30

# **Outline**

#### Critical issues when using non-invasive tests

#### • Evidence in NAFLD

• Referral pathways

### NAFLD: an under-recognised disease in Primary Health Care



#### Referral to specialist <10%

- No symptoms
- No simple diagnostic marker
- · Lack of awareness of most GP

Blais P et al. Am J Gastroenterol 2015;110:10–14

# High prevalence, low severity (F3-F4 <5%)



### Simple serum scores should be used as first-line FIB-4 vs. NFS



Sterling RK et al. Hepatology 2006;43:1317–25; Angulo P et al. Hepatology 2007;45:846–54

# FIB-4 and NFS performance according to context of use



N= 759 NAFLD patients 10 centers in Asia

Chan et al. GCH 2019; 17: 2570-80

### **Need for a second test**



Tsochatzis & Newsome. Lancet GH 2018; 3: 509-17

# **Combination: what is the best strategy?**



# **Paired combination**



N= 741 NAFLD patients ; tertiary referral center

Petta et al. APT 2017

# **Sequential combination**



N= 3,200 NAFLD patients ; tertiary referral centers; 71% F3-F4

Anstee QM et al. Hepatology 2019.

# From selected patients to real-life populations the Camden-Islington algorithm



#### Srivastava A et al. J Hepatol 2019;71:371–8

# From selected patients to real-life populations the Camden-Islington algorithm



#### Srivastava A et al. J Hepatol 2019;71:371–8

## **Impact on referrals**



Srivastava A et al. J Hepatol 2019;71:371–8

## **Screening type 2 Diabetics with VCTE**



# **Use in clinical practice**

#### **Patients in Primary Health Care**

#### **1st line: General practitioner**





# **Take Home messages**

- VCTE, FIB-4, and NAFLD fibrosis score are the most widely used and best validated tests
- Availability, cost, applicability and context of use are critical issues when using non-invasive tests
- The optimal way to identify F3-F4 NAFLD patients is the sequential use of FIB-4/NFS then VCTE to select those who should be considered for LB
- The next step is to establish effective pathways from primary health care and/or diabetes clinics where most NAFLD patients are seen in order to identify those who need to be referred to liver clinics for further assessment