***HIV Medicine*: Letter**

Title

Central obesity and non-alcoholic fatty liver disease in people living with HIV: a case for targeted screening?

Short title

NAFLD in HIV

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Main text

Sir,

Non-alcoholic fatty liver disease (NAFLD) is common in people living with HIV (PLWH) (1). A recent update to European guidance suggests screening for NAFLD in PLWH who also have metabolic syndrome (MetS) (2). Equivalent UK guidance does not yet exist. We therefore aimed to pilot a pragmatic approach to NAFLD, using data routinely collected in a UK HIV clinic setting.

Consecutive adult PLWH attending for outpatient care were reviewed, and those with recurrently abnormal liver function (defined here as ALT >ULN on ≥2 occasions in last 13 months) were identified for further evaluation. At next planned visit we assessed central obesity (CO, by waist circumference (WC), per WHO cut-offs (3)) and insulin resistance (IR, defined as type 2 diabetes mellitus and/or elevated HbA_1C >42mmol/mol). Where a presumptive diagnosis of NAFLD was made, staging was performed using the NAFLD Fibrosis Score (NAFLD-FS) (4).

544 consecutive patients were evaluated. 100 (18%) had recurrently abnormal ALT. Of these 46 were excluded owing to viral hepatitis co-infection, alcohol excess, or other liver disease, and 10 did not attend for imaging. Of the remaining 44 patients (83% male, mean age 49.2 years, mean duration of diagnosed HIV infection 9.5 years, 91% ART treated), CO was present in 74%. By body mass index,

25% were overweight (BMI 25-29.9) and 37% obese (BMI ≥30). Of note, 22% of subjects with CO had normal BMI. 23% had IR, and 14% MetS, all of whom had coexisting CO.

After other causes were excluded, NAFLD was the commonest cause of liver disease, with a prevalence of 55% (representing 24% of all those with recurrently elevated ALT). A further 18% had possible NAFLD (CO/IR with no fat on USS). 88% of NAFLD cases were previously undiagnosed. Almost all patients with NAFLD had CO (sensitivity 94%, specificity 50%). BMI-defined obesity was less sensitive (Sn 80%, Sp 47%), and most did not have overt IR (Sn 29%, Sp 88%) or MetS. There was no association between presence of NAFLD and current or nadir CD4 count, duration of HIV infection, or duration or class of ART. Of subjects with NAFLD, 74% had low, 21% indeterminate, and 5% high fibrosis risk.

The prevalence of recurrently elevated ALT in a typical HIV cohort was high. NAFLD was the commonest cause of liver disease, and a large majority of cases were previously undiagnosed. As a pragmatic study based on current UK monitoring practice, we considered only those PLWH with elevated ALT. As such, we will have underestimated the true prevalence of NAFLD. WC will identify almost all PLWH with NAFLD, but the EACS approach of screening only those with MetS, whilst highly specific, appears to be insufficiently sensitive. It is noteworthy that, in the contemporary HIV clinic, 'lean NAFLD' is uncommon.

We therefore recommend implementation of routine WC measurement in UK clinical care (this will also enhance cardiovascular risk stratification), with targeting of NAFLD screening to those PLWH with CO. Future work should compare the Sn/Sp of this approach in the presence or absence of elevated ALT.

(500w)

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Insert

Figure 1. Suggested approach to NAFLD in PLWH. CO, central obesity; IR, insulin resistance; MetS, metabolic syndrome; USS, ultrasound scan; NAFLD-FS, NAFLD fibrosis score; TE, transient elastography. Adapted from Dyson *et al.* (5)

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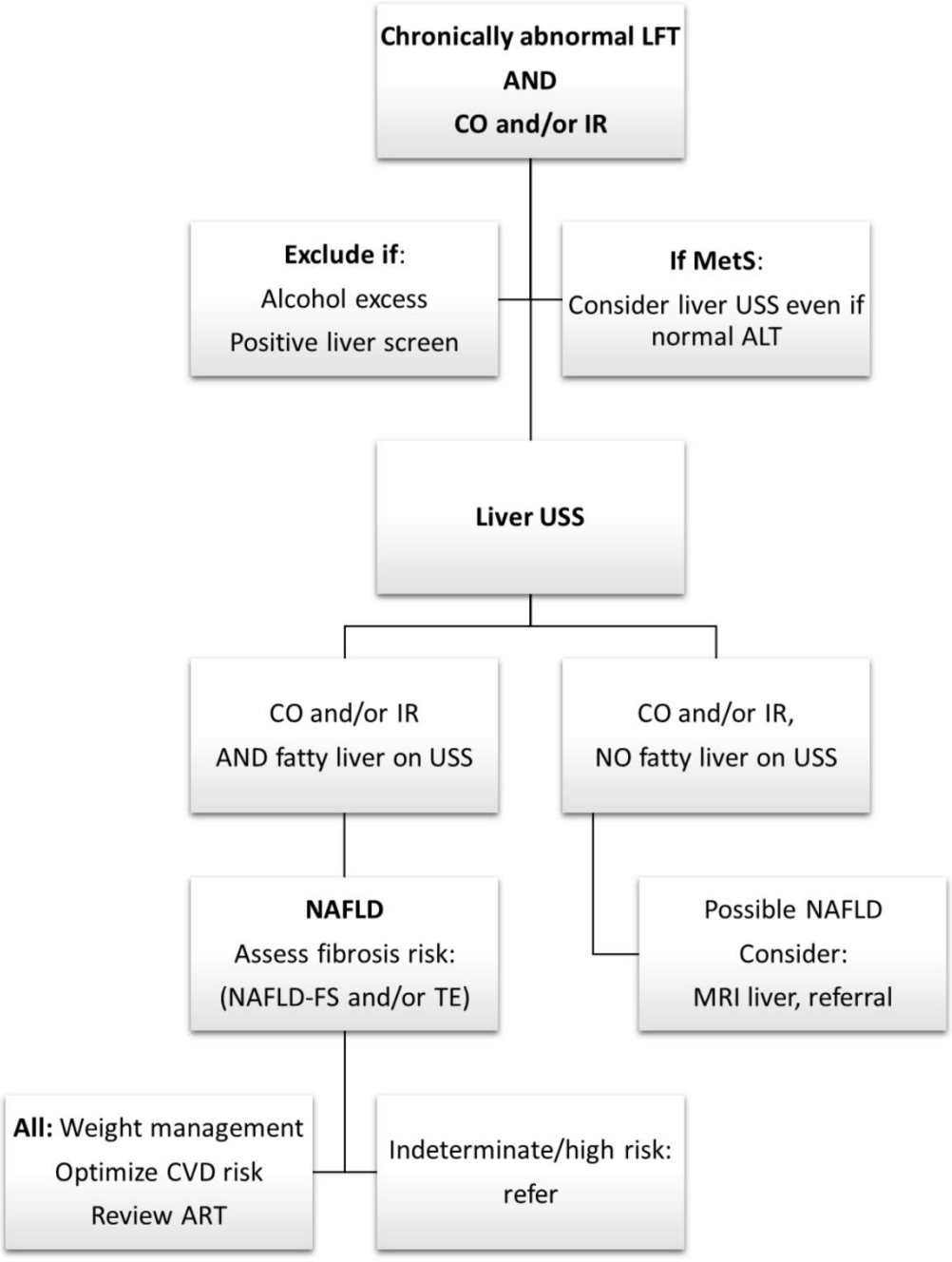
Chronically abnormal LFT
AND
CO and/or IR
Exclude if:
Alcohol excess
Positive liver screen
If MetS:
Consider liver USS even if normal ALT
Liver USS
CO and/or IR
AND fatty liver on USS
CO and/or IR,
NO fatty liver on USS
NAFLD
Assess fibrosis risk:
(NAFLD-FS and/or TE)
Possible NAFLD
Consider:
MRI liver, referral
All: Weight management
Optimize CVD risk
Review ART
Indeterminate/high risk:
refer