Out of Hours

Writing liver function test guidelines:

how hard can it be?

I was asked to write local guidelines for our referral management service for GPs to manage asymptomatic abnormal liver function tests (LFTs). *'I'd be delighted'*, I said. *'How hard can it be?'* I thought.

I was only a year off being a consultant in gastroenterology (including having worked at King's Liver Unit) when I changed to general practice. That was 10 years ago. Now half my week is as a salaried GP, and I spend the other half performing endoscopy at our district general hospital and I have close ties to the gastro department. I've got an understanding of the liver and primary care, and secondary care and the referral system. Let's crack on.

PREVALENCE OF LIVER DISEASE

We know liver disease is a problem and it is only increasing in the UK, predominantly from an increase in alcohol-related liver disease, non-alcoholic fatty liver disease (NAFLD), and hepatitis C virus (HCV). Whereas other causes of death are dropping, liver deaths are the third commonest cause of premature death in the UK and rates are soaring. Deaths are often a decade or two younger than in cardiopulmonary disease.

Up to one-third of the UK adult population have NAFLD and 2–3% have more advanced fibrotic disease: non-alcoholic steato-hepatitis (NASH).[1] Those with NAFLD are best off in primary care to control metabolic and cardiovascular risk factors but 10–20% of patients with NASH will progress to cirrhosis, where a liver death becomes more likely.

My specialist colleagues articulated how frustrating it is that three-quarters of patients with advanced liver disease present as an emergency: jaundiced, bleeding, decompensated, *in extremis*. Moreover, a large proportion of these have previously had abnormal LFTs and *'if the GP had referred them then this could have been prevented'*. Understandable frustration, I agree.

LFTs are increasingly requested from primary care, often as part of chronic disease and medication reviews rather than for symptoms. Minor abnormalities are commonplace and even with detailed workup the cause is only found about half the time.[2] Furthermore, about three-quarters of cases of advanced liver fibrosis have NORMAL LFTs. So we're planning to write guidance for insensitive, non-specific, frequently-ordered tests that are requested on a large cohort of patients that is mostly asymptomatic. Furthermore, gold standard assessment of abnormal LFTs is time consuming, of low yield, risks iatrogenic harm, and this work isn't specifically remunerated for in general practice via the QOF. Marvellous.

OUR ALGORITHM

We set to work on our algorithm, which included an extra test to the usual liver screen. Not an exotic test: the AST (aspartate aminotransferase). This is of interest because in alcohol-related and NAFLD (which accounts for about a half of abnormal LFTs when the cause is known),[3] the ratio of AST to ALT (alanine transaminase) is <0.8 in benign disease and the patient can be reassured. However, in more advanced fibrotic or cirrhotic disease this ratio can flip to ≥0.8, at which point our guideline suggested referral to the hepatologists for further testing. (This is usually a non-invasive assessment of hepatic fibrosis, where a fibroscan measures the liver's elasticity and quite accurately predicts histology.)

The guidance was drafted with the anticipation of getting the right patients into clinic early: to identify those with advanced liver fibrosis or cirrhosis and treat with intensive lifestyle modification and entry into surveillance programmes for detection of hepatoma and varices. This should have positive knock-on effects for the local and national liver strategy, emergency admissions, and transplant waiting lists.

I presented the guidance to our GP commissioners. I was asked what burden of GP workload is anticipated? How many tests? How many referrals to secondary care? What can they offer above cardiovascular and lifestyle modifications that we can do in primary care? How many patients have to be screened and referred and surveyed to prevent one decompensating or dying?

My practice population is 7200. In a recent 12-month period we requested 3245 LFTs and 468 patients had a raised ALT. This is 6.5% of our total population. Scale that up to the 550 000 population of Cornwall and we're talking 35 750 raised ALTs requiring GP assessment for alcohol, viral, and fatty liver disease with subsequent liver blood screens, ultrasound scans, and the AST.

We estimated that 10% of the ALTs would have a reversed AST: ALT ratio. That's 3500 referrals per year. At present it is 350.

I explained that in the Birmingham study 2% of abnormal LFTs have significant liver fibrosis[2] and that's not far off the 3% positive predictive value bar set by the National Institute for Health and Care Excellence (NICE) for new urgent suspected cancer referrals. We often refer patients with a much lower than 2% risk of significant disease. I explained that we don't know the numbers needed to screen or survey to prevent decompensation or death. The evidence is meagre and of low quality in NICE's draft full guidance on cirrhosis but this is what the specialist societies advise.

'We're not publishing these guidelines', I was told emphatically. I realised I knew this scenario well from my interest in overdiagnosis. As generalists we know the yield of investigating 'pre-disease' is very small, the vast majority of patients won't benefit and some will be harmed. But as specialists, day after day we live in the tip of the iceberg, which is sick, yellow, and sometimes dead and we want to make things better. As the middleman I couldn't get the generalist and specialist agendas to overlap.

In the future, with increased availability of fibroscanners, more creative service design, and integrated working (plus time, money, and effort) we could assess patients locally and get those at highest risk into the hepatology services as dreamed about in the latest draft NICE guidelines on cirrhosis.[3] But for the moment, we're stuck.

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REFERENCES

1. British Society of Gastroenterology. *Chronic management: NASH and non-alcoholic fatty liver disease*. http://www.bsg.org.uk/clinical/commissioning-report/nash-and-non-alcoholic-fatty-liver-disease.html (accessed 4 Jul 2016).
2. Armstrong MJ, Houlihan DD, Bentham L, *et al*. Presence and severity of NAFLD in a large prospective primary care cohort. *J Hepatol* 2012; **56(1):** 234–240.
3. National Institute for Health and Care Excellence. *Cirrhosis in over 16s: assessment and management*. NICE guideline: short version. 2015. https://www.nice.org.uk/guidance/GID-CGWAVE0683/documents/short-version-of-draft-guideline (accessed 4 Jul 2016).