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Title **Development of a Decision Support Tool for Primary Care Management of Patients with Abnormal Liver Function Tests Without Clinically Apparent Liver Disease: A Record-Linkage Population Cohort Study and Decision Analysis (ALFIE)**

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Aim

To determine the natural history of abnormalities in liver function tests (LFTs) before overt liver disease presents in the population, derive predictive algorithms for liver disease, and analyze cost-utility to lead to decision aids that would identify those requiring further investigation, or none, with the potential for early diagnosis or reducing National Health Service (NHS) costs.

Conclusions and results

From 1989 to 2003 in primary care, 95 977 patients had 364 194 incident-initial LFTs without obvious liver disease. This cohort had a median follow-up of 3.7 years. Of these 21.7% had at least one abnormal LFT and 1.3% (1213) developed liver disease. Elevated transaminases were strongly associated with diagnosed liver disease, hazard ratio (HR)=4.20 (3.54, 4.98) for mild levels and HR=11.99 (9.26, 15.52) for severe levels vs normal. For gamma-glutamyltransferase (GGT) these hazards were 2.46 (2.12, 2.86) and 13.21 (10.60, 16.46) respectively. Low albumin was strongly associated with all-cause mortality, 2.65 (95% CI 2.47, 2.85) for mild levels and 4.99 (95% CI 4.26, 5.84) for severe levels. Predictive algorithms were developed for three time periods; 0 to 3 months, 3 months to 1 year, and over 1 year, for liver disease diagnosis, liver mortality, and all-cause mortality using the Weibull regression model. All LFTs and several interaction terms were predictive of liver disease, and high probability of liver disease was associated with being female, methadone use, alcohol dependency, history of cancer, and deprivation. The shorter-term models had overall c-statistics of 0.85 and 0.72 for outcome of liver disease at 3 months and 1 year respectively, and 0.88 and 0.82 for all-cause mortality at 3 months and 1 year respectively. Calibration was also good for models predicting liver disease.

Recommendations

From this large population-based, data-linked database we developed several predictive algorithms, which displayed good discriminative performance and calibration. Further work will seek to develop these into user-friendly decision aids. Cost-utility analyses indicated that identifying high-risk patients for immediate referral to secondary care would be cost effective, while in low-risk patients re-testing in primary care was more cost effective.

Methods

See Executive Summary link at www.ncchta.org/project/1460.asp.

Further research/reviews required

The derived predictive algorithms could be further developed into user-friendly computerized decision aids. These could be evaluated in cluster-randomized trials to assess their value in aiding decisions in primary care. This will facilitate optimal decision-making, both for the benefit of the patient and the NHS.

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