Cardiovascular disease

ECG-based tool aids rapid risk assessment for a cardiac cause of syncope

In patients with a syncopal event, a combination of seven ECG criteria enabled a rapid assessment of the likelihood that the event was due to a cardiac cause, in a prospective multicentre trial.

A total of 2,007 patients, aged over 40 years, presenting to the emergency department with syncope within the past 12 hours were recruited to the BASEL IX study from May 2010 to July 2017. The median age of patients was 71 years and 40% were women.

The participating centres ranged from large university hospitals to smaller rural hospitals in eight countries (Switzerland, Germany, Poland, Spain, Italy, Australia, New Zealand, and the USA).

12-Lead ECG recordings were obtained at presentation following the syncopal event. The primary diagnostic outcome was a cardiac cause of syncope, and this was determined by two independent cardiologists using all available clinical information including 12-month follow-up.

The authors identified seven ECG criteria as predictors for a cardiac cause of syncope. These were: heart rate; corrected QT-interval; rhythm; atrioventricular block; ST-segment depression; bundle branch block and ventricular extrasystole/non-sustained ventricular tachycardia. These predictors were used to generate a risk score ALERT-CS.

The Improving Syncope Risk Stratification in Older Adults study was used as the external validation cohort. This prospective multicentre observational cohort study enrolled adults aged 60 years and older at 11 emergency departments in the USA, who presented with syncope or near-syncope. Median age was 72 and 48% were women.

In the BASEL IX study, the diagnostic accuracy of these combined predictors (ALERT-CS) for a cardiac cause of syncope was high with an area under the curve (AUC) 0.80 (95% CI: 0.77-0.83).

Patients with an adjudicated cardiac cause of syncope (n = 267, 16%) were older and had a higher prevalence of known cardiovascular disorders. Bradycardia (n = 121, 45%) and tachyarrhythmia (n = 60, 22%) were the two most common subtypes of a cardiac cause of syncope.

The ALERT-CS performed similarly for diagnosing cardiac causes of syncope of tachyarrhythmic origin AUC 0.82 (95% CI: 0.76-0.87) and bradyarrhythmic origin AUC 0.78 (95% CI: 0.74-0.83, P = 0.328)

Around 10% (n = 175) of patients experienced a major adverse cardiac event within 30 days of the index event, defined as all-cause death, acute myocardial infarction, life-threatening arrhythmia including cardiac arrest, pacemaker or cardioverter defibrillator implantation.

Patients in the ALERT-CS rule-in group for a cardiac cause of syncope had a significantly increased risk: HR 35.7 (95% CI: 8.8-145.5) compared with the rule-out group, which had a very low risk (HR set to 1.0 as the reference group).

Syncope is a relatively common presenting problem in primary care and often causes considerable anxiety in both physicians and patients alike, associated with diagnostic uncertainty, and may result in unnecessary investigations. Prompt determination of syncope aetiology is essential for the initiation of evidence-based therapy, particularly for patients with a cardiac cause.

However, in many cases referral to specialist cardiology services can be avoided with a careful history and 12-lead ECG. This study highlights the importance of performing a 12-lead ECG in all patients presenting with syncope and furthermore highlights criteria that can be used to judge the importance of any abnormalities seen and facilitate prompt referral of those patients with a suspected cardiac cause.

The study authors conclude: 'Combining seven ECG criteria within the simple ALERT-CS may aid emergency department physicians in the early rule-out or rule-in of a cardiac cause of syncope.'

DR PETER SAVILL

Zimmermann T, du Fay de Lavallaz J, Walter JE et al, the BASEL IX and SRS Investigators. Development of an electrocardiogram-based risk calculator for a cardiac cause of syncope. *Heart* 2021;107:1796-1804

Cardiovascular disease

Can choice of anticoagulant for AF influence risk of incident dementia?

Dementia and mild cognitive impairment were less common among patients prescribed direct oral anticoagulants (DOACs) for newly diagnosed atrial fibrillation (AF) compared with those prescribed vitamin K antagonists (VKAs), in a UK cohort study.

The authors used electronic health records from the UK Clinical Practice Research Datalink, linked to Hospital Episodes Statistics and Index of Multiple Deprivation data, to identify first-time oral anticoagulant users with non-valvular AF diagnosed between 2012 and 2018.

They compared the incidence of dementia and mild cognitive impairment in patients prescribed VKAs and those prescribed DOACs.

The statistical analysis accounted for variables such as calendar time and time on treatment, sociodemographic and lifestyle factors, clinical comorbidities and other medication.

Of 39,200 first-time oral anticoagulant users (44.6% female), median age 76 years, 20,687 (53%)

were prescribed a VKA and 18,513 (47%) a DOAC at baseline.

Demographic and lifestyle factors were similar in those prescribed DOACs and VKAs and there was no difference in the history of stroke, a major risk factor for dementia, between the different treatment groups.

A total of 1,258 patients (3.2%) had a diagnosis of dementia recorded by their GP with an incidence of 16.5 per 1,000 person-years. Overall, 1,488 patients (4.0%) received a diagnosis of mild cognitive impairment, with an incidence rate of 20.05 per 1,000 person-years.

In the whole cohort, compared with VKA therapy DOAC treatment for AF was associated with:

- 16% reduction in dementia diagnosis; adjusted hazard ratio (HR) 0.84 (95% CI: 0.73-0.98)
- 26% reduction in mild cognitive impairment; adjusted HR 0.74 (95% CI: 0.65-0.84)

Dementia risk is almost double in patients with AF. This could be due to silent cerebral infarcts, microemboli or systemic inflammation. Certainly, cerebral hypoperfusion is linked to neurodegeneration.

Oral anticoagulant treatment is recommended to reduce the risk of stroke in high-risk individuals with AF and could potentially protect patients from the excess dementia risk associated with this arrhythmia.

The authors conclude:
'We observed that individuals taking DOACs for AF were less likely to be diagnosed with dementia and mild cognitive impairment than those taking VKAs, after adjusting for potential confounding factors.

'While further evidence, including from randomised controlled trials, would strengthen this finding, it may be relevant to consider cognitive risk profile when prescribing oral anticoagulants for AF among older individuals.'

DR PETER SAVILL
Cadogan SL, Powell E, Wing K et al. Anticoagulant prescribing for atrial fibrillation and risk of incident dementia. *Heart* 2021;107:1898-1904

Gastrointestinal disease

NAFLD increases risk of all-cause mortality

In patients with non-alcoholic fatty liver disease (NAFLD), fibrosis stages F3 and F4 are associated with an increased risk of liver-related health problems and death from all causes, a large prospective study from the USA has found.

The authors followed 1,773 patients (64% women), mean age 52 years, with NAFLD for a median of four years. Participants were enrolled from multiple centres between 2009 and 2019.

Alcohol-related liver disease was excluded using the Alcohol Use Disorders Identification Test (AUDIT), and patients with liver disease from other causes, or with a history of liver transplant or hepatocellular cancer were also excluded.

All patients had undergone liver biopsy, and the stage of fibrosis for each participant was assigned by a specialist committee. More than half (55%) had definite nonalcoholic steatohepatitis (NASH), 20% had borderline NASH and 25% fatty liver without NASH.

The main outcomes included death from any cause, hepatic decompensation (clinically apparent ascites, overt encephalopathy, or variceal haemorrhage), the development of hepatocellular cancer, non-hepatic cancer, cardiovascular events, cerebrovascular events and new onset of coexisting conditions including type 2 diabetes, hypertension and chronic kidney disease.

All-cause mortality was higher in the study population than the expected background age-related rates:

- 0.57 vs 0.4 deaths per 100 person-years

All-cause mortality rates increased with increasing fibrosis:

- 0.32 deaths per 100 person-years for fibrosis stages F0 to F2 (no, mild or moderate fibrosis)
- 0.89 deaths per 100 person-years for fibrosis stage F3
- 1.76 deaths per 100 patient-years for fibrosis stage F4 (cirrhosis)

Likewise, the incidence of liver-related health problems increased with the degree of fibrosis.

Variceal haemorrhage rates:

- 0.00 per 100 person-years for F0 to F2
- 0.06 per 100 person-years for F3
- 0.70 per 100 patient-years for F4

Encephalopathy rates:

- 0.02 per 100 person-years for F0 to F2
- 0.75 per 100 person-years for F3
- 2.39 per 100 patient-years for F4

Patients with F4 fibrosis were more likely to have diabetes and a reduction of > 40% in eGFR during the study period compared with those with F0-F2 fibrosis. The incidence of cardiac events and non-hepatic cancers was similar across patients with all fibrosis stages.

When adjusted for age, gender, race, diabetes status, NASH or NAFLD and fibrosis stage at baseline, the occurrence of any hepatic decompensation event during the study period was associated with increased all-cause mortality; adjusted hazard ratio 6.8 (95% CI: 2.2-21.3).

The study authors conclude:
'This study showed an association between fibrosis stages F3 and F4 and hepatic decompensation and death in patients with NAFLD.

'These data may be helpful in the assessment of prognoses and in the use of treatments for NASH.'

The development of NAFLD is strongly linked to obesity and type 2 diabetes, and its clinical and histopathological spectrum ranges from uncomplicated fatty liver to NASH which can progress to cirrhosis.

As a GP, lifestyle change and weight loss will remain the mainstay of treatment, as not only can they promote resolution of NAFLD, but they can also help reduce the risk of related conditions including diabetes and cardiovascular disease.

DR JEZ THOMPSON
Sanyal A, Van Natta JL, Clark J et al for the NASH Clinical Research Network (CRN). Prospective study of outcomes in adults with nonalcoholic fatty liver disease. *N Engl J Med* 2021;385;1559-69 »