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Incidence and prevalence of light chain amyloidosis: a population-based study

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Background: Systemic light chain (AL) amyloidosis is considered a rare disease, but knowledge of its exact incidence and prevalence is based on old data involving limited populations.

Purpose: To determine the incidence and prevalence of AL amyloidosis in the general population.

Patients and methods: The national reference center for AL amyloidosis is located in the University Hospital of Limoges, in Limoges (France), the administrative center of the Limousin region (738,110 inhabitants in 2014). A comprehensive and exhaustive database of AL amyloidosis patients diagnosed in this region has been computerized since January 2007. All patients living in the Limousin region and with a first diagnosis of systemic AL amyloidosis between January 1, 2012, and December 31, 2016, were retrospectively included to determine the disease incidence. All departments and laboratories of pathology were contacted in the region, and any possible missing cases diagnosed during the same period were collected. Prevalence was determined as all living patients with AL amyloidosis during 2016 regardless of the diagnosis date. Cardiac involvement was defined according to current definition (ie, mean wall thickness >12 mm in the absence of other causes of left ventricular hypertrophy). Renal involvement was defined as proteinuria >0.5 g/L (predominantly albumin) in the absence of other etiology.

Results: Over the 5-year period, 46 new patients in the Limousin region had a confirmed diagnosis of AL amyloidosis (70% men; median age, 72.5 years), corresponding to a crude yearly incidence of 12.5 (95% CI, 5.6–19.4) cases per million inhabitants. The calculated prevalence of AL amyloidosis was 58 (95% CI, 43–73) cases per million inhabitants. Cardiac and renal involvement was found in 70% and 72% of cases, respectively. Mayo Clinic stages I, II, IIIA (NT-proBNP ≤8500 ng/L), and IIIB (NT-proBNP >8500 ng/L) based on cardiac biomarkers were found in 21%, 29%, 29%, and 21% of patients respectively. The underlying disease was multiple myeloma in 19 patients (41%), including smoldering myeloma in 14 patients, MGUS (monoclonal gammopathy of undetermined significance) in 22 patients (48%), IgM in 2 patients, Waldenström disease in 1 patient, low-grade lymphoma in 3 patients, plasmocytoma in 1 patient, and unknown in 1 patient. In this 5-year-period, 16 patients (35%) died.

Conclusion: This is the first report of contemporary incidence and prevalence of systemic AL amyloidosis in France. Incidence was slightly higher than the incidence (adjusted to sex and age) previously reported by Kyle & colleagues (Blood, 1992; 7:1817–1822), probably corresponding to the progress in the past 20 years in diagnosing this rare disease.

P1814

Deaths and vascular outcomes with non-vitamin K oral anticoagulants versus warfarin in patients with heart failure in the food and drug administration adverse event reporting system

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Background: Many patients with heart failure (HF) are prescribed warfarin or non-vitamin K antagonist oral anticoagulants (NOACs). We sought to identify any potential clinical benefit of NOACs relative to warfarin in HF in a large real world database.

Methods: Using the US Food and Drug Administration Adverse Event Reporting System (FAERS) database, we investigated the endpoints of all-cause mortality, myocardial infarction, and stroke for warfarin and NOACs in subjects with HF during 2015. Adverse event reports in subjects on warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban were extracted and stratified according to the absence or presence of HF. We computed odds ratios (OR; 95% confidence interval, CI) for warfarin relative to NOACs.

Results: FAERS reported 137,026 HF cases, with mortality in 42,942 (31.3%).



Odds ratios for adverse events

Among HF patients 11,278 (8.2%) were on anticoagulants, with more prescribed warfarin (n=8,260; 73%) than the four NOACs combined (n=3,018; 23%). The odds ratios (OR; 95% CI) for the composite of mortality, myocardial infarction and stroke with warfarin were 1.91 (1.76–2.07) versus apixaban, 1.92 (1.81–2.03) versus dabigatran, 1.80 (1.27–2.56) versus edoxaban and 4.09 (3.38–4.37) versus rivaroxaban (all P<0.01). Warfarin, compared to all NOACs combined demonstrated higher rates of mortality (OR=2.69; fig.1 A), myocardial infarction (OR=4.91; B), hemorrhagic stroke (OR=5.32; C) and ischemic stroke (OR=12.73; D; all P<0.001).

Conclusions: Annual 2015 FAERS profiles in HF patients reveal that warfarin was associated with higher risk of mortality, myocardial infarction and stroke compared to NOACs. These observational data provide real-world insight into a potential benefit of NOACs over warfarin in the setting of HF.

P1815

Prediction of sudden death in outpatients with heart failure: a bio-clinical approach

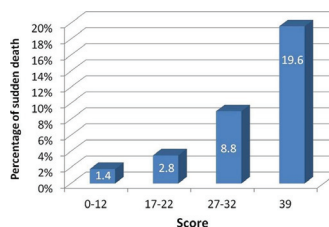
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Background: Although prevalence of sudden death (SD) has declined during last decade in patients with chronic heart failure (HF) its prediction remains a difficult challenge, not only for the diversity of parameters possibly associated with it and the difficulty of selecting the most influential but also the need of thresholding from other causes of death, currently more frequent in HF patients.

Purpose: To assess the prevalence of SD at 5 years in a real-life cohort of patients managed according to international guidelines and closely followed and to find a simple prognostic predictive model of SD.

Methods: Competing risk strategy using the Gray method was adopted in Cox regressions analyses, considering non-cardiovascular and other cardiovascular causes of death as the competing event. Statistics-C were also calculated taking into account competitive risk and time-to-event outcome. SD was considered any unexpected death, witnessed or not, occurring in a previously stable patient with no evidence of worsening HF or any other cause of death. Ambulatory patients treated at a multidisciplinary HF unit were consecutively included in the study in an outpatient setting from May 2006 to July 2010. All patients have been followed until death or completion of 5 years of follow-up.

Results: After excluding 27 patients who died from unknown causes 837 consecutive outpatients (72% men, mean age 67.9±12.2 years, LVEF 36%±14, 65.6% NYHA class II and 25.9% class III) were included. During follow-up 336 deaths occurred; causes of death were: HF 100 patients, sudden death 43, AMI 18, stroke 10, cardiovascular procedure 8, other cardiovascular 25 and non-cardiovascular 132. Variables associated with SD in univariate analyses were age (p=0.04), hemoglobin (p=0.02), eGFR (p=0.001), HF duration (p=0.02), hs-TnT (p<0.001), NTproBNP (p=0.004) and ST2 (p=0.001). In a multivariable analysis (backward stepwise) that included all these variables and also other considered clinically relevant such as sex (p=0.16), NYHA class (p=0.06), LVEF <45% (p=0.07), ischemic etiology (p=0.18), beta-blocker treatment (p=0.28), loop diuretic dose (p=0.08) and ICD (p=0.38), only HF duration (p=0.01), eGFR (p=0.009), LVEF <45% (p=0.04) and ST2 (p=0.005) remained in the model. The obtained model achieved an AUC of 0.75 (0.68–0.82) for the prediction of 5-year risk of SD. The constructed score including such variables in a dichotomous manner (ST2 >45), LVEF <45%, HF duration >3 years and eGFR <55) obtained an AUC of 0.76 (0.69–0.83).



Conclusions: In a current HF real-life cohort managed according to a structured HF clinic and international recommendations, SD accounted only for the 12% of all deaths at 5 years, affecting only to the 5.1% of the cohort. Of the 3 studied biomarkers, only ST2 remained independently associated with SD. A simple model containing ST2, eGFR, LVEF and HF duration allowed to predict the risk of SD at 5 years with an AUC of 0.76.