LEFT VENTRICULAR MASS IS A POWERFUL PROGNOSTIC FACTOR FOR ALL-CAUSE AND CV MORTALITY IN END STAGE KIDNEY DISEASE (ESKD) PATIENTS: A COMBINED ANALYSIS OF TWO EUROPEAN COHORTS

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INTRODUCTION

Left Ventricular Hypertrophy (LVH) is one of the strongest risk factors for cardiovascular morbidity and mortality in end stage kidney disease (ESKD) patients. Causality apart, the notion that LVH is useful for risk stratification in ESKD has never been formally tested by state-of-art statistical analyses, such as risk discrimination (Harrell's C index), explained variation in mortality (an index combining calibration and discrimination), and risk re-classification [net reclassification index (NRI) and integrated discrimination improvement (IDI)]. Recently, two risk scores (RS) for predicting 2-years all-cause (*Kidney Int 2015, 87: 996-1008*) and CV mortality *(Int J Cardiol 2016, in press*) in ESKD have been validated. Whether LVMI in ESKD improves the prognostic power of these simple risk prediction instruments, such as the RS, has never been explored.

Fig.1

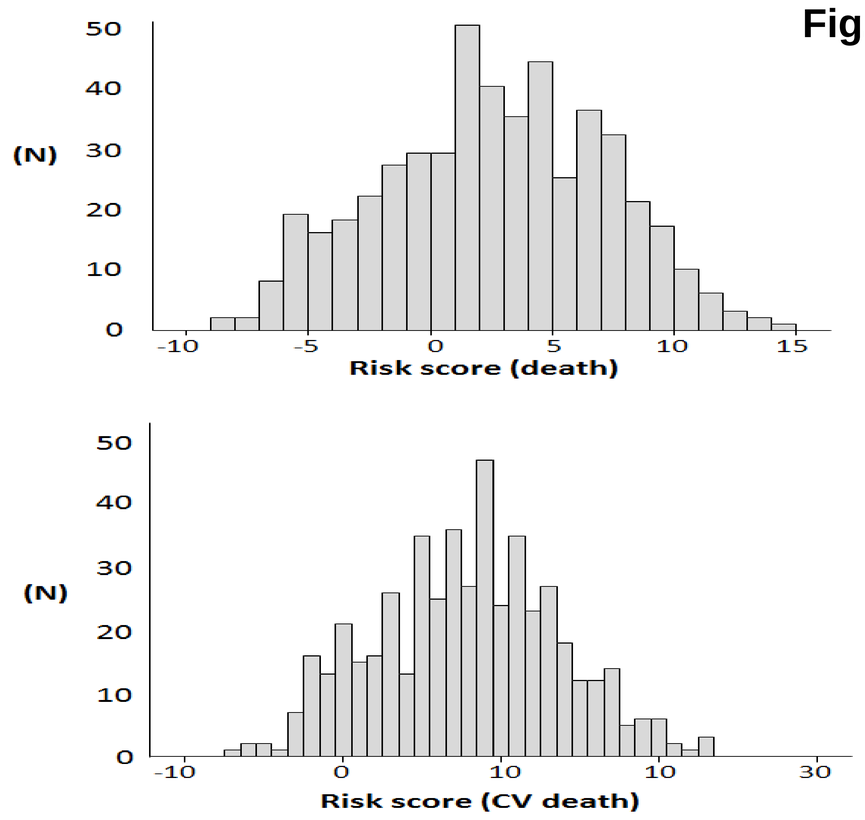
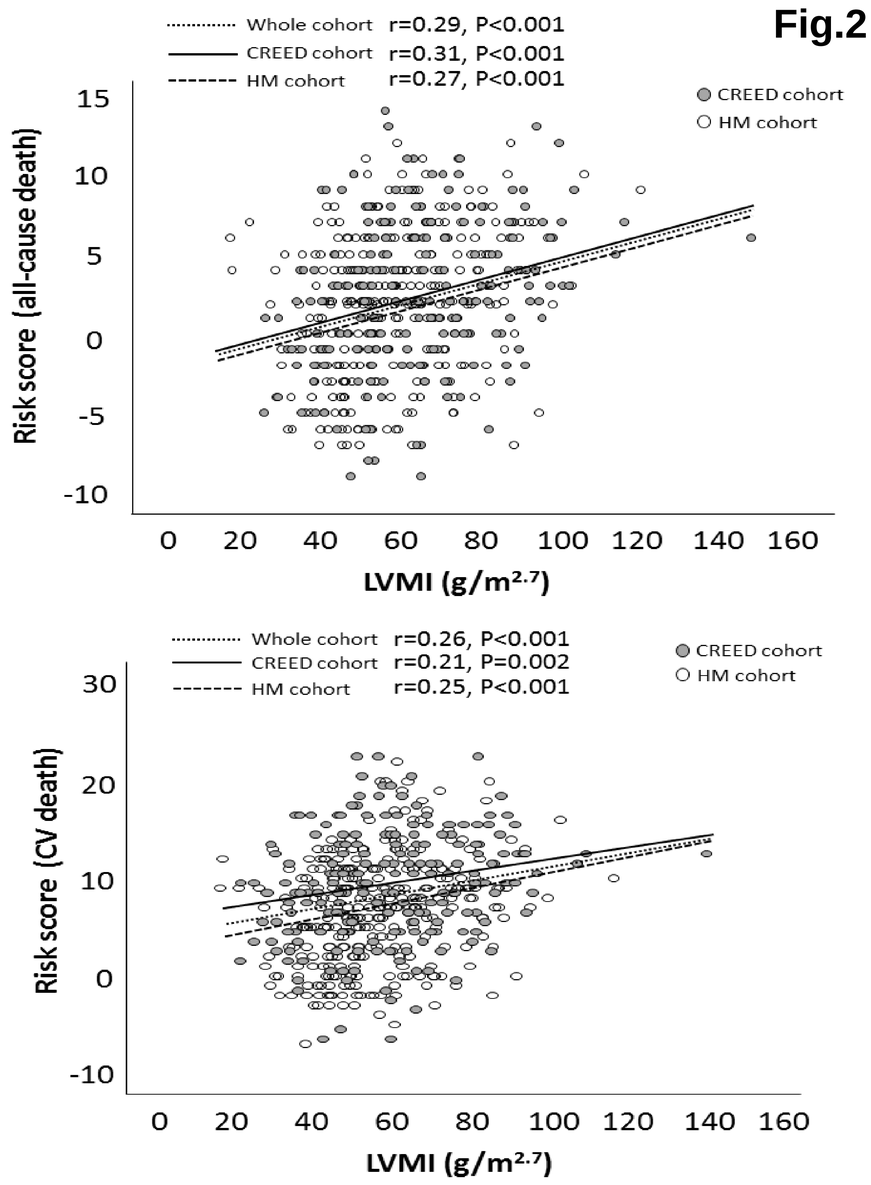
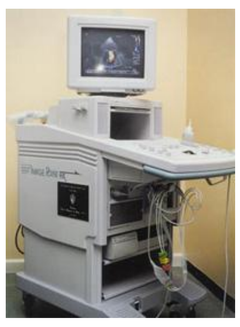


Fig.2



METHODS

We analyzed the prognostic power of LVMI, beyond and above the RS, for predicting all-cause and CV mortality over 2 years follow-up in a combined (n=489) cohort of haemodialysis patients in Italy and in France, the Cardiovascular Risk Extended Evaluation cohort (CREED cohort, n=207) and the Hospital Manhes cohort (HM cohort, n=282]. During a non dialysis day, each patient underwent a fasting blood sampling as well as a standard echocardiography. Left ventricular mass (LVM) was calculated according to the Devereux formula and indexed to height$^{2.7}$ (LVMI). LVH was defined by a LVMI >47 g/m$^{2.7}$ in women or >50 g/m$^{2.7}$ in men.



RESULTS

The study population included 489 hemodialysis patients (Table 1). The mean age of patients was 56±16 years and 12% were diabetics. The majority of patients were males (59%), about one half were on anti-hypertensive treatment (48%) and smokers (42%) and one third had background CV comorbidities (34%). LVMI was on average 59±18 g/m2.7 and the prevalence rate of LVH was 70%. The risk scores for prognosticating all-cause and cardiovascular mortality had approximately a normal distribution (Fig.1) and this was also true in a separate analysis by cohorts (data not shown). On univariate analysis, LVMI was significantly related to cause-specific risk scores (Fig.2) in both the whole study cohort as well as in the two cohorts (CREED and HM cohorts) considered separately (Fig.2). Of note, the strength of the linear association between LVMI and the two risk scores was almost identical in the CREED and HM cohort (Fig.2).

Cox regression analysis

During the 2 year follow-up period, 123 patients died, 80 of them (65%) of cardiovascular causes. In multiple Cox model, stratified by cohort (CREED and HM cohort), both variables [LVMI, hazard ratio (HR): 1.02, 95% CI: 1.01-1.03, P<0.001] and the risk score (HR: 1.20, 95% CI: 1.14-1.26, P<0.001) significantly and independently associated to all-cause mortality. The same analysis carried out according to CV mortality provided similar results (LVMI, HR: 1.03, 95% CI: 1.01-1.04, P<0.001; risk score, HR: 1.16, 95% CI: 1.11-1.21, P<0.001).

Prognostic value of LVMI

LVMI provided a Harrell's C indexes (all-cause death: 64%; CV death: 66%) and an explained variation (all-cause death: 12%; CV death: 9%) which were lower than the two risk scores (all-cause death, Harrell's C index: 74%; explained variation: 27%; CV death, Harrell's C index: 71%; explained variation: 16%). The simultaneous inclusion of LVMI and risk scores into the same Cox model, produced a joint discriminatory power for all-cause (Harrell's C index: 76%; explained variation: 30%) and CV mortality (Harrell's C index: 74%; explained variation: 18%) which were higher than those provided by the sole LVMI and risk scores (both P≤0.02).

The additional prognostic value of LVMI beyond and above the two risk scores was further investigated by the net reclassification index (NRI) and by the Integrated Discrimination Improvement (IDI). These analyses showed that LVMI had a 12.7% net reclassification index (P=0,029) for all-cause mortality. The analysis of reclassification ability of LVMI carried out by the IDI provided a 2.0% IDI for all-cause mortality, a figure which was of high statistical significance (P=0.01). Remarkably, a risk reclassification analysis carried out for cardiovascular mortality showed that the inclusion of LVMI to the risk score based model provided a 18.0% NRI (P=0.006) and a 2.3% IDI (P=0.01) for reclassifying patients who died of fatal CV events.

CONCLUSIONS

LVMI is an independent risk factor of mortality in ESKD and significantly improves the prognostic accuracy of a predictive risk score based on traditional and dialysis-related risk factors in ESKD patients. These results suggest that LVH not only remains a fundamental treatment target in ESKD but also represents an accurate prognostic factor for risk stratification in hemodialysis patients.

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