Quantitative determination of circulating L-cartinine and its derivates contributes to Heart failure diagnosis, etiology discrimination and clinical prognosis prediction

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Background: Despite the latest progress in heart failure therapy, early diagnosis and clinical prognosis prediction are still critical issues nowadays. It has been proved that carnitines play an essential role in fatty acid metabolism. However, it is unclear about the changes and clinical effects of circulating carnitines in heart failure.

Objectives: This study was designed to clarify the alteration of serum carnitine and its derivates in heart failure patients, and to verify the impact of carnitines on heart failure etiology discrimination and mortality prediction.

Methods: A total of 161 heart failure patients (Dilated cardiomyopathy: DCM, n=98; ischemia cardiomyopathy: ICM, n=63) and control patients (n=48) were enrolled from Feb to Sep in 2017. Serum L-carnitines were quantitatively measured by liquid chromatography/ mass spectrometry. All patients underwent follow-up (mean 30.8 months). Multi-variable Cox survival was performed to verify the impact of carnitines on heart failure mortality prediction.

Results: A total of 27 different carnitine derivates were detected. Compared with control group, 26 types of carnitines were increased significantly in heart failure patients. Several circulating carnitines were independent biomarkers for heart failure even adjusted by multi-variable logistic analysis. We also found 7 carnitines were obviously increased in DCM group than those in ICM group. Isobutyryl-L-carnitine and stearoyl-L-carnitine were independently associated with higher probability of DCM than ICM. DCM prediction model established by adding carnitines (isobutyryl-L-carnitine and stearoyl-L-carnitine) to age, serum creatinine and left ventricular ejection fraction,had favorable discrimination (C-index = 0.832, $P<0.01$, Figure 1A and B) and calibration efficiency (Hosmer-Lemeshow $\chi^2=7.376$, $P=0.497>0.05$).

Meanwhile, a total of 43 mortality event occurred, 18 death (31.6%) in ICM group and 25 (27.2%) in DCM group. Independent clinical risk factors for the occurrence of mortality were serum creatinine >2mg/dl, left atrial diameter 0.55mm and N-terminal pro-B-type natriuretic peptide >4000 pg/ml. Using multi-variable COX survival analysis simultaneously adjusted by serum creatinine, left atrial diameter, NT-pro-BNP and age, oleoyl L-carnitine >300nmo/L (HR=2.364, 95% CI: 1.122–4.976, P=0.024) and isovaleryl-L-carnitine <100nmol/L (HR=2.108, 95% CI: 1.091–4.074, P=0.026) were also independently associated with higher mortality.

Conclusions: As one of critical participants in fatty acid metabolism, L-carnitines alteration not only differentiates DCM patients from ICM ones, but also independently predicts the risk of long-term mortality in heart failure patients.

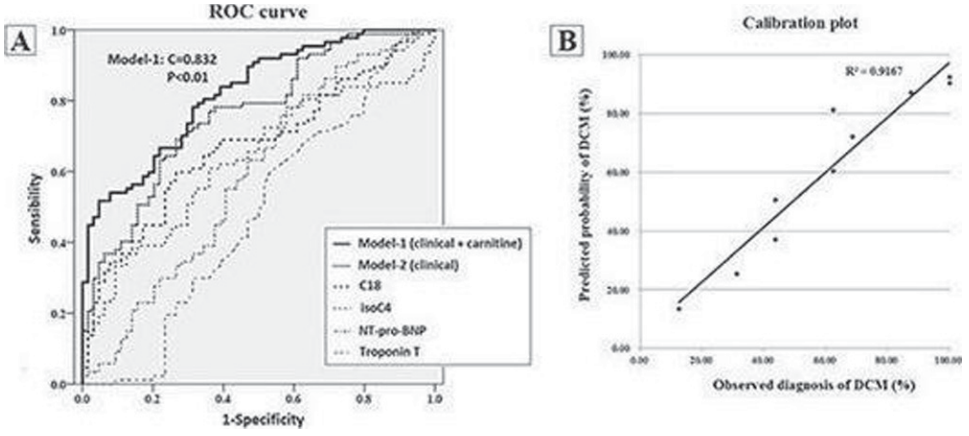

Figure 1