Plasma ß-trace protein predicts mortality in CKD: relation with endothelial dysfunction

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Introduction and aims

-BTP (lipocalin-type prostaglandin D synthase) is a low-molecular weight protein emerging as a novel glomerular filtration rate (GFR) marker.

-BTP is an important constituent of cerebrospinal fluid, but it is also found in blood. It appears to be expressed by cardiomyocytes, vascular smooth muscle cells as well as endothelial cells and has been shown to be involved in NO release, bronchoconstriction and recruitment of inflammatory cells.

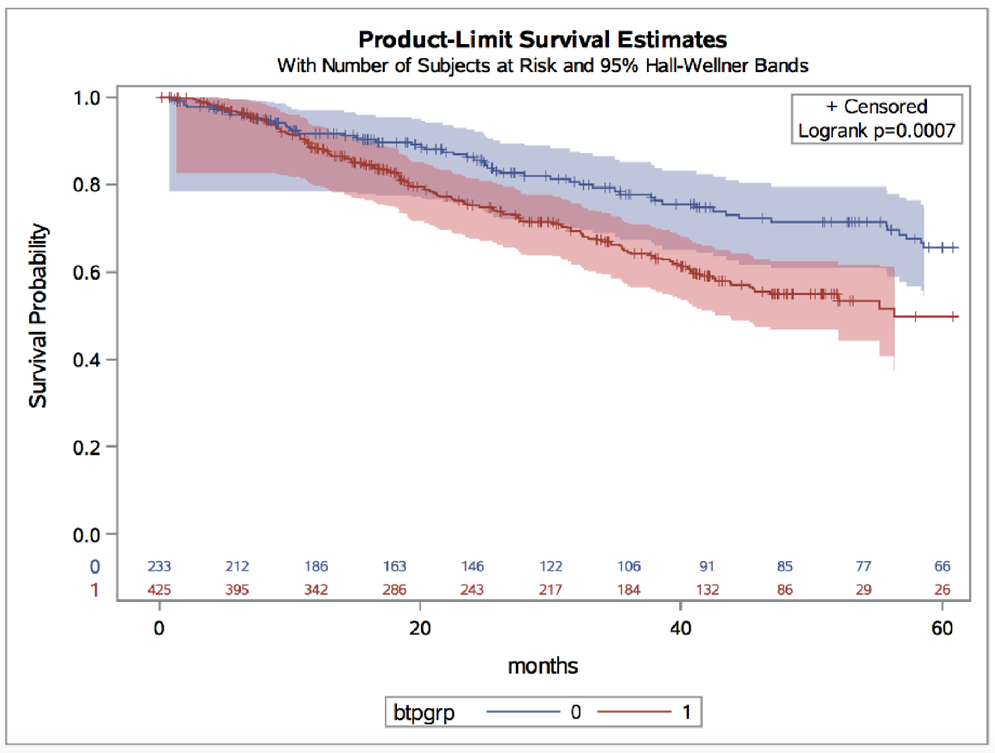
-BTP has been shown to have prognostic value regarding all-cause and cardiovascular mortality in patients with chronic kidney disease (CKD). Whether this finding reflects a more accurate estimation of GFR or an underlying pathophysiological process, such as endothelial dysfunction, still has to be explored.

Patients and methods

- Plasma levels of BTP in 663 patients with CKD were determined using a nephelometric test *(N Latex BTP, Siemens)*.
- The whole cohort was divided according to BTP tertiles.
- Soluble vascular cell adhesion molecule-1 (sVCAM-1) levels were measured in a subgroup of patients (n=355) as a surrogate marker of endothelial dysfunction.

CKD groups

CKD stage 3-4 (n=86)
CKD stage 5 on HD (n=215)
CKD stage 5 on PD (n=83)
CKD stage 5 without RRT (n=279)



Results

- Of the 663 patients studied [age 59 ± 14 yrs; 62% male; eGFR MDRD median (range) 6.2 (52) ml/min/1.73m^2], 206 patients (31%) died during a median follow-up of 31 months.
- Kaplan-Meier survival analysis shows a higher survival probability of the patients with lowest BTP (see **Figure**). In multivariate Cox proportional hazard analysis, adjusting for age, sex, presence of cardiovascular disease and diabetes as well as MDRD tertile, BTP appeared to be strongly and significantly associated with mortality (HR for middle + high vs low BTP 1.86; 95% CI 1.26- 2.75). Tertiles of MDRD had no statistical significant impact on the mortality.
- There was a positive correlation between sVCAM-1 and BTP levels (r=0.432, p <0.001), which appeared to be independent of MDRD in multivariate regression analysis (ß 0.432).

Conclusion

- BTP is a new promising GFR marker with better predictive power for mortality than eGFR from creatinine (MDRD) in patients with CKD stage 3-5.
- The strong correlation with sVCAM-1, independent of renal function, indicates endothelial dysfunction as a non-GFR determinant of BTP levels.

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53 ERA
286--SP
Chronic Kidney Disease. Clinical Epidemiology.
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DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.