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NephroCheck: should we consider urine osmolality?

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Early detection of acute kidney injury (AKI) is challenging due to the risk of morbidity and mortality and a direct impact on patients' management [1]. The diagnosis relies on the changes of serum creatinine and urine output [2], which are the main markers of kidney function. Recently, Astute Medical introduced the NephroCheck, a test that allows a bedside analysis of two biomarkers of renal damage implicated in G1 cell-cycle arrest: tissue inhibitor metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP-7) [3]. The combination of these two biomarkers led to a new score (AKIRisk™). An AKIRisk™ score > 0.3 identifies patients at risk of developing AKI with sensitivity and specificity of 92% and 46%, respectively; increasing the cutoff to 2.0, the sensitivity is 46% and the specificity is 95% [4]. The AKIRisk™ reference interval in healthy humans ranges from 0.04 to 2.22. A possible reason for this wide range could be that the score is not taking into account urine concentration.

We aimed to check the correlation between AKIRisk™ and urine osmolality, using a dehydration test. We collected urine samples from healthy volunteers after 8 h of operating room shift without drinking water (T0) and after drinking 0.5 l of water (T1). Urine samples were analyzed, and osmolality as well as biomarker concentration were measured. Complete measurements are reported in Additional file 1: Table S1. A significant difference was found between the mean AKIRisk™ at T0 (0.82, 95% CI 0.15 to 1.48) vs. T1 (0.24, 95% CI 0.02 to 0.50), $p = 0.01$ (Wilcoxon test—Fig. 1a). The Pearson correlation between osmolality and AKIRisk™ at T0 and T1 was $r = 0.93$, $p = 0.02$, and $r = 0.80$, $p = 0.03$ (Fig. 1b, c).

Our results suggest that fluid intake in the normal population is able to modify the urinary concentration of TIMP-2 and IGFB-7. It is to note that every AKIRisk™ > 0.3 occurs in people with urine osmolality > 600 mOsm/kg and that there is a good correlation between urine osmolality and AKIRisk™. Some participants still maintained AKIRisk™ > 0.3 even after fluid reintegration, maintaining a good correlation with urinary osmolality also at T1, indicating a suboptimal dehydration correction.

Our data suggest that the values of AKIRisk™ score could be related to the urine concentration; thus, urine osmolality should be considered in the interpretation of the results of the NephroCheck® test. This correlation should be checked in critically ill patients at risk of AKI.

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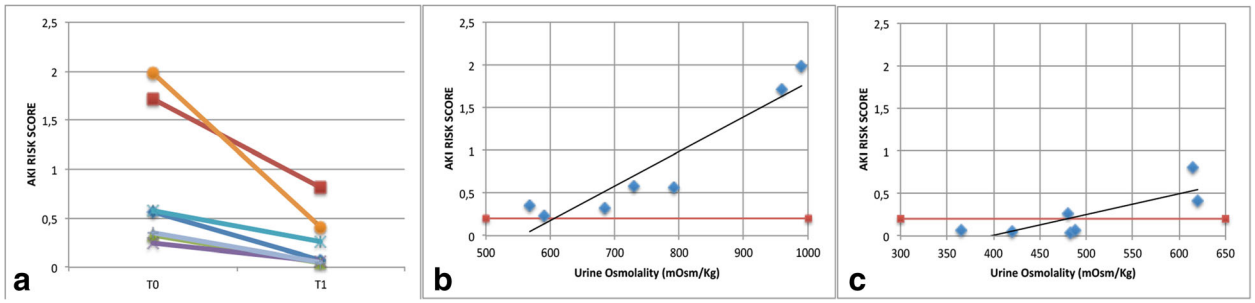

Fig. 1 **a** AKIRisk score measured at dehydration (T0) and after hydration (T1). **b**, **c** Relationship between urine osmolality and AKIRisk score measured by NephroCheck at T0 and T1. Red line represents the AKIRisk cutoff

Additional file

Additional file 1: Raw data. Urine osmolality and AKIRisk score of each patient. (DOCX 43 kb)

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