



NEPHROCHECK Biomarkers TIMP-2 and IGFBP7 Included in the ERAS “Guidelines for Perioperative Care in Cardiac Surgery”

Marcy l'Étoile (France) - May 13, 2019 – The NEPHROCHECK® Test biomarkers (TIMP-2 and IGFBP7) that indicate kidney stress in advance of acute kidney injury (AKI) have been included in the “Guidelines for Perioperative Care in Cardiac Surgery” which were published by the ERAS® (Enhanced Recovery After Surgery) Cardiac Society, an international group of leading heart surgeons, anesthesiologists and critical care specialists. This group has a formal collaborative agreement with the ERAS® Society, a multimodal, transdisciplinary care improvement initiative to promote recovery of patients undergoing surgery throughout their entire perioperative journey. The guidelines include among their various recommendations the use of the biomarkers measured by the NEPHROCHECK® Test after cardiac surgery for the early detection of kidney stress, followed by appropriately targeted interventions to avoid AKI. The NEPHROCHECK® Test is marketed in the United States as an aid in the risk assessment for moderate or severe AKI in adult ICU patients who currently have or have had, within the past 24 hours, acute cardiovascular and or respiratory compromise, and is also marketed in various European countries for risk assessment for AKI.

The ERAS® Cardiac Society guidelines recommendations were developed through a two-year formal process to provide cardiac surgical programs evidence-based protocols to enhance patient recovery following heart surgery. They were presented at the American Association for Thoracic Surgery (AATS) meeting on May 4th, 2019 and published online in JAMA Surgery on the same day.

These recommendations state that AKI complicates 22% to 36% of cardiac surgical procedures, doubling total hospital costs. Strategies to reduce AKI involve assessing which patients are at risk and then implementing specific interventions to reduce the incidence. They further describe that urinary biomarkers such as tissue inhibitor of metalloproteinases-2 (TIMP- 2) and insulin-like growth factor-binding protein 7 (IGFBP7) can identify patients as early as 1 hour after cardiopulmonary bypass who are at increased risk of developing AKI. The guideline asserts that although many risk scores for AKI after cardiac surgery have been published, these scoring systems have good discrimination in assessing low-risk groups but relatively poor discrimination in patients at moderate to high risk. It suggests that all patients undergoing cardiac surgery may benefit from detection of modifiable early kidney stress to prevent AKI. Therefore, it recommends that these biomarkers be used for early identification of patients at risk and to guide an intervention strategy to reduce AKI with a strong level of evidence.¹

“Using the urinary biomarkers IGFBP7 and TIMP-2 provides early detection of kidney stress and risk of acute kidney injury in cardiac surgery patients,” said Daniel Engelman MD, FACS, Medical Director, Heart, Vascular & Critical Care Services, Baystate Medical. *“When used as a trigger to initiate the intervention of a multidisciplinary acute kidney response team (AKRT), these urinary biomarkers can guide intervention that dramatically reduces postoperative AKI following cardiac surgery and avoid the need for dialysis and the other comorbidities that typically result from AKI.”*

¹ Guidelines for Perioperative Care in Cardiac Surgery Enhanced Recovery After Surgery Society Recommendations Daniel T. Engelman, MD; Walid Ben Ali, MD; Judson B. Williams, MD, MHS; & al



“We are thrilled by the inclusion of the NEPHROCHECK® Test biomarkers in the ERAS® Cardiac Surgery guidelines as a tool for improving patient outcomes following these important heart procedures,” said Mark Miller, Executive Vice President and Chief Medical Officer for bioMérieux. “Evidence-based patient care guidelines are crucial for standardizing medical care and enhancing patient recovery. This recognition from international experts in the ERAS® Cardiac Society illustrates our commitment to bringing high medical value tests to physicians in order to help them make important medical decisions for the ultimate benefit of patients. These important first-of-its-kind guidelines recommend the use of the NEPHROCHECK® urine biomarkers as an important tool for improving the management of adult cardiac surgery patients in order to protect their kidneys from both acute and long-term damage.”

ABOUT AKI

AKI is a frequent complication in patients undergoing major surgery, and is known to increase morbidity, mortality and costs¹. Additional AKI-associated expenses during U.S. hospitalizations have been reported at \$38,000 per patient², resulting in U.S. healthcare expenditures that may range between \$5.4 to \$24 billion annually³. Currently, changes in the available indicators of AKI, such as elevated serum creatinine and decrease urine output, may not be present by the time the kidney damage has already occurred⁴. Recent studies have called for the pursuit of innovative strategies to combat this major public health concern^{5,6}.

ABOUT NEPHROCHECK®

The NEPHROCHECK® test was developed by Astute Medical, Inc (a bioMérieux company since April 2018) and detects two biomarkers, urinary tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7), that increase in a patient's urine in response to early kidney cell stress which can lead to AKI. This allows the biomarkers to function as an early alarm of kidney stress before progression to AKI so that maneuvers to protect the kidneys can be undertaken⁷.

In the US the NEPHROCHECK® Test is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are intensive care unit (ICU) patients as an aid in the risk assessment for moderate or severe AKI within 12 hours of patient assessment. The NEPHROCHECK® Test is intended to be used in patients 21 years of age or older. For more information on the NEPHROCHECK® test visit www.NephroCheck.com



ABOUT BIOMÉRIEUX

Pioneering Diagnostics

A world leader in the field of *in vitro* diagnostics for over 55 years, bioMérieux is present in 43 countries and serves more than 160 countries with the support of a large network of distributors. In 2018, revenues reached €2.4 billion, with over 90% of international sales.

bioMérieux provides diagnostic solutions (systems, reagents, software, services) which determine the source of disease and contamination to improve patient health and ensure consumer safety. Its products are mainly used for diagnosing infectious diseases and some critical illnesses. Its diagnostic solutions are also used for detecting microorganisms in agri-food, pharmaceutical and cosmetic products.



bioMérieux is listed on the Euronext Paris stock market.

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Reuters: BIOX.PA/Bloomberg: BIM.FP

Corporate website: www.biomerieux.com. Investor website: www.biomerieux-finance.com

More about ERAS® Society: www.erassociety.org

about ERAS® Cardiac Surgery: www.erascardiac.org

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¹ Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. *Ann Surg.* 2014;00:1-8.

² Alshaikh H, Katz N, Gani F, et al. Financial Impact of Acute Kidney Injury After Cardiac Operations in the United States. *Ann Thorac Surg.* 2018 Feb;105(2):469-475.

³ Silver SA, Chertow GM. The Economic consequences of AKI. *Nephron.* 2017;137:297-301.

⁴ McCullough PA, Shaw AD, Haase M, et al. Diagnosis of acute kidney injury using functional and injury biomarkers: workgroup statements from the tenth Acute Dialysis Quality Initiative Consensus Conference. *Contrib Nephrol.* 2013;182:13-29.

⁵ Thakar CV. Acute Kidney Injury: A Paradigm In Quality and Patient Safety. *Adv Chronic Kid Dis.* 2017;24(4):192-193.

⁶ Silver SA, Chertow GM. The Economic consequences of AKI. *Nephron.* <https://doi.org/10.1159/000475607>. Published online June 9, 2017.

⁷ Kellum JA, Chawla LS. Cell-cycle arrest and acute kidney injury: the light and dark sides. *Nephrol Dial Transplant.* (2015) 0: 1–7doi: 10.1093/ndt/gfv130.