Assessing post-contrast acute kidney injury in children with congenital heart disease undergoing cardiac catheterization using cystatin C based equation for estimated glomerular filtration rate

A Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Rana Maged El-Maghrabi

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List of Abbreviations

Abbr.	Full-term
AARs	**:** Acute adverse reactions
ACEI	**:** Angiotensin converting enzyme inhibitor
AKI	**:** Acute kidney injury
AKIN	**:** Acute kidney injury network
AUC	**:** Area under Curve
BMI	**:** Body mass index
BSA	**:** Body surface area
CHD	**:** Congenital heart disease
CI-AKI	**:** Contrast-induced acute kidney injury
CIN	**:** Contrast-induced nephropathy
CM	**:** Contrast media
COA	**:** Coarctation of aorta
CpA	**:** Compound A
CT	: Computerized tomography
Cys C	**:** Cystatin C
eGFR	**:** Estimated Glomerular filtration rate
ELISA	**:** Enzyme-linked immunosorbent assay
GFR	**:** Glomerular filtration rate
HOCM	**:** High osmolar contrast media
ICM	**:** Iodine Contrast Media
IGFBP7	**:** Insulin-like growth factor–binding protein 7
IL-18	**:** Interleukin-18
IOCM	**:** Iso-osmolar CM

KDa	**:** Kilo-Dalton
KDIGO	**:** Kidney Disease: Improving Global Outcomes
KIM-1	**:** Kidney injury molecule 1
L-FABP	**:** Liver-type fatty acid binding protein
LMWH	**:** Low Molecular weight heparin
LOCM	**:** Low osmolar contrast media
MACD	**:** Maximum allowable contrast dose
MRI	**:** Magnetic resonant imaging
NGAL	**:** Neutrophil gelatinase-associated lipocalin
NSAID	**:** Nonsteroidal anti-inflammatory drugs
PA	**:** Pulmonary artery
PAS	**:** Pulmonary artery stenosis
PC-AKI	**:** Post-contrast acute kidney injury
PCI	: Percutaneous coronary intervention
PDA	**:** Patent Ductus Arteriosus
pRIFLE	**:** Pediatric Risk, Injury, Failure, Loss, End-Stage Kidney Disease
RBF	**:** Renal blood flow
ROC	**:** Receiver Operating Characteristic Curve
RV	**:** Right ventricle
sCr	**:** Serum creatinine
SD	**:** Standard deviation
TFA	**:** Tranfemoral approach
TIMP-2	**:** Tissue inhibitor of metalloproteinase-2
TRA	**:** Transradial approach
VSDs	**:** Ventricular septal defects

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Introduction

The term Post-contrast acute kidney injury (PC-AKI) is used to describe a decrease in renal function that follows intravascular administration of contrast media. The decrease in renal function is usually mild, peaking at 2-3 days, and renal function usually returns to baseline values within 1-3 weeks. Like all forms of AKI, an episode of PC-AKI is a marker for increased short-and long-term morbidity and mortality and prolonged hospital stay **(van der Molen et al., 2018).**

Contrast media (CM) used in cardiac catheterization is low osmolar non-ionic contrast media (iohexol) has less effect on cardiac function and fewer side effects than conventional ionic contrast media, Contrast material dosing is based on a standardized dosing nomogram adjusted for patient weight **(McDonald et al., 2018).**

A new biomarker Cystatin C (CysC), a non-glycosylated low-molecular-weight (13 kDa) protein encoded by the CST3 gene, a protease inhibitor, that is synthesized and released into the blood at a relatively constant rate by all nucleated cells. It is freely filtered in normal circumstances by the glomeruli and completely reabsorbed in the proximal tubule. In the absence of tubular dysfunction, its serum levels reflect glomerular filtration, therefore it could be used as a convenient measure of glomerular filtration rate **(Cecchi et al., 2017).**

As blood levels of cystatin C are not significantly affected by age, sex, race, or muscle mass, it is a better predictor for glomerular function compared with serum creatinine (sCr) in patients with chronic kidney disease **(Mostafa et al., 2016).**

Cystatin C equation: (eGFR =70.69 x $(CysC)^{-0.931}$) for estimation of GFR may have advantages over serum Creatinine-based equations **(Schwartz et al., 2012).**

In children, the revised Schwartz formula to estimate GFR is recommended. eGFR (ml/min/1.73 m^2) = 0.413 × height/sCr (sCr in mg/dl, height in cm) **(Schwartz et al., 2009)**

Also one of the promising candidate biomarker for AKI is Neutrophil gelatinase-associated lipocalin (NGAL), a 25 kDa siderophore binding protein composed of 179 amino acids, a member of the lipocalin family, covalently attached to human neutrophil gelatinase, secreted by activated neutrophils. Lipocalins are proteins binding small lipophilic molecules and transporting them between the cells of the body. NGAL is involved in processes of cell-mediated immunity, bacteriostatic effects, cell proliferation, differentiation and apoptosis processes. It increases when there are conditions such as infection and malignancy **(Lichosik et al., 2015).**

In the kidney, NGAL is mainly expressed in the loop of Henle and distal convoluted tubules. It's filtered by the renal glomeruli and reversibly reabsorbed in the proximal convoluted tubules **(Andreucci et al., 2016).**