Incidence of Acute Kidney Injury Following Initiation of SGLT2 Inhibitor in Acute Heart Failure: A Randomized Controlled Trial

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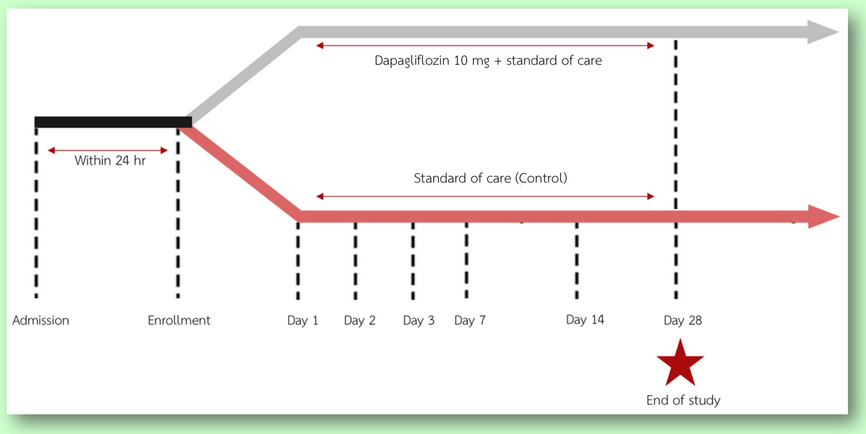
Background:
Sodium-glucose co-transporter 2 (SGLT2) inhibitors improve cardiovascular outcomes in acute heart failure (AHF) but associated with transient rise in serum creatinine. The aim of this study was to assess the incidence of acute kidney injury (AKI) following initiation of SGLT2 inhibitor in patients hospitalized with acute AHF.

Method:
An open labelled, randomized, controlled trial enrolled patients who hospitalized for AHF at Bhumibol Adulyadej Hospital. Patients who hospitalized for AHF were randomized to dapagliflozin added to standard of care or control group for 28 days. The primary outcome was the incidence of AKI by KDIGO criteria. The secondary outcome was the AKI predicted by urinary [TIMP-2] x [IGFBP-7] criteria, change from baseline eGFR, and adverse events.



Primary outcomes
- Urinary [TIMP-2] x [IGFBP7] (day 0, 7, 28)
- AKI

Secondary outcomes
- Change from baseline SCr
- Cumulative urine output
- Adverse events

Figure 1. Research methodology

Table 1. Baseline characteristics of study subjects

	Dapagliflozin (n = 13)	Controls (n = 12)	P-value
Age, years (SD)	67.0 ± 17.4	67.2 ± 13.4	0.970
Male (%)	7 (58.3)	7 (53.8)	0.821
Serum creatinine, mg/dl ± SD	1.18 ± 0.32	1.16 ± 0.42	0.886
eGFR (CKD-EPI), ml/min/1.73m² ±SD	61.3 ± 20.7	64.9 ± 24.4	0.698
Ejection Fraction, % ± SD	42.4 ± 17.0	41.8 ± 16.7	0.924
NT-proBNP, pg/ml (IQR)	8,048 (3471, 15760)	4,802 (3537, 9273)	0.505
Type of AHF (%)			
New onset	5 (41.7)	9 (69.2)	0.238
ADHF	7 (58.3)	4 (30.8)	0.238
Acute respiratory failure (%)	0 (0)	2 (15.4)	0.497
Underlying CV diseases (%)			
Coronary artery disease	5 (41.7)	4 (30.8)	0.881
Dilated cardiomyopathy	4 (33.3)	3 (23.1)	0.901
Ischemic cardiomyopathy	1(8.3)	4 (30.8)	0.368
Atrial fibrillation	1(8.3)	2 (15.4)	1.000
Valvular heart disease	3 (18.8)	2 (15.4)	0.920

ADHF, acute decompensated heart failure; AHF, acute heart failure; CV, cardiovascular; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation

Table 2. Incidence of AKI according to treatment groups

	Dapagliflozin (n=12)	Controls (n=13)	P-value
Outcomes			
AKI by serum creatinine criteria (%)*	4(33.3)	6(46.2)	0.513
AKI stage 1	4(33.3)	6(46.2)	0.513
AKI stage 2	0	0	-
AKI stage 3	0	0	-
Predicted AKI by urinary [TIMP-2] x [IGFBP7]**	3(25)	7(53.8)	0.288
AKI requiring dialysis	0	0	-

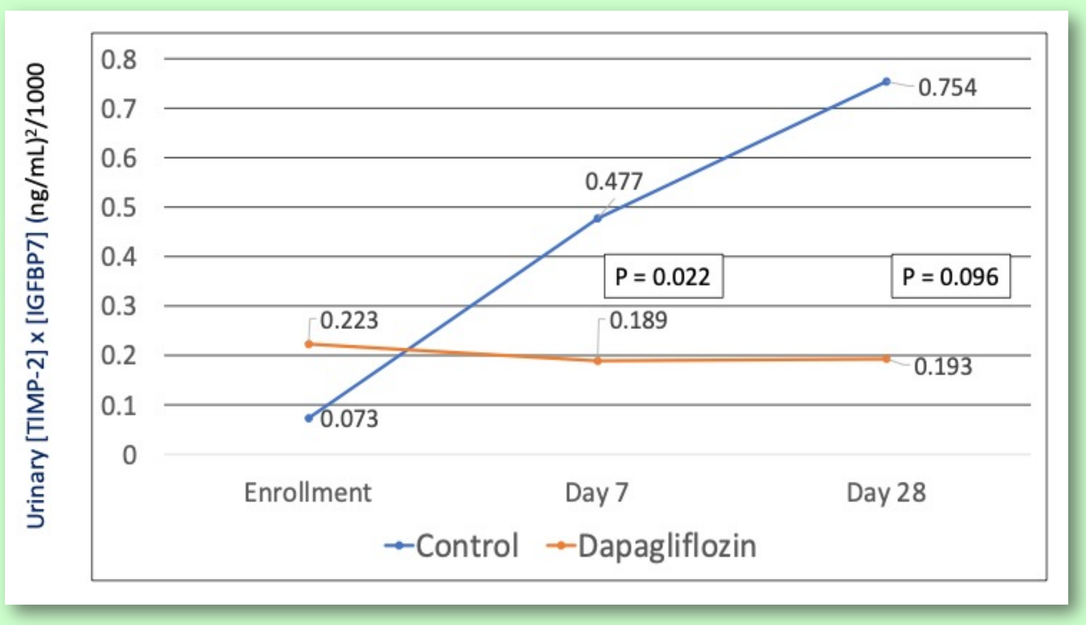


Figure 2. Effects of dapagliflozin on Urinary [TIMP-2] x [IGFBP7] in patients with AHF *(p-value compared changes from baseline between both groups)*

Results:
A total of 32 patients were enrolled. dapagliflozin group has demonstrated a trend towards decrease in AKI events compared with standard therapy (33.3% vs 46.2%; P = 0.513). In terms of AKI biomarkers, we conducted additional analysis using urinary [TIMP-2] x [IGFBP-7] at a threshold of 0.3 (ng/ml)²/1000. We also observed a trend where the number of patients with urinary [TIMP-2] x [IGFBP-7] levels exceeding 0.3 was lower in the dapagliflozin group (25.0% vs 53.8%, P = 0.288). The change from baseline eGFR, and adverse events showed no differences in both groups.

Conclusion:
In patients hospitalized for acute heart failure, SGLT2 inhibitor add on to standard therapy does not increase the incidence of AKI and appears to have a potential preventive effect on tubular injury.

Keywords: acute heart failure, acute kidney injury, urinary [TIMP-2] x [IGFBP7], SGLT2 inhibitor

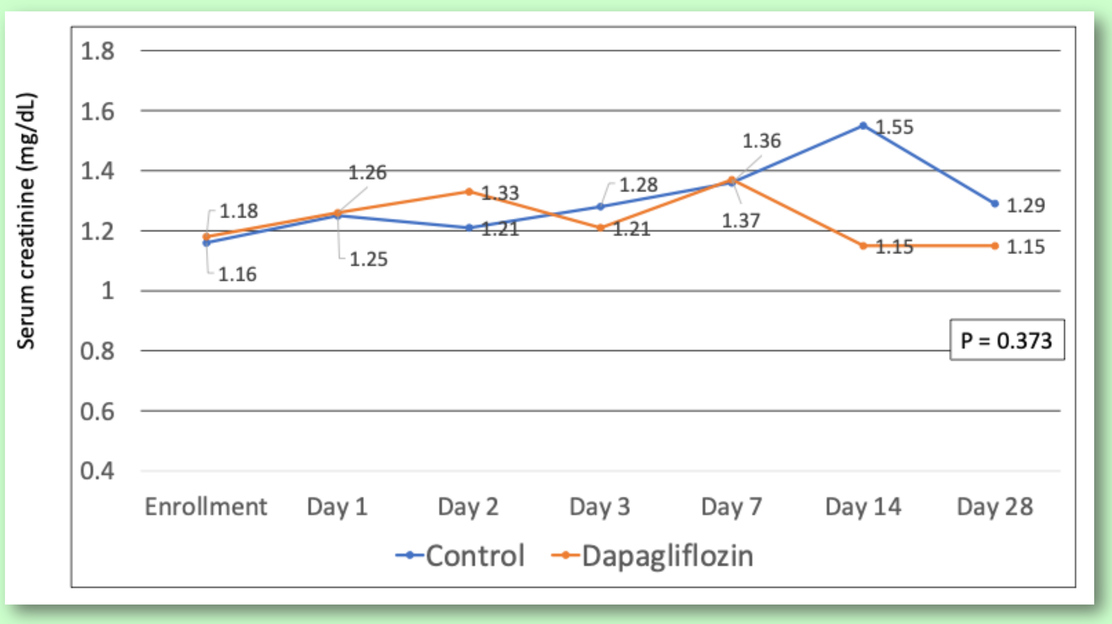


Figure 3. Effects of dapagliflozin on serum creatinine *(p-value compared changes from baseline between both groups)*

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