

## EFFECT OF PULSATILE FLOW ON RENAL FUNCTION IN ELDERLY PATIENTS UNDERGOING CORONARY ARTERY BYPASS SURGERY

**Amanj Kamal Mohammed**

MB,ChB, FIBMS Cardiovascular Surgery. Cardiac Surgeon, Division of Cardiovascular and thoracic Surgery, Slemani Cardiac Hospital. Department of Surgery, College of Medicine, University of Al-Sulaymaniyah, IRAQ.

### Abstract

The incidence of acute kidney injury (AKI) after on-pump coronary artery bypass graft (CABG) varies among studies but can be reduced if pulsatile flow is used.

The aim of this study is to evaluate pulsatile flow impact on renal function of elderly patients undergoing CABG.

Over one year (April 2014 to April 2015) 48 patients above the age of 65 underwent on-pump CABG in our institute. Patients were divided into two groups; pulsatile flow (PFG) and non-pulsatile flow (NPPFG) groups. Serum creatinine (S.Cr), creatinine clearance (Cr.Cl) and per-pfusion urine output (UO) were measured. AKI Network criteria were adopted for diagnosis.

Mean age was 68 in PFG and 69 in NPPFG. Males constituted 83.3% of PFG and 79.2% of NPPFG. Although 37.5% of PFG and 41.7% of NPPFG were hypertensive, all patients had normal ejection fraction (EF). Both groups had nearly 3 coronary anastomoses, cardiopulmonary bypass (CPB) time of 90 min, cross clamp time of 71 min and mean perfusion pressure of 70 mmHg. Mean S.Cr was the same (0.8 mg/dl) in both groups on 1st postoperative day (POD) but UO was significantly larger (708 ml in PFG vs. 648 ml in NPPFG). On 3rd POD, S. Cr didn't change in PFG but it has significantly increased in NPPFG (from 0.76 to 1.0 mg/dl). Moreover, Cr.Cl has significantly improved in PFG (81 vs. 72 ml/min in NPPFG). Seven of 48 patients (14.6 %) developed AKI (6; 25% in NPPFG).

In conclusion; Pulsatile perfusion technique is a simple and safe measure to minimize AKI in the elderly.

*Keywords: Coronary artery bypass graft, elderly, cardiopulmonary bypass, pulsatile flow, non-pulsatile flow, acute kidney injury, serum creatinine, creatinine clearance*

### Introduction

Although coronary artery bypass graft (CABG) surgery can be performed on a beating heart (off-pump), most CABG operations are still performed under cardiopulmonary bypass (CPB). When CPB is used, it has many unfavorable systemic effects on body organs due to inflammatory reactions<sup>1</sup> which may lead to organ dysfunction<sup>2</sup>. One of the devastating complications after cardiac surgery is acute kidney injury (AKI)<sup>3</sup> whose incidence ranges from 0.6%-10%<sup>4,5</sup>. Noteworthy, 20% of AKI require dialysis and are associated with a high mortality<sup>6,7</sup>. The pathogenesis

of AKI after cardiac surgery particularly CABG, is multifactorial. Prolonged aortic cross-clamping time, low perfusion pressure, non-pulsatile flow, hemo-dilution, embolic phenomenon, oxygen radicals and pro-inflammatory response are few to mention<sup>8,9</sup>.

Regarding the type of CPB; pulsatile flow may provide better microcirculation and tissue perfusion than non-pulsatile flow due to its physiological nature. Peripheral vascular resistance is one of the major determinants that affect tissue perfusion during CPB, and pulsatile flow provides lower peripheral vascular

resistance and higher blood supply than non-pulsatile flow<sup>10,11</sup>. Advanced age is considered an independent risk factor for renal disease. Previous studies revealed high incidence of acute renal failure in the elderly<sup>12</sup>. However, the exact mechanism of this correlation between renal failure and advanced age is not well-known. The role of comorbidities such as diabetes mellitus, vascular disease, and hypertension is not very clear<sup>13</sup>. The kidney of elderly patient is more vulnerable for injury than that of the young, since it has a decreased vasodilation capacity when stimulated maximally, and it has a great sensitivity to volume depletion<sup>14</sup>.

There are different methods for assessment of renal function, AKI recognition is based on a rise in serum creatinine (S.Cr), blood urea nitrogen (BUN), cystatin C and creatinine clearance (Cr.Cl). Serum creatinine and calculated creatinine clearance require a single blood sample testing and, for many decades, have been used for estimation of glomerular filtration rate (GFR)<sup>15</sup>.

This prospective study was carried in order to compare the effects of pulsatile and non-pulsatile CPB on incidence of AKI in elderly patients undergoing CABG over one year period with review of literature.

### Patients and Methods

This cross-sectional study was conducted in Slemani Cardiac Hospital, Al-Sulaimaniyah, Kurdistan, Iraq over one year period (April 2014 to April 2015).

Forty eight patients (39 males) were enrolled. Age ranged between 65 and 76 years with a mean of 68.9. All patients underwent CABG surgery with the use of CPB machine (on-pump). Patients with an ejection fraction (EF) <50%, history of renal disease, diabetes mellitus and hypertension were excluded. Furthermore, concomitant valve surgery and emergency CABG were also excluded.

Transthoracic echocardiography (TTE), coronary angiography and renal function tests were performed for all of patients.

All surgeries were performed via median sternotomy incision and CPB was established with ascending aortic cannula and two-stage venous cannula through right atrium. Myocardial protection was achieved via antegrade blood cardioplegia and moderate hypothermia (32°C). Left internal mammary artery (LIMA) was harvested and anastomosed to the left anterior descending artery (LAD) while great saphenous vein was used a conduit for other coronary arteries. Proximal anastomoses were done with aortic side-clamping.

All patients were monitored intra-operatively by electrocardiography, invasive arterial pressure, central venous catheter, pulse oximeter, and esophageal temperature probe. The standard linear (non-pulsatile) perfusion was used in 24 patients (NPPFG) while pulsatile flow was used in the remaining 24 (PFG). In all patients, the mean perfusion pressure was kept within 60-80 mmHg.

Renal function was evaluated for all patients by measuring pre-operative serum creatinine, and creatinine clearance using Cockcroft-Gault formula: Cr.Cl (male)=[(140-age)×weight in kg]/(serum creatinine×72);(multiplied by 0.85 for females)<sup>15</sup>. The same measurement was repeated after CPB, and at the third post-operative day. In addition, intra-operative and post-CPB urine output (UO) was measured. In this study, AKI was defined as reduction in urine output (oliguria of <0.5 ml/kg per hour for >6 hours), >0.3 mg/dl absolute increase in serum creatinine post-operatively (50% rise from the baseline serum creatinine level, a 1.5 fold increase from the baseline) according to AKI Network (AKIN)<sup>16</sup>.

Data were analyzed using IBM SPSS for windows version 25 software and variables of the two groups were compared. P-values <0.05 were considered significant.

## Results

A comparison of preoperative variables between the two groups is demonstrated in table I.

**Table I: Pre-operative Characteristics of Both Groups.**

Variable	Pulsatile Flow Group (PFG) (N=24)		Non-pulsatile Flow Group (NPF) (N=24)		P value
	%	Mean ± SD	%	Mean ± SD	
Age	---	68.79 ± 3.25	---	69.13 ± 3.26	0.725
Male Gender	83.3	---	79.2	---	0.712
Hypertension	37.5	---	41.7	---	0.5
EF%	---	56.7 ± 3.3	---	57.1 ± 3.1	0.653

All patients were above the age of 65 (68 years in PFG vs. 69 years in NPF). Males constituted >3 quarters of patients in both groups (83.3% in PFG vs. 79.2% in NPF). Hypertension was documented in 37.5% in PFG vs. 41.7% in NPF. All patients had a normal left ventricular EF (>55%). It was almost the same in both groups (56.7% in PFG vs. 57.1% in NPF). All differences were not statistically significant. The operative variables are shown in Table II.

**Table II: Operative Variables.**

Variable	PFG (N=24)	NPF (N=24)	P value (>0.05)
	Mean ± SD	Mean ± SD	
Mean number of anastomoses	3.0 ± 0.5	2.8 ± 0.45	0.372
CPB time (min.)	91.7 ± 5.2	91.0 ± 5.6	0.692
Cross clamp time (min.)	70.9 ± 5.2	70.7 ± 5.6	0.915
Mean perfusion pressure (mmHg)	69.2 ± 6.9	70.9 ± 6.9	0.405

It is evident that both groups had almost very similar operative variables like mean number of coronary anastomoses (≈3), CPB time (≈90 minutes), cross clamp time (≈71 minutes) and mean perfusion pressure (≈70 mmHg).

The renal function indicators in the 2 groups of patients are demonstrated in Table III.

**Table III: Renal Function Indicators in Both Groups.**

Indicator	PFG (N=24)	NPF (N=24)	P value.
	Mean ± SD	Mean ± SD	
Preoperative S. Cr. (mg/dl)	0.76±0.09	0.76±0.09	>0.05
S.Cr after weaning from CPB (mg/dl)	0.8 ± 0.1	0.8 ± 0.1	>0.05
3rd postoperative day S.Cr. (mg/dl)	0.9 ± 0.11	1.0 ± 0.12	0.002
3rd postoperative day Cr. Clearance (ml/min)	81 ± 7.5	72 ± 9.5	0.001
Urine output (ml) during CPB	708 ± 85.5	648 ± 59.8	0.007

Early after weaning from CPB, mean serum creatinine was the same (0.8 ± 0.1 mg/dl) in both groups. However, on the 3rd postoperative day, serum creatinine and creatinine clearance became significantly different between the 2 groups (p<0.05). In regard to the urine output (just after weaning from CPB), it was significantly better (larger) in the PFG (708 ± 85.5 ml vs. 648 ± 59.8 ml for the NPF) (p<0.05).

The distribution of AKI in the 2 study groups is shown in Figure 1.

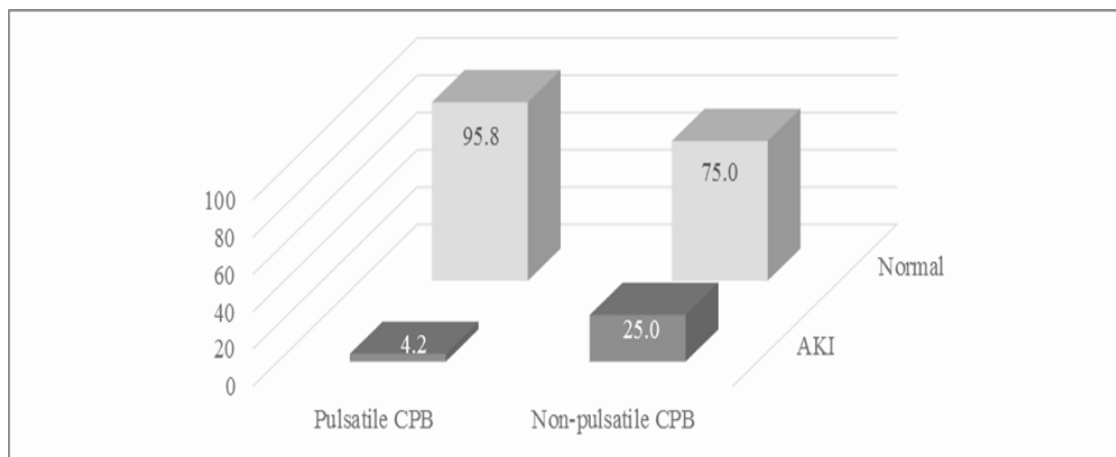


Figure 1: Distribution of AKI in both groups.

Overall 7 of 48 patients (14.6 %) had AKI. All of them were managed conservatively and none required hemodialysis. The incidence of AKI was significantly higher among patients who received non-pulsatile flow (n=6, 25%), (P value=0.04).

## Discussion

Renal function impairment and AKI after cardiac surgery is multi-factorial. Many studies have demonstrated that AKI is more common in the elderly<sup>17-19</sup>. In addition, the type of CPB flow (pulsatile or non-pulsatile) has also been shown to affect the incidence of AKI after cardiac surgery. As long as the aim of the current study was just to assess the influence of type of perfusion flow, we chose 2 groups of patients almost identical in age (mean age of 69).

Furthermore, diabetic patients were excluded because DM itself is considered an independent risk factor for AKI<sup>20-22</sup> and the incidence of AKI is higher in diabetic patients undergoing surgery<sup>23,24</sup>. The 2 groups of patients were not significantly different in the rate of hypertension (37.5% vs. 41.7%) as studies have shown a relationship between AKI and high blood pressure, especially uncontrolled hypertension<sup>25</sup>. Low ejection fraction is associated with reduced renal perfusion. Patients with EF%  $\leq$ 45% had a tenfold increase in the incidence of AKI vs. those with LVEF%  $\geq$ 45%<sup>26</sup>. For this reason, patients with low EF were excluded from the study and enrolled those with an EF  $>$ 55%. Intra-operative events have a big impact on

renal function. CPB time, ACC time, and mean perfusion pressure are strongly associated with the development of AKI post-cardiac surgery, especially after CABG<sup>27-29</sup>. Fortunately, both groups of patients in this study had almost similar CPB time, ACC time and mean perfusion pressure.

Like other studies<sup>15,30</sup> serum creatinine, and creatinine clearance were used for evaluation of renal function in this study. Other measures of assessing renal function include estimated glomerular filtration rate<sup>30</sup> and the calculated creatinine clearance<sup>15</sup>. This study showed a significant correlation between the type of perfusion flow and the postoperative renal function. Pulsatile flow was more protective from the development of post-operative renal impairment and/or AKI. Pulsatile flow preserves renal function better than standard non-pulsatile flow even in patients older than 65. Hence, pulsatile flow is recommended as the procedure of choice in this subgroup of patients<sup>31</sup>.

In this study, pulsatile flow was associated with a significantly better (larger) intraoperative urine output (708 ml vs. 648 ml). Hökenek et al<sup>32</sup> reported a similar finding with a total urine output

of 1025 ml in the pulsatile group vs. 828 ml in the non-pulsatile group. However, Milano et al. showed no significant difference in the perioperative urine output for either group in aortic valve surgery (653±353 ml for pulsatile group vs. 602±296 ml for non-pulsatile flow group with a p value of 0.60)<sup>33</sup>. Urine output in the aforementioned study was measured during the entire operation and not during CPB period as we did in our study.

Hökenek et al<sup>32</sup> observed that the mean serum creatinine level (mg/dl) for the pulsatile group (0.9±0.2) was not significantly different from the non-pulsatile group (1.0±0.1) on 1st postoperative day and did not differ significantly from the preoperative level (0.9±0.2). Likewise, our findings were the same i.e. 1st postoperative day serum creatinine was 0.8±0.1 mg/dl for both groups).

However, on the 3rd postoperative day, serum creatinine and creatinine clearance became significantly different between the 2 groups (p<0.05). In the pulsatile group no change in serum creatinine was noticed while in the non-pulsatile group it has significantly increased (from

0.76±0.1 mg/dl preoperatively to 1.0±0.12 mg/dl on 3rd postoperative day). The same was true regarding creatinine clearance i.e. it has significantly decreased in the non-pulsatile group (72±9.5) compared to the pulsatile group (81±7.5).

Natarajan et al studied 100 patients divided into 2 groups with similar CPB and ACC times and found that postoperative serum creatinine slightly increased with non-pulsatile perfusion but did not change in pulsatile perfusion<sup>34</sup>. In this study, AKI developed in 25% of patients who received non-pulsatile perfusion while it occurred in just 2.8% of patients with pulsatile perfusion (p<0.05). Literature review revealed a great variation in the incidence of AKI after cardiac surgery<sup>35,36</sup>. In this study, 7 of 48 patients (14.6%) developed AKI while others reported 30%<sup>36</sup> and even 43.7%<sup>35</sup>.

### Conclusion

Pulsatile perfusion technique has a significant effect on the outcome of elderly patients' renal function after cardiac surgery. It is a simple and safe measure for prevention of AKI after coronary surgery in this age group.

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