

# Investigation of the Effect of Pulsatile and Nonpulsatile Flow on Kidney in Coronary Surgery With NIRS

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## ABSTRACT

**Background:** Acute renal insufficiency is a significant cause of morbidity and mortality after coronary artery bypass grafting performed with cardiopulmonary bypass. Functional near-infrared spectroscopy (fNIRS) is an emerging brain-imaging technique that can be used to detect organ perfusions in adults. This study aims to determine the effects of pulsatile and nonpulsatile flow on renal circulation by using functional near-infrared spectroscopy and biochemical markers.

**Methods:** Forty patients, who had undergone isolated CABG between March 2014 and July 2014 in the authors' clinic, were included in the study. Patients were divided in the pulsatile and nonpulsatile groups by simple randomization.

**Results:** Urine outputs statistically were higher in the pulsatile group, during CPB ( $P = .045$ ). Renal perfusion measurements via fNIRS intra-operatively statistically were parallel between the groups. When we compared biochemical markers within the groups, in the nonpulsatile group, creatinin statistically is higher on the postoperative first day ( $P = .003$ ), and BUN statistically is higher on the postoperative first ( $P = .015$ ), second ( $P = .001$ ), and fifth ( $P = .020$ ) days, according to preoperative value. In the pulsatile group, only the postoperative second day BUN is higher ( $P = .007$ ).

**Conclusion:** fNIRS is being used to track cerebral functions. During operation, it also provides a correct observation for blood feeding of somatic organs, such as the kidneys, but it requires more clinical study to be accepted as routine.

## INTRODUCTION

Recent studies have shown that cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response syndrome (SIRS) [Paparella 2002]. Postoperative complications like myocardial dysfunction,

respiratory failure, renal and neurologic dysfunction, bleeding disorders, altered liver function, and ultimately, multiple organ failure (MOF) may develop by this inflammatory reaction. Even with advances in methods and technologies, post-operative acute renal insufficiency continues to be a significant cause of morbidity and mortality after coronary artery bypass grafting (CABG) performed with CPB [Sahin 2015].

Functional near-infrared spectroscopy (fNIRS), which can assess the relative changes of oxy hemoglobin (HbO), deoxy hemoglobin (Hb), and total hemoglobin (HbT) in the cortical regions of the brain, is an emerging brain-imaging technique [Sai 2014]. In the pediatric population, fNIRS also is used to detect organ perfusions like kidneys [Ricci 2015]. In a limited number of studies, fNIRS is presented to detect organ perfusions in adults [Toraman 2012].

In this prospective study, we aimed to assay the effects of pulsatile and nonpulsatile flow on renal circulation, during CPB in CABG patients by using functional near-infrared spectroscopy and biochemical markers.

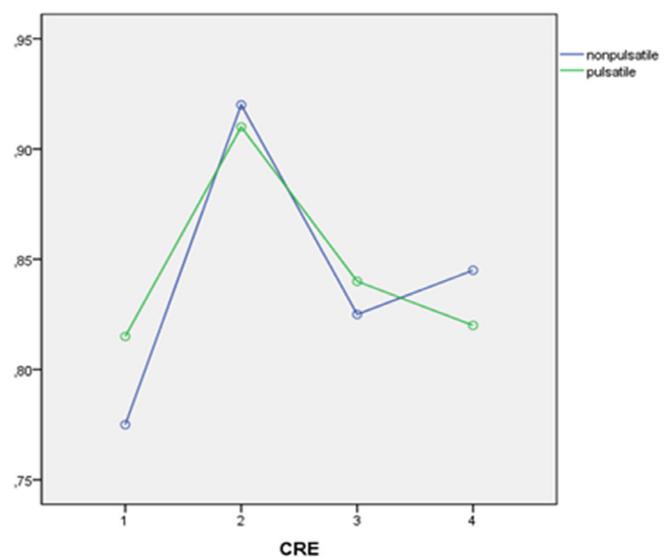


Figure 1. Creatinine measures between the different flow patterns ( $P = .953$ ).

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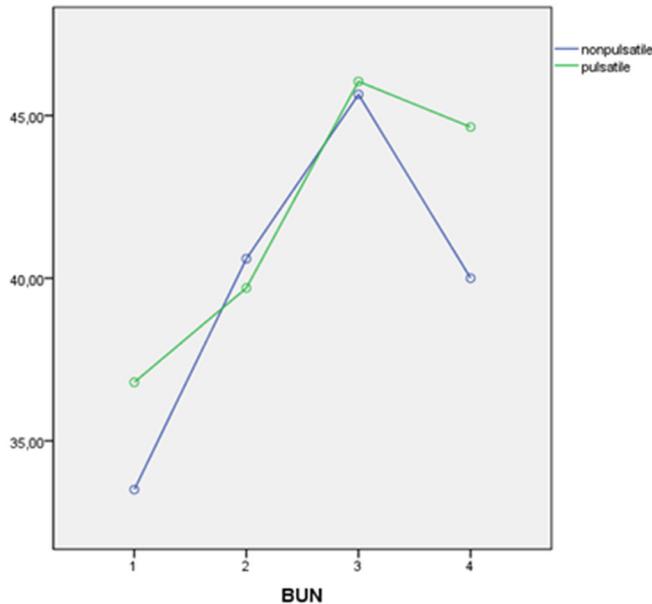


Figure 2. BUN measures between the different flow patterns ( $P = .601$ ).

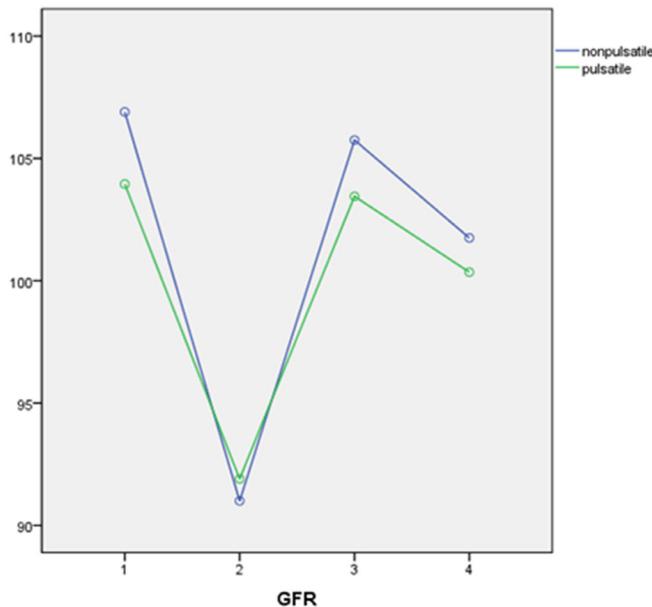


Figure 3. GFR measures between the different flow patterns ( $P = .875$ ).

## PATIENTS AND METHODS

### Study group

Forty patients, who had undergone isolated CABG between March 2014 and July 2014 in the authors' clinic, were included in the study. Patients were randomized into two groups by flipping a coin.

All patients were operated on by one expert surgeon. Patients with renal artery stenosis, renal failure, low ejection

Table 1. Preoperative demographics, clinical and echocardiographic findings of the patients

	Pulsatile (N = 20)	Nonpulsatile (N = 20)	P
Gender			
Male	17 (85%)	17 (85%)	1.000
Female	3 (15%)	3 (15%)	1.000
Age	60.45 ± 7.79	57.40 ± 7.59	.217
Hypertension	12 (60%)	14 (70%)	.507
Diabetes mellitus	3 (15%)	5 (25%)	.695
KOAH	-	2 (10%)	.487
Cigarette	15 (75%)	12 (60%)	.311
Alcohol	2 (10%)	1 (5%)	1.000
Hyperlipidemia	15 (75%)	14 (70%)	.723
SVO	-	1 (5%)	1.000
BMI (body mass index)	25.20 ± 2.80	26.32 ± 2.01	.155
EF	60.5 ± 5.59	59.5 ± 5.10	.558

Table 2. Operative variables

	Pulsatile	Nonpulsatile	P
Perfusion current (mL/min)	4070 ± 388.79	4185 ± 277.72	.289
Perfusion time (min)	88.10 ± 30.19	83.20 ± 13.18	.512
Aorta clamp time (min)	54.50 ± 18.52	57.30 ± 11.40	.569
Blood pressure (mmHg)	68.10 ± 7.43	67.75 ± 7.32	.882
CPB urine output (mL)	567.50 ± 195.6	460 ± 120.961	.045

fraction (EF), and emergency status were not included in the study. All patients gave written consent for the study and approval of the study was obtained from the hospital's ethics committee.

### NIRS

Renal doppler ultrasound (Mindray 7-convex probe) imaging preoperatively was performed to detect the optimal positioning of the NIRS probe and renal artery disease. The closer part of the skin to renal parenchyma was marked and the distance between them measured. INVOS 5100C Cerebral/Somatik oximetry probes were placed to the marked area. Peripheral oxygen saturation, blood pressure, and renal parenchyma oxygenation were measured before anesthetic induction, before intubation, initiating to CPB, fifth minute of the CPB, tenth minute of the cross clamping, twentieth minute of the cross clamping, end of the CPB, and end of the operation.

### Surgical technique

Under general anesthesia and orotracheal intubation, all patients underwent CABG after full sternotomy. After going on CPB with moderate hypothermia (nasopharyngeal

Table 3. fNIRS, blood pressure and peripheral saturation measurements during operation

		Pulsatile	Nonpulsatile	P
Pre-induction	Right/Left	80.60 ± 4.94/80.85 ± 3.32	81.40 ± 6.37/80.10 ± 5.22	.66/.59
	TA	104.35 ± 13.37	106.60 ± 20.26	.68
	PerSO <sub>2</sub>	96.30 ± 0.47	95.95 ± 1.43	.31
Post-intubation	Right/Left	82.95/83.35 ± 5.79/4.93	82.85/81.60 ± 7.05/5.59	.96/.30
	TA	87.15 ± 17.30	96.35 ± 22.14	.15
	Peripheral	99.80 ± 0.41	99.45 ± 0.60	.04*
CPB entry	Right/Left	76.45/76.80 ± 5.12/4.43	78.70/77.90 ± 6.54/5.79	.23/.50
	TA	62.35 ± 13.59	58.30 ± 12.07	.32
	Peripheral	99.35 ± 1.04	97.90 ± 4.86	.20
CPB 5th minute	Right/Left	75.15/75.60 ± 5.64/5.17	77.90/76.55 ± 6.66/6.30	.16/.60
	TA	64.10 ± 8.63	63.25 ± 10.15	.77
	Peripheral	99.45 ± 1.19	99.10 ± 1.65	.44
Cross clamp 10th minute	Right/Left	75.45/75.85 ± 5.58/5.85	78.25/77.35 ± 5.90/5.79	.13/.42
	TA	63.90 ± 11.76	60.45 ± 9.47	.31
	Peripheral	99.35 ± 0.98	98.80 ± 1.93	.26
Cross clamp 20th minute	Right/Left	75.65/76.40 ± 4.99/5.49	78.85/77.85 ± 5.42/5.18	.06/.39
	TA	65.10 ± 9.17	64.05 ± 10.40	.73
	Peripheral	99.00 ± 1.74	98.30 ± 2.08	.25
When removing cross clamp	Right/Left	74.65/76.20 ± 6.01/6.02	78.15/76.90 ± 6.93/6.92	.09/.73
	TA	61.30 ± 9.49	56.15 ± 14.70	.19
	Peripheral	99.40 ± 0.88	98.10 ± 2.61	.04*
CPB exit	Right/Left	76.70/78.10 ± 5.91/7.00	78.40/78.05 ± 6.16/5.88	.37/.98
	TA	72.55 ± 11.84	68.40 ± 11.05	.25
	Peripheral	98.60 ± 1.90	97.60 ± 3.16	.23
End of operation	Right/Left	78.10/79.50 ± 5.68/7.14	76.35/76.10 ± 8.24/7.36	.43/.14
	TA	76.10 ± 9.21	76.70 ± 11.11	.85
	Peripheral	99.40 ± 0.82	98.85 ± 1.56	.17

temperature, 30 to 32°C), (flow rate: 2.5 L/min/m<sup>2</sup>), mean systemic pressure was maintained at 60 mmHg. Myocardial protection was achieved by antegrade administration of blood cardioplegic solution on induction and continued with administration of cold-blood cardioplegic doses every 20 minutes, in accordance with our institution's routine. A final warm-blood dose was administered before releasing the cross clamp.

For half of the patients, pump was operated in pulsatile mode, while for others it was operated in nonpulsatile mode. The pump that was operated in nonpulsatile mode before placing the cross clamp in the pulsatile mode group was changed to pulsatile mode with placing the cross clamp. CPB was established with a standard 6" roller pump using the Terumo® Advanced Perfusion System 1 (Terumo Cardiovascular Group, Ann Arbor, MI) heart-lung machine. The extracorporeal circuits consisted of biocompatible custom heparin-albumin coated circuits (Bioline®, Maquet Cardiopulmonary

AG., Hirrlingen, Germany) and the membrane oxygenator was Quadrox-I Adult (Sofline® Maquet Cardiopulmonary AG., Hirrlingen, Germany). Systemic perfusion was converted to pulsatile flow at a rate of 70 beats per minute for all patients randomized into this group under cross clamp. Pulsatile flow was generated with the following set parameters: base 60% and width 60%. In contrast, the nonpulsatile group received continuous flow throughout the procedure.

### Markers

For both patient groups, in the preoperative period and on the first, second, and fifth postoperative days, patients were checked for kidney and liver functions and values of hemogram, troponin, and glucose were recorded.

Statistical analysis: Statistical evaluation was done with SPSS v16.0 (SPSS Inc., Chicago, IL) packaged software. The results were reported as mean ± standard (SD) for quantitative variables and percentages for categorical variables. Pearson

Table 4. Comparison of hemogram and biochemical data between groups

		Pulsatile	Nonpulsatile	P
WBC	Preop	7.91 ± 2.25	8.02 ± 2.38	.882
	1st day	10.51 ± 2.36	12.98 ± 3.11	.008*
	2nd day	11.97 ± 2.88	14.01 ± 3.78	.063
	5th day	8.19 ± 2.20	9.91 ± 3.29	.060
HGB	Preop	13.82 ± 1.17	13.97 ± 1.66	.735
	1st day	10.13 ± 1.31	9.37 ± 0.85	.035*
	2nd day	9.03 ± 0.73	8.29 ± 0.72	.003*
	5th day	8.57 ± 0.67	8.63 ± 0.77	.779
HCT	Preop	41.18 ± 3.32	42.27 ± 4.99	.424
	1st day	30.30 ± 4.08	28.21 ± 2.53	.059
	2nd day	27.32 ± 2.46	25.05 ± 2.00	.003*
	5th day	25.94 ± 2.08	26.10 ± 2.37	.822
PLT	Preop	218.70 ± 49.22	230.30 ± 47.88	.455
	1st day	160.05 ± 39.90	175.80 ± 40.85	.225
	2nd day	152.70 ± 37.43	173.95 ± 44.85	.112
	5th day	201.95 ± 48.37	233.50 ± 68.64	.101
BUN	Preop	37.10 ± 9.97	33.50 ± 7.96	.215
	1st day	39.70 ± 11.20	40.60 ± 13.93	.823
	2nd day	46.05 ± 16.72	45.65 ± 14.99	.937
	5th day	44.65 ± 17.73	40.00 ± 12.90	.349
CREATINE	Preop	0.81 ± 0.24	0.77 ± 0.20	.600
	1st day	0.91 ± 0.34	0.92 ± 0.30	.915
	2nd day	0.84 ± 0.33	0.82 ± 0.31	.919
	5th day	0.82 ± 0.25	0.84 ± 0.29	.769

$\chi^2$  test (or the Fisher exact test) was used for comparing categorical variables, and independent samples t-test and paired t test were used to compare continuous variables. Repeated measures analysis of variance was used to analyze biochemical markers within the groups. A *P*-value of <.05 was considered to be statistically significant.

## RESULTS

The mean age was 60.45 ± 7.79 years in the pulsatile group and 57.40 ± 7.59 years in the nonpulsatile group. Three patients (15%) were women in both groups. New Euroscore II was calculated 0.94 ± 0.40 and 0.86 ± 0.35, respectively, in the pulsatile and nonpulsatile groups (*P* = .507). Body mass index (BMI) and EF were similar in both groups, and *P* values were 0.155 and 0.558, respectively. Patient preoperative data is summarized in Table 1. Kidney to skin measurements preoperatively were recorded and statistically were similar in both groups.

The mean perfusion flow was 4070 ± 388.79 mL/minute for the pulsatile group and 4185 ± 277.72 mL/minute for the

nonpulsatile group (*P* = .289). Mean blood pressure during CPB was 68.10 ± 7.43 and 67.75 ± 7.32, respectively, in the pulsatile and nonpulsatile groups (*P* = .882). Urine output statistically was higher in the pulsatile group, during CPB (*P* = .045) (Table 2).

Renal perfusion measurements via fNIRS intra-operatively were statistically parallel between the groups (Table 3).

When complete blood count (CBC) parameters were analyzed, white blood cell (WBC) count on the postoperative first day (*P* = .008), hemoglobin values on the postoperative first (*P* = .035) and second days (*P* = .003), and hematocrit rates on the postoperative second day (*P* = .003) were statistically different in favor of the pulsatile group. There was no difference between the groups when we compare biochemical markers (Table 4).

However, when we compare biochemical markers within the groups, in the nonpulsatile group, creatinin statistically is higher on the postoperative first day (*P* = .003) and BUN statistically is higher on the postoperative first (*P* = .015), second (*P* = .001), and fifth (*P* = .020) days, according to preoperative value. In the pulsatile group, only postoperative second day BUN was higher, compared with preoperative numbers (*P* = .007) (Table 5).

Table 5. Biochemical markers within groups

		Mean ± SD	P
Nonpulsatile BUN	Preop	33.50 ± 1.78	
	Postop 1st day		.015*
	Postop 2nd day	45.65 ± 3.55	.001*
	Postop 5th day	40.00 ± 2.88	.020*
Nonpulsatile creatine	Preop	0.77 ± 0.45	
	Postop 1st day		.003*
	Postop 2nd day	0.82 ± 0.69	.141
	Postop 5th day	0.84 ± 0.66	.092
Pulsatile BUN	Preop	37.10 ± 9.97	
	Postop 1st day		.175
	Postop 2nd day	46.05 ± 16.72	.007*
	Postop 5th day	44.65 ± 17.73	.083
Pulsatile creatine	Preop	0.81 ± 0.24	
	Postop 1st day		.114
	Postop 2nd day	0.84 ± 0.33	.624
	Postop 5th day	0.82 ± 0.25	.909

## DISCUSSION

Coronary artery disease is strongly associated with chronic renal failure and changes in renal arteries [Fuiano 2005]. Patients referred for coronary artery bypass grafting are older, have poorer left ventricular function, and lower GFR because of the increased use of angioplasty [Grover 2001]. Preoperatively, GFR is the most powerful predictor of postoperative acute renal failure. CPB also is an independent predictor of renal failure after CABG [Onorati 2007].

Renal dysfunctions can occur during CPB, due to exposure of blood to a foreign surface, hemodilution, hypothermia, and nonpulsatile blood flow. Renin secretion, during nonpulsatile flow, may affect the kidneys more than other organs [Sievert 2012]. Sympathetic activation with nonpulsatile blood flow results in vasoconstriction and increased afterload. This may happen as a result of not stimulating the arterial baroreceptors to a similar degree as pulsatile devices or normal controls [Markham 2013].

Changes in kidneys or other organs give symptoms no sooner than 24 hours, and because of this detecting injuries in kidney early has become more important [Toraman 2012]. Diaz et al found that early detection of renal or hepatic injury improves the results [Diaz 2008]. In a study from the Duke University database on 2,672 patients undergoing elective CABG with CPB, acute kidney injury requiring renal replacement therapy occurred in only 0.7% of patients, but was associated with 28% mortality, compared with 1% in patients without kidney injury [Conlon 1999]. Mortality rates increase to 88% in patients with acute renal failure after cardiac surgery [Khilji 2004].

Increasing evidence supports a shift from nonpulsatility to pulsatility in open-heart surgeries, with clinical evidence

showing better cardiac, renal and pulmonary outcomes in patients receiving pulsatile perfusion [Bayram 2012]. Benefits of pulsatile flow include reduction of the systemic inflammatory response syndrome associated with bypass, decreased need for inotropic support, shortened hospital stay, and superior organ preservation [Mohammadzadeh 2013]. Our study also demonstrated improved biochemical and hemogram findings, and urine output in the pulsatile group.

The literature often states that postoperative somatic organ damage is a factor increasing cardiac surgical mortality and morbidity. Hence, there is a need for organ-protective strategies, and new tracking modalities may help with diagnosing somatic organ dysfunctions earlier [Toraman 2012]. In our study, we used fNIRS to track renal function during operations. We found that fNIRS measurements were equal for both groups; similarly, we did not observe any renal-related complications during the postoperative period in both groups.

## CONCLUSION

Presently, fNIRS is used in tracking cerebral functions during operations. It also provides accurate observation of blood feeding for somatic organs, such as the kidneys, but further clinical studies are required to justify routine usage. Due to high mortality in CABG patients having acute renal failure, fNIRS must be considered for operations with pulsatile current in high-risk groups.

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