

# The Systemic Inflammation on Transradial vs Transfemoral Approach for Coronary Angiography in Patients with Chronic Coronary Syndrome

## —Does Transradial Coronary Angiography Trigger More Inflammation?

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### Abstract

**Background:** Most of the institutions accept the Transradial Access (TRA) as the first approach for patients undergoing Coronary Angiography (CAG) and Percutaneous Coronary Interventions (PCI). Several studies clearly revealed endothelial injury of coronary arteries triggers inflammatory response. In this study, we aimed to evaluate inflammatory response to CAG and to compare the inflammatory response of TRA and Transfemoral Access (TFA). **Methods:** In this single-center prospective study 140 consecutive patients presenting with (Chronic Coronary Syndrome) CCS and underwent transradial or transfemoral CAG between December 2017 and December 2018 were included. After exclusions, left 92 patients were divided into two equal groups as TRA and TFA. The primary endpoints were 2nd hour Tumor Necrosis Factor alpha (TNF $\alpha$ ), 48<sup>th</sup> hour high-sensitivity C-Reactive Protein (hs-CRP), complication rates, amount of contrast medium, procedure time and fluoroscopy time. **Results:** Basal characteristics of TRA and TFA groups were similar. A comparison of variables demonstrated that there was no statistical significance in increase in inflammatory markers (TNF $\alpha$ , hs-CRP), complication rates, amount of contrast media and procedure time. In contrast, TRA was associated longer fluoroscopy time and higher X-ray dosage, although statistically insignificant. CAG caused a similar increase in hs-CRP in both groups, insignificantly. **Conclusion:** In contrast to previous studies reporting a higher inflammatory response with TRA, this study demonstrates that inflammatory response caused by CAG is unrelated to access site and similar in TRA and TFA. Longer fluoroscopy time, higher X-ray dosage and

longer procedure time in the TRA group indicate the importance of carefully selecting the angiographic route especially in patients with chronic heart failure, chronic renal impairment and malignancy risk. Also, these parameters place importance for physicians own health and woman planning pregnancy.

## Keywords

Transradial Coronary Angiography, Transfemoral Coronary Angiography, Inflammation, TNF $\alpha$ , hs-CRP

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## 1. Introduction

The first cardiac catheterization procedure was performed by Werner Forssmann in 1929 and selective CAG was described by Mason Sones in the early 1960s [1]. TFA approach which was commonly used, has been compared with radial approach in multiple randomized studies. TRA has been considered as the preferred vascular access site due to vessel-related complications and bleeding related increased morbidity, mortality and hospital stay with TFA, particularly when anticoagulation and antiplatelet therapy are administered [2] [3].

Most of the institutions currently accept the Transradial Access (TRA) as the first choice for patients undergoing CAG and Percutaneous Coronary Interventions (PCI) in regard of data from randomized trials which have shown TRA reduced major bleeding and major adverse cardiac events compared with Transfemoral Access (TFA). TRA has been especially investigating in high-risk population such as women, elderly patients or patients with prior CABG [4] [5] [6]. Studies clearly revealed that CAG and PCI trigger inflammatory response [7] [8] [9]. Higher inflammatory response means poorer outcome. Hs-CRP was assessed due to hs-CRP is gold standard to diagnose inflammation and recent studies have found a certain correlation between hs-CRP and atherosclerosis. TNF $\alpha$  is a powerful proinflammatory cytokine with pleiotropic properties and a key mediator of inflammation. This study is the first head-to-head comparison of inflammation between TRA and TFA in patients presenting with Chronical Coronary Syndrome (CCS) and undergoing CAG without PCI.

## 2. Methods

In this single-center prospective study 140 consecutive patients presenting with CCS and underwent transradial or transfemoral CAG between December 2017 and December 2018 were included. After exclusions, left 92 patients (41 female, 51 male) were divided into two equal groups as TRA group and TFA group. Patients with an estimated glomerular filtration rate (eGFR) of <30 ml/min/1.7m<sup>2</sup>, age > 75 years, history of CABG, inflammatory diseases or malignancies and those with procedural complications or cross over were excluded. The primary endpoints were 2<sup>nd</sup> hour TNF $\alpha$  value, 48<sup>th</sup> hour hs-CRP, complication rates, amount

of contrast medium, procedure time and fluoroscopy time. Demographic and clinical characteristics, total angiography and fluoroscopy time, contrast media volume, quantity of X-ray, access site, number of puncture attempts, use of sedation, size of sheath and catheters, occurrence of radial artery spasm, contents of intra-arterial cocktails, complications during in hospital period and angiographic findings were recorded. Venous blood samples for hs-CRP and TNF $\alpha$  levels were obtained prior to puncture and post procedure at 2<sup>nd</sup> and 48<sup>th</sup> hours. Other biochemical findings (hemogram, blood glucose, creatinine, lipids) as well as patients' height, weight and left ventricular ejection fraction were obtained from hospital records.

All statistical analysis was carried out using SPSS 24.0 software (IBM SPSS for Windows, ver.24). On detection of the sufficiency of sample size, power of all values was described at least 80% and type 1 error was accepted 5%. Shapiro-Wilko test ( $n < 50$ ) was used as test of normality. Continuous variables were presented as mean  $\pm$  standard deviation (SD). Categorical variables were presented as percentages. The Independent Samples t test compared the means of two independent groups (TRA vs TFA) in order to determine whether there is statistical evidence that the associated population means are significantly different. The test of nonparametric variables was Mann-Whitney U test. The paired t test and Wilcoxon analysis were used to compare dependent parametric values and dependent nonparametric values, significantly. The correlation values were obtained using the Spearman rank order correlation test. The enumeration data were presented as rate and compared using  $\chi^2$  test.  $P < 0.05$  was considered as statistically significant.

### 3. Results

Mean age of TRA and TFA patients were  $57.1 \pm 8.5$  and  $57.1 \pm 10.7$  years, respectively. 63.0% of TRA population and 47.8% of TFA population were male. To avoid their effects on inflammation, basal characteristics such as hypertension, diabetes mellitus, hyperlipidemia, renal failure, PCI history and smoking of TRA and TFA groups were similar. Basal TNF $\alpha$  and basal hs-CRP values of two groups were insignificant (basal hs-CRP of TRA and TFA patients  $3.70 \pm 4.31$  and  $4.20 \pm 4.48$ , respectively,  $p: 0.592$ . Basal TNF $\alpha$  of TRA and TFA patients  $7.10 \pm 3.39$  and  $6.2 \pm 2.98$ , respectively,  $p: 0.052$ ) (**Table 1**). A comparison of variables demonstrated that there was no significant increase in inflammatory markers (TNF $\alpha$ , hs-CRP), complication rates, amount of contrast media, procedure time between two groups (**Table 2**). On the other hand, TRA was associated longer fluoroscopy time than TFA ( $6.01 \pm 3.84$  vs  $3.64 \pm 1.55$ ,  $p < 0.001$ ) and insignificantly higher X-ray dosage.

### 4. Discussion

The comparison of TRA versus TFA with regard to reducing major cardiovascular and cerebrovascular complications was demonstrated with a meta-analysis

**Table 1.** Basal characteristics of TRA and TFA groups.

	TRA		TFA		P
	n	%	n	%	
Sex (male)	29	63.0	22	47.8	0.142
Hypertension	33	71.7	33	71.7	1.000
Diabetes Mellitus	22	47.8	15	32.6	0.137
Hyperlipidemia	23	50.0	18	39.1	0.294
Renal Failure	1	2.2	1	2.2	1.000
PCI history	5	10.9	10	21.7	0.158
Smoking	17	37.0	9	19.6	0.064
Acetylsalicylic acid	18	39.1	17	37.0	0.830
Clopidogrel	3	6.5	6	13.0	0.292
Ticagrelor	0	0.0	1	2.2	0.315
Statin	17	37.0	15	32.6	0.662
Betablocker	19	41.3	16	34.8	0.519
ACEI/ARB	22	47.8	25	54.3	0.532
DHP-CCB	6	13.0	8	17.4	0.562
Non-DHP-CCB	1	2.2	0	0.0	0.315

PCI: Percutaneous coronary intervention, ACEI/ARB: Angiotensin converting enzyme inhibitor/ Aldosterone receptor blocker, DHP-CCB: Dihydropyridine calcium channel blocker.

**Table 2.** Comparison of the primary endpoints.

	TRA Mean	TFA Mean	p
Hs-CRP 0 <sup>th</sup> hour (mg/dl)	3.70 ± 4.31	4.20 ± 4.48	0.592
Hs-CRP 48 <sup>th</sup> hour(mg/dl)	10.89 ± 20.34	11.75 ± 15.64	0.821
Hs-CRP 0 <sup>th</sup> - 48 <sup>th</sup> hour(mg/dl)	4.77 ± 9.73	7.56 ± 14.04	0.276
TNFα 0 <sup>th</sup> hour(pg/dl)	7.10 ± 3.39	6.2 ± 2.98	0.052
TNFα 2 <sup>nd</sup> hour (pg/dl)	6.50 ± 3.58	5.59 ± 2.97	0.064
TNFα 0 <sup>th</sup> - 2 <sup>nd</sup> hour (pg/dl)	0.23 ± 0.70	0.17 ± 0.37	0.588
X-ray (Gy)	830.32 ± 411.79	710.65 ± 203.27	0.081
Amount of contrast media (ml)	70.22 ± 22.58	62.07 ± 20.04	0.070
Procedure time (min)	12.30 ± 6.62	10.30 ± 3.62	0.076
Flouroscopy time (min)	6.01 ± 3.84	3.64 ± 1.55	<0.001

TRA: Transradial access, TFA: transfemoral access, hs-CRP: high-sensitivity C-reactive protein, hs-CRP 0: Basal high-sensitivity C-reactive protein, hs-CRP 48: 48<sup>th</sup> hour high-sensitivity C-reactive protein, hs-CRP 0 - 48: Difference between basal and 48<sup>th</sup> hour high-sensitivity C-reactive protein between, TNFα: tumor necrosis factor alpha, TNFα 0: Basal tumor necrosis factor alpha, TNFα 2: Second hour tumor necrosis factor alpha, TNFα 0 - 2: Difference between basal and 2<sup>nd</sup> hour tumor necrosis factor alpha, Gy: Gray

including four important trials called as MATRIX-ACCESS, RIVAL, SAFE-PCI and STEMI-RADIAL [10]. According to meta-analyses, TRA reduced death from

all causes during the first 30 days following intervention, bleeding and local complications at the access site. In addition, TRA was associated with a reduction in length of hospital stay and more of the patients preferred the TRA for their next procedure [11]. In patients with CCS, inflammation has been reported to be correlated with plaque progression. Even low-grade inflammation that is defined by high plasma levels of hs-CRP and TNF $\alpha$  was described a significant risk factor for coronary spasm and coronary artery disease (CAD) [12] [13]. Only rare studies are available about inflammatory response of patients who experienced CAG without PCI and our study is the first head-to-head comparison of inflammation between TRA and TFA in patients presenting with CCS and undergoing CAG without PCI.

In contrast to previous single arm studies reporting a higher inflammatory response with TRA, this study demonstrates that inflammatory response caused by CAG is unrelated to access site. This result can be related to exclusion of multiple punctures via experienced operators in TRA population. Longer fluoroscopy time, higher X-ray dosage and longer procedure time in the TRA group indicate the importance of carefully selecting the angiographic route especially in patients with chronic heart failure, chronic renal impairment and malignancy risk. Also, these parameters place importance for physicians own health and woman planning pregnancy.

## 5. Conclusion

In contrast to previous studies reporting a higher inflammatory response with TRA, this study demonstrates that inflammatory response caused by CAG is unrelated to access site and similar in TRA and TFA. Longer fluoroscopy time, higher X-ray dosage and longer procedure time in the TRA group indicate the importance of carefully selecting the angiographic route especially in patients with chronic heart failure, chronic renal impairment and malignancy risk. Also, these parameters place importance for physicians own health and woman planning pregnancy.

## 6. Limitations

Firstly, this was a single center study with a limited number of patients. Most quantitative analyses require a fairly large sample. Secondly, only the TNF $\alpha$  and hs-CRP have been assessed due to hs-CRP is gold standard to diagnose inflammation. Finally, patients with eGFR of <30 ml/min/1.7m<sup>2</sup>, age > 75 years, history of CABG, inflammatory diseases or malignancies and those with procedural complications or cross over were not included in the study group. Including these fragile patients can provide more generalizable information.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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