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Altered Hand Temperatures Following Transradial Cardiac Catheterization: A Thermography Study☆,☆☆

Katherine A. Maki [a,b], Decebal S. Griza [a], Shane A. Phillips [c], Beata M. Wolska [d,e], Mladen I. Vidovich [a,e,*]

[a] Jesse Brown VA Medical Center, Chicago, IL, United States of America
[b] College of Nursing, University of Illinois at Chicago, Chicago, IL, United States of America
[c] Department of Physical Therapy, College of Applied Health Sciences, University of Illinois at Chicago, Chicago, IL, United States of America
[d] Department of Physiology and Biophysics, Center for Cardiovascular Research, University of Illinois at Chicago, Chicago, IL, United States of America
[e] Division of Cardiology, University of Illinois at Chicago, Chicago, IL, United States of America

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ABSTRACT

Background: There is concern about potential detrimental effects of transradial access (TRA) on radial artery structure, endothelial and hand function. This thermography study evaluated TRA impact on hand microvascular perfusion.

Methods and results: We prospectively measured hand thermography, radial and ulnar artery size and blood flow velocities in both catheterization and non-catheterization hands at baseline and 30-days after TRA in 158 patients. There were no differences in radial or ulnar arterial diameters or velocities pre- and post-TRA in catheterization and non-catheterization hands ($p = NS$). The absolute total hand thermography values post-TRA were increased in both catheterization and non-catheterization hand (pre-TRA 30.4 ± 2.9 vs. post-TRA 31.6 ± 2.6 $p < 0.01$; pre-TRA 30.2 ± 2.9, post-TRA 31.6 ± 2.6 $p < 0.01$, respectively). After ulnar artery occlusion, hand temperatures decreased in both catheterization and non-catheterization hands, both pre- and post-TRA and were similar in the catheterization and non-catheterization hands ($p = NS$). Total hand temperature decreased with ulnar artery occlusion and was significantly attenuated post-TRA ($p < 0.001$ both catheterization and non-catheterization hands).

Conclusions: TRA is associated with temperature changes in both catheterization and non-catheterization hands at one month after the index procedure. These changes likely represent a systemic response to local TRA stimulus.

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1. Introduction

Compared to femoral arterial access for coronary angiography and intervention, the benefits of radial arterial access (TRA) include increased patient satisfaction, reduced bleeding complications and length of stay, and decreased mortality in high-risk settings [1]. Despite these benefits, there has been an ongoing concern about potential detrimental effects on radial artery structure, endothelial function as well as hand function after TRA [2]. Various techniques have been used to assess the effects of TRA, including Doppler ultrasonography, optical coherence tomography, measures of sensory loss, hand grip strength, lactic acid concentration and structured questionnaires [3]. These studies have yielded mixed results. Some suggest a degree of endothelial dysfunction and others short-term hand dysfunction with limited or no long-term sequelae [4–6]. Radial artery occlusion occurs in a small percentage of TRA despite anticoagulation and contemporary hemostasis techniques [7, 8].

At this time, there is limited research on microvascular perfusion pre-and post-TRA. The impact of TRA on non-intervention hand function has not been consistently studied [9–11]. To address this gap, we performed a prospective study employing hand thermography in patients undergoing TRA. Infrared thermography is a diagnostic tool that detects infrared heat from the surface of the body and quantifies skin temperature as a surrogate for blood flow. It has been used to study physiologic blood flow abnormalities related to temperature distribution in various conditions [12]. It produces a visual heat-map display and allows objective temperature measurement with regional temperature assessment to evaluate vascular perfusion [13]. We sought to determine the effects TRA on catheterization and non-catheterization hand microvascular perfusion using hand thermography.

2. Methods

Using a repeated measures design, artery diameters and hand temperatures were measured before and 30 days after elective TRA in a

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* Corresponding author at: 840 S Wood St, Suite 935, Chicago, IL 60613, United States of America.
E-mail address: miv@uic.edu (M.I. Vidovich).

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sample of Veterans subjects (n = 172). Patients were recruited from April 22, 2013 to December 21, 2015. (Fig. 1). Medical history, patient demographics and procedural details are shown in Table 1. This was the first TRA procedure for all patients and none of the patients underwent an upper extremity procedure between initial procedure and follow-up.

2.1. Pre- and post-procedure thermography measurements

Dorsal hand and individual finger temperatures were measured by thermography (FLIR A615 thermal imaging camera, FLIR Systems, Inc., Wilsonville, OR) in both hands (hand used for TRA or "catheterization hand" and control/contralateral hand) after 3 min of seated temperature acclimation. All measures were performed in a temperature-controlled room with an ambient temperature between 20 and 22 °C. Hands were placed on a cork board surface to minimize influence of surrounding surface on temperature measurements. The dorsal surface of the hand was imaged to promote natural hand position and patient comfort. The hand silhouette was used to maintain stable hand position during thermography image acquisition and the forearm was supported for patient comfort. In order to distinguish the contribution of radial arterial flow from ulnar arterial flow and to determine the sole contribution of radial artery to hand perfusion, *isolated radial artery flow* was obtained by mechanically occluding the ulnar artery with an inflatable hemostasis band (TR BAND® Radial Compression Device, Terumo Medical Corporation, Somerset, NJ). Complete ulnar artery occlusion was confirmed by temporary manual occlusion over the radial artery to verify disappearance of pulsatile plethysmography tracing waveform in the 2nd digit (manual pressure over the radial artery was subsequently released before temperature recording). After 3 min of isolated radial artery flow, a second set of thermography measures were obtained.

The average temperature of the whole hand was calculated by combining the six regional measures and averaging the temperature results. We also measured radial artery (thumb and index finger) and ulnar artery (4th and 5th digit) perfusion territory temperatures. (Fig. 2. and Fig. 3.) The non-catheterization hand (i.e., radial artery not accessed for angiography) served as the control. These temperature measures were compared in the catheterization hand and the non-catheterization hand, pre- and post-TRA. Temperature changes with *isolated radial artery flow* were calculated by subtracting the average temperature of the total hand after 3 min of mechanical ulnar artery occlusion from the average temperature of total hand prior to ulnar occlusion. Radial and ulnar perfusion territory temperature differences with *isolated radial artery flow* were also compared for regional temperature assessment. The temperature measurements between the catheterization hand and the non-catheterization hand pre-and post-TRA were compared.

Table 1
Baseline patient and procedure characteristics.

Patient characteristics	
Age, mean ± SD	64.4 ± 9.3
Male, %	94.3
African American, %	63.3
Hypertension, %	91.1
Dyslipidemia, %	81.0
Diabetes mellitus, %	49.1
Smoking history, %	77.8
Weight, (kg)	97.5 ± 23.8
Body mass index, (kg/m^2)	31.2 ± 6.8
Procedure characteristics	
Right radial access, %	92.4
5 French sheath size, %	75.3
Diagnostic cardiac catheterization, %	67.7
Percutaneous coronary intervention, %	31.7
Heparin dose, (Units)	4949 ± 1688
Use of bivalirudin, %	20.9
Activated clotting time, (sec)	227 ± 110
Air inflated in hemostasis band, (ml)	12 ± 2
Radial artery occlusion, *n* (%)	1 (0.63)

2.2. Ultrasound measurements

Transverse and gray scale ultrasound images and peak systolic Doppler flow velocity of the radial and ulnar arteries were recorded in both hands to confirm bilateral artery patency with a 10–5 MHz linear transducer (SonoSite MicroMaxx, Sonosite, Inc., Bothell, WA). Radial

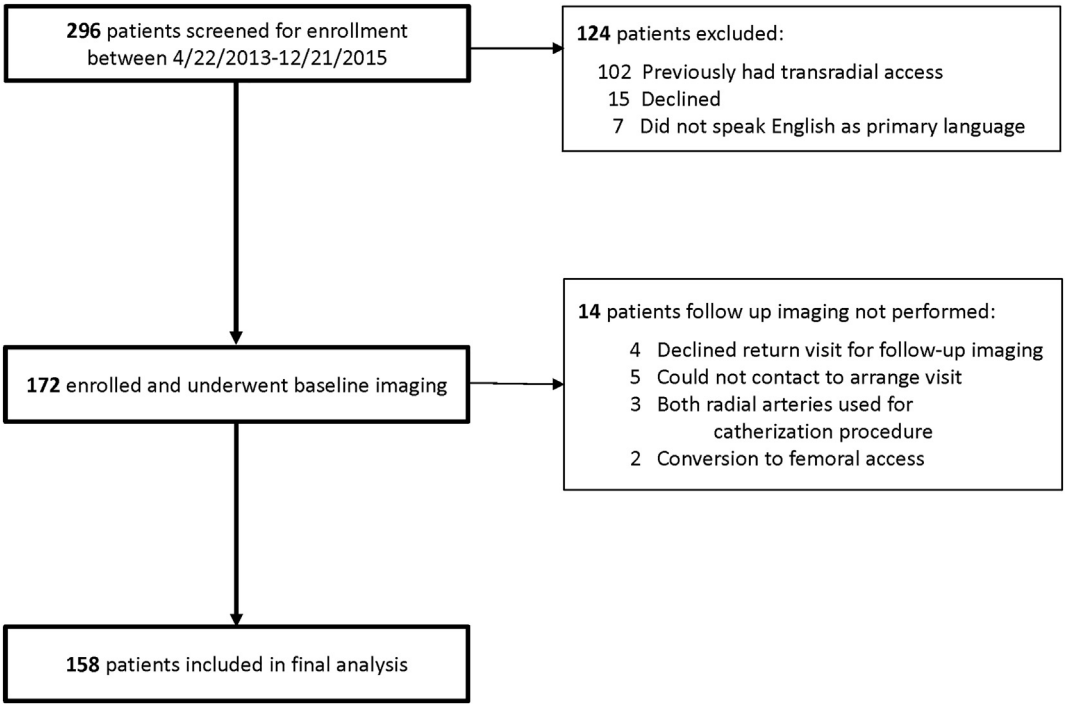

Fig. 1. Patient screening and enrollment flow chart.

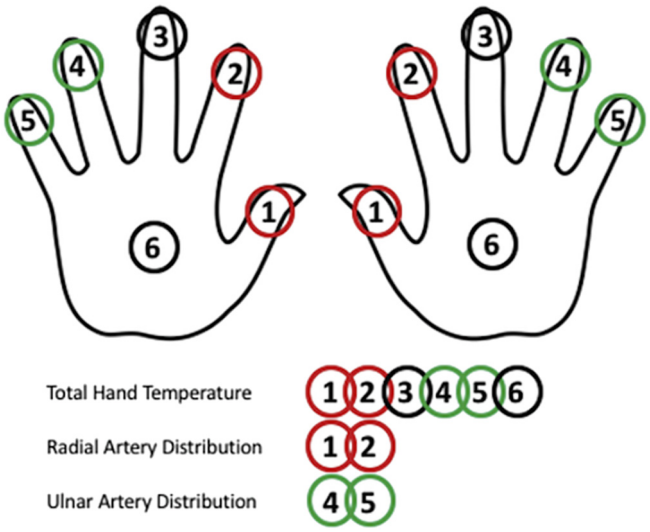

Fig. 2. Thermography temperature measurement territories. Temperature points over six regional territories were averaged to create a mean temperature for the area. These territories were digits one through five and the dorsal surface of each hand. Isolated radial perfusion territory included thumb and index and isolated ulnar perfusion territory included 4th and 5th digit.

and ulnar artery diameters were measured with three separate measurements; at the planned radial access site and 1 cm proximal and distal of the planned radial access site. The mean of these three measurements is reported. All measures were repeated during the follow-up visit after TRA following the same protocol.

2.3. Hemostasis and palmar arch patency determination

Hemostasis was achieved in all patients with the patent hemostasis protocol. We performed Allen's and Barbeau tests prior to TRA and at follow-up. Barbeau test results were dichotomized – Types A and B as "normal" and Types C and D as "abnormal".

2.4. Sample size calculation

Assuming a 20% relative hand temperature change (pre- and post-TRA), with isolated radial artery flow; between radial and ulnar perfusion territories, the sample size required to detect the specified difference with 90% power and a 2-sided α level of 0.01 (using a paired *t*-test) was 97 patients. Each subject served as their own age- and comorbidity-matched control as the catheterization and non-catheterization hand were compared both pre- and after the procedure. We increased our sample size by 50% to allow for potentially lower observed differences.

2.5. Statistical analyses

Univariate analysis was performed to summarize patient and procedural data. Continuous data are presented as a mean $\pm$ SD and categorical variables are presented as percent of total. *t*-tests were used to compare temperature values pre- and post-TRA and in catheterization hand vs. non-catheterization hand. All tests were 2-tailed, and a p-value <0.05 was considered significant for all tests. To explore influence of patient and procedural factors on hand temperature change, multivariate linear regression analyses using the least square estimation method were performed. The following covariates were included in the regression analysis: patient characteristics (age, race, BMI, smoking history, hypertension, hyperlipidemia and days to follow-up imaging) and procedural characteristics (sheath size, length of procedure, activated clotting time and amount of air in hemostasis band). Due to the small sample size, additional statistical models were explored, using a backward elimination process of highly non-significant variables, which did not reveal new significant predictors of hand temperature change in the intervention and non-intervention hand post catheterization and therefore all relevant characteristics were kept in the final models. All analyses were performed using the Stata statistical software version 14.1 (StataCorp, College Station, TX). This study has been approved by the local ethics committee and was registered at clinicaltrials.gov – NCT01996553. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government.

3. Results

A total of 173 patients were included in the study; 158 patients completed the study by returning for follow-up imaging and were included in the final analyses. Due to the population in the Veterans Health Administration, most subjects were male with a history of one or more cardiovascular risk factors, with a mean age of 65 years. (Table 1.) Mean activated clotting time prior to sheath removal was 227 $\pm$ 109 s. Average time to follow-up imaging was 33 $\pm$ 15 days.

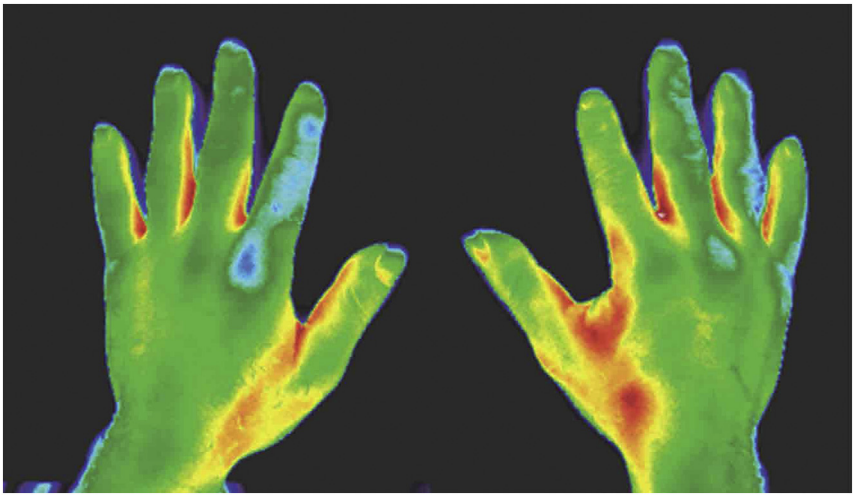

Fig. 3. Representative image of dorsal hand temperature thermography imaging.

3.1. Allen's and Barbeau tests

At baseline and during follow-up, Allen's test findings were unchanged in both the catheterization and non-catheterization hands. The Barbeau test was statistically significantly different in the non-catheterization hand (Allen's $p = 1.0$ and $p = 0.18$, respectively; Barbeau $p = 1.0$ and $p = 0.02$, respectively).

3.2. Ultrasound imaging

There were no differences in radial arterial diameters or velocities pre- and post-TRA. (Table 2). One patient demonstrated asymptomatic radial artery occlusion confirmed by ultrasound.

3.3. Absolute hand thermography imaging

Compared to pre-TRA, the average absolute total hand thermography values post-TRA were *increased* in both the catheterization and non-catheterization hand (pre-TRA 30.4 ± 2.9 vs. pre-TRA 31.6 ± 2.6 $p < 0.01$; pre-TRA 30.2 ± 2.9, pre-TRA 31.6 ± 2.6 $p < 0.01$, respectively). (Table 3.)

3.4. Isolated radial artery thermography imaging

After occlusion of the ulnar artery, total hand temperatures *decreased* in both catheterization and non-catheterization hands, both pre- and post-TRA. These observed temperature decreases were similar in the catheterization and non-catheterization hands. This total hand temperature decrease with ulnar artery occlusion was significantly *attenuated* post-TRA ($p < 0.001$ both catheterization and non-catheterization hands). Both radial and ulnar perfusion territories in the catheterization and non-catheterization hands demonstrated decrease in temperature pre-TRA ($p < 0.001$ for both). This isolated radial and ulnar territory temperature decrease was similarly attenuated post-TRA ($p < 0.001$ for both hands). (Table 3. and Fig. 4).

3.5. Multivariate analysis

There were no variables significantly associated with total hand temperature change with isolated radial artery flow in the catheterization or non-catheterization hand *pre*-TRA access. There were no procedure or patient-related predictors for the magnitude of temperature change in the catheterization hand. (Table 4.) In the non-catheterization hand, diagnostic cardiac catheterization and procedure length were associated with hand temperature change post-TRA ($p = 0.01$ and $p = 0.03$, respectively). (Table 5). Allen's and Barbeau tests were not associated with the observed hand temperature changes (pre-TRA catheterization hand: Allen $p = 0.79$, Barbeau $p = 0.31$; pre-TRA non-catheterization hand: Allen $p = 0.32$, Barbeau $p = 0.09$; post-TRA catheterization hand: Allen $p = 0.94$, Barbeau $p = 0.64$; post-TRA non-catheterization hand: Allen $p = 0.55$, Barbeau $p = 0.39$).

4. Discussion

The primary findings in this study of hand thermography and TRA are: [1] TRA attenuates the baseline hand temperature decrease observed with isolated radial flow; [2] both catheterization and non-catheterization hands demonstrate similar temperature changes after TRA; and [3] temperature changes in both hands occur without changes in radial or ulnar artery diameters or blood flow velocities.

Thermography measures thermoregulatory perfusion in the periphery and is a surrogate/indirect measure of changes in microvascular function [14]. It has been correlated with changes in hand blood flow [15] and is used as a noninvasive means of hand microvascular function assessment in Raynaud's disease, systemic sclerosis or occupational hand vibration exposure [16–18].

The relationship between skin temperature and microvascular skin perfusion is complex [19]. In the acral areas, such as the hands, changes in microcirculatory perfusion appears to be the dominant factor due to the presence of copious arteriovenous anastomoses [20]. However, multiple factors influence skin temperature - autonomic and sensory vessel innervation along with endothelium-dependent and endothelium-independent mechanisms [21]. Vessel occlusion has been used as a provocative test to measure microvascular hand function [22].

Several previous studies have demonstrated that TRA is associated with adverse effects on endothelium-dependent radial artery function. These studies reflect great heterogeneity related to study design, power, endothelial function assessment techniques, time to follow-up and control groups use [2, 9–11]. Hydrophilic coating is not associated with reduction in endothelial dysfunction [10] while procedure length and sheath size are [9]. These studies had various duration of follow-up; it appears that that the effect of TRA may persist several months after the index procedure [2].

Our observation that TRA was associated with bilateral attenuation of the temperature decrease with isolated radial flow suggests an interaction of local and systemic factors and is likely due to ischemic conditioning and neuronal and humoral signal transduction [23].

4.1. Initial stimulation

TRA and sheath insertion cause a variety of stimuli to the vasculature and peripheral sensory nerves. We performed compression of the ulnar arteries pre-TRA to simulate isolated radial artery flow which may initiate preconditioning. Subsequent sheath placement in the radial artery during TRA continues this process. The “index ischemia”, or main ischemic event, occurs from complete to partial occlusion of the radial artery during TRA. Mechanical stimuli during catheterization such as needle puncture and sheath insertion, wire and catheter exchanges, act as noxious triggers to activate peripheral nerves [24, 25]. Additionally, pharmacologic stimulation such as verapamil, saline injection and heparin contribute to these stimuli and neurohumoral activation. Hemostasis after sheath removal with the inflatable occlusive band and alteration of the physiologic blood flow across the palmar arch may act as further stimuli.

4.2. Neuronal and humoral signal transfer

As the above mechanical, pharmacologic and ischemic stimuli are transmitted from the catheterization site through nociceptors and peripheral sensory nerves to the spinal cord, signals are processed and transferred from preganglionic to postganglionic neurons of both the sympathetic and parasympathetic nervous systems [26]. Neuronal and

Table 2
Radial and ulnar artery ultrasound measures pre- and post-transradial access.

	Catheterization hand			Non-catheterization hand		
	Pre-TRA	Post-TRA	p	Pre-TRA	Post-TRA	p
Radial artery diameter (mm)	2.73 ± 0.52	2.69 ± 0.54	0.36	2.63 ± 0.61	2.63 ± 0.62	0.97
Radial artery velocity (cm/s)	53 ± 17.1	55 ± 17	0.19	50 ± 19.2	52 ± 17.9	0.18
Ulnar artery diameter (mm)	2.33 ± 0.48	2.35 ± 0.57	0.65	2.33 ± 0.57	2.29 ± 0.62	0.23
Ulnar artery velocity (cm/s)	48.8 ± 17.3	50.8 ± 17.2	0.19	50.7 ± 20.1	53.1 ± 22	0.18

Table 3
Baseline and temperature change with isolated radial artery flow pre- and post-transradial access.

	Catheterization hand			Non-catheterization hand		
	Pre-TRA (°C)	Post-TRA (°C)	p	Pre-TRA (°C)	Post-TRA (°C)	p
Baseline						
Absolute total hand temperature (Mean ± SD)	30.4 ± 2.87	31.61 ± 2.56	<0.001	30.2 ± 2.93	31.55 ± 2.59	<0.001
Isolated radial flow						
Total hand temperature change (Mean ± SD)	−0.49 ± 0.45	−0.14 ± 0.5	<0.001	−0.40 ± 0.66	−0.02 ± 0.67	<0.001
Radial perfusion territory	−0.50 ± 0.52	−0.09 ± 0.53	<0.001	−0.42 ± 0.74	−0.03 ± 0.71	<0.001
Ulnar perfusion territory	−0.6 ± 0.57	−0.24 ± 0.6	<0.001	−0.38 ± 0.83	−0.04 ± 0.71	<0.001

humoral signal transfer, stimulate the release of mediators and hypoxia-induced factors to the ipsilateral and contra-lateral hands [27].

4.3. Target effects

Through the humoral and neural activation of receptors in target organs (both catheterization and non-catheterization hands) the response to the initial stimulus appears to be a systemic response to a local ischemic event. This may originate from upregulation of anti-inflammatory and downregulation of pro-inflammatory genes [28], or release of vasodilator mediators to generate an increase in blood flow in both the ipsilateral and contralateral hand [29]. It is plausible that remote conditioning from ipsilateral TRA allows signals and mediators to travel from the spinal cord and act at the contralateral hand as a protective mechanism [23].

4.4. Implications

TRA causes a variety of morphological and functional effects on the radial artery. There is both structural injury to the radial artery and impairment of vasomotor function. TRA is associated with intimal hyperplasia, dissection, medial inflammation and tissue necrosis [30, 31], and repeated access is associated with progressive decrease in radial artery diameter [32]. As a result of these changes, the suitability of radial artery for bypass conduit after TRA has been debated [33].

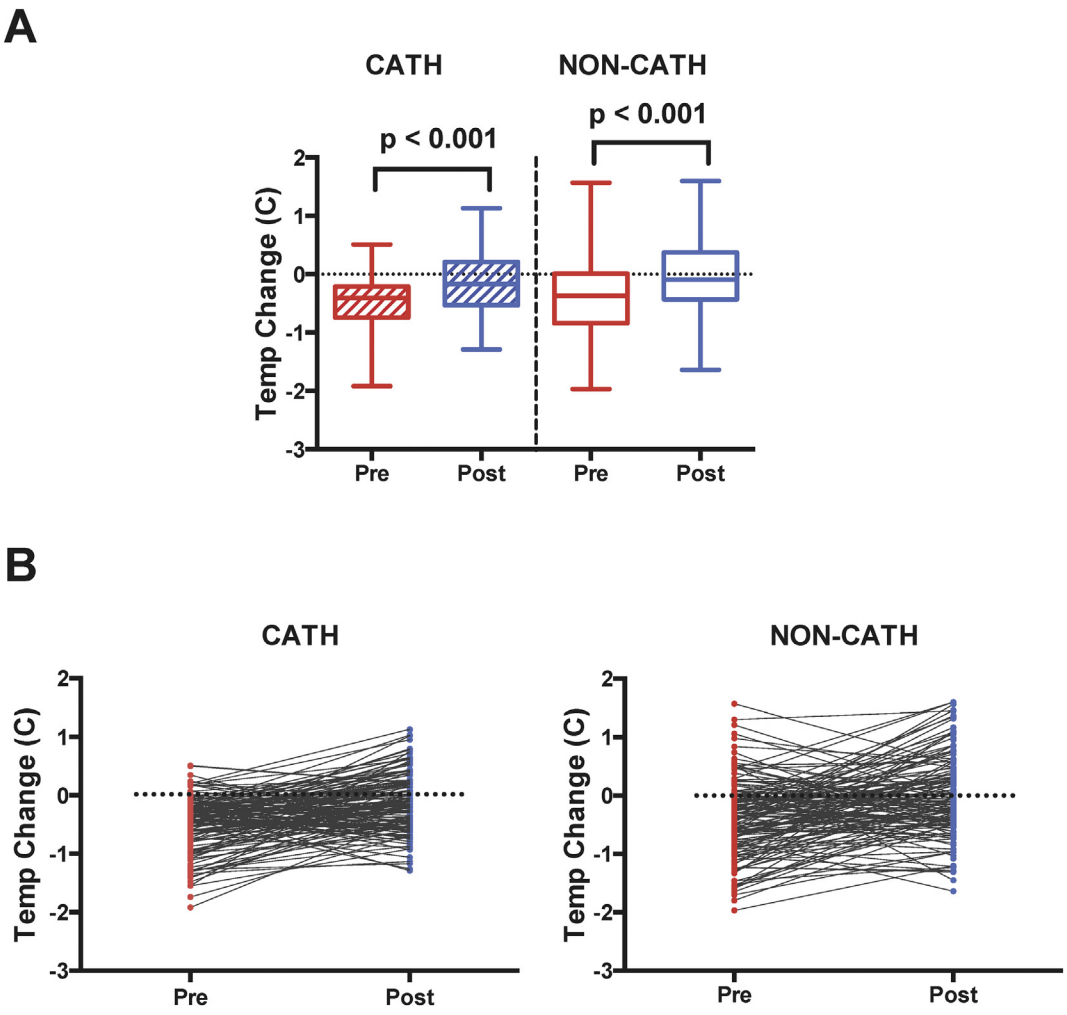

Fig. 4. Hand temperature change with isolated radial artery flow pre- and post-transradial access in catheterized and non-catheterized hands. Panel A. Box and whiskers graphs of temperature change in catheterized and non-catheterized hands. The whiskers go down to the smallest and up to the largest change in hand temperature. Panel B. Plot of all individual changes in hand temperature (catheterized hand and non-catheterized hand).

Table 4
Temperature change post-catheterization in interventional hand: multiple regression results.

	Estimate	Standard error	p-Value
Patient characteristics			
Age	0.004	0.005	0.37
Male	−0.2	0.19	0.29
African American	0.05	0.05	0.28
Hypertension	0.1	0.15	0.52
Dyslipidemia	−0.009	0.11	0.94
Diabetes mellitus	0.09	0.09	0.32
Smoking history	−0.08	0.11	0.45
Weight	−0.002	0.003	0.58
Body mass index	−0.0005	0.01	0.97
Procedural characteristics			
Right radial access	−0.3	0.17	0.08
5 French sheath size	0.25	0.16	0.13
Diagnostic catheterization	0.4	0.52	0.45
Interventional procedure	0.27	0.54	0.62
Procedure length	0.001	0.002	0.52
Heparin dose	−3.63	0.00004	0.99
Use of bivalirudin	−0.29	0.28	0.31
Activated clotting time	0.0005	0.0009	0.58
Air inflated in hemostasis band	0.009	0.02	0.71

Transient decrease in hand grip strength after TRA with eventual full return of function has been described [34]. It is quite likely that the putative neurohumoral alterations may contribute to decreased hand grip strength. We did not observe any association between the traditional Allen's and Barbeau tests and hand temperature changes. These findings are in concordance with the current data and further supports limited usefulness of pre-procedural assessment of dual circulation to the hand [6, 35].

4.5. Limitations

Thermography does not measure perfusion directly, instead it provides an indirect measurement of skin temperature. Our study was performed in a predominately male population, where arterial sizes are larger and larger the sheath-to artery ratio. This decreases the likelihood of radial artery occlusion and could potentially be a confounder in the distal blood flow measures. We observed only one patient who experienced radial artery occlusion and cannot extrapolate our findings to patients with radial artery occlusion.

Table 5
Temperature change post-catheterization in non-interventional hand: multiple regression results.

	Estimate	Standard error	p-Value
Patient characteristics			
Age	0.006	0.006	0.36
Male	−0.03	0.28	0.93
African American	0.0003	0.06	0.99
Hypertension	0.06	0.22	0.77
Dyslipidemia	0.06	0.15	0.71
Diabetes mellitus	0.03	0.12	0.82
Smoking history	−0.2	0.14	0.17
Weight	0.0003	0.004	0.94
Body mass index	−0.007	0.01	0.62
Procedural characteristics			
Right radial access	0.33	0.21	0.12
5 French sheath size	0.002	0.22	0.99
Diagnostic catheterization	1.76	0.69	0.01
Interventional procedure	1.4	0.72	0.05
Procedure length	0.007	0.003	0.03
Heparin dose	−5.27	0.00005	0.91
Use of bivalirudin	−0.29	0.37	0.44
Activated clotting time	0.002	0.001	0.19
Air inflated in hemostasis band	−0.03	0.03	0.38

We did not enroll consecutive patients, rather only patients who consented to this trial which could have influenced our observations. Acclimation time to ambient room temperature was 3 min pre-imaging and 3 min during baseline imaging, which is shorter than other published studies examining skin microcirculation. We only studied patients at one-month follow-up. We did not perform thermography or ultrasound measures in patients without TRA to evaluate the influence of time on isolated radial artery flow. The systemic medications patients were receiving may have influenced the observed differences. Although the second thermography measurement was an average of 33 days post procedure, the calcium channel blocker administered through the radial artery after TRA may have carried a larger influence on the temperature increase post catheterization than other procedural characteristics creating the initial stimulation and should be taken into consideration. Variance, although minimal, in the ambient room temperature may have influenced the magnitude of temperature change from baseline. Hand temperature changes with isolated radial artery flow may not be clinically relevant, as the compensatory flow from the ulnar artery was removed. Noninvasive methods used to assess hand microvascular flow - Laser Doppler Flowmetry and Laser Speckle Contrast Imaging were not compared to thermography.

5. Conclusions

TRA is associated with a temperature change in both catheterization and non-catheterization hands. The mechanisms of these changes are currently not well-defined but are likely a systemic response to the local TRA stimulus which warrants future investigation. These findings add to the growing body of evidence that TRA is associated with structural and functional changes to the radial artery and extend these findings to effect of TRA on the contralateral hand.

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