Original Article

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Role of Infrared Imaging for Detection of Subclinical Inflammation of Joints: A Prospective Cohort Study

Physical Medicine and Rehabilitation Section

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ABSTRACT

Introduction: The detection of inflammation is important for diagnosis of inflammatory joint diseases and its severity. There are clinically doubtful cases of inflammation of joints. Advanced thermal cameras are able to detect the presence of inflammation. Hence, thermal imaging technology has been used for detection of this type of subclinical inflammation of joints.

Aim: To study the efficacy of infrared imaging to detect the subclinical inflammation of joints in doubtful cases of arthritis.

Materials and Methods: A prospective cohort study was conducted for a period of one year from January 2016 to June 2017. The study comprised of 60 patients of all age groups. Patients with joint pain attending Outpatient Department (OPD) of Physical Medicine and Rehabilitation Department (PMR), Agartala Government Medical College (AGMC) and Govind Ballav Pant Hospital (GBPH), Agartala, India, irrespective of the duration of illness and diseases were selected considering inclusion and exclusion criteria. They were evaluated clinically (swelling, tenderness, redness, increased temperature and the presence of restriction of movement) for presence of inflammation in the joint. Blood tests were done for Acute Phase Reactant (APR) namely Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) and infrared imaging of the respective joints were taken. On the basis of clinical examination, all these patients were divided in three groups: (i) patients with inflamed joint; (ii) non inflamed joint; and (iii) doubtful inflammation of joints. Infrared imaging of all the respective joints of all the patients were compared with the respective results of APR for presence of inflammation. Values more than the normal range of APR were considered as positive marker for inflammation. The data was analysed statistically by calculating sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) using Matrix Laboratory (MATLAB) 2013b software.

Results: Out of 60 cases, 37 (61.66%) patients showed clinically inflamed joints, 10 (16.66%) showed no inflammation and 13 (21.66%) showed clinically doubtful cases of inflammation. The results were statistically analysed and the sensitivity, specificity, PPV and NPV of infrared imaging for detection of joint inflammation were 91%, 80%, 94% and 72%, respectively.

Conclusion: Infrared imaging is a very sensitive tool for the detection of inflammation of joints and is very useful for detection of subclinical inflammation of joint.

Keywords: C-reactive protein, Erythrocyte sedimentation rate, Sensitivity, Specificity

INTRODUCTION

The most important aspect in the management of arthritis is to establish the diagnosis of inflammation. Clinicians are dependent on clinical measures like joint tenderness, swelling, redness, restriction of movement and warmth of joint surface, which are all subjective identifiers for the diagnosis of the arthritis [1]. Along with these subjective measures some blood tests like ESR [2] and CRP [3] are considered for detection of inflammation in the joint. More than the normal values of either ESR (normal value in adult male is 10-12 mm in one hour and in adult female is 12-19 mm in one hour) or CRP (normal value in adult is <5 mg/dL) or both is considered to be positive evidence for inflammation of joint [4] and when both ESR and CRP values are negative, the condition is considered as negative inflammation of joint. There is no gold standard for identifying the synovitis of joints [5].

In some cases these clinical parameters collectively cannot detect the synovitis, commonly known as subclinical inflammation of joints. Imaging with Ultrasonography (USG) and Magnetic Resonance Imaging (MRI) has increased the clinicians ability to detect the effusion earlier when there is clinically doubtful synovitis (i.e., joint inflammation) [5,6]. These imaging methods are costlier. Thermal imaging has recently emerged as an important medical diagnostic tool for different disease conditions. Different research works related to thermal imaging have been mentioned in [Table/Fig-1] which provides an insight on the ability of thermal imaging in the detection of inflammation of joint [10-16]. From these studies it can be concluded that there is a relationship between the surface temperature (detected by thermograms) and radiographs of the osteosrthritis patients. Using that correlation, it was concluded that thermograms are efficient in the detection of the severity of osteoarthritis [10-12]. Wherein, [14-16] considering Rheumatoid Arthritis (RA) and to determine the applicability of thermaography in the early diagnosis of arthritis patients, its severity and disease activity. In the above mentioned studies, diagnosis of subclinical inflammation has not been considered. Whereas, the diagnosis of early subclinical inflammation may help clinicians in the initial clinical examination of patients. With this background the present study was conducted with an aim to evaluate the efficiency and accuracy of infrared imaging in the detection of inflammation of joints, particularly the subclinical inflammation.

MATERIALS AND METHODS

A prospective cohort study was conducted in the OPD of PMR Department, Agartala Government Medical College (AGMC) and Govind Ballav Pant Hospital (GBPH), Agartala, India from January 2016 to June 2017. The study was approved by the Institutional Ethical Committee of Agartala Government Medical College vide Ethics Committee approval number Ref. no. 4 (6-11)- AGMC/ Medical Education/ Ethics Com/2018/15136, dated 31st December, 2018) and written consent from all the patients was obtained.

Patients with joint pain were screened irrespective of their duration of illness considering the inclusion and exclusion criteria and a total of 60 patients were selected for the study. On the basis of clinical examination all these patients were divided in three groups;

Authors and year	Joints studied	Number of patients	Observations
Varjú G et al., 2004 [10]	Hand osteoarthritis	A total of 91 subjects were enrolled on the basis of clinical hand OA.	The earliest discernible radiographic stage of hand OA Kellgren-Lawrence 1 (KL1), was associated with higher joint surface temperature. Joints with severe radiographic OA (KL 2-4) were associated with lower surface temperatures.
Denoble AE et al., 2010 [11]	Knee osteoarthritis	A total of 30 women (15 Cases with symptomatic knee OA and 15 age-matched Controls without knee pain or knee OA) participated in this study.	They reported that the skin temperature of the patellar region correlated with x-ray severity of knee OA. This method of infrared knee imaging is reliable and an objective measure for a sign of inflammation and temperature.
Borojevic N et al., 2011 [12]	Hand rheumatoid and osteoarthritis	A total of 21 subjects (6 Healthy subject, 7 patients hospitalised due to OA, 8 patients were hospitalised due to RA) are considered for this study	They used basic statistical analysis of certain region of hands thermograms. They concluded that thermography reliable in differentiating normal subjects and RA subjects and OA subjects from each other.
Lasanen R et al., 2015[13]	Knees and ankles	Study population consist of 58 children exhibiting symptoms of joint inflammation	They found that Infrared Thermography (IRT) could be applicable for screening of ankle joint inflammation in children with Juvenile Idiopathic Arthritis (JIA) or Systemic Lupus Erythematous (SLE).
Snekhalatha U et al., 2017 [14]	Knee rheumatoid arthritis	30 RA patients and 30 age and sex-matched healthy volunteers were included in the study.	They used statistical features to correlate thermograms and radiographs to a biochemical method as standard. They observed that thermal imaging method has a competency in the diagnosis of RA by automated segmentation methods.
Pauk J et al., [2019] [15]	Hand rheumatoid arthritis	50 patients with high disease activity, 16 moderate disease activity and 42 healthy participants were included in the study.	They applied an infrared thermography sensor and a fingers examination protocol. This study shows that dynamic infrared thermography detects the RA disease activity level and can be used in clinical practice as a supportive tool in diagnosis.
Gatt A et al., [2019] [16]	Hand and wrist rheumatoid arthritis	Data from 31 RA patients were compared to that of 51 healthy controls in this study	They used statistical feature mean to compare thermogram of healthy subject to the thermogram of RA patients. These innovative findings provide evidence that baseline thermal data in RA differs significantly from healthy individuals.

[Table/Fig-1]: Review work on application of thermograms in detection of inflammation.
OA: Osteoarthritis; RA: Rheumatoid arthritis

(i) 37 (61.66%) patients with inflamed joint; (ii) 10 (16.66%) non inflamed joint; and 13 (21.66%) doubtful inflammation of joints.

Inclusion criteria: Patient in the age group between 18-60 years of either gender with joint pain, irrespective of the diseases and the duration of illness were included.

Exclusion criteria: Patients with post-traumatic joint swelling, known of malignancy, mental illness, poor general condition, fever, severe anaemia, presence of metal implant in the joint to be evaluated and presence of skin infection in or around the joint to be studied were excluded from the study.

Study Procedure

The randomly selected patients were clinically evaluated and infrared imaging of concerned joints were captured along with necessary biochemical blood tests. The infrared camera used in this study was FLIR T650sc with resolution of 640×480. The infrared images were captured from knee, ankle, elbow and wrist joints as per clinical presentation. The patients included in this study were having one among the following diagnosis namely Osteoarthritis (OA), Rheumatoid Arthritis (RA), Seronegative Spondyloarthopathy (SSpA), Ankylosing Spondylitis (AS), Reactive Arthritis (ReA), and gout [Table/Fig-2] [17-24] precisely maintaining all the protocols to create the dataset.

A number of factors can affect the thermogram acquisition adversely [24] which are categorised into four groups namely infrared camera specification, infrared camera positioning, environmental condition and patient preparation [23]. Camera specification, camera positioning and patient preparation are easy to handle manually compared to environmental condition. But the control of environmental conditions is not in the hands of human. Radiation of objects present in the surrounding environment of acquisition setup can degrade the quality of Infrared image. Other objects having radiation property may produce the artifacts on the temperature profile of the actual object during capturing, such as electric wires, pipes, outlets etc. Field of View (FOV) and required distance between object and camera with respect to the size of the room were identical for all patients. Authors also tried to control other factors such as room temperature and room humidity. The room temperature was fixed in between 220°C to 250°C and the humidity was between 40% to 60% [25].

Type of protocols	Protocol
Camera specification [23]	Camera Name: FLIR T650sc
	Sensitivity: <20 mK @ 300C
	Spectral Range: 7.5-14.0 µm
	Image Resolution: 640×480 pixels
Patient preparation [17-21]	Undressed the part to be captured
	Stabilisation for 15 minutes in at the acquisition room and should avoid contact of other parts.
	Patients should avoid smoking, nerve stimulation, acupunture, hot or cold presses, physiotherapy or intense physical exercises for 24 hours prior to thermography
	Any kind of jewelery not allowed at that time of imaging.
	Patient should avoid tight fitting clothes.
Camera positioning [22-24]	Camera positioned at a distance of 2 meter from the patient.
	The 900 alignment between the camera and the body part to be captured was also an important requirement

[Table/Fig-2]: Protocols maintained during collection of data [17-24].

A dark room made of black clothes and black coloured wood with closed windows in a closed room for acquisition of Infrared image to avoid these interferences [11]. The room was also protected from direct sunlight and air drifts [26]. To find the efficiency of thermal imaging in the above mentioned categories, a state-of-the-art experimentation framework was adopted [13,22]. Among these, it was found that the mean temperature is the most common feature used to detect arthritis from thermograms. The mean temperature can be calculated by the following formula:

$$\text{mean} \pm \text{sum}(x)/\text{size}(x)$$

Where, 'x' is the respective joint part extracted from the thermograms. Sum(x) is the sum of the intensity values present in 'x' and size(x) is the total number of pixel present in 'x'. According to the previous research works in thermal images from healthy subjects, the mean temperature of the anterior knee was 29.5±1.6°C whereas, 30.5±0.8°C and 30.7±1.3°C in thermal images from RA and OA effected subjects [26,27].

Clinical examinations, ESR and CRP were incorporated here for validation of infrared thermal imaging. Wherein, clinical examination can be defined by the subjective measures used by clinician for diagnosing inflammation. The subjective measures considered during

clinical examination were swelling, tenderness, redness, increased temperature of the joints and restriction of movement of the affected joint. Among these three factors (clinical examination, ESR, CRP), if all of them were found positive then it was considered as positive and vice-versa for negative cases. If either ESR or CRP was positive, then the condition of subclinical inflammation of joint was considered when clinical examination could not assess the inflammation clinically and ESR or CRP was found inconclusive [22].

STATISTICAL ANALYSIS

Four factors such as, sensitivity, specificity, PPV and NPV were used for analysis of the data statistically. MATLAB 2013b software (8.2 version) was used. In MATLAB, the mean values were calculated from the images. The mean value was considered as an indicator of the arthritis. Afterwards, with this mean value authors diagnose subclinical inflammation. Sensitivity, specificity, PPV and NPV are used to assess the efficacy of the mean feature and thermal imaging in detection of subclinical inflammation. In the first step, the mean feature is a dependent variable, whereas pixel values were independent variables. In the second step, specificity, sensitivity, PPV and NPV are the dependent variable and True Positive (TP), False Positive (FP), True Negative (TN) and False Negative (FN) are the independent variables.

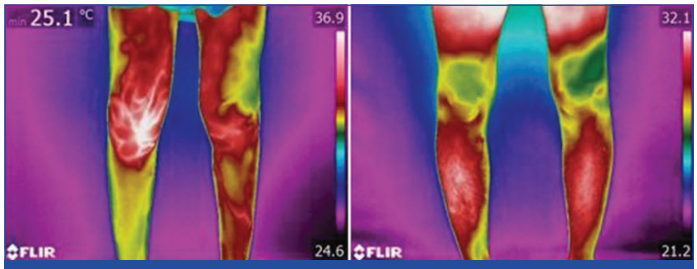
RESULTS

The study population was 60 cases with 37 females (61.7%) and 23 males (38.3%). The highest proportions of study participants were found to be suffering from OA i.e., 22 (36.67%) cases [Table/Fig-3].

Name of diseases	Number of patients n (%)
Osteoarthritis	22 (36.67)
Rheumatoid arthritis	15 (25)
Reactive arthritis	11 (18.33)
Seronegative spondyloarthopathy	7 (11.67)
Ankylosing spondylitis	3 (5)
Gouty arthritis	2 (3.33)

[Table/Fig-3]: Statistics of total dataset.
*These were the confirmed cased based on clinical signs and inflammatory markers

In [Table/Fig-4], left image shows the positive thermogram of knee with rheumatoid arthritis and right image shows the knee thermogram of normal subject.

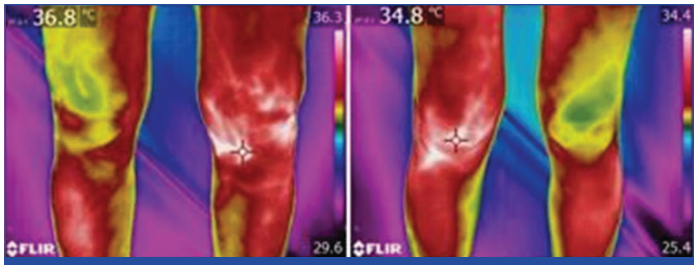


[Table/Fig-4]: Left Image: Thermogram of knee Rheumatoid Arthritis (RA) patient; Right Image: Thermogram of normal subject.

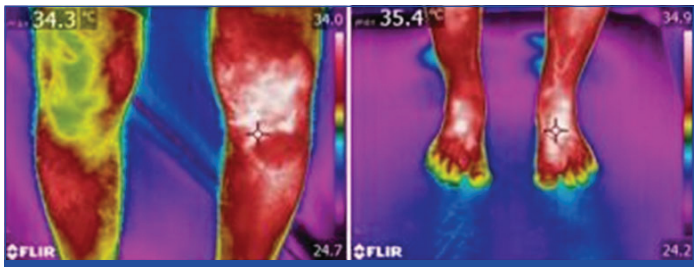
[Table/Fig-5] showing two samples of osteoarthritis, [Table/Fig-6] present samples of knee and ankle affected by Reactive Arthritis (ReA). Hands and wrist of rheumatoid arthritis patient are shown in [Table/Fig-7].

A total of 37 (61.66%) patients with clinical presence of inflammation and the average ESR and CRP values were 55.19 mm and 9.03 mg/L, respectively. Out of these cases thermal imaging was able to detect inflammation in 34 cases (91.89%). Thermal imaging failed in 3 (8.10%) cases, where it was unable to detect inflammation.

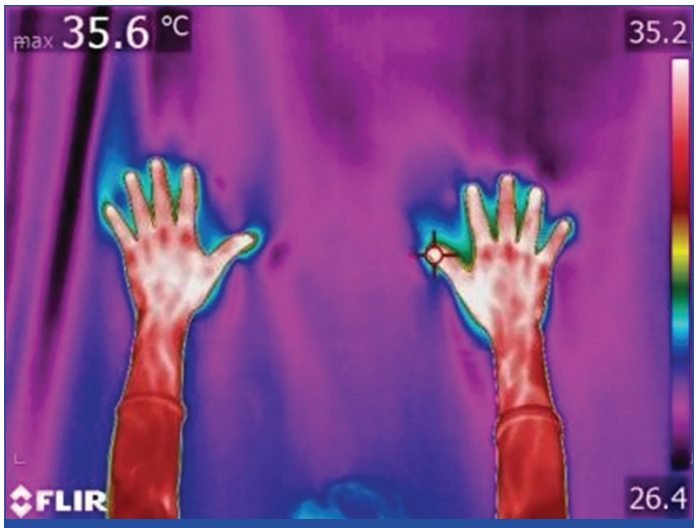
A total of 10 (16.66%) cases of clinically non inflammatory joint pain with average ESR and CRP values are 13.96 mm and 3.82 mg/L respectively. Out of these cases thermal imaging showed absence



[Table/Fig-5]: Thermograms of knees. In the right knee of the right image and in the left knee of the left image showing positive thermograms. Clinical Diagnosis: OA with effusion also considered to be inflammatory in nature.



[Table/Fig-6]: Thermogram sample: Left knee of the left image and both the ankle of right image showing positive thermograms. Clinical Diagnosis: Reactive Arthritis (ReA).



[Table/Fig-7]: Both hands and wrist are showing positive thermogram. Clinical diagnosis: rheumatoid arthritis.

of inflammation in eight cases (80%) and failed in two (20%) cases. It is worth noting that in most of the osteoarthritis cases inflammation was absent.

There were 13 (21.66%) subclinical cases in the studied population and the average ESR and CRP of these patients were 27.46 mm and 5.52 mg/L, respectively. Thermal imaging detected inflammation in 11 (84.61%) cases which is compatible with the higher value of average ESR of this group of patients [Table/Fig-8].

[Table/Fig-9] shows the performance of thermal imaging in detection of positive and negative inflammation. It shows that thermal imaging have 91% sensitivity, 80% specificity, PPV of 94% and NPV of 72%.

DISCUSSION

Increase or decrease in temperature has a direct relation with aggravation or reduction of inflammation. Acute inflammatory changes with high heat dissipation can be detected clinically but mild inflammation of joint may not give rise to significant heat to be detected by clinical examination. As a result subclinical features pose several difficulties to the clinicians in accurately diagnosing arthritis. There were number of cases having subclinical inflammation [13,14].

The observed results also indicated that thermal imaging methodology has the potential in aiding clinicians during clinical examination of the inflammation. The performance of thermal imaging in detection of

Details of patients with clinically presence of inflammation						
S. No.	Diseases	Total number of patients (%)	Avg. ESR	Avg. CRP	Thermographic value positive	Thermographic value negative
1.	Rheumatoid arthritis	12 (32.43)	55.19	9.03	91.89%	8.10%
2.	Osteoarthritis	7 (18.91)				
3.	Reactive arthritis	8 (21.62)				
4.	Ankylosing spondylitis	3 (8.10)				
5.	SSpA	5 (13.5)				
6.	Gout	2 (5.40)				
	Total	37 (61.66)			34	3
Details of patients with clinical absence of inflammation						
1.	Rheumatoid arthritis	1 (10)	13.96	3.82	80%	20%
2.	Osteoarthritis	9 (90)				
	Total	10 (16.66)			8	2
Details of patients with doubtful inflammation (subclinical inflammation)						
1.	Rheumatoid arthritis	2 (15.38)	27.46	5.52	84.61%	15.38%
2.	Osteoarthritis	6 (61.53)				
3.	Reactive arthritis	3 (7.69)				
4.	SSpA	2 (15.38)				
	Total	13 (21.66)			11	2

[Table/Fig-8]: Details of patients with clinical presence of inflammation.
SSpA: Seronegative spondyloarthopathy

S. No.	Measures	Result
1	Sensitivity	91%
2.	Specificity	80%
3.	PPV	94%
4.	NPV	72%

[Table/Fig-9]: Performance of thermal imaging in diagnosis of arthritis.

positive and negative inflammation showed thermal imaging of 91% sensitivity, 80% specificity, PPV 94% and NPV 72%. More specifically, thermal imaging have high sensitivity and specificity which inturn means that thermal imaging is effective in the detection of positive inflammation and negative inflammation with lower rate of FP and FN. The PPV and NPV also showed the efficacy of thermal imaging in detection of positive and negative inflammation. Hence, authors can conclude that thermal imaging has the potential in the detection of subclinical inflammation.

There are several reported literatures regarding thermal imaging in detection of arthritis listed in [Table/Fig-1]. Although, there are several studies [10-16,28], but according to the authors' knowledge no work concentrates on detection of subclinical inflammation using thermal imaging. Thermal imaging is an effective tool that can help the clinicians in diagnosis of subclinical inflammation. Hence, clinicians can make use of thermal imaging technology along with their observation to assess the doubtful inflammation.

Limitation(s)

In the present study, though the sample size was small, more study will be helpful to establish the role of thermal imaging in the detection of doubtful inflammation of joints.

CONCLUSION(S)

The comparison of ESR and CRP values with the infrared thermal imaging implied that thermal imaging can be considered as a tool for detection of inflammation of joint including the subclinical inflammation of joint.

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