Handheld Infrared Thermometer to Evaluate Cellulitis (HI-TEC)

Statistical Analysis Plan Version 1.0 1ˢᵗ of March 2020

Study ID: 2019-4850

NCT03846635

Participants

Eligible patients were at least 18 years of age and had suspected cellulitis restricted to an arm or leg (without involvement of the trunk, genitalia or head and neck). Consultation of an infectious disease specialist was required for enrolment. Patients were excluded if they had received empiric therapy for cellulitis for greater than 24 hours before recruitment or if they had a severe skin infection that would ultimately need operative management (such as deep abscess or necrotizing fasciitis). Patients who were unable to give informed consent, as well as patients with amputated contralateral limbs or known severe dysautonomia causing limb temperature dysregulation were also excluded.

Diagnostic Procedure

At the time of recruitment, demographic data and key clinical information including medical history and laboratory results were collected. We used a MasterCraft Digital Temperature Reader infrared thermometer (Mastercraft Canada, Toronto, Canada) to measure skin surface temperature. This thermometer was chosen because it was previously validated against a medical–grade skin temperature device (Exergen DermaTemp)[1], is inexpensive (purchased for $30.50 CAD), and is widely commercially available in Canada.

We performed duplicate measurements of the affected area, followed by measurements of the contralateral limb as close to the same location as possible. Before obtaining the measurement, patients were instructed to uncover the area for several minutes in order to avoid temperature fluctuation caused by clothing. Measurements were taken from a vertical distance of approximately 5-10 cm above the affected area. We then evaluated whether a difference in the average temperature between limbs was associated with a clinical diagnosis of cellulitis as determined by the blinded faculty infectious disease consultant. The treating team and the infectious disease specialist

remained blinded to the temperature measurements so that clinical decisions were not influenced by the results.

Analysis of Diagnosis of Cellulitis:

Our goal was to detect a 12% difference in skin surface temperature between limbs with a statistical power of 80%. Assuming an alpha value of 5%, we estimated that we would need to enroll a minimum of 31 patients. To more confidently establish sensitivity and specificity estimates and to be more certain of an adequate sample size, we sought to enrol 50 patients.

With the "cutpt" command in STATA v. 16 (Statacorp LP, USA), we will use Youden's method[2] to determine the temperature difference which best differentiated cellulitis from pseudocellulitis. We will then use bootstrapping (500 repetitions) to estimate 95% confidence intervals for the sensitivity, specificity and the area under the receiver operating curve (c–statistic). Then, using the point estimates for sensitivity and specificity we will construct a plot of pre–test vs. post–test probability as a function of test result. We will also calculate the temperature difference which gave the maximal specificity and include it for reference.

Analysis of Improvement of Cellulitis:

For those who were admitted to hospital and who agreed to be followed we will calculate the FDA criteria for early response (percent reduction in the lesion size at 48 to 72 hours compared to baseline) wherein clinical response in a patient generally is defined as a percent reduction in lesion size greater than or equal to 20 percent compared to baseline. With the "cutpt" command in STATA v. 16 (Statacorp LP, USA), we will use Youden's method[2] to determine the temperature difference which best matches early response. We will then use bootstrapping (500 repetitions) to estimate 95% confidence intervals for the sensitivity, specificity and the area under the receiver operating curve (c–

statistic). We will also calculate the temperature differences which give the maximal sensitivity and specificity and include it for reference.

We will also explore the relationship between change in lesion size and temperature difference between limbs graphically and calculate an estimate of the correlation using the most appropriate regression method based on inspection.

<div align="center">REFERENCES</div>

1.   Mufti A, Coutts P, Sibbald RG. Validation of commercially available infrared thermometers for measuring skin surface temperature associated with deep and surrounding wound infection. *Adv Skin Wound Care.* 2015;28(1):11–16.

2.   Youden WJ. Index for rating diagnostic tests. *Cancer.* 1950;3(1):32–35.