Effects of Acupuncture Stimulation on the Radial artery’s Pressure Pulse Wave in Healthy Young Participants: Protocol for a prospective, Single-Arm, Exploratory, Clinical Study

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Abstract

Introduction: This study aims to investigate the effects of acupuncture stimulation on the radial artery’s pressure pulse wave, along with various hemodynamic parameters, and to explore the possible underlying mechanism of pulse diagnosis in healthy participants in their twenties.

Methods and analysis: This study is a prospective, single-arm, exploratory clinical study. A total of 25 healthy participants, without regard to gender, in their twenties will be recruited by physicians. Written informed consent will be obtained from all participants. The participants will receive acupuncture once at ST36 on both sides. The radial arterial pulse waves will be measured on the left arm of the subjects by using an applicable pulse tonometric device (KIOM-PAS). On the right arm (appearing twice), electrocardiogram (ECG), photoplethysmogram (PPG), respiration and cardiac output (CO) signals, will be measured using a physiological data acquisition system (Biopac module), while the velocity of blood flow, and the diameter and the depth of the blood vessel will be measured using an ultrasonogram machine on the right arm (appearing twice). All measurements will be conducted before, during, and after acupuncture. The primary outcome will be the spectral energy at high frequencies above 10 Hz (SE10-30 Hz) calculated from the KIOM-PAS device signal. Secondary outcomes will be various variables obtained from the KIOM-PAS device, ECG, PPG, impedance cardiography modules, and an ultrasonogram machine.

Discussion: The results of this trial will provide information regarding the physiological and the hemodynamic mechanisms underlying acupuncture stimulation and clinical evidence for the influence of acupuncture on the pressure pulse wave in the radial artery.

Ethics and dissemination: This study was approved by the Institutional Review Board (IRB) of Kyung Hee University’s Oriental Medical Center, Seoul, Korea (KOMCIRB-150818-HR-030). The study findings will be published in peer-reviewed journals and presented at national and international conferences.

Trial registration number: This trial was registered with the Clinical Research Information Service (CRIS) at the Korea National Institute of Health (NIH), Repub-
lic of Korea (KCT0001663), which is a registry in the World Health Organization’s (WHO’s) Registry Network.

1. Introduction

Acupuncture was originally a technique employed in Korean medicine, and its efficacy has been proven by several clinical researches [1]. The World Health Organization (WHO) has publicly acknowledged that 80% of 129 countries now recognize the use of acupuncture [2]. According to the 2011 National Statistical Office survey of the Republic of Korea, 77.5% of Koreans have been treated using Korean medicine, in which acupuncture (48%) is the most frequently employed treatment [3].

One of the physiological reactions associated with acupuncture is Deqi [4, 5]. The Emperor’s Inner Canon (Huangdi Neijing) described Deqi as follows: “If there is no Deqi with one acupuncture needle insertion, keep inserting it until you generate one. If Deqi is generated after insertion of the acupuncture needle, remove it, and do not insert it again. Because acupuncture needles of different shapes have their own purposes and because it should be used according to its therapeutic purposes, the key to acupuncture treatment is Qizhi which brings about the therapeutic effect of acupuncture” [6]. Bae reported that Qizhi is a synonym for Deqi, which refers to the acupuncture sensation in a recent Korean medical theory. However, the Qizhi mentioned in the Emperor’s Inner Canon referred to changes in a pulse wave, and did not relate to the sensation occurred by acupuncture manipulation. Therefore, according to the Emperor’s Inner Canon, observing changes in the pulse wave before and after acupuncture treatment can help predict the effectiveness of acupuncture in the patients [7]. However, objective evidence is required to prove this theory.

The pulse waves measured from Chon (Cun), Gwan (Guan), and Cheok (Chi), which are three adjacent regions along the radial artery used for pulse diagnosis in traditional Korean medicine (TKM), can reveal information on the balance of Qi and blood and on the homeostasis of the body and various organ systems [8]. Changes in the pulse wave and blood flow characteristics observed before and after acupuncture treatment can be used to objectively evaluate the efficacy of acupuncture. Hence, scientific observational studies are required to understand the physiological and the hemodynamic mechanisms of acupuncture.

In previous studies on the effects of acupuncture, Bouteuyrie et al [9] observed changes in the hemodynamic characteristics by using ultrasound and found significant differences in the blood vessel diameter between the sensitized patient group and the native patients group after applying sham acupuncture and real acupuncture. Sandberg et al [10] reported that the Deqi stimulation group showed significantly elevated skin and muscle blood flow compared to the control group after acupuncture at ST36. Takayama et al [11-12] confirmed that blood flow dropped during acupuncture stimulation and contradiestinctively rose after 180 seconds of acupuncture stimulation at LS3. Huang et al [13] found that the spectral energy of the pulse wave frequency in dyspepsia patients showed a significant increase after acupuncture stimulation. The effects of acupuncture are reported to be hemodynamic changes, such as those in the heart rate variability (HRV), high blood pressure effect, cerebral blood flow, and finger photoplethysmography (PPG) after acupuncture [14-17]. In Korea, the first such study was performed in 2012 that observed changes in the pulse rate of healthy subjects before and after acupuncture treatment using a pulse wave detector [18]. However, studies on acupuncture effects with pulse wave are still rare and fundamental aspects of acupuncture effects on pulse wave need to be investigated.

This study is a prospective, single-arm, exploratory clinical study to investigate the effects of acupuncture stimulation on the radial artery pressure pulse wave in healthy participants in their twenties. The results of this study will be used as a reference for further studies on the effectiveness of acupuncture on various diseases, symptoms, ages and genders, and for establishing scientific evidences and clinical usefulness of pulse diagnosis in TKM.

2. Methods and Analysis

2.1. Study design

We will conduct a prospective, single-arm, exploratory clinical study to observe the effect of acupuncture stimulation on the radial artery’s pressure-pulse wave in healthy young participants. Because, this clinical study will be performed using a single-arm evaluation, the method of randomization and blinding do not have to be taken into consideration.

The study will be carried out at the Korean Medicine Clinical Trial Center, Kyung Hee University’s Oriental Medical Center, Seoul, South Korea, from October 12, 2015, to October 11, 2016. Healthy men and women in their twenties will be recruited, with a target sample size of 25 participants, through advertisements on hospital websites and on bulletin boards. Those responding to the advertisements will be given full information about the study, including the method of acupuncture and the instrument measuring process. Those interested in participation will be guided through the informed consent process. After informed written consent has been obtained, the participants will be asked to answer screening questions and undergo electrocardiography and a pregnancy test to determine their eligibility. If eligible, a study researcher will administer the baseline questionnaire after which the interviewer will schedule the study procedure (Fig. 1). Participants will be categorized by age and sex. Vital signs and relevant personal medical histories will be recorded. Each participant will receive one session of acupuncture over the course of this study.

The inclusion criteria are as follows: (1) age 20 to 30 years; (2) ability to communicate about one’s physical condition and to fill out a questionnaire; (3) ability to participate voluntarily; (4) clearly understanding of the purpose and the characteristics of the clinical trial; (5) provision of informed written consent form.

Participants will be excluded from the study if one or more of the following criteria are fulfilled: (1) use within...
one month of medications, such as blood pressure depres-
sants, hypoglycemic agents, sleeping drugs, tranquilizers,
antithrombotic agents, antiplatelet agents, anticoagulants,
and hormone drugs that were prescribed for an internal
medicine, surgical, or psychiatric diagnosis; (2) preg-
nancy or lactation; (3) student of Korean Medicine College or
Korean medical doctor; (4) acupuncture treatment within
the last four months; (5) physical characteristics that pre-
clude assessments using the applicable pulse tonometric
device and the ultrasonogram machine; (6) a history of
heart disease or transplant of devices such as pacemakers;
(7) participation in other clinical trials within the last three
months; (8) communication disorder; (9) drug addiction
or alcohol abuse; (10) conditions where acupuncture
might not be safe, such as an allergy to metal; (11) refus-
al to participate in the trial or to provide informed written
consent form; (12) exclusion at the investigator’s discre-
tion.

The medical history of the participants, including their
current medication status, surgical history, the presence
of other diseases, and the results of electrocardiography
and pregnancy tests, will be recorded at baseline. Data
for lifestyle factors, including exercise, smoking, caffeine
intake, and alcohol consumption, will also be document-
ed as will hypertension, height, weight, and demographic
information. Licensed Korean medicine doctors (KMDs)
are specialists or residents of Korean medicine with more
than two years of clinical experience and six years of ed-
ucation. All participating KMDs will take part in an edu-
cational course to ensure that they strictly adhere to the
study protocol. All will be familiar with administering
the study treatments and will undergo intensive, customized
training to ensure that they have a full understanding of
the “acupuncture” procedure, including details such as the
acupuncture points and depths (Table 1).

2.2. Sample size

The sample size was determined based on the difference
in spectral energy from 13 to 50 Hz (SE13-50Hz) between be-
fore and after acupuncture stimulation, as described pre-
viously by Huang et al [13]. The characteristic of SE13-50Hz
is very similar to that of SE10-30Hz, measured by using our
tonomeric device, because the variation in the spectral
energy at frequencies above 10 Hz is only 0.9% of the total
variation [19]. The formula to estimate the sample size is
as follows:

\[
N = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 \sigma^2}{\bar{D}^2}
\]

where \(\alpha\) is a significance level (type I error), \(\beta\) is a type II
error, \(\bar{D}\) is the mean difference in the SE13-50Hz between be-
fore and after acupuncture stimulation, \(\sigma^2\) is the variance
of the difference, and \(z_{1-\alpha/2}\) or \(z_{1-\beta}\) is the \((1-\alpha/2)\)
or the \((1-\beta)\)th quartile of the standard normal distribu-
tion, respectively. We acquired \(\bar{D}\) and \(\sigma^2\) from the result
of Huang’s study [13]. The mean difference \(\bar{D}\), is \(-3.38\).
The variance of the change in SE13-50Hz was estimated based on
the following formula:

\[
\sigma^2 = \frac{n(n-1)}{2} \sigma^2
\]

where \(n\) is the sample size reported previously [20, 21],
and \(t_0\) is the \(t\)-value given by the degree of freedom and
reported \(P\)-value. The sample size used previously was
30, and the \(P\)-value for the difference in SE13-50Hz between
before and after acupuncture stimulation was reported as
0.0029. Thus the value of \(t_0\) is found to be \(-3.3526\) by using
the inverse function of the \(t\) distribution. Applying the de-
scribed information and the above formula gives a \(\hat{\delta}^2\) val-
ue of 32.3958. The estimated sample size of the study is 25,
with a 5% type I error, an 80% and a 5% drop rate.

2.3. Study procedures

All study procedures will be conducted at the Korean
Medicine Clinical Trial Center, Kyung Hee University’s
Oriental Medical Center, Seoul, South Korea.

The findings from the global physical activity question-
naire (GPAQ) and the credibility/expectancy question-
naire (CEQ) will be recorded before engagement of treat-
ment-measurement protocol. After the questionnaires
have been completed, the subjects will be given a 20-min-
ute resting session. After the rest, the spectral energy at 10
- 30 Hz (SE10-30Hz), the spectral energy at 0 - 10 Hz (SE0-10
Hz), the pulse power index (PPI), the pulse depth index
(PDI), and the pulse volume index (PVI) will be measured
on the left wrist of the subjects with by using an applica-
table pulse tonometric device (KION-PAS, Korea Institute
of Oriental Medicine, Daejeon, Korea) (Fig. 1). The HRV,
the mean area under the curve of the PPG signal (MAUCp-
g), the cardiac output (CO), and the respiration (RSP)
will be measured using a physiological data acquisition
system (Biopac module, Biopac MP150, Biopac Systems
Inc., USA) (Fig. 2) while the velocity of blood flow, and the
diameter and the depth of the blood vessel will be mea-
sured using an ultrasonogram machine (Voluson 730 Pro,
GE Healthcare Austria GmbH & Co OG, Austria) (Fig. 3)
on the right wrist the before, during, and after acupunc-
ture. The environmental temperature and moisture will be
maintained at 20 — 21°C and 40% — 45 %, respectively. All
measurements will be conducted 6 times in total (once 5
minutes before the needle insertion, 3 times in 20 minutes
during the needle retention, and twice during 14 minutes
after needle removal). After the measurements have been
completed, the participants will be given the acupuncture
sensation questionnaire (ASQ) (Table 2).

2.4. Interventions

The participants will receive acupuncture once at ST36
on both sides. A previous study found that acupuncture
stimulation at ST36 can improve various features of the
biomarkers of the cardiovascular system, such as the ba-
roflex function and various hemodynamic parameters
[22, 23], thereby indicating that acupuncture stimulation
at ST36 can affect cardiovascular parameters including
the pulse wave and the heart rate. The ST36 acupuncture
points will be localized according to the ‘WHO Standard
Acupuncture Point Location in the Western Pacific Region’
protocol (Fig. 4) [24]. KMDs will perform the interventions
using disposable acupuncture needles (Seirin Co. Ltd.,
Shizuoka, Japan) which are stainless steels of the size of
0.16 mm × 40.0 mm. The Deqi sensation will be induced by
bidirectional rotation of the needles by 90° around an axis
### Table 1  STRICTA (Standards for Reporting Interventions in Clinical Trials of Acupuncture)

<table>
<thead>
<tr>
<th>Item</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Acupuncture rationale</strong></td>
<td>(a) Style of acupuncture</td>
</tr>
<tr>
<td></td>
<td>(b) Reasoning for treatment provided (based on historical context, literature sources and consensus methods)</td>
</tr>
<tr>
<td></td>
<td>(c) Extent to which treatment was varied</td>
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<tr>
<td><strong>2. Details of needling</strong></td>
<td>(a) Number of needle insertions per patient per session</td>
</tr>
<tr>
<td></td>
<td>(b) Names (or location if no standard name) of points used (uni/bilateral)</td>
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<tr>
<td></td>
<td>(c) Depth of insertion</td>
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<td></td>
<td>(d) Response sought (for example, de qi or muscle twitch response)</td>
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<tr>
<td></td>
<td>(e) Needle stimulation (for example, manual, electrical)</td>
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<tr>
<td></td>
<td>(f) Needle-retention time</td>
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<td></td>
<td>(g) Needle type (diameter, length and manufacturer or material)</td>
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<tr>
<td><strong>3. Treatment regimen</strong></td>
<td>(a) Number of treatment sessions</td>
</tr>
<tr>
<td></td>
<td>(b) Frequency and duration of treatment sessions</td>
</tr>
<tr>
<td><strong>4. Other components of treatment</strong></td>
<td>(a) Details of other interventions administered to the acupuncture group</td>
</tr>
<tr>
<td></td>
<td>(b) Setting and context of treatment, including instructions to practitioners and information and explanations to patients</td>
</tr>
<tr>
<td><strong>5. Practitioner background</strong></td>
<td>(a) Description of participating acupuncturists</td>
</tr>
<tr>
<td><strong>6. Control or comparator interventions</strong></td>
<td>(a) Rationale for the control or comparator in the context of the research question with sources that justify this choice</td>
</tr>
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<td></td>
<td>(b) Precise description of the control or comparator if sham acupuncture</td>
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</tbody>
</table>
Table 2  Schedule for study procedures

<table>
<thead>
<tr>
<th>Visit</th>
<th>Day 1</th>
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<tbody>
<tr>
<td></td>
<td>Before Measurement</td>
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<tr>
<td></td>
<td>Visit 1</td>
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<tr>
<td>Questionnaire</td>
<td></td>
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<tr>
<td>GPAQ</td>
<td>•</td>
</tr>
<tr>
<td>CEQ</td>
<td>•</td>
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<tr>
<td>ASQ</td>
<td>•</td>
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<tr>
<td>Applicable pulse tonometric device (KIOM-PAS)</td>
<td></td>
</tr>
<tr>
<td>SE_{10-30Hz}</td>
<td>•</td>
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<tr>
<td>SE_{0-10Hz}</td>
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<tr>
<td>PPI</td>
<td>•</td>
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<tr>
<td>PDI</td>
<td>•</td>
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<tr>
<td>PVI</td>
<td>•</td>
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<tr>
<td>Physiological data acquisition system (Biopac module)</td>
<td></td>
</tr>
<tr>
<td>HRV</td>
<td>•</td>
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<tr>
<td>RSP</td>
<td>•</td>
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<tr>
<td>MAUC ppg</td>
<td>•</td>
</tr>
<tr>
<td>CO</td>
<td>•</td>
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<tr>
<td>Ultrasonogram machine</td>
<td></td>
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<tr>
<td>Velocity of blood flow</td>
<td>•</td>
</tr>
<tr>
<td>Diameter of blood vessel</td>
<td>•</td>
</tr>
<tr>
<td>Depth of blood vessel</td>
<td>•</td>
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</tbody>
</table>

GPAQ, global physical activity questionnaire; CEQ, credibility/expectancy questionnaire; ASQ, acupuncture sensation questionnaire; SE_{10-30Hz}, spectral energy at 10 - 30 Hz; SE_{0-10Hz}, spectral energy at 0 - 10 Hz; PPI, pulse power index; PDI, pulse depth index; PVI, pulse volume index; HRV, heart rate variability; RSP, respiration; MAUCppg, mean area under curve of photoplethysmogram; CO, cardiac output.

perpendicular to the surface of the skin in 18 seconds, after which the needles will stay in place for 20 minutes before removal (Table 2). Any changes in medical history or vital signs and any reports of adverse events will be recorded.

2.5. Devices and measurement technique

The radial pulse signal will be measured on the left wrist of the subjects with a applicable pulse tonometric device (KIOM-PAS, Korea Institute of Oriental Medicine, Daejeon, Korea) (Fig. 1). This device consists of a main body with an arm holder and a sensing body attached to a mobile actuator. A pulse detection sensor, which is composed of 7 piezoresistive unit sensors within 9 × 9 mm², is located at the actuator tip. An example of measuring a radial pulse using the KIOM-PAS is illustrated in Fig. 1. In this study, the technician will measure the pulse signals at the Gwan (Guan) location [25].

Other Physiological data related to the HRV, RSP rate, PPG and CO will be obtained using an integrated Biopac module a (MP150, Biopac Systems Inc., USA) (Fig. 2). More specifically, the HRV signal will be obtained using an electrocardiogram module (ECG100C), the RSP signal will be obtained using a thermistor (SKT100C), the mean area under the curve of PPG (MAUCppg) signal will be obtained using a PPG module (PPG100C), and the CO signal will be obtained by an impedance cardiography module (NICO100C).

The blood flow and the diameter and depth of the artery will be obtained on the right wrist by an ultrasonogram machine (Volusion 730 Pro, GE Medical, USA) (Fig. 3). The arterial diameter and the depth will be measured in the B mode and the blood flow velocity will be measured in the
2.6. Outcome measures

The primary outcome measure will be the SE_{10-30Hz}. From the radial pulse signal obtained for 60 seconds under constant hold-down pressure at which pulse amplitude is maintained its maximum, power spectral density (PSD) will be calculated. The integrated value of the high frequency regime of PSD above 10 Hz will be defined as the spectral energy of the range of 10 - 30 Hz. The first six secondary outcomes will be as follows: (1) the SE_{0-10Hz} for which the spectral energy in the range of 0 - 10 Hz will be calculated from the PSD; (2) PPI is defined as the highest pulse amplitude of the pulse signal obtained by a continuously evolved tonometric mechanism [26]; (3) PDI is defined as the sensor displacement between the contact point of the sensor to the skin and the point at which the PPI is obtained (Fig. 5). (4) The pulse volume index (PVI) is defined as the depth window between the 30% point of the PPI and the PPI (Fig. 5). (5) HRV will be calculated by the ECG signal. More specifically, we calculate the R-R interval (NN), the standard deviation of the NN (SDNN), the root mean squared standard deviation (RMSSD), low and high frequency spectral power density (LF, HF) etc. [27]. (6) RSP For which a fast-response surface temperature thermistor will be attached to the philtrum region of participants to measure temperature changes in inspirations and exhalations through the nose. RSP rates will be calculated using...
Four more secondary outcomes are as follows:

(7) **MAUCppg** can be used to estimate the state of heart beat activity by using the optical characteristics of in-vivo tissues in which changes in the blood flow rates and the blood vessel volumes occur due to the dilatation and the contraction of the heart. The mean waveform of the PPG wave will be measured from the starting to the ending points, as will the area under the mean waveform curve.

(8) **CO** is the multiplication of the stroke volume and the heart rate and will be calculated using a standard formula with an impedance cardiology signal [28].

(9) The velocity of blood flow can be determined by using the Doppler effect of ultrasonic waves. Changes in the frequencies of ultrasonic waves emitted to blood vessels with flow rates and returned after being reflected will be sensed to estimate the maximum blood flow velocity and the mean blood flow velocity in the blood vessels.

(10) The diameter and depth of the radial artery will be determined. Ultrasonic waves emitted from an ultrasonogram machine will be used, and the time for the ultrasonic waves to return after being reflected in the human body will be calculated. The signals that return after being reflected will be expressed as the brightness of the images in the B mode of an ultrasonogram machine, and the pixels in the images in the B mode include distance information. Therefore, distances between two points in the images of ultrasonogram machine will be measured using information on the distance per pixel in the images of the ultrasonogram machine and will be used to estimate blood vessel diameters and depths.

The last three secondary outcomes are the results from the (11) GPAQ, (12) CEQ, and (13) ASQ.

The GPAQ was developed by the WHO for physical activity surveillance. It uses 16 questions (P1 — P16) to collect information on physical activity participation in three settings (or domains), as well as sedentary behavior. The domains are “activity at work,” “travel to and from places,” and “recreational activities” [29]. The GPAQ assessment will be performed before acupuncture.

The CEQ has recently been developed as measure of treatment credibility and expectancy. The questionnaire consists of one question that reflects the expectancy of acupuncture. Each participant will answer this question with a rating of 1-9 [30]. The CEQ will be assessed before...
acupuncture.

The ASQ was developed at the Department of Applied Korean Medicine, Kyung Hee University, Seoul, Korea, to measure acupuncture sensation (Deqi). The analysis of the interview transcripts will provide three categories: sensations during the insertion of the acupuncture needle (SIA), sensations during the manipulation of the acupuncture needle (SMA), and sensations during the time the acupuncture needle is in the skin (SM). In in-depth interviews, 33 items related to SIA, 59 to SMA, and 29 to SM will be addressed [31]. The ASQ will be assessed after acupuncture stimulation.

2.7. Statistical analysis

Statistical analysis will be performed using STATA version 13.1 (StataCorp, College Station, TX, USA) and R statistical software in the current version. The number of total participants actually enrolled and eligible participants will be described by using a flow chart. The significance level for all tests will be set to 0.05 (two-sided). Baseline characteristics of participants will be described with the available data. Categorical measures will be represented as the number of participants and percentages, and continuous variables will be summarized as means and standard deviations for normal data and as medians and interquartile ranges (25th and 75th quartiles) in the case of skewed data. The Shapiro-Wilk test will be used to verify the normality of quantitative measures. Analyses of the primary and the secondary outcomes will be conducted on a full analysis set (FAS) on the basis of the intention-to-treat (ITT) principle and on per protocol subsamples for the purpose of sensitivity analyses. The last observation carried forward (LOCF) method will be used to impute missing data.

The primary outcome is the change in $SE_{10-30Hz}$ at six time points (before acupuncture stimulation, immediately upon needle insertion, during stimulation measured after 7 and 14 minutes of needle insertion, immediately after removal of acupuncture needle, and 7 minutes later) will be investigated using repeated measures analysis of variance (RMANOVA) as a secondary analysis. The model of RMANOVA will include covariates (sex, age, and ASQ scale effects) and interactions between sex and time effects. The model will be modified by excluding an interaction term if it is not significant. The ANOVA table for the model will be provided, as will the least-squares mean, standard error, and 95% confidence interval at each time point. The difference in time relative to the baseline (before acupuncture) will be examined using Dunnett’s test.

2.8. Data handling and adverse events

Investigators will enter the information required by the protocol on case report forms (CRFs). Non-obvious errors or omissions will be entered on data query forms, which will be returned to the investigational site for resolution. The data from all centers will be gathered and summarized with respect to demographic baseline characteristics, effectiveness, and safety observations.

Adverse events are unexpected signs, symptoms, or diseases that occur during the clinical trial. These include not only acupuncture treatment-induced side effects but also all other abnormal findings caused for any reason. All unexpected responses related to acupuncture treatment and measurement will be reported to investigators by the participants and will be examined by the investigators. Local, general, and psychological adverse events are possible as a result of acupuncture treatments. Adverse events will be evaluated by investigators and categorized as mild, moderate, or severe according to the WHO’s Draft Guidelines for Adverse Event Reporting [32] and Spilker’s criteria [33]. If serious adverse events (SAE) occur, they will be reported to the IRB and to monitors; experimental treatments will be stopped immediately and appropriate treatments will be offered. During every visit, adverse events will be measured.
3. Discussion

The outcome measures for this study are the changes in radial artery pressure pulse, blood vessel properties, and physiological data obtained before, during, and after acupuncture at ST36. The changes in the artery pressure pulse, properties of blood vessels, and physiological data, as measured by using the SE10-30Hz, SE0-10Hz, PPI, PDI, MAUCpg, HRV, CO, RSP, blood vessel depth, blood vessel diameter, and blood velocity, before, during, and after acupuncture at ST36 will be compared. The primary comparisons will be before acupuncture versus during acupuncture versus after acupuncture. In addition, we will record the GPAQ, CEQ, and ASQ findings.

The hypotheses to be tested are as follows: 1) the radial artery’s pressure pulse wave will differ significantly between the before, during, and after acupuncture assessments; 2) the hemodynamic parameters will differ significantly between the before, during, and after acupuncture; 3) and the radial artery’s pressure-pulse wave and the hemodynamic parameters will differ significantly between the before, during, and after acupuncture assessments according to the sensitivity of the Deqi sensation.

The results from this study will determine the efficacy and the safety of stimulation of the radial artery’s pressure pulse wave in healthy individuals in their twenties. These results can provide information regarding the physiological and hemodynamic mechanisms underlying acupuncture, as well as clinical evidence for the influence of acupuncture on the radial artery pressure pulse wave; they will also clarify whether the radial artery’s pressure pulse wave can be used to objectively evaluate the efficacy of acupuncture.

The results of this trial will be available in January 2017. This study involve healthy young participants. We expect this study to provide the clinical basis and the information that are required to assess the feasibility of a future large scale trial in patients. Blinding and randomization will not be done in this trial, because this clinical study will be performed using a single-arm evaluation, so blinding the participants and the acupuncturists is not possible.

4. Ethics, dissemination, and status

The study protocol was approved by the Institutional Review Board of Kyung Hee University’s Oriental Medical Center, Seoul, Korea (KOMCIRB-150818-HR-030) and was registered with the Clinical Research Information Service (CRIS) at the Korea National Institute of Health (NIH), Republic of Korea (KCT0001663), which is a registry in the WHO’s Registry Network [34]. Written informed consent will be obtained from all participants in accordance with the Declaration of Helsinki. The study findings will be published in peer-reviewed journals and presented at national and international conferences. The trial is currently in the recruitment phase. Participant recruitment started in October 2015 and is expected to end in October 2016.

5. Authors’ contributions

JUK conceived the idea for the study and led protocol development. BCK, THK, JHB, HJC, JYS and JHL assisted with the study concept, study design, clinical interpretation, and manuscript drafting and finalization. THK will recruit the participants and conduct the trial. BCK planned the statistical analysis. JHL helped to conceive and design the study and critically reviewed the trial. JUK provided overall supervision as the primary mentor and led the team in manuscript preparation. JYS and BCK wrote the manuscript and approved the final version for publication. All authors commented upon drafts of the manuscript and approved the final version of the manuscript.

6. Registration details

This protocol was registered with the CRIS at the NIH, Republic of Korea (KCT0001663), which is a registry in the WHO’s Registry Network [19/34].

Acknowledgments

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Conflict of interest

The authors declare that there are no conflict of interest.

ORCID


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