Assessment of Post-surgical improvement in Obstructive Sleep Apnea Patients after imaging of Upper Respiratory Airway using Cone Beam Computed Tomography (CBCT) and Drug-Induced Sleep Endoscopy (DISE) versus Drug-Induced Sleep Endoscopy Only: A Validity Study

Registered at www.clinicaltrials.gov. ID: OCS05051989

Protocol submitted to
Faculty of Dentistry, Cairo University
for partial fulfilment of the requirements for the Ph.D. Degree in Oral and Maxillofacial Radiology,
Faculty of Dentistry, Cairo University

By

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Supervisors' signature

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I- Study Protocol:

A) Study design and setting

1. Study design

In this validity two-arm study, a total of (70) patients will be included; all are diagnosed with OSA and will undergo surgical treatment after appropriate planning. Patients will be classified into two equal groups (with allocation ratio 1:1). Patients of the study group will be examined after scanning with CBCT at both ends of expiration and inspiration and DISE. Control group patients will be examined by DISE only.

These (70) patients will be selected by the ENT specialist according to the following;

- A multidisciplinary approach will be performed to diagnose OSA patients who are indicated for surgery. Firstly, a comprehensive assessment of patients' history will be performed; including evaluation of all risk factors and complete sleep history ***(Epstein et al. 2009***).
- Epworth Sleepiness Scale (ESS) which consists of eight section questionnaire that defines the frequency of an individual to fall asleep during regular daily activities will be obtained from the patients (***Johns 1992, Sharkey et al. 2013***)**.**
- Afterward, a proper physical examination will be performed including a thorough clinical examination of the oropharynx, nasopharynx, and hypopharynx to evaluate any anatomical abnormalities as impotency of the nasal airway, elongated soft palate or uvula, enlarged lingual tonsils, and any other pathological conditions of tongue, palate, and tonsils.
- Then, Polysomnography (PSG) (sleep study) will be performed to allow proper evaluation of normal and abnormal physiological sleep episodes. Apnea/Hypopnea Index (AHI) will be reported to detect the severity of OSA and patients were classified into mild (AHI = 5-14 / hour), moderate (AHI = 15-30 / hour) and severe (AHI >30 / hour) (***Maspero et al. 2015***)**.**
- All patients in both groups will undergo upper airway surgery, DISE will be performed by the same ENT surgeon to detect the level of collapse in the upper airway which will be assessed by LwPTL and VOTE classifications, emphasizing on the primary structures contributing at upper airway collapse, either alone or in combination: the larynx, palate, tongue and pharyngeal lateral walls.
- Study group participants only will be scanned by CBCT twice; once at the end of inspiration and the other at the end of expiration while they are gently holding their breath for as long as possible. ***(Woodson 2003)***
- In the study group, surgical procedures decision will be taken after appropriate assessment to sites of collapse in CBCT views at both ends of expiration and inspiration vies in combination to DISE.
- Finally, strict post-operative instructions will be given to patients of both groups.

2. Settings

This study will be carried out on patients attending outpatient clinics in the ENT department, Faculty of Medicine, Mansoura University, Egypt. CBCT scans of surgical candidates of OSA patients will be included

according to the proposed eligibility criteria.

B) Participants

1. Eligibility criteria and selection methods

Inclusion Criteria:

- Patients' age is more than 18 years old.
- Patients are indicated for upper respiratory airway surgery based on adequate history taking, proper clinical examination, and sleep study.
- Patients refusing non-surgical treatment procedures as Continuous Positive Airway Pressure (CPAP) treatment.
- Systemically medically free patients.

Exclusion Criteria:

- Patients who are refusing the surgical approach as a treatment option.
- Patients who have undergone previous surgeries in the upper respiratory airway.
- Pregnant women.
- Patients who didn't follow post-operative instructions.
- Patients who are not able to come for the follow-up appointments.

Follow up:

- Patients who strictly follow post-operative instructions will perform another sleep study after 3 months from the day of the surgery.
- Percentage of AHI reduction will be calculated which in turn indicates post-surgical improvement.

2. Matching criteria and allocation ratio

The patients will be randomly allocated to the intervention groups using computer-generated random numbers that will be performed by the main investigator (Marco Isaac). The patients will be allocated in a ratio of 1:1 (35 patients in each group).

The two groups will be equally clinically examined before surgical procedures. Then the decision of which group will be scanned with CBCT and which won't will be taken according to the randomized numbers placed in opaque sealed envelopes. The number will be picked by the main investigator (Marco Isaac).

The main investigator will be responsible for the generation of allocation sequence and will assign the patients to the 2 intervention groups. The main investigator will also be responsible for patient enrolment.

C) Variables

1. Details about variables

- Mean AHI reduction percentage.
- Level of Collapse of the upper respiratory airway.
- The volume of the upper respiratory airway.

2. Data sources and management

- The level of the collapse of the upper respiratory airway will be determined by an expert ENT surgeon with DISE.
- Radiographic assessment will be performed using the iCAT FLX V17-Series CBCT machine (Imaging Science International, ISI, PA, USA). Quick scan imaging protocol of 16cm x 13cm Field Of View (FOV) (120 KV, 5 mA, 2 sec) and 0.3 mm voxel size.
- Participants are required to wear a protective lead apron during scanning. The position of the X-ray tube will be adjusted to minimize the extent of scanning and to ensure the lowest radiation dose as much as possible. To prevent motion artifacts, participants will be instructed not to move their head, body, tongue, and jaws during scanning.
- Raw DICOM data from CBCT scanning will be checked to evaluate whether there were any motion artifacts in images at coronal, horizontal, and sagittal planes.
- CBCT scans at both ends of inspiration and expiration will be analyzed using Invivo5 software.
- For the second outcome, CBCT images will be interpreted by three oral and maxillofacial radiologists independently; blinded from demographic data of the patients, DISE findings, and the results of each other.
- Each radiologist will evaluate the CBCT images for assessment of the level of collapse and assessment of the secondary outcomes. One radiologist will assess all the outcomes twice with more than 1month interval. Intra-observer and inter-observer variability of CBCT findings will be evaluated.

3. Addressing potential sources of bias

No source of bias. CBCT images will be interpreted by three oral and maxillofacial radiologists independently blinded from demographic data of the patients, DISE findings, and the results of each other.

D) Study size

1. Study size

This study aims to assess surgical improvement in OSA patients after imaging of upper Respiratory Airway using CBCT and DISE using mean AHI reduction percentage. According to the results of ***(Pang et al. 2020),*** the mean of AHI reduction percentage and the minimal clinically important difference estimated by the expert was 21.6. By adopting an alpha (α) level of 0.05 (5%) and a power of 80%, the predicted sample size is 35 per group with a total of 70. To compensate for losses during follow up, the sample will be

increased by 20% to be 84 participants in total. Sample size calculation was achieved using PS: Power and Sample Size Calculation software Version 3.1.2 (Vanderbilt University, Nashville, Tennessee, USA).

E) Quantitative variables

1. Handling of quantitative variables in the analyses

The volume of the upper respiratory airway will be determined and correlated with its level of collapse.

F) Statistical methods

1. Statistical methods

Data will be analyzed using SPSS (statistical package for social sciences) version 22. Qualitative data will be presented as number and percent, Quantitative data will be tested for normality by the Kolmogrov-Smirnov test then described as mean and standard deviation for normally distributed data and median and range for non-normally distributed. The appropriate statistical test will be applied according to the data type with the following suggested tests: Chi-Square for the categorical variable. Student t-test and Mann Whitney U test for continuous variables.

II. Ethics and dissemination:

a. Research ethics approval

The study protocol will be submitted to the Ethics commute in the Faculty of Dentistry, Cairo University for approval.

b. Protocol amendments

Any amendments in the protocol will be reported to the main and co-supervisors.

c. Informed consent

After discussing the treatment plan with the patient and educating the patient with all the data needed, an arabic consent form will be signed by the willing participants.

d. Confidentiality

- All study-related information will be stored securely.
- All reports, data, scans, and administrative forms will be identified by a coded ID (identification) number only to maintain participant confidentiality.
- All personal data that contain names or other identifiers including age, sex, identification number, address, phone number, work address, and any other information will be stored separately from the study records and identified by a code number.

e. Declaration of interest

There is no conflict of interest.

f. Access to data

Investigator, Co-supervisors, and main supervisor will have access to the final trial data set .

g. Dissemination policy

The Investigator will communicate his results with other participants and healthcare providers through the publication of the protocol and the research final results and recommendations. This will be done through publication websites and journals concerned with Oral and Maxillofacial Radiology specialty, For Sharing the recommended clinical application obtained from the final results of the research.

III- Appendix:

1- Epworth Sleepiness Scale (ESS):

Epworth Sleepiness Scale

Name: _____ Today's date: _____

Your age (Yrs): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

0 = would **never** doze
1 = **slight chance** of dozing
2 = **moderate chance** of dozing
3 = **high chance** of dozing

It is important that you answer each question as best you can.

Situation	**Chance of Dozing (0-3)**
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	

THANK YOU FOR YOUR COOPERATION

2- Informed Consent:

Faculty of Oral & Dental Medicine

Cairo University

Research Ethics Committee

Application Form

Human Subjects

Kindly fulfill the following:

Research title: Assessment of Post-surgical improvement in Obstructive Sleep Apnea Patients after imaging of Upper Respiratory Airway using Cone Beam Computed Tomography (CBCT) and Drug-Induced Sleep Endoscopy (DISE) versus Drug-Induced Sleep Endoscopy Only: A Validity Study

Master [ ] ***PHD/D [✓]*** ***others [ ]***

Full name of the researcher(s): Marco Emad Shawky Isaac

Study: A Validity Study

Objective of the research: Post-surgical Improvement, determining level of Collapse of the upper respiratory airway, and the volume of the upper respiratory airway.

- ***Steps in short and Number of visits & follow up period:***

In this validity two-arm study, all patients are diagnosed with OSA and will undergo surgical treatment after appropriate planning. Patients will be classified into two equal groups with allocation ratio (1:1). Patients of the study group will be examined after scanning with CBCT at both ends of expiration and inspiration and DISE. Control group patients will be examined by DISE only. After discussing the treatment plan with the patient and educating the patient with all the data needed, an arabic consent form will be signed by the willing participants.

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- In the study group, surgical procedures decision will be taken after appropriate assessment to sites of collapse in CBCT views at both ends of expiration and inspiration vies in combination to DISE.
- Finally, strict post-operative instructions will be given to patients of both group and a 3 months follow up would be done.

Direct benefit of the research to the human volunteer:

Patient's full knowledge of the research steps: Reading [✓] Oral explanation [✓] Other []

1. I have carefully reviewed and understood the purpose of conducting the research and the nature of this study, and I understand what is necessary to accomplish these procedures.

2. The researcher has informed me of the possible therapeutic alternatives for this research.

3. The researcher has informed me of all the possible risks of this research and how to deal with it.

4. I agree to the imaging, recording, and all types of radiology to be performed in this study, on condition of anonymity.

5. I have made an accurate report on my health history and informed the doctor of all kinds of health reactions or unusual allergies to medicines, food, insect bites, anesthetics, dust or any reactions that have occurred to me from any other substances, abnormal bleeding or any other related conditions. For my health

6. I acknowledge that I am not involved in any other research from the beginning of this research until the end of this research and that I will inform the researcher physician if I enter any other research throughout the period of this research.

7. I undertake to return the medical devices (instruments) used in the research in case of discontinuation or when the research is completed.

After knowing the available information related to the research, the volunteer or the person in charge will be able to choose freely whether or not to subscribe. In case of approval, kindly fill out the data shown. The volunteer has the right to withdraw from the research without giving reasons.

The physician in charge of the research undertakes to keep the information of the volunteer person confidential by participating in the research, stating the methods used, such as replacing names with code numbers or hiding facial features when photographing (etc.).

Signature: Marco Emad Shawky Isaac

***Date:* 22/01/2021**