THE CLINICAL ACADEMIA

We are indexed in
ASEAN citation index (ACI)

VOLUME 46 ISSUE 2
April-JUNE

WWW.KKH.GO.TH/TCA
PRINTED IN THE USA
ISSN:2465-4027

the clinical academia

Aim and Scope

Our journal is an opened access international journal devoted to peer-reviewed contributions dealing with clinical medicine and medical education from experimental to clinical aspects. Our journal publishes only high quality research, review and other types of original articles, technical and clinical reports every two months. Reviews of various global and Asian aspects will be solicited. Innovation or epidemiological aspects as well as health system research will be addressed. Rigorous systematic review and neglected tropical diseases are our priority

We.....

- are in ASEAN Citation Index (ACI)
- are in Group I of Thai Journal Citation Index (TCI)
- are open access peer-reviewed journal
- 100% check for plagiarism using "turnitin"
- are a registered member of Committee on Publication Ethics (COPE)
- publish only English articles
- publish every 2 months
- request all submitted manuscripts to be provided to with documents regarding ethical approval
- request all original database to be submitted with every manuscript
- request all submitted randomized controlled trial study to be presented with Clinical Trial Registry Number

the clinical academia

OWNED BY
The Medical Advancement Foundation

Under the Patronage of
Khon Kaen Medical Education Center
Khon Kaen Hospital
Thai Ministry of Public Health

THE ADVISORY BOARD
Chanchai Janworachaikul, M.D.
Sirijit Vasanawathana, M.D.
Prasit Hanpinitsak, M.D.
Surachai Saranrittichai, M.D.

EDITORIAL BOARD
Professor Tomono Kazunori, Osaka University Hospital, Japan
Associate Professor Hiroshi Nishigori, Kyoto University, Japan
Assistant Professor Lynette J Menezes, University of South Florida, USA
Professor Charurat Somboonwit, University of South Florida, USA
Professor.Nathorn Chaiyakunapruk, Pharm.D., Ph.D., Monash University, Malaysia
Kanokwan Sriruksa,M.D., Medical Education Center, Khon Kaen Hospital, Khon Kaen, Thailand

MANAGING EDITOR
Benjaporn Silaruks, B.Pharm., Ph.D. Khon Kaen Hospital, Khon Kaen, Thailand

EDITOR-IN-CHIEF
Thammasorn Jeeraaumponwat, M.D., Ph.D.

LAYOUT EDITOR
Ketsaraphon Chanaket, B.A.
Chanchanason Samrongphon, B.A.

Material printed in the *Journal* is covered by copyright. No copyright is claimed to any work of the Thai government. No part of this publication may be reproduced without written permission. The *Journal* does not hold itself responsible for statements made by any contributors. Statements or opinions express in the *Journal* reflect the views of the author(s) and do not represent the official policy of the *Journal* unless stated.

submission

Please visit

www.kkh.go.th/tca

For online submission

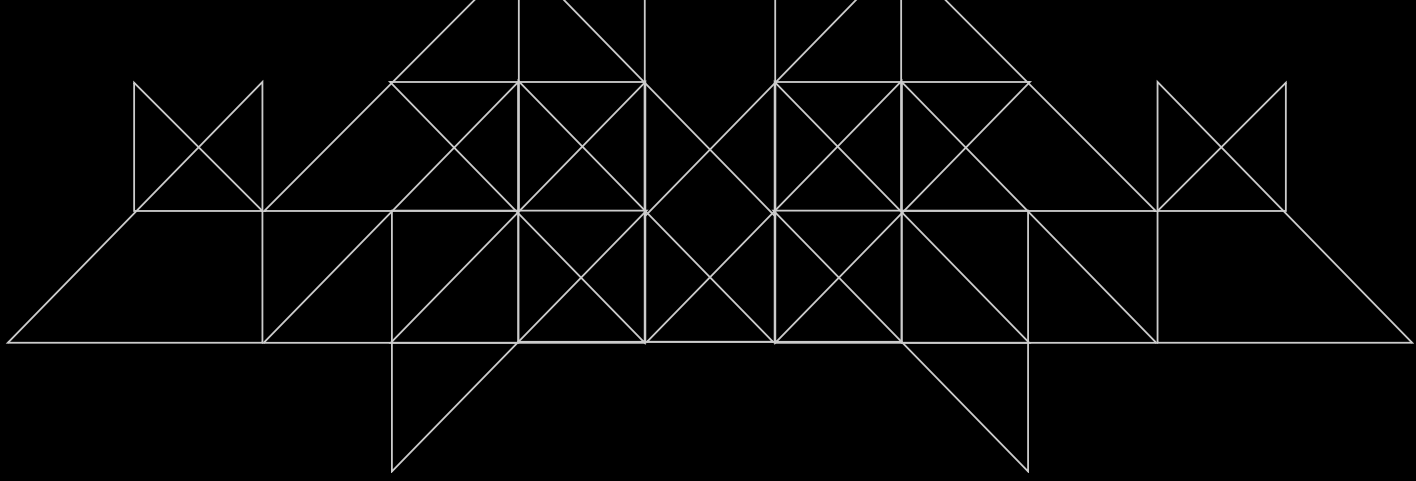
Our issues of each volume will be published online
IN
March, June, September, and December

reviewing process

All accepted articles are classified into two main categories;
"***standard submission***" with the approximated processing time of 3-4 months and "***expression submission***" with the approximated processing time of 1-2 months. For the latter category, the author must submit as standard submission with notifying our journal for express submission.

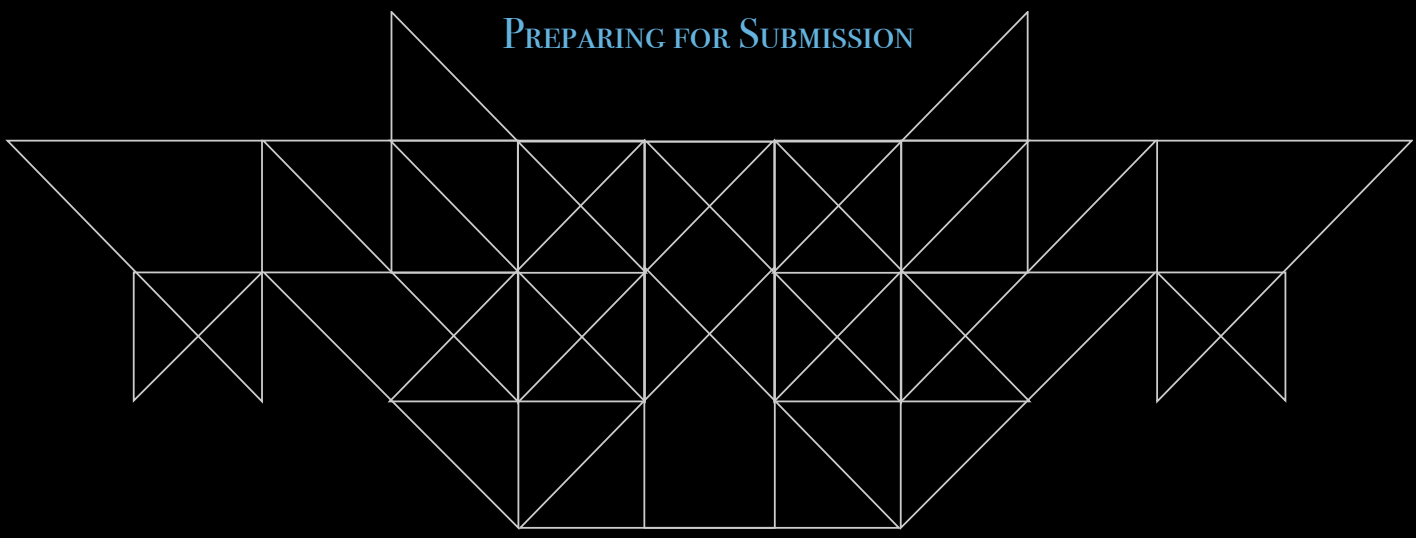
Email: theclinicalacademia@gmail.com
Telephone: (+66) 87 990 1035

Contents



International Committee of Medical Journal Editors (ICMJE)

Recommendation for Preparing for Submission



1. General Principles

The text of articles reporting original research is usually divided into Introduction, Methods, Results, and Discussion sections. This so-called "IMRAD" structure is not an arbitrary publication format but a reflection of the process of scientific discovery. Articles often need subheadings within these sections to further organize their content. Other types of articles, such as meta-analyses, may require different formats, while case reports, narrative reviews, and editorials may have less structured or unstructured formats.

Electronic formats have created opportunities for adding details or sections, layering information, cross-linking, or extracting portions of articles in electronic versions. Supplementary electronic-only material should be submitted and sent for peer review simultaneously with the primary manuscript.

2. Reporting Guidelines

Reporting guidelines have been developed for different study designs; examples include CONSORT for randomized trials, STROBE for observational studies, PRISMA for systematic reviews and meta-analyses, and STARD for studies of diagnostic accuracy. Journals are encouraged to ask authors to follow these guidelines because they help authors describe the study in enough detail for it to be evaluated by editors, reviewers, readers, and other researchers evaluating the medical literature. Authors of review manuscripts are encouraged to describe the methods used for locating, select¬ing, extracting, and synthesizing data; this is mandatory for systematic reviews. Good sources for reporting guidelines are the EQUATOR Network and the NLM's Research Reporting Guidelines and Initiatives.

3. Manuscript Sections

The following are general requirements for reporting within sections of all study designs and manuscript formats.

a. Title Page

General information about an article and its authors is presented on a manuscript title page and usually includes the article title, author information, any disclaimers, sources of support, word count, and sometimes the number of tables and figures.

Article title. The title provides a distilled description of the complete article and should include information that, along with the Abstract, will make electronic retrieval of the article sensitive and specific. Reporting guidelines recommend and some journals require that information about the study design be a part of the title (particularly important for randomized trials and systematic reviews and meta-analyses). Some journals require a short title, usually no more than 40 characters (including letters and spaces) on the title page or as a separate entry in an electronic submission system. Electronic submission systems may restrict the number of characters in the title. Author information: Each author's highest academic degrees should be listed, although some journals do not publish these. The name of the department(s) and institution(s) or organizations where the work should be attributed should be specified. Most electronic submission systems require that authors provide full contact information, including land mail and e-mail addresses, but the title page should list the corresponding authors' telephone and fax numbers and e-mail address. ICMJE encourages the listing of authors' Open Researcher and Contributor Identification (ORCID).

Disclaimers. An example of a disclaimer is an author's statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

Source(s) of support. These include grants, equipment, drugs, and/or other support that facilitated conduct of the work described in the article or the writing of the article itself.

Word count. A word count for the paper's text, excluding its abstract, acknowledgments, tables, figure legends, and references, allows editors and reviewers to assess whether the information contained in the paper warrants the paper's length, and whether the submitted manuscript fits within the journal's formats and word limits. A separate word count for the Abstract is useful for the same reason.

Number of figures and tables. Some submission systems require specification of the number of Figures and Tables before uploading the relevant files. These numbers allow editorial staff and reviewers to confirm that all figures and tables were actually included with the manuscript and, because Tables and Figures occupy space, to assess if the information provided by the figures and tables warrants the paper's length and if the manuscript fits within the journal's space limits.

Conflict of Interest declaration. Conflict of interest information for each author needs to be part of the manuscript; each journal should develop standards with regard to the form the information should take and where it will be posted. The ICMJE has developed a uniform conflict of interest disclosure form for use by ICMJE member journals and the ICMJE encourages other journals to adopt it. Despite availability of the form, editors may require conflict of interest declarations on the manuscript title page to save the work of collecting forms from each author prior to making an editorial decision or to save reviewers and readers the work of reading each author's form.

b. Abstract

Original research, systematic reviews, and meta-analyses require structured abstracts. The abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations, note important limitations, and not over-interpret findings. Clinical trial abstracts should include items that the CONSORT group has identified as essential. Funding sources should be listed separately after the Abstract to facilitate proper display and indexing for search retrieval by MEDLINE.

Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to ensure that they accurately reflect the content of the article. Unfortunately, information in abstracts often differs from that in the text. Authors and editors should work in the process of revision and review to ensure that information is consistent in both places. The format required for structured abstracts differs from journal to journal, and some journals use more than one format; authors need to prepare their abstracts in the format specified by the journal they have chosen.

The ICMJE recommends that journals publish the clinical trial registration number at the end of the abstract. The ICMJE also recommends that, when a

registration number is available, authors list that number the first time they use a trial acronym to refer to the trial they are reporting or to other trials that they mention in the manuscript. If the data have been deposited in a public repository, authors should state at the end of the abstract the data set name, repository name and number.

c. Introduction

Provide a context or background for the study (that is, the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

d. Methods

The guiding principle of the Methods section should be clarity about how and why a study was done in a particular way. Methods section should aim to be sufficiently detailed such that others with access to the data would be able to reproduce the results. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section. If an organization was paid or otherwise contracted to help conduct the research (examples include data collection and management), then this should be detailed in the methods.

The Methods section should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included.

i. Selection and Description of Participants

Clearly describe the selection of observational or experimental participants (healthy individuals or patients, including controls), including eligibility and exclusion criteria and a description of the source population. Because the relevance of such variables as age, sex, or ethnicity is not always known at the time of study design, researchers should aim for inclusion of representative populations into all study types and at a minimum provide descriptive data for these and other relevant demographic variables. If the study was done involving an exclusive population, for example in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer)." Authors should define how they measured race or ethnicity and justify their relevance.

ii. Technical Information

Specify the study's main and secondary objectives–usually identified as primary and secondary outcomes. Identify methods, equipment (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well-known; describe new or substantially modified methods, give the reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration. Identify appropriate scientific names and gene names.

iii. Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size and precision of estimates. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the statistical software package(s) and versions used. Distinguish prespecified from exploratory analyses, including subgroup analyses.

e. Results

Present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations. Provide data on all primary and secondary outcomes identified in the Methods Section. Extra or supplementary materials and technical details can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."

Separate reporting of data by demographic variables, such as age and sex, facilitate pooling of data for subgroups across studies and should be routine, unless there are compelling reasons not to stratify reporting, which should be explained.

f. Discussion

It is useful to begin the discussion by briefly summarizing the main findings, and explore possible mechanisms or explanations for these findings. Emphasize the new and important aspects of your study and put your finings in the context of the totality of the relevant evidence. State the limitations of your study, and explore the implications of your findings for future research and for clinical practice or policy. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the Introduction or the Results section.

Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly.

g. References

i. General Considerations Related to References

Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests.Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. On the other hand, extensive lists of references to original work on a topic can use excessive space. Fewer references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently.

Do not use conference abstracts as references: they can be cited in the text, in parentheses, but not as page footnotes. References to papers accepted but not yet published should be designated as "in press" or "forthcoming." Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source.

Avoid citing a "personal communication" unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, obtain written permission and confirmation of accuracy from the source of a personal communication.

Some but not all journals check the accuracy of all reference citations; thus, citation errors sometimes appear in the published version of articles. To minimize such errors, references should be verified using either an electronic bibliographic source, such as PubMed, or print copies from original sources. Authors are responsible for checking that none of the references cite retracted articles except in the context of referring to the retraction. For articles published in journals indexed in MEDLINE, the ICMJE considers PubMed the authoritative source for information about retractions. Authors can identify retracted articles in MEDLINE by searching PubMed for "Retracted publication [pt]", where the term "pt" in square brackets stands for publication type, or by going directly to the PubMed's list of retracted publications.

References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses.

References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals). Journals vary on whether they ask authors to cite electronic references within parentheses in the text or in numbered references following the text. Authors should consult with the journal to which they plan to submit their work.

ii. Reference Style and Format

References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Sample References webpage and detailed in the

NLM's Citing Medicine, 2nd edition. These resources are regularly updated as new media develop, and currently include guidance for print documents; unpublished material; audio and visual media; material on CD-ROM, DVD, or disk; and material on the Internet.

h. Tables

Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text.

Prepare tables according to the specific journal's requirements; to avoid errors it is best if tables can be directly imported into the journal's publication software. Number tables consecutively in the order of their first citation in the text and supply a title for each. Titles in tables should be short but self-explanatory, containing information that allows readers to understand the table's content without having to go back to the text. Be sure that each table is cited in the text.

Give each column a short or an abbreviated heading. Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes, and use symbols to explain information if needed. Symbols may vary from journal to journal (alphabet letter or such symbols as *, †, ‡, §), so check each journal's instructions for authors for required practice. Identify statistical measures of variations, such as standard deviation and standard error of the mean.

If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

Additional tables containing backup data too extensive to publish in print may be appropriate for publication in the electronic version of the journal, deposited with an archival service, or made available to readers directly by the authors. An appropriate statement should be added to the text to inform readers that this additional information is available and where it is located. Submit such tables for consideration with the paper so that they will be available to the peer reviewers.

i. Illustrations (Figures)

Digital images of manuscript illustrations should be submitted in a suitable format for print publication. Most submission systems have detailed instructions on the quality of images and check them after manuscript upload. For print submissions, figures should be either professionally drawn and photographed, or submitted as photographic-quality digital prints.

For X-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, send high-resolution photographic image files. Since blots are used as primary evidence in many scientific articles, editors may require deposition of the original photographs of blots on the journal's website.

Although some journals redraw figures, many do not. Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication. Figures should be made as self-explanatory as possible, since many will be used directly in slide presentations. Titles and detailed explanations belong in the legends—not on the illustrations themselves.

Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background. Explain the internal scale and identify the method of staining in photomicrographs.

Figures should be numbered consecutively according to the order in which they have been cited in the text. If a figure has been published previously, acknowledge the original source and submit written permission from the copyright holder to reproduce it. Permission is required irrespective of authorship or publisher except for documents in the public domain.

In the manuscript, legends for illustrations should be on a separate page, with Arabic numerals corresponding to the illustrations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

j. Units of Measurement

Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.

Temperatures should be in degrees Celsius. Blood pressures should be in millimeters of mercury, unless other units are specifically required by the journal.

Journals vary in the units they use for reporting hematologic, clinical chemistry, and other measurements. Authors must consult the Information for Authors of the particular journal and should report laboratory information in both local and International System of Units (SI).

Editors may request that authors add alternative or non-SI units, since SI units are not universally used. Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

k. Abbreviations and Symbols

Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

Effect of bariatric surgery using laparoscopic sleeve gastrectomy technique in patients with morbid obesity and obstructive sleep apnea

ORIGINAL ARTICLE

ORIGINAL ARTICLE BY

Piyaporn Sirijanchune,[1] M.D.; Khwannara Ketwong,[2] M.D.; Nonlawan Chueamuangphan,[1] M.D.; Chaiwetch Thanapaisal,[1] M.D.

[1]Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand.; [2]Chularat 3 International Hospital, Bangkok, Thailand.

Accepted: April 2022
Latest revision: May 2022
Printed: June 2022

Correspondence to: Piyaporn Sirijanchune; siripiyaporn@gmail.com

ABSTRACT

OBJECTIVE

To evaluate the efficacy of bariatric surgery in patients with morbid obesity and obstructive sleep apnea (OSA).

METHODS

This was a quasi-experimental before and after study to evaluate the efficacy of bariatric surgery. Our study was conducted at Chiangrai Prachanukroh Hospital, Thailand. Patients with morbid obesity and OSA undergoing bariatric surgery using laparoscopic sleeve gastrectomy technique from January 2018 to June 2020 was included in the present study. Our primary endpoint was a changes in body weight. The secondary endpoints were changes in BMI and other metabolic biological markers as well as Epworth sleepiness scale (ESS).

RESULTS

A total of 16 individuals with morbid obesity and OSA were recruited. There was reductions of the body weight (mean difference, -23 kg; $P<0.001$), BMI (mean difference, -8.6 kg/m^2; $P<0.001$), systolic blood pressure (mean difference, -16.1 mmHg; $P<0.001$), diastolic blood pressure (mean difference, -6.6 mmHg; $P=0.015$), alanine transaminase (mean difference, -18.1 IU/L; $P=0.028$), fasting blood sugar (mean difference, -22.1 mg/dL; $P=0.005$), triglyceride (mean difference, -60.1 mg/dL; $P=0.006$) as well as the ESS (mean difference, -4.4; $P<0.001$) while there was an increase of high density lipoprotein (mean difference, 6.3 mg/dL; $P=0.034$)

CONCLUSION

Bariatric surgery using laparoscopic sleeve gastrectomy technique were able to demonstrate a significant improvement in term of weight and other metabolic biological markers.

INTRODUCTION

The proportion of the population with morbid obesity is rapidly increasing.[1] There is a high prevalence of morbid obesity worldwide, the overall population prevalence range from 40 to 45%.[2,3] Morbid obesity is associated with overall poor health and quality of life, related to high morbidity and mortality, while it is also related to sleep-disordered breathing; obstructive sleep apnea (OSA) is the most common.[4] Overall prevalence of OSA is relative high, ranging from 9 to 38%, in the obese population.[5] Its prevalence is even higher in the bariatric surgery population is around 12-30 folds of the usual population,[6] and accounted for 71% of all morbid obese.[7] The initial effective treatment of OSA is weight reduction. The weight reduction through lifestyle modification, calorie restriction, and pharmacotherapy is not always effective.[8] Surgical intervention is a promising solution for morbid obesity in the OSA population after exhausting conservative treatment options.[3] Bariatric surgery is a weight-loss operation done with gastric bypass. The primary of this operation is to change the digestive system to lose weight. The benefit of bariatric surgery is weight reduction and reduces the risk of weight-related health problems.[9,10] There were various types such as Roux-Y gastric bypass, biliopancreatic diversion with duodenal switch, and sleeve gastrectomy. Laparoscopic sleeve gastrectomy (LSG) is the dominant procedure.[11,12] About 80 percent of the stomach is removed in sleeve gastrectomy and leaves a long tube-like pouch.[13,14] The procedure is related to decreased Ghrelin hormone, an appetite-regulating hormone. General bariatric surgery is recommended in those with in body mass index (BMI) of more than 40 or BMI 35 to 39.9 with weight-related health problems patient; such as coronary heart disease, obstructive sleep apnea, arterial hypertension, and type 2 diabetes.[9,15] The long-term follow-up after bariatric surgery includes monitoring weight reduction change and improvement in weight-related comorbidities.[9] However, there was limited data on outcomes after bariatric surgery using LSG technique in morbid obesity with OSA. This study aimed to evaluate the efficacy of this type of surgery in patients with morbid obesity and OSA at 1-year follow-up after the surgery.

METHODS

STUDY DESIGN

This was a quasi-experimental before and after study to evaluate efficacy of bariatric surgery using LSG technique. Our study was conducted at Chiangrai Prachanukroh Hospital, Thailand between January 2018 and June 2021. The study protocol was approved by the Ethics Committee in Human Research Chiangrai Pachanukroh Hospital (EC CHR 072/64 In), and was carried out following the Declaration of Helsinki.

PATIENTS

We included patients with morbid obesity and OSA aged more than 15 years who underwent bariatric surgery using LSG technique. Morbid obesity patients are defined as patients who had a BMI of more than 35 kg/m^2.[1] They were, later, screened for diagnosis of OSA using STOP-BANG questionnaires.[4] Patients who STOP-BANG more than 3 points would proceed to polysomnography for definite diagnosis OSA.[16,17] With the Apnea

Table 1. Baseline characteristics of the patients

Characteristic	Value (N=16)
Female – no. (%)	11 (69)
Age – yr	36.2±10.6
Hypertension – no. (%)	5 (37)
Diabetes Mellitus – no. (%)	6 (38)
Dyslipidemia – no. (%)	3 (19)
Cardiovascular disease – no. (%)	2 (13)
Weight – kg	127.5±28.3
Height – cm	161.3±9.7
Body mass index – kg/m^2	48.5±6.2
Apnea-hypopnea index – event/hr	35.0±22.6
Mean oxygen saturation overnight – %.	70.4±17.4
Minimum oxygen saturation overnight – %.	89.8±6.0
Left ventricular ejection fraction – %.	72.4±6.6
Systolic blood pressure – mmHg	141.1±16.2
Diastolic blood pressure – mmHg	84.7±9
Aspartate transaminase – IU/L	
Median	27
Interquartile range	20.5–31
Alanine transaminase – IU/L	
Median	29
Interquartile range	21.7–46

Table 1. (Continued.)

Characteristic	Value (N=16)
Albumin – g/dL	4.1±0.3
Hemoglobin – g/dL	
Median	13.4
Interquartile range	12.3–14.8
Fasting blood sugar – mg/dL	
Median	105.5
Interquartile range	93.5–138.8
Cholesterol – mg/dL	177.6±42.6
Triglyceride – mg/dL	
Median	135
Interquartile range	103.8–167.5
High density lipoprotein – mg/dL	42.2±6.8
Low density lipoprotein – mg/dL	101.5±29.8
Epworth sleepiness scale	9.8±3.6

*Plus minus values are mean±SD

Hypopnea Index (AHI) more than 5 events per hour, definite diagnosis for OSA would make.[14,15] Total of 16 morbid obesity patients with OSA were recruited in the present study.

INTERVENTIONS

All patients with morbid obesity and OSA were orientated and received conservative treatment

for weight reduction before acceptance for the bariatric surgery with preoperative evaluation at an out-patient clinic, Chiangrai Prachanukroh Hospital, Thailand. The bariatric surgery was performed by laparoscopic sleeve gastrectomy technique[1,2] for weight reduction. The LSG surgery was performed by experienced in laparoscopic bariatric surgery under general anesthesia. The operation will make five small incisions on the abdomen. The laparoscopic using the trocar pushed through the incision and completely dissection of the gastric fundus. Then the rest of the stomach will calibrate into the tube shape called sleeve gastrectomy. The operation takes about 2 hours and small amount of estimate blood loss.

DATA COLLECTION

The data of the included patients were 3-year information from January 2018 to June 2021 extracted from their medical records. Pre-operative data were reviewed regarding gender, age, preoperative weight, height, BMI, AHI, the severity of the OSA, weight-related comorbid conditions; blood pressure, liver enzyme, FBS, lipid profile and sleepiness condition. Hypertension is classified by stage of blood pressure; grade I hypertension systolic blood pressure 140-159 and/or diastolic blood pressure 90-99 mmHg, grade II hypertension systolic blood pressure >160 or diastolic blood pressure >100 mmHg.[18]

The severity of the OSA is classified as mild OSA (apnea-hypopnea index (AHI)<15 events/hour), moderate OSA (AHI 15-30 events/hour), and severe OSA (AHI>30 events/hour).[5] Sleepiness conditions evaluated by Epworth Sleepiness Scale (ESS) questionnaire which reflects daytime somnolence. ESS used the eight structure with the choice of 0 to 3 for each question, the score of more than 10 reflected daytime sleepiness.[19,20]

The one year follow up after operation data reviewed include excess weight loss, BMI points lost, percent of excess weight loss (%EWL) and follow up the effect of on weight-related comorbid conditions.[21]

OUTCOMES

At 1–year of follow-up after the bariatric surgery, we reassessed general health conditions including body weight, BMI, blood pressure, blood chemistry of cardiovascular and metabolic outcome, liver enzyme, fasting blood sugar, lipid component, and ESS. Our primary endpoint was the change in body weight. The secondary endpoint were the changes of (i) BMI, (ii) blood pressure both systolic and diastolic blood pressure, (iii) liver enzymes both aspartate transaminase (AST) and alanine transaminase (ALT), (iv) fasting blood sugar, (v) lipid metabolism both cholesterol, triglyceride, low density lipoprotein (LDL) and HDL, and (vi) ESS. We also check for nutritional status after bariatric surgery using albumin and hemoglobin level.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize findings in the included patients. These data were presented using number and percentage for categorical variables. Mean together with standard deviation (SD) were used for describe normally distributed continuous variables while median and interquartile range (IQR) were use to described non-normally distributed continuous variables. The changes of outcomes at 1–year follow-up were

Table 2. Treatment outcomes

Outcome	Baseline	One year	Mean difference (95% confidence interval)	P Value
Weight – kg	127.5±28.3	104.4±23.1	-23.0 (-31.4 to -14.6)	<0.001
BMI – kg/m^2	48.5±6.2	39.8±6.3	-8.6 (-11.4 to -5.8)	<0.001
Systolic blood pressure – mmHg	141.1±16.2	125.0± 9.7	-16.1 (-24.2 to -8)	<0.001
Diastolic blood pressure – mmHg	84.7±9	78.1±7.2	-6.6 (-11.6 to -1.5)	0.015
Aspartate transaminase – IU/L			-14.2 (-32.2 to 3.9)	0.111
Median	27	21		
Interquartile range	20.5–31	14–22		
Alanine transaminase – IU/L			-18.1 (-31.2 to -5.0)	0.028
Median	29	15		
Interquartile range	21.7–46	7–25		
Albumin – g/dL	4.1±0.3	4±0.4	-0.2 (-0.4 to 0)	0.06
Hemoglobin – g/dL			5.3 (-7.3 to 18)	0.582
Median	13.4	13.6		
Interquartile range	12.3 –14.8	12.4 –14.4		
Fasting blood sugar – mg/dL			-22.1 (-34.2 to -10.0)	0.005
Median	105.5	94		
Interquartile range	93.5–138.8	76 –115.3		
Cholesterol – mg/dL	177.6 ± 42.6	173.7 ± 36.5	-4.2 (-28.3 to 20.0)	0.707
Triglyceride – mg/dL			-60.1 (-103.3 to -17.0)	0.006
Median	135	89		
Interquartile range	03.8–167.5	69.0–113.8		
High density lipoprotein – mg/dL	42.2 ± 6.8	47.3 ± 10	6.3 (0.6 to 12.1)	0.034
Low density lipoprotein – mg/dL	101.5±29.8	104.8 ± 22.8	6.5 (-11.5 to 24.5)	0.442
Epworth sleepiness scale	9.8±3.7	5.4±1.9	-4.4 (-6.4 to -2.3)	<0.001

*Plus minus values are mean±SD

identified using paired t-test for normally distributed data and the Wilcoxon sign rank test for non-normally distributed data. $P<0.05$ was considered statistically significant difference.

RESULTS

A total of 16 individuals from January 2018 to June 2020 were enrolled in the study. Their baseline characteristics are shown in Table 1. The mean age was 36.2±10.6 years with females predominant. There were 6 patients with hypertension five patients with grade I hypertension and one patient with grade II hypertension. There was one patient with diabetes mellitus who had microvascular complications out of six patients. There were three patients with dyslipidemia and 2 patients with cardiovascular disease. The mean weight was 127.5±28.3 kilograms, the mean BMI was 48.5±6.2 kg/m^2 and the mean AHI was 35.0±22.6 events per hour.

One year after bariatric surgery (Table 2); there was a reduction in the body weight (mean difference, -23.1 kg; $P<0.001$), BMI (mean difference, -8.6 kg/m^2; $P<0.001$), systolic blood pressure (mean difference, -16.1 mmHg; $P<0.001$), diastolic blood pressure (mean difference, -6.6 mmHg; $P=0.015$), ALT (mean difference, -18.1; $P=0.028$), fasting blood sugar (mean difference, -22.1; $P=0.005$), triglyceride (mean difference, -60.1; $P=0.006$) as well as the ESS (from 9.8 to 5.4; mean difference, 4.4; $P<0.001$). We also observed an increase of HDL (mean difference, 6.5; $P=0.034$). There were no significant changes in terms of LDL

DISCUSSION

The overall number of morbid obesity in OSA individuals has increased rapidly in the last few years. An estimated overall population of morbid obesity ranges from 9 to 38%.[22] Morbid obesity has been extremely related to the development of OSA.[22,23] When combined morbid obesity with OSA, the prevalence range was extremely high to 70%. Every unit of BMI increased, and the odds ratio was 1.14 to develop the OSA.[24] The prevalence of obesity population with OSA and type 2 diabetes was extremely high to 86%.[25] This number of populations expect to increase in the upcoming future. The effects of morbid obesity in combination with OSA are multifaceted on health care. These conditions were related to cardiovascular disease, metabolic diseases, and sleep quality in daytime sleepiness. Hypertension, myocardial infarction, nonalcoholic fatty liver disease, type 2 diabetes, and dyslipidemia are frequent conditions related.[18,25,26] The weight reduction had associated with the resolution of comorbidities associated with morbid obesity with OSA. The strategies for weight reduction management; lifestyle modification with increased physical activity, restricted calorie intake, a healthy diet, pharmacotherapy and weight reduction surgery.[8,27] Bariatric surgery is considered after conservative treatment options have been exhausted. These operations corrected the morbid obesity in weight loss therapy and improved in OSA condition.[24,28] However, the resolution of comorbidities was uncertain. There have been many recent studies that reported the efficacy of bariatric surgery with improved overall morbidity.

Our study resulted in our patients being at extremely high risk for cardiovascular disease and metabolic abnormalities. Most of the individuals had a BMI of more than 40 and the AHI of more than 30 represents a severe degree of both conditions. There was a succession of significant body weight and BMI reduction after bariatric surgery. Varies studies had reported that BMI reduction was 17.9 kg/m^2 (95% CI,16.5 to 19.3). The BMI from 55.3 kg/m^2 (95% CI, 53.5 to 57.1) reduced to 37.7 kg/m^2 (95% CI, 36.6 to 38.9) after surgery which is similar to our study.[29] There were studies of bariatric studies by LSG technique.[30] From LSG at 1 year follow up, the median percent of EWL was 76.1% (48 to 112%) and the median BMI was 26.3 kg/m^2 (23 to 56.4 kg/m^2) higher than our study. The initial median BMI of this study was 46 kg/m^2 (30 to 85 kg/m2) which results in a high percent change.[31] From systematic review emphasized that weight loss surgery benefit effect in OSA patients is multi-modality.[25] The percent of EWL and BMI reduction were 18.1 and 17.9, respectively.

There were studies of bariatric study by LSG technique.[30] Similar population in Asia from China, the study report of 33±11 kg weight change after 1-year follow-up of LSG technique of bariatric surgery.[32] There was a multifactorial mechanism for bodyweight loss; increased satiety, decreased hunger, change in metabolic rate, and modulation. Our study showed improvement in cardiovascular outcome and metabolic component with a favorable outcome. The systemic review of 621 studies revealed that after post-bariatric surgery the glycemic control was 86.6% improved.[33]

Ghrelin-producing fundus completely removed from LSG operation. Resulting in improve type 2 diabetes and blood sugar reduction.[34] The other possible mechanism in improving glycemic control after weight loss surgery was gut hormone glucagon-like peptide-1 modulation.[34] This study has shown a great benefit of 98% resolution of diabetes, normalized blood sugar level, and 75% resolution of dyslipidemia after a 1-year follow-up of LSG surgery.[31] Similar to another study with 15 months of follow-up. There were favorable outcomes. There was a 100 % improvement in type 2 diabetes, 78% hypertension, and 87% in dyslipidemia.[30] In the Asian population, after a 1-year follow-up, the comorbidities after operation improved. Their resolution of the comorbidities was 39%in metabolic syndrome, 8% in hypertension, 42% in type 2 diabetes, and 42% in dyslipidemia.

There was an improvement in systemic blood pressure monitor by systolic blood pressure. The mean systolic blood pressure decreased from 149±17 to 141±20, P=0.02 in our study. Our study shows benefits in the reduction of cholesterol levels both total cholesterol and low-density lipoprotein. The triglyceride showed in reduction after 1-year follow-up but did not reach statistically significant. Conversely, with the study of 24 months follow-up, dyslipidemia improved significantly in mean triglyceride level from 1.7 to 1.3 mmol/L; P=0.008.[36] There was 59% (95% CI; 0.38 to 0.78) improvement of steatohepatitis. AST and ALT were improved with 32% of patients (95% CI: 0.22, 0.42) and 62% of patients (95% CI: 0.42, 0.82) respectively after bariatric surgery.[35] There was a correlation statistically significant between

weight reduction and fatty liver improvement (r-coefficient=0.36, p-value< 0.001).[36] The meta-analysis reported that after bariatric surgery, the liver enzyme was improved. Our study has shown that liver enzyme was improved but not statistically significant. However, our patients did not have steatohepatitis at the initiation of the study.[37,38] Obesity suffers from poor sleep, there were studies that support the association between obesity with sleep duration and quality. When obesity is associated with OSA the more regression in sleep quality.[38,39] There was an improvement in reduction of daytime sleepiness evaluated by ESS after bariatric surgery similar to our study which means a reduction in ESS was 4.38.[34,37] These results reflected that the weight reduction improved sleep quality in sleepiness symptoms. Nevertheless, there was some controversy resulting in sleep quality which was not correlated with weight reduction after bariatric surgery.[4,34] From 3–6 months post–bariatric surgery (mean 5.2±2.5 months), the mean ESS was a reduction from 8.9±3.2 to 4.03±2.15, P<0.001.[4] The weight reduction and BMI reduction were improved with clinical and statistically significant, P<0.001. But this study was no correlation between BMI with ESS, P=0.332.[4]

The strength of our study was that all patients who underwent bariatric surgery had a screening for OSA and performed polysomnography for a definite diagnosis. Our study was a 1–year follow up which was long enough to find the beneficial effect on the cardiovascular and metabolic components. There were some limitations in our study. We only collect a small number of the patients. Due to the economic barrier to participating in bariatric surgery projects. Therefore, this study was an observational case series report. From the limitation, we make the following recommendations to enroll more cases to improve the power in both clinical and statistical outcomes in further research.

In summary, morbid obesity with OSA needs a multidisciplinary team. Lifestyle modification with behavioral therapy with increased physical activity and calorie restriction is still the mainstay of first–line management of weight reduction. Bariatric surgery improves in multiple modalities. Our study had demonstrated that surgical intervention of bariatric surgery using the LSG technique was an effective treatment option for morbid obesity with OSA with an improvement in comorbidities significantly.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank the Sleep Disorder Center, Department of Medicine, and Department of Surgery of Chiangrai Prachanukroh Hospital, Chiang Rai for the data contribution.

COMPETING INTERESTS: This study has no competing on interest.

*FUNDING: T*his study has been fully supported by Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand

REFERENCES

1.Hruby, A. and F.B. Hu, The Epidemiology of Obesity: A Big Picture. PharmacoEconomics, 2015. 33(7): p. 673-689.

2.Hales, C.M., et al., Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017-2018. NCHS Data Brief, 2020(360): p. 1-8.

3.Endalifer, M.L. and G. Diress, Epidemiology, Predisposing Factors, Biomarkers, and Prevention Mechanism of Obesity: A Systematic Review. Journal of Obesity, 2020. 2020: p. 6134362.

4.Priyadarshini, P., et al., Impact of bariatric surgery on obstructive sleep apnoea-hypopnea syndrome in morbidly obese patients. Journal of minimal access surgery, 2017. 13(4): p. 291-295.

5.Senaratna, C.V., et al., Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev, 2017. 34: p. 70-81.

6.Mechanick, J.I., et al., Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient--2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. Obesity (Silver Spring, Md.), 2013. 21 Suppl 1(0 1): p. S1-S27.

7.Lopez, P.P., et al., Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. Am Surg, 2008. 74(9): p. 834-8.

8.Cowan, D.C. and E. Livingston, Obstructive sleep apnoea syndrome and weight loss: review. Sleep disorders, 2012. 2012: p. 163296-163296.

9.Wolfe, B.M., E. Kvach, and R.H. Eckel, Treatment of Obesity: Weight Loss and Bariatric Surgery. Circulation research, 2016. 118(11): p. 1844-1855.

10.Hudgel, D.W., et al., The Role of Weight Management in the Treatment of Adult Obstructive Sleep Apnea. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med, 2018. 198(6): p. e70-e87.

11.Bariatric surgery: an evidence-based analysis. Ont Health Technol Assess Ser, 2005. 5(1): p. 1-148.

12.Lee, W.-J. and O. Almalki, Recent advancements in bariatric/metabolic surgery. Annals of gastroenterological surgery, 2017. 1(3): p. 171-179.

13.Weiner, R.A., et al., Laparoscopic sleeve gastrectomy--influence of sleeve size and resected gastric volume. Obes Surg, 2007. 17(10): p. 1297-305.

14.Mognol, P., D. Chosidow, and J.P. Marmuse, Laparoscopic sleeve gastrectomy (LSG): review of a new bariatric procedure and initial results. Surg Technol Int, 2006. 15: p. 47-52.

15.Bariatric surgery for people with diabetes and morbid obesity: an evidence-based analysis. Ont Health Technol Assess Ser, 2009. 9(22): p. 1-23.

16.Pivetta, B., et al., Use and Performance of the STOP-Bang Questionnaire for Obstructive Sleep Apnea Screening Across Geographic Regions: A Systematic Review and Meta-Analysis. JAMA Network Open, 2021. 4(3): p. e211009-e211009.

17.Chung, F., H.R. Abdullah, and P. Liao, STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. Chest, 2016. 149(3): p. 631-8.

18.Drager, L.F., et al., Obstructive Sleep Apnea: A Cardiometabolic Risk in Obesity and the Metabolic Syndrome. Journal of the American College of Cardiology, 2013. 62(7): p. 569-576.

19.Boyes, J., et al., The use of an online Epworth Sleepiness Scale to assess excessive daytime sleepiness. Sleep & breathing = Schlaf & Atmung, 2017. 21(2): p. 333-340.

20.Corlateanu, A., et al., Predictors of daytime sleepiness in patients with obstructive sleep apnea. Pneumologia, 2015. 64(4): p. 21-5.

21.Montero, P.N., et al., Reported excess weight loss after bariatric surgery could vary significantly depending on calculation method: a plea for standardization. Surg Obes Relat Dis, 2011. 7(4): p. 531-4.

22.Lee, W., et al., Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. Expert review of respiratory medicine, 2008. 2(3): p. 349-364.

23. Young, T., et al., The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med, 1993. 328(17): p. 1230-5.

24. Pannain, S. and B. Mokhlesi, Bariatric surgery and its impact on sleep architecture, sleep-disordered breathing, and metabolism. Best Pract Res Clin Endocrinol Metab, 2010. 24(5): p. 745-61.

25. Ashrafian, H., et al., Metabolic surgery and obstructive sleep apnoea: the protective effects of bariatric procedures. Thorax, 2012. 67(5): p. 442.

26.Metabolic disorders associated with obstructive sleep apnea in adults. Adv Cardiol, 2011. 46: p. 67-138.

27.Jean-Louis, G., et al., Obstructive sleep apnea and cardiovascular disease: role of the metabolic syndrome and its components. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine, 2008. 4(3): p. 261-272.

28. Romero-Corral, A., et al., Interactions between obesity and obstructive sleep apnea: implications for treatment. Chest, 2010. 137(3): p. 711-719.

29. Greenburg, D.L., C.J. Lettieri, and A.H. Eliasson, Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. Am J Med, 2009. 122(6): p. 535-42.

30. Omana, J.J., et al., Comparison of comorbidity resolution and improvement between laparoscopic sleeve gastrectomy and laparoscopic adjustable gastric banding. Surg Endosc, 2010. 24(10): p. 2513-7.

31. Lakdawala, M.A., et al., Comparison between the results of laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y

gastric bypass in the Indian population: a retrospective 1 year study. Obes Surg, 2010. 20(1): p. 1-6.
32. Wong, S.K., et al., Laparoscopic bariatric surgery: a five-year review. Hong Kong Med J, 2009. 15(2): p. 100-9.
33. Buchwald, H., et al., Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med, 2009. 122(3): p. 248-256.e5.
34. Karamanakos, S.N., et al., Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. Ann Surg, 2008. 247(3): p. 401-7.
35. Fakhry, T.K., et al., Bariatric surgery improves nonalcoholic fatty liver disease: a contemporary systematic review and meta-analysis. Surg Obes Relat Dis, 2019. 15(3): p. 502-511.
36. Yeo, C., et al., Weight Loss After Bariatric Surgery Predicts an Improvement in the Non-alcoholic Fatty Liver Disease (NAFLD) Fibrosis Score. Obesity Surgery, 2019. 29.
37.Laursen, T.L., et al., Bariatric surgery in patients with non-alcoholic fatty liver disease - from pathophysiology to clinical effects. World journal of hepatology, 2019. 11(2): p. 138-149.
38.Fakhry, T., et al., Bariatric Surgery improves Nonalcoholic Fatty Liver Disease: A Contemporary Systematic Review and Meta-Analysis. Surgery for Obesity and Related Diseases, 2018. 15.
39.Patel, S.R., et al., The association between sleep duration and obesity in older adults. Int J Obes (Lond), 2008. 32(12): p. 1825-34.
40.Grunstein, R.R., et al., Two-year reduction in sleep apnea symptoms and associated diabetes incidence after weight loss in severe obesity. Sleep, 2007. 30(6): p. 703-710.

Quantitative antibodies against SARS-CoV-2 spike receptor binding domain after vaccination in healthcare workers

ORIGINAL ARTICLE

ORIGINAL ARTICLE BY

Piyaporn Sirijanchune, M.D.; Suwimon Khusuwan, M.D.; Worarat Imsaguan M.D.; Paruspak Payoong M.D.; Sureeruk Achalapong,R.N.; Chalermchai Boonlao, Sunaree Chaiyaloet, Nonlawan Chueamuangphan, M.D.

Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand.

Accepted: April 2022
Latest revision: May 2022
Printed: June 2022

Correspondence to: Piyaporn Sirijanchune; siripiyaporn@gmail.com

ABSTRACT

OBJECTIVE

To estimate the anti-S-RBD IgG level and the antibody responses after the vaccination of Sinovac-CoronaVac (COVID-19) vaccine in a healthcare worker.

METHODS

An ecological study in single-center study of healthcare workers of Chiangrai Prachanukroh Hospital, Thailand to observe the antibody response after the two-dose, four-week apart, of Sinovac-CoronaVac vaccination between April 2021 and July 2021. The anti-S-RBD IgG levels were measured within three months after the last dose of vaccination. The primary outcome was the anti-S-RBD IgG levels after vaccination within three months.

RESULTS

A total of 299 healthcare workers participate in the study. The anti-S-RBD IgG level in female was higher than male (P=0.030). The age group between 21 and 30 years had the highest anti-S-RBD IgG level (P=0.022). The age group of <40 years had higher anti-S-RBD IgG levels compared to age >40 years (P=0.048). The first two weeks after vaccination had the highest anti-S-RBD IgG level compared to other weeks (P<0.001). Comparison of anti-S-RBD IgG levels between groups of duration <4 and >4 weeks after vaccination. The former had significantly higher anti-S-RBD IgG levels (P <0.001).

CONCLUSION

Most healthcare workers developed antibodies after two-dose regimen of the vaccine, for protection against future infection, which is currently not well defined. Further studies are mandatory to confirm immune response and the protective antibodies against this disease would be warranted.

INTRODUCTION

The emergence of SARS-CoV-2 virus infection caused by Covid-19 disease is a global crisis pandemic, World Health Organization (WHO) has been assessing this outbreak since March 2020.[1] As the pandemic accelerated, effective vaccine as well as its accessibility is one of the most important problem solutions.[2] The vaccine candidates are under development and in clinical usage.[3,4] Various studies observed the IgG antibodies level to the spike protein after vaccination.[5-7] Several studies reported that neutralizing antibodies were correlated with RBD S protein antibodies.[4,7] The pre-existing antibodies could have a protective effect on Covid-19 disease.[8] The potential effectiveness of the vaccine from antibodies level of SARS-CoV-2 is an important implication of vaccine development.[9-11]

The SAR-CoV2 spike IgG antibody (anti-S-RBD IgG) is antibodies to SAR-CoV-2 viral infection. Its is used for evaluating immune status in infected individuals or individuals who received the Covid-19 vaccine by quantitatively measuring IgG antibodies against the RBD S protein of SARS-CoV-2.[12-16] Currently, serology diagnosis of Covid-19 infection has been developed based on the detection of antibodies against the S protein of SAR-CoV-2 viral infection.[17-20] As SAR-CoV-2 viral infection is a newly emerging disease, further studies for more information are needed. As a reference from WHO, Thailand's public healthcare policy recommendation suggests that the Sinovac-CoronaVac (COVID-19) vaccine is for the general population aged 18-60 years.[21-25] During the limited resource of vaccines, the healthcare workers are the first prioritized due to high-risk exposure.[26-30]

They work on the front line against the Covid-19 disease. The Sinovac-CoronaVac vaccine was an inactivated vaccine produced by China pharmaceutical company.[1,31-33] There were animals studied well responded in immunogenicity with vaccine-induced neutralizing antibodies with The SARS-CoV-2 strain.[34-36] The vaccine efficacy prevented symptomatic and severe disease with decreased hospitalization. The persistence of the antibody level after vaccination is controversial and limited. This study aims to observe the anti-S-RBD IgG level and the antibody responses after the Sinovac-CoronaVac vaccine in a healthcare worker

METHODS

STUDY DESIGN

An observational study was performed at Chiangrai Prachanukroh Hospital. We observed the antibody response of healthcare workers after the two-dose regimen of Sinovac-CoronaVac vaccination. The healthcare workers who underwent the vaccination between April 2021 and July 2021 were enrolled in the study. Our study protocol was approved by the Ethics Committee of Chiangrai Prachanukroh Hospital (EC CHR 2021 07/64 In). and was carried out following the Declaration of Helsinki. All participants were informed about the study and signed the approved consent forms.

PARTICIPANTS

The program in the present study observed the antibody response in 299 out of 3,200 healthcare workers without a previous SAR-CoV-2 infection by

Table 1. Demographic data and anti-S-RBD IgG levels

Characteristic	Value (N=299)
Age – yr	38.4±10.4
Female – no. (%)	234 (78.3)
Post vaccination duration – days	48.9±12.3
Antibody level – AU/mL	
Median	602.1
Interquartile range	322.3–1005.1
Body weight – kg	61.8±12.9
Body mass index – kg/m^2	23.8±4.7

*Plus minus values are mean±SD

determining antibodies spike protein within three months after vaccination. The sampling methods were using the convenience sampling methods. Further inclusion criteria were the age of participants between 15-60 years. All participants received two doses of the vaccine four weeks apart. The Sinovac-CoronaVac vaccine is the inactive vaccine. One dose of vaccination 0.5 ml administration via intramuscular technique contains 600 SU of SARS-CoV-2 viral antigens. The anti-S-RBD IgG levels were measured within three months after the last dose of vaccination. The demographic data were recorded for each individual.

IMMUNOASSAY

The blood samples from healthcare workers were collected with standard venipuncture and the samples were transferred for the serum separation at the hospital laboratory. The serum was obtained and stored at 2 to 10°C after vaccination within three months. The SARS-CoV-2 IgG Antibody Spike RBD Quantitative enzyme–linked immunosorbent assay (ELISA) is for the Qualitative assay of antibodies from Abbot Diagnostics.[37-39] The method employs the indirect sandwich ELISA technique with chemiluminescent microparticle immunoassay (CMIA) methods. The manufacturer's instruction method was done on the architect i2000 instrument. The dilutional assays were performed with incubated antigen-coated SARS-CoV-2. When the antibody is present, these will be bound to SARS-CoV-2 antigens coated Microparticles.

The results were reported in a unit with AU/mL.[40-42] The protein antigen was binding with the antibody of the SARS-CoV-2 virus. There was HRP-conjugated detection of IgG antibodies followed by incubation to produce the complexity. Then removal of the non-specific binding protein and added for color development for substance solution for anti-SARS-CoV-2. The absorption duration was 450 nm. The chemiluminescent reaction is reported as relative light units (RLUs). The result of the anti-S-RBD IgG antibodies in the sample was directed related to the RLUs measurement. As suggested by the manufacturer, results below 50 AU/mL were considered negative immune responses.[43,44]

OUTCOMES

Within 3 months after Sinovac-CoronaVac vaccination of healthcare workersmeasure anti-S-RBD IgG levels. Our primary outcome was the anti-S-RBD IgG levels associated with an interval

Table 2. Anti S-RBD IgG levels (AU/mL) after vaccination classified by gender, age group, duration post vaccination

Characteristic	No. (%)	Anti-S-RBD IgG levels (AU/mL) Median (IQR)	P Value
Gender – no. (%)			0.030
Female	234 (79.3)	877.9±62.0*	
Male	65 (21.7)	610.2±67.9*	
Age group – no. (%)			0.022
21–30 years	87 (29.1)	746.7 (382.8–1172.7)	
31–40 years	92 (30.8)	519.6 (315.6–932.5)	
41–50 years	70 (23.4)	576.6 (321.3–917.5)	
51–60 years	50 (16.7)	393.7 (288.8–828.7)	
Age group – no. (%)			0.048
<40 years	179 (59.9)	660.8 (339.6–1095.3)	
>40 years	129 (43.1)	471.3 (309.1–847.6)	
Duration after vaccination – no. (%)			<0.001
2 weeks	11 (3.7)	1722.9 (1172.7–2179.8)	
4 weeks	19 (6.4)	1172.4 (716.6–1690.3)	
6 weeks	26 (8.7)	776.2 (441.7–1159.1)	
8 weeks	90 (30.1)	761.8 (405.2–1151.3)	
10 weeks	151 (50.5)	389.1 (272.9–686.8)	
12 weeks	2 (0.7)	356.6 (94–619.2)	
4 weeks of vaccination – no. (%)			<0.001
<4 weeks	30 (10.1)	1367.4 (901.4–1812.3)	
>4 weeks	269 (89.9)	519.6 (315.6–864.3)	

*Plus minus values are mean±SD

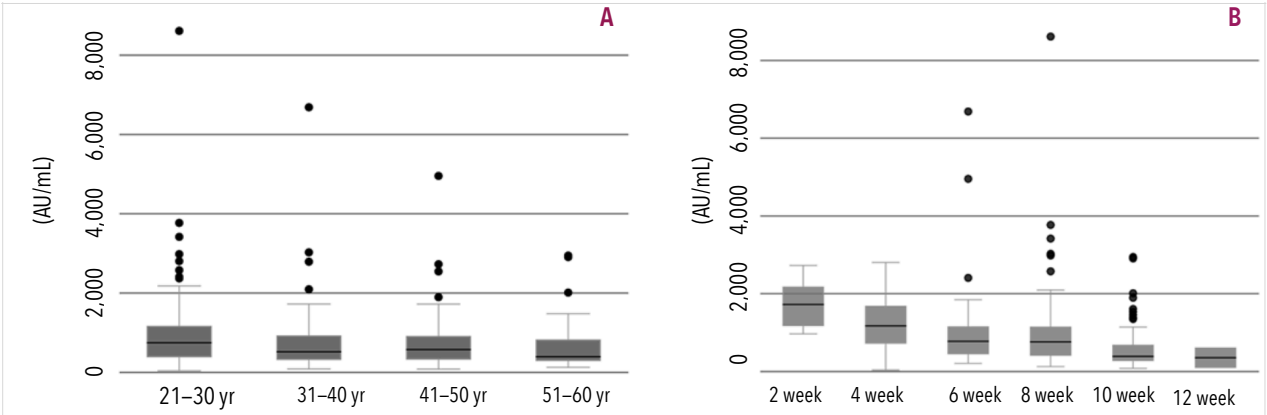


Figure 1. Anti S-RBD IgG levels
Panel A, anti S-RBD IgG levels (AU/mL) after vaccination classified by age group. Panel B, anti-S-RBD IgG levels (AU/mL) classified by duration post-vaccination.

after vaccination within three months. We also categorized the outcomes regarding age groups, and duration of vaccination.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize findings in the included patients. These data were presented using number and percentage for categorical variables. Mean together with standard deviation (SD) were used for describe normally distributed continuous variables while median and interquartile range (IQR) were use to described non-normally distributed continuous variables. The levels of anti-S-RBD IgG were present in terms of mean together with its 95% confidence interval (CI). Comparing the levels between the two groups, t-test or Mann Whitney U test was used where appropriate. Comparing the levels more than 2 groups, either analysis of variance, (ANOVA) or Kruskal-Wallis test was used. $P<0.05$ was considered statistically significant difference.

RESULTS

A total of 299 healthcare workers participate in the study. Demographic data and anti-S-RBD IgG levels were shown in Table 1. The mean age of the participants was 38.4±10.4 years. The female healthcare workers were predominant with 78.3%. The mean duration interval of post-vaccination was 48.9 days. The median of antibody level was 602.1 AU/mL

The anti-S-RBD IgG levels classified by age groups after the last dose of vaccination were shown in Table 2. The anti-S-RBD IgG level in female was higher than male (P=0.030). The age group between 21 and 30 years had the highest anti-S-RBD IgG level (P=0.022). The age group of

<40 years had higher anti-S-RBD IgG levels compared to age >40 years (P=0.048). The first two weeks after vaccination had the highest anti-S-RBD IgG level compared to other weeks (P<0.001). Comparison of anti-S-RBD IgG levels between groups of duration <4 and >4 weeks after vaccination. The former had significantly higher anti-S-RBD IgG levels (P <0.001). Figure 1 present anti-S-RBD IgG levels regarding age groups and groups of duration after vaccination.

DISCUSSION

The global pandemic of SARS-CoV-2 impacts public health worldwide by rapidly raising COVID-19 disease. Vaccine development is one of the effective solutions for controlling the diffusion of this infectious disease.[44,45] The measurement of antigen-specific antibodies is one of the vaccine efficacy immune surveillance. After vaccination, the human-produced antibodies against spike proteins, nucleocapsid, and other proteins. The S1 spike protein (S1 RBD) is the major containing a receptor-binding domain production of antibodies with binding to the human ACE2 receptor for viral replication. The antibody assay of SARS-CoV-2, primarily targets the receptor-binding domain of S1 spike protein.[46-48] There was used to evaluate the antibody response of health care workers after vaccination. These assays had a strong correlation with neutralizing antibodies. They had good potency for vaccination response and did not cross-reaction with other most common coronaviruses. These assay results in the level of an individual's immune response over time.[46,48,49] Tracking post-vaccination antibody levels monitoring for potentially assessing vaccine efficacy.

In this study, we measured the level of antibodies in the healthcare worker at Chiangrai Prachanukroh hospital after the Sinovac-CoronaVac vaccination. To the best of our knowledge, this is a large-scale study assessment of the antibody response of anti-S-RBD IgG levels in vaccinated healthcare workers in Thailand. Overall participants, there was only one participant (0.33%) who failed the antibody response with anti-S-RBD IgG levels was 39.6 AU/mL. The other participants were antibody responders after vaccination with 99.67%. The major finding of our study reported that the anti-S-RBD IgG levels were correlated significantly higher in the female gender, short-duration interval after immunization, and young age. We found that the duration post vaccination at the first two weeks was the highest and at 12 weeks there was no significant difference in antibody level response.

The younger age between 21 and 30 years had the highest antibody level response. The age group below 30 years had significantly higher antibody level responses.[50] Our findings were in accordance with the study of measurement of antibodies level against the spike protein of SARS-CoV-2 in healthcare workers after vaccination of CoronaVac vaccine (Sinovac COVID-19 vaccine). The finding had a similar result in good efficacy with 99.6 percent immune response from antibody level with a higher level of antibodies in female gender and young age group between 18 to 34 years.[51] An Asian population study done in Hong Kong showed a positive result of immune response

of a total of 187 healthcare workers after 28 days of 2 doses of CoronaVac vaccine with 94.4% antibody responders. The mean anti-S-RBD IgG levels were 1005.2 (95% CI; 850.3 to 1160.0) AU/mL, which was lower than our study.[51] In China, the anti-S-RBD IgG levels were responded well with 99.2 to 100% efficacy at 28 days post-Sinovac-CoronaVac vaccine in the healthy population.[52] The higher level of the antibodies could have been attributed to the short interval after vaccination and the young age population of the healthcare workers.[53]

In the present study, we report a significant decline of antibody post vaccination at intervals over time. The highest mean antibody titer was observed within 2 weeks after vaccination of the participants. As expected the healthcare workers significantly raised the antibody level within two weeks after vaccination.[50] After vaccination overtime of more than eight weeks, the mean antibody decreased as compared to the individual the antibody levels with no significant difference between groups. There was a rapid decline of the antibody titers after vaccination in healthcare workers at 60 days which was similar to our study.[54] Nevertheless, our study revealed that the antibody response decreased after vaccination over time. These showed that the antibody level correlated with duration decreased after vaccination over time. The anti-S-RBD IgG developed detection after 21 days after the first vaccination and reflected well antibody response after two doses of vaccination in this study.[55] The aim of this study was to observe the antibody level duration over time after vaccination. for the secondary endpoint, we had demonstrated the antibody level classified by the aged group and the duration over time post-vaccination. The younger age had higher antibody levels compared to the older population. The strength of our study was this study conducted with a large scale of healthcare workers in our country during the pandemic situation. The limitation of this study was unable to measure the level of neutralizing antibodies and the population of the healthcare worker unbalanced distribution with females predominant.

This study provided information on the antibody response in the healthcare worker after two-dose regimen of vaccination. We lack information on the antibody level after the first dose of vaccination. The potency of the antibody would develop after a complete two-dose regimen of vaccination. The information on long-term antibodies in vaccinated individuals is still limited. Further study has planned to follow up with the participants after vaccination boosted with another type of COVID vaccine with a regular schedule of antibody sampling. The measuring of anti-S-RBD IgG from this study benefits the information of antibodies level and the response after vaccination. The healthcare workers who had low antibody response after vaccination is at high risk for severe COVID-19 disease which is necessary for a booster dose to improve immunization.[56,57] Most healthcare workers developed antibodies after a two-dose regimen of the vaccine, for protection against future infection is currently not well defined. Further studies are mandatory to confirm immune response and the protective antibodies against this disease would be warranted.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank the Department of Medicine, and the Department of Human resources of Chiangrai Prachanukroh Hospital, Chiang Rai for the data contribution.

COMPETING INTERESTS: This study has no competing on interest.

FUNDING: This study has been fully supported by Chiangrai Prachanukroh Hospital, Chiang Rai. Thailand

REFERENCES

1.Cascella, M., et al., Features, Evaluation, and Treatment of Coronavirus (COVID-19), in StatPearls. 2021, StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.: Treasure Island (FL).

2.Aleem, A., A.B. Akbar Samad, and A.K. Slenker, Emerging Variants of SARS-CoV-2 And Novel Therapeutics Against Coronavirus (COVID-19), in StatPearls. 2021, StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.: Treasure Island (FL).

3.Alturki, S.O., et al., The 2020 Pandemic: Current SARS-CoV-2 Vaccine Development. Front Immunol, 2020. 11: p. 1880.

4.Dong, Y., et al., A systematic review of SARS-CoV-2 vaccine candidates. Signal Transduct Target Ther, 2020. 5(1): p. 237.

5.Yu, F., et al., Receptor-binding domain-specific human neutralizing monoclonal antibodies against SARS-CoV and SARS-CoV-2. Signal Transduct Target Ther, 2020. 5(1): p. 212.

6.Wang, R., et al., Emerging vaccine-breakthrough SARS-CoV-2 variants. ArXiv, 2021.

7.Mullen, T.E., et al., Accelerated antibody discovery targeting the SARS-CoV-2 spike protein for COVID-19 therapeutic potential. Antib Ther, 2021. 4(3): p. 185-196.

8.Jeyanathan, M., et al., Immunological considerations for COVID-19 vaccine strategies. Nat Rev Immunol, 2020. 20(10): p. 615-632.

9.Ura, T., et al., New vaccine production platforms used in developing SARS-CoV-2 vaccine candidates. Vaccine, 2021. 39(2): p. 197-201.

10.Kaur, S.P. and V. Gupta, COVID-19 Vaccine: A comprehensive status report. Virus Res, 2020. 288: p. 198114.

11.Samrat, S.K., et al., Prospect of SARS-CoV-2 spike protein: Potential role in vaccine and therapeutic development. Virus Res, 2020. 288: p. 198141.

12.Kaneko, S., et al., The dynamics of quantitative SARS-CoV-2 anti spike IgG response to BNT162b2 vaccination. Journal of Medical Virology, 2021. n/a(n/a).

13.Moura, A.D., et al., Assessment of avidity related to IgG subclasses in SARS-CoV-2 Brazilian infected patients. Scientific Reports, 2021. 11(1): p. 17642.

14.Dispinseri, S., et al., Neutralizing antibody responses to SARS-CoV-2 in symptomatic COVID-19 is persistent and critical for survival. Nature Communications, 2021. 12(1): p. 2670.

15.Indenbaum, V., et al., Testing IgG antibodies against the RBD of SARS-CoV-2 is sufficient and necessary for COVID-19 diagnosis. PLOS ONE, 2020. 15(11): p. e0241164.

16.Trougakos, I.P., et al., Comparative kinetics of SARS-CoV-2 anti-spike protein RBD IgGs and neutralizing antibodies in convalescent and naïve recipients of the BNT162b2 mRNA vaccine versus COVID-19 patients. BMC Medicine, 2021. 19(1): p. 208.

17.Gong, F., et al., Evaluation and Comparison of Serological Methods for COVID-19 Diagnosis. Frontiers in Molecular Biosciences, 2021. 8(683).

18.Kevadiya, B.D., et al., Diagnostics for SARS-CoV-2 infections. Nature Materials, 2021. 20(5): p. 593-605.

19.Burbelo, P.D., et al., Detection of Nucleocapsid Antibody to SARS-CoV-2 is More Sensitive than Antibody to Spike Protein in COVID-19 Patients. medRxiv: the preprint server for health sciences, 2020: p. 2020.04.20.20071423.

20.Li, D., J. Li, and S. Kraft Colleen, Immunologic Testing for SARS-CoV-2 Infection from the Antigen Perspective. Journal of Clinical Microbiology. 59(5): p. e02160-20.

21.Bono, S.A., et al., Factors Affecting COVID-19 Vaccine Acceptance: An International Survey among Low- and Middle-Income Countries. Vaccines, 2021. 9(5).

22.Dash, S., et al., Combating the COVID-19 infodemic: a three-level approach for low and middle-income countries. BMJ Glob Health, 2021. 6(1).

23.Lazarus, J.V., et al., A global survey of potential acceptance of a COVID-19 vaccine. Nature Medicine, 2021. 27(2): p. 225-228.

24.Pagliusi, S., et al., Emerging manufacturers engagements in the COVID-19 vaccine research, development, and supply. Vaccine, 2020. 38(34): p. 5418-5423.

25.Zhang, Y., et al., Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomizsed, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis, 2021. 21(2): p. 181-192.

26.Harapan, H., et al., Acceptance of a COVID-19 Vaccine in Southeast Asia: A Cross-Sectional Study in Indonesia. Frontiers in public health, 2020. 8: p. 381-381.
27.Bin Naeem, S. and M.N. Kamel Boulos, COVID-19 Misinformation Online and Health Literacy: A Brief Overview. Int J Environ Res Public Health, 2021. 18(15).
28.Meyer, M.N., T. Gjorgjieva, and D. Rosica, Trends in Health Care Worker Intentions to Receive a COVID-19 Vaccine and Reasons for Hesitancy. JAMA Netw Open, 2021. 4(3): p. e215344.
29.Kwok, K.O., et al., Editor's Choice: Influenza vaccine uptake, COVID-19 vaccination intention and vaccine hesitancy among nurses: A survey. Int J Nurs Stud, 2021. 114: p. 103854.
30.Hajure, M., et al., Attitude Towards COVID-19 Vaccination Among Healthcare Workers: A Systematic Review. Infection and drug resistance, 2021. 14: p. 3883-3897.
31.Sharma, O., et al., A Review of the Progress and Challenges of Developing a Vaccine for COVID-19. Front Immunol, 2020. 11: p. 585354.
32.Gao, Q., et al., Development of an inactivated vaccine candidate for SARS-CoV-2. Science, 2020. 369(6499): p. 77-81.
33.Palacios, R., et al., Double-Blind, Randomized, Placebo-Controlled Phase III Clinical Trial to Evaluate the Efficacy and Safety of treating Healthcare Professionals with the Adsorbed COVID-19 (Inactivated) Vaccine Manufactured by Sinovac - PROFISCOV: A structured summary of a study protocol for a randomizsed controlled trial. Trials, 2020. 21(1): p. 853.
34.Kalnin, K.V., et al., Immunogenicity and efficacy of mRNA COVID-19 vaccine MRT5500 in preclinical animal models. npj Vaccines, 2021. 6(1): p. 61.
35.Klasse, P.J., F. Nixon Douglas, and P. Moore John, Immunogenicity of clinically relevant SARS-CoV-2 vaccines in nonhuman primates and humans. Science Advances. 7(12): p. eabe8065.
36.Xia, S., et al., Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes: Interim Analysis of 2 Randomized Clinical Trials. JAMA, 2020. 324(10): p. 951-960.
37.English, E., et al., Performance of the Abbott SARS-CoV-2 IgG II Quantitative Antibody Assay Including the New Variants of Concern, VOC 202012/V1 (United Kingdom) and VOC 202012/V2 (South Africa), and First Steps towards Global Harmonization of COVID-19 Antibody Methods. Journal of Clinical Microbiology. 59(9): p. e00288-21.
38.Manalac, J., et al., Evaluation of Abbott anti-SARS-CoV-2 CMIA IgG and Euroimmun ELISA IgG/IgA assays in a clinical lab. Clinica Cchimica Aacta; international journal of clinical chemistry, 2020. 510: p. 687-690.
39.Perkmann, T., et al., Anti-Spike protein assays to determine post-vaccination antibody levels: a head-to-head comparison of five quantitative assays. medRxiv, 2021: p. 2021.03.05.21252977.
40.Alhajj, M. and A. Farhana, Enzyme- Linked Immunosorbent Assay, in StatPearls. 2021, StatPearls Publishing
Copyright © 2021, StatPearls Publishing LLC.: Treasure Island (FL).
41.Nicol, T., et al., Assessment of SARS-CoV-2 serological tests for the diagnosis of COVID-19 through the evaluation of three immunoassays: Two automated immunoassays (Euroimmun and Abbott) and one rapid lateral flow immunoassay (NG Biotech). J Clin Virol, 2020. 129: p. 104511.
42.Jääskeläinen, A.J., et al., Performance of six SARS-CoV-2 immunoassays in comparison with microneutralisation. J Clin Virol, 2020. 129: p. 104512.
43.Nguyen, N.N., et al., Correlation of ELISA method with three other automated serological tests for the detection of anti-SARS-CoV-2 antibodies. PloS one, 2020. 15(10): p. e0240076-e0240076.
44.Mehdi, F., et al., Development of a Fast SARS-CoV-2 IgG ELISA, Based on Receptor-Binding Domain, and Its Comparative Evaluation Using Temporally Segregated Samples From RT-PCR Positive Individuals. Frontiers in Microbiology, 2021. 11(3597).
45.Srivastava, N. and S.K. Saxena, Prevention and Control Strategies for SARS-CoV-2 Infection. Coronavirus Disease 2019 (COVID-19): Epidemiology, Pathogenesis, Diagnosis, and Therapeutics, 2020: p. 127-140.
46.Huang, Y., et al., Structural and functional properties of SARS-CoV-2 spike protein: potential antivirus drug development for COVID-19. Acta Pharmacologica Sinica, 2020. 41(9): p. 1141-1149.
47.Min, L. and Q. Sun, Antibodies and Vaccines Target RBD of SARS-CoV-2. Frontiers in Molecular Biosciences, 2021. 8(247).
48.Zhu, X., et al., Receptor-binding domain as a target for developing SARS vaccines. Journal of Thoracic Disease, 2013: p. S142-S148.
49.Sternberg, A. and C. Naujokat, Structural features of coronavirus SARS-CoV-2 spike protein: Targets for vaccination. Life sciences, 2020. 257: p. 118056-118056.
50.Wei, J., et al., Antibody responses to SARS-CoV-2 vaccines in 45,965 adults from the general population of the United Kingdom. Nature Microbiology, 2021. 6(9): p. 1140-1149.
51.Zee, J.S.T., et al., Serological response to mRNA and inactivated COVID-19 vaccine in healthcare workers in Hong Kong: preliminary results. Hong Kong Med J, 2021. 27(4): p. 312-313.
52.Li, M., et al., Healthcare workers' (HCWs) attitudes and related factors towards COVID-19 vaccination: a rapid systematic review. Postgraduate Medical Journal, 2021: p. postgrad medj-2021-140195.
53.Post, N., et al., Antibody response to SARS-CoV-2 infection in humans: A systematic review. PLoS One, 2020. 15(12): p. e0244126.
54.Self, W.H., et al., Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network - 12 States, April-August 2020. MMWR Morb Mortal Wkly Rep, 2020. 69(47): p. 1762-1766.
55.Emary, K.R.W., et al., Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Lancet, 2021. 397(10282): p. 1351-1362.
56.Thomas, S.J., et al., Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months. N Engl J Med, 2021.
57.Kamar, N., et al., Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. N Engl J Med, 2021. 385(7): p. 661-662.

Efficacy and safety of tubeless versus standard percutaneous nephrolithotomy in resource-limited setting

ORIGINAL ARTICLE

ORIGINAL ARTICLE BY

Soratree Saingarm,M.D.

Yasothon Hospital, Yasothon, Thailand.

Accepted: April 2022
Latest revision: May 2022
Printed: June 2022

Correspondence to: Soratree Saingarm; godchied@gmail.com

ABSTRACT

OBJECTIVE

To evaluate the efficacy and safety of a tubeless versus standard percutaneous nephrolithotomy (PCNL) in resource-limited setting.

METHODS

Between March 2020 and June 2021, medical records of patients undergoing PCNL, standard technique under fluoroscopic guidance, at Yasothon Hospital, Thailand were verified reviewed. At Yasothon Hospital, the standard PCNL was performed between March and October 2020 while tubeless PCNL was performed between November 2020 and June 2021. Their outcomes and complications of the two groups were compared.

RESULTS

There were 92 patients included in the present study; 46 tubeless PCNL and 46 standard PCNL. Comparing between those undergoing tubeless and standard PCNL, the former tended to have less blood loss ($P<0.001$), less drop in hematocrit ($P<0.001$), less morphine usage ($P<0.001$), requesting less for acetaminophen tablet ($P<0.001$), longer length of stay after the surgery ($P<0.001$), less VAS pain score at 12 hours after the operation ($P=0.013$). Moreover, the former was likely to have lower rate fever ($P=0.012$), and sepsis ($P=0.0004$). Aside from these, other complications were found to have similar rates between the two groups.

CONCLUSION

Tubeless PCNL was found to have similar efficacy and safety to that of standard PCNL.

INTRODUCTION

Renal calculi or renal stone is a global problem with an approximate lifetime prevalence of 15-25% with a very high recurrent rate.[1] Modality for treating renal calculi includes medical treatment and surgery, shock wave lithotripsy, ureteroscope, and percutaneous nephrolithotomy (PCNL) are the most common surgical modalities.[2] Since its first introduction in 1976 by Fernstrom and Johansson, PCNL was evolved into the standard treatment for large and complex renal stones.[3] The procedure has been widely practiced and replaced open surgical removal of large renal stones.[3,4] Inserting a nephrostomy tube after PCNL as drainage is a standard procedure. Furthermore, it also provides a tamponade effect along the PCNL tract and permits access to perform a second exploration.[5,6] In 1997, Bellman et al first reported tubeless PCNL with excellent results.[7] PCNL without postoperative nephrostomy tube placement is defined as tubeless PCNL. While neither a nephrostomy tube nor a ureteral stent is used, the procedure is defined as total tubeless PCNL.[8] Previously tubeless PCNL was done in selected patients with uncomplicated stones. The selection criteria include stone burden <3 cm, single access tract case with no significant intraoperative bleeding, no significant collecting system perforation, and no requirement for a secondary percutaneous procedure. In recent years, the tubeless PCNL technique has been applied in patients with expanded indications including complex stone, staghorn stone, multiple access tracts, bilateral simultaneous PCNL, previously operated kidneys, anatomical anomalies, and solitary kidney. Tubeless PCNL with ureteric stent had favorable outcomes with no increase in complications compared with standard PCNL in expanded indications for large renal calculi.[9,10] The objective of this study was to evaluate the efficacy and safety of tubeless and standard PCNL in settings with limited resources, Yasothon, Thailand.

METHODS

STUDY DESIGN AND OVERSIGHT

This was a retrospective case reviewed of patients under going PCNL under fluoroscopic guidance at Yasothon Hospital, Thailand between March 2020 and June 2021. The study protocol was approved by the Ethics Committee in Human Research Yasothon Hospital (EC YST 2020–12). The present study was conducted under the Declaration of Helsinki. Its preparation and execution fully complied with the fundamental ethical principles of autonomy, justice, beneficence, and non-maleficence.

PATIENTS' DATA

Using Yasothon Hospital Database, we selected data of patients undergoing PCNL regarding the mentioned study period. Patients who had coagulation problems who underwent simultaneous bilateral PCNL or lateral position PCNL were excluded. Then, we extracted data regarding age, sex, body mass index (BMI), co-mobidities (e.g., hypertension, diabetes, chronic kidney disease, and cancer), side of the stone, size of the stone, location of the stone, previous operations, urine culture findings, and the associated anomalies.

Table 1. Characteristics of the patients

Characteristic	Tubeless PCNL (N=46)	Standard PCNL (N=46)	P Value
Age – yr	57.1±7.6	57.3±10.4	0.925
Male – no. (%)	28 (61)	27 (59)	0.832
Body mass index – kg/m^2	24.2±4.6	24.2±4.2	0.976
Comorbidity – no. (%)			
Hypertension	9 (20)	17 (37)	0.064
Diabetes	6 (13)	6 (13)	>0.99
Chronic kidney disease	8 (17)	9 (20)	0.788
Cerebrovascular accident	2 (4)	0	0.153
Ischemic heart disease	1 (2)	0	>0.99
Cancer	2 (4)	2 (5)	>0.99
Others	6 (13)	5 (11)	0.748
Right side stone – no. (%)	25 (54)	23 (50)	0.676
Size of the stone – mm			<0.465
Median	30	30	
Interquartile range	28–30	29.5–30	
Location of the stone – no. (%)			
Staghorn	28 (61)	28 (61)	>0.99
Renal pelvic stone	5 (11)	9 (20)	0.246
Calyceal stone	8 (17)	7 (15)	0.778
Renal pelvic and calyces stone	6 (13)	2 (4)	0.267
Previous operation – no. (%)			
Anatrophic nephrolithotomy	4 (9)	8 (17)	0.216
Percutaneous nephrolithotomy	7 (15)	2 (4)	0.158
Extracorporeal shock wave lithotripsy	7 (15)	1 (2)	0.059
No previous operation	31 (67)	35 (76)	0.354

Table 1. (Continued.)

Characteristic	Tubeless PCNL (N=46)	Standard PCNL (N=46)	P Value
Positive preoperative urine culture – no. (%)			0.65
No growth	33 (72)	31 (67)	
Positive	13 (28)	15 (33)	
Associated anomaly – no. (%)			
Calyceal diverticulum	3 (7)	4 (9)	>0.99
Infundibular stenosis	2 (4)	2 (4)	>0.99
Ureteropelvic junction obstruction	3 (7)	0	0.242
Single kidney	1 (2)	1 (2)	>0.99
Horseshoe kidney	0	0	-
Double collecting system	0	0	-
Malrotation	1 (2)	1 (2)	>0.99

*Plus–minus values are mean±SD; PCNL= percutaneous nephrolithotomy

OPERATIVE PROCEDURES

All patients underwent intravenous pyelography or computerized tomography to evaluate stone size and location. For the PCNL, all patients were operated under general anesthesia. A 6-F open-ended ureteric catheter was placed cystoscopically before percutaneous access. Percutaneous access was performed in a prone position following the contrast media injection via ureteric catheter under fluoroscopic guidance. Metallic Alken dilators dilated the percutaneous tract and Amplatz sheath was used in all cases. The standard nephroscopy was used with a pneumatic lithotripter for stone fragmentation. At the end of the procedure, the double-J ureteric stent no.6 was indwelled by the antegrade fashion of every PCNL procedure. Nephrostomy tube 26 Fr was inserted in standard PCNL.

At Yasothon Hospital, the standard PCNL was performed between March and October 2020 while tubeless PCNL was performed between November 2020 and June 2021. From the medical record of each patient, data regarding operative time, number of tract, preparation before having surgery, and renal puncture site were extracted and collected onto spreadsheet.

OUTCOMES AND COMPLICATIONS

After the operation, outcomes regarding estimated blood loss, drop in hematocrit, morphine usage, requesting for acetaminophen tablet (500 mg), length of stay after surgery, pain score using visual analogue scale (VAS) (0 to10) at 12 hours after the operation, stone residual after the operation (the residual fragment was defined as residual stone visualized by plain kidney, ureter, bladder (KUB)

Table 2. Operative procedures

Characteristic	Tubeless PCNL (N=46)	Standard PCNL (N=46)	P Value
Operative time – min	81±26.3	97.4±30.9	0.007
Number of tract – no. (%)			0.714
1 tract	43 (94)	41 (89)	
2 tracts	3 (7)	5 (11)	
Preparation before having surgery – no. (%)			0.979
Day of surgery admission	25 (54)	30 (65)	
Admission 1 day before the surgery	21 (46)	16 (35)	
Renal puncture site			
Upper pole	39 (85)	39 (85)	>0.99
With supracostal	17 (37)	3 (7)	0.83
Middle pole	3 (7)	3 (7)	>0.99
Lower pole	7 (15)	9 (20)	0.582

*Plus minus values are mean±SD; PCNL= percutaneous nephrolithotomy

film at postoperative periods, residual stone less than 3-4 mm was considered a clinically insignificant residual fragments (CIRF), and complications (i.e., fever, sepsis, stroke, pleural effusion, re-admission, nephrocutaneous fistula, fluid collection, ureteropelvic junction injuries of the surgery) were also reviewed, verified, and extracted from the medical records of the included patients before the statistical analyses.

STATISTICAL ANALYSIS

All data were double entered. They were cleaned before the analyses. All analyses were performed using statistical software package. All analyses were performed regarding the comparison between the two groups of the patients; tubeless vs. standard PCNL. For descriptive statistics, number and percentage were used to described categorical variables. Mean and standard deviation (SD) were used to summarized normally distributed continuous variables while median and interquartile range (IQR) were used to summarized non-normally distributed continuous variables. For inferential statistics, t-test was used to compare means between the two groups while Mann-Whitney U test was used to compare sum rank test between the two groups. Chi-square or Fisher's exact test was used to compare between the two groups of categorical variables where appropriate. $P<0.05$ was considered statistical significant.

Table 3. Outcomes and complications

Outcome and complication	Tubeless PCNL (N=46)	Standard PCNL (N=46)	P Value
Estimated blood loss – ml			<0.001
Median	100	200	
Interquartile range	10–125	100–500	
Drop in hematocrit – %			<0.001
Median	1	2	
Interquartile range	1–1.25	1–5	
Morphine usage – dose			<0.001
Median	0	1	
Interquartile range	0–1	0–2	
Requesting for acetaminophen 500 mg – tab	7.1±4.7	13.8±5.9	0.002
Length of stay after the surgery-day	5.3±2.1	2.4±1.1	<0.001
VAS pain score at 12 hours after the operation	3.3±1.4	4.1±1.7	0.013
Stone residual from plain film – no. (%)			
Stone free	25 (54)	16 (35)	0.093
Residual stone	15 (33)	20 (44)	0.391
Clinically insignificant residual fragments	6 (13)	10 (22)	0.41
Complication – no.(%)	17 (37)	38 (83)	
Fever	27 (59)	38 (83)	0.012
Sepsis	2 (4)	8 (17)	0.004
Stroke	0	2 (4)	0.495
Pleural effusion	2 (4)	2 (4)	>0.99
Re–admission	2 (4)	1 (2)	>0.99
Nephrocutaneous fistula	0	5 (11)	0.056
Fluid collection	1 (2)	1 (2)	>0.99
Ureteropelvic junction injuries	0	1 (2)	>0.99

*Plus minus values are mean±SD; PCNL= percutaneous nephrolithotomy

RESULTS

PATIENTS

In total , there were 92 patients undergoing PCNL were included in the analysis; 46 tubeless and 46 standard PCNL. Mostly they were male with the mean age around 57 years old. Hypertension was the most common comorbidity. Right kidney and upper pole of the kidney were most common site of the stone with the average size of 30 mm in diameter.

Comparing between those undergoing tubeless and standard PCNL, the two groups were relatively similar in terms of age, male sex, BMI, comorbidities, side of stone, location of the stone, positive pre-operative urine culture, previous operations and associated anomalies (Table 1).

OPERATIVE PROCEDURES

For the operative procedures, the former tended to have shorter operative time (P=0.007) (Table 2). Proportion of number of tracts whether one or two tracts, preparation before having surgery, and renal puncture sites were similar between the two groups.

OUTCOMES

For the outcomes, the former tended to have less blood loss (P<0.001), less drop in hematocrit (P<0.001), less morphine usage (P<0.001), requesting less for acetaminophen tablet (P<0.001), longer length of stay after the surgery (P<0.001), less VAS pain score at 12 hours after the operation (P=0.013) (Table 3). The stone residual from plain KUB films after the surgery, the two groups were found to have similar rates. The former was likely to have lower rate fever (P=0.012), and sepsis (P=0.0004). Aside from these, rates of other complications were found to be similar between the two groups.

DISCUSSION

PCNL is the standard treatment for large and complex renal stones. A nephrostomy tube is usually left in the renal pelvis at the end of the procedure. In recent years, the procedure has been modified to the tubeless procedure in which an external nephrostomy tube was replaced by internal drainage (double J stent). Tubeless PCNL was confirmed to lower hospitalization and post-operative analgesic requirements. Previous studies demonstrated that the tubeless PCNL was safe in patients with antiplatelet use, liver cirrhosis,[9] chronic kidney disease[12], and bilateral simultaneous procedures.[13]

With expanded indications, there was no statistical difference in postoperative hemoglobin drop between the two groups and also showed that tubeless PCNL was the safe procedure.[9,10] In this study, the tubeless procedure was done in all patients in November 2020. The result of the tubeless procedure did not increase serious complications. The most common complication in both groups was fever and also lower in the tubeless group. These results corresponded with earlier studies.[9,10,14] The success rate of stone clearance may be associated with the stone characteristics which most of the stones are staghorn stones. To achieve 100% clearance may be required second or third renal access tracts that increase bleeding and arteriovenous fistula.[13] In

this study some patients performed second access. There was no difference in postoperative complication rate. On the follow-up date, patients with residual fragments got advice on the treatment similar to the standard treatment such as extracorporeal shock wave lithotripsy (ESWL), Retrograde intrarenal surgery (RIRS), or observation in asymptomatic nonobstructive stone.

The average length of hospital stay in tubeless PCNL in this study was 2.85 days (range 1–7 days) whereas the hospital stay in standard PCNL was 5.65 days. This result could be explained by the absence of nephrostomy tube clamping and removal at postoperation. The minimum day of stay in the tubeless group was only 1 day because of the day of surgery admission policy (DOSA). Preoperative investigations prior to surgery were conducted. Patients were admitted to the hospital and had surgery on the same day except for somebody who had the inconvenience to go to the hospital in the early morning or somebody who had severe underlying diseases.

Since the COVID-19 pandemic in 2020, the admission policy had been changed. All patients who had scheduled for elective surgery must be admitted one day before surgery to do nasopharyngeal swab polymerase chain reaction (PCR) for COVID-19. However, the incidence of post-operative urosepsis was no different between a day of surgery admission (DOSA) and the preoperative admission group.

Our findings conformed to multiple studies that PCNL was conducted as ambulatory surgery.[14,15] the limitation of this study is the retrospective nature with a small sample size. As a resource-limited settings, single surgeon performed the surgery in every case of PCNL in the hospital. Due to the fact that a surgeon's experience in PCNL reaches a plateau in operation and performs the procedure with competence after 45-60 operations.[18,19] For better estimation of the complication regarding surgeon experience, outcomes in later cases should be prospective collected and compared. A cluster randomized controlled trial is also suggested for fairer comparison rather than historical comparison of two different time periods in the present study that might limit the validity of the study.

ACKNOWLEDGMENTS & DECLARATION

I would like to express my sincere thanks and appreciation to Associate Professor Dr. Ekkarin Chotikawanich for study inspiration, and wonderful surgical technique. I am most grateful to Ms.Ladda Comdang, a nurse who works at urology ward, for her invaluable support, thoughtful suggestion, and enthusiastic encouragement. I wish to give the gratefulness to Dr. Thammasorn Jeeraaumponwat for guiding in the statistical analysis and giving the opportunity for publishing. Moreover, I sincerely thanks to his colleagues for statistical analysis and interpretation. In addition, I honestly thanks all of my patients who have confidence in myself. I also wish to give special thanks to all scrub nurses who assist with the surgery. Finally, my deepest gratitude intends to my family for all theirs support throughout the difficult period of this research.

COMPETING INTERESTS: This study has no competing on interest.

FUNDING: None

REFERENCES

1.Moe, O.W., 2006. Kidney stones: Pathophysiology and medical management. Lancet, 367: 333-344.

2.Srisubat A, Potisat S, Lojanapiwat B, et al. Extracorporeal shock wave lithotripsy (ESWL) versus percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS) for kidney stones. Cochrane Database Syst Rev 2014; :CD007044.

3.Fernstrom I, Johansson B. Percutaneous pyelolithotomy. A new extraction technique. Scand J Urol Nephrol 1976; 10: 257-9.

4. Türk C., Neisius A., Petrik A., Seitz C., et al. EAU Guidelines on Urolithiasis, 2017 : 1-84.

5.Istanbulluoglu MO, Cicek T, Ozturk B, Gonen M, Ozkardes H. Percutaneous nephrolithotomy: nephrostomy or tubeless or totally tubeless? Urology 2010; 75: 1043-6.

6. Srinivasan AK, Herati A, Okeke Z, Smith AD. Renal drainage after percutaneous nephrolithotomy. J Endourol 2009; 23: 1743-9.

7.Bellman GC, Davidoff R, Candela J, Gerspach J,Kurtz S, Stout L, Tubeless percutaneous renal surgery. J Urol 1997; 157: 1578-82.

8.Agrawal MS, Agrawal M. Tubeless percutaneous nephrolithotomy. Indian J Urol 2010;26:16-24.

9. Isac W, Rizkala E, Liu X, Noble M, Monga M. Tubeless percutaneous nephrolithotomy: outcomes with expanded indications. Int Braz J Urol 2014; 40: 204-11.

10.Sirithanaphol W, Jitpraphai S, Taweemonkongsap T,Nualyoung C, Chotikawanich E, Safety and Feasibility of tubeless percutaneous nephrolithotomy with expanded indication. J med assoc Thai 2017; 100: 169-173.

11. Jou YC, Shen CH, Lin CT, Cheng MC, Chen PC, Tsai YS: Safety and efficacy of tubeless percutaneous nephrolithotomy in patients on anti-platelet therapy and cirrhotic patients. Urol Res. 2011; 39: 393-6.

12. Etemadian M, Maghsoudi R, Shadpour P, Ghasemi H, Shati M: Outcomes of tubeless percutaneous nephrolithotomy in patients with chronic renal insufficiency. Iran J Kidney Dis. 2012; 6: 216-8

13. Shah HN, Kausik VB, Hegde SS, Shah JN, Bansal MB. Safety and efficacy of bilateral simultaneous tubeless percutaneous nephrolithotomy. Urology. 2005;66:500–4

14.Taylor E, Miller J, Chi T, Stoller ML. Complications associated with percutaneous nephrolithotomy. Transl Androl Urol. 2012;1(4):223-228.

15.Kukreja R, Desai M, Patel S, et al. Factors affecting blood loss during percutaneous nephrolithotomy: prospective study. J Endourol 2004;18:715-22

16.Fahmy A, Rhashad H, Algebaly O, Sameh W. Can percutaneous nephrolithotomy be performed as an outpatient procedure?. Arab J Urol. 2017;15(1):1-6.

17.Bechis SK, Han DS, Abbott JE, Holst DD, Alagh A, DiPina T, Sur RL. Outpatient Percutaneous Nephrolithotomy: The UC San Diego Health Experience. J Endourol. 2018 May;32(5):394-401

18.Ziaee SA, Sichani MM, Kashi AH, Samzadeh M. Evaluation of the learning curve for percutaneous nephrolithotomy. Urol J. 2010 Fall;7(4):226-31.

19.Allen D, O'Brien T, Tiptaft R, Glass J. Defining the learning curve for percutaneous nephrolithotomy. J Endourol. 2005 Apr;19(3):279-82.

"I shall either find a way or make one"

-Hannibal Barca


I don't want you to be only
a doctor but I also want you
to be a man